FASTING

A MEDICAL DICTIONARY, BIBLIOGRAPHY,
AND ANNOTATED RESEARCH GUIDE TO
INTERNET REFERENCES

JAMES N. PARKER, M.D.
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The collective knowledge generated from academic and applied research summarized in various references has been critical in the creation of this book which is best viewed as a comprehensive compilation and collection of information prepared by various official agencies which produce publications on fasting. Books in this series draw from various agencies and institutions associated with the United States Department of Health and Human Services, and in particular, the Office of the Secretary of Health and Human Services (OS), the Administration for Children and Families (ACF), the Administration on Aging (AOA), the Agency for Healthcare Research and Quality (AHRQ), the Agency for Toxic Substances and Disease Registry (ATSDR), the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Healthcare Financing Administration (HCFA), the Health Resources and Services Administration (HRSA), the Indian Health Service (IHS), the institutions of the National Institutes of Health (NIH), the Program Support Center (PSC), and the Substance Abuse and Mental Health Services Administration (SAMHSA). In addition to these sources, information gathered from the National Library of Medicine, the United States Patent Office, the European Union, and their related organizations has been invaluable in the creation of this book. Some of the work represented was financially supported by the Research and Development Committee at INSEAD. This support is gratefully acknowledged. Finally, special thanks are owed to Tiffany Freeman for her excellent editorial support.

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FORWARD

In March 2001, the National Institutes of Health issued the following warning: "The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading."[1] Furthermore, because of the rapid increase in Internet-based information, many hours can be wasted searching, selecting, and printing. Since only the smallest fraction of information dealing with fasting is indexed in search engines, such as **www.google.com** or others, a non-systematic approach to Internet research can be not only time consuming, but also incomplete. This book was created for medical professionals, students, and members of the general public who want to know as much as possible about fasting, using the most advanced research tools available and spending the least amount of time doing so.

In addition to offering a structured and comprehensive bibliography, the pages that follow will tell you where and how to find reliable information covering virtually all topics related to fasting, from the essentials to the most advanced areas of research. Public, academic, government, and peer-reviewed research studies are emphasized. Various abstracts are reproduced to give you some of the latest official information available to date on fasting. Abundant guidance is given on how to obtain free-of-charge primary research results via the Internet. **While this book focuses on the field of medicine, when some sources provide access to non-medical information relating to fasting, these are noted in the text.**

E-book and electronic versions of this book are fully interactive with each of the Internet sites mentioned (clicking on a hyperlink automatically opens your browser to the site indicated). If you are using the hard copy version of this book, you can access a cited Web site by typing the provided Web address directly into your Internet browser. You may find it useful to refer to synonyms or related terms when accessing these Internet databases. **NOTE:** At the time of publication, the Web addresses were functional. However, some links may fail due to URL address changes, which is a common occurrence on the Internet.

For readers unfamiliar with the Internet, detailed instructions are offered on how to access electronic resources. For readers unfamiliar with medical terminology, a comprehensive glossary is provided. For readers without access to Internet resources, a directory of medical libraries, that have or can locate references cited here, is given. We hope these resources will prove useful to the widest possible audience seeking information on fasting.

The Editors

[1] From the NIH, National Cancer Institute (NCI): **http://www.cancer.gov/cancerinfo/ten-things-to-know**.

CHAPTER 1. STUDIES ON FASTING

Overview

In this chapter, we will show you how to locate peer-reviewed references and studies on fasting.

The Combined Health Information Database

The Combined Health Information Database summarizes studies across numerous federal agencies. To limit your investigation to research studies and fasting, you will need to use the advanced search options. First, go to **http://chid.nih.gov/index.html**. From there, select the "Detailed Search" option (or go directly to that page with the following hyperlink: **http://chid.nih.gov/detail/detail.html**). The trick in extracting studies is found in the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Journal Article." At the top of the search form, select the number of records you would like to see (we recommend 100) and check the box to display "whole records." We recommend that you type "fasting" (or synonyms) into the "For these words:" box. Consider using the option "anywhere in record" to make your search as broad as possible. If you want to limit the search to only a particular field, such as the title of the journal, then select this option in the "Search in these fields" drop box. The following is what you can expect from this type of search:

- **Effects of Moderate Alcohol Intake on Fasting Insulin and Glucose Concentrations and Insulin Sensitivity in Postmenopausal Women: A Randomized Control Trial**

  Source: JAMA. Journal of the American Medical Association. 287(19): 2559-2562. May 15, 2002.

  Summary: Epidemiological data demonstrate that moderate alcohol intake is associated with improved insulin sensitivity in nondiabetic individuals. No controlled-diet studies have addressed the effects of daily moderate alcohol consumption on fasting insulin and glucose concentrations and insulin sensitivity. This article reports on a study undertaken to determine whether daily consumption of low to moderate amounts of alcohol influences fasting insulin and glucose concentrations and insulin sensitivity in nondiabetic postmenopausal women. The randomized controlled crossover trial included 63 healthy postmenopausal women. Results showed that consumption of 30

grams per day of alcohol compared with 0 grams per day reduced fasting insulin concentration by 19.2 percent and triglyceride concentration by 10.3 percent, and increased insulin sensitivity by 7.2 percent. Normal weight, overweight, and obese individuals responded in similar ways. Fasting glucose concentrations were not different across treatments. The authors conclude that consumption of 30 grams of alcohol (2 drinks per day) has beneficial effects on insulin and triglyceride concentrations and insulin sensitivity in nondiabetic postmenopausal women. 1 figure. 2 tables. 35 references.

- **Ramadan Fasting: Impact on Diabetes Mellitus and Guidelines for Care**

  Source: Practical Diabetology. 20(3): 7-11, 14. September 2001.

  Contact: Available from R.A. Rapaport Publishing, Inc. 150 West 22nd Street, New York, NY 10011. (212) 989-0200 or (773) 777-6801.

  Summary: Ramadan is the ninth lunar month in the Islamic calendar. During this month, all healthy adult Muslims, male or female, are expected to abstain from foods, fluids, oral medications, intravenous fluids and nutrients, smoking, and sexual intercourse from dawn to sunset. This article discusses the impact of this cultural and religious requirement on people who have diabetes. The classic Islamic point of view is that Ramadan fasting is good for the health and is also good for the spiritual cleanliness of Muslims. Ramadan fasting is a type of intermediate or partial fasting because individuals can eat again after 12 to 14 hours. The physiologic aspects of Ramadan are influenced by the combination of food and water deprivation, the periodic nature of fasting, and the modification of physical activities during the daytime hours. In people with diabetes, the blood glucose response to fasting is individual and variable. It has been suggested that the fasting blood glucose of such patients can be influenced by dietary noncompliance as a result of eating high carbohydrate meals (a tradition during Ramadan). This dietary factor may outweigh factors such as age, sex, and weight in influencing blood glucose in fasting patients with diabetes. The author notes that Ramadan fasting per se does not impair glycemic control in patients with diabetes. The glycemic control strategy in such patients should be considered individually in light of the control level before Ramadan, presence of complications, and course of the diabetes. The author discusses the impact of fasting on insulin, lipids (fats), renal (kidney) physiology, and body weight. Specific guidelines for diabetes care during Ramadan are outlined. A patient education handout about fasting for religious purposes and its impact on diabetes control is offered in the same journal issue. 26 references.

- **Impaired Glucose Tolerance Is a Risk Factor for Cardiovascular Disease, But Not Impaired Fasting Glucose: The Funagata Diabetes Study**

  Source: Diabetes Care. 22(6): 920-924. June 1999.

  Contact: Available from American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 232-3472. Website: www.diabetes.org.

  Summary: This article describes a cohort study designed to determine whether the new category of impaired fasting glucose (IFG) recently proposed by the Expert Committee of the American Diabetes Association was a risk factor for cardiovascular disease. Death certificates and residence transfer documents from the cohort population consisting of participants of the diabetes prevalence study conducted from 1990 to 1992 in Funagata, Yamagata prefecture, Japan, were analyzed up through the end of 1996. The cohort population was classified into 2,016 people who had normal glucose tolerance (NGT), 382 people who had impaired glucose tolerance (IGT), and 253 people who had

diabetes. Then the same population was reclassified into normal fasting glucose (NFG), IFG, and diabetic. The cumulative survival rates among the groups were compared using the classical lifetable method; age adjusted analyses, the person-year method, and Cox's proportional hazard model were then adopted. The study found that, at the end of the 7 observed years, the cumulative survival rates from cardiovascular disease of IGT and diabetes were 0.962 and 0.954, respectively. Both were significantly lower than that of NGT. The Cox's proportional hazard model analysis shows that the hazard ratio of IGT to NGT on death from cardiovascular disease was 2.219. However, the cumulative survival rate of IFG from cardiovascular disease was 0.977, not significantly lower than that of NFG. The Cox's hazard ratio of IFG to NFG on death from cardiovascular disease was 1.136, which was not significant. The article concludes that glucose intolerance, including IGT and diabetes, was a risk factor for death from cardiovascular disease, but IFG was not. Therefore, using the World Health Organization and the American Diabetes Association diagnostic criteria, with and without oral glucose tolerance test, should be routine clinical practice in diagnosing overt diabetes or detecting risk factors for cardiovascular disease. 2 figures. 3 tables. 14 references. (AA-M).

- **Fasting Plasma Homocysteine Levels in the Insulin Resistance Syndrome**

  Source: Diabetes Care. 24(8): 1403-1410. August 2001.

  Contact: Available from American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 232-3472. Website: www.diabetes.org.

  Summary: This article describes a study that examined relationships between hyperinsulinemia, phenotypes of insulin resistance syndrome (IRS), and levels of fasting homocysteine. Participants were subjects of the Framingham Offspring Study. Clinical characteristics, plasma levels of fasting homocysteine, folate, B vitamins, creatinine, and fasting and 2 hour insulin and glucose levels after a 75 gram oral glucose tolerance test were measured in 2,214 subjects without cardiovascular disease (CVD) at the fifth examination (1991 to 1995) of the Framingham Offspring Study. After excluding 203 subjects with diabetes, the remaining 2,011 subjects were categorized as having none, one, two, or all three of the phenotypes of IRS (impaired glucose tolerance, hypertension, and a central metabolic syndrome). In addition, in 1,592 subjects attending the sixth examination (1995 to 1998), the study measured the urine albumin/creatinine ratio (UACR). Age, gender, creatinine, vitamin, and UACR adjusted mean homocysteine levels or proportions with homocysteine greater than 14 umol per liter in each phenotypic category and differences between categories were assessed with regression models. The mean age of the subjects was 54 years. Men had higher mean levels of homocysteine than women, but the distribution of IRS phenotypes among men and women was similar. In this nondiabetic population, 15.9 percent of subjects had at least two IRS phenotypes and 6.6 percent had all three phenotypes. The overall prevalence of hyperinsulinemia was 12.3 percent, and subjects with the central metabolic syndrome alone or in combination with other phenotypes had higher fasting insulin levels than those without the central metabolic syndrome phenotype. Adjusted mean homocysteine levels were higher comparing those with hyperinsulinemia and those without, and they were higher among subjects with two or more IRS phenotypes compared with those with one or no phenotype. Mean UACR levels were also higher among subjects with two or more IRS phenotypes compared with those with one or no phenotype. The article concludes that hyperhomocysteinemia and abnormal urinary albumin excretion are both associated with hyperinsulinemia and may partially account for increased risk of CVD associated with insulin resistance. Observations are consistent

with the hypothesis that endothelial dysfunction is associated with expression of the IRS. 1 figure. 3 tables. 73 references. (AA-M).

- **Fasting: Can You? Should You?**

  Source: Diabetes Self-Management. 18(3): 82, 84-85. May-June 2001.

  Contact: Available from R.A. Rapaport Publishing, Inc. 150 West 22nd Street, New York, NY 10011. (800) 234-0923. Website: www.diabetes-self-mgmt.com.

  Summary: This article provides people who have diabetes with information on fasting. Throughout the ages, people have fasted for various spiritual, cultural, and health reasons. The article discusses some of the changes that occur in the body to survive a fast. This is followed by an examination of some common beliefs about fasting and the facts according to medical professionals. Some of these beliefs are that fasting can help people feel more in control of their bodies, cure illness, and promote self discipline; fasting can be done by anyone; the body needs to be periodically cleansed of toxins through fasting; fasting promotes long term weight loss and boosts energy levels; and the body needs a rest from digestion for good health. Although most of these beliefs are myths, a fast is sometimes necessary prior to a medical test or procedure. The article provides tips for maintaining blood glucose levels while fasting for tests or procedures or when participating in a religious fast.

- **Prospective Study of Hospitalization With Gallstone Disease Among Women: Role of Dietary Factors, Fasting Period, and Dieting**

  Source: American Journal of Public Health. 81(7): 880-884. July 1991.

  Summary: This article reports on a population-based prospective study that attempted to determine dietary risk factors for hospitalization with gallstone disease. The researchers evaluated the role of dietary constituents, fasting, and dieting on subsequent hospitalization with gallstone disease among 4,730 women, ages 25 to 74 years, who participated in the first follow-up of the first National Health and Nutrition Examination Survey. Results show that the hazard rate of hospitalization with gallstone disease increased with a longer overnight fasting period and with dieting. Intake of fiber showed a small protective effect. The effect of energy intake was significant only among women younger than age 50 years at baseline. Results were not affected by adjustment for known risk factors for gallstone disease or other dietary factors.

- **Comparison of a Clinical Model, the Oral Glucose Tolerance Test, and Fasting glucose for Prediction of Type 2 Diabetes Risk in Japanese Americans**

  Source: Diabetes Care. 26(3): 758-763. March 2003.

  Contact: Available from American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 232-3472. Website: www.diabetes.org.

  Summary: This article reports on a study undertaken to test the validity of a published clinical model for predicting incident (new) diabetes in Japanese Americans. A total of 465 nondiabetic Japanese Americans (243 men, 22 women), aged 34 to 75 years, were studied at baseline and at 5 to 6 years. A total of 412 subjects were studied at 10 years. The clinical model included age, sex, ethnicity, body mass index (BMI), systolic blood pressure, fasting plasma glucose (FPG), HDL cholesterol, and family history of diabetes at baseline. The diabetes risk associated with body mass index (BMI), sex, and HDL cholesterol differed by age. The authors conclude that in Japanese Americans older than 55 years, a clinical model was better than FPG for predicting diabetes after 5 to 6 years,

but not after 10 years. The model was not useful in older Japanese Americans, whereas 2 hour glucose testing was useful for predicting diabetes risk regardless of age. 3 tables. 22 references.

- **Intestinal Transport During Fasting and Malnutrition**

  Source: in McCormick, D.B., Bier, D.M., and Goodridge, A.G., eds. Annual Review of Nutrition. Palo Alto, CA: Annual Reviews Inc. 2000. Volume 20: 195-219.

  Contact: Available from Annual Reviews Inc. 4139 El Camino Way, P.O. Box 10139, Palo Alto, CA 94303-0139. (800) 523-8635. Fax (415) 424-0910. PRICE: $53.00. ISBN: 0824328167. ISSN: 01999885. Individual article reprints available from Annual Reviews Preprints and Reprints. (800) 347-8007 or (415) 259-5017. E-mail: arpr@class.org. Base price $13.50 per article.

  Summary: This article reviews the dramatic effects that fasting or malnutrition (FM) has on the small intestine mucosal structure and transport function. Fasting often means a voluntary abstinence from food, whereas starvation implies an involuntary cessation of food intake; in this review, they are considered in tandem, as their effects on the gastrointestinal tract are the same. Intestinal secretion of ions and fluid is increased by FM both under basal (basic) conditions and in response to secretory agonists (drug or other substance that causes a response). Intestinal permeability to ions and macromolecules may also be elevated by FM, which increases the potential for fluid and electrolyte losses and for anaphylactic (lifethreatening, hypersensitive)responses to luminal antigens. Mucosal atrophy induced by FM reduces total intestinal absorption of nutrients, but nutrient absorption normalized to mucosal mass may actually be enhanced by a variety of mechanisms, including increased transporter gene expression, electrochemical gradients, and ratio of mature to immature cells. This reduction in absorptive surface area of the intestine reduces its total capacity for nutrition absorption, but also reduces the proportion of total body energy and nutrient stores that must be diverted to the gut for its maintenance. The authors conclude that their observations underscore the value of enteral (supplemental nutrition using the gastrointestinal tract) feeding during health and disease. 1 figure. 104 references.

- **Elevated Nitric Oxide Production in Rheumatoid Arthritis: Detection Using the Fasting Urinary Nitrate:Creatinine Ratio**

  Source: Arthritis and Rheumatism. 39(4):643-647; April 1996.

  Summary: This journal article for health professionals describes a study that was conducted to develop a simple method for assessing endogenous nitric oxide (NO) production applicable to routine clinical practice in rheumatology. NO production was assessed in 19 patients with rheumatoid arthritis (RA) as serum nitrate levels and as the urinary nitrate:creatinine ratio in morning samples of urine following an overnight fast. The influence of dietary intake of nitrate on these measurements was investigated in 12 healthy volunteers. The clinical value of the urinary nitrate: creatinine ratio was validated in patients with infectious gastroenteritis, in whom its production is known to be increased. Results show that urinary nitrate:creatinine ratios were significantly elevated in patients with RA or infectious gastroenteritis and that serum nitrate was significantly elevated only in patients with infectious gastroenteritis. Dietary intake of nitrate had no significant influence on the fasting morning urinary nitrate:creatinine ratio in the healthy volunteers, showing that this particular parameter was a useful indicator of endogenous NO production. 20 references and 3 figures. (AA-M).

- **Diabetes, Impaired Fasting Glucose, and Elevated HbA1c in U.S. Adolescents: The Third National Health and Nutrition Examination Survey**

  Source: Diabetes Care. 24(5): 834-837. May 2001.

  Contact: Available from American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 232-3472. Website: www.diabetes.org.

  Summary: This review article describes a study that used data from the Third National Health and Nutrition Examination Survey to estimate the prevalence of diabetes, impaired fasting glucose, and elevated glycosylated hemoglobin (HbA1c) levels in U.S. adolescents during 1988 to 1994. The prevalence of diabetes was calculated for 2,867 adolescents who attended any physical examination and had glucose measured. The prevalence of impaired fasting glucose was calculated for the subsample of 1,083 adolescents who were assigned to the morning half sample, attended a morning examination, and fasted for at least 8 hours. The prevalence of elevated HbA1c was calculated for 2,852 adolescents who attended any physical examination and had HBA1c measured. The study found that 13 of the 2,867 adolescents who had glucose measured were considered to have diabetes. Of these, nine reported using insulin, two reported using oral agents only, and two did not report any treatment but had high glucose levels. Four of the cases were considered to have type 2 diabetes. The four adolescents not using insulin were non-Hispanic blacks or Mexican Americans. The estimated prevalence of diabetes per 100 adolescents ages 12 to 19 years was 0.41 percent. The prevalence of impaired fasting glucose among adolescents without diabetes who had fasted for at least 8 hours was 1.76 percent. The prevalence of elevated HbA1c was 0.39 percent. The article concludes that the national data reflect the presence of type 2 diabetes in U.S. adolescents, but the survey sample size was not large enough to obtain precise prevalence estimates because of the relatively low prevalence. 2 tables. 15 references. (AA-M).

- **Are Lower Fasting Plasma Glucose Levels at Diagnosis of Type 2 Diabetes Associated with Improved Outcomes?: U.K. Prospective Diabetes Study 61**

  Source: Diabetes Care. 25(8): 1410-1417. August 2002.

  Contact: Available from American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 232-3472. Website: www.diabetes.org.

  Summary: Type 2 diabetes may be present for several years before diagnosis, by which time many patients have already developed diabetic complications. Earlier detection and treatment may reduce this burden, but evidence to support this approach is lacking. This article reports on a study in which glycemic control and clinical and surrogate outcomes were compared for 5,088 of 5,102 United Kingdom Diabetes Prospective Study participants according to whether they had low, intermediate, or high fasting plasma glucose (FPG) levels at diagnosis. Individuals who presented with and without diabetes symptoms were also compared. Fewer people with FPG in the lowest category had retinopathy (eye disease), abnormal biothesiometer measurements, or reported erectile dysfunction (ED). The rate of increase in FPG and HbA1c (glycosylated hemoglobin, a measure of blood glucose levels over time) during the study was identical in all three groups, although absolute differences persisted. Individuals in the low FPG group had a significantly reduced risk for each predefined clinical outcome except stroke, whereas those in the intermediate group had significantly reduced risk for each outcome, except stroke and myocardial infarction. The low and intermediate FPG groups had a significantly reduced risk for progression of retinopathy, reduction in vibration sensory threshold, or development of microalbuminuria (protein in the urine, a sign of kidney

disease). The authors conclude that people presenting with type 2 diabetes with lower initial glycemia who may be earlier in the course of their disease had fewer adverse clinical outcomes despite similar glycemic progression. Since most such people are asymptomatic at diagnosis, active case detection programs would be required to identify them. 2 figures. 3 tables. 20 references.

Federally Funded Research on Fasting

The U.S. Government supports a variety of research studies relating to fasting. These studies are tracked by the Office of Extramural Research at the National Institutes of Health.[2] CRISP (Computerized Retrieval of Information on Scientific Projects) is a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other institutions.

Search the CRISP Web site at **http://crisp.cit.nih.gov/crisp/crisp_query.generate_screen**. You will have the option to perform targeted searches by various criteria, including geography, date, and topics related to fasting.

For most of the studies, the agencies reporting into CRISP provide summaries or abstracts. As opposed to clinical trial research using patients, many federally funded studies use animals or simulated models to explore fasting. The following is typical of the type of information found when searching the CRISP database for fasting:

- **Project Title: A WEIGHT CONTROL MODEL FOR INNER CITY MINORITY CHILDREN**

  Principal Investigator & Institution: Caprio, Sonia; Associate Professor of Endocrinology And; Pediatrics; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2001; Project Start 15-FEB-2001; Project End 31-JAN-2003

  Summary: Obesity is becoming a major health problem, particularly among African-Americans. Given the current inability of successfully treating obesity in both adolescents and adults, the prevention of obesity is the best way to tackle the problem. The overall objective of this pilot study is to determine whether a culturally sensitive program of nutrition counseling, supervised exercise by as former basketball African American (AA) player, can reduce the weight gain in inner city minority children of Bridgeport, CT during the transition to adolescence compared to routine clinical care and health counseling. We hypothesize that having a successful athlete as a role model in the program will enhance fitness, self-esteem and quality of life of AA children and lead them to more healthy lifestyles with respect to nutritional and physical activity. The target population will consist of AA children and their caregivers. The aims of the trial are a) to determine whether the intervention program reduces adiposity in experimental vs. control subjects. This will be assessed by differences in body mass index and body composition using BIA, b) to determine whether the intervention favorably alters the biochemical risk factors for cardiovascular disease, including **fasting** plasma lipids and basal insulin concentrations, and 3) to determine whether the intervention enhances psychosocial well being and healthy lifestyles as assessed by standard questionnaires

[2] Healthcare projects are funded by the National Institutes of Health (NIH), Substance Abuse and Mental Health Services (SAMHSA), Health Resources and Services Administration (HRSA), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDCP), Agency for Healthcare Research and Quality (AHRQ), and Office of Assistant Secretary of Health (OASH).

and activity monitoring instruments. This program will bring together a multi-disciplinary team of professions from a) the academic world (Yale University) working in the field of childhood obesity, b) the "Charles D. Smith Foundation Education Center", a non-professional organization center in Bridgeport, CT, working with inner city children and their families, and c) the children of the "Paul Laurence Dunbar School" of Bridgeport, CT. The ultimate goal of this trial is to empower AA children and caregivers with the knowledge and skills necessary to promote fitness and wellness.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ACYL-COA SYNTHETASE: STRUCTURE, FUNCTION AND REGULATION**

  Principal Investigator & Institution: Coleman, Rosalind A.; Professor of Nutrition & Pediatrics; Nutrition; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002; Project Start 15-APR-2002; Project End 31-MAR-2007

  Summary: DK59935. Intracellular lipids, particularly triacylglycerol, fatty acids, aryl-CoAs and their metabolites, provide a critical link between obesity, insulin resistance and diabetes. Between 1990 and 1998 five different rat isoforms of acyl-CoA synthetase (ACS) were cloned and it has become apparent that the different ACS isoforms probably play major roles in regulating cellular fatty acid and acyl-CoA levels. Thus, it is surprising that little information is available about the individual ACS isoforms. Using non-cross-reacting peptide antibodies, we have shown that the three isoforms expressed in liver and adipocytes, ACS1, 4, and 5 are each located in different subcellular membranes in liver, that they are inhibited by different chemical inhibitors, and that they are regulated independently in liver by **fasting** and refeeding. Further, we discovered that thiazolidinediones specifically inhibit AVCS4, suggesting that these clinically important insulin sensitizers might act, in part, by inhibiting ACS4. We now propose to focus on the function, regulation, and structure of ACS1, 4, and 5 I order to understand how each of these ACSs contributes to normal glycerolipid metabolism an what role each ACS isoform plays in promoting the lipid-related pathophysiology of insulin resistance and diabetes. In order to determine the function of the ACSs , we will over express each of the three ACS isoforms, and use selective chemical and antisense inhibitors to assess effects on synthetic and degradative pathways. We will compare the cellular locations of the ACSs with confocal microscopy and determine whether regulation of ACS activities includes phosphorylation/dephosphorylation and movement from cytosol to intracellular membranes. We will determine the topography of the acyl-CoA synthetase isoforms within membranes and their crystal structures. Finally, we will use the yeast two-hybrid system to determine whether each ACS has one or more specific metabolic partners. These studies will enable us to understand how acyl- CoAs can serve as both metabolic signals and as substrates for synthetic and energy-producing pathways, how they can be partitioned towards different metabolic fates, and how their metabolism contributes to the pathogenesis of diabetes.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: AMYLIN AND ITS RELEASING FACTOR IN THE EARLY DIAGNOSIS OF PANCREATIC CANCER**

  Principal Investigator & Institution: Adrian, Thomas E.; Professor; University of Nebraska Medical Center Omaha, Ne 681987835

  Timing: Fiscal Year 2001; Project Start 25-MAR-1999; Project End 31-JAN-2003

Summary: Pancreatic cancer is associated with profound insulin resistance, resulting in diabetes in up to 80% of patients. This metabolic abnormality is tumor dependent and disappears after tumor resection, despite the loss of islets. Amylin is a pancreatic hormone that inhibits muscle glycogen synthesis and reduces food intake. In most pancreatic cancer patients, amylin levels are elevated in the **fasting** state. Even though diabetes may not be a major problem for the management of patients with pancreatic cancer, measurement of amylin may be a valuable marker for the early diagnosis of the disease, at least in a proportion of patients. Furthermore, the increased amylin levels appear to result from stimulation of peri-tumoral islets by a tumor-derived peptide (amylin releasing peptide of ARP). It is likely that, compared with amylin, circulating ARP levels are elevated in an even higher proportion of pancreatic cancer patients. The major goals of this proposal are as follows: 1. To investigate the specificity of elevated circulating amylin in pancreatic cancer, by investigating patients with pancreatitis, biliary obstruction, newly diagnosed diabetes, pancreatic cancer or other malignancies. 2. To purify and sequence ARP and develop a radioimmunoassay to measure this peptide. 3. To establish whether ARP is a better marker for pancreatic cancer than amylin, by measurement in the above groups of patients. 4. To determine the value of amylin and ARP as early indicators of pancreatic cancer, by measuring the peptides in families with a high risk of developing the disease, and by measuring them in samples from pancreatic cancer patient collected several years prior to their cancer diagnosis. This study may aid in the development of an early screening technique for detecting pancreatic cancer at an early, curable stage. In addition, it will improve our understanding of the role played by the islets in this disease.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ANCILLARY STUDY DATA ANALYSIS IN VA-HIT**

  Principal Investigator & Institution: Rubins, Hanna; Medicine; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

  Timing: Fiscal Year 2001; Project Start 30-SEP-2001; Project End 31-AUG-2003

  Summary: The VA HDL Intervention trial (VA-HIT) was a multicenter, placebo controlled, randomized trial that showed that gemfibrozil significantly reduced major cardiovascular events in 2531 men with coronary heart disease, low levels of low density lipoprotein (LDL) cholesterol and low levels of high density lipoprotein (HDL) cholesterol. In addition to its unique lipid profile, the VA-HIT population also had a high prevalence of diabetes, impaired **fasting** glucose, or high **fasting** plasma insulin; central obesity; and hypertension, which are all components (together with high triglycerides and low ILL-cholesterol) of a constellation of risk factors known as the metabolic syndrome. Since prior clinical trials have not enrolled this type of population, the VA- HIT database is a unique resource. The purpose of the present proposal is to use this database to study additional risk markers that were measured in the study population. Specific proposed analyses are: 1. An analysis of the association between levels of glucose tolerance, insulin resistance and other features of the metabolic syndrome, occurrence of major cardiovascular outcomes, and gemfibrozil efficacy. 2. An analysis of the effect of gemfibrozil on progression of carotid atherosclerosis, as measured by B-mode ultrasound. 3. An analysis of the association between LDL particle size distribution and lipoprotein subclass distribution; homocysteine; lipoprotein(a); C-reactive protein, tissue plasminogen activator; fibrinogen; and factor VII; major cardiovascular outcomes, and gemfibrozil efficacy. Written documentation that the data will be available to us is included in the letter from Dr. Peter Peduzzi of the VA Cooperative Studies Program.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: APO B TRANSLOCATION AND DEGRADATION**

  Principal Investigator & Institution: Davis, Roger A.; Professor; Biology; San Diego State University 5250 Campanile Dr San Diego, Ca 92182

  Timing: Fiscal Year 2001; Project Start 01-JAN-1994; Project End 31-MAY-2004

  Summary: Overproduction of apo B-containing lipoproteins by the liver is responsible for a common form of familial combined hyperlipidemia associated with premature cardiovascular disease. Our proposed mechanistic studies in mice will allow us to identify the factors and processes responsible for regulating the secretion of lipoproteins in normal and hyperlipidemic animals and humans. To achieve this goal, we propose the following Specific Aims: 1) To examine the hypothesis that the relative level of expression of MTP and apo B contribute toward determining the maximal capacity of the liver to assemble and secrete apo B-containing lipoproteins. For these studies we will use inbred C57BL/6 mice which have altered expression of MTP and apo B100. 2) To examine the hypothesis that over-production and secretion of apo B-containing lipoproteins is the basis for familial combined hyperlipidemia. Using a novel mutant mouse clone displaying a genotype and phenotype that closely reflects a human form of familial combined hyperlipidemia, we will determine the molecular basis for this common hyperlipidemic disorder. 3) To define the molecular mechanism responsible for the inactivation of the MTP promoter in L35 cells. L35 cells show a phenotype similar to that of livers from abetalipoproteinemics (i.e. genetic loss of MTP expression and an inability to secrete apo B-containing lipoproteins). We will delineate the mechanism responsible for inactivation of the MTP gene in L35 cells using the promoter constructs that we have shown replicates the transcriptional activity of the endogenous MTP gene. 4) To examine the hypothesis that the relative level of expression of MTP, apo B and lipogenic enzymes displayed by individual liver cells varies dynamically with anatomical localization and changes in physiologic and nutritional state. The knowledge gained from our proposed studies in mice will allow us for the first time to determine the physiologic significance of hypotheses formulated from cultured cell models. New insights gained from these proposed studies should be useful in designing diets and pharmacologic agents that may prevent hyperlipidemia and the formation of atherosclerosis in humans.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: BIOMARKERS FOR TOTAL BODY BURDEN OF FLUORIDE**

  Principal Investigator & Institution: Shearer, Thomas R.; Professor and Chairman; Oral Molecular Biology; Oregon Health & Science University Portland, or 972393098

  Timing: Fiscal Year 2003; Project Start 01-SEP-2003; Project End 31-AUG-2005

  Summary: (provided by applicant): While the benefit of fluoridation in the prevention of dental caries has been overwhelmingly substantiated, the effect of fluoridation on other chronic health problems is less clear. For example, fluoridation has been linked with osteoporosis, bone cancer, uterine cancer, fertility rates, testosterone levels, gastro-duodenal manifestations, and otosclerosis. The majority of studies evaluating the impact of fluoridation on chronic health conditions, however, have been ecological. In ecological studies, the unit of analysis is an aggregate on individuals rather than the individual itself and, in most cases both exposure status and disease status are based on the aggregate. Aggregating exposure and disease status data can lead to inappropriate conclusions regarding relationships at the individual level (ecological fallacy). The

purpose of this research is to identify a biomarker for long-term fluoride exposure that can be used in future epidemiologic research on the impact of fluoride exposure on human health. Developing a fluoride biomarker will improve the precision of fluoride exposure measures and provide better estimates of individual level fluoride exposure. This will reduce misclassification of fluoride exposure, thereby enhancing our ability to detect dose-response relationships between fluoride exposure and health outcome measures. The fluoride content of bone appears to reflect total body burden of fluoride and is an appropriate "gold standard" for a fluoride biomarker. For this reason, we will recruit 210 patients scheduled for primary total hip or total knee replacement surgery in Portland and Salem, OR. Excised bone tissue along with **fasting** blood, **fasting** ductal saliva, and demographic information will be obtained from each study participant and analyzed for fluoride content at the Medical College of Georgia. While controlling for confounding variables, we will correlate bone fluoride to tissue fluoride in order to determine which tissue, if any, is the "best" biomarker for long-term fluoride exposure. In addition, we will obtain additional tissue samples from a subset (n=30) to evaluate the precision of the biomarker. This research is a collaborative effort between Oregon Health Sciences University and the Medical College of Georgia.

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- **Project Title: CARBOHYDRATE AND LIPID METABOLIC PATHWAYS**

  Principal Investigator & Institution: Landau, Bernard R.; Professor of Medicine and Biochemistry; Medicine; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

  Timing: Fiscal Year 2001; Project Start 01-MAY-1978; Project End 31-MAR-2002

  Summary: Our long-term objective is to develop and apply novel methods that will significantly advance our understanding of carbohydrate and lipid metabolism in physiological and pathological states, in particular diabetes. These methods have in common the safe 2H- enrichment of body water with 2H20. We plan to achieve the following seven interrelated specific aims. 1. To quantitate glycogen hydrolysis, cycling, and turnover as a function of liver glycogen content. 2. To measure the rate of de novo glycerol formation via labeling from 2H20, and to define: (i)the role of liver and kidney in glycerol production, fatty acid reesterification, and lipolysis quantitation., and (ii) the source of carbon of glycerol-3-P used by adipose tissue to reesterify fatty acids. 3. To determine the pathway(s) by which 2H20 labels H on C1 of glucose, and to define how this labeling affects calculations of gluconeogenesis and glycogenolysis. 4. To develop a method for quantitating glyconeogenesis, based on 2H-enrichment of body water. 5. To evaluate to what extent the transaldolase reactions affect quantitations of gluconeogenesis and glycogenolysis 6. To apply these techniques to measurements of gluconeogenesis (i) in subjects who are at high risk for NIDDM. (ii) in NIDDM patients, and (iii) in the NIDDM patients then treated with metformin. 7. To apply these techniques to measurements of gluconeogenesis in obese patients. The subjects will ingest 2H2O (to measure the contribution of gluconeogenesis to glucose production from the C5/C2 2H-labeling ratio in glucose), and will be infused with (6,6-2H2) glucose (to measure glucose turnover). The 2H-enrichment at the glucose carbons will be amplified six-fold by incorporating them into hexamethylenetetramine for assay. The contribution of gluconeogenesis will be related to hepatic glycogen content measured by 13C-NMR spectroscopy. Our studies will define the role of gluconeogenesis (i) in diabetic hyperglycemia, (ii) as a possible etiologic factor in the onset of NIDDM, and (iii) in the mechanism of metformin's action. They will help establish whether the propensity of upper body obese subjects to insulin resistance, NlDDM, and cardiovascular disease

is related to increased gluconeogenesis. Also, the direct conversion of glycogen to glucose may prove to be an important regulator of glycogen content. Our studies will shed new light on how glucose and lipid metabolism in adipose tissue adapts to **fasting.**

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- **Project Title: CHROMIUM PICOLINATE IN THE METABOLIC SYNDROMEN**

  Principal Investigator & Institution: Szapary, Philippe O.; Medicine; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-AUG-2005

  Summary: (provided by applicant): The metabolic syndrome (MetSyn) is a cluster of metabolic abnormalities which is characterized by abdominal obesity, impaired **fasting** glucose (IFG), dyslipidemia and raised blood pressure. The MetSyn has been linked to an increased risk of developing both type 2 diabetes mellitus (T2DM) and atherosclerotic cardiovascular disease (ASCVD). The most recent guidelines from the National Cholesterol Education Program (NCEP) include a new definition for MetSyn, and have identified it as an important target of therapy. Using this new definition, it is estimated that 22% of Americans have the MetSyn in some form. Thus, the implication is that therapies aimed specifically at the MetSyn will be very important in reducing the incidence of T2DM and ASCVD. Supplemental trivalent chromium (Cr+3) has been shown to improve insulin sensitivity in some patients with T2DM, but its effect in patients at high risk of developing T2DM is unknown. There is also intriguing literature to suggest that supplemental Cr+3 may reduce weight and improve serum lipids, all of which are important components of the MetSyn. Additionally, recent in vitro data suggests that Cr+3 may also possess antioxidant and anti-inflammatory properties, further suggesting that supplemental Cr+3 might be useful in preventing T2DM and its complications. Thus, we propose to systematically evaluate the safety and efficacy of supra-physiologic doses of Cr+3 in obese adults with NCEP-defined MetSyn and IFG in a four-month, double-blind, randomized, placebo-controlled trial. Primarily, this trial will answer whether 1000 mcg of oral chromium picolinate (CrPic) taken daily can safely improve insulin sensitivity in this high risk population as measured by several indices obtained from an intravenous frequently sampled glucose tolerance test. This study will also quantify the effects of CrPic supplementation on other important clinical features seen in MetSyn including: serum high density lipoprotein cholesterol (HDL-C) and **fasting** triglycerides (TG); weight/body composition; and blood pressure. Additionally, this study will provide the first human data on the effects of CrPic supplementation on state-of-the art readouts of oxidant stress and inflammation, which are important intermediates in the development of both T2DM and ASCVD. Finally, the study will provide evidence of the relationship between chromium status and effects on insulin sensitivity as well as information on the prevalence of chromium deficiency in the MetSyn population. The results from this clinical trial will provide ample preliminary data for future R01 grant submissions further investigating the effects of CrPic supplementation in diabetes and coronary heart disease prevention.

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- **Project Title: DECREASING WEIGHT GAIN IN AFRICAN AMERICAN PREADOLESCENT**

  Principal Investigator & Institution: Klesges, Robert C.; Executive Director; None; University of Memphis Memphis, Tn 38152

  Timing: Fiscal Year 2001; Project Start 01-AUG-1999; Project End 31-MAY-2002

Summary: In this response to NHLBI RFA Number HL-98-010, we propose, as a field center: In Phase I: To conduct a two year intervention planning phase to: (a) identify potentially modifiable social and behavioral determinants of the behaviors and processes that will form the core of the intervention program, particularly those that may have been previously unrecognized or that have different characteristics in African American girls than would be assumed based on studies in Euro American girls; (b) identify important contextual variables (e.g., cultural, situational, familial, or developmental factors that will clearly influence adoption and long term adherence, but which cannot be directly addressed by the intervention) and specify their implications for the intervention design and implementation; (c) for both the social/behavioral and contextual variables, distinguish between cultural variables that are common to African Americans across socioeconomic status from those that seem to apply primarily to high or low SES girls or their families, in order to clarify what differences in assumptions and approaches would apply to interventions stratified or not-stratified on SES; (d) refine proposed data collection methods to improve the validity and appropriateness of all measures for pre-pubertal African American girls, considering physiological and cognitive development, body composition issues, and psychosocial factors; (e) revise the proposed design, recruitment, intervention, and measurement plans as indicated; and (f) feasibility test all aspects in a formal 12 week pilot study with participants similar to those to be included in the Phase II study. In Phase II: To conduct a two year (Phase II) randomized clinical trial of two family-based interventions compared to a standard care condition. The primary outcome measure will be the between group differences in BMI and DEXA at 1 and 2 years of follow up. Secondary outcomes will be percent body fat, **fasting** insulin, glucose, and c-peptides. Intermediate outcome measures will include between group differences in dietary intake and physical activity. Measures of intervention safety and potential negative side effects of intervention will include measures of bone mass, sexual maturation, eating disorders, and rates of smoking. Because the type of intervention that will be effective will involve an interactive process of tailoring and responding to participant needs and interests, rather than fixed content offered in a fixed format, an additional aim of Phase II will be to document the interventions to allow for later dissemination. This will be accomplished through continued monitoring of the implementation process and development of a scheme for describing how the process evolves and how it can be replicated.

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- **Project Title: DIABETES EVALUATION IN WASHINGTON (DEW-IT) CLINICAL CEN***

  Principal Investigator & Institution: Hagopian, William A.; Principal Scientist; Pacific Northwest Research Institute 720 Broadway Seattle, Wa 98122

  Timing: Fiscal Year 2003; Project Start 01-MAR-2003; Project End 31-DEC-2007

  Summary: (provided by applicant): The etiology of Type 1 (autoimmune) diabetes involves both genetic and environmental influences of roughly equal magnitude. Large cooperative arrangements pooling many patient samples have aided in identification of several of the causative genetic polymorphisms. Identification of environmental factors has been more difficult, but should also benefit from a cooperative approach. The Diabetes Evaluation in Washington (DEW-IT) study is a 32,000 subject population-based screening program, which will identify more than 6,000 young children at elevated genetic risk of future diabetes. Combining subject groups with similarly sized population-based screening studies in the US and elsewhere should make it possible to achieve sufficient sample sizes and statistical power to identify common environmental

triggers. We propose to follow subjects at high genetic risk (DEW-IT family and DEW-IT general cohorts) through three putative disease stages: a) seroconversion to single antibody positivity to one of GAD, ICA512/IA2, and insulin, b) progression from one to multiple defined autoantibodies, and c) development of low beta cell function (fasting C-peptide) or clinical diabetes. First degree relatives will be followed sequentially through all stages, but stages b) and c) will be augmented by antibody-positive genetically-at-risk children from the general DEW-IT cohort, prior to intense environmental sampling. Frequent patient sampling will include serum, PBMC, throat swabs, hair, urine and stool. We will also survey children on food intake, vaccinations, allergies, illnesses and other stressors. Environmental sampling will also include selected foodstuffs identified in patient diaries. Genotyping will include HLA DR-DQ and 10 other known diabetes risk loci, as well as 10 other loci designed to detect polymorphisms at beta cell genes known to mitigate toxic exposures. Trios, including both parents, will be collected for TDT analyses. Measured environmental exposures include enteroviruses, dietary mycotoxins, environmental toxins selected by the CDC, and exposures proposed by other sites. Disease progression will be analyzed with respect to gene effects, environmental effects, and gone x environment effects. Disease staging, sample collection and analyses, and statistical approach will follow the consensus approach developed by the consortium. The overall goal is to identify environmental factors initiating and/or propagating the pathogenesis of childhood autoimmune diabetes.

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- **Project Title: DIABETES THERAPY TO IMPROVE BMI AND LUNG FUNCTION IN CF**

  Principal Investigator & Institution: Moran, Antoinette M.; Professor; Pediatrics; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

  Timing: Fiscal Year 2001; Project Start 01-JUL-2001; Project End 31-MAY-2006

  Summary: The majority of cystic fibrosis (CF) patients now survive beyond childhood, and CF related diabetes (CFRD), due to insulin deficiency, is common. CFRD without **fasting** hyperglycemia (FH) is found in 25 percent of CF adults and is associated with increased morbidity and mortality. BMI and pulmonary function deteriorate much more rapidly in these patients than in CF patients with normal glucose tolerance. Insulin deficiency alters protein and fat metabolism resulting in loss of weight and lean body mass and contributing to pulmonary disease and clinical decline. Preliminary isotopic data have shown that insulin and, to a lesser extent, the oral diabetes agent repaglinide acutely improve protein synthesis in patients with CFRD without FH. The objective of this research is to recruit 150 adult patients with CFRD without **fasting** hyperglycemia for a multi-center, twelve month, placebo- controlled intervention trial testing the ability of insulin or repaglinide to improve BMI and stabilize pulmonary function. It will test the hypotheses that: 1. Participants receiving either insulin or repaglinide will increase their BMI compared to control participants. 2. Insulin will be more effective than repaglinide at increasing BMI. 3. The increase in BMI will be primarily due to increased muscle mass. 4. The increase in BMI will be accomplished without significant changes in dietary macronutrient or calorie composition. 5. Insulin or repaglinide therapy will prevent pulmonary function decline compared to both control subjects and to their own baseline as measured the previous year. This will be associated with improvement in NIH clinical score and will be directly related to weight gain and increase in thigh muscle volume. 6. Participants receiving insulin or repaglinide will improve hand grip strength, and this will be directly related to weight gain and increase in thigh muscle

volume. If it can be shown that insulin or repaglinide also improves body mass and pulmonary function, it would have a major impact on the current therapy and prognosis for adult CF patients. The question of whether these patients should receive diabetes therapy was given the highest priority for future research funding at a national consensus conference on CFRD

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- **Project Title: DIABETES, COGNITION AND THE BRAIN**

  Principal Investigator & Institution: Convit, Antonio J.; Associate Professor of Psychiatry; Psychiatry; New York University School of Medicine 550 1St Ave New York, Ny 10016

  Timing: Fiscal Year 2003; Project Start 16-SEP-2003; Project End 31-AUG-2008

  Summary: (provided by applicant): The long-term goal of the proposed work is to increase our understanding of how brain function is impaired by diabetes and insulin resistance. The immediate objectives of the proposed work are to carefully characterize the in vivo brain in type 2 diabetes and insulin resistance syndrome (relative to age-, education-, and gender-matched nominally normal individuals with normal glucose tolerance) and to ascertain whether observed reductions in declarative memory performance among diabetics and individuals with insulin resistance are associated with specific hippocampal volume reductions. All evaluations will use standardized and reliable methods. We hypothesize that deficits will be related to the degree of insulin resistance, i.e., type 2 diabetics > non-diabetic insulin resistant > control. Because significant vascular disease can have an impact on cognitive performance, we will study individuals who do not have extensive vascular pathology, and we will monitor subtle levels of micro-vessel disease so as to be in a position to account for those effects statistically in secondary analyses. Given the extensive associations between hippocampal integrity and cortisol levels and regulation, as well as the known relationships between regulation of peripheral glucose and cortisol secretion, in secondary analyses we will account for the potential effects of cortisol on the hypothesized relationships. We propose to study three groups of age, gender, and education matched individuals, who do not have evidence of significant large vessel atherosclerosis, 45-60 years of age, with at least a high school education, and 50% female, as follows: 50 normal individuals with normal glucose tolerance, 50 individuals with **fasting** glucose levels in the non-diabetic range and with insulin resistance, and 50 patients with type-2 diabetes, who have never been treated with insulin or insulin secretagogues and who are well controlled on diet and/or oral agents. The improved understanding to be provided by this study may suggest that the brain be formally evaluated as a site of potential complications in diabetes. In addition, the proposed study may add to the rationale to use behavioral and pharmacological interventions aimed at improving insulin sensitivity to improve memory problems among mid-life individuals. Lastly, this study may also contribute to a more general understanding of hippocampal atrophy in conditions other than diabetes where there may be HPA axis dysregulation.

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- **Project Title: DIET THERAPY IN DIABETES MANAGEMENT OF MEXICAN AMERICANS**

  Principal Investigator & Institution: Briones, Esperanza R.; Univ of Texas-Pan American Edinburg, Tx

Timing: Fiscal Year 2002; Project Start 01-JUN-1977; Project End 31-JUL-2006

Summary: (provided by applicant): Diabetes in Hispanic Americans is a serious health problem. It affects 1.2 million or 10.6% of the Mexican American population. Approximately 24% of Mexican Americans in the U.S. between the ages of 45-74 have diabetes. In Hispanic adults, diabetes is primarily type 2, and its incidence is correlated with the occurrence of obesity. The purpose of the study is to conduct a two and half (2-1/2) year randomized trial of a culturally appropriate dietary and lifestyle education intervention designed for Mexican Americans with type 2 diabetes residing in Rio Grande Valley. Both males and females, with type 2 diabetes will be recruited, with two age subgroups, ages 45-59 and 60 and above. Eligible participants will be randomized into two groups. Group 1 will receive the conventional dietary counseling and group 2 will receive additional sessions and follow-up. The specific objectives of the study are: to assess the effectiveness of a culturally appropriate intervention to improve participants' adherence to dietary modifications, medication schedules, and promote sustained improvements in lifestyle behaviors; to assess the anthropometric measurements, health habits, and nutrient consumption of subjects at baseline and after dietary and educational sessions; to determine **fasting** serum glucose and glycosylated hemoglobin in assessing the level of diabetes control; and to assess the lipid profile (serum cholesterol, triglycerides, high density lipoprotein cholesterol) which are associated with the development of coronary heart disease in diabetes. Statistical calculations will be used to evaluate the differences between the two groups.

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- **Project Title: DIETARY COMPOSITION, OBESITY, AND CARDIOVASCULAR RISK**

  Principal Investigator & Institution: Schaefer, Ernst J.; Professor; None; Tufts University Boston Boston, Ma 02111

  Timing: Fiscal Year 2001; Project Start 01-JUL-1999; Project End 31-MAY-2004

  Summary: Coronary heart disease (CHD) is a major cause of death and disability in our society. Obesity increases CHD risk by adversely affecting glucose, lipoproteins, and blood pressure. There is consensus that dietary saturated fat and cholesterol (C) restriction is beneficial for low density lipoprotein (LDL) lowering and CHD risk reduction, but there controversy about other aspects of the diet. We propose to examine the effects of three diets meeting National Cholesterol Education program Step 2 diet criteria on body weight and composition and on CHD risk factors (LDL C, HDL C, remnant lipoprotein C, Lp(a) C, insulin, glycosylated hemoglobin, glucose, and blood pressure) in the **fasting** and nonfasting state (4 hours after a meal) in 80 men and women (men greater than or equal to 50 and less than 65 years of age, women postmenopausal and less than 65) with LDL C values greater than or equal to 130 mg/dI and a body mass index greater than or equal to 28 and less than 38 kg/m2. A four phase study will be conducted in which all food and drink is provided during the first 3 phases, while diet is recommended but not provided in the fourth phase. In phase 1, all subjects will initially be placed on an average isoweight U.S. diet for 5 weeks (15 percent protein, 35 percent fat; 15 percent saturated fat; 15 percent monounsaturated (mono) fat; 6 percent polyunsaturated (poly) fat, with 150 mg of cholesterol/1000 calories and 10 g/1000 cal. of fiber). For phase 2, subjects will then be equally randomized to one of 3 diets, all containing 15 percent protein, 5 percent saturated fat and 60 mg of cholesterol/1000 calories: 1) high complex carbohydrate (CHO): 15 percent fat, 5 percent mono, 5 percent poly, and 70 percent CHO (mainly complex with relatively high glycemic index), 16 g/1000 cal of fiber, and low dietary caloric density of 1.10 cal/gm; 2)

high mono: identical to diet 1 except that the fat content will be 30 percent (15 percent mono) and 55 percent CHO with CHO of high glycemic index and high caloric density, 1.25 cal/gm; and 3) composite: identical to diet 2 except that there will be lower glycemic index and low dietary caloric density of 1.10 g/1000 cal). These diets will be given ad libitum, and subjects can adjust their calorie level using 200 calorie casseroles from 66 percent to 133 percent of calories needed to maintain weight, for a 12 week period. Subjects will then be continued on these same diets isoweight for an additional 5 weeks under controlled circumstances in phase 3, and then for one year (phase 4) under uncontrolled circumstances where they will receive dietary instruction and menus, but not food. Body weight and blood pressure will be assessed three times per week, and plasma lipoproteins (LDL, HDL, remnants, and Lp[a]), glucose, glycosylated hemoglobin, and insulin levels will be assessed three times in the **fasting** state and once in the fed state at the end of each controlled dietary period and at 3, 6, 9, and 12 months in the long-term follow-up period. In addition, body weight, body energy expenditure, physical activity, body composition, anthropometics, and metabolic rate will be measured at regular intervals during all phases. Our hypothesis is that the fat-restricted diet rich in complex carbohydrate and low in caloric density and the composite diet low in caloric density and glycemic index will have a more favorable effect on CHD risk factors, body weight, body composition and energy expenditure than the Step 2 diet higher in mono fat, glycemic index, and caloric density.

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- **Project Title: DIETARY PATTERNS AND RISK OF CARDIOVASCULAR DISEASE**

  Principal Investigator & Institution: Hu, Frank B.; Nutrition; Harvard University (Sch of Public Hlth) Public Health Campus Boston, Ma 02460

  Timing: Fiscal Year 2001; Project Start 01-AUG-1998; Project End 31-JUL-2003

  Summary: This new application presents plans to study, prospectively, the association between dietary patterns and risk of coronary heart disease (CHD), ischemic stroke, and hemorrhagic stroke in cohort studies of 121,700 women age 30 to 55 years at baseline in 1976 (the Nurses; Health Study; NHS) and 51,529 men aged 40-75 years at baseline in 1986 (the Health Professionals Follow-up Study; HPFS). Food consumption data were collected through semiquantitative food frequency questionnaires at baseline and during follow-up in each of the cohorts. Dietary patterns are derived from the food consumption data using factor analysis, cluster analysis, and dietary indexes (based on prevailing dietary recommendations). In addition, using existing datasets from dietary validation studies in sub-samples of the two cohorts, the investigators propos to evaluate the reproducibility and validity of dietary patterns defined by factor/cluster analysis and dietary indexes. Further, using prospectively collected and stored bloods in the NHS (n-32, 826) during 1989-1990 and the HPFS (n-18, 000) during 1993-1994, we propose to examine whether observed associations between dietary patterns and CHD are explained by (or mediated through) plasma biochemical measurements (including serum lipids, thrombotic factors, antioxidants, **fasting** insulin, and homocysteine levels) in a nested case-control design; and they propose to assess prospectively the relationship between dietary patterns and these biomarkers in the control samples. The funded NHS and HPFS will provide follow-up and documentation of CHD and stroke in addition to covariate information. Assays of biomarkers in the two cohorts are funded through other grants. Overall, the large size of these cohorts, the prospective design, the high follow-up rates, and the availability of archived blood specimens provide a unique opportunity to study the relationship between overall dietary patterns and cardiovascular disease in an extremely cost-efficient manner. This would be the first

study to characterize dietary patterns in large cohorts of men and women and relate dietary patterns to CHD and stroke. Finally, this project will enable evaluation of prevailing dietary recommendations in relation to both biomarkers of risk as well as clinical cardiovascular diseases.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DIETARY PROTEIN REQUIREMENTS IN HEMODIALYSIS PATIENTS**

  Principal Investigator & Institution: Kopple, Joel D.; Professor; Harbor-Ucla Research & Educ Inst 1124 W Carson St Torrance, Ca 90502

  Timing: Fiscal Year 2003; Project Start 16-MAY-2003; Project End 31-JAN-2008

  Summary: (provided by applicant): A high proportion of maintenance hemodialysis (MHD) patients have protein-energy malnutrition (PEM), which is a powerful predictor of high morbidity and mortality. Although inflammation may contribute to PEM, low dietary protein intake (DPI) is often a contributing factor. The usual DPI of MHD patients is about 1.0 g protein/kg/day, whereas expert groups recommend = 1.20 g protein/kg/day. However, these recommendations are based upon few studies, often of insufficient duration, that were usually carried out with obsolete types of dialysis therapy. This project has two primary aims: Study 1. To assess dietary protein requirements in clinically stable MHD patients. It is hypothesized that the average DPI that will maintain nitrogen balance is 1.00 g protein/kg/day, but that a safe intake that maintains balance in almost all MHD patients is about 1.25 g protein/kg/day. Study 2. To test the hypothesis that in clinically stable MHD patients with PEM, treatment for 5 months with a DPI of 1.30 g/kg/day, but not 1.00 g/kg/day, is associated with a significant increase in urea-free total body nitrogen (TBNuf). In Study 1, 9 patients will be studied in a clinical research center while they are fed, in random order, the following 5 DPIs, each for 17 days: 0.60, 0.80, 1.00, 1.15 and 1.30 g/kg/day. Energy intake for each patient will be based on their indirect calorimetry. The key outcome measure is nitrogen balance. We will assess the effects of these DPIs on total body (13C-leucine) protein synthesis and degradation and 13C-leucine oxidation during **fasting** and feeding, plasma amino acids, dialysate amino acids, peptides and proteins, and body composition (anthropometry, dual x-ray photon absorptiometry (DXA)). We will attempt to define more precisely the relationships between urea nitrogen appearance (UNA), protein nitrogen appearance (PNA) and DPI and investigate the validity of urea kinetic equations for estimating UNA, PNA, DPI and urea pools. In Study 2, 70 MHD outpatients will be randomly assigned to a DPI of 1.00 or 1.30 g/kg/day for 5 months each, utilizing dietary counseling and food supplements. Before and after these 5 months, total body protein will be assessed by TBNuf, body cell mass (TBK), and other components of body composition using anthropometry, DXA, and near infra-red interactance.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DIFFERENTIAL METABOLISM OF DIETARY FATTY ACIDS**

  Principal Investigator & Institution: Kien, C Lawrence.; Professor; Pediatrics; University of Texas Medical Br Galveston 301 University Blvd Galveston, Tx 77555

  Timing: Fiscal Year 2002; Project Start 01-SEP-2000; Project End 31-AUG-2004

  Summary: Preliminary data indicate that the rate of oleic acid oxidation is 21 percent increased compared to palmitic acid. If the ratio of OA to PA in the diet were to increase, the rate of total fatty acid oxidation in the fed state also may increase; thus, daily fat

balance might be decreased in humans fed diets enriched in OA. This would have significance to the treatment and prevention of obesity. Indirect calorimetry will be performed in the fed and **fasting** state in 34 young, healthy adults who will be studied under two conditions: after a 30-day, solid food diet ("run-in phase") and again, after a 30-day formula diet. The subjects will be randomized to receive either a Control Formula similar to the solid food diet (OA=PA=16.4 percent total kcal) or a High Oleic Acid Formula (OA=31.4 percent kcal; PA=1.7 percent kcal). Using dual-energy x-ray absorptiometry, body composition will be monitored before and after the formula diet. The principal investigator (PI) will address four specific aims. In specific aim 1, the PI will determine if a higher intake of oleic acid (and a reciprocally lower intake of palmitic acid) is associated with a higher rate of fat oxidation. The PI hypothesizes that the rate of fat oxidation (g/hr) in the fed state, adjusted for the covariate effect of the rate of fat oxidation on the solid food diet, will be higher (30 percent) in those subjects randomized to the OA-enriched diet compared to controls. In the specific aim 2, the PI will measure energy intake required to maintain constant body weight during each diet and to measure fat-free mass and fat mass, before and after each dietary change. The PI hypothesizes that a higher rate of fat oxidation on the high OA diet will be associated with a higher energy intake required to maintain constant body weight. In specific aim 3, the PI will compare fat oxidation on the liquid formula diet with that observed on the solid food diet. The PI hypothesizes that fat oxidation will increase in those fed the OA-enriched diet. In specific aim 4, the PI will measure the thermic effect of feeding during both the solid food and formula diet periods. The PI hypothesizes that the high OA feeding will be associated with a higher thermic effect of feeding.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DISTINCT HUMAN MACROPHAGE RECEPTOR FOR ABNORMAL VLDL**

  Principal Investigator & Institution: Gianturco, Sandra H.; Prof/Div/Gerontology/Geriatric Medicine; Medicine; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2001; Project Start 01-JAN-1991; Project End 31-DEC-2002

  Summary: Cardiovascular disease (CVD) due to atherosclerosis is the major cause of death on the US. Monocyte-macrophage (MM)-derived, lipid-filled "foam cells" are hallmarks of both early fatty streak and later, rupture-prone, thrombogenic lesions. Elevated plasma triglycerides [hyper (H) TG, **fasting** or post-prandial] are emerging risk factors for atherothrombotic disease; the mechanistic links are not known. One potential mechanism is via a MM receptor (R) we identified that binds apoB of TG-rich lipoproteins (TGRLP), including apoB-48 of chylomicrons (CM), inducing foam cells in vitro like those in vivo in atherosclerotic lesions and in the bone marrow, skin, and spleen in humans with persistent CMs and remnants. We have cloned the human R's cDNA (3773 bp). It encodes a new, unique R that induces TGRLP uptake and foam cell formation when transfected into R- negative CHO-K1 cells. Its approximately 3.8 kb mRNA is expressed in THP-1 monocytes, placenta, peripheral mononuclear leukocytes, bone marrow, spleen, tonsil, lymph node, and appendix, a distribution like that of foam cells in vivo in humans with persistent CMs. Immunohistochemical studies show R expression in foam cells of human aortic fatty streaks, advanced coronary and carotid lesions and MM of immune tissues. We hypothesize that the receptor's normal role is to ensure efficient delivery of essential dietary lipids and lipid-soluble vitamins to monocytes and accessible macrophages of the immune system; when overwhelmed, as in states with persistent CMs, it is involved in foam cell formation and atherogenesis. To

test this hypothesis in vivo, homologous recombination in murine embryonic stem (ES) cells will be used to make R deficient (R-/- and R-/+) mice and tissue specific, over-expressing transgenics. Effects of gene dosage on lipoprotein profiles and atherosclerosis susceptibility in these and in crosses with murine models of atherosclerosis (apoE-/-, LDLR-/-) and HTG (apoCIII, and apoCI transgenics) will help clarify this R's role in lipoprotein metabolism and atherogenesis in vivo. Studies in vitro in monocytes and transfected CHOs will define mechanisms of the R's synthesis, processing, cycling, and uptake of core lipids. The potential impact of this R on CVD warrants the proposed studies to provide cellular, molecular, and in vivo functional rationales for therapeutic interventions.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DNA METHYLATION AND COLORECTAL POLYPS**

  Principal Investigator & Institution: Haile, Robert W.; Professor; Preventive Medicine; University of Southern California 2250 Alcazar Street, Csc-219 Los Angeles, Ca 90033

  Timing: Fiscal Year 2001; Project Start 20-JAN-2000; Project End 31-DEC-2003

  Summary: (Adapted from the Applicant's Abstract): Our overall objective is to better define the role DNA methylation in the etiology of colorectal adenomas, and to assess potential risk factors for de novo methylation in adenomas. We propose to accomplish our objective by adding a methylation component onto an existing sigmoidoscopy-based case-control study of environmental and genetic risk factors for adenomatous polyps of the large bowel that will have 1,000 cases and 1,000 controls, with food frequency and risk factors questionnaires, a **fasting** blood sample, and, for cases, pathology reports and tumor blocks. We propose the following aims: First, we will conduct a descriptive study of de novo methylation in five specific genes, three known tumor suppressor genes (APC, hMLH1, and p16) involved in colorectal of hypermethylation of the promoter region cancer, the estrogen receptor (ER), which may or may not be directly involved in the etiology of colorectal polyps, and a "control" gene, MYOD, that is clearly not involved in colorectal cancer. Second, we will assess two hypotheses regarding risk factors for hypermethylation. The first is that decreased dietary or RBC folic acid will be associated with an increase prevalence of hypermethylation of the promoter region of the ER. As part of this hypothesis, we will assess modification of the folic acid-methylation relationship by a gene, methylene-tetrahydrofolate reductase (MTHFR), that is involved in folic acid metabolism. The second hypothesis is that use of postmenopausal hormones will be associated with a lower prevalence of hypermethylation of the ER. Third, we will determine if there are differences in the methylation status of the five target genes in adenomas with the replication error phenotype (RER+) compared to adenomas without that phenotype (RER-). We propose to measure methylation status with a new procedure (COBRA), developed by Dr. Peter Laird , that more sensitive and quantitative than other assays that can feasibly be conducted on a large sampled of paraffin-embedded tissue. Combining this assay with our ongoing study will provide us with a powerful means of addressing important questions about methylation and its role on cancer. We propose to measure methylation status with a new procedure (COBRA), developed by Dr. Peter Laird, that is more sensitive and quantitative than other assay with our ongoing study will provide a powerful means of addressing important questions about methylation and its role on cancer etiology.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DOES HYPERGLYCEMIA PREDICT PANCREATIC CANCER DIAGNOSIS?**

  Principal Investigator & Institution: Chari, Suresh T.; Mayo Clinic Rochester 200 1St St Sw Rochester, Mn 55905

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2007

  Summary: (provided by applicant): Pancreatic cancer causes glucose intolerance and diabetes in up to 80% of patients. Pancreatic cancer induced diabetes (PaCDM) is often asymptomatic, of short duration (50 years of age may have PaCDM. We propose to establish whether newly elevated **fasting** blood glucose (FBG) is indicative of underlying pancreatic cancer as evidenced by diagnosis of pancreatic cancer within 3 years of the FBG measurement. If so, this would provide an entirely novel approach to screening for sporadic pancreatic cancer. We hypothesize that the 3-year likelihood of diagnosis of pancreatic cancer will be high in subjects: a) equal to or > 50 years of age with newly elevated FBG, b) with elevated **fasting** glucose who have known risk factors for pancreatic cancer (e.g. smoking), and/or c) who manifest an abrupt increase in FBG in serial measurements over time. We will identify visits to Mayo Clinic between years 1988 to 2002 by subjects equal to or >50 years of age who resided in its surrounding catchment area and had a routine physical examination that included a FBG. Preliminary data reveal that about 150,000 different subjects made >300,000 such visits during this time period providing >1 million person-years of follow-up. We will electronically retrieve clinical, and laboratory data and examine 3-year follow-up from date of FBG measurement to identify those diagnosed with pancreatic cancer. We expect 340 to 510 pancreatic cancer events in this cohort. Our Specific Aims are: Aim 1A). To test if FBG drawn during routine physical examination predicts likelihood of underlying pancreatic cancer and to test for non-linearity of this association. Aim 1B) To establish a FBG threshold that predicts a high 3-year likelihood of diagnosis of pancreatic cancer. Aim 2). To estimate the extent to which known risk factors for pancreatic cancer (age, smoking, obesity and family history) modify the likelihood of underlying pancreatic cancer in subjects with FBG greater than the threshold defined by Aim 1B. Aim 3). To test if patterns of change in serial measurements of FBG over time predict likelihood of underlying pancreatic cancer. The clinical and research implications of this study are considerable. These data may lead to delineation of individuals who have a high likelihood of existing pancreatic cancer, and who may be ideal candidates for more intensive screening or early detection regimens. The research described in this application is 100% relevant to pancreatic cancer.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DYNAMIC FMRI ANALYSES OF HYPOGLYCEMIA UNAWARENESS**

  Principal Investigator & Institution: Liu, Yijun; Psychiatry; University of Florida Gainesville, Fl 32611

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 31-JUL-2004

  Summary: (provided by applicant): We propose a functional MRI (fMRI) study to probe the timing and location of neuro-hormonal interaction following food ingestion in humans. The proposal presents an explorative fMRI project by developing in vivo methods to characterize brain activity during hypoglycemia induced by prolonged **fasting.** We will examine brain responses during a real-time transition from **fasting** hypoglycemia to normoglycemia attained by eating (i.e., by oral glucose intake), focusing on the hypothalamus and its associated neural circuits. In particular, this project underscores two novel dynamic imaging approaches for tracing the time course

of brain-hormone interaction during the transition. These approaches, namely (1) temporal clustering analysis (TCA) and (2) within-condition interregional covariance analysis (WICA), are critical to the timing of neuronal events that are interacting with hormonal processes, such as glucose-insulin regulation. Modeling of both temporal and spatial information about brain-hormone interaction will be our first step toward establishing a functional marker of hypoglycemia unawareness. By the functional marker we mean noninvasively -measured neuroendocrinal signals in response to a physiological challenge, such as **fasting** or eating. We hypothesize that alteration of such signals is implicated in the development of hypoglycemia unawareness, as in insulin-dependent diabetes mellitus (IDDM) accompanied by recurrent hypoglycemia. Although the ultimate goal of this project is to directly test this hypothesis in patient population under long-term intensive insulin treatment, which may require large-scale clinical trials, the current R21 proposal aims to develop new fMRI methodology involving a small number of subjects imaged under well-controlled conditions. While functional imaging methods may reflect a departure from traditional, symptom-dependent assessment of hypoglycemia unawareness (e.g., cognitive task testing or objective neurophysiological evaluation), it is still important to correlate fMRI analyses with routine clinical measurements, such as counterregulatory hormone levels by blood sampling. This correlation may provide information for delineating the neural bases about how internal biochemical signals give rise to the awareness of hunger or satiation, and for understanding the phenomenon of hypoglycemia unawareness. Two specific aims are to be accomplished in this two-year project: Aim 1. Development of a fasting-eating fMRI paradigm by correlating functional imaging signal with biochemical measurement; and Aim 2. Development of both temporal and spatial reference systems for the in vivo modeling of glycemia regulation and hypoglycemia unawareness.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: EFFECT OF DIETARY LIPIDS ON THE FUNCTION OF CHYLOMICRONS**

  Principal Investigator & Institution: Chung, Byung-Hong H.; Medicine; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2001; Project Start 15-SEP-1999; Project End 31-AUG-2003

  Summary: Although numerous diet studies have demonstrated that dietary fat composition of chronic diets alters **fasting** plasma lipoprotein cholesterol (CH) levels and the risk of developing atherosclerosis, the specific mechanisms responsible for these alterations are not well established. Dietary fat and CH are the exclusive precursors of postprandial (PP) chylomicrons, but they do not enter into the formation of endogenous lipoproteins in **fasting** blood. The working hypothesis of this proposal is that dietary fat composition alters endogenous lipoprotein CH levels in **fasting** plasma and the risks of developing atherosclerosis by influencing the ability of PP chylomicrons to accept CH molecules from endogenous lipoproteins and cell membranes through the reactions catalyzed by lecithin cholesterol acyltransferase (LCAT) and/or cholesterylester transfer proteins (CETP) and by influencing the rate of the clearance of CH-enriched chylomicron remnants from circulating blood. To test this hypothesis, this study will examine the acute and chronic effect of altering dietary fat composition on 1) level, composition and density spectrums of plasma lipoprotein CH and TG, 2) the extent of LCAT and CETP-mediated transfer of CH from endogenous lipoproteins and/or cell membranes into PP TG-rich lipoproteins in vivo and in vitro, 3) intraplasma metabolic activities that promote the reverse cholesterol transport (RCT) in vivo and 4) the extent of accumulation of chylomicrons and their remnants in the blood at a late clearance

stage of PP lipemia. Study subjects (n=32) will be recruited from a pool of normolipidemic adult males and will be rotated through three experimental diets (saturated fat, polyunsaturated fat, and monounsaturated fat), each diet lasting for 20 days. Three oral fat loading studies will be conducted during each dietary intervention period. Each subject will serve as his own control. The studies determining the chronic and acute effect of dietary fat composition on the potencies of PP chylomicrons to accept CH from endogenous lipoproteins and cell membranes and to deliver their CH to the liver for excretion should provide additional information about the mechanisms by which the dietary fat composition alters the development of atherosclerosis.

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- **Project Title: EFFICACY OF THE KETOGENIC DIET--A BLINDED STUDY**

  Principal Investigator & Institution: Freeman, John M.; Neurology; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2001; Project Start 15-JUL-1997; Project End 31-MAR-2002

  Summary: This study is designed to establish the efficacy of the ketogenic diet in a blinded, placebo-controlled fashion. Twenty to thirty percent of children with epilepsy remain refractory to currently available anticoveulsant medications. The frequent atonic-myoclonic seizures of the Lennox-Gastaut Syndrome (LGS), are particularly handicapping. Preliminary date suggest that even when other medications have failed, these seizures respond rapidly and dramatically to a high-fat-low-carbohydrate ketogenic diet. Twenty children with LGS having more 15 atonic/ myoclonic seizures/day will enter a randomized, blinded, crossover protocol to evaluate the efficacy of this diet. Efficacy will be defined as greater than 50% decrease from baseline seizure frequency utilizing continuous EEG monitoring obtained just prior to **fasting.** The diet will be instituted in a standard fashion following 36 hours of **fasting.** Children will be randomized to a liquid supplement containing either placebo (maintaining ketosis) or glucose negating ketosis). Seizure frequency (utilizing 24 hours continuous EEG monitoring) will be evaluated after full diet initiation (5 days). The child will be re-fasted for 24 hours and crossed to the alternate liquid supplement. At the end of 5 days on the second arm, a repeat 24 hours continuous EEG monitoring will be obtained, and the child will be discharged on the routine ketogenic diet. The primary endpoint will be the number of EEG documented seizures on the last day of each treatment period. We do not believe that there will be substantive sequence or carry- over effect. However, these assumptions will be examined, first by comparing the seizure frequency after the placebo diet to the frequency measured at baseline, and then by calculating the total seizure frequency for each sequence and comparing the two sequences. After discharge, each child's diet will be "fine-tuned" to optimize seizure control, followed in routine fashion with monthly seizure calenders maintained by the parents. Each child will return for follow-up at six months and one year. Twenty-four hour continuous EEG monitoring will be obtained at each of these visits. The secondary question of whether control can be maintained overtime will consist of either a simple proportion (with confidence interval), or will use survival methods, if those are indicated because of poor compliance or loss to follow-up. Analysis will be done both by intention to treat and by those on treatment.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: EXTRACELLULAR REGULATION OF LIPOPROTEIN LIPASE ACTIVITY**

  Principal Investigator & Institution: Goldberg, Ira J.; Professor of Medicine; Medicine; Columbia University Health Sciences New York, Ny 10032

  Timing: Fiscal Year 2001; Project Start 01-APR-1991; Project End 31-MAR-2005

  Summary: Lipoprotein lipase (LpL) is the principal enzyme responsible for hydrolysis of triglyceride in circulating lipoproteins. Changes in LpL activity are a basic mechanism used to modulate uptake of free fatty acids and perhaps fat-soluble vitamins by tissues. Regulation of LpL involves a number of post-secretory processes. By investigating these processes basic biological insights into the interaction of proteins with heparan sulfate proteoglycans (HSPGs) have been obtained. In this renewal, a series of experiments are proposed to understand how LpL is transferred from its sites of synthesis, principally adipocytes and myocytes, to the luminal surface of endothelial cells. Aim 1 is to determine the pathways required for LPL transport across endothelial cell monolayers. We have observed that LpL transcytosis across endothelial monolayers is reduced by RAP, the 39 kDa inhibitor of the LDL receptor related protein and other receptors in this family. In this Aim we will assess the role of these receptors and HSPGs in the transcytosis of normal and mutant LpL. The importance of this pathway and the association of LpL with proteoglycans will also be studied in vivo. Aim 2 proposes to study how LPL interaction with HSPGs regulates HSPG binding. Using these mice and new mice expressing a tethered dimer of mutated LpL, the importance of LpL-HSPG interactions will be studied. Aim 3 will study how the VLDL receptor and other RAP-sensitive receptor, and LpL monomizerization participate in the physiological regulation of LPL actions. We will assess the importance of LpL transcytosis pathways in wildtype and heterozygous LpL transcytosis pathways in wild type and heterozygous LpL knockout mice, the role of RAP-sensitive receptors in regulation of LpL activity with feeding/fasting, and modulation of tissue LpL in mice that cannot covert dimeric LpL to inactive monomers. These experiments will provide information about how a secreted protein transfers from the subendothelial space into the bloodstream and the importance of protein dimerization and HSPG binding in this process. Moreover by understanding the regulation of LpL activity, these investigations will may means to change human caloric and vitamin disposal; processes that are often abnormal in humans with lipoprotein disorders and diabetes.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: FATTY ACIDS, ANGIOTENSIN AND OXIDATIVE STRESS**

  Principal Investigator & Institution: Egan, Brent M.; Associate Professor; Pharmacology; Medical University of South Carolina 171 Ashley Ave Charleston, Sc 29425

  Timing: Fiscal Year 2002; Project Start 15-AUG-1997; Project End 31-MAR-2005

  Summary: (provided by applicant): BACKGROUND: Obese hypertensives have elevated plasma non-esterified fatty acids (NEFAs) including oleic acid. Oleic acid induces a PKC-dependent increase of reactive oxygen species in vascular smooth muscle cells. In volunteers consuming diets low in anti-oxidants for 3 weeks, raising plasma NEFAs with an infusion of Intralipid and heparin increased blood pressure (BP) about l4/8 mmHg and elevated plasma F2-isoprostanes, an index of oxidative stress, p<O.O5. The rise in NEFAs correlated with the increase of plasma F2-isoprostanes NEFAs (N=30, r=O.53, p<O.Ol). The increase of plasma F2-isoprostanes, in turn, correlated with the rise in systolic BP (N 30, r= 0.44, p<O.O5). The findings support the HYPOTHESIS that fatty acids elevate BP through oxidative stress-sensitive mechanisms. SPECIFIC AIM:

Determine the effects of isocaloric high and low anti-oxidant diets with equal daily amounts of Na* (3000 mg), K+ (4000 mg), Ca2+ (1000 mg), and Mg2+ (500 mg) and fiber for 4 weeks each on BP and plasma isoprostanes at baseline and during a 4-hour infusion of Intralipid and heparin to raise plasma NEFAs in obese, dyslipidemic hypertensive and lean normotensive volunteers. METHODS: Complete data will be obtained on 30 lean (BMI 150 mg/dl, HDL-C <45 mg/dl, BP 130-159/85-99). Subjects are studied first on their usual diets, then randomized to either the low or high anti-oxidant diet for 4 weeks prior to the second study. They undergo a third study after 4 weeks on the complementary phase of the high or low anti-oxidant diet. Each study includes a two-day assessment. On day one, volunteers have measurements of glucose and NEFAs under **fasting** conditions and during a 15-minute insulin tolerance test to assess insulin action. A 24-hour BP monitor is placed. On day two, subjects undergo testing that includes hemodynamics (BP, heart rate, stroke volume, cardiac output, calculated vascular resistance, arterial compliance) and indices of oxidative stress (plasma and urine F2-isoprostanes and other secondary markers). Anti-oxidant capacity will be assessed by assaying the ferric reducing activity of plasma (FRAP) and by measuring reduced and oxidized glutathione in plasma and RBCs. Plasma NEFAs, lipids, and insulin will be obtained. Measurements will be obtained in the **fasting** state and during a 4-hour infusion of Intralipid and heparin to raise plasma NEFAs. SIGNIFICANCE: The mechanisms by which obesity raises BP are not well defined. Evidence supports the notion that resistance to insulin's NEFAs lowering action contributes to elevated BP through oxidant-sensitive mechanisms. This study is designed to clarify the capacity of dietary anti-oxidants to modulate BP and measures of oxidative stress under basal, **fasting** conditions and in response to acute dyslipidemia under controlled laboratory conditions. We believe the information generated by the proposed studies has the potential for elucidating biological mechanisms underlying obesity-associated hypertension and the potential for dietary anti-oxidants to modulate BP.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: FETAL BRANCHED CHAIN AMINO ACID AND KETOACID METABOLISM**

  Principal Investigator & Institution: Liechty, Edward A.; Professor; Pediatrics; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, in 462025167

  Timing: Fiscal Year 2001; Project Start 01-AUG-1987; Project End 31-MAY-2004

  Summary: The regulation of fetal growth is coordinated by a complex interaction of substrate supply and endocrine signals of fetal and placental origin: insulin and insulin-like growth factor 1 are believed to have the major regulatory roles. We have been investigating the regulatory roles of these hormones in the ovine fetus, particularly their regulation of proteolysis and amino acid catabolism. We have found that the fetus is resistant to insulin's effect to suppress proteolysis, but insulin is potent inhibitor of amino acid catabolism. IGF-1 inhibits proteolysis by 30%, but has a lessor effect on acid catabolism. The hypothesis of the present proposal is that during brief elevations of insulin and IGF-1, the hormones act in distinct but synergistic manners to promote tissue accretion, insulin by promoting carbohydrate utilization and suppressing amino acid catabolism, and IGF-1 by suppression proteolysis. Insulin acts to reduce amino acid catabolism, directly affecting the activity state of enzymes responsible for amino acid catabolism. IGF-1 acts independent of insulin to decrease proteolysis by suppressing the ubiquitin proteolytic system in the fetus. However, as the length of time in the elevation of plasma IGF-1 progresses, stimulation of protein synthesis becomes predominant, and

suppression of proteolysis decreases. Finally, we hypothesize that circulating fetal IGF-1 acts primarily on fetal tissues, but also has effects on placental tissues to alter metabolism and/or transport. These hypotheses will be investigated through three specific aims. 1. To verify that the branched chain dehydrogenase complex in the fetus is a) regulated by the phosphorylation/dephosphorylation; and b) that insulin and insulin-like growth factor act by regulation of the activity state of the complex. 2. To investigate the mechanisms by which IGF-1 inhibits fetal proteolysis. The ubiquitin system will be investigated. We hypothesize the IGF-1 inhibits the ubiquitin system at the gene transcription level, thereby inhibiting fetal proteolysis. 3. To investigate the transplacental flux rates of important fetal substrates during infusion of IGF-1 and/or insulin. 4. To compare and contrast the acute versus chronic effects of increased plasma IGF-1 on fetal growth and protein kinetics. Investigations will be carried out in the chronically catheterized fetal lamb. IGF-1 and insulin will be infused singly and in combination, with detailed analysis of fetal protein kinetics and placental substrate transfer rates determined. In addition, hormonal regulation of the branched chain ketoacid decarboxylase complex and the ubiquitin proteolytic will be examined in detail at the cellular level. These studies will result in important new information system regarding the mechanisms of fetal protein accretion, which will be important in evaluations of the potential for IGF-1 and/or insulin therapy for intrauterine growth restriction or inadequate postnatal growth in premature infants.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: GENETIC ANALYSIS OF CVD RISK FACTORS**

  Principal Investigator & Institution: Maccluer, Jean W.; Scientist; Southwest Foundation for Biomedical Res San Antonio, Tx 782450549

  Timing: Fiscal Year 2002; Project Start 01-JUL-2002; Project End 31-MAY-2007

  Summary: (provided by the applicant): The objective of Project 1 is to detect, map and characterize polymorphic genes that contribute to variation in risk of cardiovascular disease (CVD). The focus in this Program Project (the San Antonio Family Hearth Study, SAFHS) is on extended Mexican American families ascertained without regard to disease status. During the current grant period each family member is being genotyped for 414 short tandem repeat markers in a 10 centimorgan map. Using genome screen data from the first ten genotyped families (Pedigree Set A, with nearly 500 individuals), QTLs have been detected and mapped that influence leptin, fat mass, BMI, insulin, 2 hour glucose, LDL-3-C, HDL-C, HDL2a unesterified cholesterol, evidence for linkage, additional, more closely spaced markers are being typed for use in finer scale mapping strategies. Identification of the functional alleles for a few of the best characterized of these genes will be pursued in Project 3. In Project 1, taking advantage of the resource of families with extensive genotypic and phenotypic data that has been created in the past ten years, linkage analyses will be pursued for phenotypes that exhibit substantial heritabilities but for which significant linkages were not detected in Pedigree Set A (e.g., apolipoproteins, selected lipoproteins size classes, **fasting** glucose, 2-hour insulin, fibrinogen, C-reactive protein, and measures of carotid intima-media thickness). Linkage signals also will be strengthened and refined for other QTLs for which significant evidence of linkage already has been detected (e.g., QTLs for BMI on chromosome 17, HDL-C on chromosome 16, insulin/glucose ratio on chromosome 3, and HDL2a unesterfied cholesterol on chromosome 8). These analyses will incorporate additional markers, and associations will be sought with polymorphisms in positional candidate genes. Several new phenotypes related to the role of adipose tissue as an endocrine organ will be examined, and the pleiotropic effects of QTLs detected in the

current and proposed grant periods, on other CVD risk factors will be characterized. The longitudinal data being accumulated for the families in the SAFHS will be exploited to examine genetic effects on age-related changes in CVD risk.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: GENETIC AND PHYSIOLOGICAL REGULATION IN BROWN ADIPOCYTES**

  Principal Investigator & Institution: Graves, Reed A.; Associate Professor; Medicine; University of Chicago 5801 S Ellis Ave Chicago, Il 60637

  Timing: Fiscal Year 2001; Project Start 01-AUG-1996; Project End 31-JUL-2004

  Summary: The long-term objective is to understand the physiologic and developmental regulation of brown adipose tissue (BAT). The thermogenic activity of brown adipose tissue (BAT) is regulated in response to a number of physiologic signals including cold-exposure, arousal from hibernation and overfeeding. The unique thermogenic properties of BAT derive from the uncoupling of mitochondrial respiration and oxidative phosphorylation through the action of the BAT-specific uncoupling protein (UCPI). Because heat production is equivalent to energy expenditure, BAT can play a dual role in the organism of ensuring homeothermy and energy balance. Ablation of BAT in transgenic mice causes obesity in the absence of hyperphagia confirming the important role of BAT in energy balance. Obesity is a major risk factor for the development of diabetes, hypertension and coronary artery disease. A deeper understanding of the mechanisms controlling BAT growth and development may lead to the development of novel therapeutic approaches to the problem of obesity. UCP1 controls the thermogenic activity of BAT and is the defining gene product of the brown adipocyte. Thus, the regulatory factors controlling UCP1 expression are likely to be fundamental determinants of brown adipocyte differentiation and physiologic regulation. The HIB-1B cell line derived from a brown fat cell tumor differentiates into brown adipocytes that appropriately express the UCP1 gene. The UCP1 enhancer located at -2.5 to -2.3 kb is capable of directing high level gene expression to BAT of transgenic mice and expression is regulated by physiological stimuli such as cold exposure and fasting/refeeding. Specific aim 1 will utilize the HIB-1B cells to systematically identify the cis-acting elements within this enhancer. Specific aim 2 will examine the regulation of a novel BAT coactivator PGC1. Specific aim 3 examines the role of cAMP and retinoic acid response elements in mediating the response to cold exposure and fasting/feeding.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: GENETICS OF THE METABOLIC SYNDROME IN JAPANESE AMERICANS**

  Principal Investigator & Institution: Austin, Melissa A.; Professor; Epidemiology; University of Washington Seattle, Wa 98195

  Timing: Fiscal Year 2001; Project Start 01-JAN-1994; Project End 31-MAY-2003

  Summary: (Adapted from Investigator's Abstract) The long-term goal of this project is to understand genetic susceptibility to cardiovascular disease (CVD) and non-insulin dependent diabetes mellitus (NIDDM) in Japanese-American kindreds by characterizing the genetic basis of the risk factors of the metabolic syndrome (insulin resistance syndrome). During the first four years of the project, three specific aims are being addressed, as follow: 1) to determine if variation in the diameter of the major low-density lipoprotein subclass (LDL size) is inherited as a single gene trait in Japanese-

American families, and to determine if LDL size is associated with risk factors of the syndrome; 2) to characterize the inheritance of lipoprotein (a) and apolipoprotein (a) isoforms in Japanese Americans; and 3) to establish a repository of white blood cells and plasma aliquots for genetic studies. These aims will be accomplished by the end of the initial 4-year project period, based on data from 400 study participants, including pedigree information, extensive laboratory results, medical history questionnaire data and nutritional data. The project proposed here will enhance these studies by recruiting and sampling approximately 350 additional relatives of local, married-in Japanese-American spouses, with 3 new specific aims: 1) to identify genetic influences on the risk factors that characterize the syndrome (including **fasting** insulin, proinsulin, C-peptide and glucose; body weight and waist circumference; lipoproteins; blood pressure; fibrinogen, factor VII and plasminogen activator inhibitor-1) using statistical genetic analysis approaches, including univariate complex segregation analysis, factor analysis, and quantitative multivariate genetic analysis; 2) to test for genetic linkage between specific candidate genes involved in lipid metabolism, carbohydrate metabolism, blood pressure, obesity, and hemostasis with genetically influenced risk factors of the metabolic syndrome in Japanese-Americans, using established linkage analysis approaches in sibships and in kindreds; and 3) when the DNA repository has been completed (750 samples by the end of year 4), to apply to the NHLBI Mammalian Genotyping Service to perform a whole genome screen to identify new genes involved in susceptibility to the metabolic syndrome. The investigators state that the studies proposed in this renewal application represent effective ways to characterize genetic susceptibility to the metabolic syndrome and subsequent risk of cardiovascular disease and non-insulin-dependent diabetes among Japanese-American families, and may lead to targeted intervention strategies to prevent these diseases.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: GLP-1 IN NORMAL AND ABNORMAL GLUCOSE TOLERANCE**

  Principal Investigator & Institution: D'alessio, David A.; Associate Professor of Medicine; Internal Medicine; University of Cincinnati 2624 Clifton Ave Cincinnati, Oh 45221

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-JAN-2004

  Summary: The overall goal of this proposal is to determine the role of the insulinotropic GI hormone glucagon-like peptide 1 (GLP-1) in persons with normal glucose tolerance, and with type 2 diabetes. In normal subjects the action of GLP-1 and other gut factors accounts for 30-60 percent of the insulin secreted after eating. This effect is severely impaired in persons with type 2 diabetes suggesting defects in the secretion or action of gut peptides. In addition to its action on the -cell, we have recently observed a novel effect of GLP-1 to suppress endogenous glucose production (EGP) independent of its effects on islet hormone secretion. When given to persons with type 2 diabetes in pharmacologic amounts, GLP-1 normalizes both **fasting** and post-prandial hyperglycemia, and so has potential as a therapeutic agent. Therefore, it is important to understand the mechanisms by which GLP-1 lowers blood glucose levels in persons with diabetes, and whether defects in the secretion or action of the hormone contribute to the pathogenesis of diabetes. The specific aims of this project are to determine: 1) the mechanism by which GLP-1 normalizes **fasting** hyperglycemia in diabetic subjects. 2) whether GLP-1 suppresses EGP by inhibition of glycogenolysis, gluconeogenesis, or both. 3) whether the deficient incretin effect in persons with type 2 diabetes is due to decreased levels of GLP-1, or impaired sensitivity of insulin secretion to GLP-1. To address these aims: 1) Glucose turnover will be measured in diabetic subjects before and

during GLP-1 infusions, to determine the contributions of islet hormones, and islet hormone-independent effects of GLP-1 to lower blood glucose. 2) EGP will be measured in healthy subjects, and rates of gluconeogenesis and glycogenolysis determined before and after GLP-1 using the 2H2O method. 3) Secretion, and metabolism of GLP-1 in diabetic and control subjects will be compared using a new assay we have developed with greatly increased specificity for GLP-1. In addition, GLP-1 will be infused over a wide range of doses to measure the sensitivity of the insulin response in diabetic and control subjects. The results of these studies will expand the understanding of glucose homeostasis, and promote the development of new strategies to treat type 2 diabetes.

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- **Project Title: HAPO: DATA COORDINATING CENTER**

  Principal Investigator & Institution: Dyer, Alan R.; Professor and Associate Chair; Preventive Medicine; Northwestern University Office of Sponsored Programs Chicago, Il 60611

  Timing: Fiscal Year 2001; Project Start 04-MAY-1999; Project End 31-MAR-2004

  Summary: There is a consensus that overt diabetes mellitus (DM), whether or not accompanied by symptoms or signs of metabolic decompensation, is associated with a significant risk of adverse pregnancy outcome. On the other hand, the risk of adverse outcome associated with degrees of glucose intolerance less severe than overt DM is controversial. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study is a basic epidemiologic investigation aiming to clarify unanswered questions on the association of various levels of glucose intolerance during the third trimester of pregnancy and risk of adverse outcomes. Its General Aim -- by means of an international cooperative study involving 16 centers and approximately 25,000 pregnant women -- is to achieve a major advance in knowledge on levels of glucose during pregnancy that place the mother, fetus, and neonate at increased risk. The primary hypothesis is that hyperglycemia during pregnancy, less severe than overt DM, is associated with increased risk of adverse maternal, fetal, and neonatal outcome that is independently related to the degree of metabolic disturbance. Specific Aims of HAPO are: 1. to examine glucose tolerance in a large, heterogeneous, multinational, multicultural, ethnically diverse cohort of women in the third trimester of gestation with medical caregivers "blinded" to status of glucose tolerance (except in those instances where **fasting** and/or two hour OGTT plasma glucose concentration exceeds a predefined cutoff value); and 2. to derive internationally acceptable criteria for the diagnosis and classification of gestational diabetes mellitus (GDM) based on the specific relationships between maternal glycemia and the risk of specific adverse outcomes that are established through this study. The study is to be accomplished with high quality standardized data collection on the women during the third trimester of gestation (including the OGTT) and at time of delivery for assessment of adverse outcomes, including operative delivery (caesarean section), increased fetal size (macrosomia/obesity), neonatal morbidity (hypoglycemia), and fetal hyperinsulinism. HAPO is to include a Clinical Coordinating Center and Data Coordinating Center, both located at the Northwestern University Medical School in Chicago, as well as a Central Laboratory located in Belfast, United Kingdom. This application requests support for the Data Coordinating Center for HAPO. Cost effectiveness for HAPO is enhanced through cost sharing by colleagues in non-U.S. centers.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HIGH GLYCEMIC DIET AND RISK OF NIDDM AND CHD**

  Principal Investigator & Institution: Liu, Simin; Assistant Professor of Medicine; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

  Timing: Fiscal Year 2001; Project Start 15-AUG-2000; Project End 31-JUL-2003

  Summary: (adapted from the application) This is a resubmission of DK02767 "High glycemic diet and risk of type 2 DM and CRD, " a K08 program for advanced training and research leading to a career as an independent clinical scientist in diabetes and cardiovascular epidemiology with particular emphasis on nutrition and prevention of chronic disease. The candidate will develop, refine, and validate the Nurses' Health Study (NHS) database for both the glycemic and insulin indices to assess each NHS participant's long term dietary glycemic load and insulin demand and evaluate their potential effects on the incidence of type 2 diabetes mellitus (DM) and coronary heart disease (CHD). In this resubmission, we have substantially revised the proposal, taking into account each of the major concerns raised by the reviewers. We continue to focus on a comprehensive evaluation of the effects of carbohydrates on disease risk using prospectively collected dietary data and blood samples in the NHS. We have added two new components including a) validating the two dietary variables-glycemic index and insulinemic index-using a series of biomarkers including glycosylated hemoglobin Alc (HbAlc), C-peptide, triglyceride (TG), and insulin; and b) expanding the scope of the nested case-control studies to further understand the relations of dietary carbohydrate, glycemic index and load, and insulin index and load with risk of type 2 LIM and CHD. Further, we provide new preliminary data relating dietary glycemic index and carbohydrate intake assessed by our food frequency questionnaire to **fasting** TG in a sample of nurses without DM and CHD who provided **fasting** blood samples. In addition, we provide a critical review of the available literature regarding the clinical usefulness of glycemic index. We believe that the detailed exposure information and multiple dietary assessments in this large prospective cohort of 121, 700 women offer a unique opportunity to study the controversial topic of the health effects of carbohydrate quality. Through the process, Dr. Liu will acquire ample skills and experience to become an independent clinician scientist and educator in the field of nutrition and chronic disease prevention and control.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HOMOCYSTEINE AND COAGULATION IN SICKLE CELL DISEASE**

  Principal Investigator & Institution: Balasa, Vinod; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 45229

  Timing: Fiscal Year 2003; Project Start 11-JUL-2003; Project End 31-MAR-2008

  Summary: The coagulation system and endothelial cells are believed to contribute to the vascular pathology of sickle cell disease (SCD). Elevated plasma homocysteine (Hcy) is associated with vascular disease and thrombosis in the general population and is believed to induce endothelial cell dysfunction and activate the coagulation system. Patients with SCD exhibit activation of coagulation and an increase in activated circulating endothelial cells (CEC). Preliminary data demonstrate that hyperhomocysteinemia (HHcy) is present in 38% of patients with SCD and that a majority (62%) of these individuals have pyridoxine deficiency, compared to race and age-matched controls. It is hypothesized that HHcy is associated with activation of coagulation and CEC in SCD and that a lowering of Hcy with pyridoxine supplementation will reduce this activation. Therefore, the aims of this study are to determine the following in patients with SCD: (1) prevalence of HHcy and its

association with vitamin cofactor deficiencies (2) correlation of HHcy with activation of CEC and coagulation (3) responsiveness of HHcy to pyridoxine supplementation (4) correlation of a decrease in Hcy levels with reduction in the activation of CEC and coagulation. The following laboratory determinations will be made in patients with SCD and in race and age-matched controls: **fasting** and post-methionine load Hcy, levels of red cell folate, serum vitamin B12, pyridoxal 5'-phosphate, the C677T MTHFR genotype; markers of activation of coagulation (prothrombin fragment 1.2, thrombin:antithrombin complexes), and fibrinolysis (plasmin:antiplasmin complexes, D-dimer); enumeration of CECs and the presence of activation markers VCAM-1 and tissue factor on CECs. SCD patients with HHcy will be randomized to receive a 6-week trial of pyridoxine supplementation or placebo and levels of Hcy, pyridoxine, and determination of markers of activation of coagulation and CECs will be repeated. This study is a collaborative trial open to all the sickle cell centers and at least 248 SCD patients and 248 controls will be recruited. Hey levels will be regressed on age in the controls and 95% confidence intervals will be determined. The chi-square statistic will be used to test the difference. Linear regression will be used to determine the relationship between Hcy and the activation markers. Paired t-tests will be used to test the other hypotheses. Pyridoxine supplementation is a simple therapy with the potential to reduce thrombotic complications of sickle cell disease.

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- **Project Title: HOSTILITY, RACE, AND GLUCOSE METABOLISM**

  Principal Investigator & Institution: Surwit, Richard S.; Professor; Psychiatry; Duke University Durham, Nc 27706

  Timing: Fiscal Year 2003; Project Start 01-SEP-2003; Project End 31-AUG-2007

  Summary: (provided by applicant): Recent research in our laboratory has provided evidence that the metabolic correlates of hostility may play a role in the racial disparity in the prevalence of type 2 diabetes. We propose to study how hostility is differentially related to glucose metabolism in healthy African-Americans and Caucasians, to determine the underlying behavioral and physiologic mechanisms of these relationships, and to investigate the possibility that race and sex interact in determining this relationship. We will assess the multi-factorial nature of hostility in 400 healthy African-American and Caucasian men and women. These psychometric measures will be examined in relation to **fasting** and two-hour post-prandial glucose and insulin as well as hemoglobin AIC (HbAIC) on all subjects. We will test the hypothesis that hostility is related to insulin resistance in Caucasians and to glucose production and defective glucose-stimulated insulin secretion in African-Americans, putting hostile African-Americans at greater risk for developing diabetes. Accordingly, we will assess glucose-stimulated insulin release, insulin resistance, hepatic glucose production and glucose effectiveness utilizing an IV GTT with labeled glucose in a subset of our sample. We will begin to determine the mechanism by which hostility impacts glucose metabolism in an African-American and Caucasian population. Three sets of mediators will be examined in the subjects studied parameters of hypothalamic-pituitary-adrenal (HPA) axis activity, measures of body mass and fat distribution, and measures of behavioral factors including calorie intake and exercise habits. It is further hypothesized that while the relationship of hostility to **fasting** insulin and insulin sensitivity in Caucasians is mediated by BMI and behavioral variables, the relationship of hostility to **fasting** glucose in African-Americans will depend on neuroendocrine factors influencing hepatic glucose production and insulin secretion. These studies will further

our understanding of the differences in the etiology of diabetes in these ethnic groups and may help explain the racial disparity in this disease.

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- **Project Title: HUMAN BRAIN METABOLISM IN KETOSIS**

  Principal Investigator & Institution: Pan, Jullie W.; Associate Director of Neurology and Neur; Neurology; Yeshiva University 500 W 185Th St New York, Ny 10033

  Timing: Fiscal Year 2002; Project Start 01-FEB-2002; Project End 31-JAN-2005

  Summary: (provided by applicant): It is well known that the brain can switch from its primary fuel of glucose to ketone bodies under states of **fasting,** vigorous exercise, specific diets as well as a number of clinical disorders. However, specifically how the human brain uses ketones is not well defined. This question is of major interest particularly since the ketogenic diet (KD) is known to be of significant therapeutic value in the treatment of intractable epilepsies. In order to understand how the metabolic state of ketosis is affecting brain function inepileptic patients, an understanding of how ketosis affects the non-epileptic brain is critical. Human brain ketone metabolism is thought to be limited by plasma levels and blood brain barrier transport reflecting the belief that brain ketone oxidation is rapid, thus preventing accumulation of ketones. However, recent human brain data have shown that significant accumulation of b-hydroxybutyrate (BHB) can occur. Since the brain pool of ketones is not negligible, especially during ketotic states such as **fasting,** this implies that oxidation of ketones is limited relative to its net influx. In this proposal we will investigate the brain accumulation of ketones to define its transport in healthy fasted and non-fasted adults, to determine whether induction of transport occurs with **fasting.** We will investigate how much ketones fractionally contribute towards oxidative flow, and determine how much this contribution changes with chronic (fasting induced) ketosis. These data will define the baseline effects of ketosis. In the last part of this application we will apply this work in adult and pediatric epilepsy patients being treated with the ketogenic diet. We will determine whether accumulation of cerebral ketonesin these two patient groups is comparable to healthy controls. In doing so, we will establish a means by which the cerebral metabolic evaluation of the patients on the ketogenic diet can be made. We anticipate that these data will contribute towards better understanding of themechanism of seizure control by theketogenic diet.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HYPERHOMOCYSTEINEMIA IN ALZHEIMER'S DISEASE**

  Principal Investigator & Institution: Diaz-Arrastia, Ramon R.; Associate Professor; Neurology; University of Texas Sw Med Ctr/Dallas Dallas, Tx 753909105

  Timing: Fiscal Year 2001; Project Start 15-AUG-2001; Project End 31-JUL-2004

  Summary: In the past years, two independent case control studies have established a correlation between elevated homocysteine levels and Alzheimer's Disease (AD). Since vitamin supplementation with folic acid, vitamin B12, and pyridoxine can lower homocysteine levels, this association raises the exciting possibility that polyvitamin therapy may decrease the incidence of AD. The goal of this proposal is to obtain pilot data necessary to design a large multicenter trial to determine whether vitamin therapy lowers the risk of AD. We plan to do this through the following specific aims: (a) Determine whether **fasting** or post-methionine load (PML) are best associated with AD. The published studies analyzed homocysteine levels in **fasting** or randomly drawn serum samples. Since many patients have elevations in homocysteine levels only after a

methionine load, and both **fasting** and PML hyperhomocysteinemia may be associated with dementia, we will determine whether **fasting** hyperhomocysteinemia, PML hyperhomocysteinemia, or both, are linked to a higher risk of AD. We will also determine whether plasma levels of S-adenosylhomocysteine (SAH) and S-adenosylmethionine (SAM) are nire sensitive markers of functional hyperhomocysteinemia (b) Determine the relative importance of nutritional and genetic factors as determinants of hyperhomocysteinemia. Elevated homocysteine levels result from a complex interplay of genetic and acquired factors, and the link between hyperhomocysteinemia and AD has so far been reported only in Europeans. In an attempt to determine which of these factors is most important in an ethnically and culturally heterogeneous US population, we will administer a nutritional questionnaire and measure vitamin levels in our patients, as well as determine the allelic frequency of the C677T polymorphism of MTHFR, a major genetic determinant of hyperhomocysteinemia. (c) Determine whether vitamin therapy is effective in lowering homocysteine levels in patients with hyperhomocysteinemia. All subjects will be treated sequentially for 12 weeks first with low dose vitamin supplementation, followed by high-dose vitamin supplementation. The effectiveness, compliance rates, and potential side effects of these therapies will be monitored. Each of these specific aims is essential to rationally design a large multicenter trial to determine whether polyvitamin therapy lowers AD risk.

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- **Project Title: IMMUNOTHERAPY TRIAL IN NEW ONSET TYPE 1 DIABETES**

  Principal Investigator & Institution: Gottlieb, Peter A.; Assistant Professor; Pediatrics; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, Co 800450508

  Timing: Fiscal Year 2001; Project Start 30-SEP-2000; Project End 31-AUG-2003

  Summary: (adapted from the application) We propose a two arm randomized, partially blinded, placebo-controlled clinical trial to test the hypothesis that mycophenolate mofetil (MMF) alone or with daclizurnab (DZB) will prolong the period of C-peptide production in subjects with new onset type I diabetes. A second aim of this study will provide the clinical material for the validation of surrogate markers for immunity to islet Beta cells. The study will be conducted jointly by the Barbara Davis Center for Childhood Diabetes in Denver and the Virginia Mason Research Center in Seattle and takes advantage of the annual accrual of over 80 new onset type-l diabetes at these institutions. The metabolic end-points of this study will be **fasting** and stimulated C-peptide, hemoglobin Alc, and total insulin dose. Levels of autoantibodies and T cell reactivity to islet autoantigens, both of which are surrogate immunological parameters specific for type I diabetes, will be followed. Measures of immune modulation will include serologic and T cell reactivity to recall antigens. The subject number allows for 80 percent power to detect differences significant at a 5 percent level. The study is innovative in that the agents to be tested have not previously been evaluated in type I diabetes, but are rational choices for interventions in an autoimmune disorder. The proposed surrogate markers use peptide tetramers to identify and enumerate antigen-responsive T cells. We believe the study is timely in that far less toxic immunosuppressive agents have been developed in the 10 year interval since Cyclosporine was found to preserve C-peptide production in new-onset patients. Our power projections are based on our extensive previous intervention studies and the choice of agents to be tested is supported by animal studies. MMF is an effective component of anti-rejection treatment of heart, kidney and liver recipients. It is effective

for the treatment of psoriasis. The DZB anti-IL2 receptor antibody selected for use with MMF is effective in the treatment of acute renal rejection episodes. The safety of these agents in clinical use justifies a trial in type I diabetes, where 30 percent of new onset subjects run HbAlc levels that put them at high risk for vascular disease within 20 years.

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- **Project Title: IMPAIRED GLUCOSE METABOLISM IN HIV-INFECTED DRUG USERS**

  Principal Investigator & Institution: Howard, Andrea A.; Montefiore Medical Center (Bronx, Ny) Bronx, Ny 104672490

  Timing: Fiscal Year 2003; Project Start 01-FEB-2003; Project End 31-JAN-2008

  Summary: (provided by applicant): HIV-infected drug users may be at heightened risk for impaired glucose tolerance and type 2 diabetes mellitus in association with protease inhibitor (PI) therapy and co-infection with hepatitis C virus (HCV). To address these issues, the candidate proposes a five-year prospective study of 300 individuals with or at risk for HIV infection in order to examine the associations of HIV, PI therapy, and HCV infection with impaired glucose tolerance and type 2 diabetes. By nesting this study in two ongoing longitudinal studies of drug users in the Bronx, NY, the candidate will benefit from an extensive database and an established research infrastructure as well as the guidance of a group of experienced independent investigators. The specific aims of the project are: 1. To determine the prevalence of and factors associated with impaired glucose tolerance and type 2 diabetes in HIV-infected drug users, including PI therapy, HCV infection, sociodemographics, body mass index, and family history of diabetes. 2. To determine prospectively the impact of HIV infection, PI therapy, and HCV infection on the incidence of impaired glucose tolerance and type 2 diabetes. At semi-annual research visits, participants will undergo standardized interviews to assess sociodemographics, medical history, and drug use behavior, measurement of height, weight, and waist/hip ratio, and blood tests for CD4+ count, HIV viral load, HCV antibody, and HCV RNA level. In addition, **fasting** lipid profiles and body composition analysis using dual x-ray absorptiometry will be obtained. Oral glucose tolerance tests will be performed annually to screen for impaired glucose tolerance and diabetes. Active surveillance for clinical disease events will also be performed. The candidate's long term career goal is to become an independent investigator of HIV epidemiology in drug users. To achieve this goal, she will work closely with a multidisciplinary group of mentors with expertise in research related to HIV, diabetes, hepatitis C, and substance abuse. She will also complete coursework in the conduct of diabetes-related clinical research, addiction medicine, and the responsible conduct of research.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: INCREASED GLUCONEOGENESIS IS ONE CAUSE OF CFRD**

  Principal Investigator & Institution: Hardin, Dana S.; Associate Professor; Pediatrics; University of Texas Sw Med Ctr/Dallas Dallas, Tx 753909105

  Timing: Fiscal Year 2002; Project Start 01-SEP-2002; Project End 31-AUG-2007

  Summary: The incidence of impaired glucose tolerance and diabetes (called CFRD) is high in cystic fibrosis (CF), and is expected to increase due to increased life-span of the patients. CFRD is an important cause of worsened morbidity and mortality, thus understanding the pathophysiology underlying its development is imperative. Insulin deficiency has been recognized as one cause of CFRD; however it is clear the etiology is more complex. The applicant's long-range goal is to understand the pathophysiologic

changes which cause CFRD. Studies proposed in this application will allow us to characterize alterations in normal metabolism of glucose and protein which contribute to CFRD. Our global hypothesis is that increased rates of gluconeogenesis (GNG) result in hyperglycemia. This excess is not caused simply by portal hypoinsulinemia alone, but rather is driven by excessive amino acid substrate availability secondary to cytokine-mediated protein catabolism. We will recruit 48 adult CF subjects (12 per glucose tolerance category: normal, impaired, CFRD with **fasting** hyperglycemia and CFRD without **fasting** hyperglycemia) and 20 normal volunteers matched for age and gender. Subjects will recruited from the CF centers at The University and the South Central CF Consortium (all CF centers in Texas, Oklahoma and Arkansas). Subjects will be categorized according to clinical status (pulmonary function and modified NIH score), and we will measure cytokines TNF-a, IL- 6, IL-10 and TNF receptor antibodies. We will also measure thyroid function, estrogen and testosterone and IGF-1 levels. GNG and glycogenolysis will be quantified by measuring the incorporation 2H into the 2nd, 5th and 6th carbons of glucose, and reported as percentage of total hepatic glucose production (measured using [6,6-2H2]glucose). Whole body protein turnover (WBPT) will be measured using [15N]urea and [1-13C]leucine, and we will conduct a sub-study to evaluate the effect of intravenous protein hyperalimentation on GNG and WBPT. Insulin secretion will be quantified using a hyperglycemic clamp (target glucose levels 160 mg/dl and 350 mg/dl). Insulin effect on GNG and WBPT, as well as peripheral insulin sensitivity will be determined using a step-wise hyperinsulinemic euglycemic clamp (insulin doses of 10,20 and 120 mU/m2/min). We will measure resting energy expenditure using indirect calorimetry and intake of carbohydrate, protein and fat will be quantified with a three day food journal. Important support for this proposal includes the excellent scientific community at UT-Southwestern, the consultant role of Dr. Satish Kalhan, a noted expert in substrate metabolism, ready access to a GC mass spectrometer, institutional support, and an established track record of performing complex metabolic studies in CF subjects. It is therefore expected that these studies will provide new information regarding potential causes of CF related diabetes and protein catabolism.

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- **Project Title: INSTABILITY OF TUMOR PROMOTION IN HEPATOCARCINOGENESIS**

  Principal Investigator & Institution: Pitot, Henry C.; Professor (Emeritus); Oncology; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2001; Project Start 01-JUN-1997; Project End 31-MAR-2002

  Summary: The long-term objective of the studies outlined in this proposal is to better our understanding of the cell and molecular mechanisms involved in the stages of initiation and promotion in multistage hepatocarcinogenesis in the rat. A series of five experiments will be performed to test the thesis that single glutathione-S transferase, placental form (PGST)-positive (+) hepatocytes comprise a significant part of the initiated cell population. During the stage of promotion altered hepatic foci (AHF) comprise only about 1% of the number of single PGST+ hepatocytes. Reasons for this difference will be sought in determining ploidy characteristics of the single PGST+ hepatocytes as well as the phenotypic distributions of AHF induced by different promoting agents. The operational reversibility of AHF growth during the stage of promotion will be investigated by combining the removal of the -promoting agent after 4 months of administration, together with two sequential periods of short-term **fasting** in order to obtain the most effective loss of AHF within a relatively short time period.

Parameters involved in the acute loss of hepatocytes within AHF by this procedure will be studied by determining the most effective format of the **fasting** period(s), the effect of the time of tumor promotion prior to the **fasting** period, the effect of continued administration of the promoting agent during the **fasting** period, and the effects of omission and addition of the same or other promoting agents or inhibitors of the stage of promotion during the refeeding period on the AHF number and growth. Since apoptosis is reportedly a principal mechanism in the loss of cells from AHF upon removal of the promoting stimulus, as well as in liver on acute **fasting,** we will investigate both in vivo and in hepatocyte culture in normal hepatocytes and those of AHF levels of the growth factors, TGF-(, HGF, and TGF-(1, as well as TNF-(, and their receptors during and following the period of **fasting** and promoting agent removal. The effect of **fasting** on the expression of members of the Bcl-2 and Bax gene families will also be investigated. From these studies we hope to better establish the cell biology of the stage of initiation and develop a better understanding of mechanisms involved in the reversibility of the stage of tumor promotion as induced by a combination of removal of the promoting agent and acute dietary restriction in the form of **fasting.**

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- **Project Title: INSULIN RESISTANCE /DIET OF HISPANIC WOMEN W/ BREAST CAN**

  Principal Investigator & Institution: Duarte-Gardea, Maria O.; University of Texas El Paso El Paso, Tx 79968

  Timing: Fiscal Year 2003; Project Start 01-JUN-2003; Project End 31-MAY-2007

  Summary: (provided by applicant): Background: Breast cancer is the most common cancer among women. A relationship has been hypothesized between insulin resistance and breast cancer. To our knowledge, no study has investigated the relationship among insulin resistance, energy and fat intake, and breast cancer in Hispanic women. The purpose of this project is to test the hypothesis that **fasting** insulin and other markers of insulin resistance, along with energy intake and dietary fat, will be significantly higher among Hispanic women diagnosed with breast cancer compared to those with no indication of cancer. Specific aims: Our aims are to compare the following characteristics among women with and without breast cancer: Aim 1) markers of insulin resistance and Aim 2) total energy and total fat intake. Aims 3) demographic, anthropometric, and reproductive, and Aim 4) lifestyle and dietary factors and their association with diagnosis of breast cancer. Design/Methods: A prospective case-control study of Hispanic women attending the University Breast Care Center at Texas Tech University Health Sciences Center at El Paso for routine breast examination will be conducted. Markers of insulin resistance including obesity, waist/hip ratio, blood pressure, acanthosis nigricans, **fasting** insulin, **fasting** glucose, and lipid profile will be performed in four hundred eligible participants. Subjects will complete a three-day food record to determine total energy and fat intake. Case and control groups will be formulated once the data are collected and after mammogram and pathology reports have been filed. The case group includes 100 subjects with breast cancer. Three controls (matched by age +/- 5 years) and menopausal status) for each case will be located from the pool of total participants. We will perform correlation and factor analyses to identify variables and/or factors which would best represent each of the four classes of independent variables as outlined in the specific aims section. We will then use logistic regression analysis to examine the relationship between the categorical response (diagnosed with and without breast cancer) with the set of independent variables identified above. The proposed work will advance the understanding of the associations of insulin resistance,

diet and breast cancer in Hispanic women. Individual risk factors (anthropometric, health, reproductive, lifestyle and dietary) may be identified. There is a need for research that focuses on a comprehensive approach to insulin resistance, dietary lifestyle choices, and breast cancer and that emphasizes a fat-caloric intake-insulin resistance linkage. Such information is critical for the design of health education interventions that seek the adoption of healthy lifestyle in low income Hispanic population through community-based culturally relevant and tailored prevention programs, and public policy recommendations.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: INSULIN RESISTANCE IN TISSUE SPECIFIC IKKB TRANSGENICS**

  Principal Investigator & Institution: Lee, Jongsoon; Joslin Diabetes Center Boston, Ma 02215

  Timing: Fiscal Year 2003; Project Start 01-JAN-2003; Project End 31-DEC-2004

  Summary: (provided by applicant): Our studies in insulin resistant cells and animals, and type 2 diabetic patients showed that the IkappaB kinase, IKKbeta, plays a central role in acquired insulin resistance. In 3T3-L1 adipocytes and Fao hepatoma cells, activation of IKKbeta by treatment of TNF or by transfection of upstream kinase, NIK, or constitutively active IKK, induced cellular insulin resistance-decreased insulin-stimulated Tyr phosphorylation of IR and IRSs. Inhibition of IKKbeta by specific inhibitors- high doses of salicylates (NaS) or aspirin (ASA)- or by transfection of dominant negative IKKbeta reversed TNF-induced insulin resistance. Treatment of high doses of NaS or ASA to type 2 diabetes patients or obese and insulin resistant animals reversed insulin resistance as judged by glucose tolerance test (GTT), insulin tolerance test (ITT) and hyperinsulinemic, euglycemic clamp studies. Hyperglycemia, hyperinsulinemia, and dyslipidemia are normalized by ASA treatment. Insulin signaling studies conducted with tissues isolated from the rodents show that insulin-stimulated Tyr phosphorylation of IR and IRS are increased due to decrease in inhibitory Ser/Thr phosphorylation of IRSs. Heterozygous deletion (IkkBeta +/-) in mice reduced **fasting** glucose and insulin concentrations, and protected against the development of insulin resistance during high-fat feeding and in obese Lep-ob/ob mice. We also found that obese animals have higher IKK kinase activity than control animals. To study which tissue(s) are important for IKK-mediated insulin resistance and for the reversal of insulin resistance by salicylates, we generated mice expressing constitutively active IKKbeta in fat, muscle and liver with the hypothesis that increasing IKKbeta activity in animal tissues may itself induce insulin resistance. We now have colonies of all three tissue transgenic mice and found that fat- and liver-specific transgenic mice have developed insulin resistance as early as 4 week-old. We will characterize these mice to determine which tissue is responsible for IKKbeta-induced insulin resistance and how activation of IKKbeta in one tissue can induce whole body insulin resistance. These experiments will validate IKKbeta as a major mediator of insulin resistance and as a useful target for the discovery of new drugs to treat type 2 diabetes and insulin resistance.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: INTRA-ABDOMINAL FAT AND RISK OF DISEASE IN ADOLESCENTS**

  Principal Investigator & Institution: Goran, Michael I.; Associate Director and Professor; Preventive Medicine; University of Southern California 2250 Alcazar Street, Csc-219 Los Angeles, Ca 90033

Timing: Fiscal Year 2001; Project Start 01-AUG-1999; Project End 31-MAY-2002

Summary: There are distinct gaps in our understanding of the link between obesity and/or fat distribution and increased disease risk in adolescent children. We propose a 5-year longitudinal study to examine the temporal relationships between changes in body fat, body fat pattern, insulin sensitivity, lipd profile, physical activity, and sex hormones during adolescent growth. We will use state-of-the-art techniques for measuring total body fat (4-compartment model), body fat pattern (dual energy X-ray absorptiometry, computed tomography), physical activity (combination of doubly labeled water and indirect calorimetry), and whole-body insulin sensitivity (Bergman Minimal model). We will examine blood pressure and circulation lipid and lipoprotein levels as risk factors for cardiovascular disease, and **fasting** indulin and insulin sensitivity as risk factors for non-insulin dependent diabetes mellitus. We propose to study Caucasian and African American adolescents because these groups are at increased risk of obesity and related diseases and have not been thoroughly examined. Preliminary data and recent publications from other investigators support the concept that accumulation of body fat in the intra- abdominal region begins to occur before and during adolescence. Moreover, these data provide evidence that the relationship between obesity and disease risk in adolescents may be explained by accumulation of intra-abdominal adipose tissue (IAAT). Thus, we propose to examine the following hypotheses: 1) The relationship between obesity and disease risk in Caucasian and African American adolescents is due specifically to the accumulation of IAAT; 2) Physical inactivity, total body fat, and sex hormone levels contribute to the development of IAAT during adolescence, which leads to the development of insulin resistance which in turn leads to the development of dyslipidemia. The strength of these cause and effect relationships will not be significantly influenced by ethnicity, or gender; and ,3) IAAT can be accurately predicted from anthropometry, and more accurate equations can be developed by inclusion of total abdominal fat by dual energy X-ray absorptiometry. Our unifying hypothesis is that the development of IAAT during adolescence is the specific cause of increased risk of disease resulting from obesity. This longitudinal study will add to our understanding of the etiology of obesity and the emergence of different body fat patterns during adolescent development. The study will yield substantial information of the mechanism(s) relating obesity to increased disease risk in Caucasian and African American adolescents, and this information will be useful for the design of prevention and intervention programs aimed at reducing long term risk of disease.

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- **Project Title: ISOTHIOCYANATE EXCRETION, BRASSICA, AND BREAST CANCER**

  Principal Investigator & Institution: Fowke, Jay; Epidemiology and Biostatistics; University of South Carolina at Columbia Byrnes Bldg., Room 501 Columbia, Sc 29208

  Timing: Fiscal Year 2001; Project Start 15-FEB-2001; Project End 31-JUL-2001

  Summary: Dietary factors play an important role in the etiology of breast cancer. Vegetables of the Brassica genus, such as broccoli and cabbage, contain isothiocyanates (ITC) which increase glutathione-S-transferase (GST) activity, leading to the excretion of potentially carcinogenic compounds. Brassica vegetable administration prevented mammary tumor development in animal models of breast cancer, and it is therefore conceivable that Brassica consumption could reduce breast cancer risk in humans. Preliminary results from our pilot study suggest that high levels of urinary ITC excretion, indicative of greater Brassica vegetable intake, were associated with a greater than 50% reduction in breast cancer risk. We propose to analyze urine samples collected

from a larger subset (n=350 case-control pairs) of study participants recruited into the Shanghai Breast Cancer Study, a NCI-funded population-based case- control study among Chinese women in Shanghai (RF01 CA64271). In addition to in-person interviews, **fasting** blood and urine samples have been collected from over 80% of the 3000 women included in this parent study. These samples are being used for several ancillary studies, including NCI-funded studies to evaluate the relation of estrogens, IGFs, pesticides, genetic factors, and phytoestrogens, with breast cancer risk (R03CA80655, R03CA83050, R03CA86119, NCI contract). For this newly proposed individual matched case-control study, urinary ITC levels will be analyzed by HPLC, and GST genotype determined from blood DNA. Because recruitment, questionnaire data, and specimen collection have been completed by existing studies, this project will be very cost-efficient. Urinary ITC excretion predicts habitual Brassica intake within Asian populations, as people in China or Japan typically consume 200 g/day/person of Brassica. Since Brassica vegetables are widely available and without toxicity, a protective association between urinary ITC levels and breast cancer could suggest that dietary recommendations to reduce breast cancer risk should include greater Brassica consumption.

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- **Project Title: LEPTIN SIGNALING IN PRIMATE DEVELOPMENT**

  Principal Investigator & Institution: Wilson, Mark E.; Research Professor and Chief; Medicine; Emory University 1784 North Decatur Road Atlanta, Ga 30322

  Timing: Fiscal Year 2001; Project Start 01-AUG-2000; Project End 31-JUL-2002

  Summary: (Adapted from applicant's description): Acquisition of a critical body mass is thought to be important for the initiation of puberty. Although a number of studies in a variety of species have linked body size to puberty, the signal responsible for increasing pulsatile gonadotropin hormone releasing hormone (GnRH) secretion and initiating puberty is unknown. However, the recent identification of the protein leptin has lead to the hypothesis that a developmental increase in leptin, derived from accumulating fat mass, acts centrally to increase GnRI-1 secretion and a parallel increase in the pituitary release of the gonadotropins, resulting in gonadal activation. While the hypothesis that leptin initiates puberty has yet to be adequately tested in primates which, unlike rodents, show a protracted period of post-natal development prior to puberty. Before prospective studies can be initiated in primates, additional preliminary data derived from a female monkey model are needed to A) define precisely the temporal relationship between prepubertal increases in diurnal leptin concentrations and the emergence of nocturnal gonadotropin release and B) develop a protocol to assess how the sustained administration of leptin affects GnRH secretion in well nourished females. Specific Aim 1 will test the hypothesis that the developmental rise in nocturnal leptin secretion precedes the emergence nocturnal gonadotropin secretion in females. Specific Aim 2 will test the hypothesis that the timing of daytime food intake influences the pattern but not amplitude of the diurnal leptin secretion. Specific Aim 3 will determine the dose of sustained administration leptin that reverses the fasting-induced suppression of gonadotropin secretion and will test the hypothesis that leptin binding protein facilitates leptin's access to the brain and effects on neuroendocrine systems. Specific Aim 4 will obtain information on the efficacy of leptin administration to immature females on metabolic and reproductive parameters.

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- **Project Title: LIPID METABOLISM IN OBESITY, WEIGHT LOSS AND EXERCISE**

  Principal Investigator & Institution: Houmard, Joseph A.; Professor and Director; Human Performance Laboratory; East Carolina University 1000 E 5Th St Greenville, Nc 27858

  Timing: Fiscal Year 2001; Project Start 15-AUG-2000; Project End 31-JUL-2005

  Summary: (Adapted from the applicant's abstract):The long-term objective of this research is to better understand defects in human skeletal muscle that contribute to the morbidity and mortality evident with obesity. There is evidence that lipid metabolism in the skeletal muscle of obese individuals is altered in a manner favoring lipid storage. For example, some data indicate that obese skeletal muscle has a reduced capacity to oxidize lipid. There is also evidence that muscle-associated triglyceride concentration increases with obesity. These are important observations as the accumulation of lipid in skeletal muscle is associated with insulin resistance. The storage of lipid in skeletal muscle may thus predispose obese individuals toward insulin resistance and the many conditions linked with insulin resistance (hypertension, coronary artery disease, diabetes mellitus). Despite these important implications, the cellular mechanism that promotes lipid accretion in obese skeletal muscle is not evident. In the current application experiments are proposed that will determine the mechanism(s) responsible for promoting lipid storage in skeletal muscle with obesity and if intervention compensates or corrects the initial defect(s). The primary hypothesis is that postabsorptive (fasting) lipid metabolism in skeletal muscle is altered with obesity in a manner that promotes lipid accumulation in this tissue. This hypothesis is based upon preliminary work, where it was observed that lipid oxidation is depressed in the muscle of obese individuals in conjunction with reductions in oxidative enzyme activities. These preliminary data form the basis for the working hypothesis that lipid oxidation is depressed in skeletal muscle with obesity which promotes lipid storage. The secondary hypothesis is that weight loss does not enhance lipid oxidation, but reduces muscle triglyceride stores by an alternative mechanism. The tertiary hypothesis is that exercise training reverses the initial decrement in lipid oxidation evident with obesity, promoting lipid utilization. To test these hypotheses it will be determined: Specific Aim I - if postabsorptive lipid metabolism is impaired in skeletal muscle from obese individuals in a manner that promotes the accumulation of lipid; Specific Aim II - if the impairment in postabsorptive lipid metabolism in the skeletal muscle of obese individuals is corrected or compensated for with weight loss and; Specific Aim III - if exercise training enhances postabsorptive lipid metabolism in obese individuals and the cellular mechanisms responsible. Findings will be important as little is known concerning the mechanisms responsible for the defects in lipid metabolism with obesity and the impact of intervention.

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- **Project Title: LONGEVITY AND METABOLISM MEDIATED BY FASTING**

  Principal Investigator & Institution: Waddle, James A.; Assistant Professor of Molecular Biology; Molecular Biology; University of Texas Sw Med Ctr/Dallas Dallas, Tx 753909105

  Timing: Fiscal Year 2001; Project Start 01-SEP-2001; Project End 31-AUG-2006

  Summary: (provided by applicant): The broad, long-term objective of this proposal is to understand which tissues and genes respond to caloric restriction, and to explain how such changes affect the overall physiology, health and longevity of animals, including humans. The hypotheses to be tested are: (1) An H1 linker histone, HIS-41, is a direct target of DAF-16 and is one key transcriptional output of scenarios that increase

longevity. (2) HIS-41 is necessary, but not sufficient, for the metabolic shift and increased longevity conferred by reduced insulin-like signaling or caloric restriction. (3) Distinct longevity mutants induce different HIS-41 accumulation patterns appropriate for the affected target tissue. (4) Caloric restriction extends life span by activating two synergistic processes: HIS-41 dependent silencing that reduces metabolic rate and reactive oxygen species levels; and increased production of factors that are co-regulated with HIS-41, such as superoxide dismutase. The specific aims are: (1) Identify the sequence elements required for DAF-l6- dependent induction of his-41 in vivo (hypothesis 1). (2) Assay fat accumulation and life span in calorie restricted his-41 mutants or his-41- gerontogene double mutants; and determine whether forced HIS-41 expression is sufficient to phenocopy longevity mutants (hypothesis 2). (3) Identify genes that regulate HIS-41 levels and genes that are coordinately regulated with his-41 (hypotheses 1,2). (4) Determine the cell type specificity of HIS-41 accumulation in calorie restricted vs. single and double mutant combinations of distinct longevity pathways (hypothesis 3). (5) Measure the life span of transgenic animals that constitutively express HIS-41, SOD-3, and genes that are co-regulated with HIS-41 (hypothesis 4). A central view of this proposal is that widespread genomic silencing, mediated by an H1 linker histone, is a common feature of many genetic pathways that extend life span and increase stress resistance. Environmental factors, including caloric restriction, increase longevity by turning on the H1- mediated repression of genes for rapid growth and glucose-based metabolism, thereby reducing the overall rate of metabolism and the production of reactive oxygen species. The activation of the H1 repression system is done by the same transcription factor (DAF-l6/forkhead protein) known to up regulate enzymes for fat storage and utilization, as well as enhanced life maintenance (e.g. superoxide dismutase).

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- **Project Title: MATERNAL LIVER DISEASE AND FATTY ACID OXIDATION DEFECTS**

  Principal Investigator & Institution: Ibdah, Jamal A.; Internal Medicine; Wake Forest University Health Sciences Winston-Salem, Nc 27157

  Timing: Fiscal Year 2001; Project Start 21-SEP-2001; Project End 31-AUG-2006

  Summary: Mitochondrial trifunctional protein (TFP) catalyzes the last 3 steps in the beta-oxidation spiral of long chain fatty acids and consists of 4 alpha and 4 beta subunits. Long chain 3- hydroxyacyl Co-A dehydrogenase (LCHAD) resides in the alpha- subunit. Mutations in the alpha-subunit such as the prevalent G1528C mutation cause "isolated" LCHAD deficiency. Other mutations cause complete TFP deficiency (all the 3 enzymes are deficient). Recently, we have documented a fetal-maternal interaction that causes maternal liver disease in heterozygote women who carry fetuses with isolated LCHAD deficiency. This raises several questions. First, what is the mechanism of this fetal-maternal interaction? Second, what is the effect of environmental factors such as high fat diet and **fasting** on the development of maternal liver disease in the susceptible heterozygotes? Our hypothesis is that heterozygote women develop acute fatty liver of pregnancy (AFLP) or HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome due to accumulation of hepato-toxic fatty acid metabolites generated by either the affected fetus or the susceptible heterozygote under conditions of oxidative stress. To test this hypothesis we propose the following studies. 1) To use conventional and inducible Cre/lox P strategies to generate and characterize two knockout mice models for complete TFP deficiency (null mutation) and isolated LCHAD deficiency (G1528C mutation). Clinical, biochemical, histological, and molecular

analyses will be performed. Tissue-specific and developmental stage-specific gene expression will also be characterized in these mice. Differences in the accumulated fatty acid metabolites will be correlated to the genotypes and phenotypes to elucidate the role of fatty acid metabolites in the genotype-phenotype correlations in these disorders. 2) To employ preimplantation genotyping and embryo transfer to independently study the effects of fetal and maternal genotypes on development of maternal liver disease in knockout mice. Pregnant dams will be monitored for evidence of liver disease. Fatty acid metabolites will be measured in fetal and maternal sera, fetal and maternal livers, and placentas, and will be correlated to the fetal/maternal genotypes and maternal phenotypes to identify the fatty acid metabolites that are potentially toxic to the maternal liver. 3) To conduct dietary studies in knockout mice to elucidate the effects of high fat diet and **fasting** on pregnant heterozygotes while carrying unaffected fetuses. Four different high fat diets will be studied to elucidate the effects of fat content, fatty acid configuration, and protein/carbohydrate contents.

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- **Project Title: MENOPAUSE, LPL GENOTYPE AND METABOLISM AFTER WEIGHT LOSS**

  Principal Investigator & Institution: Goldberg, Andrew P.; Professor; Medicine; University of Maryland Balt Prof School Baltimore, Md 21201

  Timing: Fiscal Year 2001; Project Start 01-SEP-2000; Project End 31-JUL-2005

  Summary: This research is designed to determine whether obese postmenopausal women with a common polymorphism in the lipoprotein lipase (LPL) PvuII gene, i.e. the (+) allele have less favorable metabolic responses to weight loss (WL) treatment than women without the LPL PvuII cut-site (-/-). The hypothesis is that the LPL PvuII genotype affects **fasting** muscle and adipose tissue and LPL activity and the metabolic responses to hypocaloric feeding-induced WL in a dose-dependent manner to affect the magnitude of the reduction of total and visceral fat, and improvements in glucose/insulin and lipoprotein lipid metabolism following WL in postmenopausal women. Specific aims determine whether obese women who are homozygous for the LPL PvuII (+) cut-site, i.e. the (+/+) genotype, have greater increases in adipose tissue LPL and decreases in muscle LPL activity and larger decreases in resting metabolic rate (RMR) and fat oxidation than heterozygotes during hypocaloric diets, that are associated with: 1) the loss of less total body and visceral fat; and 2) smaller improvements in lipid and glucose metabolism than women without the cut-site, i.e., (-/-). We will study healthy, obese (Body Mass Index, 30-40 kg/m2) 50-60 year old women within 5 years of menopause. The statistical power to test our hypothesis is based on preliminary data showing differences in adipose tissue LPL responses to WL between LPL PvuII (+/+) and (-/-) genotypes, and requires 27 women/genotype. Subjects will be entered prospectively based on their LPL genotype to ensure a homogeneous group of obese menopausal women are studied to eliminate confounding factors of gender, age, duration from menopause and body composition on the metabolic responses to WL treatment. Metabolic studies are performed on prepared calculated weight maintaining eucaloric diets for 2-3 weeks at baseline and after 6-mo WL to ensure metabolic stability, and on hypocaloric diets after the short-term study to assess metabolic responses to negative energy balance. We will measure muscle and adipose tissue LPL activity, RMR, fat oxidation, total and visceral body fat (DXA and CT scans) lipoprotein lipids and. glucose/insulin responses during an oral glucose tolerance test. Following the post-WL metabolic evaluations, subjects enter a 6- mo follow-up period followed by metabolic testing to assess long- term metabolic

adaptations and weight regain by genotype. Collectively, these findings will enhance our understanding of obesity by assessing the gene-metabolic mechanisms underlying the predisposition of some obese women to more favorable metabolic health benefits from WL. This would allow the targeting of WL treatments to women more likely to respond, and pharmacologic and other treatments to those less likely to respond to WL. This optimistic outcome would reduce prevalence of obesity and risk for CVD in older women.

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- **Project Title: METABOLIC CONTROL OF FEEDING BEHAVIOR**

  Principal Investigator & Institution: Friedman, Mark I.; Associate Director; Monell Chemical Senses Center 3500 Market St Philadelphia, Pa 19104

  Timing: Fiscal Year 2003; Project Start 01-AUG-1993; Project End 31-MAR-2006

  Summary: (provided by applicant): Postabsorptive fuel metabolism is an important factor in the control of food intake. Sensors in brain and liver that are sensitive to various metabolic parameters have been implicated in this control. In liver, considerable evidence indicates that changes in energy metabolism produce a stimulus or stimuli that are transduced into a neural signal that carries this metabolic information to the central nervous system for use in controlling food intake. In particular, changes in hepatic ATP content, or some closely related change in liver energy status, generate signals that initiate or terminate feeding behavior under various conditions, such as fasting-refeeding, type I diabetes, and treatment with metabolic inhibitors. Recent studies in this laboratory have revealed that three different animal models of obesity (genetic, dietary and neurological) show reduced hepatic energy status, suggesting that changes in liver energy status are also involved in overeating and the development of obesity. The overall goal of this project is to assess whether and how altered hepatic energy metabolism is a contributing cause of hyperphagia (overeating) that leads to obesity. Some rats overeat and become obese when fed a diet high in fat content (obesity-prone), whereas others of the same strain do not (obesity-resistant). The proposed research will use this diet-induced animal model of obesity because it appears most comparable to the obesity commonly seen in humans. We hypothesize that, during the development of obesity, hyperphagia may be driven at least in part by decreased liver energy status, which is secondary to the redirection of fuels into storage and away from oxidative pathways. Overeating could result from a faster decline in hepatic energy status between meals or a slower recovery in hepatic energy status during and after a meal. The project has three specific aims: (1) Determine whether overeating in obesity prone rats is due to an enhanced susceptibility to reductions in liver energy status. (2) Determine whether overeating in obesity prone rats is due to a slow restoration of liver energy status. (3) Determine whether calcium signaling during metabolic stimulus transduction differs in hepatocytes from lean and obese rats.

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- **Project Title: MOBILITY AMONG OLDER AFRICAN AMERICANS AND WHITES**

  Principal Investigator & Institution: Allman, Richard M.; Professor; Medicine; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2003; Project Start 30-SEP-1998; Project End 31-JUL-2008

  Summary: (provided by applicant) The hypotheses underlying the proposed research are that potentially modifiable factors predict mobility (life-space) trajectories associated with aging among community-dwelling African Americans (AAs) and whites.

Moreover, there are racial differences in these trajectories and in risk factors for life-space changes. The research team proposes to continue a prospective, observational study of a population-based sample of 1000 community-dwelling older adults (251 African American (AA) males, 249 AA females, 250 white males and 250 white females; 54 percent rural) for a total of 7 years of follow-up. New specific aims include: (1) Assess the predictors of life-space trajectories; (2) Identify predictors of transitions to restricted life-space, homebound status, and nursing home placement; (3) Examine proximate causes of life-space transitions; 4) Evaluate changes in hypothesized risk factors as predictors of life-space trajectories; (5) Determine the relationship of nutritional status with subsequent life-space trajectories; (6) Evaluate specific markers of inflammation as potential predictors of life-space. Repeat in-home assessments (N=780) 48-months after the baseline (1999-2001) in-home assessment will permit documentation of changes in disease and geriatric syndrome status, europsychological factors, nutritional status, health behaviors, and medication use since baseline. **Fasting** blood specimens (N=662) will be obtained within one month of the 48-month in-home assessment to assess nutrition-related lab tests, measures of inflammation, and other lab tests reflecting disease severity or management. Three 24-hour recall dietary intakes also will be obtained within 3 weeks of the in-home assessment. Telephone follow-up interviews every 6 months will be used to ascertain subsequent life-space. Multivariable, hierarchical mixed model growth curve analyses and generalized estimating equation (GEE) approaches will be used for analyses to permit identification of predictors of life-space trajectories and of specific life-space transitions. The results of this research will lead to interventions that will foster independence of older AAs and whites.

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- **Project Title: MOLECULAR CONTROL OF MITOCHONDRIAL FATTY ACID OXIDATION**

  Principal Investigator & Institution: Kelly, Daniel P.; Professor; Internal Medicine; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2001; Project Start 30-SEP-1992; Project End 31-JAN-2005

  Summary: Mitochondrial fatty acid oxidation (FAQ) serves as a chief energy transduction pathway in tissues with high oxidative energy demands such as heart and liver. The capacity for cellular FAQ is altered in a variety of inherited and acquired human diseases including cardiomyopathy, diabetes mellitus, and obesity. Recent studies have identified a role for the lipid-activated nuclear receptor, the peroxisome proliferator-activated receptor a (PPARa) and its coactivator, PPARy coactivator-1 (PGC-1), in the transcriptional control of genes encoding mitochondrial FAQ enzymes. This renewal proposal is designed to test the hypothesis that the PPARa/PGC-1 transcriptional regulatory complex serves a critical role in the control of FAQ enzyme gene expression under physiologic conditions known to alter energy demands and substrate availability. Experiments proposed in Specific Aim 1 are designed to further characterize the role of the PPARa/PGC-1 complex in the control of FAQ and other mitochondrial energy metabolic pathways. The goal of Specific Aim 2 is to extend our studies aimed at the characterization of the role of the PPARcL regulatory complex in the transcriptional control of FAQ enzyme gene expression in response to physiologic conditions known to precipitate clinical manifestations in humans with inborn errors in FAO enzymes. First, the proximal regulatory pathways involved in the activation of PPARa and PGC-1 in response to short-term **fasting** will be characterized. Second, exercise studies will be performed with wild-type and PPARcL-null mice to evaluate the potential role of PPARcL in mediating the known augmentation of skeletal muscle

mitochondrial FAQ enzyme expression in response to training. Specific Aims 3 and 4 are designed to develop mice with altered PGC-1 function in heart using transgenic and cre-lox-mediated gene disruption approaches. The PGC-1-nulLmice will be evaluated in the physiologic contexts described in Specific Aim 2 in order to rigorously define the role played by this coactivator as a transducer of physiologic stimuli to the control of mitochondrial FAQ. The long-term objective of this project is to develop novel experimental and, ultimately, therapeutic strategies to modulate mitochondrial FAQ capacity in vivo in the context of human diseases such as obesity, heart failure, and diabetes mellitus.

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- **Project Title: NEUROENDOCRINE CONTROL OF ANTERIOR PITUITARY HORMONES**

  Principal Investigator & Institution: Kineman, Rhonda D.; Assistant Professor; Medicine; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

  Timing: Fiscal Year 2003; Project Start 02-JUL-1981; Project End 31-JAN-2007

  Summary: (provided by applicant): Growth hormone (GH) promotes protein synthesis and lipolysis. In turn, metabolic disturbances are associated with alteration in GH production which contribute to the pathophysiology of clinically relevant disorders such as malnutrition, anorexia nervosa, obesity and diabetes. Despite the strong association between metabolism and GH, little is known regarding the basic mechanisms by which perturbations in metabolic pathways bring about changes in GH synthesis and release. Therefore, this application will determine the mechanisms by which alterations in nutrient availability; 1) regulate hypothalamic expression of neuropeptides essential for normal pituitary GH production (GH-releasing hormone [GHRH] and somatostatin [SRIF]), and 2) modify pituitary sensitivity to the GH-stimulatory peptides, GHRH and ghrelin. It has been proposed that changes in circulating leptin (an adipocyte factor) and ghrelin (a GH-releasing peptide produced in the stomach) mediates hypothalamic expression of GHRH and SRIF through activation of neuropeptide Y (NPY) neurons. To test this hypothesis, the effects of **fasting** on neuropeptide mRNA levels, in mice harboring defects in leptin synthesis (ob/ob), tissue source of leptin (AZIP-F1), NPY synthesis (NPY-/-), SRIF synthesis (smst-/-) and SRIF signaling (ss1l/2-/-) will be examined by ribonuclease protection assay and in situ hybridization. Also the effects of **fasting** in normal mice following exogenous hormone replacement (to increase NPY, leptin or ghrelin), pharmacological treatment (to block endogenous NPY production) or passive immunoneutralization (to block the actions of ghrelin) will be tested. **Fasting** not only alters expression of GH-regulatory neuropeptides but also enhances pituitary sensitivity to GHRH and ghrelin by increasing GHRH-R and GHS-R mRNA levels. In vitro, FFAs alone or in conjunction with glucocorticoids increase GHS-R synthesis. Therefore it is hypothesized that **fasting** induced elevations in FFA and glucocorticoids are required to enhance pituitary receptor synthesis and sensitivity, and thus compensate for fasting-induced alteration in central signals. To test this hypothesis, studies will examine the ability of **fasting** to alter pituitary receptor expression (by quantitative RT-PCR) and dynamic GH release (by RIA of serial blood samples) following blockade of FFA formation (by the anti-lipolytic Acipimox) or glucocorticoid actions (by the glucocorticoid receptor antagonist, RU-486). Also primary rat and non-human primate (baboon) pituitary call cultures will be used to determine if FFA and glucocorticoids mediate their effects on receptor synthesis via transcriptional or post-transcriptional processes and if the effects of FFA can be mimicked by activation of the putative FFA nuclear receptors, peroxisome proliferator-activated receptors (PPAR).

This is the second revision of a competitive renewal of an RO1 application which continues to study the regulation of the GH axis. The current application centers on the interrelationship between changes in metabolic function and the GH axis.

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- **Project Title: NEUROENDOCRINOLOGY OF PUBERTY**

  Principal Investigator & Institution: Foster, Douglas L.; Professor & Research Scientist; Obstetrics and Gynecology; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2001; Project Start 01-MAR-1984; Project End 31-JAN-2005

  Summary: When nourishment is inadequate or energy expenditure is great, fertility is reduced in the adult, and puberty is delayed in the developing individual. This suppression of reproductive activity is not understood mechanistically. We believe this to be an integrative problem at this stage of inquiry that requires both physiologic and pharmacologic approaches to answer broad questions about how the brain discriminates how well nourished and how mature the body is. Our broad objective is to understand the physiological mechanisms by which changes in nutrition and metabolism control reproduction, specifically the signals, sensors, and pathways whereby blood-borne information regulates GnRH secretion. To progress further in understanding the relationship between growth, metabolism and production of high frequency GnRH pulses during development, we must first determine how energy metabolism regulates GnRH secretion. To progress further in understanding the relationship between growth , metabolism and production of high frequency GnRH pulses during development, we must first determine how energy metabolism regulates GnRH secretion in the adult. Thus, we will first evaluate how changes in glucose availability and leptin modify GnRH secretion during adulthood and then determine if such a mechanism might be timing puberty during growth. The sheep will be used because its large size and long lifespan permits individuals to be studied longitudinally through their development and permits detailed studies in adults. Importantly, it is well suited for the characterization of hypophysiotrophic hormone patterns. Specific Aim 1 will determine if the hindbrain and the liver contain sensors that transmit information about glucose availability to regulated GnRH secretion. We will both increase and decrease availability locally in each site to establish their function and their interrelationships. Specific Aim 2 will determine the role of leptin as a signal to regulate the pulsatile secretion of GnRH. This will be achieved through central administration of leptin during both acute **fasting** and chronic low nutrition. Although widely studied in feeding behavior, we have little understanding of its physiologic role in regulating GnRH secretion. Specific Aim 3 will assess "nutritional stress" as a cause hypogonadotropism through reduced GnRH secretion by monitoring of stress peptides in the pituitary portal circulation and by antagonizing their action during acute **fasting** and chronic low nutrition. Specific Aim 4 will determine if glucose availability times the pubertal GnRH increase by using the power of our large animal model in which we can chronically administer metabolically important signals such as insulin and leptin. Understanding the metabolic control of GnRH secretion has broad application both to growth and maturation and to other physiologic conditions in which reduced GnRH secretion may contribute to infertility because of altered energy metabolism. These include dietary malnutrition from eating disorders; during high-energy expenditure, as in exercise- induced amenorrhea and lactational anovulation; during type 1-diabetes-induced infertility.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NEUROPEPTIDE Y--EFFECTS ON ENERGY METABOLISM**

  Principal Investigator & Institution: Billington, Charles J.; Professor of Medicine; Medicine; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

  Timing: Fiscal Year 2001; Project Start 10-AUG-1991; Project End 31-MAR-2002

  Summary: The brain's critical role in regulating energy and fat balance has never been more apparent. Several recent developments (see (l)) have focused attention on brain regulatory systems: leptin, the product of the ob gene, appears to signal fat status to the brain; the tubby gene appears to code for a protein expressed in hypothalamus; and a new satiety- inducing neuroregulator GLP-1 and feeding stimulator, melanocyte-concentrating hormone have been found to work in hypothalamus. It is evident that abnormalities in brain regulatory mechanisms may be responsible for alterations in energy balance (obesity, anorexia, etc.) in animals and in humans. Neuropeptide Y (NPY) is the most potent known neuroregulator of appetite and can be used, as described herein, to functionally map one brain system regulating energy balance (appetite and energy metabolism), which in this proposal we will call the Neuropeptide Y-Coded Energy Management Network (NEMN). The goal of these investigations is to define the central organization of one brain system regulating energy balance (appetite and energy metabolism), which in this proposal we will call the Neuropeptide Y-Coded Energy Management Network (NEMN). Abnormalities and disturbances in NEMN regulatory mechanisms could be responsible for alterations in energy balance (obesity, anorexia, etc.) in animals and in humans. Neuropeptide Y (NPY) is the most potent known orexigenic agent. We will utilize NPY administration into the hypothalamic paraventricular nucleus as the primary tool to functionally map the circuitry of the NEMN. We hypothesize a distributed energy management network in the brain, which can be traced using the stimulus of NPY. OBJECTIVES: (1) Define the neuronal sites activated by NPY in hypothalamic paraventricular nucleus, opioids in nucleus of the solitary tract, and by food deprivation through examining site specific expression of the immediate early gene, c-fos; (2) Verify the functional efferent link between NPY activity in the PVN and opioidergic activity in the NTS: (3) Functionally define the next circuit projections for the NPY-Coded Energy Management Network, (4) Define the site of action and regulatory significance of serotonin blockade of NPY effects on energy metabolism.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NIACIN, N-3 FATTY ACIDS AND INSULIN RESISTANCE**

  Principal Investigator & Institution: Harris, William S.; Professor; St. Luke's Hospital 4401 Wornall Rd Kansas City, Mo 64111

  Timing: Fiscal Year 2003; Project Start 20-FEB-2003; Project End 31-JAN-2008

  Summary: (provided by applicant): The insulin resistance syndrome (IRS) afflicts approximately 47 million Americans. Its principal components include central obesity, elevated triglycerides, decreased high density lipoprotein cholesterol (HDL-C) levels, **fasting** hyperglycemia, and/or hypertension. Individuals with the IRS are at significantly increased risk for developing type 2 diabetes mellitus and/or coronary heart disease (CHD). While diet and exercise can improve some manifestations of the IRS, pharmacotherapy is often needed to normalize other components. In recent studies from our laboratory, niacin and fish oil (n-3 fatty acids, FA) used in combination in individuals with the IRS improved the lipid phenotype, but also, unexpectedly, the mealinduced suppression of free fatty acid (FFA) flux (an important indicator of adipose

tissue insulin sensitivity). This project will explore the clinical efficacy of combined (and mono-) therapy with n-3 FA and niacin on CHD risk factors, on triglyceride and FFA kinetics and on glucose disposal rates in subjects with the IRS. We will conduct a single, randomized, parallel-arm, placebo-controlled trial. Subjects with the IRS (per the NCEP ATP-itl guidelines) will be randomly allocated to one of four intervention groups after a one-month dual placebo run-in period. The groups will be: n-3 FA (3.4 g/d), crystalline niacin (3 g/d), the combination, or duat placebo. The latter two groups will include 20 subjects each while the two-monotherapy arms will have 10 subjects each. Effects on endpoints will be determined at baseline and after four months of treatment. The CHD risk factors include serum lipids and lipoproteins; lipoprotein(a); subfractions of HDL and of low density tipoproteins; tissue plasminogen activator and plasminogen activator inhibitor-1; and blood pressure. Triglyceride kinetics will be determined by bolus injection of 2H/5-glycerol, and FFA kinetics by isotope dilution using a constant infusion of 3H-palmitate in the **fasting** state, after a standard mixed meal and during the hyperinsulinemic-euglycemic clamp procedure used to evaluate glucose disposal rates. At the completion of these studies, we expect to have detailed information on the potential therapeutic efficacy and the kinetic mechanisms of action of these two nutritional agents. This should lead to more effective therapy for the dyslipidemia of insulin resistance and ultimately to reduced risk for CHD in this burgeoning patient population.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NUTRITIONAL & METABOLIC REGULATION OF BODY WEIGHT**

  Principal Investigator & Institution: Galbraith, Richard A.; Professor; Medicine; University of Vermont & St Agric College 340 Waterman Building Burlington, Vt 05405

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2004

  Summary: The health of the people and the economy of the United States of America remain under siege from obesity. Nutrient intake is an important variable in the control of body weight and its dysregulation can lead to obesity. Numerous afferent stimuli, including hormones both old and new, have been implicated in the nutritional and metabolic regulation of body weight, but the neurochemical basis for their integration remains elusive. A newly recognized neurotransmitter, nitric oxide, has been implicated in the neurochemical regulation of various central nervous system processes, including the ingestion of food and water. There is evidence, derived from the observation that inhibitors of nitric oxide synthase oppose the hyperphagia caused by many disparate stimuli, to suggest that the locus of action of nitric oxide may be distal to the level of many of the transmitter-receptor systems in the hypothalamus which play a role in the regulation of food intake. This grant is focused on the further evaluation of the contribution of this neurotransmitter to the control of body weight and to test the overall hypothesis that nitric oxide is a common downstream effector linking and intergrating multiple diverse stimuli with increased food intake. Specific aims are to directly inject, into the brain of rats, substances known to increase or decrease the concentration of nitric oxide and to correlate changes in food ingestion and body weight with histochemical and biochemical alterations in the levels of protein and gene expression, catalytic activity and product of the enzymes responsible for the synthesis of nitric oxide. Because nitric oxide contributes to the regulation of many central nervous system processes, specificity will be increased by focusing on the areas which are activated to express the Fos protein in response to stimuli which regulate food intake. The secondary hypothesis is that alterations in this nitric oxide-dependent pathway may account for the prolonged and marked anorectic effect of cobalt protoporphyrin, a synthetic

analogue of heme, which leads to profound and sustained weight loss. Experiments to test this secondary hypothesis will be carried out in addition to experiments to examine the molecular mechanism of these actions of cobalt protoporphyrin. This approach is expected to further our understanding of the physiology of appetite and body weight regulation in the central nervous system and eventually may assist in the development of strategies to combat the epidemic of obesity in western societies.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NUTRITIONAL CONTROL OF REPRODUCTIVE AND STRESS AXES**

  Principal Investigator & Institution: Thompson, Robert C.; Co-Director, Mhri Psychiatry; Psychiatry; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2003

  Summary: Our overall goal is determine how endocrine and sensory information associated with altered states of nutrition is relayed to the reproductive system. This proposal is based upon our observation that the metabolic hormone, leptin, administered alone during food restriction maintains pulsatile LH secretion. Conditions which limit food or metabolic fuels can profoundly effect the reproductive axis. In this proposal, we test the hypothesis that these compromised metabolic conditions are "sensed" by the brain as a "stress" and it is this "stress" that leads to an inhibition in LH pulses. According to this hypothesis, leptin acts by inhibiting this "stress" reaction via brain sites thereby maintaining pulsatile LH secretion. In Specific aim one, we will determine if **fasting** activates the stress axis concurrently with the inhibition of pulsatile LH secretion and if leptin administration during the **fasting** period blocks the stress activation as well as LH pulse inhibition. Additionally in this aim, we determine if CRH neurons in the paraventricular nucleus (PVN) as well as in other non-PVN CRH sites are regulated by **fasting** and if leptin reverses this regulation. In Specific aim two, we will determine if acute reductions in brain leptin (immunoneutralization) activate the stress axis while inhibiting pulsatile LH secretion. It also determines if these neuroendocrine changes are mediated by the stress peptide, corticotropin releasing hormone, CRH. Further in this aim, we will identify those neurons activated by reduced brain leptin (cfos activation) in an attempt to identify those cells responding to the reduced availability of this metabolic hormone. The last study in this aim, identifies the neuropeptide phenotype of cfos activated cells due to reductions in brain leptin. Using this anatomical data together with the data on CRH, we expect to identify neuropeptide systems responding to reduced brain leptin and potential mediators of the neuroendocrine changes. In Specific aim three, we will use anatomical tract tracing methods and receptor mRNA colocalization studies to determine if CRH (or other suggested leptin sensitive neuropeptides) project directly or indirectly to GnRH neurons. This project is relevant to human health because it addresses the underlying mechanisms and anatomical pathways that are regulated by the fat hormone leptin, a hormone critical to the proper functioning of many neuroendocrine systems. This work should help explain the basis for disruption of neuroendocrine functions in several metabolic disorders as well as provide insight into understanding the endocrine complexities observed in several animal models of obesity.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PACEI-DP: AN INTERVENTION FOR YOUTH AT RISK FOR DIABETES**

  Principal Investigator & Institution: Patrick, Kevin M.; Adjunct Professor; Family and Preventive Medicine; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, Ca 92093

  Timing: Fiscal Year 2003; Project Start 01-SEP-2003; Project End 31-JUL-2007

  Summary: (provided by applicant): Improved physical activity (PA) and dietary behaviors and reductions in overweight or obesity show great promise to reduce the risk of type 2 diabetes in adults. However, very few interventions have been reported that address this issue, and none that are useful for primary care providers or that address reducing diabetes risk in adolescents. We propose a randomized controlled trial to evaluate whether an integrated primary care and web-based intervention, PACEi-DP, can produce initial and sustained improvements in anthropometric, behavioral, metabolic, and physiological outcomes in adolescents who meet the ADA criteria for "high risk" for type 2 diabetes. PACEi-DP is a 1- year intervention involving: a) pre-primary care visit web assessment and progress planning; b) clinician counseling; c) 12 months of web-based, phone and/or group-based follow-up. Pilot studies based upon selected elements of PACEi-DP demonstrate its promise in improving dietary & PA behaviors and in stabilizing BMI in overweight adolescents. We will recruit 93 adolescents, age 12 to 16 years, who meet the ADA criteria for high risk of Type 2 diabetes. Subjects will be recruited from 5 healthcare settings and the community and randomly assigned to one of three conditions: 1) usual medical care; 2) a web-based version of PACEi-DP where the follow-up component involves asynchronous web-based contact with subjects and their parent/guardian; or 3) a multi-modal PACEi-DP where the follow-up component adds phone and group contact. PACEi-DP will target 4 behaviors: 1) total energy expenditure from moderate and vigorous PA; 2) sedentary behavior and recreational media use; 3) Fruit/Vegetable/Fiber consumption (5 or more servings/day of fruits/vegetables and 3 or more servings/day of whole grains or legumes); and 4) total fat as percent of energy consumed. The intervention guides patients to select PA & diet target behaviors for which they develop action plans to discuss with the clinician. The clinician endorses or modifies the action plan and encourages participation in the ongoing intervention. Web-tutorials, continuous web access, e-mail interaction, and (in Group 3) phone counseling and group meetings guide patients and parent/guardian to use cognitive & behavioral skills to change behaviors. PACEi-DP enables participants to receive tailored, stage-appropriate intervention on their diet & PA goals. The primary outcome will be the effect of PACEi-DP on BMI at 12 months. Secondary outcomes (at 6 and 12 mo.) will be: a) metabolic and physiological measures of insulin resistance (fasting insulin, **fasting** blood glucose, blood lipids, microalbuminuria, acanthosis nigricans, and blood pressure; b) anthropometric measures (percent body fat by DEXA (at 12 months), waist/hip ratios; c) behavioral measures (moderate & vigorous PA; total energy expenditure; CSA; measures of sedentary behavior & recreational media use; servings of fruits, vegetables & fiber; and total fat as a percent of energy consumed. Exploratory measures will include psychosocial mediators of change; measures of parent/guardians' BMI and waist/hip ratios, and process, satisfaction & cost-effectiveness measures of each study arm. The PACEi-DP intervention is particularly innovative because its three components - pre-visit web assessment and behavior change planning, primary care provider counseling, and the ongoing web or web/phone/group intervention -are unified through a common behavioral theoretical framework.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PERIODONTAL INFECTION AND PREDIABETIC CONDITIONS**

  Principal Investigator & Institution: Offenbacher, Steven; Professor of Periodontology; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, Nc 27599

  Timing: Fiscal Year 2001; Project Start 01-AUG-1999; Project End 31-JUL-2002

  Summary: Antecedent systemic inflammation has recently been demonstrated to be associated with an increased risk of incident type 2 diabetes. This is manifest as elevations in fibrinogen increased while blood cell count, decreased serum albumin and elevations in certain coagulation factors including factor VIII. Our new findings demonstrate that among non- diabetics, periodontal disease is associated with impaired **fasting** glucose (IFG) but not impaired glucose tolerance (IGT), suggesting that periodontitis may contribute to the metabolic abnormalities seen in this one subset of pre-diabetic subjects. To further examine this relationship we propose to conduct a randomized, no-treatment controlled, study in 96 subjects with IFG and 96 with IGT to determine where periodontal therapy reduces clinical biomarkers of poor metabolic control **fasting** glucose, **fasting** insulin and C-peptide), acute phase reactants in serum (C-reactive protein and IL-6) and oxidative stress (serum 8-iso PGF/2alpha). These changes will be determined treating half of the subjects in each group with scaling and root planing and measuring each of these biomarkers at 6 weeks, 3, 6,9 and 12 months. The remaining half of the patients will serve as delayed treatment controls and will be treated at exit. We expect to see a lowering of **fasting** blood glucose levels in response to periodontal treatment indicating that periodontal infection contributes to the metabolic dysfunction seen in pre-diabetes. If proved this may represent a new primary intervention strategy to prevent new cases of type 2 diabetes.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PLACENTAL VASCULAR COMPROMISE AND PRETERM DELIVERY**

  Principal Investigator & Institution: Thorp, John M.; Professor; Obstetrics and Gynecology; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, Nc 27599

  Timing: Fiscal Year 2001; Project Start 01-SEP-2001; Project End 31-AUG-2006

  Summary: (provided by applicant): There is substantial interest in determining the etiology of preterm delivery (PTD). Despite much effort, the cause remains elusive and effective prevention measures do not exist. Uteroplacental vascular compromise (UPVC) via inflammation, thrombosis, or atherosis is a biologically plausible cause of preterm delivery, albeit not adequately explored. We propose to test his hypothesis by conducting a prospective, epidemiologic study of UPVC and by integrating information about known risk factors for PTD. Placental histopathologic examination and morphometric analysis of the basal plate will be done to assess compromise of placental vessels. We will explore novel, possible antecedents of such compromise, dyslipidemia and insulin resistance, using nuclear magnetic resonance analysis of lipid subclasses and **fasting** insulin-glucose ratios. Given the inaccessibility of the uteroplacental vasculature in ongoing gestations at midpregnancy, we will utilize non-invasive measures of UPVC, Doppler velocimetry of the uterine artery, and maternal serum alpha fetoprotein to indirectly evaluate vascular function. In addition, we will carefully evaluate tobacco and cocaine use, nutrition, and changes in vaginal microflora within our cohort. The data will enable us to thoroughly assess whether UPVC constitutes a distinct etiologic pathway for PTD and help to identify modifiable risk factors. We will utilize cohort and

case-cohort techniques, refined in our present research, to answer these questions. Blood, urine and vaginal fluid are collected twice between 15 and 20 weeks and between 24 and 29 weeks gestation. Hair will be collected after delivery. All subjects will complete two telephone interviews and two self administered questionnaires regarding various behaviors, dietary intake, physical activity, and psychosocial stressors. Placentas will be collected at the time of delivery and histopathologic analysis will be completed by an experienced perinatal pathologist for cases and a non-case subgroup. Nuclear magnetic resonance measurement of lipoprotein subclasses will be done to assess dyslipidemia. Insulin glucose ratios will be measured from **fasting** blood samples. We expect to enroll a cohort of 1800 women with 250 preterm deliveries and a randomly selected non-case subgroup (n=500). We will analyze the relationship between UPVC and PTD using logistic regression. Given 1) the size of the study, 2) thorough histopathologic assessment of the placenta, 3) extensive questionnaire data, 4) biologic markers of exposure to bacterial vaginosis, insulin resistance, dyslipidemia, and cocaine use, and 5) the careful assessment of potential confounding factors, this study promises to markedly advance our knowledge of the potential role of UPVC in the etiology of PTD.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PLAINS INDIANS TRADITIONAL DIETS AND DIABETES CONTROL**

  Principal Investigator & Institution: Kattelmann, Kendra K.; Nutrition, Food Science and Hospitality; South Dakota State University Brookings, Sd 57007

  Timing: Fiscal Year 2003; Project Start 01-SEP-2003; Project End 31-AUG-2006

  Summary: (provided by applicant): At present, there are no specific dietary guidelines for the Northern Plains Indian with type 2 diabetes. Current medical nutrition therapy practices base the diabetic therapeutic guidelines on the Food Guide Pyramid that encourages a grain-based diet. Anecdotally, Northern Plains Indians have reported a better control of their type 2 diabetes when following a diet higher in protein. Genetic differences may contribute to decreased adaptation to higher carbohydrate loads among Northern Plains Indians compared to Northern European descendents. A diet patterned after the historical hunter-gatherer type diet, or even the early reservation diet (with higher proportion of energy being supplied from protein), may lower the circulating insulin levels and provide better blood glucose control in Northern Plains Indians with type 2 diabetes. The hypothesis of this application is that Northern Plains Indians with non-insulin dependent, type 2 diabetes who receive an educational lesson that promotes a diet patterned according to the traditional consumption of macronutrients (25% calories from protein, 45-50% from carbohydrate, and 25-30% from fat) will have a better control of their diabetes as measured by their HbA1C, blood glucose, and circulating insulin concentrations compared to those educated to consume a grain-based diet that supplies a more typical mix of macronutrients (10-15% calories from protein, 50-55% from carbohydrate, and 30-35% from fat). A 26- week, dietary educational intervention given monthly will be conducted in the Northern Plains Indians from the Cheyenne River Reservation (Lakota Sioux). Adult Lakota volunteers with type 2 diabetes will be recruited and randomized to an experimental (Medicine Wheel Model) or control (Usual Care) group. The experimental group will receive dietary training using the Medicine Wheel Model for Native Nutrition, which promotes a diet patterned according to the traditional consumption of macronutrients. The control group will receive the usual care dietary training based on the Food Guide Pyramid. Primary outcome variables of HbA1C, **fasting** blood glucose, and circulating insulin concentrations and secondary

outcome variables of blood lipid concentrations will be measured at the beginning and end of trial. Measurements of potential confounders of weight, height, usual dietary intake, activity levels, medication use, and incidence of infection will be taken at the beginning and end of the study period.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PLANT-BASED DIETRY INTERVENTION IN TYPE 2 DIABETES**

  Principal Investigator & Institution: Barnard, Neal D.; Physicians Committee for Responsible Med Responsible Medicine Washington, Dc 20016

  Timing: Fiscal Year 2003; Project Start 01-SEP-2003; Project End 31-AUG-2005

  Summary: (provided by applicant): Diabetes often leads to serious complications, including coronary heart disease, kidney disease, and blindness, among others. Previous studies have suggested that low-fat, plant-based diets can have a strongly favorable effect on the management of type 2 diabetes mellitus, as well as on the elevations of body weight and serum cholesterol that often accompany it, reducing the risk of complications, and raising the possibility of reducing or even eliminating medication use for many individuals. Evidence suggests that the dietary recommendations that are most effective in diabetes management may be similar to the low-fat, vegetarian diets that have demonstrated utility in reversing coronary artery blockages. However, no study to date has examined the effect of a low-fat, vegetarian diet as an intervention for diabetes in a substantial number of participants, and most studies using plant-based (near-vegetarian) diets have also included exercise as a major intervention component, making it impossible to separate the effects of physical activity from those of diet or to reach any definitive conclusion as to which type of dietary intervention is best. This study, which follows an encouraging preliminary trial reported in Preventive Medicine in 1999, will test the hypothesis that a low-fat, vegetarian diet yields significant improvements in key indices of diabetic control, including glycosylated hemoglobin, **fasting** serum glucose and insulin concentrations, microalbuminuria, and medication requirements, as well as in cardiovascular risk factors, such as body weight, serum lipids, and blood pressure, in a 22-week intervention controlled throughout for exercise, with a 1-year follow-up. Sixty-eight volunteers with type 2 diabetes will be randomly assigned to a low-fat, vegan (intervention) diet or a control diet deriving 15-20percent of energy from protein and < 7percent of energy from saturated fats, with carbohydrate and monounsaturated fats together providing 60-70percent of energy intake, based on current American Diabetes Association guidelines. Participants in both groups will be asked to attend weekly meetings for nutrition and cooking instruction and group support, and will be asked not to alter their exercise patterns. Physical activity will be monitored by use of the Bouchard 3-Day Physical Activity Record. (Bouchard 1983) Diets will be assessed at baseline and 11, 22, and 74 weeks, using a 3-day dietary record. **Fasting** serum glucose will be monitored for the study duration and will be used to adjust medications according to a set protocol. Glycosylated hemoglobin, insulin concentrations, 24-hour urinary albumin, body weight, blood pressure, serum lipids, and related cardiovascular risk factors will be measured at baseline, 22 weeks, and 74 weeks.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: POSTPRANDIAL LIPEMIA AND ENDOTHELIAL FUNCTION IN ACCORD**

  Principal Investigator & Institution: Ginsberg, Henry N.; Professor; Medicine; Columbia University Health Sciences New York, Ny 10032

Timing: Fiscal Year 2001; Project Start 01-SEP-2001; Project End 31-AUG-2005

Summary: (provided by applicant): The ACCORD trial will use two connected 2x2 designs to test the efficacy of (a) optimal glucose control (HbA1c = 6.0%) versus standard control (HbA1c + 7.5%) in 10,000 patients with type 2 diabetes mellitus, (b) more intense systolic blood pressure control (120 mm Hg) versus less intense control (140 mm Hg) in 4,200 of those patients, and (c) combined low density lipoprotein cholesterol lowering, triglyceride lowering, and high density lipoprotein cholesterol raising versus only low density lipoprotein cholesterol lowering in 5,800 of those patients. The primary outcome for the overall ACCORD trial is a combination of non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death. The comparison of lipid-altering therapies will be carried out in the Lipid Arm of ACCORD, in which the 5,800 subjects will all be treated with simvastatin and, in addition, be randomly assigned to receive either fenofibrate or placebo. The main ACCORD trial will measure only **fasting** blood samples for lipids, lipoprotein fractions, and apolipoproteins. In the proposed ancillary study, we will compare the effects of simvastatin plus fenofibrate with the effects of simvastatin alone on postprandial lipemia in 250 ACCORD patients at 4 sites in the Northeast Network. In addition, we will compare the effects of the two treatment strategies on baseline and postprandial endothelial function, and on markers of coagulation, endothelial function, and oxidative stress. The propose ancillary study will provide a unique opportunity to determine possible mechanisms whereby simvastatin plus fenofibrate therapy will be associated with reduced cardiovascular events in the overall ACCORD trail. The study is divided into three specific aims. Specific Aim A: To carry out high fat load studies of postprandial lipemia in patients who are participating in the Lipid Arm of the ACCORD trial and compare postprandial excursions of triglycerides, triglyceride-rich lipoproteins, retinyl palmitate, and remnant lipoprotein cholesterol in patients receiving fenofibrate plus simvastatin with those postprandial excursions in patients receiving only simvastatin. Specific Aim B: To determine brachial artery dilatation in response to increased blood flow post- forearm ischemia just prior to, and five hours after, ingestion of a high fat load in the two patient groups. Specific Aim C: To determine baseline levels of PAI-1, fibrinogen and factor VII, and postprandial excursions of factor VII, sVCAM-1, sICAM-1, and sE-selectin in the two patient groups. ACCORD provides a unique opportunity to compare, in detail, the effects of statin therapy alone with statin plus fibrate therapy on several emerging risk factors for atherosclerotic cardiovascular disease in a representative subgroup of the ACCORD cohort that is being followed for cardiovascular endpoints.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PREMIER--LIFESTYLE INTERVEN FOR BLOOD PRESSURE CONTROL**

  Principal Investigator & Institution: Elmer, Patricia J.; Senior Investigator and Professor; Kaiser Foundation Research Institute 1800 Harrison St, 16Th Fl Oakland, Ca 94612

  Timing: Fiscal Year 2001; Project Start 25-SEP-1998; Project End 31-AUG-2003

  Summary: This application is part of a set of applications from five participating institutions. PREMIER, a randomized clinical trial, will determine how two multi-component lifestyle interventions affect blood pressure (BP). Although numerous organizations recommend lifestyle change to control BP and potentially prevent hypertension, practical implementation strategies have yet to be developed and tested. The two lifestyle interventions to be tested in PREMIER include a "comprehensive" intervention implementing current recommendations for BP control (reduced salt intake; increased physical activity, moderation of alcohol intake; and weight loss, if

appropriate), and a "comprehensive plus DASH" intervention implementing current recommendations plus the Dietary Approaches to Stop Hypertension (DASH) dietary pattern (rich in fruits, vegetables, and low-fat dairy products, and reduced in saturated fat, total fat, and cholesterol). These lifestyle intervention programs will consist of a series of group and individual counseling sessions similar in intensity to health education programs currently provided by health care delivery systems for other conditions. Study participants (n=800) will be 25 years of age or older, with systolic BP of 120-159 mmHg and diastolic BP of 80-95 mmHg. Approximately half of the participants will be female, 40 percent will be African American, and 30 percent will have stage 1 hypertension. After three screening visits, participants Will be randomly assigned to one of the two lifestyle interventions or a usual care control group. Follow-up will last 18 months after randomization. The primary outcome will be systolic BP with diastolic BP as a secondary outcome. Additional outcome variables will include **fasting** lipids, **fasting** glucose, insulin, and homocysteine. The trial hypotheses will be examined in all participants as well as separately in non-hypertensive and hypertensive subgroups. Results from PREMIER will provide the scientific rationale for routinely implementing comprehensive lifestyle intervention programs to control BP and ultimately prevent BP-related cardiovascular disease.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PREMIER--LIFESTYLE INTERVENE FOR BLOOD PRESSURE CONTRL**

  Principal Investigator & Institution: Stevens, Victor J.; Professor; Kaiser Foundation Research Institute 1800 Harrison St, 16Th Fl Oakland, Ca 94612

  Timing: Fiscal Year 2001; Project Start 01-SEP-1998; Project End 31-AUG-2003

  Summary: This coordinating center application is part of a set of applications from five participating institutions. PREMIER, a randomized clinical trial, will determine how two multi-component lifestyle interventions affect blood pressure (BP). Although numerous organizations recommend lifestyle change to control BP and potentially prevent hypertension, practical implementation strategies have yet to be developed and tested. The two lifestyle interventions to be tested in PREMIER include a "comprehensive" intervention implementing current recommendations for BP control (reduced salt intake; increased physical activity; moderation of alcohol intake; and weight loss, if appropriate), and a "comprehensive plus DASH" intervention implementing current recommendations plus the Dietary Approaches to Stop Hypertension (DASH) dietary pattern (rich in fruits, vegetables, and low fat dairy products, and reduced in saturated fat, total fat, and cholesterol). These lifestyle intervention programs will consist of a series of group and individual counseling sessions similar in intensity to health education programs currently provided by health care delivery systems for other conditions. Study participants (n=800) will be 25 years of age or older, with systolic BP of 120-159 mmHg and diastolic BP of 80-95 mmHg. Approximately half of the participants will be female, 40 percent will be African American, and 30 percent will have stage 1 hypertension. After three screening visits, participants will be randomly assigned to one of the two lifestyle interventions or a usual care control group. Follow-up will last 18 months after randomization. The primary outcome will be systolic BP with diastolic BP as a secondary outcome. Additional outcome variables will include **fasting** lipids, **fasting** glucose, insulin, and homocysteine. The trial hypotheses will be examined in all participants as well as separately in non hypertensive and hypertensive subgroups. Results from PREMIER will provide the scientific rationale for routinely

implementing comprehensive lifestyle intervention programs to control BP and ultimately prevent BP-related cardiovascular disease.

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- **Project Title: PREMIER--LIFESTYLE INTERVENE FOR BLOOD PRESSURE CONTRL**

  Principal Investigator & Institution: Harsha, David W.; None; Lsu Pennington Biomedical Research Ctr 6400 Perkins Rd Baton Rouge, La 70808

  Timing: Fiscal Year 2001; Project Start 01-SEP-1998; Project End 31-AUG-2003

  Summary: This clinical center application is part of a set of applications from five participating institutions. PREMIER, a randomized clinical trial, will determine how two multi-component lifestyle interventions affect blood pressure (BP). Although numerous organizations recommend lifestyle change to control BP and potentially prevent hypertension, practical implementation strategies have yet to be developed and tested. The two lifestyle interventions to be tested in PREMIER include a "comprehensive" intervention implementing current recommendations for BP control (reduced salt intake; increased physical activity; moderation of alcohol intake; and weight loss, if appropriate), and a "comprehensive plus DASH" intervention implementing current recommendations plus the Dietary Approaches to Stop Hypertension (DASH) dietary pattern (rich in fruits, vegetables, and low fat dairy products, and reduced in saturated fat, total fat, and cholesterol). These lifestyle intervention programs will consist of a series of group and individual counseling sessions similar in intensity to health education programs currently provided by health care delivery systems for other conditions. Study participants (n=800) will be 25 years of age or older, with systolic BP of 120 159 mmHg and diastolic BP of 80 95 mmHg. Approximately half of the participants will be female, 40 percent will be African American, and 30 percent will have stage 1 hypertension. After three screening visits, participants will be randomly assigned to one of the two lifestyle interventions or a usual care control group. Follow up will last 18 months after randomization. The primary outcome will be systolic BP with diastolic BP as a secondary outcome. Additional outcome variables will include **fasting** lipids, **fasting** glucose, insulin, and homocysteine. The trial hypotheses will be examined in all participants as well as separately in non hypertensive and hypertensive subgroups. Results from PREMIER will provide the scientific rationale for routinely implementing comprehensive lifestyle intervention programs to control BP and ultimately prevent BP related cardiovascular disease.

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- **Project Title: PREMIER--LIFESTYLE INTERVENTION BLOOD PRESSURE CONTROL**

  Principal Investigator & Institution: Svetkey, Laura P.; Assistant Professor; Medicine; Duke University Durham, Nc 27706

  Timing: Fiscal Year 2001; Project Start 01-SEP-1998; Project End 31-AUG-2003

  Summary: This clinical center application is part of a set of applications from five participating institutions. PREMIER, a randomized clinical trial, will determine how two multi-component lifestyle interventions affect blood pressure (BP). Although numerous organizations recommend lifestyle change to control BP and potentially prevent hypertension, practical implementation strategies have yet to be developed and tested. The two lifestyle interventions to be tested in PREMIER include a "comprehensive" intervention implementing current recommendations for BP control (reduced salt

intake; increased physical activity; moderation of alcohol intake, and weight loss, if appropriate), and a "comprehensive plus DASH" intervention implementing current recommendations plus the Dietary Approaches to Stop Hypertension (DASH) dietary pattern (rich in fruits, vegetables, and low fat dairy products, and reduced in saturated fat, total fat, and cholesterol). These lifestyle intervention programs will consist of a series of group and individual counseling sessions similar in intensity to health education programs currently provided by health care delivery systems for other conditions. Study participants (n=800) will be 25 years of age or older, with systolic BP of 120-159 mmHg and diastolic BP of 80- 95 mmHg. Approximately half of the participants will be female, 40 percent will be African American, and 30 percent will have stage I hypertension. After three screening visits, participants will be randomly assigned to one of the two lifestyle interventions or a usual care control group. Follow up will last 18 months after randomization. The primary outcome will be systolic BP with diastolic BP as a secondary outcome. Additional outcome variables will include **fasting** lipids, **fasting** glucose, insulin, and homocysteine. The trial hypotheses will be examined in all participants as well as separately in non hypertensive and hypertensive subgroups. Results from PREMIER will provide the scientific rationale for routinely implementing comprehensive lifestyle intervention programs to control BP and ultimately prevent BP related cardiovascular disease.

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- **Project Title: R21 PROJECT: ANTI-DIABETIC EFFECTS OF PANAX GINSENG**

  Principal Investigator & Institution: Yuan, Chun-Su; Anesthesia and Critical Care; University of Chicago 5801 S Ellis Ave Chicago, Il 60637

  Timing: Fiscal Year 2002; Project Start 15-MAR-2002; Project End 31-JAN-2004

  Summary: Diabetes mellitus or diabetes is a chronic metabolic disease that can cause blindness, kidney failure, nerve damage, and confers an increased risk of ischemic heart disease, stroke and peripheral vascular disease. Diabetes is divided into two major categories: type 1 or insulin- dependent diabetes mellitus (IDDM), and type 2 or non-insulin dependent diabetes mellitus (NIDDM). In this country, the incidence of diabetes is approximately 4.5%, of which 90% is type 2 diabetes. In 1992, diabetes care required roughly 14.6% of the total U.S. health care expenditure ($105 billion). Many of these patients also suffer from diabetic complications. Considering the heterogeneity of this disease, and the limitations of current therapies, such as high secondary failure rates and side effects, there is an urgent need to explore new anti- diabetic agents. This research project is related to the development of useful products in the field of complementary and alternative medicine. This proposal will focus on our studies on anti-diabetic effects of Panax ginseng, and this project is a continuation of our previous ginseng pharmacological studies. Recently, in our preliminary studies, we observed exciting results on anti-diabetic actions in ob/ob mice using Panax ginseng berry (or fruit) extract, other than the commonly used root extract. The ob/ob mice is a genetic model for type 2 diabetes, and these animals are extremely insulin resistant and have **fasting** blood glucose levels that are significantly higher than that of lean mice. Data from our pilot observation showed that extract of Panax ginseng berry normalized hyperglycemia and increased insulin sensitivity in ob/ob mice. In addition, we analyzed the constituents of the ginseng berry by HPLC analysis and found that, compared to ginseng root, the ginseng berry has a distinctive profile of ginsenosides, the vital constituent of ginseng. In this revised proposal, we will test the hypothesis that Panax ginseng berry extract has significant anti-hyperglycemic activity. The project aims to identify the anti-hyperglycemic constituents of Panax ginseng berry, and synergistic

effects between these constituents. We will also investigate mechanisms of action of these active component(s). Our strategy is to use an in vivo-guided chemical fractionation method to isolate the pure, biologically active, anti-hyperglycemic compound(s) from Panax ginseng berry using the ob/ob mouse. Improvements in glucose homeostasis, glucose tolerance, and in vivo insulin sensitivity will be tested. The results of the proposed project will also help fill gaps in our knowledge before therapeutic agents can be developed.

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- **Project Title: REGIONAL ADIPOSITY AND SYNDROME X IN SPINAL CORD INJURY**

  Principal Investigator & Institution: Braunschweig, Carol; Human Nutrition and Dietetics; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

  Timing: Fiscal Year 2003; Project Start 01-JAN-2003; Project End 31-DEC-2004

  Summary: (provided by applicant): Total and abdominal obesity frequently occur following SCI. Excessive total body adiposity, particularly excessive visceral abdominal adipose tissue (VAAT), and thigh skeletal muscle adiposity (TSKMAT), measured by magnetic resonance imaging (MRI), have been associated with a low-grade systemic inflammation and the metabolic syndrome (MS) (also called syndrome X) which has been defined as the presence of three or more of the following features: waist circumference (WC) greater than 40 inches, **fasting** triglycerides of at least 150 mg/dl, glucose equal or greater than 110 mg/dl, HDL cholesterol equal or less than 40 mg/dl and/or blood pressure of at least 130/85 mmHg. People with the MS are predisposed to developing insulin resistance and increased risks for diabetes mellitus, hypertension, and cardiovascular disease. Individuals with SCI have higher prevalence rates for these diseases than able-bodied individuals, however, measures of VAAT or TSKMAT volumes and their relation to a measure for inflammation, features of the MS or insulin resistance have not been reported for this population. This is unfortunate given that body fat distribution and inflammatory status are both modifiable risk factors. The purpose of this pilot investigation is to explore the association between measures of adiposity (total, abdominal, VAAT and TSKMAT), a sensitive marker of inflammation (CRP), features of the MS, and insulin resistance in paraplegic men compared to similar able-bodied men. The investigators propose a cross sectional investigation of community dwelling males (N = 60) recruited from urban SCI rehabilitation and trauma centers to determine whether the volume of VAAT, its anthropometric surrogates (WC and/or sagittal diameter), and/or the volume of TSKMAT predict concentrations of CRP, levels and numbers of features of the MS, and insulin resistance in paraplegic men and whether these variables are similar in direction, magnitude and association to those observed in able-bodied men. Four groups of men more than one year post SCI or trauma, frequency matched for age and ethnicity (15/group; 30 paraplegic SCI and 30 able-bodied men with a history of trauma resulting in a hospital stay over 5 days), will be recruited as follows: group 1 lean SCI (WC 40 inches), group 3 lean able-bodied (WC 40 inches). Correlation analysis, multiple regression, and analysis of variance will be used to determine the association between CRP, the MS, insulin sensitivity, and various measures of regional adiposity between these groups.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ROLE OF FOOD INTAKE AND CORTISOL ON LEPTIN IN HUMANS.**

  Principal Investigator & Institution: Laferrere, Blandine B.; St. Luke's-Roosevelt Inst for Hlth Scis Health Sciences New York, Ny 10019

Timing: Fiscal Year 2003; Project Start 01-FEB-2003; Project End 31-JAN-2005

Summary: (provided by applicant): The adipocyte hormone leptin plays a key role in the control of energy balance. We and others have demonstrated a synergistic effect of administered glucocorticoids (GC) and food intake (or insulin) on leptin in lean and obese subjects. Morning food intake produces an increase in insulin, a midday spike of cortisol and an increase of leptin at night. During **fasting,** neither insulin or cortisol peak in midday, and leptin does not rise at night. Administration of insulin alone cannot produce the meal-entrained nocturnal rise in serum leptin. We hypothesize that the spike of cortisol occurring with feeding is permissive for post-prandial insulin effects on nighttime leptin. Thus we anticipate that administration of metyrapone, a blocker of cortisol production, should blunt the leptin response to food intake. Accordingly, the administration of hydrocortisone to subjects receiving metyrapone, by artificially simulating the midday surge of cortisol, will restore the leptin response to the meal. This mechanistic experiment will be conducted in lean subjects. Obesity, particularly abdominal obesity, is associated with perturbations of the hypothalamic-pituitary-adrenal (HPA) axis. The response of plasma cortisol to stressors, such as a lunch meal, is increased. The leptin response to the administration of GC is also elevated. Thus, we will also investigate whether the relationship between the meal-entrained cortisol secretion and leptin night rise is perturbed in upper body obese (UBO). UBO have a high risk of developing metabolic complications, and represent a subgroup of obese with the most well-characterized abnormalities of the HPA axis. We hypothesize that UBO will exhibit a more robust and homogenous response to cortisol manipulations than a random subset of obese individuals. Taken together, these experiments should provide information on basic mechanisms of nutritional/hormonal effects on serum leptin, as well as preliminary data on how these mechanisms may be altered in obesity. Ultimately, these results would lead to a better understanding of the mechanisms of leptin dysregulation in obese subjects

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- **Project Title: ROLE OF WNT IN WHITE AND BROWN ADIPOSE DEVELOPMENT**

  Principal Investigator & Institution: Macdougald, Ormond A.; Associate Professor; Physiology; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2003; Project Start 01-FEB-2003; Project End 31-JAN-2008

  Summary: (provided by applicant): The long-term goal of my research program is to determine the molecular mechanisms by which extracellular signals regulate adipocyte differentiation and metabolism. We have pioneered investigations into the role of Wnt signaling as a potent, endogenously produced inhibitor of adipogenesis. Wnt10b acts as an adipogenic switch, which must be shut off for cultured preadipocyte models to differentiate in vitro. Based on the role of Wnt10b in white adipogenesis in cell culture, we hypothesize that Wntl0b also regulates development of white adipose tissue (WAT) and brown adipose tissue (BAT) in the integrative setting of the organism. To test this hypothesis, we have created transgenic mice in which Wnt10b is expressed under control of the adipocyte-specific promoter, 422/aP2. Our preliminary data indicate that Wnt10b transgenic mice are almost devoid of WAT. In addition to its effects on development of WAT, our data suggest that Wnt10b also inhibits development of brown adipocytes within mice and within cultured cell models. Because little is known about the regulation of BAT development, our studies will be seminal to our understanding of this important metabolic and thermogenic tissue. The role of Wnt10b in development of adipose tissues will also be explored in Wnt10b -/- mice. Thus, the Specific Aims of this

proposal are to:1) Investigate the role of Wnt10b in development of WAT. Experiments include molecular and mechanistic analyses of how Wnt10b regulates adipocyte differentiation and metabolism,1) Investigate the role of Wnt10b in development of BAT. Experiments include molecular and mechanistic analyses of how Wnt 10b regulates BAT development in vivo and brown adipogenesis in cultured cells.1) Determine effects of Wnt10b on energy balance. Variables measured will include food intake, weight gain, body composition, metabolic rate, respiratory quotient, locomotor activity, and body temperature. Effects on energy balance will be determined as control and Wnt transgenic or null mice adapt to **fasting,** cold stress, genetic or diet-induced obesity.Understanding the role of Wnt signaling in the development of WAT and BAT will provide important insight into the medical problems of obesity and type II diabetes, two major health risks in the United States. The identification of Wnt10b as a susceptibility gene for dysregulated development of WAT in mice will provide proof of principle that Wnt10b is important for normal and pathological development of adipose tissue in the human population.

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- **Project Title: SAFETY OF ESTROGEN IN LUPUS ERYTHEMATOSUS**

  Principal Investigator & Institution: Buyon, Jill P.; Professor; Hospital for Joint Diseases Ortho Inst Orthopaedic Institute New York, Ny 10003

  Timing: Fiscal Year 2001; Project Start 30-SEP-1995; Project End 31-AUG-2006

  Summary: (provided by applicant): The Safety of Estrogens in Lupus Erythematosus, National Assessment (SELENA) consists of two randomized double blind placebo-controlled equivalence trials. The first examines the effect of hormonal replacement therapy (HRT) on disease activity in postmenopausal women with SLE, the primary outcome being severe flare. Current enrollment is 314 patients and should reach the target of 350 by April 2001. The second trial, initiated in April 1997, examines the effect of oral contraceptive pills (OCP) on disease activity. To date, 159 subjects have been enrolled at an average rate of month. This application seeks an additional 5 years of enrollment for the OCP trial to achieve adequate power for assessing equivalence in severe flare rates across treatment arms; determining potential salutary effects of estrogens on two clinical concerns in SLE, osteoporosis and atherosclerosis; and studying two research themes often linked to estrogen use, autoimmunity and thrombosis. Three new investigations have been added to the proposal, each of which optimally utilizes the unique resources of this prospective clinical trial. These complementary projects have a dual purpose: to evaluate hormonal effects in vitro with respect to fundamental pathophysiologic questions, and to determine whether laboratory markers can be established to select subsets of patients who may either benefit from OCP or be at increased risk for exacerbation of 1upus or cardiovascular sequelae. Accordingly, 4 specific aims are proposed in this application. Specific Aim 1: To evaluate the safety of OCP by assessing whether the rates of severe flare in the OCP and placebo groups are clinically equivalent. Specific Aim 2: To assess protection from and risk of osteoporosis and atherosclerosis by pre- and post-study evaluation of DEXA scans, **fasting** lipids, fibrinogen, CRP, plasminogen activator inhibitor, homocysteine, lipoprotein(a), and carotid duplex. Specific Aim 3: To understand whether there is a change in B cell subsets in the peripheral blood of SLE patients receiving OCP; whether there are changes in expression of candidate autoimmunity genes in peripheral blood B cells (including SHP-1, VCAM-1, Bcl-2, and CD22); and whether there are changes in the number or phenotype of B cells spontaneously secreting anti-DNA antibody. Specific Aim 4: To address the hemostatic effects of estrogen (with focus on the protein S system)

which may increase the risk for thrombosis even in patients screened out by virtue of high levels of anticardiolipin antibodies or a lupus anticoagulant. The SELENA-OCP trial offers the best (and perhaps only) opportunity to firmly answer the concerns of clinical safety and potential cardiovascular and skeletal efficacy of exogenous hormones in women with SLE. Moreover, this translational research trial, at least with regard to the estrogen and progesterone load imposed by OCP, will facilitate answers to the ever-pressing basic biologic issues of the effect of female hormones on autoimmunity and thrombosis.

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- **Project Title: SELENODEIODINASE PROCESSING BY THE PROTEASOME SYSTEM**

  Principal Investigator & Institution: Larsen, Philip R.; Professor; Brigham and Women's Hospital 75 Francis Street Boston, Ma 02115

  Timing: Fiscal Year 2001; Project Start 01-FEB-2001; Project End 31-JAN-2004

  Summary: (Adapted from the applicant's abstract) This is a new proposal to determine the mechanisms regulating the rate-limiting steps in the ubiquitin proteasome system leading to the controlled degradation of the Types 1, 2 and 3 selenodeiodinases. D2 is a critical enzyme regulating the first step in thyroid hormone action, the conversion of the prohormone T4 to the active hormone, T3. This process occurs intracellularly in brain, pituitary and brown fat in which the T3 produced constitutes a major fraction of the nuclear receptor-bound hormone. Furthermore, it appears that, in humans, unlike in adult rodents, D2 may also generate a significant fraction of plasma T3 by virtue of its wide tissue expression in skeletal muscle. It has been known for a number of years that post-translational regulation of D2 by substrate is a major regulatory step in determining the tissue level of the active enzyme. Recent studies have shown that degradation of D2 occurs in proteasomes, that its half-life is quite short (<1 hr), that its degradation is accelerated 2-fold by exposure to substrate and that this process requires interaction of substrate with a D2 enzyme which has either selenocysteine or cysteine in its active center. To define the regulatory steps in this process, the investigator will use several complementary systems. These include transient expression in HEK-293 cells and a temperature-sensitive CHO cell line containing a mutant UB-1 enzyme. A third strategy will be to exploit the fact that D2 can be expressed in yeast with well-documented mutations in the ubiquitin-proteasome degradation pathway and that it is possible to express both wild type and epitope-labeled protein to evaluate changes in activity those in D2 protein levels. Lastly, the investigator will employ cell-free systems which will allow the study of specific components of the ubiquitin proteasome system in the metabolism of D2 and compare results with those for Dl and D3 which have significantly longer half-lives. From a physiological perspective, it is quite conceivable that the accelerated proteolysis of D2 in human skeletal muscle during starvation or illness could explain the rapid onset of the "low T3 syndrome." This is a well-recognized but poorly understood phenomenon which occurs in every human under food restriction or with significant systemic illness.

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- **Project Title: SKELETAL MUSCLE METABOLISM OF FATTY ACIDS**

  Principal Investigator & Institution: Kelley, David E.; Professor; Medicine; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2001; Project Start 01-APR-2000; Project End 31-DEC-2004

Summary: Skeletal muscle has a crucial role in substrate metabolism and energy balance and perturbations can have major implications for health, as exemplified by the important role of skeletal muscle insulin resistance in obesity and Type 2 diabetes mellitus (DM). A major focus of the candidate's research has been to better understand the interaction between glucose and fatty acid metabolism in the pathogenesis of skeletal muscle insulin resistance. This research has led to the hypothesis that skeletal muscle in obesity and Type 2 DM has a reduced capacity for fat oxidation, that this impairment is most clearly manifest during **fasting** conditions and causes lipid accumulation within muscle; a process that aggravates insulin resistant glucose metabolism. The thrust of this proposal is to further test this hypothesis. We will seek to do this by developing several novel approaches to the clinical investigation of skeletal muscle metabolism of fatty acids. During the past 11 years of clinical investigation, the candidate has mastered the use of arterio-venous leg balance, radioactive fatty acid and glucose isotope dilution, systemic and regional (limb) indirect calorimetry, euglycemic insulin infusions and percutaneous muscle biopsy as methods to evaluate skeletal muscle physiology in Type 2 DM and obesity. All of these techniques have been in use for at least several decades. This field of clinical investigation could benefit considerably by application of exciting new modalities, including non-invasive imaging of metabolism and tissue composition. During the next five years, with the support of a MidCareer Investigator Award, the candidate will work within a multidisciplinary collaborative effort, including young colleagues to develop three methods: 1) a stable isotope method for in vivo determination of fatty acid uptake and oxidation in skeletal muscle; 2) spiral magnetic resonance imaging method for non-invasive determination of skeletal muscle lipid content; and 3) positron emission tomography (PET) imaging of skeletal muscle fatty acid uptake and oxidation. These methods will be used for testing the hypothesis of that skeletal muscle oxidation of fatty acids is decreased while fatty acid esterification is increased in obesity-related insulin- resistance.

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- **Project Title: STRENGTH TRAINING FOLLOWING GASTRIC BYPASS FOR OBESITY**

  Principal Investigator & Institution: Geliebter, Allan; St. Luke's-Roosevelt Inst for Hlth Scis Health Sciences New York, Ny 10019

  Timing: Fiscal Year 2003; Project Start 01-MAR-2003; Project End 31-DEC-2004

  Summary: (provided by applicant): As the incidence of obesity rises dramatically in the United States, more and more severely obese individuals are undergoing surgical treatment to reduce body weight and associated risk factors. Roux-en-Y gastric bypass (RYGB) is now the most common operation to treat morbid obesity in the US. However, little is known about the effects of RYGB on body composition and resting energy expenditure (REE). The main objectives of this study are to determine: 1) the composition of weight loss following surgery, 2) whether protein supplementation and strength training can limit the expected reduction of lean mass and REE. The study candidates will be morbidly obese women with a body mass index (BMI) of 40-56 kg/m2, be 18 - 49 y.o. and premenopausal. Except for severe obesity, they will be relatively healthy with a history of diet failure. They will be sedentary except for walking. There will be 36 study participants who, after stratifying by race, will be randomly assigned to three treatment groups (n = 12): 1) standard postoperative nutritional counseling only, 2) protein supplementation and standard postoperative nutritional counseling, or 3) protein supplementation plus strength training and standard postoperative nutritional counseling. The protein supplementation will begin

shortly after surgery and increase from 40 g/day to 80 g/d at 4 weeks. Strength training will begin 8 weeks postoperation, to allow for adequate wound healing, and will consist of twice weekly progressive resistance training for upper and lower body for a period of 12 weeks. A battery of test measurements following a 12 h overnight fast will be conducted prior to surgery and repeated postoperatively at 8 and 20 weeks. These tests will include measurement of REE and body composition using underwater weighing, air displacement (BODPOD), dual xray absorptiometry (DEXA), magnetic resonance imaging (MRI), isotope dilution (D20), sodium bromide, and regional anthropometrics. There also will be assessments of arm and leg strength. Additionally, there will be measures of **fasting** glucose and body weight related hormones insulin, leptin, cortisol, and the recently discovered ghrelin. The predictions are that during the dramatic weight loss after surgery, the loss of some lean tissue, which could adversely impact skeletal muscle and vital organs, will be reduced by enhanced protein intake and weight training. There also may be greater conservation of REE and bone density. Plasma glucose and hormones should all decrease, especially with exercise, except for ghrelin, which should increase. The findings should improve understanding of surgical weight loss in morbidly obese patients and have clinical applications in the postoperative care of such patients.

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- **Project Title: THERMOGENESIS AND EXERCISE IN LEAN AND OBESE MAN**

  Principal Investigator & Institution: Klein, Samuel; Professor of Medicine and Director; Internal Medicine; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2001; Project Start 01-DEC-1986; Project End 31-AUG-2003

  Summary: Women normally have more body fat, a different distribution of fat, and a greater prevalence of obesity than men. Despite their greater body fat, premenopausal women are less prone to develop insulin resistance diseases associated with obesity. Therefore, an understanding of gender differences in fat metabolism has important physiological and clinical implications. However, few studies have evaluated the effect of gender on in vivo regulation of fat metabolism in humans. Moreover, the available data is largely confounded by differences in body composition, which independently influence substrate metabolism. The main purpose of this proposal is to determine the independent effects of gender and adiposity on fat metabolism during the major physiological conditions which decrease lipolysis and fat oxidation (hyperinsulinemia) or increase the mobilization and use of fat as a fuel (fasting and endurance exercise). We hypothesize that differences in fat metabolism between men and women will become more apparent during the physiological challenges of hyperinsulinemia, exercise, and **fasting.** The proposed studies will elucidate the independent effects of gender and adiposity in men and premenopausal women, matched by adiposity at three levels (22-25%, 28-31%, and 35-38% body fat), on: 1) insulin action in different tissues: adipose tissue (suppression of whole- body and regional adipose tissue lipolysis), liver (inhibition of glucose production), and skeletal muscle (stimulation of glucose uptake) (Study 1); the metabolic responses to short-term **fasting** (whole-body and regional adipose tissue lipolysis and its hormonal regulation) (Study 2); and 3) the metabolic responses to endurance exercise (whole-body and regional adipose tissue lipolysis, intramuscular triglyceride lipolysis, whole body fat oxidation, plasma fatty acid oxidation, and intramuscular triglyceride oxidation rates) (Study 3). These endpoints will be evaluated by performing isotope infusion experiments during 1) a multistage hyperinsulinemic pancreatic hormonal clamp, 2) short-term **fasting,** and 3) cycling exercise using state-of-the-art in vivo methodologies, including stable isotope tracers to

measure substrate and norepinephrine kinetics, indirect calorimetry to evaluate substrate oxidation, microdialysis and abdominal vein catheterization to assess regional (abdominal/femoral adipose tissue and skeletal muscle) substrate and hormone metabolism, and 133Xe clearance and venous occlusion plethysmography to measure adipose tissue and muscle blood flow, respectively. The information derived from these studies may improve our understanding of the regulation fat metabolism and the underlying metabolic factors which lead to obesity-related comorbidities.

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- **Project Title: TRANSCRIPTIONAL REGULATION OF A SURFACTANT ENZYMEN**

  Principal Investigator & Institution: Mallampalli, Rama K.; Professor; Internal Medicine; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 18-FEB-2002; Project End 31-JAN-2004

  Summary: (provided by applicant): The developing fetal lung critically relies on the availability of maternal lipoproteins to maintain adequate synthesis of surfactant by alveolar type II epithelial cells. Lipoproteins are a rich source of fatty acids, which serve as substrates for synthesis of phosphatidylcholine (PC), the major 1ipid of surfactant. Lipoproteins also serve as potent post-transnational activators of the rate-limiting enzyme required for surfactant PC synthesis, cytidylyltransferase (CT). Although much is known about post-transnational control of CT, transcriptional regulation of this enzyme has not been evaluated. In addition, feedback control mechanisms that exist in the lung to maintain surfactant PC homeostasis under conditions of lipoprotein deficiency remain largely unknown. The revised proposal expands from recent advances made in our laboratory showing that chronic lipoprotein deficiency increases CT activity and surfactant synthesis in fetal type II cells by increasing transcription of the CT gene. These in vitro results suggest that lipoprotein deprivation stimulates CT gene transcription as a novel compensatory mechanism. These preliminary results led us to hypothesize that CT is regulated, in vivo, at the transcriptional level. We propose to test this hypothesis by generating a CT promoter-reporter mouse (AIM 1). This transgenetic mouse will be used to study constitutive and induced CT transcription after lipoprotein deprivation during various phases of fetal lung development (AIM 2). In addition, transgenic mice harboring specific CT promoter segments linked to the beta-galactosidase (beta gal) reporter gene will be used to determine the functional relevance of regulatory elements within the 5' flanking region of the CT promoter in vivo. To achieve our Aims, maternal and fetal lungs will be analyzed for reporter expression by tissue immunohistochemical staining, immunoblotting, beta gal activity, and Northern analysis for beta gal. Results will be correlated with endogenous CT expression and surfactant production. These in vivo studies will be supplemented by use of a lipoprotein-sensitive type II line. The unique contributions of this proposal impacting the field of surfactant metabolism include providing a springboard by which investigators can understand for the first time how the CT gene is regulated transcriptionally, in vitro and in vivo. Ultimately, the results from these studies could lead to therapeutic strategies directed at modulating expression of this key surfactant enzyme at the molecular level.

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- **Project Title: TRH REGULATION/BIOSYNTHESIS AND PARAVENTRICULAR NUCLEUS**

  Principal Investigator & Institution: Lechan, Ronald M.; Professor of Medicine; New England Medical Center Hospitals 750 Washington St Boston, Ma 021111533

Timing: Fiscal Year 2002; Project Start 01-FEB-1986; Project End 31-MAY-2007

Summary: The long term goals of this program are to elucidate the mechanisms of control of the biosynthesis of thyrotropin- releasing hormone (TRH) in a population of neurons in the hypothalamic paraventricular nucleus (PVN) that comprise a critical component of the hypothalamic-pituitary-thyroid (HPT) axis and determine how these neurons alter their response to feedback signals by thyroid hormone during adaptive and pathological conditions that comprise the nonthyroidal illness syndrome observed in man, including **fasting** and infection. The importance of neuropeptide Y (NPY), agouti-related protein (AGRP), GABA, alpha-MSH and CART in mediating the regulatory role of leptin to reset the HPT axis to feedback signals by circulating thyroid hormone, will be studied. Synthetic peptides, agonists and/or antagonists will be infused individually or in combination into the cerebrospinal fluid of rats or in transgenic mice with targeted deletion of melanocortin receptors 3,4, or both 3 and 4, to determine whether the effect of **fasting** on the HPT axis can be replicated in fed animals or prevented in **fasting** animals, and/or to identify the specific receptors involved. The importance of the hypothalamic dorsomedial nucleus (DMN) as a relay nucleus to TRH neurons in the PVN via a multisynaptic pathway that involves leptin- responsive neurons in the arcuate nucleus will also be explored. The chemical mediators of DMN projections to TRH neurons in the PVN will be identified; the leptin-regulated, arcuate-DMN-PVN multisynaptic pathway to TRH neurons defined; and the role of the DMN to modulate the set point for TRH gene expression in the PVN by **fasting** and leptin administration determined, the latter by unilateral ablation of the DMN or microinjections of alpha-MSH into the DMN and PVN. Similarly, the importance of the brainstem nucleus tractus soitarius (NTS) in leptin-mediated regulation of the HPT axis will be studied in animals with surgical disconnection the NTS from the PVN, and by determining whether glucagon-like peptide-1 (GLP-1) alters TRH gene expression. Finally, the mechanism for suppression of the HPT axis during infection will be elucidated using endotoxin (bacterial lipopolysaccharide or LPS) to replicate the inflammatory cascade caused by infection. Direct or indirect inhibitory effects on hypophysiotropic TRH neurons will be studied by determining whether cytokine-inducible inhibitors of signaling (SOCS-1 and SOCS-3) are increased in TRH neurons in the PVN following LPS administration mediated by the negative regulator of gene transcription, STAT3beta, and/or through effects on the melanocortin signaling system, NPY, GABA, CRH and/or prostaglandins in the PVN or other loci in the brain, mediated by the cAMP-responsive modifier CREM/ICER.

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- **Project Title: TRIALNET: DIABETESTYPE 1 PREVENTION TRIAL**

  Principal Investigator & Institution: Chase, H Peter.; B Davis Ctr/Childhood Diabetes; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, Co 800450508

  Timing: Fiscal Year 2001; Project Start 30-SEP-2001; Project End 31-AUG-2008

  Summary: (provided by applicant) Long Term Objective: to determine whether early interventional therapies can delay, prevent, or reverse the development of Type 1 diabetes. Specific Aims: intervention trials for subjects with pre-diabetes and new onset diabetes The Diabetes Prevention Trial - Type 1 (DPT-1): to determine whether the early intervention use of insulin in nondiabetic relatives of persons with Type 1 diabetes can delay their development of Type 1 diabetes as a clinical disease. Insulin is used for this purpose since it is a well characterized antigen specifically produced by beta cells. Research design: the parenteral antigen protocol enrolled subjects found to be at high

risk (greater than 50 percent) for development of diabetes in the next 5 years. Subjects randomized to the insulin-treated group received insulin intravenously for 4 days each year and two injections of Ultralente each day (before breakfast and before bedtime). The oral antigen protocol enrolls subjects found to be at intermediate risk (25-50 percent) for the development of Type 1 diabetes in the next 5 years. This is a double-blind study and all subjects take 1 capsule daily, with half receiving the antigen and the others receiving a placebo. Levels of antibodies, insulin, C-peptide, HbA1C and glucose are followed. The main study endpoint is two ?diabetic? oral glucose tolerance tests (OGTT) performed on different days. Immunotherapy Trial in New Onset Type 1 Diabetes: to test the hypothesis that mycophenolate mofetil (MMF alone or with daclizumab (DZB) will prolong the period of C-peptide production in subjects with new onset Type 1 diabetes. A secondary aim is to provide the clinical material for the validation of surrogate markers for immunity to islet beta-cells. This study is innovative in that these agents have not been previously evaluated but are rational choices for intervention in an autoimmune disorder. Research design: Levels of autoantibodies and T cell reactivity to islet autoantigens, both of which are surrogate immunological parameters specific for Type 1 diabetes will be followed. Measures of immune modulation will include serologic and T cell reactivity to recall antigens. The metabolic end-points of this study will be **fasting** and stimulated C-peptide, hemoglobin A1C, and total insulin dose. If this study has a positive outcome, then we would propose a similar study in people at high risk for developing Type 1 diabetes.

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- **Project Title: TYPE 2 DIABETES PRIMARY PREVENTION FOR AT RISK GIRLS**

  Principal Investigator & Institution: Robinson, Thomas N.; Assistant Professor Of; Medicine; Stanford University Stanford, Ca 94305

  Timing: Fiscal Year 2002; Project Start 15-AUG-2002; Project End 31-JUL-2006

  Summary: (provided by applicant): We propose to test the efficacy of an after school dance program to reduce weight gain and risk for type 2 diabetes in a sample of predominantly Latina, Pacific Islander, Filipina and African-American pre-adolescent girls. Over the past two decades we have witnessed an emerging epidemic of type 2 diabetes in children, adolescents and young adults. The rise in type 2 diabetes has been attributed, in large part, to the accompanying epidemic of obesity. Girls and children of non-European ancestry are at highest risk for pediatric type 2 diabetes. After school dance programs may be a generalizable environmental strategy to promote long-term moderate-to vigorous physical activity among girls. Two pilot studies of dance in predominantly low-income African-American and Latina samples confirmed that (1) dance is a highly attractive and feasible form of activity for preadolescent girls and (2) a dance intervention can result in reduced body mass index (BMI) and increased fitness among girls. We propose a 2-year randomized, controlled trial involving 240 2nd, 3rd and 4th grade girls and their families, from low-income, ethnically diverse elementary schools. Girls will be randomized to the after school dance intervention or a non-specific "active placebo" control group. Dance classes will be conducted at their school sites. Both social and performance dance will be taught, emphasizing ethnic dance styles and traditions. In-home/school-based measures of height, weight, waist circumference, triceps skinfold thickness, blood pressure, resting heart rate, and self-reports of physical activity and sedentary behaviors will be collected every six months and **fasting** insulin, glucose, and lipoprotein levels, and four days of physical activity monitoring and three 24-hour dietary recalls will be obtained annually. We will use random regression models to test the following primary hypothesis: Compared to controls, girls in the

dance intervention treatment group will significantly reduce their weight gain over a 2-year study period. Body mass index (BMI, kg/m2) will be the primary measure of body fatness. Secondary outcomes include **fasting** insulin, **fasting** lipoproteins, blood pressure and resting heart rate, physical activity levels, and dietary calorie and fat intake. We will also perform baseline and prospective risk factor/targeting studies and process studies, to better understand the relevance of the results and the intervention.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: WEIGHT LOSS MAINTENANCE IN PRIMARY CARE**

  Principal Investigator & Institution: Lowe, Michael R.; Professor of Psychology; Psychology; Drexel University 3201 Arch Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-JUL-2008

  Summary: (provided by applicant): The rising prevalence of obesity is taking an increasingly severe toll on the nation's health. Achieving and maintaining a medically significant weight loss is of particular importance for those overweight individuals who have, or who are at greatest risk for developing, one of the many medical conditions associated with obesity. The present proposal is aimed at evaluating three treatments for weight loss maintenance in primary care practices where such patients are routinely treated. One treatment consists of a conventional lifestyle change program (based on the LEARN manual). The second consists of the LEARN program plus the use of meal replacements (MRs) to facilitate weight loss maintenance. The third consists of LEARN+MR and a Reduced Energy Density Eating program (REDE). The three treatments will be administered using two different modes of delivering the programs, one group-based (where an outside expert leads a traditional weight control program) and the other practice-based (where physicians and a practice-based care manager collaborate to deliver the program to individual patients). Participants will consist of 312 overweight and obese primary care patients. All participants will initially lose weight on identical 1,200-1,500 kcal/day diets (consisting of two MRs and a healthy dinner), after which one of the three maintenance interventions will be introduced. A second aim of the study is to investigate the mechanisms responsible for differential weight maintenance outcomes. A final aim is to examine several individual difference measures as potential moderators of study outcomes, both alone and in combination with treatment condition. This study is important because it may identify better ways of promoting long-term improvements in diet and body weight in overweight patients seen in primary care settings. Participants will receive treatment during a one-year period and follow-up assessments will be conducted one and two years after treatment ends. Outcome will be assessed in terms of changes in body weight and composition, nutritional composition of the diet, measures of eating control, overeating, and quality of life, physical activity, patient and physician satisfaction ratings, cost-effectiveness, and several medical risk factors (blood pressure, lipids, **fasting** glucose, and HbAlc).

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: WISCONSIN EPIDEMIOLOGICAL STUDY OF CARDIOVASCULAR DISEAS**

  Principal Investigator & Institution: Klein, Ronald; Professor; Ophthalmology and Visual Sci; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2001; Project Start 01-FEB-1999; Project End 31-JAN-2003

  Summary: This proposal describes a population-based cohort aimed at determining the prevalence and incidence of cardiovascular disease morbidity and mortality in people

with Type 1 diabetes of long-duration. For this epidemiologic study, subjects include all insulin-taking persons who: (1) were less than 30 years of age at the time of their diagnosis, (2) had received primary medical care in an 11-county area of south-central Wisconsin, and (3) were first identified in 1979-80. Standardized protocols for examinations and interviews have been employed during the baseline, 4-, 10-, and 14-year follow up examinations. Refusal rates have been low. The mean age of the cohort and the long duration of diabetes provide an opportunity to document the prevalence and incidence of coronary heart disease, myocardial infarction, angina, congestive heart failure, stroke, transient ischemic attacks, peripheral vascular disease, and cardiovascular disease mortality in a large population-based group of persons with Type 1 diabetes. Retinal photographs of each study participant were taken at the baseline examination. This will permit us to test the predictive ability of focal and generalized retinal arteriolar narrowing and arterio-venous cross changes (i.e. A/V nicking) for subsequent macrovascular events controlling for other risk factors. These factors include blood pressure, cigarette smoking, serum lipids, body mass index, duration of diabetes, and glycemia. We plan to reexamine this cohort to obtain ECGs, blood lipid fractions not previously measured, and fibrinogen, as well as upper and lower extremity blood pressures, urine specimens, and medical records. This will provide information about silent about silent infarctions and other cardiographic abnormalities as well as previously doctor-diagnosed macrovascular events in long-term survivors of Type 1 diabetes. Study examinations will be performed in a mobile van. Participants will provide two urine specimens for determination of urinary albumin excretion. **Fasting** blood will be obtained for determination of glycosylated hemoglobin Alc, blood sugar, serum cholesterol, triglycerides, HDL- cholesterol, LDL-cholesterol, VDL-cholesterol, LDL particle size, serum creatinine, and fibrinogen. Additional study procedures include measurements of weight and height, waist and hip girth, and brachial and ankle blood pressures. Electrocardiography will also be performed. A questionnaire will be administered Participants will subsequently be interviewed yearly and clinical and hospital records and death certificates will be collected to document new cardiovascular disease events. Findings regarding the prevalence and incidence of cardiovascular disease and associated risk factors will be of great public health importance in directing further at preventing these conditions in people with Type 1 diabetes of long duration.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

E-Journals: PubMed Central[3]

PubMed Central (PMC) is a digital archive of life sciences journal literature developed and managed by the National Center for Biotechnology Information (NCBI) at the U.S. National Library of Medicine (NLM).[4] Access to this growing archive of e-journals is free and unrestricted.[5] To search, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Pmc**, and type "fasting" (or synonyms) into the search box. This search gives you access to full-

[3] Adapted from the National Library of Medicine: **http://www.pubmedcentral.nih.gov/about/intro.html**.

[4] With PubMed Central, NCBI is taking the lead in preservation and maintenance of open access to electronic literature, just as NLM has done for decades with printed biomedical literature. PubMed Central aims to become a world-class library of the digital age.

[5] The value of PubMed Central, in addition to its role as an archive, lies in the availability of data from diverse sources stored in a common format in a single repository. Many journals already have online publishing operations, and there is a growing tendency to publish material online only, to the exclusion of print.

text articles. The following is a sample of items found for fasting in the PubMed Central database:

- **A critical role for the peroxisome proliferator-activated receptor [alpha] (PPAR[alpha]) in the cellular fasting response: The PPAR[alpha]-null mouse as a model of fatty acid oxidation disorders.** by Leone TC, Weinheimer CJ, Kelly DP.; 1999 Jun 22;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=22110
- **An observational study comparing 2-hour 75-g oral glucose tolerance with fasting plasma glucose in pregnant women: both poorly predictive of birth weight.** by Ouzilleau C, Roy MA, Leblanc L, Carpentier A, Maheux P.; 2003 Feb 18;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=143544
- **Attitudes of Mexican anesthesiologists to indicate preoperative fasting periods: A cross-sectional survey.** by Ramirez-Mora JC, Moyao-Garcia D, Nava-Ocampo AA.; 2002;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=116440
- **Effect of Fasting on Temporal Variation in the Nephrotoxicity of Amphotericin B in Rats.** by LeBrun M, Grenier L, Bergeron MG, Thibault L, Labrecque G, Beauchamp D.; 1999 Mar;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=89154
- **Effects of fasting on temporal variations in nephrotoxicity of gentamicin in rats.** by Beauchamp D, Collin P, Grenier L, LeBrun M, Couture M, Thibault L, Labrecque G, Bergeron MG.; 1996 Mar;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=163178
- **Effects of Greek orthodox christian church fasting on serum lipids and obesity.** by Sarri KO, Tzanakis NE, Linardakis MK, Mamalakis GD, Kafatos AG.; 2003;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=156653
- **High Density Lipoprotein is the Major Carrier of Lipid Hydroperoxides in Human Blood Plasma from Fasting Donors.** by Bowry VW, Stanley KK, Stocker R.; 1992 Nov 1;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=50329
- **Is fasting a necessary preparation for abdominal ultrasound?** by Sinan T, Leven H, Sheikh M.; 2003;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=183866
- **Obese Gene Expression: Reduction by Fasting and Stimulation by Insulin and Glucose in Lean Mice, and Persistent Elevation in Acquired (Diet-Induced) and Genetic (Yellow Agouti) Obesity.** by Mizuno TM, Bergen H, Funabashi T, Kleopoulos SP, Zhong Y, Bauman WA, Mobbs CV.; 1996 Apr 16;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=39626
- **Pharmacokinetics of Ethambutol under Fasting Conditions, with Food, and with Antacids.** by Peloquin CA, Bulpitt AE, Jaresko GS, Jelliffe RW, Childs JM, Nix DE.; 1999 Mar;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=89161
- **Pharmacokinetics of Ethionamide Administered under Fasting Conditions or with Orange Juice, Food, or Antacids.** by Auclair B, Nix DE, Adam RD, James GT, Peloquin CA.; 2001 Mar;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=90379

- **QT Interval Lengthening after Fasting Complicated by a Sudden Attack of Torsades de Pointes.** by Petrov DB.; 2003;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=152848
- **Role of glucocorticoids in mediating effects of fasting and diabetes on hypothalamic gene expression.** by Makimura H, Mizuno TM, Isoda F, Beasley J, Silverstein JH, Mobbs CV.; 2003;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=179893
- **Using fasting plasma glucose concentrations to screen for gestational diabetes mellitus: prospective population based study.** by Perucchini D, Fischer U, Spinas GA, Huch R, Huch A, Lehmann R.; 1999 Sep 25;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=28232

The National Library of Medicine: PubMed

One of the quickest and most comprehensive ways to find academic studies in both English and other languages is to use PubMed, maintained by the National Library of Medicine.[6] The advantage of PubMed over previously mentioned sources is that it covers a greater number of domestic and foreign references. It is also free to use. If the publisher has a Web site that offers full text of its journals, PubMed will provide links to that site, as well as to sites offering other related data. User registration, a subscription fee, or some other type of fee may be required to access the full text of articles in some journals.

To generate your own bibliography of studies dealing with fasting, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "fasting" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for fasting (hyperlinks lead to article summaries):

- **A liberalized fasting guideline for formula-fed infants does not increase average gastric fluid volume before elective surgery.**
  Author(s): Cook-Sather SD, Harris KA, Chiavacci R, Gallagher PR, Schreiner MS.
  Source: Anesthesia and Analgesia. 2003 April; 96(4): 965-9, Table of Contents.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12651643&dopt=Abstract

- **A novel mitochondrial carnitine-acylcarnitine translocase induced by partial hepatectomy and fasting.**
  Author(s): Sekoguchi E, Sato N, Yasui A, Fukada S, Nimura Y, Aburatani H, Ikeda K, Matsuura A.
  Source: The Journal of Biological Chemistry. 2003 October 3; 278(40): 38796-802. Epub 2003 July 25.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12882971&dopt=Abstract

[6] PubMed was developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM) at the National Institutes of Health (NIH). The PubMed database was developed in conjunction with publishers of biomedical literature as a search tool for accessing literature citations and linking to full-text journal articles at Web sites of participating publishers. Publishers that participate in PubMed supply NLM with their citations electronically prior to or at the time of publication.

- **A postnatal fasting plasma glucose is useful in determining which women with gestational diabetes should undergo a postnatal oral glucose tolerance test.**
  Author(s): Holt RI, Goddard JR, Clarke P, Coleman MA.
  Source: Diabetic Medicine : a Journal of the British Diabetic Association. 2003 July; 20(7): 594-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12823243&dopt=Abstract

- **Advising patients with diabetes about fasting during Ramadhan.**
  Author(s): Khodabukus R.
  Source: Nurs Times. 2003 July 15-21; 99(28): 26-7. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12889305&dopt=Abstract

- **Alcohol consumption and risk for development of impaired fasting glucose or type 2 diabetes in middle-aged Japanese men.**
  Author(s): Nakanishi N, Suzuki K, Tatara K.
  Source: Diabetes Care. 2003 January; 26(1): 48-54.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12502657&dopt=Abstract

- **An observational study comparing 2-hour 75-g oral glucose tolerance with fasting plasma glucose in pregnant women: both poorly predictive of birth weight.**
  Author(s): Ouzilleau C, Roy MA, Leblanc L, Carpentier A, Maheux P.
  Source: Cmaj : Canadian Medical Association Journal = Journal De L'association Medicale Canadienne. 2003 February 18; 168(4): 403-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12591779&dopt=Abstract

- **Assessment of insulin sensitivity based on a fasting blood sample in men with liver cirrhosis before and after liver transplantation.**
  Author(s): Perseghin G, Caumo A, Mazzaferro V, Pulvirenti A, Piceni Sereni L, Romito R, Lattuada G, Coppa J, Costantino F, Regalia E, Luzi L.
  Source: Transplantation. 2003 August 27; 76(4): 697-702.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12973112&dopt=Abstract

- **Association between insulin resistance and carotid arteriosclerosis in subjects with normal fasting glucose and normal glucose tolerance.**
  Author(s): Ishizaka N, Ishizaka Y, Takahashi E, Unuma T, Tooda E, Nagai R, Togo M, Tsukamoto K, Hashimoto H, Yamakado M.
  Source: Arteriosclerosis, Thrombosis, and Vascular Biology. 2003 February 1; 23(2): 295-301.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12588774&dopt=Abstract

- **Association between weight fluctuation and fasting insulin concentration in Japanese men.**
  Author(s): Yatsuya H, Tamakoshi K, Yoshida T, Hori Y, Zhang H, Ishikawa M, Zhu S, Kondo T, Toyoshima H.
  Source: International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity. 2003 April; 27(4): 478-83.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12664081&dopt=Abstract

- **Association of the hormone sensitive lipase -60C > G variant with fasting insulin levels in healthy young men.**
  Author(s): Talmud PJ, Palmen J, Nicaud V, Tiret L; European Atherosclerosis Research II Study.
  Source: Nutr Metab Cardiovasc Dis. 2002 August; 12(4): 173-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12514936&dopt=Abstract

- **Blood pressure, serum lipids, fasting insulin, and adrenal hormones in 12-year-old children born with maternal preeclampsia.**
  Author(s): Tenhola S, Rahiala E, Martikainen A, Halonen P, Voutilainen R.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2003 March; 88(3): 1217-22.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12629109&dopt=Abstract

- **Blunted lipolytic response to fasting in abdominally obese women: evidence for involvement of hyposomatotropism.**
  Author(s): Buijs MM, Burggraaf J, Wijbrandts C, de Kam ML, Frolich M, Cohen AF, Romijn JA, Sauerwein HP, Meinders AE, Pijl H.
  Source: The American Journal of Clinical Nutrition. 2003 March; 77(3): 544-50.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12600841&dopt=Abstract

- **Both fasting-induced leptin reduction and GH increase are blunted in Cushing's syndrome and in simple obesity.**
  Author(s): Grottoli S, Gauna C, Tassone F, Aimaretti G, Corneli G, Wu Z, Strasburger CJ, Dieguez C, Casanueva FF, Ghigo E, Maccario M.
  Source: Clinical Endocrinology. 2003 February; 58(2): 220-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12580939&dopt=Abstract

- **Central fat predicts deterioration of insulin secretion index and fasting glycaemia: 6-year follow-up of subjects at varying risk of Type 2 diabetes mellitus.**
  Author(s): Kriketos AD, Carey DG, Jenkins AB, Chisholm DJ, Furler SM, Campbell LV.
  Source: Diabetic Medicine : a Journal of the British Diabetic Association. 2003 April; 20(4): 294-300.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12675643&dopt=Abstract

- **Circulating resistin levels are not associated with obesity or insulin resistance in humans and are not regulated by fasting or leptin administration: cross-sectional and interventional studies in normal, insulin-resistant, and diabetic subjects.**
  Author(s): Lee JH, Chan JL, Yiannakouris N, Kontogianni M, Estrada E, Seip R, Orlova C, Mantzoros CS.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2003 October; 88(10): 4848-56.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14557464&dopt=Abstract

- **Colonic preparation correlates with fasting breath hydrogen in patients undergoing colonoscopy.**
  Author(s): Mann NS, Condon DS, Leung JW.
  Source: Hepatogastroenterology. 2003 January-February; 50(49): 85-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12629997&dopt=Abstract

- **Comparison of a clinical model, the oral glucose tolerance test, and fasting glucose for prediction of type 2 diabetes risk in Japanese Americans.**
  Author(s): McNeely MJ, Boyko EJ, Leonetti DL, Kahn SE, Fujimoto WY.
  Source: Diabetes Care. 2003 March; 26(3): 758-63.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12610034&dopt=Abstract

- **Contributions of fasting and postprandial plasma glucose increments to the overall diurnal hyperglycemia of type 2 diabetic patients: variations with increasing levels of HbA(1c).**
  Author(s): Monnier L, Lapinski H, Colette C.
  Source: Diabetes Care. 2003 March; 26(3): 881-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12610053&dopt=Abstract

- **C-reactive protein is more strongly related to post-glucose load glucose than to fasting glucose in non-diabetic subjects; the Insulin Resistance Atherosclerosis Study.**
  Author(s): Festa A, D'Agostino R Jr, Tracy RP, Haffner SM.
  Source: Diabetic Medicine : a Journal of the British Diabetic Association. 2002 November; 19(11): 939-43.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12421431&dopt=Abstract

- **Cross-sectional and prospective relationships of fasting plasma ghrelin concentrations with anthropometric measures in pima Indian children.**
  Author(s): Bunt JC, Salbe AD, Tschop MH, DelParigi A, Daychild P, Tataranni PA.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2003 August; 88(8): 3756-61.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12915665&dopt=Abstract

- **Daytime sleepiness during Ramadan intermittent fasting: polysomnographic and quantitative waking EEG study.**
  Author(s): Roky R, Chapotot F, Benchekroun MT, Benaji B, Hakkou F, Elkhalifi H, Buguet A.
  Source: Journal of Sleep Research. 2003 June; 12(2): 95-101.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12753346&dopt=Abstract

- **Decreased glucagon-like peptide 1 fasting levels in type 2 diabetes.**
  Author(s): Legakis IN, Tzioras C, Phenekos C.
  Source: Diabetes Care. 2003 January; 26(1): 252.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12502699&dopt=Abstract

- **Decreasing serum concentrations of all-trans, 13-cis retinoic acids and retinol during fasting and caloric restriction.**
  Author(s): Berggren Soderlund M, Fex G, Nilsson-Ehle P.
  Source: Journal of Internal Medicine. 2003 March; 253(3): 375-80.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12603506&dopt=Abstract

- **Diabetes and impaired fasting glycemia in a rural population of Bangladesh.**
  Author(s): Sayeed MA, Mahtab H, Akter Khanam P, Abdul Latif Z, Keramat Ali SM, Banu A, Ahren B, Azad Khan AK.
  Source: Diabetes Care. 2003 April; 26(4): 1034-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12663569&dopt=Abstract

- **Disproportionately elevated fasting proinsulin levels in normoglycemic patients with thalassemia major are correlated to the degree of iron overload.**
  Author(s): Cario H, Holl RW, Debatin KM, Kohne E.
  Source: Hormone Research. 2003; 59(2): 73-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12589110&dopt=Abstract

- **Distribution of fasting plasma insulin, free fatty acids, and glucose concentrations and of homeostasis model assessment of insulin resistance in a representative sample of Quebec children and adolescents.**
  Author(s): Allard P, Delvin EE, Paradis G, Hanley JA, O'Loughlin J, Lavallee C, Levy E, Lambert M.
  Source: Clinical Chemistry. 2003 April; 49(4): 644-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12651818&dopt=Abstract

- **Does a homeopathic ultramolecular dilution of Thyroidinum 30cH affect the rate of body weight reduction in fasting patients? A randomised placebo-controlled double-blind clinical trial.**
  Author(s): Schmidt JM, Ostermayr B.
  Source: Homeopathy. 2002 October; 91(4): 197-206.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12422922&dopt=Abstract

- **Does fasting during Ramadan alter body composition, blood constituents and physical performance?**
  Author(s): Ramadan J.
  Source: Medical Principles and Practice : International Journal of the Kuwait University, Health Science Centre. 2002; 11 Suppl 2: 41-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12444309&dopt=Abstract

- **Effect of desirable fasting triglycerides on the postprandial response to dietary fat.**
  Author(s): Miller M, Zhan M, Georgopoulos A.
  Source: Journal of Investigative Medicine : the Official Publication of the American Federation for Clinical Research. 2003 February; 51(1): 50-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12580321&dopt=Abstract

- **Effect of fasting glucose levels on mortality rate in patients with and without diabetes mellitus and coronary artery disease undergoing percutaneous coronary intervention.**
  Author(s): Muhlestein JB, Anderson JL, Horne BD, Lavasani F, Allen Maycock CA, Bair TL, Pearson RR, Carlquist JF; Intermountain Heart Collaborative Study Group.
  Source: American Heart Journal. 2003 August; 146(2): 351-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12891207&dopt=Abstract

- **Effect of short-term fasting and refeeding on transcriptional regulation of metabolic genes in human skeletal muscle.**
  Author(s): Pilegaard H, Saltin B, Neufer PD.
  Source: Diabetes. 2003 March; 52(3): 657-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12606505&dopt=Abstract

- **Effects of acute administration of doxazosin on fasting and postprandial haemodynamics and lipid metabolism in healthy subjects.**
  Author(s): Ulahannan TJ, Karpe F, Humphreys SM, Matthews DR, Frayn KN.
  Source: Hormone and Metabolic Research. Hormon- Und Stoffwechselforschung. Hormones Et Metabolisme. 2002 September; 34(9): 499-503.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12384826&dopt=Abstract

- **Effects of dietary fat quantity and composition on fasting and postprandial levels of coagulation factor VII and serum choline-containing phospholipids.**
  Author(s): Lindman AS, Muller H, Seljeflot I, Prydz H, Veierod M, Pedersen JI.
  Source: The British Journal of Nutrition. 2003 August; 90(2): 329-36.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12908893&dopt=Abstract

- **Effects of dietary saturated, monounsaturated and n-3 fatty acids on fasting lipoproteins, LDL size and post-prandial lipid metabolism in healthy subjects.**
  Author(s): Rivellese AA, Maffettone A, Vessby B, Uusitupa M, Hermansen K, Berglund L, Louheranta A, Meyer BJ, Riccardi G.
  Source: Atherosclerosis. 2003 March; 167(1): 149-58.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12618280&dopt=Abstract

- **Effects of GH on urea, glucose and lipid metabolism, and insulin sensitivity during fasting in GH-deficient patients.**
  Author(s): Norrelund H, Djurhuus C, Jorgensen JO, Nielsen S, Nair KS, Schmitz O, Christiansen JS, Moller N.
  Source: American Journal of Physiology. Endocrinology and Metabolism. 2003 October; 285(4): E737-43. Epub 2003 June 10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12799313&dopt=Abstract

- **Effects of ileal bile salts on fasting small intestinal and gallbladder motility.**
  Author(s): Van Ooteghem NA, Van Erpecum KJ, Van Berge-Henegouwen GP.
  Source: Neurogastroenterology and Motility : the Official Journal of the European Gastrointestinal Motility Society. 2002 October; 14(5): 527-33.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12358681&dopt=Abstract

- **Effects of long-term fasting on insulin responses to fatty acids in man.**
  Author(s): Qvigstad E, Bjerve KS, Grill V.
  Source: Scandinavian Journal of Clinical and Laboratory Investigation. 2002; 62(4): 271-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12476925&dopt=Abstract

- **Effects of one week juice fasting on lipid metabolism: a cohort study in healthy subjects.**
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  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12742806&dopt=Abstract

- **Serum adiponectin levels are inversely associated with overall and central fat distribution but are not directly regulated by acute fasting or leptin administration in humans: cross-sectional and interventional studies.**
  Author(s): Gavrila A, Chan JL, Yiannakouris N, Kontogianni M, Miller LC, Orlova C, Mantzoros CS.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2003 October; 88(10): 4823-31.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14557461&dopt=Abstract

- **Serum gamma-glutamyltransferase and development of impaired fasting glucose or type 2 diabetes in middle-aged Japanese men.**
  Author(s): Nakanishi N, Nishina K, Li W, Sato M, Suzuki K, Tatara K.
  Source: Journal of Internal Medicine. 2003 September; 254(3): 287-95.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12930239&dopt=Abstract

- **Serum leptin levels in acromegaly--a significant role for adipose tissue and fasting insulin/glucose ratio.**
  Author(s): Bolanowski M, Milewicz A, Bidzinska B, Jedrzejuk D, Daroszewski J, Mikulski E.
  Source: Medical Science Monitor : International Medical Journal of Experimental and Clinical Research. 2002 October; 8(10): Cr685-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12388920&dopt=Abstract

- **Serum sialic acid, a possible cardiovascular risk factor is not increased in Fijian Melanesians with impaired glucose tolerance or impaired fasting glucose.**
  Author(s): Crook MA, Goldsmith L, Ameerally P, Lumb P, Singh N, Miell J, Russell-Jones D.
  Source: Annals of Clinical Biochemistry. 2002 November; 39(Pt 6): 606-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12564845&dopt=Abstract

- **Synthetic exendin-4 (exenatide) significantly reduces postprandial and fasting plasma glucose in subjects with type 2 diabetes.**
  Author(s): Kolterman OG, Buse JB, Fineman MS, Gaines E, Heintz S, Bicsak TA, Taylor K, Kim D, Aisporna M, Wang Y, Baron AD.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2003 July; 88(7): 3082-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12843147&dopt=Abstract

- **The decisive role of free fatty acids for protein conservation during fasting in humans with and without growth hormone.**
  Author(s): Norrelund H, Nair KS, Nielsen S, Frystyk J, Ivarsen P, Jorgensen JO, Christiansen JS, Moller N.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2003 September; 88(9): 4371-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12970312&dopt=Abstract

- **The diagnosis of fasting hypoglycemia due to an islet-cell tumor obscured by a highly specific insulin assay.**
  Author(s): Chia CW, Saudek CD.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2003 April; 88(4): 1464-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12679423&dopt=Abstract

- **The effect of dehydration and fasting on ocular blood flow.**
  Author(s): Inan UU, Yucel A, Ermis SS, Ozturk F.
  Source: Journal of Glaucoma. 2002 October; 11(5): 411-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12362080&dopt=Abstract

- **The effect of growth hormone on the insulin-like growth factor system during fasting.**
  Author(s): Norrelund H, Frystyk J, Jorgensen JO, Moller N, Christiansen JS, Orskov H, Flyvbjerg A.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2003 July; 88(7): 3292-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12843178&dopt=Abstract

- **The effect of maternal fasting on the fetal biophysical profile.**
  Author(s): Mirghani HM, Weerasinghe DS, Ezimokhai M, Smith JR.
  Source: International Journal of Gynaecology and Obstetrics: the Official Organ of the International Federation of Gynaecology and Obstetrics. 2003 April; 81(1): 17-21.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12676388&dopt=Abstract

- **The presence of a common mitochondrial DNA variant is associated with fasting insulin levels in Europeans in Auckland.**
  Author(s): Poulton J, Bednarz AL, Scott-Brown M, Thompson C, Macaulay VA, Simmons D.
  Source: Diabetic Medicine : a Journal of the British Diabetic Association. 2002 November; 19(11): 969-71.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12421439&dopt=Abstract

- **The quantitative insulin sensitivity check index QUICKI predicts the onset of type 2 diabetes better than fasting plasma insulin in obese subjects: a 5-year follow-up study.**
  Author(s): Vanhala P, Vanhala M, Kumpusalo E, Keinanen-Kiukaanniemi S.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2002 December; 87(12): 5834-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12466395&dopt=Abstract

- **The relationship between nonfasting and fasting lipid measurements in patients with or without type 2 diabetes mellitus receiving treatment with 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors.**
  Author(s): Weiss R, Harder M, Rowe J.
  Source: Clinical Therapeutics. 2003 May; 25(5): 1490-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12867223&dopt=Abstract

- **The role of growth hormone in the regulation of protein metabolism with particular reference to conditions of fasting.**
  Author(s): Moller N, Norrelund H.
  Source: Hormone Research. 2003; 59 Suppl 1: 62-8. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12566723&dopt=Abstract

- **The short-term effects of fasting on the neuroendocrine system in patients with chronic pain syndromes.**
  Author(s): Michalsen A, Schneider S, Rodenbeck A, Ludtke R, Huether G, Dobos GJ.
  Source: Nutritional Neuroscience. 2003 February; 6(1): 11-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12608732&dopt=Abstract

- **The vitamin D receptor gene variant and physical activity predicts fasting glucose levels in healthy young men.**
  Author(s): Ortlepp JR, Metrikat J, Albrecht M, von Korff A, Hanrath P, Hoffmann R.
  Source: Diabetic Medicine : a Journal of the British Diabetic Association. 2003 June; 20(6): 451-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12786678&dopt=Abstract

- **Time-course of adiposity and fasting insulin from childhood to young adulthood in offspring of parents with coronary artery disease: the Bogalusa Heart Study.**
  Author(s): Youssef AA, Valdez R, Elkasabany A, Srinivasan SR, Berenson GS.
  Source: Annals of Epidemiology. 2002 November; 12(8): 553-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12495828&dopt=Abstract

- **Urinary cadmium, impaired fasting glucose, and diabetes in the NHANES III.**
  Author(s): Schwartz GG, Il'yasova D, Ivanova A.
  Source: Diabetes Care. 2003 February; 26(2): 468-70.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12547882&dopt=Abstract

- **U-shaped association between white blood cell count and fasting plasma glucose level.**
  Author(s): Tamakoshi K, Yatsuya H, Kondo T, Hori Y, Zhang H, Ishikawa M, Murata C, Otsuka R, Zhu S, Toyoshima H.
  Source: Diabetes Care. 2003 March; 26(3): 950.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12610067&dopt=Abstract

CHAPTER 2. NUTRITION AND FASTING

Overview

In this chapter, we will show you how to find studies dedicated specifically to nutrition and fasting.

Finding Nutrition Studies on Fasting

The National Institutes of Health's Office of Dietary Supplements (ODS) offers a searchable bibliographic database called the IBIDS (International Bibliographic Information on Dietary Supplements; National Institutes of Health, Building 31, Room 1B29, 31 Center Drive, MSC 2086, Bethesda, Maryland 20892-2086, Tel: 301-435-2920, Fax: 301-480-1845, E-mail: ods@nih.gov). The IBIDS contains over 460,000 scientific citations and summaries about dietary supplements and nutrition as well as references to published international, scientific literature on dietary supplements such as vitamins, minerals, and botanicals.[7] The IBIDS includes references and citations to both human and animal research studies.

As a service of the ODS, access to the IBIDS database is available free of charge at the following Web address: **http://ods.od.nih.gov/databases/ibids.html**. After entering the search area, you have three choices: (1) IBIDS Consumer Database, (2) Full IBIDS Database, or (3) Peer Reviewed Citations Only.

Now that you have selected a database, click on the "Advanced" tab. An advanced search allows you to retrieve up to 100 fully explained references in a comprehensive format. Type "fasting" (or synonyms) into the search box, and click "Go." To narrow the search, you can also select the "Title" field.

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[7] Adapted from **http://ods.od.nih.gov**. IBIDS is produced by the Office of Dietary Supplements (ODS) at the National Institutes of Health to assist the public, healthcare providers, educators, and researchers in locating credible, scientific information on dietary supplements. IBIDS was developed and will be maintained through an interagency partnership with the Food and Nutrition Information Center of the National Agricultural Library, U.S. Department of Agriculture.

The following is a typical result when searching for recently indexed consumer information on fasting:

- **A biochemical study of fasting, subfeeding, and recovery processes in yellow-legged gulls.**
  Author(s): Department of Applied Biology, Estacion Biologica de Donana, Pabellon del Peru, Consejo Superior de Investigaciones Cientificas, Avenida de Maria Luisa s/n 41013 Seville, Spain. alonso@ebd.csic.es
  Source: Alonso Alvarez, C Ferrer, M Physiol-Biochem-Zool. 2001 Sep-October; 74(5): 703-13 1522-2152

- **Beta(1)/beta(2)/beta(3)-adrenoceptor knockout mice are obese and cold-sensitive but have normal lipolytic responses to fasting.**
  Author(s): Departement de Biochimie Medicale, Centre Medical Universitaire, 1, rue Michel-Servet, 1211 Geneve 4, Switzerland. maria.jimenez@medecine.unige.ch
  Source: Jimenez, M Leger, B Canola, K Lehr, L Arboit, P Seydoux, J Russell, A P Giacobino, J P Muzzin, P Preitner, F FEBS-Lett. 2002 October 23; 530(1-3): 37-40 0014-5793

- **Blood sugar control among fasting Muslims with type 2 diabetes mellitus in Ilorin.**
  Author(s): Department of Medicine, University of Ilorin, Ilorin.
  Source: Katibi, I A Akande, A A Bojuwoye, B J Okesina, A B Niger-J-Med. 2001 Jul-September; 10(3): 132-4 1115-2613

- **Determinants of fasting glucose in young Guatemalan adults.**
  Author(s): Department of International Health, Rollins School of Public Health Atlanta, GA 30322, USA. aconlis@emory.edu
  Source: Conlisk, A J Stein, A D Schroeder, D G Torun, B Grajeda, R Martorell, R Ethn-Dis. 2001 Fall; 11(4): 585-97 1049-510X

- **Effects of fasting on corticosterone production by zona fasciculata-reticularis cells in ovariectomized rats.**
  Author(s): Department of Chemical Engineering, Chinese Culture University, Taipei, Taiwan, Republic of China.
  Source: Chang, Ling Ling Kau, Mei Mei Wun, Wan Song Alfred Ho, Low Tone Wang, Paulus S J-Investig-Med. 2002 March; 50(2): 86-94 1081-5589

- **Effects of short-term modest weight loss on fasting and post-prandial lipoprotein sub-fractions in type 2 diabetes mellitus patients.**
  Author(s): Departamento de obstetricia y gynecologia, Instituto Universitario Dexeus, Universidad autonoma de Barcelona, Barcelona, Spain.
  Source: Ybarra, J James, R W Makoundou, V Bioletto, S Golay, A Diabetes-Metab. 2001 December; 27(6): 701-8 1262-3636

- **Fasting and lactation effect fat-soluble vitamin A and E levels in blood and their distribution in tissue of grey seals (Halichoerus grypus).**
  Author(s): Institute of Nutritional Science, University of Potsdam, Arthur-Scheunert-Allee 114-116, D-14558 Bergholz-Rehbrucke, Potsdam, Germany. fjschwei@rz.uni-potsdam.de
  Source: Schweigert, Florian J Luppertz, Martina Stobo, Wayne T Comp-Biochem-Physiol-A-Mol-Integr-Physiol. 2002 April; 131(4): 901-8 1095-6433

- **Fasting limits the increase in intracellular calcium during ischemia in isolated rat hearts.**
  Author(s): Columbia University, Dept. of Cardiology, New York, NY 10032, USA.

Source: Ramasamy, R Liu, H Cherednichenko, G Schaefer, S Basic-Res-Cardiol. 2001 September; 96(5): 463-70 0300-8428

- **Impaired fasting glycaemia and undiagnosed diabetes: prevalence, cardiovascular and behavioural risk factors.**
  Author(s): Department of Endocrinology, Centre Hospitalo-Universitaire, Tours, France. lecomte@med.univ-tours.fr
  Source: Lecomte, P Vol, S Caces, E Lasfargues, G Combe, H Laurent, S Tichet, J Diabetes-Metab. 2002 September; 28(4 Pt 1): 311-20 1262-3636

- **Intermittent fasting during winter and spring affects body composition and reproduction of a migratory duck.**
  Author(s): Institute of Arctic Biology, and Department of Biology and Wildlife, University of Alaska Fairbanks, PO Box 757000, Room 311 Irving I, Fairbanks AK 99775-7000 USA. ffpsb@uaf.edu
  Source: Barboza, P S Jorde, D G J-Comp-Physiol-[B]. 2002 July; 172(5): 419-34 0174-1578

- **Low fasting serum triglyceride and high free fatty acid levels in pulmonary fibrosis: a previously unreported finding.**
  Author(s): Department of Medicina Interna e Patologie Sistemiche, University of Catania Medical School, Garibaldi Hospital, 95123 Catania, Italy.
  Source: Iannello, Silvia Cavaleri, Antonina Camuto, Massimo Pisano, Maria Grazia Milazzo, Paolina Belfiore, Francesco MedGenMed. 2002 June 14; 4(2): 5 1531-0132

- **Muscarinic cholinergic receptor blockade impairs free fatty acid mobilization during fasting in pigeons (Columba livia).**
  Author(s): Department of Physiological Sciences, CCB, Federal University of Santa Catarina, Florianopolis SC, Brazil.
  Source: de Azevedo, L C Zizemer, J R Hackl, L P Marino Neto, J Paschoalini, M A J-Comp-Physiol-[B]. 2002 February; 172(2): 115-23 0174-1578

- **Myocardial FDG-PET examination during fasting and glucose loading states by means of a one-day protocol.**
  Author(s): Department of Radiology, Fukui Medical University, Matsuoka, Japan. tsucchy@fmsrsa.fukui-med.ac.jp
  Source: Tsuchida, T Sadato, N Yonekura, Y Sugimoto, K Nakano, A Lee, J D Takahashi, N Waki, A Ishii, Y Itoh, H Ann-Nucl-Med. 2001 October; 15(5): 433-8 0914-7187

- **Proposed biomolecular theory of fasting during fevers due to infection.**
  Author(s): Botanical Medicine Academy, 69113 Camp Polk Rd, Sisters OR 97759, USA. dryarnell@bendnet.com
  Source: Yarnell, E Altern-Med-Revolume 2001 October; 6(5): 482-7 1089-5159

- **Severe catabolic state after prolonged fasting in cirrhotic patients: effect of oral branched-chain amino-acid-enriched nutrient mixture.**
  Author(s): Department of Nutrition, The University of Tokushima, School of Medicine, Japan.
  Source: Nakaya, Y Harada, N Kakui, S Okada, K Takahashi, A Inoi, J Ito, S J-Gastroenterol. 2002; 37(7): 531-6 0944-1174

- **The dietary composition of pre-fast meals and its effect on 24 hour food and water fasting.**
  Author(s): Department of Cardiology, Sieff Government Hospital, Safed, Israel. blond@netvision.net.il
  Source: Blondheim, D S Blondheim, O Blondheim, S H Isr-Med-Assoc-J. 2001 September; 3(9): 657-62 1565-1088

- **The effects of vitamin B2 deficiency on stored fuel utilization during 3 days fasting or 6 days underfeeding in rats.**
  Author(s): Duksung Women' s University, Seoul (Korea Republic). Department of Food and Nutrition
  Source: Cho, Y.O. Sul, S.M. Choi, S.S. Journal-of-the-Korean-Society-of-Food-and-Nutrition (Korea Republic). (April 1996). volume 25(2) page 181-187. 0253-3154

- **The NEPI antidiabetes study (NANSY). 1: short-term dose-effect relations of glimepiride in subjects with impaired fasting glucose.**
  Author(s): Skaraborg Institute, Skovde, Sweden.
  Source: Lindblad, U Lindwall, K Sjostrand, A Ranstam, J Melander, A Diabetes-Obes-Metab. 2001 December; 3(6): 443-51 1462-8902

- **Tumour necrosis factor-alpha induced inhibition of protein synthesis in rat aortic smooth muscle: effect of glucose and branched-chain amino acids during fasting.**
  Author(s): Department of Biology, Bethune-Cookman College, Daytona Beach, Florida 32114 (USA)
  Source: Cheema, I.R. Hermann, C. Scott, T. Postell, S. Biomedical-Letters (United Kingdom). (1998). volume 57(226) page 93-100.

- **VGF is required for obesity induced by diet, gold thioglucose treatment, and agouti and is differentially regulated in pro-opiomelanocortin- and neuropeptide Y-containing arcuate neurons in response to fasting.**
  Author(s): Fishberg Research Center for Neurobiology, Mount Sinai School of Medicine, New York, New York 10029, USA.
  Source: Hahm, Seung Fekete, Csaba Mizuno, Tooru M Windsor, Joan Yan, Hai Boozer, Carol N Lee, Charlotte Elmquist, Joel K Lechan, Ronald M Mobbs, Charles V Salton, Stephen R J J-Neurosci. 2002 August 15; 22(16): 6929-38 1529-2401

The following information is typical of that found when using the "Full IBIDS Database" to search for "fasting" (or a synonym):

- **A biochemical study of fasting, subfeeding, and recovery processes in yellow-legged gulls.**
  Author(s): Department of Applied Biology, Estacion Biologica de Donana, Pabellon del Peru, Consejo Superior de Investigaciones Cientificas, Avenida de Maria Luisa s/n 41013 Seville, Spain. alonso@ebd.csic.es
  Source: Alonso Alvarez, C Ferrer, M Physiol-Biochem-Zool. 2001 Sep-October; 74(5): 703-13 1522-2152

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  Source: Chang, Ling Ling Kau, Mei Mei Wun, Wan Song Alfred Ho, Low Tone Wang, Paulus S J-Investig-Med. 2002 March; 50(2): 86-94 1081-5589

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  Source: Lindblad, U Lindwall, K Sjostrand, A Ranstam, J Melander, A Diabetes-Obes-Metab. 2001 December; 3(6): 443-51 1462-8902

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Federal Resources on Nutrition

In addition to the IBIDS, the United States Department of Health and Human Services (HHS) and the United States Department of Agriculture (USDA) provide many sources of information on general nutrition and health. Recommended resources include:

- healthfinder®, HHS's gateway to health information, including diet and nutrition: **http://www.healthfinder.gov/scripts/SearchContext.asp?topic=238&page=0**
- The United States Department of Agriculture's Web site dedicated to nutrition information: **www.nutrition.gov**
- The Food and Drug Administration's Web site for federal food safety information: **www.foodsafety.gov**
- The National Action Plan on Overweight and Obesity sponsored by the United States Surgeon General: **http://www.surgeongeneral.gov/topics/obesity/**
- The Center for Food Safety and Applied Nutrition has an Internet site sponsored by the Food and Drug Administration and the Department of Health and Human Services: **http://vm.cfsan.fda.gov/**
- Center for Nutrition Policy and Promotion sponsored by the United States Department of Agriculture: **http://www.usda.gov/cnpp/**
- Food and Nutrition Information Center, National Agricultural Library sponsored by the United States Department of Agriculture: **http://www.nal.usda.gov/fnic/**
- Food and Nutrition Service sponsored by the United States Department of Agriculture: **http://www.fns.usda.gov/fns/**

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering food and nutrition. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=174&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/med_nutrition.html**
- Google: **http://directory.google.com/Top/Health/Nutrition/**
- Healthnotes: **http://www.healthnotes.com/**
- Open Directory Project: **http://dmoz.org/Health/Nutrition/**
- Yahoo.com: **http://dir.yahoo.com/Health/Nutrition/**
- WebMD®Health: **http://my.webmd.com/nutrition**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**

The following is a specific Web list relating to fasting; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **Vitamins**

  Folic Acid
  Source: Healthnotes, Inc.; www.healthnotes.com

  Pyridoxine
  Source: Integrative Medicine Communications; www.drkoop.com

  Vitamin B6
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Vitamin B6 (pyridoxine)
  Source: Integrative Medicine Communications; www.drkoop.com

- **Minerals**

  Betaine Hydrochloride
  Source: Healthnotes, Inc.; www.healthnotes.com

  Chromium
  Source: Integrative Medicine Communications; www.drkoop.com

  Chromium
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Sulfur
  Source: Integrative Medicine Communications; www.drkoop.com

- **Food and Diet**

  Diabetes
  Source: Healthnotes, Inc.; www.healthnotes.com

  Fasting Diet
  Source: Healthnotes, Inc.; www.healthnotes.com

  Fructo-oligosaccharides (FOS) and Other Oligosaccharides
  Source: Healthnotes, Inc.; www.healthnotes.com

  Gluten-free Diet
  Source: Healthnotes, Inc.; www.healthnotes.com

  Special Diets Index
  Source: Healthnotes, Inc.; www.healthnotes.com

  Weight Management Index
  Source: Healthnotes, Inc.; www.healthnotes.com

CHAPTER 3. ALTERNATIVE MEDICINE AND FASTING

Overview

In this chapter, we will begin by introducing you to official information sources on complementary and alternative medicine (CAM) relating to fasting. At the conclusion of this chapter, we will provide additional sources.

National Center for Complementary and Alternative Medicine

The National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (**http://nccam.nih.gov/**) has created a link to the National Library of Medicine's databases to facilitate research for articles that specifically relate to fasting and complementary medicine. To search the database, go to the following Web site: **http://www.nlm.nih.gov/nccam/camonpubmed.html**. Select "CAM on PubMed." Enter "fasting" (or synonyms) into the search box. Click "Go." The following references provide information on particular aspects of complementary and alternative medicine that are related to fasting:

- **A preliminary fast may potentiate response to a subsequent low-salt, low-fat vegan diet in the management of hypertension - fasting as a strategy for breaking metabolic vicious cycles.**
  Author(s): McCarty MF.
  Source: Medical Hypotheses. 2003 May; 60(5): 624-33.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12710893&dopt=Abstract

- **Aqueous extract of Ocimum canum decreases levels of fasting blood glucose and free radicals and increases antiatherogenic lipid levels in mice.**
  Author(s): Nyarko AK, Asare-Anane H, Ofosuhene M, Addy ME, Teye K, Addo P.
  Source: Vascular Pharmacology. 2002 December; 39(6): 273-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14567064&dopt=Abstract

- **Assessing plasma pharmacokinetics of cholesterol following oral coadministration with a novel vegetable stanol mixture to fasting rats.**

Author(s): Wasan KM, Holtorf L, Subramanian R, Cassidy SM, Pritchard PH, Stewart DJ, Novak E, Moghadasian MH.
Source: Journal of Pharmaceutical Sciences. 2001 January; 90(1): 23-8.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11064375&dopt=Abstract

- **Attitudes and practices of breastfeeding mothers regarding fasting in Ramadan.**
  Author(s): Ertem IO, Kaynak G, Kaynak C, Ulukol B, Gulnar SB.
  Source: Child: Care, Health and Development. 2001 November; 27(6): 545-54.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11737021&dopt=Abstract

- **Beneficial changes in serum apo A-1 and its ratio to apo B and HDL in stable hyperlipidaemic subjects after Ramadan fasting in Kuwait.**
  Author(s): Akanji AO, Mojiminiyi OA, Abdella N.
  Source: European Journal of Clinical Nutrition. 2000 June; 54(6): 508-13.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10878654&dopt=Abstract

- **Brief case reports of medically supervised, water-only fasting associated with remission of autoimmune disease.**
  Author(s): Fuhrman J, Sarter B, Calabro DJ.
  Source: Alternative Therapies in Health and Medicine. 2002 July-August; 8(4): 112, 110-1.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12126162&dopt=Abstract

- **Compromised hepatic detoxification in companion animals and its correction via nutritional supplementation and modified fasting.**
  Author(s): Scanlan N.
  Source: Alternative Medicine Review : a Journal of Clinical Therapeutic. 2001 September; 6 Suppl: S24-37. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11591171&dopt=Abstract

- **Decreasing serum concentrations of all-trans, 13-cis retinoic acids and retinol during fasting and caloric restriction.**
  Author(s): Berggren Soderlund M, Fex G, Nilsson-Ehle P.
  Source: Journal of Internal Medicine. 2003 March; 253(3): 375-80.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12603506&dopt=Abstract

- **Dietary L-carnitine supplementation in obese cats alters carnitine metabolism and decreases ketosis during fasting and induced hepatic lipidosis.**
  Author(s): Blanchard G, Paragon BM, Milliat F, Lutton C.
  Source: The Journal of Nutrition. 2002 February; 132(2): 204-10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11823579&dopt=Abstract

- **Does a homeopathic ultramolecular dilution of Thyroidinum 30cH affect the rate of body weight reduction in fasting patients? A randomised placebo-controlled double-blind clinical trial.**
  Author(s): Schmidt JM, Ostermayr B.
  Source: Homeopathy. 2002 October; 91(4): 197-206.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12422922&dopt=Abstract

- **Effect of a lacto-ovo vegetarian diet on fasting small intestinal motility.**
  Author(s): Andrews JM, Doran SM, Di Matteo AC, Leong L, Macintosh C, Chiu CJ, Read NW, Fraser RJ.
  Source: Scandinavian Journal of Gastroenterology. 2001 October; 36(10): 1037-43.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11589375&dopt=Abstract

- **Effect of green tea in the prevention and reversal of fasting-induced intestinal mucosal damage.**
  Author(s): Asfar S, Abdeen S, Dashti H, Khoursheed M, Al-Sayer H, Mathew T, Al-Bader A.
  Source: Nutrition (Burbank, Los Angeles County, Calif.). 2003 June; 19(6): 536-40.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12781855&dopt=Abstract

- **Effect of long-chain n-3 polyunsaturated fatty acids on fasting and postprandial triacylglycerol metabolism.**
  Author(s): Roche HM, Gibney MJ.
  Source: The American Journal of Clinical Nutrition. 2000 January; 71(1 Suppl): 232S-7S. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10617977&dopt=Abstract

- **Effect of Momordica charantia (Karolla) extracts on fasting and postprandial serum glucose levels in NIDDM patients.**
  Author(s): Ahmad N, Hassan MR, Halder H, Bennoor KS.
  Source: Bangladesh Med Res Counc Bull. 1999 April; 25(1): 11-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10758656&dopt=Abstract

- **Effects of dietary fat quantity and composition on fasting and postprandial levels of coagulation factor VII and serum choline-containing phospholipids.**
  Author(s): Lindman AS, Muller H, Seljeflot I, Prydz H, Veierod M, Pedersen JI.
  Source: The British Journal of Nutrition. 2003 August; 90(2): 329-36.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12908893&dopt=Abstract

- **Effects of dietary saturated, monounsaturated and n-3 fatty acids on fasting lipoproteins, LDL size and post-prandial lipid metabolism in healthy subjects.**
  Author(s): Rivellese AA, Maffettone A, Vessby B, Uusitupa M, Hermansen K, Berglund L, Louheranta A, Meyer BJ, Riccardi G.

Source: Atherosclerosis. 2003 March; 167(1): 149-58.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12618280&dopt=Abstract

- **Effects of fasting on muscle mitochondrial energetics and fatty acid metabolism in Ucp3(-/-) and wild-type mice.**
  Author(s): Bezaire V, Hofmann W, Kramer JK, Kozak LP, Harper ME.
  Source: American Journal of Physiology. Endocrinology and Metabolism. 2001 November; 281(5): E975-82.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11595653&dopt=Abstract

- **Effects of L-glutamate supplementation mimic effects of fasting in the ischemic heart.**
  Author(s): Kristiansen SB, Henning O, Nielsen-Kudsk JE, Botker HE, Nielsen TT.
  Source: Apmis. Supplementum. 2003; (109): 117-21.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12874962&dopt=Abstract

- **Effects of one week juice fasting on lipid metabolism: a cohort study in healthy subjects.**
  Author(s): Huber R, Nauck M, Ludtke R, Scharnagl H.
  Source: Forschende Komplementarmedizin Und Klassische Naturheilkunde = Research in Complementary and Natural Classical Medicine. 2003 February; 10(1): 7-10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12624474&dopt=Abstract

- **Experimental observations and clinical implications of fasting and diet supplementation in fatty livers.**
  Author(s): Grattagliano I, Portincasa P, Caraceni P, Palmieri VO, Domenicali M, Bernardi M, Palasciano G.
  Source: Eur Rev Med Pharmacol Sci. 2003 January-February; 7(1): 1-7. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12908728&dopt=Abstract

- **Fasting followed by vegetarian diet in patients with rheumatoid arthritis: a systematic review.**
  Author(s): Muller H, de Toledo FW, Resch KL.
  Source: Scandinavian Journal of Rheumatology. 2001; 30(1): 1-10. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11252685&dopt=Abstract

- **Fasting lipids: the carrot in the snowman.**
  Author(s): Spence JD.
  Source: The Canadian Journal of Cardiology. 2003 July; 19(8): 890-2. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12876608&dopt=Abstract

- **Fasting lipoprotein and postprandial triacylglycerol responses to a low-carbohydrate diet supplemented with n-3 fatty acids.**
  Author(s): Volek JS, Gomez AL, Kraemer WJ.

Source: Journal of the American College of Nutrition. 2000 June; 19(3): 383-91.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10872901&dopt=Abstract

- **Fasting plasma concentrations of selected flavonoids as markers of their ordinary dietary intake.**
  Author(s): Radtke J, Linseisen J, Wolfram G.
  Source: European Journal of Nutrition. 2002 October; 41(5): 203-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12395214&dopt=Abstract

- **Fasting plasma glucose as a screening test for gestational diabetes in a multi-ethnic, high-risk population.**
  Author(s): Agarwal MM, Hughes PF, Punnose J, Ezimokhai M.
  Source: Diabetic Medicine : a Journal of the British Diabetic Association. 2000 October; 17(10): 720-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11110505&dopt=Abstract

- **Historical continuities and discontinuities between religious and medical interpretations of extreme fasting. The background to Giovanni Brugnoli's description of two cases of anorexia nervosa in 1875.**
  Author(s): Habermas T.
  Source: History of Psychiatry. 1992 December; 3(12): 431-55.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11612915&dopt=Abstract

- **Holy anorexia revisited: the reputation of fasting in the case of Maria Janis.**
  Author(s): Carroll LL.
  Source: Psychohist Rev. 1998 Winter; 26(2): 115-36. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11619952&dopt=Abstract

- **Initial cost of care results in medically supervised water-only fasting for treating high blood pressure and diabetes.**
  Author(s): Goldhamer AC.
  Source: Journal of Alternative and Complementary Medicine (New York, N.Y.). 2002 December; 8(6): 696-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12614522&dopt=Abstract

- **Intermittent fasting and dietary supplementation with 2-deoxy-D-glucose improve functional and metabolic cardiovascular risk factors in rats.**
  Author(s): Wan R, Camandola S, Mattson MP.
  Source: The Faseb Journal : Official Publication of the Federation of American Societies for Experimental Biology. 2003 June; 17(9): 1133-4. Epub 2003 April 22.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12709404&dopt=Abstract

- **Low-dose vitamin B-6 effectively lowers fasting plasma homocysteine in healthy elderly persons who are folate and riboflavin replete.**
  Author(s): McKinley MC, McNulty H, McPartlin J, Strain JJ, Pentieva K, Ward M, Weir DG, Scott JM.
  Source: The American Journal of Clinical Nutrition. 2001 April; 73(4): 759-64.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11273851&dopt=Abstract

- **Medically supervised water-only fasting in the treatment of borderline hypertension.**
  Author(s): Goldhamer AC, Lisle DJ, Sultana P, Anderson SV, Parpia B, Hughes B, Campbell TC.
  Source: Journal of Alternative and Complementary Medicine (New York, N.Y.). 2002 October; 8(5): 643-50.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12470446&dopt=Abstract

- **Medically supervised water-only fasting in the treatment of hypertension.**
  Author(s): Ciurleo A, Marchese M.
  Source: Journal of Manipulative and Physiological Therapeutics. 2002 February; 25(2): 138-9; Author Reply 139.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11896385&dopt=Abstract

- **Medically supervised water-only fasting in the treatment of hypertension.**
  Author(s): Goldhamer A, Lisle D, Parpia B, Anderson SV, Campbell TC.
  Source: Journal of Manipulative and Physiological Therapeutics. 2001 June; 24(5): 335-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11416824&dopt=Abstract

- **Moderate-intensity physical activity and fasting insulin levels in women.**
  Author(s): Caspersen CJ, Zack MM, Fulton JE.
  Source: Diabetes Care. 2000 November; 23(11): 1712-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11092306&dopt=Abstract

- **Moderate-intensity physical activity and fasting insulin levels in women: the Cross-Cultural Activity Participation Study.**
  Author(s): Irwin ML, Mayer-Davis EJ, Addy CL, Pate RR, Durstine JL, Stolarczyk LM, Ainsworth BE.
  Source: Diabetes Care. 2000 April; 23(4): 449-54.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10857933&dopt=Abstract

- **Plant- and marine-derived n-3 polyunsaturated fatty acids have differential effects on fasting and postprandial blood lipid concentrations and on the susceptibility of LDL to oxidative modification in moderately hyperlipidemic subjects.**
  Author(s): Finnegan YE, Minihane AM, Leigh-Firbank EC, Kew S, Meijer GW, Muggli R, Calder PC, Williams CM.

Source: The American Journal of Clinical Nutrition. 2003 April; 77(4): 783-95.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12663273&dopt=Abstract

- **Prayer and fasting in the halls of Congress: a pastoral approach to lobbying.**
  Author(s): Duncombe DC.
  Source: J Pastoral Care. 2001 Spring; 55(1): 7-16.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11303455&dopt=Abstract

- **Proposed biomolecular theory of fasting during fevers due to infection.**
  Author(s): Yarnell E.
  Source: Alternative Medicine Review : a Journal of Clinical Therapeutic. 2001 October; 6(5): 482-7. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11703168&dopt=Abstract

- **Rapid hypotensive response to fasting in spontaneously hypertensive rats.**
  Author(s): Fitzgerald SM, Hall JE, Brands MW.
  Source: American Journal of Hypertension : Journal of the American Society of Hypertension. 2001 November; 14(11 Pt 1): 1123-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11724211&dopt=Abstract

- **Regulation of uncoupling protein (UCP) 2 and 3 in adipose and muscle tissue by fasting and growth hormone treatment in obese humans.**
  Author(s): Pedersen SB, Borglum JD, Kristensen K, Norrelund H, Otto J, Jorgensen L, Richelsen B.
  Source: International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity. 2000 August; 24(8): 968-75.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10951534&dopt=Abstract

- **Serum fatty acid composition predicts development of impaired fasting glycaemia and diabetes in middle-aged men.**
  Author(s): Laaksonen DE, Lakka TA, Lakka HM, Nyyssonen K, Rissanen T, Niskanen LK, Salonen JT.
  Source: Diabetic Medicine : a Journal of the British Diabetic Association. 2002 June; 19(6): 456-64.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12060056&dopt=Abstract

- **Serum levels of interleukin-6 and dehydroepiandrosterone sulphate in response to either fasting or a ketogenic diet in rheumatoid arthritis patients.**
  Author(s): Fraser DA, Thoen J, Djoseland O, Forre O, Kjeldsen-Kragh J.
  Source: Clin Exp Rheumatol. 2000 May-June; 18(3): 357-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10895373&dopt=Abstract

- **Synthetic exendin-4 (exenatide) significantly reduces postprandial and fasting plasma glucose in subjects with type 2 diabetes.**
  Author(s): Kolterman OG, Buse JB, Fineman MS, Gaines E, Heintz S, Bicsak TA, Taylor K, Kim D, Aisporna M, Wang Y, Baron AD.
  Source: The Journal of Clinical Endocrinology and Metabolism. 2003 July; 88(7): 3082-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12843147&dopt=Abstract

- **The cholesterol-lowering property of soybeans fed to rats is related to the fasting duration.**
  Author(s): Guermani-Nicolle L, Villaume C, Bau HM, Schwertz A, Nicolas JP, Mejean L.
  Source: Plant Foods for Human Nutrition (Dordrecht, Netherlands). 2001; 56(3): 239-49.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11442224&dopt=Abstract

- **The effect of fasting on the pulse spectrum.**
  Author(s): Su YC, Huang KF, Chang YH, Li TC, Huang WS, Lin JG.
  Source: The American Journal of Chinese Medicine. 2000; 28(3-4): 409-17.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11154055&dopt=Abstract

- **The pregnancy-related decrease in fasting plasma homocysteine is not explained by folic acid supplementation, hemodilution, or a decrease in albumin in a longitudinal study.**
  Author(s): Murphy MM, Scott JM, McPartlin JM, Fernandez-Ballart JD.
  Source: The American Journal of Clinical Nutrition. 2002 September; 76(3): 614-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12198008&dopt=Abstract

- **The short-term effects of fasting on the neuroendocrine system in patients with chronic pain syndromes.**
  Author(s): Michalsen A, Schneider S, Rodenbeck A, Ludtke R, Huether G, Dobos GJ.
  Source: Nutritional Neuroscience. 2003 February; 6(1): 11-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12608732&dopt=Abstract

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering CAM and related topics. The following is a representative sample:

- Alternative Medicine Foundation, Inc.: **http://www.herbmed.org/**
- AOL: **http://search.aol.com/cat.adp?id=169&layer=&from=subcats**
- Chinese Medicine: **http://www.newcenturynutrition.com/**
- drkoop.com®: **http://www.drkoop.com/InteractiveMedicine/IndexC.html**
- Family Village: **http://www.familyvillage.wisc.edu/med_altn.htm**
- Google: **http://directory.google.com/Top/Health/Alternative/**

- Healthnotes: **http://www.healthnotes.com/**
- MedWebPlus: **http://medwebplus.com/subject/Alternative_and_Complementary_Medicine**
- Open Directory Project: **http://dmoz.org/Health/Alternative/**
- HealthGate: **http://www.tnp.com/**
- WebMD®Health: **http://my.webmd.com/drugs_and_herbs**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**
- Yahoo.com: **http://dir.yahoo.com/Health/Alternative_Medicine/**

The following is a specific Web list relating to fasting; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **General Overview**

  Acne Rosacea
  Source: Healthnotes, Inc.; www.healthnotes.com

  Atherosclerosis
  Source: Healthnotes, Inc.; www.healthnotes.com

  Bulimia Nervosa
  Source: Integrative Medicine Communications; www.drkoop.com

  Diabetes
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Diabetes Mellitus
  Source: Integrative Medicine Communications; www.drkoop.com

  Epilepsy
  Source: Healthnotes, Inc.; www.healthnotes.com

  Gestational Hypertension
  Source: Healthnotes, Inc.; www.healthnotes.com

  Heart Attack
  Source: Healthnotes, Inc.; www.healthnotes.com

  Heat Exhaustion
  Source: Integrative Medicine Communications; www.drkoop.com

  High Cholesterol
  Source: Integrative Medicine Communications; www.drkoop.com

  High Homocysteine
  Source: Healthnotes, Inc.; www.healthnotes.com

High Triglycerides
Source: Healthnotes, Inc.; www.healthnotes.com

Hypercholesterolemia
Source: Integrative Medicine Communications; www.drkoop.com

Pancreatitis
Source: Integrative Medicine Communications; www.drkoop.com

Pms
Source: Integrative Medicine Communications; www.drkoop.com

Premenstrual Syndrome
Source: Integrative Medicine Communications; www.drkoop.com

Rheumatoid Arthritis
Source: Healthnotes, Inc.; www.healthnotes.com

Rheumatoid Arthritis
Source: Prima Communications, Inc.www.personalhealthzone.com

- **Alternative Therapy**

Detoxification Therapy
Source: Healthnotes, Inc.; www.healthnotes.com

Detoxification Therapy
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10119,00.html

Dr. Lynch's Holistic Self-health Program
Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D.
Hyperlink: http://www.canoe.ca/AltmedDictionary/d.html

Ehretism
Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D.
Hyperlink: http://www.canoe.ca/AltmedDictionary/e.html

Fasting
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,694,00.html

Mucusless Diet Healing System
Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D.
Hyperlink: http://www.canoe.ca/AltmedDictionary/m.html

Natural Hygiene
Alternative names: Hygienic Health System Life Science
Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D.
Hyperlink: http://www.canoe.ca/AltmedDictionary/n.html

Nature Cure
Alternative names: Nature Care
Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D.
Hyperlink: http://www.canoe.ca/AltmedDictionary/n.html

Naturopathy
Source: Integrative Medicine Communications; www.drkoop.com

Naturopathy
Alternative names: natural healing natural health natural medicine natural therapies nature cure naturology naturopathic healing naturopathic health care naturopathic medicine
Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D.
Hyperlink: http://www.canoe.ca/AltmedDictionary/n.html

Naturopathy
Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,722,00.html

Rational Fasting
Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D.
Hyperlink: http://www.canoe.ca/AltmedDictionary/r.html

Sufi Healing
Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D.
Hyperlink: http://www.canoe.ca/AltmedDictionary/s.html

Superior Fast
Alternative names: superior fasting
Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D.
Hyperlink: http://www.canoe.ca/AltmedDictionary/s.html

Testing for Stomach Acidity
Source: Healthnotes, Inc.; www.healthnotes.com

Vitality Fasting and Rejuvenation
Source: The Canoe version of A Dictionary of Alternative-Medicine Methods, by Priorities for Health editor Jack Raso, M.S., R.D.
Hyperlink: http://www.canoe.ca/AltmedDictionary/v.html

- **Herbs and Supplements**

  Aloe
  Alternative names: Aloe vera L.
  Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

  Betaine (trimethylglycine)
  Source: Healthnotes, Inc.; www.healthnotes.com

  Betula
  Alternative names: Birch; Betula sp.
  Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

  Fenugreek
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Glutamine
  Source: Healthnotes, Inc.; www.healthnotes.com

  Momordica
  Alternative names: Bitter Gourd, Karela; Momordica charantia Linn.
  Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

  Ocimum
  Alternative names: Basil, Albahaca; Ocimum basilicum
  Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

  Plantago Psyllium
  Alternative names: Psyllium, Ispaghula; Plantago psyllium/ovata
  Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

  Silybum
  Alternative names: Milk Thistle; Silybum marianum (L.) Gaertn.
  Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

  Trigonella
  Alternative names: Fenugreek; Trigonella foenum graecum L.
  Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

General References

A good place to find general background information on CAM is the National Library of Medicine. It has prepared within the MEDLINEplus system an information topic page dedicated to complementary and alternative medicine. To access this page, go to the MEDLINEplus site at **http://www.nlm.nih.gov/medlineplus/alternativemedicine.html**. This Web site provides a general overview of various topics and can lead to a number of general sources.

CHAPTER 4. DISSERTATIONS ON FASTING

Overview

In this chapter, we will give you a bibliography on recent dissertations relating to fasting. We will also provide you with information on how to use the Internet to stay current on dissertations. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical dissertations that use the generic term "fasting" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on fasting, we have not necessarily excluded non-medical dissertations in this bibliography.

Dissertations on Fasting

ProQuest Digital Dissertations, the largest archive of academic dissertations available, is located at the following Web address: **http://wwwlib.umi.com/dissertations**. From this archive, we have compiled the following list covering dissertations devoted to fasting. You will see that the information provided includes the dissertation's title, its author, and the institution with which the author is associated. The following covers recent dissertations found when using this search procedure:

- **A Study of the Relationship between Biblical Fasting and Financial Prosperity** by Rodgers, Robert Waymon; DMIN from Oral Roberts University, 2002, 244 pages
  http://wwwlib.umi.com/dissertations/fullcit/3062598
- **An Edition and Study of the Old English 'seasons for Fasting'** by Hilton, Chadwick Buford, Jr., PhD from The University of Tennessee, 1983, 92 pages
  http://wwwlib.umi.com/dissertations/fullcit/8402737
- **Christian Fasting: a Theological Approach** by Berghuis, Kent D.; PhD from Trinity Evangelical Divinity School, 2002, 393 pages
  http://wwwlib.umi.com/dissertations/fullcit/3068014
- **Early Christian Fasting: a Study of Creative Adaptation** by Rufe, Joan Brueggeman, PhD from University of Virginia, 1994, 328 pages
  http://wwwlib.umi.com/dissertations/fullcit/9424472

- **Effect of Fasting on Esterification by Rat Adipose Tissue in Vitro** by Daniel, Anna M.; Advdeg from Mcgill University (Canada), 1966
  http://wwwlib.umi.com/dissertations/fullcit/NK00300
- **Factors Related to Fasting Behavior among American Adults (recovery)** by Cho, Ho Sam, EDD from Temple University, 1995, 72 pages
  http://wwwlib.umi.com/dissertations/fullcit/9600015
- **Fasting and Feasting: a Study of an Antithesis by Analogy and Association As an Inquiry into Literature and Culture** by Kotzamanidou, Maria, PhD from University of California, Berkeley, 1983, 327 pages
  http://wwwlib.umi.com/dissertations/fullcit/8413457
- **Fasting Women and Anorexia Nervosa: Gestures of Spiritual Self-transformation** by Patterson, Barbara A. B., PhD from Emory University, 1994, 403 pages
  http://wwwlib.umi.com/dissertations/fullcit/9505706
- **Feasting and Fasting: the Meaning of Muslim Food in Delhi (symbolism, Ethnic Identity, Marriage, Hospitality, Piety, India)** by Murphy, Christopher Patrick Hussey, PhD from University of Virginia, 1985, 447 pages
  http://wwwlib.umi.com/dissertations/fullcit/8615559
- **Feasting and Fasting: the Vrata Tradition and Its Significance for Hindu Women (india)** by Mcgee, Mary, ThD from Harvard University, 1987, 930 pages
  http://wwwlib.umi.com/dissertations/fullcit/8819001
- **Food, Feasting and Fasting in the Nineteenth Century British Novel.** by Carter, Ann Alexandra, PhD from The University of Wisconsin - Madison, 1978, 318 pages
  http://wwwlib.umi.com/dissertations/fullcit/7915071
- **Formation of Monounsaturated Fatty Acids by Desaturation in Rat Brain in Vitro: Some Properties and Effects of Age, Fasting and Refeeding with Comparison to Liver Enzyme** by Cook, Harold William; PhD from Dalhousie University (Canada), 1973
  http://wwwlib.umi.com/dissertations/fullcit/NK18585
- **Obesity: an Investigation of Personality Characteristics of Patients Participating in a Behaviorally-oriented Supplemented Fasting Program** by Spiegelberg, Jane Slater, PhD from Kent State University, 1988, 176 pages
  http://wwwlib.umi.com/dissertations/fullcit/9332877
- **Prayer and Fasting As Foundation for Evangelization Through the Community Worship Center, Church of the Nazarene (new York City)** by Gillett, Elmer Lyle; DMIN from Fuller Theological Seminary, Doctor of Ministry Program, 2000, 224 pages
  http://wwwlib.umi.com/dissertations/fullcit/9974132
- **Relapse Prevention Model for Enhancing Compliance in a Very Low Calorie Diet Program (fasting)** by Levick, Keith, PhD from Wayne State University, 1992, 115 pages
  http://wwwlib.umi.com/dissertations/fullcit/9225895
- **Responses of Body Condition and Composition of Juvenile Rainbow Trout to Fasting, Activity, and Water Temperature** by Simpkins, Darin Gary; PhD from University of Wyoming, 2002, 170 pages
  http://wwwlib.umi.com/dissertations/fullcit/3079591
- **Shakespeare's Festive History: Feasting, Festivity, Fasting, and Lent in the Second Henriad (william Shakespeare)** by Ruiter, David Arthur; PhD from Baylor University, 2000, 210 pages
  http://wwwlib.umi.com/dissertations/fullcit/9956099

- **Substrate Utilization and Fasting Metabolism during Postnatal Development Ot the Pig** by Atkinson, James Lockie; PhD from University of Guelph (Canada), 1978
  http://wwwlib.umi.com/dissertations/fullcit/NK37380
- **The 'Burden of the Flesh': Fasting and the Female Body in Early Christian Ascetic Theory** by Shaw, Teresa Marie, PhD from Duke University, 1992, 371 pages
  http://wwwlib.umi.com/dissertations/fullcit/9237879
- **The Effect of Menstrual Cycle on Fasting Blood Glucose Patterns of Insulin Dependent Women with Diabetes Mellitus** by Kandt, Denise Charmane, EDD from University of Arkansas, 1992, 159 pages
  http://wwwlib.umi.com/dissertations/fullcit/9334094
- **The Effect of Training on Fasting Levels of Serum Cholesterol and Triglyceride.** by Moss, Raymond Fidalis, PhD from The University of Texas at Austin, 1976, 156 pages
  http://wwwlib.umi.com/dissertations/fullcit/7626679
- **The Formation of a Christian Fasting Ministry Within Castleberry Baptist Church and Christian Fasting's Relationship to Personal Renewal (Texas)** by Cornell, Larry Harold; Dmin from University of Dubuque Theological Seminary, 2001, 119 pages
  http://wwwlib.umi.com/dissertations/fullcit/3003547
- **The Informational Value and Usefulness of Serum Retinoid Measurements. Studies on Biological Variation, Including Infancy and Pregnancy, and Influence of Fasting, Antiepileptic Drugs and Ethanol** by Soderlund, Maria Berggren; PhD from Lunds Universitet (Sweden), 2003, 95 pages
  http://wwwlib.umi.com/dissertations/fullcit/f152929
- **The Necessity of Fasting and Prayer in the Pastoral Ministry--with Special Reference to Yeong-sin Presbyterian Church. (Korean Text)** by Yoo, Yeon-wang, DMIN from Fuller Theological Seminary, Doctor of Ministry Program, 1987, 155 pages
  http://wwwlib.umi.com/dissertations/fullcit/8815981
- **The Responses in the New Testament to the Practice of Fasting.** by Fink, Marion Michael, Jr., PhD from The Southern Baptist Theological Seminary, 1974, 330 pages
  http://wwwlib.umi.com/dissertations/fullcit/7504068
- **Two Old English Observance Poems: 'seasons for Fasting' and 'the Menologium' - an Edition. (Old English Text)** by Greerson, Hoyt St. Clair, Jr., PhD from University of Oregon, 1970, 355 pages
  http://wwwlib.umi.com/dissertations/fullcit/7101315

Keeping Current

Ask the medical librarian at your library if it has full and unlimited access to the *ProQuest Digital Dissertations* database. From the library, you should be able to do more complete searches via **http://wwwlib.umi.com/dissertations**.

CHAPTER 5. PATENTS ON FASTING

Overview

Patents can be physical innovations (e.g. chemicals, pharmaceuticals, medical equipment) or processes (e.g. treatments or diagnostic procedures). The United States Patent and Trademark Office defines a patent as a grant of a property right to the inventor, issued by the Patent and Trademark Office.[8] Patents, therefore, are intellectual property. For the United States, the term of a new patent is 20 years from the date when the patent application was filed. If the inventor wishes to receive economic benefits, it is likely that the invention will become commercially available within 20 years of the initial filing. It is important to understand, therefore, that an inventor's patent does not indicate that a product or service is or will be commercially available. The patent implies only that the inventor has "the right to exclude others from making, using, offering for sale, or selling" the invention in the United States. While this relates to U.S. patents, similar rules govern foreign patents.

In this chapter, we show you how to locate information on patents and their inventors. If you find a patent that is particularly interesting to you, contact the inventor or the assignee for further information. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical patents that use the generic term "fasting" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on fasting, we have not necessarily excluded non-medical patents in this bibliography.

Patents on Fasting

By performing a patent search focusing on fasting, you can obtain information such as the title of the invention, the names of the inventor(s), the assignee(s) or the company that owns or controls the patent, a short abstract that summarizes the patent, and a few excerpts from the description of the patent. The abstract of a patent tends to be more technical in nature, while the description is often written for the public. Full patent descriptions contain much more information than is presented here (e.g. claims, references, figures, diagrams, etc.). We

[8]Adapted from the United States Patent and Trademark Office:
http://www.uspto.gov/web/offices/pac/doc/general/whatis.htm.

will tell you how to obtain this information later in the chapter. The following is an example of the type of information that you can expect to obtain from a patent search on fasting:

- **2,5-anhydro-1,6-dihalo-1,6-dideoxy-D-mannitol**

  Inventor(s): DiNovi; Michael J. (Philadelphia, PA), Friedman; Mark I. (Merion, PA), Rafka; Robert J. (Groton Long Point, CT), Tordoff; Michael G. (Philadelphia, PA)

  Assignee(s): Monell Chemical Senses Center (Philadelphia, PA)

  Patent Number: 4,871,776

  Date filed: October 22, 1987

  Abstract: A novel fructose analog is disclosed which has been found to modify the food intake of mammals. If administered during the diurnal **fasting** period, the mammals increase their food intakes. If administered during the diurnal feeding period, food intake is decreased. The compound is 2,5-anhydro-1,6-dihalo-1,6-dideoxy-D-mannitol, preferably 2,5-anhydro-1,6-dichloro-dideoxy-D-mannitol ("Charmitol").

  Excerpt(s): The present invention relates to the field of food intake modifiers, and more particularly to the field of modifiers that can be administered to increase or decrease mammalian food intake. The physiology of the control of food intake is not well understood. Many cogent theories have been advanced based on data and observation. Several of these theories are discussed in "Physiology of the Control of Food Intake", Kissileff et al, Ann. Rev. Nutr., 2:371-418 (1982); Russek "Current Status of the Hepatostatic Theory of Food Intake Control", Appetite, 2:137-143 (1981); and Friedman et al, "The Physiological Psychology of Hunger: A Physiological Perspective", Physiological Review, 83(6):409-431 (1976). Notwithstanding the current knowledge in this area, the effect that the administration of any given substance will have upon a mammal's food intake is normally difficult if not impossible to predict in the absence of significant food intake data stemming from prior experience with that compound or substance. The present invention relates in particular to the effects of a dichloro derivative of 2,5-anhydro-D-mannitol and its effect on the food intake behavior of mammals. 2,5-anhydro-D-mannitol is a known fructose analog. The literature contains several reports concerning the possible biochemical and/or metabolic effects of 2,5-anhydro-D-mannitol (hereinafter referred to as 2,5-AM). See Riquelme et al, "Mechanism of Action of 2,5- anhydro-D-mannitol in Hepatocytes", Journal of Biological Chemistry, 259(8):5115-5123 (Apr. 25, 1984); Stevens et al, "2,5-anhydro-mannitol Inhibits Gluconeogenesis from Dihydroxyacetone in Rat Hepatocytes", Fed. Proc. 42 (Part II) Abstract No. 2384 (1983); Stevens et al, "2,5-anhydro-D-mannitol Inhibits Glycogenolysis in Isolated Rat Hepatocytes", Fed. Proc. 40 (Part I) Abstract No. 3479 (1981); Hanson et al, "Hypoglycemic Effect of 2,5-anhydro-D-mannitol", Fed. Proc. 42 (Part II), Abstract No. 1453 (1983); Raushel et al, "The Substrate in Anomeric Specificity of Fructokinase", Journal of Biological Chemistry, 248 (23):8174-8177 (Dec. 10, 1973); Riquelme et al, "Inhibition by 2,5-anhydro-mannitol of Glycolysis in Isolated Rat Hepatocytes and in Ehrlich Ascites Cells", Proc. Natl. Acad. Sci. U.S.A., 82:78-82 (January, 1985) Riquelme, "Regulation of Carbohydrate Metabolism by 2,5-anhydro-D-mannitol", Proc. Natl. Acad. Sci. U.S.A., 80:4301-4305 (July, 1983); and Hanson et al, "Inhibition of Gluconeogenesis and Glycogenolysis by 2,5-anhydro-D-mannitol", Journal of Biological Chemistry, 259(1):218-223 Jan. 10, 1984). While most of these papers address the effect of 2,5-AM at cellular and intracellular levels, please note that Hanson et al (1984) discloses the administration of 2,5-AM to **fasting** mice and rats. Hanson et al

fails to report any food intake data, nor does Hanson suggest what effect, if any, 2,5-AM might have in altering food intake.

Web site: http://www.delphion.com/details?pn=US04871776__

- **Amino acid supplementation of dietary proteins**

  Inventor(s): Jarowski; Charles I. (67 Harbor La., Massapequa Park, NY 11762)

  Assignee(s): none reported

  Patent Number: 5,559,142

  Date filed: September 22, 1994

  Abstract: A universal dietary supplement for proteins consisting of a blend of four essential amino acids was developed. A unit dose consisting of a blend of 80 mg of L-Tryptophan, 90 mg of L-Methionine, 103 mg of L-Valine and 128 mg of L-Lysine Monohydrochloride; taken after meals, will improve the biological value and net protein utilization of individual and combinations of proteins. The levels of supplementation were derived by taking into consideration the average **fasting** plasma concentrations of the eight essential amino acids, and two nonessential amino acids. L-Tyrosine and L-Cystine, of several adult males and females. The two nonessential amino acids were included since they are phenylalanine and methionine sparing, respectively. The ideal protein for humans is considered to be a multiple of the **fasting** plasma concentrations expressed in millimoles. The variation in protein composition makes it impractical to attain the ideal. However, a study of the essential amino acid composition of 61 commonly consumed proteins revealed that three of the ones present in the lowest concentrations, in other words, the first, second and third limiting essential amino acids, will become less limiting after administration of the unit dose. In all cases at least three of the essential amino acids in the unit dose will match the first three limiting ones in the various proteins. Such strategic supplementation will result in greater net protein utilization and lower excesses of underutilized amino acids, thereby reducing the possibility of their being converted to undesirable metabolic products, such as, urea, cholesterol and triglycerides.

  Excerpt(s): This invention relates to the supplementation of dietary proteins with a selected blend of four essential amino acids to improve their biologic value and net protein utilization. Nutritionists have established that several amino acids are essential for normal growth and well-being in animals, including man. Since they cannot be synthesized by the body, they must be provided in free or combined form in the diet to meet the requirements of cellular protein synthesis and to fulfill other metabolic roles. For most of the animals studied it is generally agreed that the essential amino acids include, L-arginine, L-histidine, L-isoleucine, L-leucine, L-Lysine, L-methionine, L-phenylalanine, L-valine, L-threonine and L-tryptophan. In humans, the first two mentioned are regarded as non-essential. Scientists have also established that a part of the methionine requirement can be replaced by cystine and cysteine. In addition, a part of the phenylalanine requirement can be replaced by tyrosine. This information is obviously very useful in evaluating potential dietary sources of protein. Thus, for example, gelatin, which contains practically no tryptophan, is clearly inadequate as a sole source of dietary protein. Likewise zein, which is deficient in tryptophan and lysine, is inadequate as a sole source of dietary protein. The net protein utilization and biologic value of gelatin will be improved by supplementation with L-tryptophan. Similarly, the nutritional value of zein will be enhanced by supplementation with L-tryptophan and L-lysine.

Web site: http://www.delphion.com/details?pn=US05559142__

- **Compositions comprising D-chiro inositol and sulfonylureas and methods of treatment thereof**

  Inventor(s): Allan; Geoffrey (Richmond, VA), Sleevi; Mark (Midlothian, VA)

  Assignee(s): Insmed, Incorporated (Glen Allen, VA)

  Patent Number: 6,492,339

  Date filed: October 26, 2001

  Abstract: The present invention provides compositions comprising synergistically effective amounts of D-chiro-inositol and sulfonylureas. The present invention also provides methods to treat a subject with insulin resistance comprising administration of D-chiro-inositol and sulfonylurea, either as concurrent single agents or as a combined composition. In particular the methods of the present invention are useful in maintaining pancreatic beta cell function/viability and thus delay diabetes progression. The methods and compositions of the present invention are particularly efficacious in treating insulin resistant subjects with a **fasting** blood glucose level of less than or equal to 180 mg/dL.

  Excerpt(s): The present invention provides methods to treat a subject with insulin resistance comprising administration of D-chiro-inositol and sulfonylurea, either as concurrent single agents or as a combined composition. The present invention also provides compositions comprising therapeutically effective amounts of D-chiro-inositol and sulfonylureas. The present invention also provides methods to treat a subject with insulin resistance comprising administration of D-chiro-inositol and sulfonylurea, either as concurrent single agents or as a combined composition. In particular, the methods of the present invention are useful in maintaining pancreatic beta cell function/viability and thus, delay diabetes progression. The methods and compositions of the present invention are particularly efficacious in treating insulin resistant subjects with a **fasting** blood glucose level of less than or equal to 180 mg/dL. Non-insulin dependent diabetes (NIDDM, or type 2 diabetes) is a worldwide health problem. According to the World Health Organization, an estimated 30 million people worldwide had diabetes in 1985. This number increased to 135 million people by 1995 and the WHO predicts a rise to 300 million people by 2025. The insidious nature of type 2 diabetes progression and medical complications that arise from hyperglycemia extract a heavy toll on the individual, healthcare resources, and society. As such, there is a continuing need for new therapeutic agents and therapeutic regimens that prevent diabetes, prevent or delay the progression of diabetes, or prevent or delay diabetic complications. It is generally desirable to treat a subject with diabetes or at risk of developing diabetes in ways that reestablish or maintain the balance between insulin secretion and insulin sensitivity. It is highly desirable to employ methods that avoid administration of exogenous insulin. Therefore a regimen of diet and exercise is primarily used to attempt to establish more physiologic glycemic control. Sadly, however, pharmacological intervention becomes necessary. The current "second line" of therapies includes administration of pharmacological agents including sulfonylureas (e.g. GLUCOTROL.RTM.), biguanides (e.g. metformin), and PPAR gamma agonists (e.g. rosiglitazone) alone or in combination, which are used to increase endogenous insulin production, decrease hepatic glucose output, and increase periperial insulin sensitivity (Kobayashi, Diabetes Obes. Metab., 1(Suppl 1): S32-S40 (1999); Brown et al., J. Natl. Med. Assoc., 91(7): 389-395 (1999)). Sulfonylureas are compounds that stimulate insulin secretion from beta cells in islet

tissue of the pancreas and are currently the most frequently prescribed oral hypoglycemic drugs. Increased insulin secretion by sulfonylureas may lead to hypoglycemia (Imura, N. Engl. J. Med., 338: 908-909 (1998)). Unfortunately, prolonged use of sulfonylureas results in unfavorable side effects, particularly desensitization and/or apoptosis of the beta cells resulting in decreased insulin production. The effect is particularly manifest in subjects who have more severe insulin resistance in conjunction with less insulin (Kobayashi, Diabetes Obes. Metab., 1(Suppl 1): S32-S40 (1999); Kolterman et al., Diabetes Care, 7(Suppl 1): 81-89 (1984)). Biguanides are compounds that decrease hepatic glucose output, and thus aid in controlling hyperglycemia. PPAR gamma agonists are insulin-sensitizing compounds that increase the cell's ability to respond to smaller quantities of insulin. Eventually these therapies fail and exogenous insulin is required to maintain a balance of glucose metabolism.

Web site: http://www.delphion.com/details?pn=US06492339__

- **Dry sustained release theophylline oral formulation**

  Inventor(s): Chang; Richard (Miramar, FL), Giannini; Robert P. (Plantation, FL), Hsaio; Charles (Cooper City, FL)

  Assignee(s): Schering Corporation (Kenilworth, NJ)

  Patent Number: 4,786,509

  Date filed: May 18, 1987

  Abstract: A sustained release theophylline containing oral dosage formulation comprising theophylline containing micropellets coated with from about 0.5% to about 2% by weight of a pharmaceutically acceptable water-insoluble film former, preferably ethyl cellulose and having first order release. The formulation is an improvement over theophylline containing micropellets coated with two film formers which have zero order release. The oral dosage formulation has superior non-fasting release and absorption characteristics when compared to the zero order release formulation.

  Excerpt(s): A zero order release theophylline product, THEO-DUR SPRINKLE.TM., by Key Pharmaceuticals, has received widespread acceptance in the marketplace and among the medical profession as a bronchodilator. The product is a formulation of dry sustained release oral dosage micropellets in a capsule which includes upper and lower connectible parts which are easily separable from each other. The micropellets provide sustained release of theoohylline when taken by a patient and are comprised of inner seeds coated with theophylline which in turn is coated with a mixture of ethylcellulose and hydroxypropylcellulose. The oral dosage formulation is administered by separatinq the upper and lower parts of the capsule and placing the micropellets on food, the food is then eaten. The preparation of the product is described in U.S. Pat. No. 4,587,118. Pedersen et al, PEDIATRICS, 74 (4), 534, (Oct. 4, 1984) discovered, in a clinical study involving asthmatic children using THEO-DUR SPRINKLE theophylline micropellets, that the bioavailability and absorption pattern of the theophylline were satisfactory under **fasting** conditions but both absorption pattern and bioavailability were severely adversely affected by concomitant food intake. A dela y in absorption was found and the bioavailability was reduced from 91% (fasting) to 44% ($P<0.001$). They concluded that the erratic absorption of theophylline after food intake complicates safe therapy with the preparation. This is a serious problem since the dosage form was developed for use with food by those having difficulty swallowing tablets or capsules, e.g. the elderly and children.

Web site: http://www.delphion.com/details?pn=US04786509__

- **Effects of 17.alpha.-dihydroequilenin on plasma lipid and lipoprotein, glucose, insulin concentrations, coronary artery vasomotor function, and reproductive organ and mammary gland proliferation in atherosclerotic mammals**

  Inventor(s): Adams; Michael R. (Clemmons, NC), Adelman; Steven J. (Hatfield, PA), Clarkson; Thomas B. (Clemmons, NC), Cline; J. Mark (Winston-Salem, NC), Register; Thomas C. (Clemmons, NC), Wagner; Janice D. (Kernersville, NC), Washburn; Scott A. (Winston-Salem, NC), Williams; J. Koudy (Clemmons, NC)

  Assignee(s): American Home Products Corporation (Madison, NJ), Wake Forest University (Winston-Salem, NC)

  Patent Number: 5,994,337

  Date filed: January 12, 1998

  Abstract: The present invention relates to a method of using 17.alpha.-dihydroequilenin and metabolic conjugates thereof to prevent and reduce atherogenesis in males and females without causing endometrial proliferation in females and without producing feminizing changes in males. 17.alpha.-dihydroequilenin was evaluated for its effects on plasma lipid and lipoprotein, glucose, insulin concentrations, coronary artery vasomotor function, and reproductive organ and mammary gland proliferation in atherosclerotic mammals. 17.alpha.-dihydroequilenin was found to prevent endothelium-dependent vasoconstriction in males ($p<0.05$) and ovariectomized females ($p<0.08$). 17.alpha.-dihydroequilenin treatment increased plasma apolipoprotein A-l concentrations ($p<0.05$) and lowered **fasting** insulin concentrations ($p<0.05$) without changing **fasting** plasma glucose concentrations in males. 17.alpha.-dihydroequilenin had no other effects on plasma lipid and lipoprotein concentrations in either males or females. Also, 17.alpha.-dihydroequilenin exhibited no trophic effects on the uterus, endometrium, or breast, and no effect on either prostatic or testicular weight. Thus, 17.alpha.-dihydroequilenin may prevent breast and prostatic hyperplasia and neoplasia, and has no feminizing effects on the male urogenital system or mammary gland.

  Excerpt(s): The present invention relates to a method of using 17.alpha.-dihydroequilenin and metabolic conjugates thereof to reduce and prevent ischemic heart disease in males and females without causing endometrial proliferation in females and without producing feminizing changes in males. More particularly, the present invention relates to the use of 17.alpha.-dihydroequilenin in atherosclerotic mammals and to evaluate its effects on plasma apolipoprotein, glucose, insulin concentrations, coronary artery vasomotor function, and reproductive organ and mammary gland proliferation. Postmenopausal estrogen replacement therapy has gained wide recognition as a lifelong preventive regimen for the reduction of osteoporotic fracture and ischemic heart disease. Unfortunately, good scientific evidence has failed to persuade the majority of menopausal women that the benefits of long-term estrogen replacement therapy are worth the inconvenience or anxiety resulting from its side effects, especially vaginal bleeding and the putative increase in breast cancer risk. Additionally, most of the evidence of estrogen effects in preventing ischemic heart disease in the United States is from studies that used unopposed conjugated equine estrogens. The current evidence is unclear as to whether the addition of progestins, necessary to prevent iatrogenically induced endometrial carcinoma, may either partially or completely negate the cardioprotective effect of unopposed estrogens. Several of the inventors have described a component of Premarin.RTM. (Wyeth-Ayerst, Princeton,

N.J.), 17.alpha.(-dihydroequilenin (DHEN), that caused no uterine hypertrophy in ovariectomized rats compared with ovariectomized controls and compared with a doubling of uterine weight in Premarin treated ovariectomized rats. [Washburn S A et al., A conjugated equine estrogen with differential effects on uterine weight and plasma cholesterol in the rat. Am J Obstet Gynecol 1993;169:251-6]. It was determined that DHEN caused a 70% reduction in total plasma cholesterol concentrations compared with ovariectomized controls and compared with a 15% reduction of total plasma cholesterol in ovariectomized rats treated with oral Premarin.RTM. Currently, there are no hormone replacement therapies that deliver established benefits to menopausal females and males such as the prevention and/or reduction of atherosclerotic heart disease without causing endometrial proliferation or other side effects of the type previously mentioned. Thus, there remains a need for an alternative hormone replacement therapy for menopausal women and men without side effects or the need to take concomitant progestin therapy.

Web site: http://www.delphion.com/details?pn=US05994337__

- **Erythromycin base tablets**

  Inventor(s): Kriesel; Douglas C. (Lake Bluff, IL), Mehta; Shashi P. (Libertyville, IL)

  Assignee(s): Abbott Laboratories (North Chicago, IL)

  Patent Number: 4,340,582

  Date filed: January 15, 1981

  Abstract: An enteric coated erythromycin tablet is provided that produces essentially the same blood levels in **fasting** and nonfasting subjects. The tablet contains erythromycin base dihydrate and a highly water-soluble nontoxic salt in the core and the coating polymer is a hydroxypropyl methylcellulose phthalate.

  Excerpt(s): Erythromycin has been a leading antibiotic for many years and recently, more of the manufacturers for several reasons are providing erythromycin in the form of the simple base, in contrast of previous esters and salts. Unfortunately, erythromycin is sensitive to the juices of the stomach and if exposed to the high acidity there, only very little of the dosage administered to a warm-blooded animal passes into the blood stream. A common solution to this problem is to apply an enteric coating to the tablet cores containing the antibiotic. Some of the currently marketed erythromycin base tablets have been provided with enteric coatings or similar systems which prevent premature degradation in the digestive system. Most of these tablets must be ingested on a **fasting** stomach in order to provide adequate blood levels. Also, some of the currently available erythromycin tablets are provided with an enteric coating which have prolonged dissolution rates after long term storage. These and other factors cause some of the marketed erythromycin tablets to show erratic absorption. It has now been found that the above difficulties can be overcome by providing an enteric coated erythromycin base tablet consisting essentially of a tablet core and a tablet coating, said core consisting essentially of 250 parts of erythromycin base in the form of its dihydrate, 35 to 100 parts of a water soluble nontoxic ingestible salt, and 40 to 175 parts of the usual tableting excipients including diluents, binders, disentegrants and lubricants, said core being coated from a hydro-alcoholic solvent containing, per table core, 16 to 25 parts of hydroxypropyl methylcellulose phthalate (hereinafter referred to as HPMCP) and 1 to 10 parts of customary coating excipients including dyes, pigments and plasticizers. All references to "parts" herein and hereinafter is based on weight parts.

Web site: http://www.delphion.com/details?pn=US04340582__

- **Hyper-absorption of vitamin E combined with milk protein**

  Inventor(s): Hayes; Kenneth C. (Wellesley, MA), Perlman; Daniel (Arlington, MA)

  Assignee(s): Brandeis University (Waltham, MA)

  Patent Number: 6,503,545

  Date filed: September 28, 2000

  Abstract: A milk product providing an individual at least 31 IU (International Units) of vitamin E per serving, or an ingestible blend of at least one mammalian milk protein or fragment thereof, and vitamin E or other fat-soluble micronutrient or pharmacological agent is described. The vitamin E is uniformly microdispersed throughout the milk product, and ingestion of at least 100 IU of vitamin E per day in the product is sufficient to cause the **fasting** plasma vitamin E/cholesterol ratio in human subjects to be elevated at least 50% above the basal **fasting** level of vitamin E measured in the same subjects consuming no vitamin E dietary supplements. A method for elevating the plasma vitamin E level at least 50% in human subjects is also described. The method includes ingesting a milk product as described. A method for increasing the bioavailability of an orally administered fat-soluble micronutrient or pharmaceutical agent is also described. The method includes providing a microdispersed mixture of at least one fat-soluble micronutrient or pharmaceutical agent, and at least one mammalian milk protein or fragment thereof, in which the weight ratio of the milk protein to the micronutrient or pharmaceutical agent is between 1:1 and 1000:1.

  Excerpt(s): This invention relates to milk-based food products, and in particular to the microdispersal of vitamin E in milks (milkfat-based milk, skim milk, vegetable oil-filled milk, and blends thereof) at a level providing at least 31 IU (International Units) per serving. The invention also relates to a substantially lactose-free and milkfat-free composition for oral administration to a human or other mammal, including a microdispersed mixture of at least one mammalian milk protein or fragment thereof, and at least one fat-soluble micronutrient or pharmaceutical agent, where the weight ratio of said mammalian milk protein to said fat-soluble micronutrient or pharmaceutical agent is between 1:1 and 1000:1. The information provided herein is solely to assist the understanding of the reader; none of that information or cited references is admitted to be prior art to the present invention. In the past five years several major prospective health studies have been published demonstrating that vitamin E supplement ingestion is associated with a reduced risk of coronary heart disease (CHD) in both women and men (e.g., Stampfer et al., NEJM, 328, 1444-1449, 1993 Rimm et al., NEJM, 328, 1450-1456, 1993). In a four year study of nearly 40,000 males, Rimm et al., showed that the risk of CHD diminished significantly as the daily supplemental level of vitamin E increased. This study indicates that the current Recommended Daily Allowance (RDA) of 30 international units (IU) of vitamin E is insufficient for obtaining the full protective benefits of vitamin E. In fact, the study data suggest that for most adult males, a daily supplement of at least 100 IU of vitamin E is appropriate for helping to protect against CHD. In another prospective study, long-term ingestion of vitamin E was tested for its ability to reduce the incidence of myocardial infarction in patients having a documented condition of coronary atherosclerosis (Stephens et al., Lancet, 347, 781-786, 1996). In this study, it was shown that sustained supplementation of the patients' diets with 400 IU of RRR-.alpha.-tocopherol ingested once per day in capsules was sufficient to reduce the risk of non-fatal heart attacks by

77%. This protective effect became apparent after about 200 days of treatment with the vitamin. In still another study (Losonczy et al., Am. J. Clin. Nutr. 64, 190-196, 1996), individuals in an elderly population (n=11,178) aged 67-105, were each followed for 6 years, and their uses of vitamin E and/or vitamin C supplements were correlated with their risk of developing cancer and CHD. While vitamin C supplements could not be shown to have a significant protective effect over the 6 year period, vitamin E supplements (greater than 100 IU per day) were shown to reduce all-cause mortality 27-34%, CHD mortality 41-47%, and cancer mortality 22-23% (in these ranges, the first number is the age and sex-adjusted risk, and the second is a multi-covariable adjusted risk).

Web site: http://www.delphion.com/details?pn=US06503545__

- **Method for improving the glucose metabolism of an animal having diabetic tendencies**

  Inventor(s): Stanko; Ronald T. (Pittsburgh, PA)

  Assignee(s): Montefiore Hospital Association of Western Pennsylvania (Pittsburgh, PA)

  Patent Number: 4,874,790

  Date filed: August 15, 1988

  Abstract: A method for treating animals having diabetic tendencies to improve the glucose metabolism of the animal by oral administration of therapeutically effective amounts of pyruvate and dihydroxyacetone. The treatment lowers Glucose Tolerance Test Values and lowers **Fasting** Blood Glucose Test values.

  Excerpt(s): This invention concerns oral administration of pyruvate and dihydoxyacetone to animals having diabetic tendencies to improve the glucose metalbolism of said animals. U.S. Pat. No. 4,158,057 describes oral administration of pyruvate and dihydroxyacetone to prevent excessive accumulation of fatty deposits in a mammal liver due to ethanol ingestion. U.S. Pat. No. 4,351,835 describes oral administration of pyruvate and dihydroxyacetone to reduce an expected weight gain from a given diet or to induce a weight loss in a mammal. The patent also describes oral administration of pyruvate and dihydroxyacetone to athletes prior to strenuous athletic events to increase endurance and/or performance.

  Web site: http://www.delphion.com/details?pn=US04874790__

- **Method for use of magnetic resonance imaging to image pancreas using secretin**

  Inventor(s): Bis; Kostaki G. (Troy, MI)

  Assignee(s): Wayne State University (Detroit, MI)

  Patent Number: 5,094,837

  Date filed: January 22, 1990

  Abstract: Structural and functional imaging of the pancreas can be achieved with magnetic resonance imaging and a secretin solution. An amount of secretin is placed in solution and administered to a patient for the purpose of pancreatic imaging. Because the secretin solution changes the signal intensity of the pancreas, it can be imaged relative to baseline **fasting** studies for the purposes of tumor detection and qualification of exocrine dysfunction.

Excerpt(s): The field of this invention is that of contrast agents for magnetic resonance imaging (MRI) for pancreatic imaging. This invention relates to a non-invasive method of magnetic resonance imaging (MRI) of the pancreas using a secretin solution and a kit for use in such imaging. Diagnostic methods currently used for evaluating the pancreas include computed tomography, ultrasound, angiography, and endoscopic retrograde cholangiopancreatography. For the most part, these methods. Only provide anatomical information. Heretofore, the evaluation of pancreatic exocrine function relied on several biochemical analyses. Among these, exogenous hormonal stimulation with secretin, alone, or in combination with cholecystokinin (CCK), is the standard test for measuring pancreatic exocrine function. Secretin is a naturally occurring heptacosa-peptide. It has advantages as a diagnostic agent since it is commercially available and free of adverse reactions. The use of secretin as a diagnostic agent, therefore, is currently limited to evaluating pancreatic exocrine function. However, this is an invasive and technically difficult examination requiring gastric and duodenal intubation.

Web site: http://www.delphion.com/details?pn=US05094837__

- **Method of administering pyruvate and methods of synthesizing pyruvate precursors**

  Inventor(s): Cipollo; Kent L. (Westerville, OH), Dhaon; Madhup K. (Mundelein, IL), Houbion; John A. (Vernon Hills, IL), Lundell; Edwin O. (Libertyville, IL), Miller; Robert H. (Worthington, OH), Parlet; Nickki L. (Columbus, OH)

  Assignee(s): Abbott Laboratories ()

  Patent Number: 5,256,697

  Date filed: April 16, 1992

  Abstract: A method for administering pyruvate is disclosed which comprises administering a therapeutically effective amount of a pyruvate precursor to a mammal in the form of pyruvamide or a pyruvyl-amino acid. The pyruvyl-amino acid is preferably selected from the group comprising pyruvyl-glycine, pyruvyl-alanine, pyruvyl-leucine, pyruvyl-valine, pyruvyl-isoleucine, pyruvyl-phenylalanine, pyruvyl-proline and pyruvyl-sarcosine, and their amides and esters as well as their salts. Associated with the administration of a pyruvate precursor to a mammal in accordance with this invention are improved insulin resistance, lower **fasting** insulin levels, and reduced fat gain. Novel methods of synthesizing several pyruvate precursors are also disclosed.

  Excerpt(s): present invention relates generally to a method of administering pyruvate to mammals, and to methods of synthesizing non-salt precursors to pyruvate. Obesity is a multifactorial disease which affects upwards of 25% of the adult population in the United States of America. It is estimated that in the U.S.A. between 34-50 million adults are obese, with at least 5 million of those adults receiving medical treatment for their obesity. The etiology of obesity can range from simple overeating to severe hormonal imbalance. However, the great majority of obesity is probably due to a complex relationship between the many factors that regulate energy intake and utilization. Teleologically, obese individuals may be better prepared for survival in time of limited food supply because of their ability to utilize energy in a more efficient manner. However, given that there is almost an unlimited food supply in the U.S.A., this efficiency of energy utilization probably leads to obesity. Furthermore, obesity is associated with an increased risk of cardiovascular disease, an increased risk of Type II diabetes, an increased risk of coronary artery disease, and other chronic diseases. For

example, it is believed that in the U.S.A. there are over 6 million diagnosed cases of obese Type II diabetes, with an estimated 4 million cases being undiagnosed.

Web site: http://www.delphion.com/details?pn=US05256697__

- **Method of diagnosing gestational diabetes**

  Inventor(s): Peterson; Charles M. (Santa Barbara, CA), Peterson; Lois G. (Santa Barbara, CA)

  Assignee(s): Sansum Medical Research Foundation (Santa Barbara, CA)

  Patent Number: 5,670,377

  Date filed: March 14, 1996

  Abstract: Methods of diagnosis of gestational diabetes mellitus are disclosed. In preferred embodiments, a blood sample is obtained from a pregnant female in the 24th to 28th week of pregnancy after an overnight fast, after a 1-hour 50-gram glucose challenge test, or at the 1-hour time point during a 3-hour 100-gram oral glucose tolerance test. The concentrations of **fasting** plasma glucose and glycosylated plasma proteins in this blood sample are then determined. A **fasting** plasma glucose concentration equal to or exceeding 90 mg/dL is 100% sensitive and 64% specific in predicting glucose-related macrosomia (i.e., birth weight above 4000 grams). A glycosylated plasma protein concentration equal to or exceeding 23% is 100% sensitive and 52% specific in predicting glucose-related macrosomia. A **fasting** plasma protein value equal to or exceeding 90 mg/dL and a glycosylated plasma protein value equal to or exceeding 23% is 100% sensitive and 93% specific in predicting glucose-related macrosomia.

  Excerpt(s): The present invention is broadly concerned with methods of diagnosing gestational diabetes mellitus (GDM). More particularly, in these methods, the concentrations of **fasting** plasma glucose (FPG) and glycosylated plasma protein (GPP) in the blood of a female in the 24th to 28th week of pregnancy are determined; concentrations of FPG and GPP equal to or exceeding 90 mg/dL and 23%, respectively, indicate that the pregnant female may be suffering from GDM and is therefore at risk of giving birth to a macrosomic infant. Measurement of glycosylated hemoglobin (GHb) levels, a single test and an indicator of long-term glucose control, lacks the sensitivity needed to screen for GDM, let alone milder elevations of glucose levels (7, 12). Therefore, it is unlikely that GHb is useful in screening for macrosomia. The studies on the use of GHb to predict macrosomia have been controversial and generally are retrospective, with measurement of GHb levels performed at delivery (24, 25). Studies on the use of glycosylated albumin, glycosylated serum protein (GSP), and fructosamine (8-14) have shown that these glycosylated proteins are not useful indicators of GDM. Some researchers have examined glucose concentrations determined on the glucose challenge test (GCT) and the oral glucose tolerance test (OGTT) to predict macrosomia (6, 15, 26-29). Sacks et al. (15) reported that the **fasting** blood glucose concentration on the OGTT performed in those women with a positive GCT correlated with macrosomia. Magee et al. (27) found that the frequency of macrosomia was 27% in women who screened negative on the GCT, 19% in women who screened positive on the GCT and negative on the OGTT, and 27% in women who screened positive on the GCT and on the OGTT. Little and coworkers (28) found that FPG concentrations and 2-hour plasma glucose concentrations on the OGTT were higher in those mothers who delivered an infant large for gestational age. Jovanovic and Peterson (6) showed that an elevated 1-hour plasma glucose concentration on the GCT correlated with an increased risk of

macrosomia despite normal results on the OGTT. Skyler and coworkers (29) showed that a FPG concentration above 90 mg/dL increased the risk for macrosomia.

Web site: http://www.delphion.com/details?pn=US05670377__

- **Method of treating rheumatoid arthritis using tetracycline**

  Inventor(s): Cabezas; Orestes (10201 Fontainebleau Blvd., Unit 205, Miami, FL 33172)

  Assignee(s): none reported

  Patent Number: 5,250,442

  Date filed: April 8, 1993

  Abstract: A method of treating rheumatoid arthritis which includes first, taking a blood test to determine a rate of erythrocyte sedimentation and a rheumatoid factor, and then **fasting** for a 12-hour period prior to orally administering a 500 milligram dosage of tetracycline achromycin, and observing any change in the symptoms of the rheumatoid arthritis including reduction of swelling and pain in the affected sites. This process is repeated over 24-hour cycles until the rheumatoid factor has decreased by at least 50% from the first determined level prior to treatment and erythrocyte sedimentation decreased, at which point the 24-hour cycles are continued, reducing the dosage of tetracycline achromycin to 250 milligrams until the symptoms of the rheumatoid arthritis condition disappear.

  Excerpt(s): The present invention relates to a method for treating rheumatoid arthritis to alleviate the symptoms thereof. Presently, an estimated 7,000,000 Americans suffer from rheumatoid arthritis. The symptoms of rheumatoid arthritis including pain and swelling of the smaller joints in the hands and feet. The affected joints become swollen, painful and warm to the touch during the initial attack and ensuing flare-ups. Often, the joints in the hands and the feet will ache or become stiff after extended periods of motionless such as after sleeping. Rheumatoid arthritis is believed to be an autoimmune disease in which the body's immune system literally attacks itself. It is believed that rheumatoid arthritis initially develops from a virus which upsets the immune system. In response, the body's disease fighting cells attack the joints causing inflammation.

  Web site: http://www.delphion.com/details?pn=US05250442__

- **Methods and formulations for the treatment of obesity**

  Inventor(s): Howard; Alan Norman (10 Topcliffe Way, Cambridge, EN)

  Assignee(s): none reported

  Patent Number: 4,009,265

  Date filed: March 5, 1973

  Abstract: It has been discovered that the unfavorable effects observed in weight reduction treatments based on severe dietary restriction (less than 600 Kcals/day) or total **fasting** (as regards fat, carbohydrates and aminoacids) are avoided by the administration of aminoacids and carbohydrates in critical but much lower amounts than has been believed to be necessary. Nitrogen loss with aminoacid intake between about 15 and 30 g per day is affected by carbohydrate intake. Nitrogen balance is maintained and ketosis and water retention are controlled when the daily intake includes, in addition to necessary minerals and vitamins, at least 15 g of aminoacids in

the proportions required by man, and from 15 to 75 g, preferably 30 to 45 g, of carbohydrates, with a total caloric value of from 160 to about 600 Kcals, preferably less than 400 Kcals, very desirably less than 360 Kcals, and optimally in the range of from 180 to 360 Kcals. Formulations are described in which the least amount containing the minimum daily requirement of minerals also contains at least 15 g of aminoacids (as a monomeric aminoacid mixture or as natural protein) and from 15 to 75 g, preferably from 30 to 45 g, of carbohydrates, together with optional other constituents.

Excerpt(s): This invention relates to methods and formulations for the treatment of obesity. When it is required to bring about weight reduction in over-weight patients, it is naturally necessary to reduce their food intake, since the object of the weight-reduction treatment is to cause the body to consume its own fatty tissues in meeting its energy requirements. To this end, it has hitherto been necessary for the diet of the patients to be very strictly controlled and supervised during the period of weight-reduction, which might extend to several months. To exercise so complete a control over the patient's diet it is most convenient to incorporate all the food requirements of the patients into a single dietary composition, and this has been the normal practice. Unfortunately, such controlled diets have hitherto been very unsatisfying, and the patients feel constantly hungry, which is of course very unpleasant. This causes many patients to break off the diet; and even those patients who are motivated sufficiently strongly to stay the course often find that the diet is almost intolerable. Furthermore, many physiological and psychological problems have hitherto been associated with the clinical use of severe dietary restriction. One of these problems arises from the fact that the body requires a constant supply of nitrogen (in the form of aminoacids or their polymers) to replace the endogenous nitrogen losses resulting from the normal "wear and tear" of the body's protein. If an adequate amount of aminoacids is not supplied there is a loss of body protein, with consequent reduction in muscle mass; this leaves the patient feeling weak and languid. If this protein loss continues for too long it can be dangerous, and even the heart muscle may suffer damage. In fact, this loss of muscle mass is one of the main reasons why total **fasting** is not favoured as a weight-reduction treatment.

Web site: http://www.delphion.com/details?pn=US04009265__

- **Prediction of diabetes impaired wound healing by urinary nitrate assay**

  Inventor(s): Boykin, Jr.; Joseph V. (12600 Nightingale Dr., Chester, VA 23831)

  Assignee(s): none reported

  Patent Number: 6,312,663

  Date filed: March 1, 2000

  Abstract: Wound healing is impaired in many diabetics, who suffer increased risk of chronic foot ulceration and amputation. Diabetic patients with poor healing ability were found to possess significantly lower **fasting** urinary nitrate levels than diabetic patients with normal healing ability or non-diabetic controls, implicating decreased endogenous nitric oxide activity as the mediator of diabetes-impaired wound healing. Methods and kits are provided for predicting the wound healing ability of diabetic patients based on the levels of nitric oxide related products such as nitrate or nitrite in urine or other specimens. Methods are also provided for treating non-wound healing diabetics and monitoring diabetic ulcer treatment.

Excerpt(s): The invention is related to the area of wound healing in diabetes. In particular it is related to assays for the level of nitric oxide in non-healing diabetics. Diabetes affects an estimated 15 million people in the United States. Within the diabetic population are individuals with chronic, non-healing lower extremity ulceration (LEU), which is associated with significant morbidity and treatment costs. Chronic, non-healing LEU precedes about 85% of the lower extremity amputations (LEA) that over 50,000 diabetics experience annually (GE Reiber, E J Boyko, D G Smith, in Diabetes in America, NIH Publication No. 95-1468, Bethesda, Md., ed. 2, 1995, pp. 409-428). This represents more than half of all individuals receiving LEA in this country. While only 6% of diabetic hospitalizations are associated with LEU, the total government reimbursement for diabetic lower extremity complications in 1992 exceeded $1.5 billion, not including costs for limb amputation and rehabilitation. Clinical pathophysiologic risk factors for LEA include diabetic neuropathy, lower extremity ischemia, and chronic, non-healing diabetic foot ulcers. The underlying problem in diabetics with LEU is impaired wound healing, which is poorly understood. While the majority of diabetics exhibit "normal" wound healing, those presenting with chronic LEU often demonstrate decreased wound inflammation, recurrent wound infections, decreased cutaneous vascular perfusion, poor wound collagen deposition, and scar maturation. Platelet derived growth factor (PDGF) deficiency is associated with the chronic diabetic ulcer and contributes to impaired healing (H D Beer, M T Longaker, S Werner, J Invest Dermatol 109, 132 (1997)). Clinical trials using Regranex.RTM. have shown efficacy in improving chronic foot ulcer healing in only half or less of the patients evaluated (D L Steed, J Vasc Surg, 21, 71 (1995)).

Web site: http://www.delphion.com/details?pn=US06312663__

- **Pre-operative beverage composition and method of treatment**

  Inventor(s): Marsh; M. Lou (Del Mar, CA)

  Assignee(s): Ohana Medical Concepts, LLC (Del Mar, CA)

  Patent Number: 6,069,131

  Date filed: April 17, 1998

  Abstract: A specially formulated beverage composition designed to be ingested by a pre-operative patient at least about 2 hours prior to administration of anesthesia is provided herein. The beverage composition is preferably provided in a single-serving volume containing at least about 200 Calories, which Calories are primarily from a non-protein, non-fat source, such as one or more carbohydrates. In a most preferred embodiment, the composition includes about 48 grams maltodextrin, about 6 grams fructose and about 6 grams glucose, in water with enough citric acid to provide a final solution pH of about 4.3. This beverage composition, when ingested during pre-operative **fasting,** at least about 2 hours prior to administration of anesthesia, encourages compliance with pre-operative **fasting** requirements; reduces the incidence of symptoms associated with prolonged **fasting,** such as feelings of hunger and thirst, lightheadedness, irritability and headache; and should reduce the risk of aspiration pneumonia by providing a residual gastric volume and gastric pH within generally accepted ranges. Also, contemplated herein is the method of using this beverage composition to increase compliance with pre-operative **fasting** guidelines and thereby decrease the risk of aspiration pneumonia in the anesthetized/sedated patient.

  Excerpt(s): The subject matter disclosed and claimed herein relates to a specially formulated beverage composition designed to be administered to a patient, prior to

anesthesia and/or sedation, to reduce the risk of aspiration pneumonia at least by increasing compliance with pre-anesthesia/pre-sedation **fasting** guidelines. In particular, the beverage composition is specially designed to be taken orally, by a patient, within a specified short period of time prior to administration of an anesthesia and/or sedative/analgesic. Further described herein is the method of use of the beverage composition, which method is designed to optimize the benefits of the beverage. Most preferably, the method includes providing a written label of instructions affixed to the beverage container which instructions positively direct the patient's ingestion of the beverage composition and complete **fasting** thereafter. While conscious and in the erect position, the lower esophageal sphincter (LES) and laryngeal closing reflex of a healthy person prevent regurgitation and aspiration of stomach contents. Administration of anesthesia and/or sedative/analgesic drugs often compromises many natural reflexes, including these reflexes that help protect one's airway from such regurgitation and aspiration. Upon induction of and emergence from anesthesia, as well as intravenous sedation, a patient is at greatest risk for aspiration of gastric contents, particularly because the patient is usually supine. One study has suggested that as many as 20% of patients given general anesthesia for surgery suffer at least some regurgitation and subsequent aspiration. See, Harris, et al., Can. Anaesth. Soc. J., 31:599 (1984). More than fifty years ago, C. L. Mendelson thoroughly described, for the first time, the symptoms of aspiration of stomach contents into the lungs, now known generally as aspiration pneumonia. Mendelson, C. L., Am. J. Obstet. Gynecol. 52:191 (1946). Mendelson's observations, which were made of pregnant women anesthetized during labor, led him to describe two types of aspiration: 1) aspiration of solid gastric material, resulting in blockage of the patient's airway and risk of subsequent suffocation and/or pneumonia; and 2) aspiration of liquid gastric material, resulting in pneumonia and/or other asthma-like symptoms. Aspiration pneumonia, also sometimes referred to as Mendelson's Syndrome, was reproduced experimentally by injecting human acidic vomitus into rabbit tracheas. However, injection of neutralized vomitus caused no such symptoms. It is observations such as these that have led researchers to the conclusion that the acidity of the material aspirated from the stomach is the primary causative factor in aspiration pneumonia. See for example, Kinni, et al., J. Oral Maxillofac. Surg. 44:378-384 (1986); and Mendelson, C. L., Am. J. Obstet. Gynecol. 52:191 (1946).

Web site: http://www.delphion.com/details?pn=US06069131__

- **Serum bilirubin and liver function tests as risk predictors for coronary artery disease**

  Inventor(s): Schwertner; Harvey A. (San Antonio, TX)

  Assignee(s): The United States of America as represented by the Secretary of the Air (Washington, DC)

  Patent Number: 5,380,667

  Date filed: October 30, 1992

  Abstract: A new series of non-lipid risk factors for predicting coronary artery disease (CAD) are disclosed. The level of serum total bilirubin was found to be a statistically significant independent risk factor for CAD and to be inversely related to CAD. Similarly, the levels of **fasting** blood sugar, serum glutamate pyruvate transaminase and the ratio of total cholesterol to serum total bilirubin were found to be significant univariate predictors of CAD.

  Excerpt(s): The present invention relates generally to predictive tests for early onset of coronary artery disease, and more particularly to the use of serum bilirubin, **fasting**

blood sugar and liver function tests as risk predictors for coronary artery disease. Cholesterol, smoking, and hypertension are widely recognized as major risk factors for coronary artery disease (CAD), often referred to by the more general term coronary heart disease. Of these risk factors, cholesterol has consistently been found to have the highest association with coronary artery disease and to be its best predictor. Accordingly, much attention has been focused on cholesterol as a risk factor. More recently, a number of lipoproteins and apolipoproteins have been identified as major risk predictors and some of them, for example, high density lipoprotein (HDL) cholesterol, have been identified as independent risk factors. A particular problem of CAD and other related heart diseases is that most individuals with heart disease are largely asymptomatic until their first heart attack. Unfortunately, the major risk factors thus far identified in the prior art are not perfect predictors, particularly for predicting the risk of coronary artery disease in any single individual. Thirty to forty percent of the population is still misdiagnosed using the known major risk factors.

Web site: http://www.delphion.com/details?pn=US05380667__

- **Transgenic animal models for type II diabetes mellitus**

  Inventor(s): Carty; Maynard D. (Gales Ferry, CT), Kreutter; David K. (Madison, CT), Soeller; Walter C. (Mystic, CT)

  Assignee(s): Pfizer Inc (New York, NY)

  Patent Number: 6,187,991

  Date filed: May 23, 1995

  Abstract: The generation of transgenic animal models for testing various treatments of Type II Diabetes Mellitus are described. The DNA construct allows pancreatic.beta. cell-specific expression of human islet associated polypeptide (IAPP) under the regulation of the rat insulin II promoter in both cell lines and transgenic animals. The DNA construct is introduced into animal embryos by microinjection as one or multiple copies or into established cell lines by electroporation. The transgenic animals develop amyloid plaque deposits in the islets of Langerhans in the pancreas, **fasting** hyperglycemia, glycouria and diabetic glomerulosclerosis at 3 to 5 months of age. The cell lines can be screened for treatments that inhibit expression of human IAPP; the transgenic animals can be screened for treatments that either enhance or inhibit the progression of this disease phenotype.

  Excerpt(s): This invention relates to a process for genetic alteration of mammalian cell lines and animals such that they express the protein encoded by the human Islet Amyloid Polypeptide (IAPP) gene. IAPP, formerly known as amylin, is the major protein component of pancreatic islet amyloid that forms in the pancreata of Non-insulin Dependent Diabetes Mellitus (NIDDM) patients. Recent studies of IAPP structural and functional characteristics suggest that IAPP, along with insulin and other hormones, plays a major role in carbohydrate metabolism. IAPP is produced, stored and secreted by pancreatic.beta. cells in the islets of Langerhans. It can mimic the phenomenon of insulin resistance seen in NIDDM by inhibiting glucose uptake and glycogen synthesis in muscle, and liver tissue. The generation of amyloid deposits in humans is thought to be due to the ability of the center portion of the peptide (amino acids 20-29) to form a.beta. pleated sheet structure, Rodent IAPP differs from human IAPP in that the sequences in this otherwise highly conserved protein between amino acids 20-29 are not conserved and amyloid deposits do not form in rodent pancreata. A working hypothesis is that overexpression of human IAPP leads to insulin resistance in

peripheral tissues and in the formation of amyloid deposits. Transgenic animals, especially mice, have proven to be very useful in dissecting complex systems to generate new information about human disease. Selective expression of human genes in such mice has generated novel model systems to study disease, especially when overexpression of a gene results in a disease state. With such transgenic mice, one can address issues concerning (1) tissue specificity of expression; (2) testing of hypotheses that overexpression of a particular gene leads to disease; (3) the number and identity of tissues/organs that are affected by this overexpression; and (4) effects of various treatments, including drugs, on the progression or amelioration of the disease phenotype. The generation of transgenic mice that express human IAPP has been reported in the literature, though none of these animals developed a diabetic phenotype. Niles Fox et al. (FEBS Letters 323, 40-44 [1993]) constructed a transgene that fused the rat insulin promoter sequence to a genomic DNA fragment containing the entire human IAPP gene (exons 1-3 and introns 1 and 2). Transgene RNA expression was detected in pancreas, anterior pituitary and brain. Although plasma IAPP levels were 5-fold elevated relative to nontransgenic littermates, no metabolic consequence of this elevation was observed. C. B. Verchere et al. (Diabetologia 37, 725-729 [1994]) used a 600 bp fragment encoding the entire human proIAPP sequence. Their transgenic animals exhibited greater pancreatic content of both IAPP and insulin relative to nontransgenic littermate controls. Increased secretion of both hormones was also detected in perfused pancreas studies. No clinical manifestations of this enhanced storage and secretion were observed. Hoppener et. al. (Diabetologia 36, 1258-1265 [1993]) described the generation of multiple transgenic lines that expressed either human or rat IAPP in the mouse endocrine pancreas. Hoppener's group used a 703 bp rat insulin II promoter fragment to drive expression of human or rat IAPP from genomic DNA fragments. Plasma IAPP levels were up to 15 fold elevated but no hyperglycemia nor hyperinsulinemia were observed. In a subsequent study, no amyloid plaque was seen to accumulate in vivo but intra- and extracellular amyliod fibrils did form when islets from these transgenics were cultured in vitro under conditions mimicking hyperglycemia (De Koning et al. Proc. Natl. Acad. Sci. 91, 8467-8471 [1994]).

Web site: http://www.delphion.com/details?pn=US06187991__

- **Treatment for hypoglycemia**

  Inventor(s): Geho; W. Blair (Wooster, OH)

  Assignee(s): Technology Unlimited Inc. (West Wooster, OH)

  Patent Number: 4,602,043

  Date filed: April 26, 1984

  Abstract: This invention is for an improved method of treating the disease of hypoglycemia (low blood glucose), based on the discovery by the inventor of the etiology of the disease. The genesis of this invention is in the discovery that insulin alone does not control the uptake and regeneration of glucose by the liver. It has been discovered that hepatic storage of glucose following a meal requires the related function of insulin and serotonin. Hypoglycemia occurs during **fasting** and is due to an inappropriate release of serotonin to the liver. From this, the method of using a serotonin antagonist or an agent to block synthesis and/or storage of serotonin in timed relationship to ingested food to stop the action or the production of serotonin after glucose is no longer supplied to the portal vein is described. Then the liver can cease

glucose uptake and begin production of glucose for the peripheral blood supply. The preferred antagonist is cyproheptadine.

Excerpt(s): Therapeutic methods for control of low blood sugar levels in warm blooded animals, including humans. Glucose in the blood is a primary energy nutrient for the body. Its level in the blood is carefully controlled so that it neither goes too high nor too low. Maintaining a constant blood level of glucose is so important that the body has, within the limits of current understanding of physiology, surprisingly sophisticated hormonal systems to prevent both hyperglycemia (blood glucose too high) and hypoglycemia (blood glucose too low). The body has diseases that are characterized by blood glucose levels that are either too high (i.e., Diabetes Mellitus types I and II) or too low (i.e., hypoglycemia). This disclosure describes improved therapeutic means to correct abnormally depressed blood glucose levels.

Web site: http://www.delphion.com/details?pn=US04602043__

- **Use of gut-trophic growth factors to improve oxidative status**

  Inventor(s): Jones; Dean P. (Decatur, GA), Ziegler; Thomas R. (Lilburn, GA)

  Assignee(s): Emory University (Atlanta, GA)

  Patent Number: 6,335,317

  Date filed: April 9, 1999

  Abstract: The present disclosure describes methods for minimizing oxidative damage in an animal or human during or after malnutrition, underfeeding or **fasting,** especially during refeeding after undernutrition or malnutrition, and for minimizing oxidant damage during or after toxicity resulting from chemotherapy, alcoholism, irradiation therapy or chemical or environmental exposure to a toxic compound. Administration of an effective amount of a gut trophic growth factor (GTGF) effective for improving gut and/or systemic antioxidant status results in improved clinical condition and/or outcome for the patient or animal to which the GTGF has been administered. In the context of the present disclosure, GTGF includes fibroblast growth factors, keratinocyte growth factor, hepatocyte growth factor, insulin-like growth factor I, glucagon, glicentin, and glucagon-like peptide.

  Excerpt(s): Growth of the gastrointestinal mucosa is markedly influenced by nutritional status and enteral nutrient availability. This is evidenced by the disproportionate loss of gut mucosal mass relative to body weight during starvation and other states of malnutrition (1-2). **Fasting** or severe protein-calorie restriction result in mucosal cell atrophy, decreased digestive enzyme activity and absorptive capacity, and impaired intestinal barrier function (3-4). Malnutrition is also associated with reduced antioxidant capacity in the intestinal mucosa (5). Enteral refeeding after a period of malnutrition rapidly regenerates intestinal cellularity and mucosal mass (3-5). The tripeptide glutathione (L-glutamyl-L-cysteinyl-glycine, GSH) is the most abundant low molecular weight thiol in mammalian cells and plays a key role in the detoxification of cellular free radicals, chemical toxins, and carcinogens (16). GSH deactivates potentially harmful oxidants by serving as a hydrogen donor to reduce reactive molecules with concomitant conversion to its oxidized disulfide form, GSSG (6). GSH is synthesized endogenously in mucosal cells utilizing specific amino acid substrates, can be derived exogenously from dietary sources, or may enter the gut lumen via bile and by direct secretion from mucosal cells (7-8). GSH present in the gut lumen and within enterocytes appears to be required for normal intestinal function, in part, by protecting intestinal epithelial cells

from damage by dietary electrophiles and fatty acid hydroperoxides (9-11). GSH also appears to play a role in maintaining the proper sulfhydryl/disulfide balance of gut luminal proteins, potentially modulating activity of thiol-containing enzymes on the brush border (12-13). Previous studies demonstrate that malnutrition reduces tissue GSH content (5, 15-16). In animal models, **fasting** or an insufficient dietary supply of amino acids that may serve as GSH substrates (e.g., glutamine and cysteine) depletes GSH levels in both small intestine and colon (5, 16, 17). Therefore, malnutrition-associated depletion of cellular GSH in gut epithelial cells may increase their susceptibility to oxidative injury and exacerbate the degeneration of the intestinal mucosa (17). Also, there is evidence to suggest that GSH is involved in regulation of cell growth (18).

Web site: http://www.delphion.com/details?pn=US06335317__

- **Use of oral diazoxide for the treatment of disorders in glucose metabolism**

  Inventor(s): Paulsen; Elsa P. (1115 Hilltop Rd., Charlottesville, VA 22903)

  Assignee(s): none reported

  Patent Number: 5,284,845

  Date filed: August 27, 1992

  Abstract: A method is disclosed for normalizing blood glucose and insulin levels as measured by an oral glucose tolerance test in an individual exhibiting normal **fasting** blood glucose and insulin levels and exhibiting in an oral glucose tolerance test elevated glucose levels and at least one insulin level abnormality selected from the group consisting of a delayed insulin peak, an exaggerated insulin peak and a secondary elevated insulin peak. The method comprises administering diazoxide to the individual before ingestion of a food source in an amount effective to normalize the blood glucose and insulin levels. Diazoxide is administered in an amount from about 0.4 to about 0.8 mg/kg body weight before each meal.

  Excerpt(s): This invention relates to the utilization of oral diazoxide for the treatment of disorders caused by defects in glucose metabolism, including hyperglycemia and hypoglycemia. This invention also relates to use of diazoxide to delay or prevent onset of insulin dependency in Type II diabetic subjects. The responsiveness of patients to diazoxide treatment may also provide a useful tool for diagnosing Type II or pre-Type II diabetes. The central role of insulin in human metabolism is to aid in the transport of glucose into muscle and fat cells. The disease states, such as diabetes mellitus, which result from defects in either the ability of the body to produce insulin or in defective insulin binding are well documented. Type I or insulin dependent diabetes is characterized by decreased insulin production leading to hyperglycemia, ketoacidosis, thirst and weight loss. In general, defects in insulin production or activity are associated with hyperglycemia, i.e. the failure of cells to take up glucose and subsequent high circulating blood levels.

  Web site: http://www.delphion.com/details?pn=US05284845__

- **Weight loss induced by alpha interferon and gamma interferon**

  Inventor(s): Ericsson; Arthur Dale (Houston, TX)

  Assignee(s): RX/IBR Corporation (Houston, TX)

  Patent Number: 6,270,756

  Date filed: August 30, 1999

  Abstract: The invention is based on the discovery that substances which release ZAG proteins from lymphocytes also cause accelerated weight loss in humans. By administering an amount of the substance which is effective to cause the weight loss but is beneath an amount which causes side effects, a very desirable "dieter's aid" is provided. A dilute mixture of alfa interferon and gamma interferon in an aqueous medium is highly suitable for this purpose. It is administered at a much lower dosage than is generally employed for antibiotic purposes, thereby avoiding generally universal side effects. For periods of time extending at least for a few days, the weight loss composition of the invention causes weight loss at a greater weight than would be expected from **fasting,** at least for seriously overweight individuals.

  Excerpt(s): Body weight and obesity are like the weather: Everyone talks about it, but no one seems able to do much about it. In recent years researchers have learned a great deal about the cause and ramifications of obesity. Metabolism-the way we absorb, utilize, break down and eliminate the waste from food stuffs-is only a part of the difference between individuals. In order to understand these differences, the playing field must be analyzed, not a macro-cellular level, but rather at a micro-cellular level. At the micro-cellular level, uncoupling proteins (UCPs) have been found to exist and they dissociate the reactions that break down food from those that produce the body's chemical energy. These UCPs let hydrogen ions pass through the cellular inner mitochondrial membrane, thereby abolishing the hydrogen ion gradient needed to drive ATP synthesis. If the UCPs activity could be increased by 1-2% then there would be an increase fat oxidation and thermogenesis. This would translate into a boost in resting metabolic rates and subsequent weight loss for millions of individuals. A technique to increase the action of the body's own uncoupling proteins would be very desirable, and could add years of life for certain individuals. In one embodiment of the invention, there is provided a method for promoting weight loss in humans. The method is carried out by administering effective amount of a substance which actuates the production and release of ZAG proteins from lymphocytes, but preferably beneath an amount which causes side effects.

  Web site: http://www.delphion.com/details?pn=US06270756__

Patent Applications on Fasting

As of December 2000, U.S. patent applications are open to public viewing.[9] Applications are patent requests which have yet to be granted. (The process to achieve a patent can take several years.) The following patent applications have been filed since December 2000 relating to fasting:

[9] This has been a common practice outside the United States prior to December 2000.

- **Antidiabetic preparation for oral administration**

  Inventor(s): Kato, Nobuo; (Tokyo, JP), Makino, Chisato; (Kawasaki-Shi, JP), Ninomiya, Nobutaka; (Kawasaki-Shi, JP), Orita, Haruo; (Kawasaki-Shi, JP), Sakai, Hidetoshi; (Kawasaki-Shi, JP), Shioya, Shigeru; (Tokyo, JP), Yabuki, Akira; (Kawasaki-Shi, JP)

  Correspondence: Oblon Spivak Mcclelland Maier & Neustadt PC; Fourth Floor; 1755 Jefferson Davis Highway; Arlington; VA; 22202; US

  Patent Application Number: 20030021843

  Date filed: June 28, 2002

  Abstract: There is provided a single preparation which directly decreases both of the post prandial blood glucose level and the **fasting** blood glucose level close to normal levels, by release-sustaining a drug capable of decreasing the post prandial blood glucose level of diabetic patients close to the normal level, or mixing a controlled release drug capable of decreasing the post prandial blood glucose level close to the normal level with an immediate release drug. It is particularly preferable that the drug capable of decreasing the post prandial blood glucose level close to the normal level is nateglinide.

  Excerpt(s): The present invention relates to an antidiabetic, particularly to a preparation for directly controlling, namely decreasing both a post prandial blood glucose level and a **fasting** blood glucose level of diabetic patients with one preparation to make these levels close to normal levels. Ordinary antidiabetics are antidiabetics for decreasing either a post prandial blood glucose level or a **fasting** blood glucose level to make it close to a normal level. As antidiabetics for decreasing a post prandial blood glucose level to make it close to a normal level, nateglinide has been developed, and it is described in, for example, Japanese Patent Publication No. 15,221/1992 or Japanese Patent Laid-Open No. 194,969/1998. Further, antidiabetics for decreasing a **fasting** blood glucose level to make it close to a normal level are described in, for example, Kondo Nobuo, Nippon Rinsho, vol. 55, 1997, extra ed., p. 159 and the like. In recent years, for treating diabetes, it has been considered important that both a post prandial blood glucose level and a **fasting** blood glucose level are decreased to make them close to normal levels. However, there have been no preparations for decreasing both levels to make them close to normal levels.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Combinations comprising dipeptidylpeptidase-iv inhibitor**

  Inventor(s): Balkan, Bork; (Madison, CT), Holmes, David Grenville; (Binningen, CH), Hughes, Thomas Edward; (Somerville, NJ), Villhauer, Edwin Bernard; (Morristown, NJ)

  Correspondence: Thomas Hoxie; Novartis, Patent And Trademark Department; One Health Plaza 430/2; East Hanover; NJ; 07936-1080; US

  Patent Application Number: 20030139434

  Date filed: October 10, 2002

  Abstract: The invention relates to a combination which comprises a DPP-IV inhibitor and at least one further antidiabetic compound, preferably selected from the group consisting of insulin signalling pathway modulators, like inhibitors of protein tyrosine phosphatases (PTPases), non-small molecule mimetic compounds and inhibitors of glutamine-fructose-6-phosphate amidotransferase (GFAT), compounds influencing a

dysregulated hepatic glucose production, like inhibitors of glucose-6-phosphatase (G6Pase), inhibitors of fructose-1,6-bisphosphatase (F-1,6-BPase), inhibitors of glycogen phosphorylase (GP), glucagon receptor antagonists and inhibitors of phosphoenolpyruvate carboxykinase (PEPCK), pyruvate dehydrogenase kinase (PDHK) inhibitors, insulin sensitivity enhancers, insulin secretion enhancers,.alpha.-glucosidase inhibitors, inhibitors of gastric emptying, insulin, and.alpha.sub.2-adrenergic antagonists, for simultaneous, separate or sequential use in the prevention, delay of progression or treatment of conditions mediated by dipeptidylpeptidase-IV (DPP-IV), in particular diabetes, more especially type 2 diabetes mellitus, conditions of impaired glucose tolerance (IGT), conditions of impaired **fasting** plasma glucose, metabolic acidosis, ketosis, arthritis, obesity and osteoporosis; and the use of such combination for the cosmetic treatment of a mammal in order to effect a cosmetically beneficial loss of body weight.

Excerpt(s): The invention relates to a combination, such as a combined preparation or pharmaceutical composition, respectively, which comprises a dipeptidylpeptidase-IV (DPP-IV) inhibitor and at least one further antidiabetic compound, preferably selected from the group consisting of insulin signalling pathway modulators, like inhibitors of protein tyrosine phosphatases (PTPases), non-small molecule mimetic compounds and inhibitors of glutamine-fructose-6-phosphate amidotransferase (GFAT), compounds influencing a dysregulated hepatic glucose production, like inhibitors of glucose-6-phosphatase (G6Pase), inhibitors of fructose-1,6-bisphosphatase (F-1,6-BPase), inhibitors of glycogen phosphorylase (GP), glucagon receptor antagonists and inhibitors of phosphoenolpyruvate carboxykinase (PEPCK), pyruvate dehydrogenase kinase (PDHK) inhibitors, insulin sensitivity enhancers, insulin secretion enhancers,.alpha.-glucosidase inhibitors, inhibitors of gastric emptying, insulin, and a.sub.2-adrenergic antagonists, for simultaneous, separate or sequential use, especially in the prevention, delay of progression or treatment of conditions mediated by dipeptidylpeptidase-IV (DPP-IV), in particular diabetes, more particular type 2 diabetes mellitus, conditions of impaired glucose tolerance (IGT), conditions of impaired **fasting** plasma glucose, metabolic acidosis, ketosis, arthritis, obesity and osteoporosis; the use of such combination for the preparation of a pharmaceutical preparation for the prevention, delay of progression or treatment of such conditions; the use of such combination for the cosmetic treatment of a mammal in order to effect a cosmetically beneficial loss of body weight; a method of prevention, delay of progression or treatment of conditions mediated by DPP-IV; a method of improving the bodily appearance of a warm-blooded animal. DPP-IV is responsible for inactivating GLP-1. More particularly, DPP-IV generates a GLP-1 receptor antagonist and thereby shortens the physiological response to GLP-1. GLP-1 is a major stimulator of pancreatic insulin secretion and has direct beneficial effects on glucose disposal. Non-insulin dependent diabetes mellitus (type 2 diabetes mellitus) is characterized by both increased peripheral insulin resistance and abnormal insulin secretion. At least three abnormalities of insulin secretion are recognized: in the first phase, insulin secretion is lost and in the second phase insulin is both delayed and inadequate in the face of elevated circulating glucose levels. Several metabolic, hormonal, and pharmacological entities are known to stimulate insulin secretion including glucose, amino-acids and gastrointestinal peptides. The Diabetes Control and Complications Trial (DCCT) has established that lowering of blood glucose is associated with decreases in the onset and progression of diabetic microvascular complications (Diabetes Control and Complications Trial Research Group; N. Engl. J. Med. 1993, 329, 977-986). IGT is an impairment of glucose homeostasis closely related to type 2 diabetes mellitus. Both conditions convey a great risk of macrovascular disease. Therefore, one therapeutic focus is on optimizing and potentially normalizing glycemic control in

subjects with type 2 diabetes mellitus, conditions of impaired **fasting** plasma glucose, or IGT. Presently available agents need to be improved in order to better meet this therapeutic challenge.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **COMPOSITIONS AND METHOD FOR IMPROVING INSULIN SENSIVITY AND GLUCOSE METABOLISM IN INDIVIDUALS WITH IMPAIRED FASTING GLUCOSE OR IMPAIRED GLUCOSE TOLERANCE**

  Inventor(s): ALLAN, GEOFFREY; (RICHMOND, VA)

  Correspondence: Sterne Kessler Goldstein & Fox; 1100 New York Ave NW; Suite 600; Washington; DC; 200053934

  Patent Application Number: 20010039297

  Date filed: May 19, 1998

  Abstract: The current invention relates to the use of D-chiro-inositol in improving insulin sensitivity and glucose metabolism in individuals with abnormal glucose tolerance who do not have Type 2 diabetes. D-chiro-inositol and related oral compositions may be used in treating abnormal glucose tolerance and metabolism and insulin sensitivity in mammals, and thus help prevent the progression to insulin-resistant Type 2 diabetes.

  Excerpt(s): Abnormal glucose tolerance refers to metabolic stages intermediary to normal glucose homeostasis and Type 2 diabetes; this includes conditions like impaired glucose tolerance (IGT) and impaired **fasting** glucose (IFG) where glucose values are above the conventional normal range and are often accompanied by a decrease in insulin sensitivity. Impaired glucose tolerance (IGT) and impaired **fasting** glucose (IFG) are transient, intermediate stages in the development of Type 2 diabetes. Within ten years of diagnosis, approximately 30% of IGT subjects will progress to Type 2 diabetes and potentially to health problems that accompany this disease, including retinopathy, nephropathy, and peripheral neuropathy. In addition, abnormal glucose tolerance and decreased insulin sensitivity are associated with a high risk for the development of hypertension, dyslipidemia and an increase incidence of coronary artery disease. Abnormal glucose tolerance and decreased insulin sensitivity can be attributed to a wide range of causes including obesity, age, physical activity level, certain medication or drugs, genetic factors, and some endocrine related disorders. The truncal distribution of weight as determined by a high waist to hip ratio (WHR) is a good predictor of abnormal insulin sensitivity, and there is an excellent correlation between a high body mass index (BMI) and decreased insulin sensitivity. Approximately 33% of the population in the United States is obese and the majority of these individuals have decreased insulin sensitivity, are hyperinsulinemic, and often have abnormal glucose tolerance.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **GPCR-like retinoic acid-induced gene 1 protein and nucleic acid**

  Inventor(s): Lewin, David A.; (New Haven, CT), Stewart, Timothy A.; (San Francisco, CA)

  Correspondence: Sonnenschein Nath & Rosenthal; P.O. Box 061080; Wacker Drive Station; Chicago; IL; 60606-1080; US

  Patent Application Number: 20030207288

  Date filed: August 20, 2002

  Abstract: A novel G-protein coupled receptor-like retinoic acid induced molecule was identified as being differentially expressed (GPCR-like RAIG1) in an animal model of **fasting** and feeding. Compositions and methods pertaining to treatment and diagnosis of various metabolic disorders, such as cachexia and obesity.

  Excerpt(s): This application claims priority to No. 60/313,940 filed Aug. 20, 2001, the entirety of which is herein incorporated by reference. Millions of people throughout the world are affected daily by metabolic disorders such as obesity, anorexia, cachexia, and diabetes. Though the causes for these disorders are as varied as the disorders themselves, many candidate genes and gene products, such as insulin, leptin, and ghrelin, have been identified as potential drug targets for treatment of these disorders. Understanding metabolic disorders has been hampered by the absence of an animal model that immediately reflects the human situation. Human metabolic disorders do not generally follow a Mendelian inheritance pattern, wherein a single gene determines a metabolic disorder phenotype (physical manifestation of a gene's expression; Weigle and Kuijper, 1996), although there are several rodent models that do (Spiegelman and Flier, 1996; Weigle and Kuijper, 1996). Human metabolism is a quantitative trait with many genes, as well as environmental and behavioral aspects, responsible for metabolic activities and disorders (Clement et al., 1998; Montague et al., 1997; Comuzzie and Allison, 1998; Hill and Peters, 1998).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Hereditary postprandial hypertriglyceridemic rabbit model**

  Inventor(s): Ito, Tsunekata; (Yamagata City, JP), Owada, Kazuo; (Yamagata City, JP), Tomoike, Hitonobu; (Yamagata City, JP)

  Correspondence: Robert G. Mukai; Burns, Doane, Swecker & Mathis, L.L.P.; P.O. Box 1404; Alexandria; VA; 22313-1404; US

  Patent Application Number: 20010027568

  Date filed: November 29, 2000

  Abstract: In attempts to determine the cause of hypertriglyceridemia, a model animal was established. This model is useful to analyze on the relationship between food ingestion and hypertriglyceridemia. When backcrossing of the Watanabe heritable hyperlipidemic rabbit and the Japanese white rabbit, individual rabbits with high triglyceride values were identified. A novel hereditary postprandial hypertriglyceridemic rabbit, characterized by normal serum triglyceride values under conditions of **fasting** and high levels of serum triglyceride value by ingestion of food was thus obtained.

  Excerpt(s): The three main causes of death worldwide are cancer, cardiac and cerebrovascular-related diseases. The number 1 cause of mortality in the United States is

coronary heart disease. Accordingly, to limit the occurrence of vascular diseases is one of the most important medical challenges for the 21st century. The main underlying cause of vascular diseases is atherosclerosis. Factors closely related to the occurrence and severity of atherosclerosis have been elucidated in epidemiological studies and these factors are designated "risk factors". Known risk factors for atherosclerotic heart disease are hyperlipidemia, hypertension, diabetes, tobacco use and gender (male, menopausal females). Hyperlipidemia includes hypercholesterolemia, hypertriglyceridemia and a combination of these lipid abnormalities. The objective of this invention was to design an animal model with high levels of serum lipid following ingestion of food. Hyperlipidemia is a well accelerating factor for atherosclerosis. The effect of diet on lipid and lipoprotein concentration is well established. In clinical situations where hyperlipidemia is the main pathogenesis of atherosclerosis, postprandial hyperlipidemia has been considered a serious risk factor, which aggravates vascular diseases. However, whether postprandial hyperlipidemia is acquired or is heritable in nature, the characteristics of lipid metabolism in postprandial hyperlipidemia and how and when these lipid metabolisms aggregate have not investigated systematically. The model animal designed here will be used widely as a clinical specimen to explore these questions. The Watanabe heritable hyperlipidemic rabbit (WHHL) has hyperlipidemia, and a pure line of rabbits with heritable combined hypercholesterolemia and hypertriglyceridemia after selected inbreedings was obtained and has been designated a hereditary hypertriglyceridemic rabbit (TGH: TG=triglyceride, H=high). Hypercholesterolemia in WHHL is caused by a genetic anomaly on LDL (low-density lipoprotein) receptor. The hereditary hypertriglyceridemia rabbit was selected from a WHHL rabbit sub-line, characterized by unusual high levels of triglyceride. The workers crossed TGH and Japanese White rabbit (JW) to determine the mode inheritance and individual rabbits with hypertriglyceridemia only after ingestion of food were identified. There have been no descriptions of a model animal with the hereditary trait of hypertriglyceridemia only after ingestion of food.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method for the reduction of fasting plasma glucose and hemoglobin AIC levels**

  Inventor(s): Bailey, William L.; (Mendham, NJ), Jewell, Jeffrey T.; (Morrisville, NC), Wingertzahn, Mark A.; (Stroudsburg, PA)

  Correspondence: Bruce D. Radin; Budd Larner Rosenbaum,; Greenberg & Sade, P.C.; 150 John F. Kennedy Parkway; Short Hills; NJ; 07078; US

  Patent Application Number: 20030175237

  Date filed: February 26, 2003

  Abstract: A method of reducing levels of **fasting** plasma glucose and/or hemoglobin A.sub.1C in patients by the administration of an aliphatic amine polymer, such as colesevelam HC1, either alone or in combination with a statin. In particular, the invention reduces LDL-cholesterol, FPG and HbA.sub.1c in patients with or without glucose intolerance. Also, the invention provides a method of treating hyperglycemia and prevent or delay associated microvasular complications in patients with impaired **fasting** glucose, T2DM and insulin resistance.

  Excerpt(s): This application claims the benefit of priority of U.S. Provisional Application No. 60/359,890, filed on Feb. 26, 2002. The entire teaching of the above-referenced application is incorporated herein by reference. The present invention relates to a

method of reducing levels of **fasting** plasma glucose and/or hemoglobin A.sub.1c by the administration of an aliphatic amine polymer, such as colesevelam HC1, either alone or in combination with a statin.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method of decreasing fasting sugars and weight gains in diabetic patients**

  Inventor(s): Landschulz, William H.; (East Lyme, CT)

  Correspondence: Pfizer INC.; Patent Department, Ms8260-1611; Eastern Point Road; Groton; CT; 06340; US

  Patent Application Number: 20030079747

  Date filed: June 19, 2002

  Abstract: Inhaled insulin, relative to subcutaneously and/or transdermally administered insulin, can be used to prevent the rate of weight gain and to lower the levels of **fasting** glucose in diabetic patients.

  Excerpt(s): This invention is directed to a method of reducing the rate of weight gain and/or to lowering **fasting** blood sugars in a diabetic patient who is using exogenous insulin to control blood sugars, and who is taking said insulin by other than a pulmonary route of administration, comprising administering said insulin to said patient by the pulmonary route, i.e. as inhaled insulin. Additionally, the invention relates to starting a patient on inhaled insulin who is at risk for gaining weight or developing high **fasting** blood sugars. Diabetes mellitus is a serious metabolic disease that is defined by the presence of chronically elevated levels of blood glucose. Classic symptoms of diabetes mellitus in adults are polyuria and polydipsia together with elevated levels of plasma glucose. Normal **fasting** plasma glucose concentrations are less than 110 milligrams per deciliter. In diabetic patients, **fasting** concentrations are found to be at or above 126 milligrams per deciliter. In general, diabetes mellitus develops in response to damage to, or to defects in, the beta cells of the pancreas. Primary diabetes mellitus is classified as Type 1 diabetes (also called insulin-dependent diabetes mellitus or IDDM) and Type 2 diabetes mellitus (also called non-insulin dependent diabetes mellitus or IDDM). Type I (juvenile onset or insulin-dependent) diabetes is a well-known hormone deficient state, in which the pancreatic beta cells appear to have been destroyed by the body's own immune defense mechanisms. Patients with Type I diabetes mellitus have little or no endogenous insulin secretory capacity. These patients develop extreme hyperglycemia. Type I diabetes was fatal until the introduction of insulin replacement therapy some 70 years ago--first using insulins from animal sources, and more recently, using human insulin made by recombinant DNA technology.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Oral administration of interferon-tau**

  Inventor(s): Liu, Chih-Ping; (San Francisco, CA), Sokawa, Yoshihiro; (Kyoto, JP)

  Correspondence: Perkins Coie Llp; P.O. Box 2168; Menlo Park; CA; 94026; US

  Patent Application Number: 20030219405

  Date filed: January 16, 2003

Abstract: A method of administering interferon-.tau. to a subject subsequent to a defined food and/or water intake regimen is described. The method comprises administering orally to the subject, subsequent to **fasting** and/or **fasting** combined with a controlled or absence of fluid intake, an amount of interferon-.tau. that is effective to achieve an increased level of 2',5'-oligoadenylate synthetase (OAS) activity in whole blood relative to that achieved from oral administration to a subject also treated with interferon-.tau. but not held to the defined food and/or water intake regimen.

Excerpt(s): This application claims the benefit of U.S. Provisional Application No. 60/349,658, filed Jan. 16, 2002, incorporated herein by reference in its entirety. The present invention relates generally to oral delivery of cytokines and more particularly to oral delivery of interferons. In recent years, the variety of therapeutic agents for treatment of physiological conditions and disease states has expanded considerably, due in large part to the growing use of polypeptides and proteins as therapeutic agents. The important role of peptides in replacement therapy and as pharmaceutical agents is reflected in the efforts toward synthesis of large quantities of proteins by recombinant DNA technology.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Prediction of wound healing by urinary nitrate assay**

  Inventor(s): Boykin, Joseph V. JR.; (Chester, VA)

  Correspondence: Banner & Witcoff; 1001 G Street N W; Suite 1100; Washington; DC; 20001; US

  Patent Application Number: 20010047035

  Date filed: February 6, 2001

  Abstract: Wound healing is impaired in many diabetics, who suffer increased risk of chronic foot ulceration and amputation. Diabetic patients with poor healing ability were found to possess significantly lower **fasting** urinary nitrate levels than diabetic patients with normal healing ability or non-diabetic controls, implicating decreased endogenous nitric oxide activity as the mediator of diabetes-impaired wound healing. Methods and kits are provided for predicting the wound healing ability of diabetic patients and patients with venous stasis ulceration or another disease or condition characterized by chronically impaired cutaneous wound healing in some patients based on the levels of nitric oxide related products such as nitrate or nitrite in urine or other specimens. Methods are also provided for treating non-wound healing patients and monitoring diabetic ulcer treatment.

  Excerpt(s): This application is a continuation-in-part of U.S. Application No. 09/516,584, filed Mar. 1, 2000, which claims the benefit of U.S. Provisional Application No. 60/125,284, filed Mar. 19, 1999, each of which is hereby incorporated by reference in its entirety. The invention is related to the area of wound healing. In particular it is related to assays for the level of nitric oxide in wound-healing and non-wound healing patients. Diabetes affects an estimated 15 million people in the United States. Within the diabetic population are individuals with chronic, non-healing lower extremity ulceration (LEU), which is associated with significant morbidity and treatment costs. Chronic, non-healing LEU precedes about 85% of the lower extremity amputations (LEA) that over 50,000 diabetics experience annually (GE Reiber, E J Boyko, D G Smith, in Diabetes in America, NIH Publication No. 95-1468, Bethesda, Md., ed. 2, 1995, pp. 409-428). This represents more than half of all individuals receiving LEA in this country. While only 6% of

diabetic hospitalizations are associated with LEU, the total government reimbursement for diabetic lower extremity complications in 1992 exceeded $1.5 billion, not including costs for limb amputation and rehabilitation. Clinical pathophysiologic risk factors for LEA include diabetic neuropathy, lower extremity ischemia, and chronic, non-healing diabetic foot ulcers.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Prolonged efficacy of islet neogenesis therapy methods with a gastrin/CCK receptor ligand and an EGF receptor ligand composition in subjects with preexisting diabetes**

  Inventor(s): Brand, Stephen J.; (Lincoln, MA)

  Correspondence: Sonia K. Guterman, ESQ.; Mintz, Levin, Cohn, Ferris, Glovsky And Popeo, P.C; One Financial Center; Boston; MA; 02111; US

  Patent Application Number: 20020098178

  Date filed: January 11, 2002

  Abstract: Compositions and methods are provided for achieving in vivo islet cell regeneration in subjects with preexisting diabetes. The methods comprise short term treatment with a composition having a gastrin/cholecystokinin receptor ligand and an EGF receptor ligand. Treatment with such a composition for a short term resulted in a prolonged period of increased insulin release, decreased **fasting** blood glucose, and improved glucose tolerance, the prolonged efficacy, the period being considered from the time of cessation of treatment.

  Excerpt(s): The present application claims priority from provisional application serial No. 60/261,638, filed on Jan. 12, 2001. The present application is related to U.S. Pat. Nos. 5,885,956, filed Dec. 14, 1992 and issued Mar. 23, 1999, and 6,288,301 issued Sep. 11, 2001, all of which are hereby incorporated by reference herein. Embodiments of the invention are directed to compositions and methods for a short course of systemic treatment of diabetic patients with a gastrin/cholecystokinin (CCK) receptor ligand and an epidermal growth factor (EGF) receptor ligand, such treatment initiating pancreatic islet neogenesis when administered to subjects, and providing remission of diabetes for a prolonged period of time following cessation of treatment. About 800,000 people in the United States population suffer from insulin deficiency diabetes (also known as juvenile or type I diabetes), and about 30,000 new cases arise each year. Further, an extremely large and rapidly increasing number of patients have forms of type II diabetes (also called adult onset or insulin-resistance diabetes), in this population at a level of epidemic proportions, that cause pancreatic exhaustion and insulin insufficiency. Diabetes type I is generally treated with insulin injection in response to blood glucose levels determined by patient glucose self-monitoring. A variety of forms of insulin, for example, slow and fast acting, and systems and devices suitable for insulin delivery by injection, for example a delivery pen, are used by the growing population of diabetics.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Protective shield apparatus for fork lift trucks**

  Inventor(s): Kunch, Timothy R.; (Glendale, AZ)

  Correspondence: H. Gordon Shields; 7830 North 23rd Avenue; Phoenix; AZ; 85021; US

  Patent Application Number: 20030206792

  Date filed: May 6, 2002

  Abstract: Shield apparatus for a fork lift truck includes a flat stiff plate securable to the mast or vertical portion of a carriage of a fork lift truck. The shield apparatus includes **fasting** elements which are adjustable to fit different sized mast elements of fork lift trucks made by different manufacturers. The shield apparatus comprises a relatively large and flat plate to fit the entire width of the carriage, including the vertical mast elements for the purpose of protecting material with relatively delicate edges, such as wall board, from being damaged while the material is being transported by the fork lift truck. Included are handle elements which allow the shield apparatus to be easily placed on and removed from a fork lift truck.

  Excerpt(s): This invention relates to fork lift trucks and, more particularly, to a shield for protecting materials from being damaged by the mast of a fork lift truck. U.S. Pat. No. 2,956,701 (Larson) discloses a fork lift truck with a vertical element adjacent to the horizontal forks for protecting a pallet while the pallet is being lifted. U.S. Pat. No. 3,625,385 (Ide) discloses a limit plate secured to the forks of a fork lift truck to limit the distance that a pallet may move on the forks. The purpose of the limit element is to protect adjacent cargo while the fork lift truck is loading pallets from rows of cargo laden pallets.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **SELECTED ESSENTIAL AMINO ACID SUPPLEMENTATION OF DIETARY PROTEINS TO LOWER URINARY UREA AND PEAK GLUCOSE LEVELS**

  Inventor(s): Jarowski, Charles Ignatius; (Massapequa Park, NY)

  Correspondence: DR. Charles I. Jarowski; 67 Harbor Lane; Massapequa Park; NY; 11762; US

  Patent Application Number: 20030139465

  Date filed: January 23, 2002

  Abstract: Depending upon the quantity of protein being consumed, one or more unit doses of a blend consisting of L-Tryptophan (80 mgs), L-Methionine (90 mgs), L-Valine (103 mgs) and L-Lysine Monohydrochloride (128 mgs), added as a dietary supplement, will improve the efficiency of amino acid utilization and thereby lower urinary urea excretion and control peak post-prandial blood glucose levels. The levels of supplementation are derived by taking into consideration the average human **fasting** plasma concentrations of essential amino acids and L-Tyrosine and L-Cystine.

  Excerpt(s): Depending upon the quantity of protein being consumed, one or more unit doses of a blend of L-Tryptophan (80 mgs), L-Methionine (90 mgs), L-Valine (103 mgs) and L-Lysine monohydrochloride (128 mgs) was calculated to be a universal dietary supplement for 61 commonly used foods (C. I. Jarowski, U.S. Pat. No. 5,559,142). The levels of supplementation were derived by taking into account the average human **fasting** plasma concentrations of the eight essential amino acids plus L-Tyrosine and L-Cystine. The latter two non-essential amino acids were included since they are L-

Phenylalanine-sparing and L-Methionine-sparing respectively. Earlier studies in Sprague-Dawley rats demonstrated that essential amino acid supplemented rations lowered serum urea levels 44% (G. M. Torre, V. D. Lynch and C. I. Jarowski, J. Pharm. Sci., 70, 114 (1981). The levels of L-Tryptophan, L-Lysine and L-Threonine used to supplement the commercial rat ration were derived by taking into account the average **fasting** plasma concentrations of the essential amino acids of Sprague-Dawley rats. Breakfast: One-half cup of rice (6.9 grams of protein), 2 cups of water, one chicken egg (12.8 gms of protein), one-half cup of Cow's Milk (4.03 grams of protein), one half of a banana, a cup of coffee, 10 ml of evaporated milk (0.7 gram of protein), a glass of orange juice, 10 Ritz crackers (10 grams of wheat protein), one teaspoon of Psyllium Hydrocolloid and one Multivitamin/Multimineral tablet. Total protein: 34.43 grams.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Use of a celecoxib composition for fast pain relief**

  Inventor(s): Brugger, Andrew M.; (Libertyville, IL), Forbes, James C.; (Glenview, IL), Gao, Ping; (Portage, MI), Hassan, Fred; (Peapack, NJ), Karim, Aziz; (Skokie, IL)

  Correspondence: Harness, Dickey, & Pierce, P.L.C; 7700 Bonhomme, Ste 400; ST. Louis; MO; 63105; US

  Patent Application Number: 20020028238

  Date filed: May 25, 2001

  Abstract: There is provided a method of rapidly relieving pain in a mammalian, preferably human, subject. The method comprises orally administering to the subject an effective pain-relieving amount of a composition comprising celecoxib formulated in such a way as to provide, when tested in **fasting** humans in accordance with standard pharmacokinetic practice, a blood plasma concentration profile of celecoxib in which a concentration of about 250 ng/ml is attained not later than about 30 minutes after oral administration.

  Excerpt(s): This application claims priority to U.S. application Ser. No. 60/207,729 filed May 26, 2000. The present invention relates to new uses of certain orally deliverable pharmaceutical formulations containing the selective cyclooxygenase-2 inhibitory drug celecoxib, for fast relief of pain, and for manufacture of medicaments useful in treatment of pain. A need for orally deliverable pharmaceutical compositions giving fast relief of pain exists. A particular need exists for such compositions giving fast relief of pain through selective inhibition of cyclooxygenase-2 (COX-2), without the undesirable side effects associated with inhibition of cyclooxygenase-1 (COX-1) that can occur with conventional non-steroidal anti-inflammatory drugs (NSAIDs). An especial need exists for such compositions giving fast relief of pain through selective inhibition of COX-2, yet exhibiting an onset of effective pain relief at least as rapid as standard NSAIDs used in the art, for example ibuprofen.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Use of amylin agonists to modulate triglycerides**

  Inventor(s): Fineman, Mark; (San Diego, CA), Kolterman, Orville G.; (Poway, CA), Maggs, David G.; (Del Mar, CA), Weyer, Christian; (San Diego, CA)

  Correspondence: Arnold & Porter; IP Docketing Department; RM 1126(b); 555 12th Street, N.W.; Washington; DC; 20004-1206; US

  Patent Application Number: 20030130177

  Date filed: January 8, 2003

  Abstract: Methods of improving lipid profile, including methods for lowering **fasting** triglyceride levels and post-prandial triglyceride excursions are disclosed comprising administering an effective amount of an amylin or amylin agonist.

  Excerpt(s): This application claims the benefit of and priority to U.S. Provisional Application No. 60/347,128, filed Jan. 8, 2002, which is incorporated herein by reference in its entirety. The field of the invention is modulation of circulating lipid levels, especially triglyceride levels. Amylin is a 37-amino acid polypeptide hormone normally co-secreted with insulin by pancreatic beta cells in response to nutrient intake (see, e.g., Koda et al., Lancet 339:1179-1180, 1992). Preclinical studies indicate that amylin acts as a neuroendocrine hormone that complements the actions of insulin in post-prandial glucose control via several effects that collectively reduce the influx of glucose into the circulation to a rate that better matches the rate of insulin-mediated glucose efflux (Weyer et al., Curr Pharm Des 7:1353-73, 2001; Young, Curr Opin Endocrinol Diab 4:282-290, 1997). These effects include a slowing of the rate at which nutrients are delivered from the stomach to the small intestine for absorption (Young et al., Diabetologia 38:642-648, 1995), and a suppression of nutrient-stimulated glucagon secretion (Gedulin et al., Metabolism 46:67-70, 1997). Pramlintide (.sup.25, 28, 29Pro-h-amylin) is a synthetic, soluble, non-aggregating analog of human amylin under development as an adjunct to insulin therapy in both type-1 and type-2 diabetes (Weyer et al., Curr Pharm Des 7:1353-73, 2001; Buse et al Clin Diabetes 20: 137-144, 2002; Edelman and Weyer, Diabetes Technology and Therapeutics 4: 175-189, 2002). Short-term clinical studies in patients with type-1 diabetes have shown that mealtime amylin replacement with subcutaneous (s.c.) injections of pramlintide, in addition to mealtime insulin, slows the rate of gastric emptying (Kong et al., Diabetologia 41:577-583, 1998), suppresses mealtime glucagon secretion (Nyholm et al, Metabolism 48:935-941, 1999; Fineman et al., Metabolism,51:636-641, 2002) and, consequently, improves post-prandial glucose excursions (Nyholm et al., Metabolism 48:935-941, 1999; Thompson et al., Diabetes 46:632-636, 1997).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

Keeping Current

In order to stay informed about patents and patent applications dealing with fasting, you can access the U.S. Patent Office archive via the Internet at the following Web address: **http://www.uspto.gov/patft/index.html**. You will see two broad options: (1) Issued Patent, and (2) Published Applications. To see a list of issued patents, perform the following steps: Under "Issued Patents," click "Quick Search." Then, type "fasting" (or synonyms) into the "Term 1" box. After clicking on the search button, scroll down to see the various patents which have been granted to date on fasting.

You can also use this procedure to view pending patent applications concerning fasting. Simply go back to **http://www.uspto.gov/patft/index.html**. Select "Quick Search" under "Published Applications." Then proceed with the steps listed above.

CHAPTER 6. BOOKS ON FASTING

Overview

This chapter provides bibliographic book references relating to fasting. In addition to online booksellers such as **www.amazon.com** and **www.bn.com**, excellent sources for book titles on fasting include the Combined Health Information Database and the National Library of Medicine. Your local medical library also may have these titles available for loan.

Book Summaries: Federal Agencies

The Combined Health Information Database collects various book abstracts from a variety of healthcare institutions and federal agencies. To access these summaries, go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. You will need to use the "Detailed Search" option. To find book summaries, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer. For the format option, select "Monograph/Book." Now type "fasting" (or synonyms) into the "For these words:" box. You should check back periodically with this database which is updated every three months. The following is a typical result when searching for books on fasting:

- **Practical Insulin: A Handbook for Prescribers**

  Source: Alexandria, VA: American Diabetes Association. 2002. 60 p.

  Contact: Available from American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 232-3472. E-mail: AskADA@diabetes.org. Fax: (770) 442-9742. Website: www.diabetes.org. PRICE: $7.95; plus shipping and handling. ISBN: 580401538.

  Summary: Insulin therapy is a medical necessity for all patients with type 1 diabetes and the many patients with type 2 diabetes who cannot reach their glycemic goals without insulin therapy. This pocket handbook to prescribing insulin is designed to help primary care providers handle ever-increasing numbers of patients with diabetes. The handbook covers patient selection, insulin choices, insulin character, insulin absorption, mixing insulins, insulin regimens, insulin for type 1 patients, insulin for type 2 patients, troubleshooting (patient resistance to starting insulin, weight gain, **fasting**

hyperglycemia, hypoglycemia, and hypoglycemia unawareness), patient SMBG (self monitoring of blood glucose) records, and patient education. Lengthy appendices cover endogenous insulin action, insulin storage, insulin potency, additives, insulin delivery, insulin pumps, and determining insulin to carbohydrate ratio. The handbook concludes with a brief description of the American Diabetes Association and its contact information (www.diabetes.org).

- **Annual Review of Diabetes 2002**

  Source: Alexandria, VA: American Diabetes Association. 2002. 284 p.

  Contact: Available from American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 232-3472. E-mail: AskADA@diabetes.org. Fax: (770) 442-9742. Website: www.diabetes.org. PRICE: $49.95 plus shipping and handling.

  Summary: This issue of the Annual Review of Diabetes includes twenty-one research articles in three categories: epidemiology and pathogenesis, treatment, and complications. Specific topics include neurovascular dysfunction in type 2 diabetes; fatty acid metabolism in the etiology (cause) of type 2 diabetes; diabetes, impaired **fasting** glucose, and elevated HbA1c levels in adolescents; projection of diabetes burden through 2050; autoimmune diabetes; high familial risk and genetic susceptibility in early onset childhood diabetes; **fasting** versus postload glucose levels; influence of intensive diabetes treatment on body weight and composition of adults with type 1 diabetes; interventions to improve the management of diabetes in primary care, outpatient, and community settings; evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications; select vitamins and minerals in the management of diabetes; biological complementary therapies (botanical products in diabetes); effect of metformin in pediatric patients with type 2 diabetes; pump therapy for children; gene and cell-replacement therapy in type 1 diabetes; the prevalence of comorbid depression in adults with diabetes; preventing cardiovascular complications of type 2 diabetes by lipid management; diabetic ketoacidosis and hyperglycemic hyperosmolar syndrome; the barrier of hypoglycemia; and the treatment of hypertension in adult patients with diabetes. Each article concludes with a list of references.

- **Diabetes Mellitus in the Elderly**

  Source: Binghamton, NY: Pharmaceutical Products Press. 1999. 84 p.

  Contact: Available from Pharmaceutical Products Press. 10 Alice Stret, Binghamton, NY 13904-1580. (800)429-6784. E-mail: getinfo@haworthpressinc.com. Website: www.haworthpressinc.com. PRICE: $49.95 plus shipping and handling. ISBN: 0789006820.

  Summary: This volume is devoted to the diagnosis and treatment of diabetes mellitus in the elderly. The first chapter in the monograph addresses the frustration and futility health care providers and ministers sometimes experience in attempting to help patients with diabetes care for themselves. The monograph then includes four articles: the pathophysiology of diabetes in aging; the management of type 2 diabetes in the elderly patient; the use of acarbose in Europe; and insulin use in the elderly. The first article stresses that the recently revised American Diabetes Association (ADA) guidelines that include impaired glucose tolerance (IGT) and a lower level of **fasting** plasma glucose for the diagnosis of diabetes underscore the need for earlier detection of diabetes in the older adult and the relationship of diabetes with obesity. The articles on drug therapy offer practical insight to using the four new oral agents (acarbose, metformin,

repaglinide and troglitazone) for type 2 diabetes, particularly in light of the ADA revised guidelines that suggest the trial of all oral agents before resorting to insulin. The last article discusses the comorbidities (other illnesses present at the same time as the diabetes), nutritional issues, pharmacodynamics, and physiologic effects of various insulin preparations and regimens. Each chapter concludes with a list of references and a subject index concludes the volume. This monograph has been copublished simultaneously as Journal of Geriatric Drug Therapy, Volume 12, Number 2, 1999.

Book Summaries: Online Booksellers

Commercial Internet-based booksellers, such as Amazon.com and Barnes&Noble.com, offer summaries which have been supplied by each title's publisher. Some summaries also include customer reviews. Your local bookseller may have access to in-house and commercial databases that index all published books (e.g. Books in Print®). **IMPORTANT NOTE:** Online booksellers typically produce search results for medical and non-medical books. When searching for "fasting" at online booksellers' Web sites, you may discover non-medical books that use the generic term "fasting" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "fasting" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **A Book of Fasting** by Ahmed Lemu (1996); ISBN: 1881963012; http://www.amazon.com/exec/obidos/ASIN/1881963012/icongroupinterna
- **A Hunger for God: Desiring God Through Fasting and Prayer** by John Piper (1997); ISBN: 0891079661; http://www.amazon.com/exec/obidos/ASIN/0891079661/icongroupinterna
- **Bible Studies for Fasting: For Personal & Group Study** by Cindy G. Spear (Editor), Elmer L. Towns (1997); ISBN: 1570520666; http://www.amazon.com/exec/obidos/ASIN/1570520666/icongroupinterna
- **Ceremonies and Celebrations: Feasts and Fasting (Ceremonies and Celebrations)** by Kerena Marchant; ISBN: 0750237082; http://www.amazon.com/exec/obidos/ASIN/0750237082/icongroupinterna
- **Christotherapy II: The Fasting and Feasting Heart** by Bernard J. Tyrrell (1999); ISBN: 1579102328; http://www.amazon.com/exec/obidos/ASIN/1579102328/icongroupinterna
- **Commonsense Guide to Fasting** by Kenneth E. Hagin (1981); ISBN: 0892764031; http://www.amazon.com/exec/obidos/ASIN/0892764031/icongroupinterna
- **Cross Training Senior High Volume 6: Power of Prayer-Daily Prayer, Practice Fasting, Engage in Warfare Prayer, Issues of Faith-Equip to Handle Tough Q** by Charisma Life Publishers (1997); ISBN: 1574051067; http://www.amazon.com/exec/obidos/ASIN/1574051067/icongroupinterna
- **Dedication Through Fasting and Prayer** by Nils-Erik Bergstrom, Nils-Erik Bergstrom (2001); ISBN: 1565990447; http://www.amazon.com/exec/obidos/ASIN/1565990447/icongroupinterna
- **Destroying the Works of Witchcraft Through Fasting & Prayer** by Ruth Brown (1995); ISBN: 0892281103; http://www.amazon.com/exec/obidos/ASIN/0892281103/icongroupinterna

- **El Ayuno / Fasting** by Slavko Barbaric (1994); ISBN: 0940535181; http://www.amazon.com/exec/obidos/ASIN/0940535181/icongroupinterna
- **Fasting** by Slavko Barbaric (1994); ISBN: 0940535122; http://www.amazon.com/exec/obidos/ASIN/0940535122/icongroupinterna
- **Fasting** by Derek Prince (1993); ISBN: 0883682583; http://www.amazon.com/exec/obidos/ASIN/0883682583/icongroupinterna
- **Fasting A Step Toward Intimacy With God** by James J. Aplin, et al; ISBN: 1891734059; http://www.amazon.com/exec/obidos/ASIN/1891734059/icongroupinterna
- **Fasting and fast days**; ISBN: 0706515404; http://www.amazon.com/exec/obidos/ASIN/0706515404/icongroupinterna
- **Fasting and Feasting in Morocco: Women's Participation in Ramadan (Mediterranean Series)** by Marjo Buitelaar (1994); ISBN: 0854963219; http://www.amazon.com/exec/obidos/ASIN/0854963219/icongroupinterna
- **Fasting and Man's Correct Diet** by R. B. Pearson (1993); ISBN: 0787306614; http://www.amazon.com/exec/obidos/ASIN/0787306614/icongroupinterna
- **Fasting and Science** by Bishop Auxentios of Photiki, et al (1998); ISBN: 0911165142; http://www.amazon.com/exec/obidos/ASIN/0911165142/icongroupinterna
- **Fasting As Unto the Lord** by Marilyn Salmonson, Lloyd Bustard (2003); ISBN: 0883688778; http://www.amazon.com/exec/obidos/ASIN/0883688778/icongroupinterna
- **Fasting Can Change Your Life** by Jerry Falwell (Editor), Elmer L. Towns (Editor) (1998); ISBN: 0830721975; http://www.amazon.com/exec/obidos/ASIN/0830721975/icongroupinterna
- **Fasting Can Save Your Life** by Ronald G. Cridland (Introduction), Herbert M. Shelton (1996); ISBN: 0914532421; http://www.amazon.com/exec/obidos/ASIN/0914532421/icongroupinterna
- **Fasting Cure 1911** by Upton Sinclair (2003); ISBN: 076613251X; http://www.amazon.com/exec/obidos/ASIN/076613251X/icongroupinterna
- **Fasting for Financial Breakthrough** by Elmer, Dr Towns, Elmer L. Towns (2002); ISBN: 0830729631; http://www.amazon.com/exec/obidos/ASIN/0830729631/icongroupinterna
- **Fasting for Spiritual Breakthrough** by Elmer L. Towns, Elmer Town (1996); ISBN: 0830718397; http://www.amazon.com/exec/obidos/ASIN/0830718397/icongroupinterna
- **Fasting for Spiritual Breakthrough Video Curriculum: A Guide to Nine Biblical Fasts** by Elmer L. Towns (1996); ISBN: 1570520593; http://www.amazon.com/exec/obidos/ASIN/1570520593/icongroupinterna
- **Fasting Girls** (1989); ISBN: 9994839853; http://www.amazon.com/exec/obidos/ASIN/9994839853/icongroupinterna
- **Fasting Girls: The Emergence of Anorexia As a Modern Disease** by Joan Jacobs Brumberg (1988); ISBN: 0674295013; http://www.amazon.com/exec/obidos/ASIN/0674295013/icongroupinterna

- **Fasting in the New Testament: A Study in Biblical Theology (141P)** by Joseph F. Wimmer; ISBN: 0809124203; http://www.amazon.com/exec/obidos/ASIN/0809124203/icongroupinterna
- **Fasting in the Orthodox Church: Its Theological, Pastoral, and Social Implications** by Archimandrite Akakios (1996); ISBN: 0911165169; http://www.amazon.com/exec/obidos/ASIN/0911165169/icongroupinterna
- **Fasting Prayer: Finding Strength Through Weakness** by John Shuey (1997); ISBN: 0875097421; http://www.amazon.com/exec/obidos/ASIN/0875097421/icongroupinterna
- **Fasting, Feasting** by Anita Desai (Author) (2000); ISBN: 0618065822; http://www.amazon.com/exec/obidos/ASIN/0618065822/icongroupinterna
- **Fasting: A Baha'i Handbook** by Duane L. Herrmann (1989); ISBN: 0853982805; http://www.amazon.com/exec/obidos/ASIN/0853982805/icongroupinterna
- **Fasting: A Neglected Discipline** by D. Smith (1998); ISBN: 0875085156; http://www.amazon.com/exec/obidos/ASIN/0875085156/icongroupinterna
- **Fasting: Signs and Symptoms: A Clinical Guide** by Trevor Salloum (1992); ISBN: 0962351849; http://www.amazon.com/exec/obidos/ASIN/0962351849/icongroupinterna
- **Fasting: The Delightful Discipline** by K. Neill Foster (1995); ISBN: 0875096123; http://www.amazon.com/exec/obidos/ASIN/0875096123/icongroupinterna
- **Fasting: The Phenomenon of Self-Denial** by E. Rogers; ISBN: 0525664629; http://www.amazon.com/exec/obidos/ASIN/0525664629/icongroupinterna
- **Feasting & Fasting** by Harlan Walker (Editor) (1991); ISBN: 0907325467; http://www.amazon.com/exec/obidos/ASIN/0907325467/icongroupinterna
- **Feasts and Fasting (Ceremonies and Celebrations (Raintree Steck-Vaughn Publishers).)** by Kerena Marchant, et al (2001); ISBN: 0739832689; http://www.amazon.com/exec/obidos/ASIN/0739832689/icongroupinterna
- **Fiqh Us-Sunnah Vol 3.: Alms Tax & Fasting, Set** by As-Sayyed Sabiq, et al (1983); ISBN: 0892590335; http://www.amazon.com/exec/obidos/ASIN/0892590335/icongroupinterna
- **Five Steps to Fasting & Prayer** by Bill Bright (1998); ISBN: 1563991160; http://www.amazon.com/exec/obidos/ASIN/1563991160/icongroupinterna
- **Food & Celebration from Fasting to Feasting: Proceedings of the 13th Conference of the International Commission for Ethnological Food Research, Ljubljana, Preddvor, & Piran, Slovenia, June 5-11,** by Patricia Lysaght (Editor) (2002); ISBN: 9616358545; http://www.amazon.com/exec/obidos/ASIN/9616358545/icongroupinterna
- **From Fasting Saints to Anorexic Girls: The History of Self-Starvation** by Walter Vandereycken, Ron Van Deth (Contributor) (1994); ISBN: 0814787843; http://www.amazon.com/exec/obidos/ASIN/0814787843/icongroupinterna
- **From Fasting Saints to Anorexic Girls: The History of Self-Starvation** by Walter Vandereycken, Ron Van Deth (1990); ISBN: 0756762782; http://www.amazon.com/exec/obidos/ASIN/0756762782/icongroupinterna
- **From Feasting To Fasting [DOWNLOAD: MICROSOFT READER]** by Veronika Grimm (1996); ISBN: B0000AFXHK; http://www.amazon.com/exec/obidos/ASIN/B0000AFXHK/icongroupinterna

- **From Feasting to Fasting, the Evolution of a Sin: Attitudes to Food in Late Antiquity** by Veronika E. Grimm (1996); ISBN: 0415135958; http://www.amazon.com/exec/obidos/ASIN/0415135958/icongroupinterna
- **Health Through New Thought and Fasting** by Wallace D. Wattles (2001); ISBN: 0787309362; http://www.amazon.com/exec/obidos/ASIN/0787309362/icongroupinterna
- **Hints on Fasting Well** by Marie P. Sweet (1956); ISBN: 0787312266; http://www.amazon.com/exec/obidos/ASIN/0787312266/icongroupinterna
- **Holy Men and Hunger Artists: Fasting and Asceticism in Rabbinic Culture** by Eliezer Diamond (2003); ISBN: 0195137507; http://www.amazon.com/exec/obidos/ASIN/0195137507/icongroupinterna
- **Honey from a Weed: Fasting and Feasting in Tuscany Catalonia the Cyclades and Apulia** by Patience Gray, Corinna Sargood (Illustrator); ISBN: 0865474184; http://www.amazon.com/exec/obidos/ASIN/0865474184/icongroupinterna
- **Honey from a Weed: Fasting and Festing in Tuscany, Catalonia: The Cyclades and Apulia** by Patience Gray (1986); ISBN: 190301820X; http://www.amazon.com/exec/obidos/ASIN/190301820X/icongroupinterna
- **How to Keep Slim, Healthy and Young With Juice Fasting** by Paavo Airola (1984); ISBN: 0932090028; http://www.amazon.com/exec/obidos/ASIN/0932090028/icongroupinterna
- **How to Keep Slim, Healthy and Young With Juice Fasting**; ISBN: 0685421686; http://www.amazon.com/exec/obidos/ASIN/0685421686/icongroupinterna
- **Instructions for Fasting and Dieting** by Arnold Ehret (2002); ISBN: 0879040033; http://www.amazon.com/exec/obidos/ASIN/0879040033/icongroupinterna
- **Juice Fasting and Detoxification: Use the Healing Power of Fresh Juice to Feel Young and Look Great: The Fastest Way to Restore Your Health** by Steve Meyerowitz, et al (1999); ISBN: 1878736655; http://www.amazon.com/exec/obidos/ASIN/1878736655/icongroupinterna
- **Keys to God's Grace: The Hidden Joy of Prayer, Fasting, and Almsgiving** by Word Among Us Press (2001); ISBN: 0932085334; http://www.amazon.com/exec/obidos/ASIN/0932085334/icongroupinterna
- **Ministry of Fasting** by Zacharias T. Fomum; ISBN: 0533082811; http://www.amazon.com/exec/obidos/ASIN/0533082811/icongroupinterna
- **Miracle of Fasting, 49th Edition** by Patricia Bragg (2002); ISBN: 0877900388; http://www.amazon.com/exec/obidos/ASIN/0877900388/icongroupinterna
- **Mishnah Berurah: Laws of Chol Ha-Mo'Ed, Tishah Beav and Other Fasts and Fasting** by Israel (1997); ISBN: 0873068548; http://www.amazon.com/exec/obidos/ASIN/0873068548/icongroupinterna
- **Mysteries of Fasting** by Abu H. Ghazali (1998); ISBN: 1850340498; http://www.amazon.com/exec/obidos/ASIN/1850340498/icongroupinterna
- **Mysteries of Fasting Being a Translation With Notes of the Kitabasr** by Al Ghazzali; ISBN: 0879020520; http://www.amazon.com/exec/obidos/ASIN/0879020520/icongroupinterna
- **On Fasting & Feasting** by Davidson (1988); ISBN: 0356156370; http://www.amazon.com/exec/obidos/ASIN/0356156370/icongroupinterna

- **Prayer & Fasting** by Kingsley A. Fletcher (1999); ISBN: 0883685434; http://www.amazon.com/exec/obidos/ASIN/0883685434/icongroupinterna
- **Prayer & Fasting** by W. E. McCumber (1990); ISBN: 0834113791; http://www.amazon.com/exec/obidos/ASIN/0834113791/icongroupinterna
- **Prayer and Fasting** by Gordon Lindsay (1988); ISBN: 0899850766; http://www.amazon.com/exec/obidos/ASIN/0899850766/icongroupinterna
- **Preparing for the Coming Revival: How to Lead a Successful Fasting and Prayer Gathering** by Bill Bright (2002); ISBN: 156399075X; http://www.amazon.com/exec/obidos/ASIN/156399075X/icongroupinterna
- **Quick Fasting** by Nathaniel, H. Bronner; ISBN: 0963107518; http://www.amazon.com/exec/obidos/ASIN/0963107518/icongroupinterna
- **Radical Fasting** by Dave Williams; ISBN: 0938020692; http://www.amazon.com/exec/obidos/ASIN/0938020692/icongroupinterna
- **Ramadan Fasting & Medical Science** by M. Ghulam Muazzam (1991); ISBN: 0722325452; http://www.amazon.com/exec/obidos/ASIN/0722325452/icongroupinterna
- **Rejuvenating the Body Through Fasting With Spirulina Plankton** by Christopher Hills (1980); ISBN: 091643835X; http://www.amazon.com/exec/obidos/ASIN/091643835X/icongroupinterna
- **Revival Now Through Prayer & Fasting** by Gordon Cove (1988); ISBN: 0880192275; http://www.amazon.com/exec/obidos/ASIN/0880192275/icongroupinterna
- **Scientific Fasting** by Linda Hazzard (1998); ISBN: 0787303909; http://www.amazon.com/exec/obidos/ASIN/0787303909/icongroupinterna
- **Scientific Fasting: The Ancient & Modern Key to Health** by Linda Burfield Hazzard (1997); ISBN: 1564598268; http://www.amazon.com/exec/obidos/ASIN/1564598268/icongroupinterna
- **Shakespeare's Festive History: Feasting, Festivity, Fasting, and Lent in the Second Henriad** by David Arthur Ruiter (2003); ISBN: 0754606260; http://www.amazon.com/exec/obidos/ASIN/0754606260/icongroupinterna
- **Shaping History Through Prayer and Fasting** by Derek Prince; ISBN: 0883683393; http://www.amazon.com/exec/obidos/ASIN/0883683393/icongroupinterna
- **Shaping History Through Prayer and Fasting: How Christians Can Change World Events Through the Simple, Yet Powerful Tools of Prayer and Fasting.** by Derek. Prince; ISBN: 0800706161; http://www.amazon.com/exec/obidos/ASIN/0800706161/icongroupinterna
- **Short Cut: Regeneration Through Fasting, 1929** by Julia Seton (1998); ISBN: 0766102769; http://www.amazon.com/exec/obidos/ASIN/0766102769/icongroupinterna
- **Simplicity & Fasting (Spiritual Disciplines Bible Studies)** by Janet L. Johnson, Jan Johnson (2003); ISBN: 0830820949; http://www.amazon.com/exec/obidos/ASIN/0830820949/icongroupinterna
- **Spued: How to Cast Out Lukewarm Christianity Through Fasting and a Fasted Lifestyle** by Beth M. Ley (2003); ISBN: 1890766224; http://www.amazon.com/exec/obidos/ASIN/1890766224/icongroupinterna

- **Successful Fasting: The Easy Way to Cleanse Your Body of Its Poisons** by Hellmut Lutzner; ISBN: 0722521308; http://www.amazon.com/exec/obidos/ASIN/0722521308/icongroupinterna
- **The Ancient Cookfire: How to Rejuventate Body and Spirit Through Seasonal Foods and Fasting** by Carrie L'Esperance; ISBN: 1879181517; http://www.amazon.com/exec/obidos/ASIN/1879181517/icongroupinterna
- **The Beginner's Guide to Fasting** by Elmer L. Towns (2001); ISBN: 1569552266; http://www.amazon.com/exec/obidos/ASIN/1569552266/icongroupinterna
- **The Burden of the Flesh: Fasting and Sexuality in Early Christianity** by Teresa M. Shaw (1998); ISBN: 0800627652; http://www.amazon.com/exec/obidos/ASIN/0800627652/icongroupinterna
- **The Essene Science of Fasting and the Art of Sobriety: Guide to Regeneration in Health and Disease** by Edmond Bordeaux Szekely (1981); ISBN: 0895640112; http://www.amazon.com/exec/obidos/ASIN/0895640112/icongroupinterna
- **The Fasting Girl: A True Victorian Medical Mystery** by Michelle Stacey (2003); ISBN: 1585422487; http://www.amazon.com/exec/obidos/ASIN/1585422487/icongroupinterna
- **The Fasting Key: How You Can Unlock Doors to Spiritual Blessing** by Mark Nysewander, Mike Bickle (2003); ISBN: 1569553637; http://www.amazon.com/exec/obidos/ASIN/1569553637/icongroupinterna
- **The Fasting Path: For Spiritual, Emotional, and Physical Healing and Renewal** by Stephen Harrod Buhner (2003); ISBN: 1583331700; http://www.amazon.com/exec/obidos/ASIN/1583331700/icongroupinterna
- **The Fasting Story** (1998); ISBN: 0787308528; http://www.amazon.com/exec/obidos/ASIN/0787308528/icongroupinterna
- **The Miracle Results of Fasting** by Dave Williams; ISBN: 0938020501; http://www.amazon.com/exec/obidos/ASIN/0938020501/icongroupinterna
- **The Mysteries of Fasting: Being a Translation with Notes of the Kitab Asrar Al-sawm of Al-Ghazali's Ihya' Ulum-al-Din** by Nabih Amin Faris (1992); ISBN: 8171511600; http://www.amazon.com/exec/obidos/ASIN/8171511600/icongroupinterna
- **The No Breakfast Plan & the Fasting Cure** by Edward H Dewey (1962); ISBN: 078730283X; http://www.amazon.com/exec/obidos/ASIN/078730283X/icongroupinterna
- **The Philosophy of Fasting** by Edward Perinton (1986); ISBN: 1852283599; http://www.amazon.com/exec/obidos/ASIN/1852283599/icongroupinterna
- **The Power of Prayer and Fasting: 10 Secrets of Spiritual Strength** by Ronnie W. Floyd, Bill Bright (1997); ISBN: 0805401644; http://www.amazon.com/exec/obidos/ASIN/0805401644/icongroupinterna
- **The Practical Management of Therapeutic Fasting** by Lew Strogat, Jack E. Evans (Translator) (1992); ISBN: 0911971688; http://www.amazon.com/exec/obidos/ASIN/0911971688/icongroupinterna
- **The Roots and Fruits of Fasting** by Mary R. Swope (1998); ISBN: 0960693696; http://www.amazon.com/exec/obidos/ASIN/0960693696/icongroupinterna

- **The Transforming Power of Fasting: Personal Accounts of Spiritual Renewal** by Bill Bright, Bill McCartney (1997); ISBN: 1563990903; http://www.amazon.com/exec/obidos/ASIN/1563990903/icongroupinterna
- **Tony Evans Speaks Out on Fasting** by Tony Evans (2000); ISBN: 0802443664; http://www.amazon.com/exec/obidos/ASIN/0802443664/icongroupinterna
- **Toxic Relief: Restore Health and Energy Through Fasting and Detoxification** by Don, MD Colbert (2003); ISBN: 1591852137; http://www.amazon.com/exec/obidos/ASIN/1591852137/icongroupinterna
- **Treaties on Zakat & Fasting** by Abdul-Aziz BinBaz (1996); ISBN: 9960740730; http://www.amazon.com/exec/obidos/ASIN/9960740730/icongroupinterna
- **True Fasting: A Heart in Anguish in Search of Grace** by Ohene Aku Kwapong (2001); ISBN: 0759652430; http://www.amazon.com/exec/obidos/ASIN/0759652430/icongroupinterna
- **Vitality, Fasting and Nutrition: A Physiological Study of the Curative Power of Fasting, Together With a New Theory of the Relation of Food to Human Vitality** by Hereward Carrington (1997); ISBN: 1564599159; http://www.amazon.com/exec/obidos/ASIN/1564599159/icongroupinterna

The National Library of Medicine Book Index

The National Library of Medicine at the National Institutes of Health has a massive database of books published on healthcare and biomedicine. Go to the following Internet site, **http://locatorplus.gov/**, and then select "Search LOCATORplus." Once you are in the search area, simply type "fasting" (or synonyms) into the search box, and select "books only." From there, results can be sorted by publication date, author, or relevance. The following was recently catalogued by the National Library of Medicine:[10]

- **"A wonderful little girl": the true story of Sarah Jacob, the Welsh fasting girl** Author: Busby, Siân.; Year: 1968; London: Short Books, 2003; ISBN: 1904095437 http://www.amazon.com/exec/obidos/ASIN/1904095437/icongroupinterna
- **A study of the relationship between the in vitro survival of human red blood cells and the fasting state of the blood donor using the autohemolysis test.** Author: Allen, Turman Earl.; Year: 1969; [Columbus] 1968
- **A treatise on the virtues and efficacy of a crust of bread, eat early in a morning fasting: to which are added, some particular remarks concerning cures accomplished by the saliva, or fasting- spittle, as well when externally applied as when internally given, in the scurvy, gravel, stone, rheumatism, and divers other diseases, arising from obstructions. By an eminent physician.** Author: Robinson, Nicholas,; Year: 1960; London, Printed for A. and C. Corbett, and sold by J. Crouse, in Norwich, 1763

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[10] In addition to LOCATORPlus, in collaboration with authors and publishers, the National Center for Biotechnology Information (NCBI) is currently adapting biomedical books for the Web. The books may be accessed in two ways: (1) by searching directly using any search term or phrase (in the same way as the bibliographic database PubMed), or (2) by following the links to PubMed abstracts. Each PubMed abstract has a "Books" button that displays a facsimile of the abstract in which some phrases are hypertext links. These phrases are also found in the books available at NCBI. Click on hyperlinked results in the list of books in which the phrase is found. Currently, the majority of the links are between the books and PubMed. In the future, more links will be created between the books and other types of information, such as gene and protein sequences and macromolecular structures. See **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books**.

- **About fasting; translated from the German by Geoffrey A. Dudley.** Author: Buchinger, Otto Hermann Ferdinand,; Year: 1968; London, Thorsons [1961]
- **Fasting and grape cure.** Author: Székely, Edmond Bordeaux.; Year: 1960; [Tecate, Calif.] Essene School of Life, 1949
- **Fasting can save your life** Author: Shelton, Herbert M. (Herbert McGolphin),; Year: 1974; Tampa, FL: American Natural Hygiene Society, 1978 (1991 printing); ISBN: 0914532235
- **Fasting for health and life.** Author: Oldfield, Josiah,; Year: 1962; London, Daniel [1932]
- **Fasting for health and long life.** Author: Carrington, Hereward,; Year: 1966; Mokelumne Hill, Calif., Health Research, 1956 [c1953]
- **Fasting, the master remedy** Author: Carrington, Hereward,; Year: 1950; Lucknow: Nature Cure Research Hospital, c1978
- **From fasting saints to anorexic girls: the history of self-starvation** Author: Vandereycken, Walter,; Year: 1935; London: Atglone Press, 1994; ISBN: 0485240106 http://www.amazon.com/exec/obidos/ASIN/0485240106/icongroupinterna
- **Macfadden's fasting, hydropathy and exercise; nature's wonderful remedies for the cure of all chronic and acute diseases. By Bernarr Macfadden and Felix Oswald.** Author: Macfadden, Bernarr,; Year: 1966; London, B. Macfadden; New York, printed [1903]
- **Metabolic studies in New Guineans; oxygen uptake and carbon dioxide excretion during fasting-resting and exercising conditions.** Author: Hipsley, Eben H.; Year: 1793; Noumea, New Caledonia, 1969
- **Rational fasting for physical, mental, and spiritual rejuvenation, by Arnold Ehret. Also, Health and happiness through fasting, by Fred S. Hirsch.** Author: Ehret, Arnold.; Year: 1968; Beaumont, Calif., Ehret Literature Pub. Co. [c1971]
- **The fast way to health; being, as to the first part, an exposition of the fasting cure and its application to the prevalent disorders, and, as to the second part, a treatise on food, together with diets for the well, by Dr. Frank McCoy.** Author: McCoy, Frank.; Year: 1965; Los Angeles, McCoy publications, inc., 1926
- **The natural way to health through controlled fasting.** Author: Wade, Carlson.; Year: 1968; West Nyack, N. Y., Parker [c1968]
- **The no-breakfast plan and the fasting-cure.** Author: Dewey, Edward Hooker,; Year: 1956; Passaic, N. J., Health Culture Co. [c1900]
- **The one-hour oral glucose tolerance test. Response of middle-aged men to 100-gram and 50-gram doses of glucose given fasting and 1, 2, and 3 hours after meal.** Author: National Center for Health Statistics (U.S.); Year: 1903; Washington, 1963
- **Therapeutic fasting.** Author: De Vries, Arnold Paul,; Year: 1968; Chicago, Dahlstrom [c1951]

Chapters on Fasting

In order to find chapters that specifically relate to fasting, an excellent source of abstracts is the Combined Health Information Database. You will need to limit your search to book chapters and fasting using the "Detailed Search" option. Go to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find book chapters, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and

language you prefer, and the format option "Book Chapter." Type "fasting" (or synonyms) into the "For these words:" box. The following is a typical result when searching for book chapters on fasting:

- **Acarbose: 'The European Experience'**

  Source: in Cooper, J.W. Diabetes Mellitus in the Elderly. Binghamton, NY: Pharmaceutical Products Press. 1999. p. 47-59.

  Contact: Available from Pharmaceutical Products Press. 10 Alice Stret, Binghamton, NY 13904-1580. (800)429-6784. E-mail: getinfo@haworthpressinc.com. Website: www.haworthpressinc.com. PRICE: $49.95 plus shipping and handling. ISBN: 0789006820.

  Summary: Acarbose, an alpha glucosidase inhibitor, delays carbohydrate digestion, and thereby decreases postprandial (after a meal) blood glucose (sugar) levels. Acarbose is a useful drug, especially for the treatment of obese subjects with type 2 diabetes mellitus who fail first line therapy with diet and exercise. This article on the use of acarbose is from a volume that is devoted to the diagnosis and treatment of diabetes mellitus in the elderly. The authors present 'The European Experience' with acarbose, noting its use as first line therapy in individuals with diabetes in whom postprandial hyperglycemia (high levels of blood glucose) is significantly greater than **fasting** hyperglycemia, and in elderly patients with mild diabetes who are at high risk for hypoglycemia (low levels of blood glucose). No weight gain has been described with acarbose and it is effective with high carbohydrate intake. The drug is also useful in combinations with other oral hypoglycemic agents and with insulin. In type 1 subjects, acarbose may reduce glycemic fluctuations and reduce insulin dosage. Acarbose may reduce episodes of midevening and nocturnal hypoglycemia. The disadvantage of acarbose is its gastrointestinal side effects of flatulence (gas) and diarrhea; these side effects can be minimized by slowly adjusting the doses according to the patient's symptoms. 59 references.

- **Fatty Acid Oxidation Inhibitors**

  Source: in LeRoith, D.; Taylor, S.I.; Olefsky, J.M., eds. Diabetes Mellitus: A Fundamental and Clinical Text. Philadelphia, PA: Lippincott-Raven Publishers. 1996. p. 668-674.

  Contact: Available from Lippincott-Raven Publishers. 12107 Insurance Way, Hagerstown, MD 21740-5184. (800) 777-2295. Fax (301) 824-7390. PRICE: $199.00. ISBN: 0397514565.

  Summary: Although fatty acid oxidation (FAO) inhibitors are not currently available as drug therapy, their potential for the treatment of diabetes has been appreciated due to the association between the hypoglycemic effect of hypoglycin and its ability to inhibit FAO. In this chapter, from a medical textbook on diabetes, the authors cover the potential use of FAO inhibitors in the treatment of diabetes. The authors examine the role of FAO in both prandial (meal) glucose utilization and **fasting** glucose production. The authors also explore strategies for inhibiting FAO pharmacologically. They conclude that FAO inhibitors may be a feasible improvement on low-dose insulin therapy at bedtime for the treatment of excessive glucose production during the overnight fast. Liver-selective, reversible carnitine palmitoyltransferase (CPT) inhibitors that do not require activation to coenzyme A esters may be the most desirable approach to inhibiting fatty acid oxidation. 9 figures. 79 references.

- **Metabolic Changes During Normal and Diabetic Pregnancies**

  Source: in Reece, E.A.; Coustan, D.R., eds. Diabetes Mellitus in Pregnancy. 2nd ed. New York, NY: Churchill Livingstone. 1995. p. 59-77.

  Contact: Available from Churchill Livingstone. 300 Lighting Way, Secaucus, NJ 07094. (800) 553-5426. PRICE: $92.00. ISBN: 0443089795.

  Summary: In women with limited beta cell secretory capacity (for example, women with diabetes mellitus), maternal metabolic responses to pregnancy are abnormal in ways that can be detrimental to both the mother and her developing infant. This chapter, from a medical textbook on diabetes mellitus in pregnancy, reviews normal maternal metabolism during pregnancy and the metabolic abnormalities that occur in women with diabetes mellitus. Topics include glucose metabolism, insulin resistance and hyperinsulinemia; the adaptive significance of insulin resistance; lipids and amino acids; metabolic changes during **fasting,** including lowered **fasting** glucose levels, accelerated lipolysis and ketogenesis, and the adaptive significance of these changes; the impact on maternal nutrient concentrations; diabetes mellitus in nonpregnant individuals, notably the effect of diabetes on circulating nutrients; and metabolic changes in pregestational diabetes, pregestational NIDDM, and gestational diabetes. The author reiterates that the metabolic demands of the developing fetus dictate that maternal metabolism must change markedly during pregnancy to allow efficient nutrient storage during feeding and rapid use of the stored nutrients with minimal catabolism of maternal protein during **fasting.** The three most prominent changes are progressive insulin resistance, accelerated fat catabolism, and **fasting** hypoglycemia. 7 figures. 1 table. 126 references.

- **Reactive Hypoglycemia**

  Source: in American Dietetic Association. Manual of Clinical Dietetics, Sixth Edition. Chicago, IL: American Dietetic Association. 2000. p. 337-340.

  Contact: Available from American Dietetic Association. 216 West Jackson Boulevard, Chicago, IL 60606. (800) 877-1600 or (312) 899-0040. Fax (312) 899-4899. PRICE: $59.95 for members, $70.00 for nonmembers. ISBN: 0880911875.

  Summary: Medical nutrition therapy (MNT) can be used to prevent symptoms of hypoglycemia (low blood glucose levels) after food ingestion in patients sensitive to carbohydrates (reactive hypoglycemia). This chapter on reactive hypoglycemia is from a comprehensive manual of clinical dietetics designed to help dietitians, physicians, and nurses deliver quality nutrition care. The chapter includes the purpose of nutrition care, the indications for use, a description of the diet, meal planning approaches, a definition of the disease or condition, and a discussion section. The authors describe the differences between **fasting** and postprandial (after a meal, also called reactive) hypoglycemia. 14 references.

- **Diabetes Mellitus**

  Source: in American Dietetic Association. Manual of Clinical Dietetics, Sixth Edition. Chicago, IL: American Dietetic Association. 2000. p. 301-336.

  Contact: Available from American Dietetic Association. 216 West Jackson Boulevard, Chicago, IL 60606. (800) 877-1600 or (312) 899-0040. Fax (312) 899-4899. PRICE: $59.95 for members, $70.00 for nonmembers. ISBN: 0880911875.

  Summary: Medical nutrition therapy (MNT) is used for patients with diabetes to achieve and maintain optimal blood glucose (sugar) and lipid (fats) levels through appropriate

food choices; to improve quality of life and overall health; to empower persons to self-manage their diabetes by providing information to increase their knowledge and skills; to provide adequate energy and nutrients; to teach prevention and treatment of acute complications such as hypoglycemia (low blood glucose), hyperglycemia (high blood glucose), and sick day management; and to prevent or delay long term complications, including retinopathy (eye disease), nephropathy (kidney disease), neuropathy (nerve disease), and cardiovascular disease. This chapter on diabetes mellitus is from a comprehensive manual of clinical dietetics designed to help dietitians, physicians, and nurses deliver quality nutrition care. The chapter includes the purpose of nutrition care, the indications for use, a description of the diet, meal planning approaches, a definition of the disease or condition, and a discussion section. The guidelines provided are for use with individuals diagnosed with type 1 diabetes, type 2 diabetes, gestational diabetes, impaired glucose tolerance (IGT), and impaired **fasting** glucose (IFG). The chapter concludes with resources through which readers can obtain additional information. 3 figures. 13 tables. 47 references.

- **Physiology of Gastric Motility and Gastric Emptying**

  Source: in Textbook of Gastroenterology. 4th ed. [2-volume set]. Hagerstown, MD: Lippincott Williams and Wilkins. 2003. p. 195-219.

  Contact: Available from Lippincott Williams and Wilkins. P.O. Box 1600, Hagerstown, MD 21741. (800) 638-6423. Fax: (301) 223-2400. Website: www.lww.com. PRICE: $289.00. ISBN: 781728614.

  Summary: Motor activity of the stomach serves distinct roles under **fasting** and fed conditions. Interdigestive patterns clear out undigested debris and sloughed epithelial (lining) cells. After eating, the stomach accommodates the ingested bolus, which is then ground and dispersed into fine particles that are delivered to the duodenum at a controlled rate. Coordinated actions of the three regions of the stomach, with feedback control from the small intestine, regulate the emptying of gastric contents. This chapter on the physiology of gastric motility and gastric emptying is from a lengthy, two-volume textbook that integrates the various demands of science, technology, expanding information, good judgment, and common sense into the diagnosis and management of gastrointestine patients. This chapter discusses smooth muscle characteristics of the stomach, innervation of the stomach, regional motor patterns in the stomach and duodenum, and gastric emptying. 14 figures. 336 references.

- **Motility of the Small Intestine and Colon**

  Source: in Textbook of Gastroenterology. 4th ed. [2-volume set]. Hagerstown, MD: Lippincott Williams and Wilkins. 2003. p. 220-247.

  Contact: Available from Lippincott Williams and Wilkins. P.O. Box 1600, Hagerstown, MD 21741. (800) 638-6423. Fax: (301) 223-2400. Website: www.lww.com. PRICE: $289.00. ISBN: 781728614.

  Summary: The motor activities of the small intestine and colon are characterized by contractile patterns that serve the requirements of each organ. The small intestine processes and absorbs nutrients for distribution to the rest of the body, whereas the colon extracts water, digests some meal residue, and processes feces for expulsion. Two basic motor functions, mixing and propulsion, subserve these functions. This chapter on the motility of the small intestinal and colon is from a lengthy, two-volume textbook that integrates the various demands of science, technology, expanding information, good judgment, and common sense into the diagnosis and management of

gastrointestinal patients. This chapter discusses anatomic considerations, small intestinal and colonic smooth muscle, innervation of the small intestine and colon, physiological and pathophysiological motor patterns under basal **fasting** conditions, the physiological and pathophysiological modulators of small intestinal and colonic motility, correlation of motor patterns with small intestinal and colonic transit, and sphincteric function of the lower gastrointestinal tract. 15 figures. 402 references.

- **Pathophysiology of Diabetes in Aging**

  Source: in Cooper, J.W. Diabetes Mellitus in the Elderly. Binghamton, NY: Pharmaceutical Products Press. 1999. p. 5-20.

  Contact: Available from Pharmaceutical Products Press. 10 Alice Stret, Binghamton, NY 13904-1580. (800)429-6784. E-mail: getinfo@haworthpressinc.com. Website: www.haworthpressinc.com. PRICE: $49.95 plus shipping and handling. ISBN: 0789006820.

  Summary: This article on the pathophysiology of diabetes in aging is from a volume that is devoted to the diagnosis and treatment of diabetes mellitus in the elderly. The first article stresses that the recently revised American Diabetes Association (ADA) guidelines that include impaired glucose tolerance (IGT) and a lower level of **fasting** plasma glucose for the diagnosis of diabetes underscore the need for earlier detection of diabetes in the older adult and the relationship of diabetes with obesity. Glucose (sugar) levels are tightly regulated by the combined function of the muscle to dispose of postprandial (after a meal) glucose, the liver to provide for **fasting** glucose production, and the beta cells of the pancreas to regulate both processes by secreting appropriate amounts of insulin. Aging is known to be an insulin resistant state; insulin resistance is also associated with increases in total and visceral fat mass which are typical of aging. Insulin resistance is also associated with risk factors for accelerated atherosclerosis and coronary artery disease, hypertension (high blood pressure) and hyperlipidemia (high levels of fats in the blood). While beta cell insulin secretion may compensate for the resistance to insulin action of the muscle and liver, elderly subjects with and without obesity may fail to respond by secreting adequate amounts of insulin, and will develop diabetes mellitus. The onset of frank diabetes mellitus is accompanied by further deterioration in muscle, liver, and beta cell function, a phenomenon referred to as 'glucose toxicity.' The authors stress that understanding the multi organ pathophysiology of diabetes in the elderly is clinically relevant, because present and future drug therapies aim to reverse specific organ defects, and often act together to decrease hyperglycemia (high levels of blood glucose). 4 figure. 62 references.

- **Glucose Homeostasis and Hypoglycemia**

  Source: in Wilson, J.D., et al., eds. Williams Textbook of Endocrinology. 9th ed. Philadelphia, PA: W.B. Saunders Company. 1998. p. 939-971.

  Contact: Available from W.B. Saunders Company. Book Order Fulfillment Department. 11830 Westline Industrial Drive, Saint Louis, MO 63146-9988. (800) 545-2522 or (314) 453-7010. Fax (800) 568-5136 or (314) 453-7095. E-mail: wbsbcs@harcourt.com. Website: www.wbsaunders.com. PRICE: $150.00 plus shipping and handling. ISBN: 0721661521.

  Summary: This chapter focuses on glucose homeostasis and hypoglycemia. The chapter begins with a discussion of the physiology of systemic glucoregulation, including glucose metabolism; the effect of **fasting,** feeding, and exercise on systemic glucose balance; hormonal, neural, and substrate glucoregulatory factors; and glucose counterregulation. Topics related to glucose metabolism include the origin and fate of

glucose, hepatic glucose metabolism, and glucose utilization. Other topics include the control of glucoregulatory factors, the correction and prevention of hypoglycemia, and the principles of glucose counterregulation. The chapter next examines the pathophysiology of hypoglycemia, focusing on the clinical manifestations of hypoglycemia, the diagnosis of hypoglycemia, postabsorptive versus postprandial hypoglycemia, and the clinical classification of hypoglycemia. This is followed by a discussion of hypoglycemia in type 1 and type 2 diabetes. Topics related to hypoglycemia in type 1 diabetes include the frequency, impact, prevention, and treatment of hypoglycemia and the risk factors for this condition. The chapter continues with a discussion of the causes of postabsorptive hypoglycemia including drugs such as insulin or a sulfonylurea; hepatic, cardiac, and renal diseases, sepsis, and inanition; cortisol and growth hormone deficiencies and glucagon and epinephrine deficiencies; nonbeta cell tumors; and endogenous hyperinsulinism. Causes of hypoglycemia unique to infancy or childhood include transient intolerance of **fasting,** maternal diabetes, and enzymatic defects. Final topics include postprandial hypoglycemia, treatment of postabsorptive hypoglycemia, and care of the patient with suspected hypoglycemia. 22 figures. 3 tables. 391 references.

- **Nutrition, Diabetes, and Hypoglycemia**

  Source: in Whitney, E.N., Cataldo, C.B., and Rolfes, S.R. Understanding Normal and Clinical Nutrition. 4th ed. St. Paul, MN: West Publishing Company. 1994. p. 842-878.

  Contact: Available from West Publishing. 620 Opperman Drive, St. Paul, MN 55164. (800) 340-9378 or (612) 687-7000. PRICE: $67.00. ISBN: 0314041788.

  Summary: This chapter from a nutrition textbook covers nutrition, diabetes, and hypoglycemia. Topics include insulin-dependent and noninsulin-dependent diabetes (IDDM and NIDDM, respectively); diabetes-related disorders; the acute and chronic complications of diabetes; treatment for IDDM, including measuring glucose control, insulin, diet, physical activity, treating hyperglycemia and hypoglycemia, and special issues for children and elderly people with diabetes; treatment of NIDDM, including the crucial role of diet; treatment of diabetes during pregnancy, including IDDM and NIDDM during pregnancy, as well as gestational diabetes; reactive and **fasting** hypoglycemia; the treatment of hypoglycemia; and nutrition assessment. The chapter concludes with study questions, clinical application questions, and a 'highlight' of one patient with IDDM, focusing on the practical questions of incorporating all the diabetes management information into the reality of daily living. 1 figure. 9 tables. 15 references.

- **Who Gets Diabetes?**

  Source: in Hirsch, I.B. 12 Things You Must Know About Diabetes Care Right Now!. Alexandria, VA: American Diabetes Association. 2000. p. 9-19.

  Contact: Available from American Diabetes Association (ADA). Order Fulfillment Department, P.O. Box 930850, Atlanta, GA 31193-0850. (800) 232-6733. Fax (770) 442-9742. Website: www.diabetes.org. PRICE: $14.95 plus shipping and handling. ISBN: 1580400612.

  Summary: This chapter is devoted to nonmodifiable and modifiable risk factors for diabetes. Nonmodifiable risk factors include heredity, race, and a history of diabetes during pregnancy. Although type 2 diabetes is more closely linked to genetics, there is also a genetic link with type 1 diabetes. Certain minorities, including Native Americans, Hispanics, African Americans, and Asian Americans, are at higher risk for developing type 2 diabetes. In addition, women who have had gestational diabetes are at higher risk

of developing diabetes later in life. Modifiable risk factors include impaired glucose tolerance, medications, high blood pressure or high blood fat, and obesity. People who have impaired glucose tolerance will not develop the eye, kidney, and nerve diseases linked with diabetes, but they are at a higher risk of developing heart disease and stroke. Certain medications can cause impaired glucose tolerance, impaired **fasting** glucose, or even diabetes. People who have high blood pressure or high levels of lipids are at higher risk of developing diabetes. One of the most important modifiable risk factors is obesity, so weight loss is a way to modify this risk factor. The chapter concludes with American Diabetes Association guidelines on screening for type 2 diabetes. The chapter includes a list of questions a patient may ask a doctor and questions a doctor may ask a patient. 2 tables.

- **Your Batting Average**

  Source: in Lincoln, T.A.; Eaddy, J.A. Beating the Blood Sugar Blues. Alexandria, VA: American Diabetes Association. 2001. p.26-31.

  Contact: Available from American Diabetes Association (ADA). Order Fulfillment Department, P.O. Box 930850, Atlanta, GA 31193-0850. (800) 232-6733. Fax (770) 442-9742. Website: www.diabetes.org. PRICE: $12.95 plus shipping and handling. ISBN: 1580400485.

  Summary: This chapter is from a book that offers first hand knowledge from two doctors who have more than 100 years of combined experienced with the day-to-day balancing act of blood glucose (sugar) and diabetes. The authors, both of whom have type 1 diabetes, share their own stories as well as those of over 40 of their patients. In this chapter, the authors describe the role of glycosylated hemoglobin (HbA1c) testing, a measure of blood glucose levels over time (a period of 2 to 3 months). Using the metaphor of a batting average, the authors explain how the HbA1c test can help patients monitor their overall diabetes management approach. Topics include the physiology of hemoglobin and glucose, recommended goals for HbA1c levels, the interplay between glucose level and **fasting** HbA1c levels, other factors that may have an impact on HbA1c levels (including illness), and the benefits of following an intensive program of diabetes control on a regular basis. 1 table.

- **Gallstone Management in Inflammatory Bowel Disease**

  Source: in Bayless, T.M. and Hanauer, S.B. Advanced Therapy of Inflammatory Bowel Disease. Hamilton, Ontario: B.C. Decker Inc. 2001. p. 317-320.

  Contact: Available from B.C. Decker Inc. 20 Hughson Street South, P.O. Box 620, L.C.D. 1 Hamilton, Ontario L8N 3K7. (905) 522-7017 or (800) 568-7281. Fax (905) 522-7839. Email: info@bcdecker.com. Website: www.bcdecker.com. PRICE: $129.00 plus shipping and handling. ISBN: 1550091220.

  Summary: This chapter on gallstone (cholelithiasis) management in inflammatory bowel disease (IBD) is from the second edition of a book devoted to the details of medical, surgical, and supportive management of patients with Crohn's disease (CD) and Ulcerative Colitis (UC), together known as IBD. The association between IBD and hepatobiliary (liver, gallstone, bile ducts) disorders has been well established. Both CD and chronic Ulcerative Colitis (UC) can affect the liver and biliary system. Indeed, hepatobiliary involvement in patients with IBD varies from the asymptomatic state to the development of symptomatic complications related to chronic liver injury. Gallstones represent one of the most frequently encountered clinical hepatobiliary problems in patients with IBD especially those with Crohn's disease. In this chapter, the

authors present an overview of the management of gallbladder stones and biliary sludge in patients with IBD. A summary of the epidemiology and pathogenesis of gallstones and biliary sludge in these patients is provided to guide therapeutic decision-making, which should aim not only to address symptomatic stones but also to prevent their development. Precipitating factors or conditions including prolonged **fasting,** total parenteral nutrition (TPN), and use of the drugs ceftriazone or octreotide must be avoided. Patients with symptomatic sludge or complications should have cholecystectomy (removal of the gallbladder). In poor surgical candidates, alternative interventions include oral agents for bile acid dissolution and percutaneous cholecystostomy. 1 figure. 1 table. 8 references.

- **Gallstones**

  Source: in King, J.E., ed. Mayo Clinic on Digestive Health. Rochester, MN: Mayo Clinic. 2000. p. 133-142.

  Contact: Available from Mayo Clinic Health Information. 5505 36th Street, SE, Grand Rapids, MI 49512. (800) 291-1128. Website: www.mayoclinic.com. PRICE: $14.95 plus shipping and handling. ISBN: 1893005046.

  Summary: This chapter on gallstones (cholelithiasis) is from a comprehensive guidebook from the Mayo Clinic that focuses on a variety of digestive symptoms, including heartburn, abdominal pain, constipation, and diarrhea, and the common conditions that are often responsible for these symptoms. Written in nontechnical language, the book includes practical information on how the digestive system works, factors that can interfere with its normal functioning, and how to prevent digestive problems. This chapter first reviews the key signs and symptoms of gallstones, including upper abdominal pain; pain in the back, chest, or right shoulder blade; and nausea and vomiting. Gallbladder pain, commonly called a gallbladder attack, occurs when stones in the gallbladder become lodged in the neck of the gallbladder or the cystic duct and obstruct the gallbladder's opening. This leads to a buildup of pressure in the gallbladder as it slowly contracts, causing constant pain and often nausea. The authors review how gallstones form and the three most common types: cholesterol stones, pigment stones, and primary bile duct stones. Risk factors for gallstones include being female, excess weight, diet and dieting (diet high in fat and sugar, **fasting,** and rapid weight loss diets are particularly risky), age, family history, and ethnic group. Gallstones are diagnosed with the assistance of ultrasound, computed tomography (CT scan), radionuclide scan, blood tests, and endoscopic retrograde cholangiopancreatography (ERCP). Treatment options range from watchful waiting to bile salt tablets, MTBE (methyl tertiary butyl ether) injection, sound wave therapy (extracorporeal shock wave lithotripsy), to surgery, either open or through the use of laparoscopy. One sidebar reviews the home remedies that are purported to prevent gallstones (none are supported), noting that the best preventive steps are to maintain a healthy weight and avoid crash diets. 1 figure.

- **Pathophysiology and Natural History**

  Source: in Edelman, S.V. and Henry, R.R. Diagnosis and Management of Type 2 Diabetes. Caddo, OK: Professional Communications, Inc. 2002. p. 19-27.

  Contact: Available from Professional Communications, Inc., Fulfillment Center, PO Box 10, Caddo, OK 74729-0010. (800)337-9838. Fax (580)367-9989. E-mail: profcomm@netcommander.com. ISBN: 1884735754. PRICE: $21.95, plus shipping and handling.

Summary: This chapter on pathophysiology and natural history is from a handbook for primary care providers that offers a concise overview of the diagnosis and management of type 2 diabetes. The authors briefly discuss genetics and then not that most patients with type 2 diabetes and **fasting** hyperglycemia (high blood glucose levels) are characterized by insulin resistance, impaired insulin secretion, and increased hepatic (liver) glucose production. The authors suggest that the etiologic (causative) sequence is that insulin resistance (probably genetic in origin) and abnormalities of pancreatic insulin secretion are manifested initially. The pancreas tries to compensate for insulin resistance which leads to increased insulin secretion to maintain the prediabetic state. In time, the compensation fails and beta cell function declines, leading to hyperglycemia. The authors stress that the potential benefits of intervening before the onset of diabetes, and aggressive treatment once the disease becomes manifest, are tremendous. The primary care provider is uniquely posed to promote and provide early prevention and to have a substantial impact on lessening the burden placed on individuals and society by type 2 diabetes. 1 figure. 29 references.

- **Small Intestinal Motor Physiology**

  Source: in Feldman, M.; Friedman, L.S.; Sleisenger, M.H. Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management. 7th ed. [2-volume set]. St. Louis, MO: Saunders. 2002. p. 1665-1678.

  Contact: Available from Elsevier. 11830 Westline Industrial Drive, St. Louis, MO 63146. (800) 545-2522. Fax (800) 568-5136. Website: www.us.elsevierhealth.com. PRICE: $229.00 plus shipping and handling. ISBN: 0721689736.

  Summary: This chapter on small intestinal motor physiology is from a comprehensive and authoritative textbook that covers disorders of the gastrointestinal tract, biliary tree, pancreas, and liver, as well as the related topics of nutrition and peritoneal disorders. Topics include the evaluation of small intestinal motility (insights and limitations of measurements); structural elements that determine small intestinal motility, including general anatomy, small intestinal smooth muscles, interstitial cells of Cajal, and the neural control system; control of motor activity; the clinical measurement of small intestinal motility; normal small intestinal motor function in humans, including fed and **fasting** motor patterns; clinical consequences of disordered small intestinal motor function; and the recommended approach to patients with possibly disordered small intestinal motor function. The chapter includes a mini-outline with page citations, full-color illustrations, and extensive references. 7 figures. 1 table. 33 references.

- **Physical and Metabolic Characteristics of Persons with Diabetes**

  Source: in Harris, M.I., et al., eds., for the National Diabetes Data Group (NDDG). Diabetes in America. 2nd ed. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health. 1995. p. 117-164.

  Contact: Available from National Diabetes Information Clearinghouse (NDIC). 1 Information Way, Bethesda, MD 20892-3560. (800) 860-8747 or (301) 654-3327. Fax (301) 634-0716. E-mail: ndic@info.niddk.nih.gov. Also available at http://www.niddk.nih.gov/. PRICE: Full-text book and chapter available online at no charge; book may be purchased for $20.00. Order number: DM-96 (book).

  Summary: This chapter on the physical and metabolic characteristics of persons with diabetes is from a compilation and assessment of data on diabetes and its complications in the United States. The primary data sources used by the authors are the 1989 National Health Interview Survey (NHIS), a household interview survey of a representative

sample of the U.S. civilian, noninstitutionalized population older than 18 years of age; the 1976-1980 Second National Health and Nutrition Examination Survey (NHANES II), which included a representative sample of the U.S. population age 20 to 74 years who were administered a household interview, a physical examination with certain clinical and laboratory tests, and an oral glucose tolerance test (OGTT) to detect undiagnosed diabetes; and the 1982-1984 Hispanic Health and Nutrition Examination Survey (HHANES), which included Mexican Americans, Puerto Ricans, and Cuban Americans age 20 to 74 years from certain regions of the United States and employed methods similar to those used in the NHANES II. By definition, persons with NIDDM have much higher **fasting** plasma glucose levels than persons with impaired glucose tolerance (IGT). A family history of diabetes is more frequent in NIDDM than in other groups. Mean body mass index (BMI) is highest in persons with NIDDM, followed by those with IGT, and persons with normal glucose tolerance. In general, mean blood pressure is as high in persons with undiagnosed NIDDM and IGT as in persons with a medical history of NIDDM, but lower in persons with normal glucose tolerance. Compared with nondiabetic persons, persons with NIDDM have higher mean total cholesterol, low density lipoprotein (LDL) cholesterol, and triglycerides, and lower mean high-density lipoprotein (HDL) cholesterol. Parity (number of children) is greater in persons with NIDDM than in nondiabetic persons. Except at youngest ages, a slightly higher percent of nondiabetic persons smoke (26.1 percent) than do persons with diabetes (20.1 percent). Excellent or very good health status was reported in 64.9 percent of nondiabetic adults, but only in 19.5 percent of persons with NIDDM. 50 appendices. 28 figures. 19 references. (AA-M).

- **Plasma Glucose**

  Source: in Office of Disease Prevention and Health Promotion, U.S. Public Health Service. Put Prevention Into Practice: Clinician's Handbook of Preventive Services. 2nd ed. Germantown, MD: International Medical Publishing, Inc. 1998. p. 272-276.

  Contact: Available from International Medical Publishing, Inc. Reiter's Scientific and Professional Books, 2021 K Street, NW, Washington, DC 20006. (800) 591-2713 or (202) 223-3327. Fax (202) 296-9103. PRICE: $20.00 plus shipping and handling. ISBN: 1883205328. Also available from the U.S. Government Printing Office. Superintendent of Documents, P.O. Box 371954, Pittsburgh, PA 15250-7954. (202) 512-1800. Fax (202) 512-2250.

  Summary: This chapter presents recommendations of major authorities on screening for diabetes mellitus. Approximately 5 percent of those who have diabetes have type 1, and they require insulin for survival. They usually have symptoms and are diagnosed soon after clinical onset. The remaining 95 percent have type 2 diabetes. People who have this type can be relatively symptom free for years before diagnosis. The prevalence of diabetes is significantly higher among certain ethnic groups, including Hispanics, African Americans, and Native Americans. Diabetes complications include end-stage renal disease, blindness, nontraumatic lower extremity amputation, neuropathy, cardiovascular disease, and peripheral vascular disease. The most accurate method of screening is by measuring **fasting** plasma glucose. The American College of Obstetricians and Gynecologists, the American College of Physicians, the Canadian Task Force on the Periodic Health Examination, and the U.S. Preventive Services Task Force recommend diabetes screening for patients who have various risk factors for the disease. The American Diabetes Association recommends diabetes screening every 3 years for all adults 45 years old or older and screening for younger people who have various risk factors. The chapter provides guidelines on plasma glucose screening, lists patient

resources, and presents criteria for diagnosing diabetes in nonpregnant adults. 16 references.

- **Other Diabetes**

  Source: in Hiser, E. Other Diabetes: Living and Eating Well with Type 2 Diabetes. New York, NY: William Morrow. 1999. p. 1-9.

  Contact: Available from William Morrow. 39 Plymouth Street, Fairfield, NJ 07004. (800) 843-9389. Fax (888) 775-3260. PRICE: $23.00 plus shipping and handling.

  Summary: This chapter provides an overview of type 2 diabetes. This form, which is more common than type 1 diabetes, typically starts out with high insulin levels. Although type 1 diabetes is an immediate threat to life because of the requirement for insulin, type 2 is more insidious because half of the people who have it do not know they have it. Risk factors for type 2 diabetes include excess body fat, genetic susceptibility, and sedentary lifestyle. The chapter explains how the body systems that keep humans alive by managing energy and nutrients evolved through natural selection and reviews technological advances that have led Americans to become overweight. In addition, the chapter discusses the interrelationship among obesity and type 2 diabetes, genetics, and environment among Pima Indians, a group of North Americans with the highest rate of type 2 diabetes in the world. Although much still has to be done to completely understand the genetics of type 2 diabetes, researchers know that insulin resistance is the key. Insulin resistance occurs when too much body fat impairs the body's ability to properly use insulin. In a state of insulin resistance, the insulin receptors on cell membranes do not respond properly to insulin, so glucose backs up in the blood. If blood sugar stays a lot higher than normal between meals and in the **fasting** state, a diagnosis of type 2 diabetes is made. A goal for managing type 2 diabetes is to increase insulin sensitivity so that glucose can be effectively cleared from the blood. Ways to increase insulin sensitivity include reducing caloric intake, exercising, and eating a reasonable amount of carbohydrates.

- **What You Need to Know About Lipids and Exercise**

  Source: in Hirsch, I.B. 12 Things You Must Know About Diabetes Care Right Now!. Alexandria, VA: American Diabetes Association. 2000. p. 115-130.

  Contact: Available from American Diabetes Association (ADA). Order Fulfillment Department, P.O. Box 930850, Atlanta, GA 31193-0850. (800) 232-6733. Fax (770) 442-9742. Website: www.diabetes.org. PRICE: $14.95 plus shipping and handling. ISBN: 1580400612.

  Summary: This chapter provides information on blood lipids and exercise to treat lipid problems. Lipids, which are body fats, include triglycerides and cholesterol. Neither triglycerides nor cholesterol can be dissolved in blood, so they travel in the blood by joining with proteins called lipoproteins. Low density lipoprotein (LDL) is the major carrier for cholesterol in the blood. An excess of LDL causes atherosclerosis. High density lipoprotein (HDL), however, takes cholesterol away from the blood vessel walls and into the liver. Problems occur when levels of triglycerides and LDL and HDL cholesterol are out of balance. The most common problems in people who have type 2 diabetes have to do with triglycerides and HDL cholesterol. People who have type 1 diabetes and poor glucose control will have high triglyceride and LDL cholesterol levels. Adults who have high or out of balance lipids should be tested each year for total cholesterol, **fasting** triglycerides, and HDL and LDL cholesterol. The first approach to balancing lipid levels should be to improve blood glucose control with weight loss,

exercise, and better meal planning. When lipid levels do not improve with meal planning, exercise, and glucose control, treatment with lipid lowering drugs is recommended. Drugs used to treat lipid problems include bile acid binding resins, fibric acid derivatives, HMG-CoA reductase inhibitors, nicotinic acid, estrogen, and aspirin. The chapter discusses the effects of these drugs and presents guidelines on coronary disease screening. In addition, the chapter includes a list of questions a patient may ask a doctor and questions a doctor may ask a patient. 3 tables.

- **What Should Happen at Each Doctor's Appointment?**

  Source: in Hirsch, I.B. 12 Things You Must Know About Diabetes Care Right Now!. Alexandria, VA: American Diabetes Association. 2000. p. 49-59.

  Contact: Available from American Diabetes Association (ADA). Order Fulfillment Department, P.O. Box 930850, Atlanta, GA 31193-0850. (800) 232-6733. Fax (770) 442-9742. Website: www.diabetes.org. PRICE: $14.95 plus shipping and handling. ISBN: 1580400612.

  Summary: This chapter provides people who have diabetes with information on what should happen at each doctor's appointment. The American Diabetes Association recommends that people who treat their diabetes with insulin should visit their health care provider at least four times a year and those who do not use insulin should visit their health care provider two to four times per year. At each visit, the doctor and patient will review blood glucose control, consider any changes that may need to be made to the diabetes care plan, and discuss symptoms of developing complications and other health concerns. A physical examination should also be repeated at all visits. At every visit, weight and blood pressure should be measured, feet should be examined, and eyes checked for retinopathy. Ongoing laboratory work includes tests for glycated hemoglobin level, **fasting** blood glucose level, lipid levels, and urine albumin. In addition, the patient and doctor should review the patient's management plan to find problems and check the patient's progress in meeting goals. The chapter includes a list of questions a patient may ask a doctor and questions a doctor may ask a patient.

- **Endocrine Emergencies: Hypoglycemic and Hyperglycemic Crises**

  Source: in Clark, O.H. and Duh, Q. Textbook of Endocrine Surgery. Philadelphia, PA: W.B. Saunders Company. 1997. p. 651-661.

  Contact: Available from W.B. Saunders Company. Order Fulfillment, 6277 Sea Harbor Drive, Orlando, FL 32887. (800) 545-2522. Fax (800) 874-6418 or (407) 352-3445. PRICE: $155.00. ISBN: 0721658822.

  Summary: This chapter, from a book on endocrine surgery, provides health professionals with a review of the pathophysiology of hypoglycemic and hyperglycemic crises, which are seen most commonly in patients with diabetes. Such endocrine emergencies can be life-threatening and are encountered with some frequency in the surgical setting. Topics include the physiology of systemic glucose homeostasis, hormonal regulation of glucose metabolism, and management of the surgical patient with diabetes. For both hypoglycemic and hyperglycemic crises, the authors discuss clinical presentation, pathogenesis, and recommended therapy. Hypoglycemic crises may be due to diabetic ketoacidosis or a hyperglycemic hyperosmolar nonketotic state. Hypoglycemic crises are classified as postprandial hypoglycemia or **fasting** hypoglycemia. In most surgical patients, endocrine crises are due primarily to inadequate or excessive insulin secretion or administration; patients with diabetes are at particular risk. Appropriate monitoring of glucose levels and management with

intravenous saline, insulin, and glucose are fundamental to treatment. 3 figures. 1 table. 62 references. (AA-M).

- **Role of the Kidney in Divalent Mineral Nutrition**

  Source: in Anderson, J.J.B., and Garner, S.C. Calcium and Phosphorus in Health and Disease. Boca Raton, FL: CRC Press. 1995. p. 63-81.

  Contact: Available from CRC Press. 2000 Corporate Boulevard NW., Boca Raton, FL 33431. (800) 272-7737 or (561) 994-0555. Fax (800) 374-3401. E-mail: orders@crcpress.com. Website: http://www.crcpress.com. PRICE: $159.00. ISBN: 0849378451.

  Summary: This chapter, from a medical reference text on calcium and phosphorus, covers the role of the kidney in divalent mineral nutrition. The author overviews the mechanisms of normal renal handling of calcium (Ca) and phosphorus (P), as well as their control by the calciotropic hormones. The primary renal responses to nutritional changes in Ca and P are also reviewed. The dietary regulation sections cover the role of dietary calcium and dietary phosphate; the effect of vitamin D deficiency; the effect of dietary protein, carbohydrate, and sodium; and the effect of **fasting.** 12 figures. 56 references. (AA-M).

- **Management of Gestational Diabetes**

  Source: in Reece, E.A.; Coustan, D.R., eds. Diabetes Mellitus in Pregnancy. 2nd ed. New York, NY: Churchill Livingstone. 1995. p. 277-286.

  Contact: Available from Churchill Livingstone. 300 Lighting Way, Secaucus, NJ 07094. (800) 553-5426. PRICE: $92.00. ISBN: 0443089795.

  Summary: This chapter, from a medical textbook on diabetes mellitus in pregnancy, discusses the management of gestational diabetes (GDM). The author stresses that the most important step in the management of GDM is its diagnosis. Once this has been achieved, almost every type of management protocol has been associated with a reduction in the perinatal mortality rate. The author briefly discusses the goals of management, then outlines a plan for achieving these goals. Steps in the plan include dietary therapy, glucose monitoring, oral hypoglycemic agents, insulin therapy, and the use of insulin to prevent morbidity (prophylactic insulin). The author concludes the chapter with a discussion of recommended fetal evaluation tests, and delivery considerations. The author stresses that all women diagnosed with GDM should be given dietary counseling and should be monitored at least weekly for **fasting** and postprandial hyperglycemia. Should hyperglycemia occur, insulin should be administered to restore glucose homeostasis and reduce perinatal mortality risks. Intervention to reduce perinatal morbidity is less clear. 1 figure. 2 tables. 53 references.

- **Approach to the Patient with Hypoglycemia**

  Source: Kelley, W.N., ed. Textbook of Internal Medicine. 3rd ed. Vol 2. Philadelphia, PA: Lippincott-Raven Publishers. 1997. p. 2166-2168.

  Contact: Available from Lippincott-Raven Publishers. P.O. Box 1600, Hagerstown, MD 21741. (800) 638-3030 or (301) 714-2300. Fax (301) 824-7390. PRICE: $125.00 (2 volume edition) or $99.00 (single volume edition). ISBN: 0397515405 (2 volume set); 0397517297 (volume 1); 0397517300 (volume 2); 039751283x (paper).

  Summary: This chapter, from a textbook on internal medicine, describes for health professionals the therapeutic approach to hypoglycemia in adults. Topics include

etiology, signs and symptoms, differential diagnosis, and strategies for optimal care management. The author points out that evaluation of suspected hypoglycemia requires consideration of both blood glucose level and the presence or absence of associated symptoms. Classifying specific disorders as reactive (occurring between 1 and 5 hours after eating) or **fasting** (occurring more than 5 hours afterwards) is the first step in approaching a diagnosis and understanding the underlying pathophysiologic mechanism. Differential diagnosis is usually not difficult after consideration of the individual patient's history and the clinical setting. In many cases, the probable diagnosis is apparent and it is possible to initiate appropriate therapy and conduct confirmatory tests. Clinical management of reactive hypoglycemia favors prevention of future episodes over emergency treatment of a single episode, which is often mild and transient. Patients with various causes of **fasting** hypoglycemia may have extremely low blood glucose levels that require immediate intervention. Definitive treatment of **fasting** hypoglycemia is determined by the specific underlying disease. 2 tables. 5 references. (AA-M).

- **Hypoglycemia**

  Source: in Adler, S.N., et al. Pocket Manual of Differential Diagnosis. 3rd ed. Boston, MA: Little, Brown and Company. 1994. p. 120-122.

  Contact: Available from Lippincott-Raven Publishers. 12107 Insurance Way, Hagerstown, MD 21740-5184. (800) 777-2295. Fax (301) 824-7390. E-mail: lrorders@phl.lrpub.com. Website: http://www.lrpub.com. PRICE: $24.95. ISBN: 0316011096.

  Summary: This section is from a chapter on the endocrine/metabolic system in a pocket manual of differential diagnosis; the section focuses on hypoglycemia. The section consists of listings of factors causing hypoglycemia, separated into two groups: **fasting** hypoglycemia and reactive hypoglycemia. 3 references.

- **Diagnosis and Management of Diabetes**

  Source: in Hall, J.E.; Nieman, L.K., eds. Handbook of Diagnostic Endocrinology. Totowa, NJ: The Humana Press, Inc. 2003. p. 157-177.

  Contact: Humana Press, Inc. 999 Riverview Dr., Suite 208 Totowa, NJ 07512. (973) 256-1699. Fax (973) 256-8341. E-mail: humana@humanapr.com PRICE: $99.50 plus shipping and handling. ISBN: 0896037576.

  Summary: With the rapid development of new and more reliable diagnostic tests, and aided by the molecular and genetic approaches that continue to deepen the understanding of these diseases, the ability to diagnose patients with endocrine disease has dramatically increased. This chapter on the diagnosis and management of diabetes is from a book that explains the pathophysiology and clinical manifestations of endocrine disorders and surveys all the latest laboratory tests used in their diagnosis. Diabetes mellitus represents a heterogeneous group of metabolic disorders characterized by decreased insulin secretion, insulin action, or both. In this chapter, the author discusses the diagnosis of diabetes, impaired **fasting** glucose and impaired glucose tolerance, and gestational diabetes; monitoring glycemia (levels of blood glucose) in the patient with diabetes; protein glycation; and the diagnosis and monitoring of diabetes-related complications, including retinopathy (eye disease), neuropathy (nerve disease), nephropathy (kidney disease), and cardiovascular disease. The author stresses that because safe and effective medical therapies are available to improve metabolic control and large-scale clinical trials have demonstrated reduced

complications with treatments for both types 1 and 2 diabetes, diagnostic procedures are vital. 5 tables. 50 references.

CHAPTER 7. MULTIMEDIA ON FASTING

Overview

In this chapter, we show you how to keep current on multimedia sources of information on fasting. We start with sources that have been summarized by federal agencies, and then show you how to find bibliographic information catalogued by the National Library of Medicine.

Video Recordings

An excellent source of multimedia information on fasting is the Combined Health Information Database. You will need to limit your search to "Videorecording" and "fasting" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find video productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Videorecording (videotape, videocassette, etc.)." Type "fasting" (or synonyms) into the "For these words:" box. The following is a typical result when searching for video recordings on fasting:

- **Behavioral Approaches to the Treatment of Obesity and Type II Diabetes**

  Source: Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, 1992, 60 minutes.

  Contact: WIN, 1 WIN WAY, Bethesda, MD 20892-3665.

  Summary: Dr. Wing's lecture discusses recent changes in behavioral treatment methods for treating obese patients with and without Type II diabetes (noninsulin-dependent diabetes mellitus). In the 1980s, the typical behavioral treatment-based weight loss program lasted from 20 to 25 weeks. The patient followed a 1,000- to 1,500-calorie diet and attended weekly sessions to learn self-monitoring and reinforcing strategies such as keeping a food diary and removing high-calorie foods from the home. The typical result was a weight loss of 20 pounds (11 pound weight loss maintained after 1 year). Researchers have found that patients who maintain a 15 to 30 pound weight loss after one year have significant improvements of their **fasting** blood sugar, insulin, triglyceride, and HDL levels. In the 1990s, researchers have utilized more aggressive

behavioral interventions to overcome the weight regain that occurs in virtually all patients. These include: (1) The chronic disease model, or treating obesity as a lifelong disease. Dr. Wing shares the results of a study that found that patients who followed an 18-month program of biweekly sessions lost more weight and maintained weight loss more successfully than those on a standard 20-week program. (2) Providing incentives such as prepackaged food or monetary compensation for achieving weight loss. Dr. Wing discusses the results of a study that found that providing people with weekly boxes of prepackaged meals, coupled with standard behavioral treatment, was more successful in achieving weight loss than giving patients money or by behavioral treatment alone. (3) Combining standard behavior interventions with very-low-calorie diets (VLCDs) or diets containing about 400 calories per day. Dr. Wing reviews the results of a study in which patients who went on VLCDs twice in one year combined with behavioral treatment, lost more weight and maintained weight loss better than patients on behavioral treatment alone. However, patients had trouble adhering to the second VLCD. Dr. Wing feels that more research on the appropriate use of VLCDs is warranted. (4) Using a diet that restricts fat as well as calories, Dr. Wing shows the results of a study that found that patients on a low-fat diet (less than 20 percent of calories from fat) for 16 weeks lost more weight and kept if off better than patients on behavioral treatment alone. The results also show that such a diet improved glycemic and lipid levels in obese Type II diabetics. (5) Combining diet and exercise. Dr. Wing shows preliminary results of a study in which patients who attended aerobic exercise classes while dieting lost more weight and kept it off better after 1 year than those who dieted without exercise. Surprisingly, patients who were dieting attended more exercise sessions than a third group of patients who were exercising without dieting.

- **Managing Diabetes in the Primary Care Setting: A Team Approach**

  Source: Secaucus, NJ: Network for Continuing Medical Education. 1997. (videocassette).

  Contact: Available from Network for Continuing Medical Education. 1425 Broad Street, Clifton, NJ 07013. (800) 223-0272 or (973) 473-9500. Fax (973) 591-1224. PRICE: Call for pricing information. Order number 726.

  Summary: In this telecourse video, Dr. Bruce A. Ellsweig addresses current issues in diagnosis, tight glucose control, lifestyle modification, and pharmacologic therapy to illustrate the primary care physician's role in the team approach to managing diabetes. Dr. Ellsweig refers to diabetes as a group of disorders characterized by an impaired ability to manage glucose in the body. Specific topics include the **fasting** plasma glucose test, the revised diabetes nomenclature, American Diabetes Association testing recommendations, oral agents and insulin, HbA1c, the Diabetes Control and Complications Trial (DCCT), patient compliance, patient referral, and diabetic emergencies. The video emphasizes the role of a team approach to diabetes management. Three case presentations address the importance of patient compliance. After completing this telecourse, participating physicians should be able to identify patients at risk for developing type 2 diabetes, explain insulin resistance and its consequences, describe the utility of 'tight control' in managing diabetes, describe the roles of various team members in diabetes management, and list the therapeutic options for diabetes management. A post-telecourse quiz concludes the video. (AA-M).

- **Strategies for the Prevention and Treatment of Macrovascular Complications of Type 2 Diabetes**

  Source: Kansas City, MO: American Academy of Family Physicians. 1998. (videocassette).

Contact: Available from American Academy of Family Physicians. 8880 Ward Parkway, Kansas City, MO 64114-2797. (800) 274-2237. PRICE: $17.95 for members; $25.00 for non-members, plus shipping and handling.

Summary: The macrovascular (large blood vessel) complications of diabetes account for the majority of the morbidity (related illness) and mortality (death) associated with the disease. In particular, people with type 2 diabetes are at increased risk for cardiovascular disease, since they exhibit many independent risk factors for heart disease, including obesity, hypertension (high blood pressure), and dyslipidemia (disordered levels of fats in the blood). This continuing education program features a videocassette and study guide that discuss why people with diabetes are at increased risk for macrovascular complications and how to reduce the patient's risk of cardiovascular disease. Topics include hyperglycemia (high blood glucose levels) and cardiovascular disease, insulin resistance and cardiovascular disease, the benefits of improved glycemic control, recommended target glycemic goals, nonpharmacologic therapies for diabetes (diet, exercise, patient education), pharmacologic (drug) therapies for diabetes (insulin secretagogues, insulin sensitizers, alpha-glucosidase inhibitors, and insulin), determining the optimal drug treatment regimen for individual patients, and treating cardiovascular risk factors. The program recommends that patients should be seen quarterly or more often, depending upon the severity of their disease, and target goals for HbA1c (glycosylated hemoglobin, a measurement of blood glucose levels over time) and **fasting** blood glucose should be established at the initial visit and discussed directly with the patient. Patients should be reminded at every office visit that weight loss and regular exercise are the most important aspects of controlling their diabetes and reducing the risk of macrovascular disease. A sample patient education hand out is included in the study guide. Through this program, users can qualify for one credit hour of Continuing Medical Education (CME) in category 1; the appropriate posttest is provided. 5 figures. 14 tables. 15 references.

- **New Definition of Diabetes**

  Source: Los Angeles, CA: National Health Video, Inc. 1998. (videocassette).

  Contact: Available from National Health Video, Inc. 12021 Wilshire Blvd., Suite 550, Los Angeles, CA 90025. (800) 543-6803. Fax (310) 477-8198. E-mail: Healthvid@aol.com. PRICE: $89.00 plus shipping and handling. Order number 283.

  Summary: This videotape provides people who have diabetes with information on the new definition of the disease. The videotape begins by explaining the revised **fasting** plasma glucose (FPG) criteria and their diagnostic implications and discussing the impaired **fasting** glucose (IFG) category. Diabetes is diagnosed as a FPG level of 126 or above. The criteria for diagnosis were lowered to allow for earlier identification of diabetes so that complications can be prevented. IFG is defined as a blood glucose level of 110 to 125. People with such a value do not yet have diabetes, but they are at risk of developing it. The video continues by identifying factors that indicate the need for diabetes testing, including excessive thirst, frequent urination, weight loss, a family member who has diabetes, age over 45, and obesity. This is followed by an explanation of type 1 and type 2 diabetes. In addition, the videotape presents the food guide pyramid tailored for persons who have diabetes and provides suggestions on food preparation and exercise.

- **Living with Diabetes: Making the Diagnosis**

  Source: Madison, WI: University of Wisconsin Hospitals and Clinics, Department of Outreach Education. 1999. (videocassette).

  Contact: Available from University of Wisconsin Hospital and Clinics. Picture of Health, 702 North Blackhawk Avenue, Suite 215, Madison, WI 53705-3357. (800) 757-4354 or (608) 263-6510. Fax (608) 262-7172. PRICE: $19.95 plus shipping and handling; bulk copies available. Order number 071899A.

  Summary: This videotape, part of a series on living with diabetes, focuses on the diagnosis of diabetes. A moderator discusses the new criteria for the diagnosis and classification of diabetes, the rise in the incidence of diabetes, the symptoms of diabetes, and the prevention of diabetes with an endocrinologist. The videotape begins with a discussion of what diabetes is, how insulin works, the types of diabetes, and risk factors for diabetes. Type 1 diabetes, which was formerly known as insulin dependent diabetes, usually develops quickly, whereas type 2 diabetes, which was formerly known as noninsulin dependent diabetes, usually has a gradual onset. The symptoms of diabetes, which are generally the same regardless of the type, are related to high blood sugar. They include excessive urination and thirst, fatigue, hunger, weight loss, and blurred vision. Risk factors for type 1 diabetes include a genetic predisposition for developing the disease. Risk factors for type 2 diabetes include being overweight, sedentary, and over 45 years old; having a history of stillbirth or gestational diabetes; having high blood pressure and high cholesterol; being African American, Hispanic, or Native American; and having previously been identified with impaired glucose tolerance. The acute complications of diabetes include ketoacidosis, nonketotic hyperosmolar syndrome, and hypoglycemia. The chronic complications are divided into microvascular and macrovascular complications. Microvascular complications include retinopathy, neuropathy, and nephropathy. Macrovascular complications include heart attack, stroke, and peripheral vascular disease. Early diagnosis is important in preventing complications. Diagnosis is based on blood sugar levels obtained from a blood glucose test, a **fasting** plasma glucose test, or an oral glucose tolerance test. The risk of developing type 2 diabetes may be reduced by eating properly, maintaining an ideal weight, and exercising. The videotape includes a self test that viewers can take to assess their risk of developing type 2 diabetes.

CHAPTER 8. PERIODICALS AND NEWS ON FASTING

Overview

In this chapter, we suggest a number of news sources and present various periodicals that cover fasting.

News Services and Press Releases

One of the simplest ways of tracking press releases on fasting is to search the news wires. In the following sample of sources, we will briefly describe how to access each service. These services only post recent news intended for public viewing.

PR Newswire

To access the PR Newswire archive, simply go to **http://www.prnewswire.com/**. Select your country. Type "fasting" (or synonyms) into the search box. You will automatically receive information on relevant news releases posted within the last 30 days. The search results are shown by order of relevance.

Reuters Health

The Reuters' Medical News and Health eLine databases can be very useful in exploring news archives relating to fasting. While some of the listed articles are free to view, others are available for purchase for a nominal fee. To access this archive, go to **http://www.reutershealth.com/en/index.html** and search by "fasting" (or synonyms). The following was recently listed in this archive for fasting:

- **Threshold for diagnosing impaired fasting glucose lowered**
  Source: Reuters Medical News
  Date: October 24, 2003

The NIH

Within MEDLINEplus, the NIH has made an agreement with the New York Times Syndicate, the AP News Service, and Reuters to deliver news that can be browsed by the public. Search news releases at **http://www.nlm.nih.gov/medlineplus/alphanews_a.html**. MEDLINEplus allows you to browse across an alphabetical index. Or you can search by date at the following Web page: **http://www.nlm.nih.gov/medlineplus/newsbydate.html**. Often, news items are indexed by MEDLINEplus within its search engine.

Business Wire

Business Wire is similar to PR Newswire. To access this archive, simply go to **http://www.businesswire.com/**. You can scan the news by industry category or company name.

Market Wire

Market Wire is more focused on technology than the other wires. To browse the latest press releases by topic, such as alternative medicine, biotechnology, fitness, healthcare, legal, nutrition, and pharmaceuticals, access Market Wire's Medical/Health channel at **http://www.marketwire.com/mw/release_index?channel=MedicalHealth**. Or simply go to Market Wire's home page at **http://www.marketwire.com/mw/home**, type "fasting" (or synonyms) into the search box, and click on "Search News." As this service is technology oriented, you may wish to use it when searching for press releases covering diagnostic procedures or tests.

Search Engines

Medical news is also available in the news sections of commercial Internet search engines. See the health news page at Yahoo (**http://dir.yahoo.com/Health/News_and_Media/**), or you can use this Web site's general news search page at **http://news.yahoo.com/**. Type in "fasting" (or synonyms). If you know the name of a company that is relevant to fasting, you can go to any stock trading Web site (such as **http://www.etrade.com/**) and search for the company name there. News items across various news sources are reported on indicated hyperlinks. Google offers a similar service at **http://news.google.com/**.

BBC

Covering news from a more European perspective, the British Broadcasting Corporation (BBC) allows the public free access to their news archive located at **http://www.bbc.co.uk/**. Search by "fasting" (or synonyms).

Newsletter Articles

Use the Combined Health Information Database, and limit your search criteria to "newsletter articles." Again, you will need to use the "Detailed Search" option. Go directly

to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter Article." Type "fasting" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months. The following is a typical result when searching for newsletter articles on fasting:

- **Dangerous Dieting Threatens Young Athletes' Health**

  Source: Fit Society Page. p. 5-6. April-June 2001.

  Contact: American College of Sports Medicine. PO Box 1440, Indianapolis, IN 46206-1440.

  Summary: Adolescents, particularly girls, are typically concerned about their body weight. Many are dissatisfied with their weight and may resort to unhealthy weight-control methods such as **fasting,** diet pills, vomiting, and laxatives or diuretic abuse. Female athletes are more likely than male athletes to worry about their weight or undertake unhealthy weight-control behaviors. Research indicates that athletes, particularly athletes who participate in sports emphasizing thinness or a low body weight, are at a greater risk of developing eating disorders than nonathletes. Many of the personal traits that make for a successful athlete also encourage eating disorders. The article provides a list of signs and symptoms to alert parents to the potential of excessive weight concern in their children. The author discusses how parents should promote healthy eating in their children, and what to do if they suspect their child suffers from an eating disorder.

- **Upper GI Endoscopy: What to Expect**

  Source: Digestive Health Matters. 2(1): 3-4. Spring 2000.

  Contact: Available from International Foundation for Functional Gastrointestinal Disorders (IFFGD). P.O. Box 170864, Milwaukee, WI 53217. (888) 964-2001 or (414) 964-1799. Fax (414) 964-7176. Website: www.iffgd.org.

  Summary: Endoscopy is an examination using a tubular device with a light on the end through which the examiner can see the gastrointestinal (GI) tract. This article, from a health education newsletter on gastroesophageal reflux disease (GERD), and esophageal and upper gastrointestinal health, informs readers about the procedure of upper GI endoscopy (esophagogastroduodenoscopy) and what they can expect while undergoing this procedure. The author reminds readers that this article provides only a general description; each patient should discuss the test thoroughly before the procedure to allow for variances in specific medical facilities and for any medical requirements the patient may present. An endoscopy is indicated when there are upper gastrointestinal symptoms that are unexplained or unresponsive to trials of diet modification or drugs. The author reviews where the procedure usually takes place, defines the procedure and the indications for its use (most commonly, dyspepsia, persistent heartburn, acute bleeding, and anemia), the preparation to be done before the test (fasting), the use of a medical consent form, conscious sedation, local anesthesia on the throat (for ease of swallowing the endoscopy tube), the procedure itself, and postprocedure recovery. 1 figure.

- **Cyclic Vomiting in Mitochondrial Disease**

  Source: Code V. 8(2): 5-7. Summer 2000.

Contact: Available from Cyclic Vomiting Syndrome Association (CVSA). 3585 Cedar Hill Road, NW, Canal Winchester, OH 43110. (614) 837-2586. Fax (614) 837-2586. Website: www.beaker.iupui.edu/cvsa.

Summary: Gastrointestinal (GI) symptoms are commonly encountered in patients with mitochondrial disease. In particular, vomiting is common among people with many different mitochondrial disorders, and among these individuals, the vomiting has many different causes. This article discusses one particular type of vomiting disorder, called cyclic vomiting. Cyclic vomiting refers to discrete and severe episodes of vomiting, nausea, and lethargy (severe tiredness). Episodes are discrete in that the person is free of nausea and vomiting between episodes. Vomiting and loss of appetite in this condition can be severe enough to necessitate hospitalization for intravenous fluids with each episodes. In other cases, nausea and lethargy may be much more troublesome than vomiting. Treatments are available for cyclic vomiting in individuals with mitochondrial disease. In mitochondrial disease, symptoms are believed to occur when the energy supply cannot meet energy demand. Since often little can be done to increase energy supply, decreasing energy demand is a major part of therapy. In practical terms, this means the reduction of stress, including the avoidance of **fasting,** and prompt treatment of infections and dehydration. Cyclic vomiting and other symptoms often improve with frequent feedings of complex carbohydrate, including between meals and at bedtime. Confirming the diagnosis of mitochondrial disease and ruling out other treatable metabolic disorders should be pursued. The author concludes by providing some website addresses for parents seeking additional information about cyclic vomiting and mitochondrial disease. 4 references.

- **Syndrome X**

  Source: Nutrition Action Healthletter. 29(3):3. April 2002.

  Contact: Center for Science in the Public Interest. 1875 Connecticut Ave., NW, Suite 300, Washington, DC 20009-5728. www.cspinet.org.

  Summary: Metabolic syndrome is a group of abnormalities that raise the risk of heart disease. A national survey published in the Journal of the American Medical Association (JAMA) found that one in five Americans have metabolic syndrome, also known as Syndrome X. Two in five adults between the ages of 60 and 70 years have it. It is diagnosed if three or more of the following criteria are present: blood pressure of at least 130 (systolic) or 85 (diastolic), **fasting** blood sugar of at least 110, triglycerides of at least 150, HDL cholesterol of less than 40 in men or less than 50 in women, and a waist measurement of at least 35 inches in women or at least 40 inches in men. Exercise, even in the absence of weight loss; losing a small amount of weight; and replacing carbohydrates like sweets, bread, and pasta with small amounts of unsaturated fats from oils, nuts, and salad dressing may help reverse metabolic syndrome.

- **How to Cut Your Risk of Diabetes**

  Source: Nutrition Action Healthletter. 28(4): 1, 3-8. May 2001.

  Contact: Center for Science in the Public Interest. 1875 Connecticut Avenue NW, Suite 300, Washington, DC 20009-5728.

  Summary: The author explores reducing the risk of developing diabetes. As the incidence of obesity increases in the United States, so too have diabetes rates. The article discusses the risks of high-blood sugar levels and above- optimal blood sugar. According to Frank Vinicor of the Centers for Disease Control and Prevention (CDC), 'as

of 1997, the total direct and indirect cost of diabetes was roughly 100 billion dollars a year. The major direct costs are due to hospitalization for coronary heart disease and kidney disease,' although 'blindness and amputations take the greatest toll on quality of life.' To cut diabetes risk, the article advocates losing weight if overweight, walking or being physically active for at least 30 minutes a day, eating whole-grain breads and cereals rather than refined starches and sugars, eating more fruits and vegetables, getting **fasting** blood sugar tested every 3 years starting at age 45, and using diet and exercise to keep blood pressure and cholesterol at optimal levels if **fasting** blood glucose consistently exceeds 110 mg/dL. Liebman also discusses a test for a longer term indication of blood sugar called glycated hemoglobin and lists risk factors and warning signs for diabetes, including tips on how to eat wisely to lower diabetes risk. A chart shows how to check Body Mass Index (BMI) to rate weight and diabetes risk.

- **Food Myths**

  Source: Mayo Clinic health Letter. May 1994.

  Contact: Mayo Clinic Health Letter, 200 First St., SW, Rochester, MN 55905. (800) 333-9038.

  Summary: This article describes several myths about food and explains why they are false. These myths include: the only way to lose weight is to eat less; vitamins provide energy; individuals are born to be fat; butter has more calories than oil; and **fasting** flushes the body of impurities.

- **Extreme Eating: Are Teens Compromising Their Health?**

  Source: Food Insight. p.1, 4-5. November- December 1998.

  Contact: International Food Information Council Foundation, 1100 Connecticut Ave., NW, Suite 430, Washington, DC 20036. http://ificinfo.health.org.

  Summary: This article examines the eating habits of adolescents. Many activities and products use the term `extreme,' and the author says it can also be applied to how adolescents eat. According to experts interviewed for this article, many teenagers do not get the nutrients they need most. These include calcium, zinc, and iron. Issues include athletes who feel they should be a certain weight, self-esteem, and appearance concerns. The greatest danger, says the author, is the methods many adolescents use to control their weight. These may include purging, **fasting,** taking diuretics, and over- exercising. Some experts also point to family difficulties, often an area for conflict, as making eating problems worse. The author suggests finding the proper motivator for each individual adolescent, which may be athletics, performance, or body image.

- **The History of Dieting and Its Effectiveness**

  Source: Healthy Weight Journal. 11(2):28-29; Mar/Apr 1997.

  Contact: Healthy Living Institute, 402 S. 14th St., Hettinger, ND 58639. (701) 567-2645.

  Summary: This article reviews the history of dieting from the 1950s to the present. Several programs and plans are discussed, such as **fasting,** very low-calorie liquid protein diets, low fat diets, nutrition education, and behavior modification. Finally, the author reports on a National Institutes of Health Technology Conference, which concluded that only individualized programs of decreased calorie intake, behavior modification, and exercise could achieve success.

- **Autoimmune Thyroid Disorders and Systemic Lupus**

  Source: Lupus News. 22(1): 15-18. Spring 2002.

  Contact: Available from Lupus Foundation of America. 1300 Piccard Drive, Suite 200, Rockville, MD 20850-4303. (800) 558-0121 or (301) 670-9292. Fax (301) 670-9486. Website: www.lupus.org/lupus.

  Summary: This newsletter article provides people who have lupus with information on autoimmune thyroid disorders (AITDs) and systemic lupus erythematosus (SLE). AITDs are a group of common medical problems that involve antibody reactions against the thyroid gland. The thyroid may become either underactive or overactive. Although AITD and SLE coexist with more frequency than would be expected by chance, there are no specific guidelines to testing for AITD in patients with SLE or other autoimmune rheumatologic disorders. Test results can be difficult to interpret when a patient is ill from any cause. For example, lupus flare, infections, and **fasting** will modify the thyroid hormone tests without necessarily meaning that there is true thyroid disease. A test for thyroid stimulating hormone (TSH) levels is a good screening method for minor or early thyroid gland dysfunction. However, in many cases, thyroid treatment should not be initiated unless a complete set of thyroid function tests is conducted. The article describes the symptoms of Graves' disease (overactive thyroid) and Hashimoto's thyroiditis (underactive thyroid) and discusses the overlap of these disorders. The article recommends that physicians consider screening patients with lupus and other autoimmune disorders for AITD every 2 to 3 years using a serum TSH measurement. 1 figure and 5 references.

- **Antroduodenal Manometry**

  Source: Messenger. 8(2): 9. 1996.

  Contact: Available from American Pseudo-obstruction and Hirschsprung's Disease Society (APHS). 158 Pleasant Street, North Andover, MA 01845. (978) 685-4477. Fax (978) 685-4488. E-mail: aphs@tiac.net.

  Summary: This newsletter article uses a fact sheet approach to explain antrodudoenal manometry to parents of children who may be undergoing this procedure. Written in a question and answer format, the fact sheet covers gastrointestinal motility problems in general, the technique of antroduodenal manometry, what to expect during the procedure (including pain or discomfort), and how long the procedure takes. Gastrointestinal motility is the movement of the food through the entire digestive tract (about 30 feet from the mouth to the rectum). Common examples of symptoms related to motility problems are heartburn and constipation. Antroduodenal manometry is a way to measure the strength of muscle contractions in the stomach and the duodenum. The antrum is the lower part of the stomach next to the intestines, and the duodenum is the first portion of the intestines closest to the stomach. The test may be used to help your child's doctor identify abnormalities in the strength or coordination of stomach muscles and intestinal contractions. Abnormalities may cause improper digestion and result in symptoms such as anorexia, nausea, gagging, vomiting, abdominal distention, abdominal pain, diarrhea, and constipation. The manometry tube is placed when the child is sedated; the measurement of pressure will start once the child is awake, usually the day afterward. Recordings are continued for 4 or 5 hours of **fasting,** then the child is given a meal. After the meal, recordings are continued for another 2 hours. The child will feel some discomfort from the IV (for the sedation), from lying still for a long time, and possibly from injections of medicine.

Academic Periodicals covering Fasting

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to fasting. In addition to these sources, you can search for articles covering fasting that have been published by any of the periodicals listed in previous chapters. To find the latest studies published, go to **http://www.ncbi.nlm.nih.gov/pubmed**, type the name of the periodical into the search box, and click "Go."

If you want complete details about the historical contents of a journal, you can also visit the following Web site: **http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi**. Here, type in the name of the journal or its abbreviation, and you will receive an index of published articles. At **http://locatorplus.gov/**, you can retrieve more indexing information on medical periodicals (e.g. the name of the publisher). Select the button "Search LOCATORplus." Then type in the name of the journal and select the advanced search option "Journal Title Search."

CHAPTER 9. RESEARCHING MEDICATIONS

Overview

While a number of hard copy or CD-ROM resources are available for researching medications, a more flexible method is to use Internet-based databases. Broadly speaking, there are two sources of information on approved medications: public sources and private sources. We will emphasize free-to-use public sources.

U.S. Pharmacopeia

Because of historical investments by various organizations and the emergence of the Internet, it has become rather simple to learn about the medications recommended for fasting. One such source is the United States Pharmacopeia. In 1820, eleven physicians met in Washington, D.C. to establish the first compendium of standard drugs for the United States. They called this compendium the U.S. Pharmacopeia (USP). Today, the USP is a non-profit organization consisting of 800 volunteer scientists, eleven elected officials, and 400 representatives of state associations and colleges of medicine and pharmacy. The USP is located in Rockville, Maryland, and its home page is located at **http://www.usp.org/**. The USP currently provides standards for over 3,700 medications. The resulting USP DI® Advice for the Patient® can be accessed through the National Library of Medicine of the National Institutes of Health. The database is partially derived from lists of federally approved medications in the Food and Drug Administration's (FDA) Drug Approvals database, located at **http://www.fda.gov/cder/da/da.htm**.

While the FDA database is rather large and difficult to navigate, the Phamacopeia is both user-friendly and free to use. It covers more than 9,000 prescription and over-the-counter medications. To access this database, simply type the following hyperlink into your Web browser: **http://www.nlm.nih.gov/medlineplus/druginformation.html**. To view examples of a given medication (brand names, category, description, preparation, proper use, precautions, side effects, etc.), simply follow the hyperlinks indicated within the United States Pharmacopeia (USP).

Below, we have compiled a list of medications associated with fasting. If you would like more information on a particular medication, the provided hyperlinks will direct you to ample documentation (e.g. typical dosage, side effects, drug-interaction risks, etc.). The

following drugs have been mentioned in the Pharmacopeia and other sources as being potentially applicable to fasting:

Albendazole

- **Systemic - U.S. Brands:** Albenza; Eskazole; Zentel
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202668.html

Bronchodilators, Theophylline

- **Systemic - U.S. Brands:** Aerolate Sr; Asmalix; Choledyl; Choledyl SA; Elixophyllin; Lanophyllin; Phyllocontin; Quibron-T Dividose; Quibron-T/SR Dividose; Respbid; Slo-Bid Gyrocaps; Slo-Phyllin; Theo-24; Theobid Duracaps; Theochron; Theo-Dur; Theolair; Theolair-SR; Theo-Time; Th
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/201945.html

Mebendazole

- **Systemic - U.S. Brands:** Vermox
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202339.html

Niclosamide

- **Oral - U.S. Brands:** Niclocide
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202406.html

Praziquantel

- **Systemic - U.S. Brands:** Biltricide
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202474.html

Pyrantel

- **Oral - U.S. Brands:** Pin-X
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202490.html

Repaglinide

- **Systemic - U.S. Brands:** Prandin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203463.html

Thiabendazole

- **Systemic - U.S. Brands:** Mintezol
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202558.html

Commercial Databases

In addition to the medications listed in the USP above, a number of commercial sites are available by subscription to physicians and their institutions. Or, you may be able to access these sources from your local medical library.

Mosby's Drug Consult™

Mosby's Drug Consult™ database (also available on CD-ROM and book format) covers 45,000 drug products including generics and international brands. It provides prescribing information, drug interactions, and patient information. Subscription information is available at the following hyperlink: **http://www.mosbysdrugconsult.com/**.

PDR*health*

The PDR*health* database is a free-to-use, drug information search engine that has been written for the public in layman's terms. It contains FDA-approved drug information adapted from the Physicians' Desk Reference (PDR) database. PDR*health* can be searched by brand name, generic name, or indication. It features multiple drug interactions reports. Search PDR*health* at **http://www.pdrhealth.com/drug_info/index.html**.

Other Web Sites

Drugs.com (**www.drugs.com**) reproduces the information in the Pharmacopeia as well as commercial information. You may also want to consider the Web site of the Medical Letter, Inc. (**http://www.medletter.com/**) which allows users to download articles on various drugs and therapeutics for a nominal fee.

If you have any questions about a medical treatment, the FDA may have an office near you. Look for their number in the blue pages of the phone book. You can also contact the FDA through its toll-free number, 1-888-INFO-FDA (1-888-463-6332), or on the World Wide Web at **www.fda.gov**.

APPENDICES

APPENDIX A. PHYSICIAN RESOURCES

Overview

In this chapter, we focus on databases and Internet-based guidelines and information resources created or written for a professional audience.

NIH Guidelines

Commonly referred to as "clinical" or "professional" guidelines, the National Institutes of Health publish physician guidelines for the most common diseases. Publications are available at the following by relevant Institute[11]:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Institute of General Medical Sciences (NIGMS); fact sheets available at **http://www.nigms.nih.gov/news/facts/**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines: **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Cancer Institute (NCI); guidelines available at **http://www.cancer.gov/cancerinfo/list.aspx?viewid=5f35036e-5497-4d86-8c2c-714a9f7c8d25**
- National Eye Institute (NEI); guidelines available at **http://www.nei.nih.gov/order/index.htm**
- National Heart, Lung, and Blood Institute (NHLBI); guidelines available at **http://www.nhlbi.nih.gov/guidelines/index.htm**
- National Human Genome Research Institute (NHGRI); research available at **http://www.genome.gov/page.cfm?pageID=10000375**
- National Institute on Aging (NIA); guidelines available at **http://www.nia.nih.gov/health/**

[11] These publications are typically written by one or more of the various NIH Institutes.

- National Institute on Alcohol Abuse and Alcoholism (NIAAA); guidelines available at **http://www.niaaa.nih.gov/publications/publications.htm**
- National Institute of Allergy and Infectious Diseases (NIAID); guidelines available at **http://www.niaid.nih.gov/publications/**
- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); fact sheets and guidelines available at **http://www.niams.nih.gov/hi/index.htm**
- National Institute of Child Health and Human Development (NICHD); guidelines available at **http://www.nichd.nih.gov/publications/pubskey.cfm**
- National Institute on Deafness and Other Communication Disorders (NIDCD); fact sheets and guidelines at **http://www.nidcd.nih.gov/health/**
- National Institute of Dental and Craniofacial Research (NIDCR); guidelines available at **http://www.nidr.nih.gov/health/**
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); guidelines available at **http://www.niddk.nih.gov/health/health.htm**
- National Institute on Drug Abuse (NIDA); guidelines available at **http://www.nida.nih.gov/DrugAbuse.html**
- National Institute of Environmental Health Sciences (NIEHS); environmental health information available at **http://www.niehs.nih.gov/external/facts.htm**
- National Institute of Mental Health (NIMH); guidelines available at **http://www.nimh.nih.gov/practitioners/index.cfm**
- National Institute of Neurological Disorders and Stroke (NINDS); neurological disorder information pages available at **http://www.ninds.nih.gov/health_and_medical/disorder_index.htm**
- National Institute of Nursing Research (NINR); publications on selected illnesses at **http://www.nih.gov/ninr/news-info/publications.html**
- National Institute of Biomedical Imaging and Bioengineering; general information at **http://grants.nih.gov/grants/becon/becon_info.htm**
- Center for Information Technology (CIT); referrals to other agencies based on keyword searches available at **http://kb.nih.gov/www_query_main.asp**
- National Center for Complementary and Alternative Medicine (NCCAM); health information available at **http://nccam.nih.gov/health/**
- National Center for Research Resources (NCRR); various information directories available at **http://www.ncrr.nih.gov/publications.asp**
- Office of Rare Diseases; various fact sheets available at **http://rarediseases.info.nih.gov/html/resources/rep_pubs.html**
- Centers for Disease Control and Prevention; various fact sheets on infectious diseases available at **http://www.cdc.gov/publications.htm**

NIH Databases

In addition to the various Institutes of Health that publish professional guidelines, the NIH has designed a number of databases for professionals.[12] Physician-oriented resources provide a wide variety of information related to the biomedical and health sciences, both past and present. The format of these resources varies. Searchable databases, bibliographic citations, full-text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine:[13]

- **Bioethics:** Access to published literature on the ethical, legal, and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**
- **Cancer Information:** Access to cancer-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**
- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**

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[12] Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINE*plus* (**http://medlineplus.gov/** or **http://www.nlm.nih.gov/medlineplus/databases.html**).

[13] See **http://www.nlm.nih.gov/databases/databases.html**.

- **Toxicology and Environmental Health Information (TOXNET):** Databases covering toxicology and environmental health: **http://sis.nlm.nih.gov/Tox/ToxMain.html**
- **Visible Human Interface:** Anatomically detailed, three-dimensional representations of normal male and female human bodies: **http://www.nlm.nih.gov/research/visible/visible_human.html**

The Combined Health Information Database

A comprehensive source of information on clinical guidelines written for professionals is the Combined Health Information Database. You will need to limit your search to one of the following: Brochure/Pamphlet, Fact Sheet, or Information Package, and "fasting" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For the publication date, select "All Years." Select your preferred language and the format option "Fact Sheet." Type "fasting" (or synonyms) into the "For these words:" box. The following is a sample result:

- **Prevalence of Diabetes, Impaired Fasting Glucose, and Impaired Glucose Tolerance in U.S. Adults: The Third National Health and Nutrition Examination Survey, 1988-1994**

  Source: Diabetes Care. 21(4): 518-524. April 1998.

  Contact: Available from American Diabetes Association. 1701 North Beauregard Street, Alexandria, VA 22311. (800) 232-3472. Website: www.diabetes.org.

  Summary: This review article evaluates the prevalence and time trends for diagnosed and undiagnosed diabetes, impaired fasting glucose, and impaired glucose tolerance in US adults by age, sex, and race or ethnic group. The evaluations are based on data from the Third National Health and Nutrition Examination Survey (NHANES III) and prior Health and Nutrition Examination Surveys (HANESs). For US adults at least 20 years of age, the prevalence of diagnosed diabetes between 1988 and 1994 was estimated to be 5.1 percent. Using American Diabetes Association criteria, the prevalence of undiagnosed diabetes was 2.7 percent, and the prevalence of impaired fasting glucose was 6.9 percent. While the rates of diabetes for women and men were similar, the rates for non Hispanic blacks and Mexican-Americans were 1.6 and 1.9 times the rate for non-Hispanic whites. According to American Diabetes Association criteria, prevalence of diabetes (diagnosed plus undiagnosed) in the total population of people aged 40 to 74 years increased from 8.9 percent (1976 to 1980) to 12.3 percent (1988 to 1994). The authors conclude that the high rates of abnormal fasting and postchallenge glucose found in NHANES III, together with the increasing frequency of obesity and sedentary lifestyles in the population, make it likely that diabetes will continue to be a major health problem in the United States. 3 figures. 4 tables. 27 references. (AA-M).

The NLM Gateway[14]

The NLM (National Library of Medicine) Gateway is a Web-based system that lets users search simultaneously in multiple retrieval systems at the U.S. National Library of Medicine (NLM). It allows users of NLM services to initiate searches from one Web interface,

[14] Adapted from NLM: **http://gateway.nlm.nih.gov/gw/Cmd?Overview.x**.

providing one-stop searching for many of NLM's information resources or databases.[15] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "fasting" (or synonyms) into the search box and click "Search." The results will be presented in a tabular form, indicating the number of references in each database category.

Results Summary

Category	Items Found
Journal Articles	44680
Books / Periodicals / Audio Visual	265
Consumer Health	938
Meeting Abstracts	260
Other Collections	2
Total	46145

HSTAT[16]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[17] These documents include clinical practice guidelines, quick-reference guides for clinicians, consumer health brochures, evidence reports and technology assessments from the Agency for Healthcare Research and Quality (AHRQ), as well as AHRQ's Put Prevention Into Practice.[18] Simply search by "fasting" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

Coffee Break: Tutorials for Biologists[19]

Coffee Break is a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. Here you will find a collection of short reports on recent biological discoveries. Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[20] Each report is about 400 words and is usually based on a discovery reported in one or more articles from recently published, peer-reviewed literature.[21] This site has new articles

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[15] The NLM Gateway is currently being developed by the Lister Hill National Center for Biomedical Communications (LHNCBC) at the National Library of Medicine (NLM) of the National Institutes of Health (NIH).

[16] Adapted from HSTAT: **http://www.nlm.nih.gov/pubs/factsheets/hstat.html**.

[17] The HSTAT URL is **http://hstat.nlm.nih.gov/**.

[18] Other important documents in HSTAT include: the National Institutes of Health (NIH) Consensus Conference Reports and Technology Assessment Reports; the HIV/AIDS Treatment Information Service (ATIS) resource documents; the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT) Treatment Improvement Protocols (TIP) and Center for Substance Abuse Prevention (SAMHSA/CSAP) Prevention Enhancement Protocols System (PEPS); the Public Health Service (PHS) Preventive Services Task Force's *Guide to Clinical Preventive Services*; the independent, nonfederal Task Force on Community Services' *Guide to Community Preventive Services*; and the Health Technology Advisory Committee (HTAC) of the Minnesota Health Care Commission (MHCC) health technology evaluations.

[19] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

[20] The figure that accompanies each article is frequently supplied by an expert external to NCBI, in which case the source of the figure is cited. The result is an interactive tutorial that tells a biological story.

[21] After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each

every few weeks, so it can be considered an online magazine of sorts. It is intended for general background information. You can access the Coffee Break Web site at the following hyperlink: **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.

The Genome Project and Fasting

In the following section, we will discuss databases and references which relate to the Genome Project and fasting.

Online Mendelian Inheritance in Man (OMIM)

The Online Mendelian Inheritance in Man (OMIM) database is a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere. OMIM was developed for the World Wide Web by the National Center for Biotechnology Information (NCBI).[22] The database contains textual information, pictures, and reference information. It also contains copious links to NCBI's Entrez database of MEDLINE articles and sequence information.

To search the database, go to **http://www.ncbi.nlm.nih.gov/Omim/searchomim.html**. Type "fasting" (or synonyms) into the search box, and click "Submit Search." If too many results appear, you can narrow the search by adding the word "clinical." Each report will have additional links to related research and databases. In particular, the option "Database Links" will search across technical databases that offer an abundance of information. The following is an example of the results you can obtain from the OMIM for fasting:

- **Fasting Glucose and Specific Insulin Levels**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?606035

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vignette is accompanied by a figure and hypertext links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

[22] Adapted from **http://www.ncbi.nlm.nih.gov/**. Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information--all for the better understanding of molecular processes affecting human health and disease.

Genes and Disease (NCBI - Map)

The Genes and Disease database is produced by the National Center for Biotechnology Information of the National Library of Medicine at the National Institutes of Health. This Web site categorizes each disorder by system of the body. Go to **http://www.ncbi.nlm.nih.gov/disease/**, and browse the system pages to have a full view of important conditions linked to human genes. Since this site is regularly updated, you may wish to revisit it from time to time. The following systems and associated disorders are addressed:

- **Cancer:** Uncontrolled cell division.
  Examples: Breast and ovarian cancer, Burkitt lymphoma, chronic myeloid leukemia, colon cancer, lung cancer, malignant melanoma, multiple endocrine neoplasia, neurofibromatosis, p53 tumor suppressor, pancreatic cancer, prostate cancer, Ras oncogene, RB: retinoblastoma, von Hippel-Lindau syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Cancer.html**
- **Immune System:** Fights invaders.
  Examples: Asthma, autoimmune polyglandular syndrome, Crohn's disease, DiGeorge syndrome, familial Mediterranean fever, immunodeficiency with Hyper-IgM, severe combined immunodeficiency.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Immune.html**
- **Metabolism:** Food and energy.
  Examples: Adreno-leukodystrophy, atherosclerosis, Best disease, Gaucher disease, glucose galactose malabsorption, gyrate atrophy, juvenile-onset diabetes, obesity, paroxysmal nocturnal hemoglobinuria, phenylketonuria, Refsum disease, Tangier disease, Tay-Sachs disease.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Metabolism.html**
- **Muscle and Bone:** Movement and growth.
  Examples: Duchenne muscular dystrophy, Ellis-van Creveld syndrome, Marfan syndrome, myotonic dystrophy, spinal muscular atrophy.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Muscle.html**
- **Nervous System:** Mind and body.
  Examples: Alzheimer disease, amyotrophic lateral sclerosis, Angelman syndrome, Charcot-Marie-Tooth disease, epilepsy, essential tremor, fragile X syndrome, Friedreich's ataxia, Huntington disease, Niemann-Pick disease, Parkinson disease, Prader-Willi syndrome, Rett syndrome, spinocerebellar atrophy, Williams syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Brain.html**
- **Signals:** Cellular messages.
  Examples: Ataxia telangiectasia, Cockayne syndrome, glaucoma, male-patterned baldness, SRY: sex determination, tuberous sclerosis, Waardenburg syndrome, Werner syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Signals.html**
- **Transporters:** Pumps and channels.
  Examples: Cystic fibrosis, deafness, diastrophic dysplasia, Hemophilia A, long-QT syndrome, Menkes syndrome, Pendred syndrome, polycystic kidney disease, sickle cell anemia, Wilson's disease, Zellweger syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Transporters.html**

Entrez

Entrez is a search and retrieval system that integrates several linked databases at the National Center for Biotechnology Information (NCBI). These databases include nucleotide sequences, protein sequences, macromolecular structures, whole genomes, and MEDLINE through PubMed. Entrez provides access to the following databases:

- **3D Domains:** Domains from Entrez Structure,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Books:** Online books,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books**
- **Genome:** Complete genome assemblies,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome**
- **NCBI's Protein Sequence Information Survey Results:**
  Web site: **http://www.ncbi.nlm.nih.gov/About/proteinsurvey/**
- **Nucleotide Sequence Database (Genbank):**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide**
- **OMIM:** Online Mendelian Inheritance in Man,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM**
- **PopSet:** Population study data sets,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Popset**
- **ProbeSet:** Gene Expression Omnibus (GEO),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Protein Sequence Database:**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein**
- **PubMed:** Biomedical literature (PubMed),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed**
- **Structure:** Three-dimensional macromolecular structures,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Structure**
- **Taxonomy:** Organisms in GenBank,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Taxonomy**

To access the Entrez system at the National Center for Biotechnology Information, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=genome**, and then select the database that you would like to search. The databases available are listed in the drop box next to "Search." Enter "fasting" (or synonyms) into the search box and click "Go."

Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database[23]

This online resource has been developed to facilitate the identification and differentiation of syndromic entities. Special attention is given to the type of information that is usually

[23] Adapted from the National Library of Medicine:
http://www.nlm.nih.gov/mesh/jablonski/about_syndrome.html.

limited or completely omitted in existing reference sources due to space limitations of the printed form.

At **http://www.nlm.nih.gov/mesh/jablonski/syndrome_toc/toc_a.html**, you can search across syndromes using an alphabetical index**.** Search by keywords at **http://www.nlm.nih.gov/mesh/jablonski/syndrome_db.html**.

The Genome Database[24]

Established at Johns Hopkins University in Baltimore, Maryland in 1990, the Genome Database (GDB) is the official central repository for genomic mapping data resulting from the Human Genome Initiative. In the spring of 1999, the Bioinformatics Supercomputing Centre (BiSC) at the Hospital for Sick Children in Toronto, Ontario assumed the management of GDB. The Human Genome Initiative is a worldwide research effort focusing on structural analysis of human DNA to determine the location and sequence of the estimated 100,000 human genes. In support of this project, GDB stores and curates data generated by researchers worldwide who are engaged in the mapping effort of the Human Genome Project (HGP). GDB's mission is to provide scientists with an encyclopedia of the human genome which is continually revised and updated to reflect the current state of scientific knowledge. Although GDB has historically focused on gene mapping, its focus will broaden as the Genome Project moves from mapping to sequence, and finally, to functional analysis.

To access the GDB, simply go to the following hyperlink: **http://www.gdb.org/**. Search "All Biological Data" by "Keyword." Type "fasting" (or synonyms) into the search box, and review the results. If more than one word is used in the search box, then separate each one with the word "and" or "or" (using "or" might be useful when using synonyms).

[24] Adapted from the Genome Database: **http://gdbwww.gdb.org/gdb/aboutGDB.html - mission**.

APPENDIX B. PATIENT RESOURCES

Overview

Official agencies, as well as federally funded institutions supported by national grants, frequently publish a variety of guidelines written with the patient in mind. These are typically called "Fact Sheets" or "Guidelines." They can take the form of a brochure, information kit, pamphlet, or flyer. Often they are only a few pages in length. Since new guidelines on fasting can appear at any moment and be published by a number of sources, the best approach to finding guidelines is to systematically scan the Internet-based services that post them.

Patient Guideline Sources

The remainder of this chapter directs you to sources which either publish or can help you find additional guidelines on topics related to fasting. Due to space limitations, these sources are listed in a concise manner. Do not hesitate to consult the following sources by either using the Internet hyperlink provided, or, in cases where the contact information is provided, contacting the publisher or author directly.

The National Institutes of Health

The NIH gateway to patients is located at **http://health.nih.gov/**. From this site, you can search across various sources and institutes, a number of which are summarized below.

Topic Pages: MEDLINEplus

The National Library of Medicine has created a vast and patient-oriented healthcare information portal called MEDLINEplus. Within this Internet-based system are "health topic pages" which list links to available materials relevant to fasting. To access this system, log on to **http://www.nlm.nih.gov/medlineplus/healthtopics.html**. From there you can either search using the alphabetical index or browse by broad topic areas. Recently, MEDLINEplus listed the following when searched for "fasting":

- Other guides

  Diabetes
  http://www.nlm.nih.gov/medlineplus/diabetes.html

  Heart Diseases
  http://www.nlm.nih.gov/medlineplus/heartdiseases.html

  Juvenile Diabetes
  http://www.nlm.nih.gov/medlineplus/juvenilediabetes.html

  Metabolic Syndrome X
  http://www.nlm.nih.gov/medlineplus/metabolicsyndromex.html

  Ovarian Cysts
  http://www.nlm.nih.gov/medlineplus/ovariancysts.html

You may also choose to use the search utility provided by MEDLINEplus at the following Web address: **http://www.nlm.nih.gov/medlineplus/**. Simply type a keyword into the search box and click "Search." This utility is similar to the NIH search utility, with the exception that it only includes materials that are linked within the MEDLINEplus system (mostly patient-oriented information). It also has the disadvantage of generating unstructured results. We recommend, therefore, that you use this method only if you have a very targeted search.

The Combined Health Information Database (CHID)

CHID Online is a reference tool that maintains a database directory of thousands of journal articles and patient education guidelines on fasting. CHID offers summaries that describe the guidelines available, including contact information and pricing. CHID's general Web site is **http://chid.nih.gov/**. To search this database, go to **http://chid.nih.gov/detail/detail.html**. In particular, you can use the advanced search options to look up pamphlets, reports, brochures, and information kits. The following was recently posted in this archive:

- **Reactive and Fasting Hypoglycemia**

  Source: Minneapolis, MN: International Diabetes Center. 1998. 4 p.

  Contact: Available from International Diabetes Center. Park Nicollet HealthSource. 3800 Park Nicollet Boulevard, Minneapolis, MN 55416. (800) 372-7776 or (612) 993-3534. Fax (612) 993-1840. PRICE: $1.00 for one copy; $0.90 each for 10 copies; $0.80 each for 100 copies; $0.70 for 500 copies; plus shipping and handling. ISBN: 1885115474.

  Summary: This pamphlet uses a question and answer format to provide information on reactive and fasting hypoglycemia. It defines hypoglycemia, lists the causes and symptoms of hypoglycemia, presents the features of fasting and reactive hypoglycemia, and explains how the symptoms of hypoglycemia can be avoided and how hypoglycemia is treated. Eating habits that may help avoid the symptoms of hypoglycemia include eating 5 to 6 small meals or snacks each day, spreading one's intake of carbohydrate foods throughout the day, avoiding foods that contain large amounts of carbohydrate, avoiding beverages and foods containing caffeine, and limiting or avoiding alcoholic beverages. The pamphlet highlights good food choices and foods to use less often in the categories of starches, fruit, milk, vegetables, meat and meat substitutes, fats and oils, beverages, and other. It also presents a sample menu that provides approximately 1,550 calories among three meals and two snacks.

The National Guideline Clearinghouse™

The National Guideline Clearinghouse™ offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search this site located at **http://www.guideline.gov/** by using the keyword "fasting" (or synonyms). The following was recently posted:

- **Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration**

  Source: American Society of Anesthesiologists - Medical Specialty Society; 1999; 10 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=1854&nbr=1080&string=fasting

Healthfinder™

Healthfinder™ is sponsored by the U.S. Department of Health and Human Services and offers links to hundreds of other sites that contain healthcare information. This Web site is located at **http://www.healthfinder.gov**. Again, keyword searches can be used to find guidelines. The following was recently found in this database:

- **Diabetes Diagnosis**

  Summary: This online fact sheet discusses the renaming of the two most common types of diabetes and the new lower fasting plasma glucose number used to diagnose diabetes.

  Source: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=4658

The NIH Search Utility

The NIH search utility allows you to search for documents on over 100 selected Web sites that comprise the NIH-WEB-SPACE. Each of these servers is "crawled" and indexed on an ongoing basis. Your search will produce a list of various documents, all of which will relate in some way to fasting. The drawbacks of this approach are that the information is not organized by theme and that the references are often a mix of information for professionals and patients. Nevertheless, a large number of the listed Web sites provide useful background information. We can only recommend this route, therefore, for relatively rare or specific disorders, or when using highly targeted searches. To use the NIH search utility, visit the following Web page: **http://search.nih.gov/index.html**.

Additional Web Sources

A number of Web sites are available to the public that often link to government sites. These can also point you in the direction of essential information. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=168&layer=&from=subcats**

- Family Village: **http://www.familyvillage.wisc.edu/specific.htm**
- Google: **http://directory.google.com/Top/Health/Conditions_and_Diseases/**
- Med Help International: **http://www.medhelp.org/HealthTopics/A.html**
- Open Directory Project: **http://dmoz.org/Health/Conditions_and_Diseases/**
- Yahoo.com: **http://dir.yahoo.com/Health/Diseases_and_Conditions/**
- WebMD®Health: **http://my.webmd.com/health_topics**

Finding Associations

There are several Internet directories that provide lists of medical associations with information on or resources relating to fasting. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with fasting.

The National Health Information Center (NHIC)

The National Health Information Center (NHIC) offers a free referral service to help people find organizations that provide information about fasting. For more information, see the NHIC's Web site at **http://www.health.gov/NHIC/** or contact an information specialist by calling 1-800-336-4797.

Directory of Health Organizations

The Directory of Health Organizations, provided by the National Library of Medicine Specialized Information Services, is a comprehensive source of information on associations. The Directory of Health Organizations database can be accessed via the Internet at **http://www.sis.nlm.nih.gov/Dir/DirMain.html**. It is composed of two parts: DIRLINE and Health Hotlines.

The DIRLINE database comprises some 10,000 records of organizations, research centers, and government institutes and associations that primarily focus on health and biomedicine. To access DIRLINE directly, go to the following Web site: **http://dirline.nlm.nih.gov/**. Simply type in "fasting" (or a synonym), and you will receive information on all relevant organizations listed in the database.

Health Hotlines directs you to toll-free numbers to over 300 organizations. You can access this database directly at **http://www.sis.nlm.nih.gov/hotlines/**. On this page, you are given the option to search by keyword or by browsing the subject list. When you have received your search results, click on the name of the organization for its description and contact information.

The Combined Health Information Database

Another comprehensive source of information on healthcare associations is the Combined Health Information Database. Using the "Detailed Search" option, you will need to limit

your search to "Organizations" and "fasting". Type the following hyperlink into your Web browser: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Then, select your preferred language and the format option "Organization Resource Sheet." Type "fasting" (or synonyms) into the "For these words:" box. You should check back periodically with this database since it is updated every three months.

The National Organization for Rare Disorders, Inc.

The National Organization for Rare Disorders, Inc. has prepared a Web site that provides, at no charge, lists of associations organized by health topic. You can access this database at the following Web site: **http://www.rarediseases.org/search/orgsearch.html**. Type "fasting" (or a synonym) into the search box, and click "Submit Query."

APPENDIX C. FINDING MEDICAL LIBRARIES

Overview

In this Appendix, we show you how to quickly find a medical library in your area.

Preparation

Your local public library and medical libraries have interlibrary loan programs with the National Library of Medicine (NLM), one of the largest medical collections in the world. According to the NLM, most of the literature in the general and historical collections of the National Library of Medicine is available on interlibrary loan to any library. If you would like to access NLM medical literature, then visit a library in your area that can request the publications for you.[25]

Finding a Local Medical Library

The quickest method to locate medical libraries is to use the Internet-based directory published by the National Network of Libraries of Medicine (NN/LM). This network includes 4626 members and affiliates that provide many services to librarians, health professionals, and the public. To find a library in your area, simply visit **http://nnlm.gov/members/adv.html** or call 1-800-338-7657.

Medical Libraries in the U.S. and Canada

In addition to the NN/LM, the National Library of Medicine (NLM) lists a number of libraries with reference facilities that are open to the public. The following is the NLM's list and includes hyperlinks to each library's Web site. These Web pages can provide information on hours of operation and other restrictions. The list below is a small sample of

[25] Adapted from the NLM: **http://www.nlm.nih.gov/psd/cas/interlibrary.html**.

libraries recommended by the National Library of Medicine (sorted alphabetically by name of the U.S. state or Canadian province where the library is located)[26]:

- **Alabama:** Health InfoNet of Jefferson County (Jefferson County Library Cooperative, Lister Hill Library of the Health Sciences), **http://www.uab.edu/infonet/**
- **Alabama:** Richard M. Scrushy Library (American Sports Medicine Institute)
- **Arizona:** Samaritan Regional Medical Center: The Learning Center (Samaritan Health System, Phoenix, Arizona), **http://www.samaritan.edu/library/bannerlibs.htm**
- **California:** Kris Kelly Health Information Center (St. Joseph Health System, Humboldt), **http://www.humboldt1.com/~kkhic/index.html**
- **California:** Community Health Library of Los Gatos, **http://www.healthlib.org/orgresources.html**
- **California:** Consumer Health Program and Services (CHIPS) (County of Los Angeles Public Library, Los Angeles County Harbor-UCLA Medical Center Library) - Carson, CA, **http://www.colapublib.org/services/chips.html**
- **California:** Gateway Health Library (Sutter Gould Medical Foundation)
- **California:** Health Library (Stanford University Medical Center), **http://www-med.stanford.edu/healthlibrary/**
- **California:** Patient Education Resource Center - Health Information and Resources (University of California, San Francisco), **http://sfghdean.ucsf.edu/barnett/PERC/default.asp**
- **California:** Redwood Health Library (Petaluma Health Care District), **http://www.phcd.org/rdwdlib.html**
- **California:** Los Gatos PlaneTree Health Library, **http://planetreesanjose.org/**
- **California:** Sutter Resource Library (Sutter Hospitals Foundation, Sacramento), **http://suttermedicalcenter.org/library/**
- **California:** Health Sciences Libraries (University of California, Davis), **http://www.lib.ucdavis.edu/healthsci/**
- **California:** ValleyCare Health Library & Ryan Comer Cancer Resource Center (ValleyCare Health System, Pleasanton), **http://gaelnet.stmarys-ca.edu/other.libs/gbal/east/vchl.html**
- **California:** Washington Community Health Resource Library (Fremont), **http://www.healthlibrary.org/**
- **Colorado:** William V. Gervasini Memorial Library (Exempla Healthcare), **http://www.saintjosephdenver.org/yourhealth/libraries/**
- **Connecticut:** Hartford Hospital Health Science Libraries (Hartford Hospital), **http://www.harthosp.org/library/**
- **Connecticut:** Healthnet: Connecticut Consumer Health Information Center (University of Connecticut Health Center, Lyman Maynard Stowe Library), **http://library.uchc.edu/departm/hnet/**

[26] Abstracted from **http://www.nlm.nih.gov/medlineplus/libraries.html**.

- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital, Waterbury), **http://www.waterburyhospital.com/library/consumer.shtml**
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute, Wilmington), **http://www.christianacare.org/health_guide/health_guide_pmri_health_info.cfm**
- **Delaware:** Lewis B. Flinn Library (Delaware Academy of Medicine, Wilmington), **http://www.delamed.org/chls.html**
- **Georgia:** Family Resource Library (Medical College of Georgia, Augusta), **http://cmc.mcg.edu/kids_families/fam_resources/fam_res_lib/frl.htm**
- **Georgia:** Health Resource Center (Medical Center of Central Georgia, Macon), **http://www.mccg.org/hrc/hrchome.asp**
- **Hawaii:** Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library, Honolulu), **http://hml.org/CHIS/**
- **Idaho:** DeArmond Consumer Health Library (Kootenai Medical Center, Coeur d'Alene), **http://www.nicon.org/DeArmond/index.htm**
- **Illinois:** Health Learning Center of Northwestern Memorial Hospital (Chicago), **http://www.nmh.org/health_info/hlc.html**
- **Illinois:** Medical Library (OSF Saint Francis Medical Center, Peoria), **http://www.osfsaintfrancis.org/general/library/**
- **Kentucky:** Medical Library - Services for Patients, Families, Students & the Public (Central Baptist Hospital, Lexington), **http://www.centralbap.com/education/community/library.cfm**
- **Kentucky:** University of Kentucky - Health Information Library (Chandler Medical Center, Lexington), **http://www.mc.uky.edu/PatientEd/**
- **Louisiana:** Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation, New Orleans), **http://www.ochsner.org/library/**
- **Louisiana:** Louisiana State University Health Sciences Center Medical Library-Shreveport, **http://lib-sh.lsuhsc.edu/**
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital, Farmington), **http://www.fchn.org/fmh/lib.htm**
- **Maine:** Gerrish-True Health Sciences Library (Central Maine Medical Center, Lewiston), **http://www.cmmc.org/library/library.html**
- **Maine:** Hadley Parrot Health Science Library (Eastern Maine Healthcare, Bangor), **http://www.emh.org/hll/hpl/guide.htm**
- **Maine:** Maine Medical Center Library (Maine Medical Center, Portland), **http://www.mmc.org/library/**
- **Maine:** Parkview Hospital (Brunswick), **http://www.parkviewhospital.org/**
- **Maine:** Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center, Biddeford), **http://www.smmc.org/services/service.php3?choice=10**
- **Maine:** Stephens Memorial Hospital's Health Information Library (Western Maine Health, Norway), **http://www.wmhcc.org/Library/**

- **Manitoba, Canada:** Consumer & Patient Health Information Service (University of Manitoba Libraries), **http://www.umanitoba.ca/libraries/units/health/reference/chis.html**
- **Manitoba, Canada:** J.W. Crane Memorial Library (Deer Lodge Centre, Winnipeg), **http://www.deerlodge.mb.ca/crane_library/about.asp**
- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Dept. of Public Libraries, Wheaton Regional Library), **http://www.mont.lib.md.us/healthinfo/hic.asp**
- **Massachusetts:** Baystate Medical Center Library (Baystate Health System), **http://www.baystatehealth.com/1024/**
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), **http://med-libwww.bu.edu/library/lib.html**
- **Massachusetts:** Lowell General Hospital Health Sciences Library (Lowell General Hospital, Lowell), **http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm**
- **Massachusetts:** Paul E. Woodard Health Sciences Library (New England Baptist Hospital, Boston), **http://www.nebh.org/health_lib.asp**
- **Massachusetts:** St. Luke's Hospital Health Sciences Library (St. Luke's Hospital, Southcoast Health System, New Bedford), **http://www.southcoast.org/library/**
- **Massachusetts:** Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), **http://www.mgh.harvard.edu/library/chrcindex.html**
- **Massachusetts:** UMass HealthNet (University of Massachusetts Medical School, Worchester), **http://healthnet.umassmed.edu/**
- **Michigan:** Botsford General Hospital Library - Consumer Health (Botsford General Hospital, Library & Internet Services), **http://www.botsfordlibrary.org/consumer.htm**
- **Michigan:** Helen DeRoy Medical Library (Providence Hospital and Medical Centers), **http://www.providence-hospital.org/library/**
- **Michigan:** Marquette General Hospital - Consumer Health Library (Marquette General Hospital, Health Information Center), **http://www.mgh.org/center.html**
- **Michigan:** Patient Education Resouce Center - University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center, Ann Arbor), **http://www.cancer.med.umich.edu/learn/leares.htm**
- **Michigan:** Sladen Library & Center for Health Information Resources - Consumer Health Information (Detroit), **http://www.henryford.com/body.cfm?id=39330**
- **Montana:** Center for Health Information (St. Patrick Hospital and Health Sciences Center, Missoula)
- **National:** Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), **http://caphis.mlanet.org/directory/index.html**
- **National:** National Network of Libraries of Medicine (National Library of Medicine) - provides library services for health professionals in the United States who do not have access to a medical library, **http://nnlm.gov/**
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), **http://nnlm.gov/members/**

- **Nevada:** Health Science Library, West Charleston Library (Las Vegas-Clark County Library District, Las Vegas), **http://www.lvccld.org/special_collections/medical/index.htm**
- **New Hampshire:** Dartmouth Biomedical Libraries (Dartmouth College Library, Hanover), **http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/**
- **New Jersey:** Consumer Health Library (Rahway Hospital, Rahway), **http://www.rahwayhospital.com/library.htm**
- **New Jersey:** Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center, Englewood), **http://www.englewoodhospital.com/links/index.htm**
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center, Englewood), **http://www.geocities.com/ResearchTriangle/9360/**
- **New York:** Choices in Health Information (New York Public Library) - NLM Consumer Pilot Project participant, **http://www.nypl.org/branch/health/links.html**
- **New York:** Health Information Center (Upstate Medical University, State University of New York, Syracuse), **http://www.upstate.edu/library/hic/**
- **New York:** Health Sciences Library (Long Island Jewish Medical Center, New Hyde Park), **http://www.lij.edu/library/library.html**
- **New York:** ViaHealth Medical Library (Rochester General Hospital), **http://www.nyam.org/library/**
- **Ohio:** Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), **http://www.akrongeneral.org/hwlibrary.htm**
- **Oklahoma:** The Health Information Center at Saint Francis Hospital (Saint Francis Health System, Tulsa), **http://www.sfh-tulsa.com/services/healthinfo.asp**
- **Oregon:** Planetree Health Resource Center (Mid-Columbia Medical Center, The Dalles), **http://www.mcmc.net/phrc/**
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center, Hershey), **http://www.hmc.psu.edu/commhealth/**
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center, Danville), **http://www.geisinger.edu/education/commlib.shtml**
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital, Scranton), **http://www.mth.org/healthwellness.html**
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System, Pittsburgh), **http://www.hsls.pitt.edu/guides/chi/hopwood/index_html**
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), **http://www.collphyphil.org/kooppg1.shtml**
- **Pennsylvania:** Learning Resources Center - Medical Library (Susquehanna Health System, Williamsport), **http://www.shscares.org/services/lrc/index.asp**
- **Pennsylvania:** Medical Library (UPMC Health System, Pittsburgh), **http://www.upmc.edu/passavant/library.htm**
- **Quebec, Canada:** Medical Library (Montreal General Hospital), **http://www.mghlib.mcgill.ca/**

- **South Dakota:** Rapid City Regional Hospital Medical Library (Rapid City Regional Hospital), **http://www.rcrh.org/Services/Library/Default.asp**
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), **http://hhw.library.tmc.edu/**
- **Washington:** Community Health Library (Kittitas Valley Community Hospital), **http://www.kvch.com/**
- **Washington:** Southwest Washington Medical Center Library (Southwest Washington Medical Center, Vancouver), **http://www.swmedicalcenter.com/body.cfm?id=72**

ONLINE GLOSSARIES

The Internet provides access to a number of free-to-use medical dictionaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): **http://www.medterms.com/Script/Main/hp.asp**
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): **http://www.intelihealth.com/IH/**
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: **http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html**
- On-line Medical Dictionary (CancerWEB): **http://cancerweb.ncl.ac.uk/omd/**
- Rare Diseases Terms (Office of Rare Diseases): **http://ord.aspensys.com/asp/diseases/diseases.asp**
- Technology Glossary (National Library of Medicine) - Health Care Technology: **http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm**

Beyond these, MEDLINEplus contains a very patient-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia can be accessed at **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**. ADAM is also available on commercial Web sites such as drkoop.com (**http://www.drkoop.com/**) and Web MD (**http://my.webmd.com/adam/asset/adam_disease_articles/a_to_z/a**).

Online Dictionary Directories

The following are additional online directories compiled by the National Library of Medicine, including a number of specialized medical dictionaries:

- Medical Dictionaries: Medical & Biological (World Health Organization): **http://www.who.int/hlt/virtuallibrary/English/diction.htm#Medical**
- MEL-Michigan Electronic Library List of Online Health and Medical Dictionaries (Michigan Electronic Library): **http://mel.lib.mi.us/health/health-dictionaries.html**
- Patient Education: Glossaries (DMOZ Open Directory Project): **http://dmoz.org/Health/Education/Patient_Education/Glossaries/**
- Web of Online Dictionaries (Bucknell University): **http://www.yourdictionary.com/diction5.html#medicine**

FASTING DICTIONARY

The definitions below are derived from official public sources, including the National Institutes of Health [NIH] and the European Union [EU].

Abdomen: That portion of the body that lies between the thorax and the pelvis. [NIH]

Abdominal: Having to do with the abdomen, which is the part of the body between the chest and the hips that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Abdominal fat: Fat (adipose tissue) that is centrally distributed between the thorax and pelvis and that induces greater health risk. [NIH]

Abdominal Pain: Sensation of discomfort, distress, or agony in the abdominal region. [NIH]

Ablation: The removal of an organ by surgery. [NIH]

Acanthosis Nigricans: A circumscribed melanosis consisting of a brown-pigmented, velvety verrucosity or fine papillomatosis appearing in the axillae and other body folds. It occurs in association with endocrine disorders, underlying malignancy, administration of certain drugs, or as in inherited disorder. [NIH]

Acceptor: A substance which, while normally not oxidized by oxygen or reduced by hydrogen, can be oxidized or reduced in presence of a substance which is itself undergoing oxidation or reduction. [NIH]

Acetone: A colorless liquid used as a solvent and an antiseptic. It is one of the ketone bodies produced during ketoacidosis. [NIH]

Acetylcholine: A neurotransmitter. Acetylcholine in vertebrates is the major transmitter at neuromuscular junctions, autonomic ganglia, parasympathetic effector junctions, a subset of sympathetic effector junctions, and at many sites in the central nervous system. It is generally not used as an administered drug because it is broken down very rapidly by cholinesterases, but it is useful in some ophthalmological applications. [NIH]

Acidosis: A pathologic condition resulting from accumulation of acid or depletion of the alkaline reserve (bicarbonate content) in the blood and body tissues, and characterized by an increase in hydrogen ion concentration. [EU]

Actin: Essential component of the cell skeleton. [NIH]

Acute Disease: Disease having a short and relatively severe course. [NIH]

Acute renal: A condition in which the kidneys suddenly stop working. In most cases, kidneys can recover from almost complete loss of function. [NIH]

Acyl: Chemical signal used by bacteria to communicate. [NIH]

Adaptation: 1. The adjustment of an organism to its environment, or the process by which it enhances such fitness. 2. The normal ability of the eye to adjust itself to variations in the intensity of light; the adjustment to such variations. 3. The decline in the frequency of firing of a neuron, particularly of a receptor, under conditions of constant stimulation. 4. In dentistry, (a) the proper fitting of a denture, (b) the degree of proximity and interlocking of restorative material to a tooth preparation, (c) the exact adjustment of bands to teeth. 5. In microbiology, the adjustment of bacterial physiology to a new environment. [EU]

Adenosine: A nucleoside that is composed of adenine and d-ribose. Adenosine or adenosine derivatives play many important biological roles in addition to being components of DNA and RNA. Adenosine itself is a neurotransmitter. [NIH]

Adipocytes: Fat-storing cells found mostly in the abdominal cavity and subcutaneous tissue. Fat is usually stored in the form of tryglycerides. [NIH]

Adipose Tissue: Connective tissue composed of fat cells lodged in the meshes of areolar tissue. [NIH]

Adjustment: The dynamic process wherein the thoughts, feelings, behavior, and biophysiological mechanisms of the individual continually change to adjust to the environment. [NIH]

Adjuvant: A substance which aids another, such as an auxiliary remedy; in immunology, nonspecific stimulator (e.g., BCG vaccine) of the immune response. [EU]

Adolescence: The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

Adrenal Cortex: The outer layer of the adrenal gland. It secretes mineralocorticoids, androgens, and glucocorticoids. [NIH]

Adrenal Medulla: The inner part of the adrenal gland; it synthesizes, stores and releases catecholamines. [NIH]

Adrenergic: Activated by, characteristic of, or secreting epinephrine or substances with similar activity; the term is applied to those nerve fibres that liberate norepinephrine at a synapse when a nerve impulse passes, i.e., the sympathetic fibres. [EU]

Adrenergic Antagonists: Drugs that bind to but do not activate adrenergic receptors. Adrenergic antagonists block the actions of the endogenous adrenergic transmitters epinephrine and norepinephrine. [NIH]

Adverse Effect: An unwanted side effect of treatment. [NIH]

Aerobic: In biochemistry, reactions that need oxygen to happen or happen when oxygen is present. [NIH]

Aerobic Exercise: A type of physical activity that includes walking, jogging, running, and dancing. Aerobic training improves the efficiency of the aerobic energy-producing systems that can improve cardiorespiratory endurance. [NIH]

Afferent: Concerned with the transmission of neural impulse toward the central part of the nervous system. [NIH]

Affinity: 1. Inherent likeness or relationship. 2. A special attraction for a specific element, organ, or structure. 3. Chemical affinity; the force that binds atoms in molecules; the tendency of substances to combine by chemical reaction. 4. The strength of noncovalent chemical binding between two substances as measured by the dissociation constant of the complex. 5. In immunology, a thermodynamic expression of the strength of interaction between a single antigen-binding site and a single antigenic determinant (and thus of the stereochemical compatibility between them), most accurately applied to interactions among simple, uniform antigenic determinants such as haptens. Expressed as the association constant (K litres mole -1), which, owing to the heterogeneity of affinities in a population of antibody molecules of a given specificity, actually represents an average value (mean intrinsic association constant). 6. The reciprocal of the dissociation constant. [EU]

Agar: A complex sulfated polymer of galactose units, extracted from Gelidium cartilagineum, Gracilaria confervoides, and related red algae. It is used as a gel in the preparation of solid culture media for microorganisms, as a bulk laxative, in making emulsions, and as a supporting medium for immunodiffusion and immunoelectrophoresis. [NIH]

Age of Onset: The age or period of life at which a disease or the initial symptoms or

manifestations of a disease appear in an individual. [NIH]

Agonist: In anatomy, a prime mover. In pharmacology, a drug that has affinity for and stimulates physiologic activity at cell receptors normally stimulated by naturally occurring substances. [EU]

Airway: A device for securing unobstructed passage of air into and out of the lungs during general anesthesia. [NIH]

Alanine: A non-essential amino acid that occurs in high levels in its free state in plasma. It is produced from pyruvate by transamination. It is involved in sugar and acid metabolism, increases immunity, and provides energy for muscle tissue, brain, and the central nervous system. [NIH]

Albumin: 1. Any protein that is soluble in water and moderately concentrated salt solutions and is coagulable by heat. 2. Serum albumin; the major plasma protein (approximately 60 per cent of the total), which is responsible for much of the plasma colloidal osmotic pressure and serves as a transport protein carrying large organic anions, such as fatty acids, bilirubin, and many drugs, and also carrying certain hormones, such as cortisol and thyroxine, when their specific binding globulins are saturated. Albumin is synthesized in the liver. Low serum levels occur in protein malnutrition, active inflammation and serious hepatic and renal disease. [EU]

Alertness: A state of readiness to detect and respond to certain specified small changes occurring at random intervals in the environment. [NIH]

Algorithms: A procedure consisting of a sequence of algebraic formulas and/or logical steps to calculate or determine a given task. [NIH]

Alimentary: Pertaining to food or nutritive material, or to the organs of digestion. [EU]

Alkaline: Having the reactions of an alkali. [EU]

Alkaloid: A member of a large group of chemicals that are made by plants and have nitrogen in them. Some alkaloids have been shown to work against cancer. [NIH]

Alleles: Mutually exclusive forms of the same gene, occupying the same locus on homologous chromosomes, and governing the same biochemical and developmental process. [NIH]

Allergen: An antigenic substance capable of producing immediate-type hypersensitivity (allergy). [EU]

Allylamine: Possesses an unusual and selective cytotoxicity for vascular smooth muscle cells in dogs and rats. Useful for experiments dealing with arterial injury, myocardial fibrosis or cardiac decompensation. [NIH]

Alpha-1: A protein with the property of inactivating proteolytic enzymes such as leucocyte collagenase and elastase. [NIH]

Alpha-fetoprotein: AFP. A protein normally produced by a developing fetus. AFP levels are usually undetectable in the blood of healthy nonpregnant adults. An elevated level of AFP suggests the presence of either a primary liver cancer or germ cell tumor. [NIH]

Alternative medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used instead of standard treatments. Alternative medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Alveoli: Tiny air sacs at the end of the bronchioles in the lungs. [NIH]

Amenorrhea: Absence of menstruation. [NIH]

Amine: An organic compound containing nitrogen; any member of a group of chemical compounds formed from ammonia by replacement of one or more of the hydrogen atoms by organic (hydrocarbon) radicals. The amines are distinguished as primary, secondary, and tertiary, according to whether one, two, or three hydrogen atoms are replaced. The amines include allylamine, amylamine, ethylamine, methylamine, phenylamine, propylamine, and many other compounds. [EU]

Amino Acid Sequence: The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Ammonia: A colorless alkaline gas. It is formed in the body during decomposition of organic materials during a large number of metabolically important reactions. [NIH]

Amniotic Fluid: Amniotic cavity fluid which is produced by the amnion and fetal lungs and kidneys. [NIH]

Amphetamines: Analogs or derivatives of amphetamine. Many are sympathomimetics and central nervous system stimulators causing excitation, vasopression, bronchodilation, and to varying degrees, anorexia, analepsis, nasal decongestion, and some smooth muscle relaxation. [NIH]

Ampulla: A sac-like enlargement of a canal or duct. [NIH]

Amputation: Surgery to remove part or all of a limb or appendage. [NIH]

Amyloid: A general term for a variety of different proteins that accumulate as extracellular fibrils of 7-10 nm and have common structural features, including a beta-pleated sheet conformation and the ability to bind such dyes as Congo red and thioflavine (Kandel, Schwartz, and Jessel, Principles of Neural Science, 3rd ed). [NIH]

Anaerobic: 1. Lacking molecular oxygen. 2. Growing, living, or occurring in the absence of molecular oxygen; pertaining to an anaerobe. [EU]

Anaesthesia: Loss of feeling or sensation. Although the term is used for loss of tactile sensibility, or of any of the other senses, it is applied especially to loss of the sensation of pain, as it is induced to permit performance of surgery or other painful procedures. [EU]

Anal: Having to do with the anus, which is the posterior opening of the large bowel. [NIH]

Analgesic: An agent that alleviates pain without causing loss of consciousness. [EU]

Analog: In chemistry, a substance that is similar, but not identical, to another. [NIH]

Analogous: Resembling or similar in some respects, as in function or appearance, but not in origin or development;. [EU]

Analysis of Variance: A statistical technique that isolates and assesses the contributions of categorical independent variables to variation in the mean of a continuous dependent variable. [NIH]

Anaphylactic: Pertaining to anaphylaxis. [EU]

Anaphylaxis: An acute hypersensitivity reaction due to exposure to a previously encountered antigen. The reaction may include rapidly progressing urticaria, respiratory distress, vascular collapse, systemic shock, and death. [NIH]

Anastomosis: A procedure to connect healthy sections of tubular structures in the body after the diseased portion has been surgically removed. [NIH]

Anatomical: Pertaining to anatomy, or to the structure of the organism. [EU]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

Anesthesia: A state characterized by loss of feeling or sensation. This depression of nerve function is usually the result of pharmacologic action and is induced to allow performance of surgery or other painful procedures. [NIH]

Anesthetics: Agents that are capable of inducing a total or partial loss of sensation, especially tactile sensation and pain. They may act to induce general anesthesia, in which an unconscious state is achieved, or may act locally to induce numbness or lack of sensation at a targeted site. [NIH]

Angina: Chest pain that originates in the heart. [NIH]

Angiography: Radiography of blood vessels after injection of a contrast medium. [NIH]

Animal model: An animal with a disease either the same as or like a disease in humans. Animal models are used to study the development and progression of diseases and to test new treatments before they are given to humans. Animals with transplanted human cancers or other tissues are called xenograft models. [NIH]

Anions: Negatively charged atoms, radicals or groups of atoms which travel to the anode or positive pole during electrolysis. [NIH]

Ankle: That part of the lower limb directly above the foot. [NIH]

Anorexia: Lack or loss of appetite for food. Appetite is psychologic, dependent on memory and associations. Anorexia can be brought about by unattractive food, surroundings, or company. [NIH]

Anorexia Nervosa: The chief symptoms are inability to eat, weight loss, and amenorrhea. [NIH]

Anovulation: Suspension or cessation of ovulation in animals and humans. [NIH]

Antagonism: Interference with, or inhibition of, the growth of a living organism by another living organism, due either to creation of unfavorable conditions (e. g. exhaustion of food supplies) or to production of a specific antibiotic substance (e. g. penicillin). [NIH]

Anthropometric measurements: Measurements of human body height, weight, and size of component parts, including skinfold measurement. Used to study and compare the relative proportions under normal and abnormal conditions. [NIH]

Anthropometry: The technique that deals with the measurement of the size, weight, and proportions of the human or other primate body. [NIH]

Antiallergic: Counteracting allergy or allergic conditions. [EU]

Antibacterial: A substance that destroys bacteria or suppresses their growth or reproduction. [EU]

Antibiotic: A drug used to treat infections caused by bacteria and other microorganisms. [NIH]

Antibodies: Immunoglobulin molecules having a specific amino acid sequence by virtue of which they interact only with the antigen that induced their synthesis in cells of the lymphoid series (especially plasma cells), or with an antigen closely related to it. [NIH]

Antibody: A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on

the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. [NIH]

Anticoagulant: A drug that helps prevent blood clots from forming. Also called a blood thinner. [NIH]

Antidiabetic: An agent that prevents or alleviates diabetes. [EU]

Antiepileptic: An agent that combats epilepsy. [EU]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Anti-inflammatory: Having to do with reducing inflammation. [NIH]

Anti-Inflammatory Agents: Substances that reduce or suppress inflammation. [NIH]

Antioxidant: A substance that prevents damage caused by free radicals. Free radicals are highly reactive chemicals that often contain oxygen. They are produced when molecules are split to give products that have unpaired electrons. This process is called oxidation. [NIH]

Antiplasmin: A member of the serpin superfamily found in human plasma that inhibits the lysis of fibrin clots which are induced by plasminogen activator. It is a glycoprotein, molecular weight approximately 70,000 that migrates in the alpha 2 region in immunoelectrophoresis. It is the principal plasmin inactivator in blood, rapidly forming a very stable complex with plasmin. [NIH]

Antipruritic: Relieving or preventing itching. [EU]

Antipyretic: An agent that relieves or reduces fever. Called also antifebrile, antithermic and febrifuge. [EU]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Anuria: Inability to form or excrete urine. [NIH]

Anus: The opening of the rectum to the outside of the body. [NIH]

Anxiety: Persistent feeling of dread, apprehension, and impending disaster. [NIH]

Apolipoproteins: The protein components of lipoproteins which remain after the lipids to which the proteins are bound have been removed. They play an important role in lipid transport and metabolism. [NIH]

Apolipoproteins A: Lipoproteins found in human blood serum in the high-density and very-high-density lipoprotein fraction (HDL, VHDL). They consist of several different polypeptides, the most important of which are apolipoprotein A-I and A-II. They maintain the structural integrity of the HDL particles and are activators of lecithin:cholesterol acyltransferase (LCAT). Atherosclerotic patients show low apolipoprotein A levels and these apolipoproteins are either absent or present in extremely low plasma concentration in Tangier disease. [NIH]

Apoptosis: One of the two mechanisms by which cell death occurs (the other being the pathological process of necrosis). Apoptosis is the mechanism responsible for the physiological deletion of cells and appears to be intrinsically programmed. It is characterized by distinctive morphologic changes in the nucleus and cytoplasm, chromatin cleavage at regularly spaced sites, and the endonucleolytic cleavage of genomic DNA (DNA fragmentation) at internucleosomal sites. This mode of cell death serves as a balance to

mitosis in regulating the size of animal tissues and in mediating pathologic processes associated with tumor growth. [NIH]

Aqueous: Having to do with water. [NIH]

Arachidonic Acid: An unsaturated, essential fatty acid. It is found in animal and human fat as well as in the liver, brain, and glandular organs, and is a constituent of animal phosphatides. It is formed by the synthesis from dietary linoleic acid and is a precursor in the biosynthesis of prostaglandins, thromboxanes, and leukotrienes. [NIH]

Arcuate Nucleus: A nucleus located in the middle hypothalamus in the most ventral part of the third ventricle near the entrance of the infundibular recess. Its small cells are in close contact with the ependyma. [NIH]

Arginine: An essential amino acid that is physiologically active in the L-form. [NIH]

Aromatic: Having a spicy odour. [EU]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arteriolar: Pertaining to or resembling arterioles. [EU]

Arterioles: The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

Arteriolosclerosis: Sclerosis and thickening of the walls of the smaller arteries (arterioles). Hyaline arteriolosclerosis, in which there is homogeneous pink hyaline thickening of the arteriolar walls, is associated with benign nephrosclerosis. Hyperplastic arteriolosclerosis, in which there is a concentric thickening with progressive narrowing of the lumina may be associated with malignant hypertension, nephrosclerosis, and scleroderma. [EU]

Arteriosclerosis: Thickening and loss of elasticity of arterial walls. Atherosclerosis is the most common form of arteriosclerosis and involves lipid deposition and thickening of the intimal cell layers within arteries. Additional forms of arteriosclerosis involve calcification of the media of muscular arteries (Monkeberg medial calcific sclerosis) and thickening of the walls of small arteries or arterioles due to cell proliferation or hyaline deposition (arteriolosclerosis). [NIH]

Aspiration: The act of inhaling. [NIH]

Aspirin: A drug that reduces pain, fever, inflammation, and blood clotting. Aspirin belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is also being studied in cancer prevention. [NIH]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Astrocytes: The largest and most numerous neuroglial cells in the brain and spinal cord. Astrocytes (from "star" cells) are irregularly shaped with many long processes, including those with "end feet" which form the glial (limiting) membrane and directly and indirectly contribute to the blood brain barrier. They regulate the extracellular ionic and chemical environment, and "reactive astrocytes" (along with microglia) respond to injury. Astrocytes have high- affinity transmitter uptake systems, voltage-dependent and transmitter-gated ion channels, and can release transmitter, but their role in signaling (as in many other functions) is not well understood. [NIH]

Asymptomatic: Having no signs or symptoms of disease. [NIH]

Asynchronous: Pacing mode where only one timing interval exists, that between the stimuli. While the duration of this interval may be varied, it is not modified by any sensed event once set. As no sensing occurs, the upper and lower rate intervals are the same as the

pacema. [NIH]

Ataxia: Impairment of the ability to perform smoothly coordinated voluntary movements. This condition may affect the limbs, trunk, eyes, pharnyx, larnyx, and other structures. Ataxia may result from impaired sensory or motor function. Sensory ataxia may result from posterior column injury or peripheral nerve diseases. Motor ataxia may be associated with cerebellar diseases; cerebral cortex diseases; thalamic diseases; basal ganglia diseases; injury to the red nucleus; and other conditions. [NIH]

Atrial: Pertaining to an atrium. [EU]

Atrioventricular: Pertaining to an atrium of the heart and to a ventricle. [EU]

Atrium: A chamber; used in anatomical nomenclature to designate a chamber affording entrance to another structure or organ. Usually used alone to designate an atrium of the heart. [EU]

Atrophy: Decrease in the size of a cell, tissue, organ, or multiple organs, associated with a variety of pathological conditions such as abnormal cellular changes, ischemia, malnutrition, or hormonal changes. [NIH]

Attenuated: Strain with weakened or reduced virulence. [NIH]

Autoantibodies: Antibodies that react with self-antigens (autoantigens) of the organism that produced them. [NIH]

Autoantigens: Endogenous tissue constituents that have the ability to interact with autoantibodies and cause an immune response. [NIH]

Autodigestion: Autolysis; a condition found in disease of the stomach: the stomach wall is digested by the gastric juice. [NIH]

Autoimmune disease: A condition in which the body recognizes its own tissues as foreign and directs an immune response against them. [NIH]

Autoimmunity: Process whereby the immune system reacts against the body's own tissues. Autoimmunity may produce or be caused by autoimmune diseases. [NIH]

Autonomic: Self-controlling; functionally independent. [EU]

Axillary: Pertaining to the armpit area, including the lymph nodes that are located there. [NIH]

Axillary Artery: The continuation of the subclavian artery; it distributes over the upper limb, axilla, chest and shoulder. [NIH]

Bacteria: Unicellular prokaryotic microorganisms which generally possess rigid cell walls, multiply by cell division, and exhibit three principal forms: round or coccal, rodlike or bacillary, and spiral or spirochetal. [NIH]

Bacterial Physiology: Physiological processes and activities of bacteria. [NIH]

Bactericidal: Substance lethal to bacteria; substance capable of killing bacteria. [NIH]

Bacteriophage: A virus whose host is a bacterial cell; A virus that exclusively infects bacteria. It generally has a protein coat surrounding the genome (DNA or RNA). One of the coliphages most extensively studied is the lambda phage, which is also one of the most important. [NIH]

Bacteriostatic: 1. Inhibiting the growth or multiplication of bacteria. 2. An agent that inhibits the growth or multiplication of bacteria. [EU]

Basal Ganglia: Large subcortical nuclear masses derived from the telencephalon and located in the basal regions of the cerebral hemispheres. [NIH]

Basal Ganglia Diseases: Diseases of the basal ganglia including the putamen; globus

pallidus; claustrum; amygdala; and caudate nucleus. Dyskinesias (most notably involuntary movements and alterations of the rate of movement) represent the primary clinical manifestations of these disorders. Common etiologies include cerebrovascular disease; neurodegenerative diseases; and craniocerebral trauma. [NIH]

Base: In chemistry, the nonacid part of a salt; a substance that combines with acids to form salts; a substance that dissociates to give hydroxide ions in aqueous solutions; a substance whose molecule or ion can combine with a proton (hydrogen ion); a substance capable of donating a pair of electrons (to an acid) for the formation of a coordinate covalent bond. [EU]

Basophils: Granular leukocytes characterized by a relatively pale-staining, lobate nucleus and cytoplasm containing coarse dark-staining granules of variable size and stainable by basic dyes. [NIH]

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

Beta-Galactosidase: A group of enzymes that catalyzes the hydrolysis of terminal, non-reducing beta-D-galactose residues in beta-galactosides. Deficiency of beta-Galactosidase A1 may cause gangliodisosis GM1. EC 3.2.1.23. [NIH]

Beta-pleated: Particular three-dimensional pattern of amyloidoses. [NIH]

Bilateral: Affecting both the right and left side of body. [NIH]

Bile: An emulsifying agent produced in the liver and secreted into the duodenum. Its composition includes bile acids and salts, cholesterol, and electrolytes. It aids digestion of fats in the duodenum. [NIH]

Bile Acids: Acids made by the liver that work with bile to break down fats. [NIH]

Bile Acids and Salts: Steroid acids and salts. The primary bile acids are derived from cholesterol in the liver and usually conjugated with glycine or taurine. The secondary bile acids are further modified by bacteria in the intestine. They play an important role in the digestion and absorption of fat. They have also been used pharmacologically, especially in the treatment of gallstones. [NIH]

Bile Ducts: Tubes that carry bile from the liver to the gallbladder for storage and to the small intestine for use in digestion. [NIH]

Biliary: Having to do with the liver, bile ducts, and/or gallbladder. [NIH]

Biliary Tract: The gallbladder and its ducts. [NIH]

Bilirubin: A bile pigment that is a degradation product of heme. [NIH]

Bioavailability: The degree to which a drug or other substance becomes available to the target tissue after administration. [EU]

Biochemical: Relating to biochemistry; characterized by, produced by, or involving chemical reactions in living organisms. [EU]

Biological response modifier: BRM. A substance that stimulates the body's response to infection and disease. [NIH]

Biological therapy: Treatment to stimulate or restore the ability of the immune system to fight infection and disease. Also used to lessen side effects that may be caused by some cancer treatments. Also known as immunotherapy, biotherapy, or biological response modifier (BRM) therapy. [NIH]

Biomarkers: Substances sometimes found in an increased amount in the blood, other body fluids, or tissues and that may suggest the presence of some types of cancer. Biomarkers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and GI tract cancers), and PSA (prostate cancer). Also called tumor markers. [NIH]

Biomolecular: A scientific field at the interface between advanced computing and biotechnology. [NIH]

Biopsy: Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

Biosynthesis: The building up of a chemical compound in the physiologic processes of a living organism. [EU]

Biotechnology: Body of knowledge related to the use of organisms, cells or cell-derived constituents for the purpose of developing products which are technically, scientifically and clinically useful. Alteration of biologic function at the molecular level (i.e., genetic engineering) is a central focus; laboratory methods used include transfection and cloning technologies, sequence and structure analysis algorithms, computer databases, and gene and protein structure function analysis and prediction. [NIH]

Bladder: The organ that stores urine. [NIH]

Blastocyst: The mammalian embryo in the post-morula stage in which a fluid-filled cavity, enclosed primarily by trophoblast, contains an inner cell mass which becomes the embryonic disc. [NIH]

Blood Cell Count: A count of the number of leukocytes and erythrocytes per unit volume in a sample of venous blood. A complete blood count (CBC) also includes measurement of the hemoglobin, hematocrit, and erythrocyte indices. [NIH]

Blood Coagulation: The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [NIH]

Blood Glucose: Glucose in blood. [NIH]

Blood Platelets: Non-nucleated disk-shaped cells formed in the megakaryocyte and found in the blood of all mammals. They are mainly involved in blood coagulation. [NIH]

Blood Preservation: The process by which blood or its components are kept viable outside of the organism from which they are derived (i.e., kept from decay by means of a chemical agent, cooling, or a fluid substitute that mimics the natural state within the organism). [NIH]

Blood pressure: The pressure of blood against the walls of a blood vessel or heart chamber. Unless there is reference to another location, such as the pulmonary artery or one of the heart chambers, it refers to the pressure in the systemic arteries, as measured, for example, in the forearm. [NIH]

Blood transfusion: The administration of blood or blood products into a blood vessel. [NIH]

Blood vessel: A tube in the body through which blood circulates. Blood vessels include a network of arteries, arterioles, capillaries, venules, and veins. [NIH]

Blood Viscosity: The internal resistance of the blood to shear forces. The in vitro measure of whole blood viscosity is of limited clinical utility because it bears little relationship to the actual viscosity within the circulation, but an increase in the viscosity of circulating blood can contribute to morbidity in patients suffering from disorders such as sickle cell anemia and polycythemia. [NIH]

Blot: To transfer DNA, RNA, or proteins to an immobilizing matrix such as nitrocellulose. [NIH]

Blotting, Western: Identification of proteins or peptides that have been electrophoretically separated by blotting and transferred to strips of nitrocellulose paper. The blots are then detected by radiolabeled antibody probes. [NIH]

Body Burden: The total amount of a chemical, metal or radioactive substance present at any time after absorption in the body of man or animal. [NIH]

Body Composition: The relative amounts of various components in the body, such as percent body fat. [NIH]

Body Fluids: Liquid components of living organisms. [NIH]

Body Image: Individuals' personal concept of their bodies as objects in and bound by space, independently and apart from all other objects. [NIH]

Body Mass Index: One of the anthropometric measures of body mass; it has the highest correlation with skinfold thickness or body density. [NIH]

Bolus: A single dose of drug usually injected into a blood vessel over a short period of time. Also called bolus infusion. [NIH]

Bolus infusion: A single dose of drug usually injected into a blood vessel over a short period of time. Also called bolus. [NIH]

Bolus injection: The injection of a drug (or drugs) in a high quantity (called a bolus) at once, the opposite of gradual administration (as in intravenous infusion). [EU]

Bone Density: The amount of mineral per square centimeter of bone. This is the definition used in clinical practice. Actual bone density would be expressed in grams per milliliter. It is most frequently measured by photon absorptiometry or x-ray computed tomography. [NIH]

Bone Marrow: The soft tissue filling the cavities of bones. Bone marrow exists in two types, yellow and red. Yellow marrow is found in the large cavities of large bones and consists mostly of fat cells and a few primitive blood cells. Red marrow is a hematopoietic tissue and is the site of production of erythrocytes and granular leukocytes. Bone marrow is made up of a framework of connective tissue containing branching fibers with the frame being filled with marrow cells. [NIH]

Bone scan: A technique to create images of bones on a computer screen or on film. A small amount of radioactive material is injected into a blood vessel and travels through the bloodstream; it collects in the bones and is detected by a scanner. [NIH]

Bowel: The long tube-shaped organ in the abdomen that completes the process of digestion. There is both a small and a large bowel. Also called the intestine. [NIH]

Bowel Movement: Body wastes passed through the rectum and anus. [NIH]

Brachial: All the nerves from the arm are ripped from the spinal cord. [NIH]

Brachial Artery: The continuation of the axillary artery; it branches into the radial and ulnar arteries. [NIH]

Brachytherapy: A collective term for interstitial, intracavity, and surface radiotherapy. It uses small sealed or partly-sealed sources that may be placed on or near the body surface or within a natural body cavity or implanted directly into the tissues. [NIH]

Bradykinin: A nonapeptide messenger that is enzymatically produced from kallidin in the blood where it is a potent but short-lived agent of arteriolar dilation and increased capillary permeability. Bradykinin is also released from mast cells during asthma attacks, from gut walls as a gastrointestinal vasodilator, from damaged tissues as a pain signal, and may be a neurotransmitter. [NIH]

Branch: Most commonly used for branches of nerves, but applied also to other structures. [NIH]

Breakdown: A physical, metal, or nervous collapse. [NIH]

Bronchi: The larger air passages of the lungs arising from the terminal bifurcation of the trachea. [NIH]

Bronchial: Pertaining to one or more bronchi. [EU]

Bronchodilator: A drug that relaxes the smooth muscles in the constricted airway. [NIH]

Brown Fat: A thermogenic form of adipose tissue found in newborns of many species, including humans, and in hibernating mammals. The tissue is capable of rapid liberation of energy and seems to be important in the maintenance of body temperature immediately after birth and upon waking from hibernation. [NIH]

Buccal: Pertaining to or directed toward the cheek. In dental anatomy, used to refer to the buccal surface of a tooth. [EU]

Cachexia: General ill health, malnutrition, and weight loss, usually associated with chronic disease. [NIH]

Cadmium: An element with atomic symbol Cd, atomic number 48, and atomic weight 114. It is a metal and ingestion will lead to cadmium poisoning. [NIH]

Cadmium Poisoning: Poisoning occurring after exposure to cadmium compounds or fumes. It may cause gastrointestinal syndromes, anemia, or pneumonitis. [NIH]

Caesarean section: A surgical incision through the abdominal and uterine walls in order to deliver a baby. [NIH]

Caffeine: A methylxanthine naturally occurring in some beverages and also used as a pharmacological agent. Caffeine's most notable pharmacological effect is as a central nervous system stimulant, increasing alertness and producing agitation. It also relaxes smooth muscle, stimulates cardiac muscle, stimulates diuresis, and appears to be useful in the treatment of some types of headache. Several cellular actions of caffeine have been observed, but it is not entirely clear how each contributes to its pharmacological profile. Among the most important are inhibition of cyclic nucleotide phosphodiesterases, antagonism of adenosine receptors, and modulation of intracellular calcium handling. [NIH]

Calcification: Deposits of calcium in the tissues of the breast. Calcification in the breast can be seen on a mammogram, but cannot be detected by touch. There are two types of breast calcification, macrocalcification and microcalcification. Macrocalcifications are large deposits and are usually not related to cancer. Microcalcifications are specks of calcium that may be found in an area of rapidly dividing cells. Many microcalcifications clustered together may be a sign of cancer. [NIH]

Calcium: A basic element found in nearly all organized tissues. It is a member of the alkaline earth family of metals with the atomic symbol Ca, atomic number 20, and atomic weight 40. Calcium is the most abundant mineral in the body and combines with phosphorus to form calcium phosphate in the bones and teeth. It is essential for the normal functioning of nerves and muscles and plays a role in blood coagulation (as factor IV) and in many enzymatic processes. [NIH]

Calcium Signaling: Signal transduction mechanisms whereby calcium mobilization (from outside the cell or from intracellular storage pools) to the cytoplasm is triggered by external stimuli. Calcium signals are often seen to propagate as waves, oscillations, spikes or puffs. The calcium acts as an intracellular messenger by activating calcium-responsive proteins. [NIH]

Caloric intake: Refers to the number of calories (energy content) consumed. [NIH]

Capillary: Any one of the minute vessels that connect the arterioles and venules, forming a network in nearly all parts of the body. Their walls act as semipermeable membranes for the interchange of various substances, including fluids, between the blood and tissue fluid; called also vas capillare. [EU]

Capsules: Hard or soft soluble containers used for the oral administration of medicine. [NIH]

Carbohydrate: An aldehyde or ketone derivative of a polyhydric alcohol, particularly of the

pentahydric and hexahydric alcohols. They are so named because the hydrogen and oxygen are usually in the proportion to form water, (CH2O)n. The most important carbohydrates are the starches, sugars, celluloses, and gums. They are classified into mono-, di-, tri-, poly- and heterosaccharides. [EU]

Carbon Dioxide: A colorless, odorless gas that can be formed by the body and is necessary for the respiration cycle of plants and animals. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Carcinogens: Substances that increase the risk of neoplasms in humans or animals. Both genotoxic chemicals, which affect DNA directly, and nongenotoxic chemicals, which induce neoplasms by other mechanism, are included. [NIH]

Carcinoma: Cancer that begins in the skin or in tissues that line or cover internal organs. [NIH]

Cardiac: Having to do with the heart. [NIH]

Cardiac Output: The volume of blood passing through the heart per unit of time. It is usually expressed as liters (volume) per minute so as not to be confused with stroke volume (volume per beat). [NIH]

Cardiomyopathy: A general diagnostic term designating primary myocardial disease, often of obscure or unknown etiology. [EU]

Cardiopulmonary: Having to do with the heart and lungs. [NIH]

Cardiopulmonary Bypass: Diversion of the flow of blood from the entrance of the right atrium directly to the aorta (or femoral artery) via an oxygenator thus bypassing both the heart and lungs. [NIH]

Cardiorespiratory: Relating to the heart and lungs and their function. [EU]

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

Cardiovascular disease: Any abnormal condition characterized by dysfunction of the heart and blood vessels. CVD includes atherosclerosis (especially coronary heart disease, which can lead to heart attacks), cerebrovascular disease (e.g., stroke), and hypertension (high blood pressure). [NIH]

Carnitine: Constituent of striated muscle and liver. It is used therapeutically to stimulate gastric and pancreatic secretions and in the treatment of hyperlipoproteinemias. [NIH]

Carotene: The general name for a group of pigments found in green, yellow, and leafy vegetables, and yellow fruits. The pigments are fat-soluble, unsaturated aliphatic hydrocarbons functioning as provitamins and are converted to vitamin A through enzymatic processes in the intestinal wall. [NIH]

Carrier Proteins: Transport proteins that carry specific substances in the blood or across cell membranes. [NIH]

Case report: A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

Case series: A group or series of case reports involving patients who were given similar treatment. Reports of case series usually contain detailed information about the individual patients. This includes demographic information (for example, age, gender, ethnic origin) and information on diagnosis, treatment, response to treatment, and follow-up after treatment. [NIH]

Case-Control Studies: Studies which start with the identification of persons with a disease of interest and a control (comparison, referent) group without the disease. The relationship

of an attribute to the disease is examined by comparing diseased and non-diseased persons with regard to the frequency or levels of the attribute in each group. [NIH]

Catabolism: Any destructive metabolic process by which organisms convert substances into excreted compounds. [EU]

Catalyse: To speed up a chemical reaction. [EU]

Catecholamine: A group of chemical substances manufactured by the adrenal medulla and secreted during physiological stress. [NIH]

Catheterization: Use or insertion of a tubular device into a duct, blood vessel, hollow organ, or body cavity for injecting or withdrawing fluids for diagnostic or therapeutic purposes. It differs from intubation in that the tube here is used to restore or maintain patency in obstructions. [NIH]

Cations: Postively charged atoms, radicals or groups of atoms which travel to the cathode or negative pole during electrolysis. [NIH]

Caudal: Denoting a position more toward the cauda, or tail, than some specified point of reference; same as inferior, in human anatomy. [EU]

Causal: Pertaining to a cause; directed against a cause. [EU]

Cause of Death: Factors which produce cessation of all vital bodily functions. They can be analyzed from an epidemiologic viewpoint. [NIH]

Celecoxib: A drug that reduces pain. Celecoxib belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is being studied for cancer prevention. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cell Death: The termination of the cell's ability to carry out vital functions such as metabolism, growth, reproduction, responsiveness, and adaptability. [NIH]

Cell Division: The fission of a cell. [NIH]

Cell membrane: Cell membrane = plasma membrane. The structure enveloping a cell, enclosing the cytoplasm, and forming a selective permeability barrier; it consists of lipids, proteins, and some carbohydrates, the lipids thought to form a bilayer in which integral proteins are embedded to varying degrees. [EU]

Cell motility: The ability of a cell to move. [NIH]

Cell proliferation: An increase in the number of cells as a result of cell growth and cell division. [NIH]

Cell Respiration: The metabolic process of all living cells (animal and plant) in which oxygen is used to provide a source of energy for the cell. [NIH]

Cell Survival: The span of viability of a cell characterized by the capacity to perform certain functions such as metabolism, growth, reproduction, some form of responsiveness, and adaptability. [NIH]

Cellobiose: A disaccharide consisting of two glucose units in beta (1-4) glycosidic linkage. Obtained from the partial hydrolysis of cellulose. [NIH]

Cellulose: A polysaccharide with glucose units linked as in cellobiose. It is the chief constituent of plant fibers, cotton being the purest natural form of the substance. As a raw material, it forms the basis for many derivatives used in chromatography, ion exchange materials, explosives manufacturing, and pharmaceutical preparations. [NIH]

Central fat distribution: The waist circumference is an index of body fat distribution. Increasing waist circumference is accompanied by increasing frequencies of overt type 2

diabetes, dyslipidemia, hypertension, coronary heart disease, stroke, and early mortality. In the body fat patterns called android type (apple shaped) fat is deposited around the waist and upper abdominal area and appears most often in men. Abdominal body fat is thought to be associated with a rapid mobilization of fatty acids rather than resulting from other fat depots, although it remains a point of contention. If abdominal fat is indeed more active than other fat depots, it would then provide a mechanism by which we could explain (in part) the increase in blood lipid and glucose levels. The latter have been clearly associated with an increased risk for cardiovascular disease, hypertension, and type 2 diabetes. The gynoid type (pear-shaped) of body fat is usually seen in women. The fat is deposited around the hips, thighs, and buttocks, and presumably is used as energy reserve during pregnancy and lactation. [NIH]

Central Nervous System: The main information-processing organs of the nervous system, consisting of the brain, spinal cord, and meninges. [NIH]

Central Nervous System Infections: Pathogenic infections of the brain, spinal cord, and meninges. DNA virus infections; RNA virus infections; bacterial infections; mycoplasma infections; Spirochaetales infections; fungal infections; protozoan infections; helminthiasis; and prion diseases may involve the central nervous system as a primary or secondary process. [NIH]

Cerebellar: Pertaining to the cerebellum. [EU]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cerebrospinal: Pertaining to the brain and spinal cord. [EU]

Cerebrospinal fluid: CSF. The fluid flowing around the brain and spinal cord. Cerebrospinal fluid is produced in the ventricles in the brain. [NIH]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Cerebrum: The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

Cervix: The lower, narrow end of the uterus that forms a canal between the uterus and vagina. [NIH]

Character: In current usage, approximately equivalent to personality. The sum of the relatively fixed personality traits and habitual modes of response of an individual. [NIH]

Chemotherapy: Treatment with anticancer drugs. [NIH]

Cholecystectomy: Surgical removal of the gallbladder. [NIH]

Cholecystokinin: A 33-amino acid peptide secreted by the upper intestinal mucosa and also found in the central nervous system. It causes gallbladder contraction, release of pancreatic exocrine (or digestive) enzymes, and affects other gastrointestinal functions. Cholecystokinin may be the mediator of satiety. [NIH]

Cholecystostomy: Establishment of an opening into the gallbladder either for drainage or surgical communication with another part of the digestive tract, usually the duodenum or jejunum. [NIH]

Cholelithiasis: Presence or formation of gallstones. [NIH]

Cholesterol: The principal sterol of all higher animals, distributed in body tissues, especially the brain and spinal cord, and in animal fats and oils. [NIH]

Cholesterol Esters: Fatty acid esters of cholesterol which constitute about two-thirds of the cholesterol in the plasma. The accumulation of cholesterol esters in the arterial intima is a characteristic feature of atherosclerosis. [NIH]

Choline: A basic constituent of lecithin that is found in many plants and animal organs. It is important as a precursor of acetylcholine, as a methyl donor in various metabolic processes, and in lipid metabolism. [NIH]

Cholinergic: Resembling acetylcholine in pharmacological action; stimulated by or releasing acetylcholine or a related compound. [EU]

Chromatin: The material of chromosomes. It is a complex of DNA, histones, and nonhistone proteins (chromosomal proteins, non-histone) found within the nucleus of a cell. [NIH]

Chromium: A trace element that plays a role in glucose metabolism. It has the atomic symbol Cr, atomic number 24, and atomic weight 52. According to the Fourth Annual Report on Carcinogens (NTP85-002,1985), chromium and some of its compounds have been listed as known carcinogens. [NIH]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

Chronic: A disease or condition that persists or progresses over a long period of time. [NIH]

Chronic Disease: Disease or ailment of long duration. [NIH]

Chronic renal: Slow and progressive loss of kidney function over several years, often resulting in end-stage renal disease. People with end-stage renal disease need dialysis or transplantation to replace the work of the kidneys. [NIH]

Chylomicrons: A class of lipoproteins that carry dietary cholesterol and triglycerides from the small intestines to the tissues. [NIH]

CIS: Cancer Information Service. The CIS is the National Cancer Institute's link to the public, interpreting and explaining research findings in a clear and understandable manner, and providing personalized responses to specific questions about cancer. Access the CIS by calling 1-800-4-CANCER, or by using the Web site at http://cis.nci.nih.gov. [NIH]

Citric Acid: A key intermediate in metabolism. It is an acid compound found in citrus fruits. The salts of citric acid (citrates) can be used as anticoagulants due to their calcium chelating ability. [NIH]

Citrus: Any tree or shrub of the Rue family or the fruit of these plants. [NIH]

Clamp: A u-shaped steel rod used with a pin or wire for skeletal traction in the treatment of certain fractures. [NIH]

Clinical Medicine: The study and practice of medicine by direct examination of the patient. [NIH]

Clinical study: A research study in which patients receive treatment in a clinic or other medical facility. Reports of clinical studies can contain results for single patients (case reports) or many patients (case series or clinical trials). [NIH]

Clinical trial: A research study that tests how well new medical treatments or other interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. [NIH]

Clone: The term "clone" has acquired a new meaning. It is applied specifically to the bits of inserted foreign DNA in the hybrid molecules of the population. Each inserted segment originally resided in the DNA of a complex genome amid millions of other DNA segment. [NIH]

Cloning: The production of a number of genetically identical individuals; in genetic engineering, a process for the efficient replication of a great number of identical DNA molecules. [NIH]

Clot Retraction: Retraction of a clot resulting from contraction of platelet pseudopods

attached to fibrin strands that is dependent on the contractile protein thrombosthenin. Used as a measure of platelet function. [NIH]

Cluster Analysis: A set of statistical methods used to group variables or observations into strongly inter-related subgroups. In epidemiology, it may be used to analyze a closely grouped series of events or cases of disease or other health-related phenomenon with well-defined distribution patterns in relation to time or place or both. [NIH]

Coagulation: 1. The process of clot formation. 2. In colloid chemistry, the solidification of a sol into a gelatinous mass; an alteration of a disperse phase or of a dissolved solid which causes the separation of the system into a liquid phase and an insoluble mass called the clot or curd. Coagulation is usually irreversible. 3. In surgery, the disruption of tissue by physical means to form an amorphous residuum, as in electrocoagulation and photocoagulation. [EU]

Cobalt: A trace element that is a component of vitamin B12. It has the atomic symbol Co, atomic number 27, and atomic weight 58.93. It is used in nuclear weapons, alloys, and pigments. Deficiency in animals leads to anemia; its excess in humans can lead to erythrocytosis. [NIH]

Coca: Any of several South American shrubs of the Erythroxylon genus (and family) that yield cocaine; the leaves are chewed with alum for CNS stimulation. [NIH]

Cocaine: An alkaloid ester extracted from the leaves of plants including coca. It is a local anesthetic and vasoconstrictor and is clinically used for that purpose, particularly in the eye, ear, nose, and throat. It also has powerful central nervous system effects similar to the amphetamines and is a drug of abuse. Cocaine, like amphetamines, acts by multiple mechanisms on brain catecholaminergic neurons; the mechanism of its reinforcing effects is thought to involve inhibition of dopamine uptake. [NIH]

Codon: A set of three nucleotides in a protein coding sequence that specifies individual amino acids or a termination signal (codon, terminator). Most codons are universal, but some organisms do not produce the transfer RNAs (RNA, transfer) complementary to all codons. These codons are referred to as unassigned codons (codons, nonsense). [NIH]

Coenzyme: An organic nonprotein molecule, frequently a phosphorylated derivative of a water-soluble vitamin, that binds with the protein molecule (apoenzyme) to form the active enzyme (holoenzyme). [EU]

Cofactor: A substance, microorganism or environmental factor that activates or enhances the action of another entity such as a disease-causing agent. [NIH]

Cohort Studies: Studies in which subsets of a defined population are identified. These groups may or may not be exposed to factors hypothesized to influence the probability of the occurrence of a particular disease or other outcome. Cohorts are defined populations which, as a whole, are followed in an attempt to determine distinguishing subgroup characteristics. [NIH]

Colitis: Inflammation of the colon. [NIH]

Collagen: A polypeptide substance comprising about one third of the total protein in mammalian organisms. It is the main constituent of skin, connective tissue, and the organic substance of bones and teeth. Different forms of collagen are produced in the body but all consist of three alpha-polypeptide chains arranged in a triple helix. Collagen is differentiated from other fibrous proteins, such as elastin, by the content of proline, hydroxyproline, and hydroxylysine; by the absence of tryptophan; and particularly by the high content of polar groups which are responsible for its swelling properties. [NIH]

Collagen disease: A term previously used to describe chronic diseases of the connective tissue (e.g., rheumatoid arthritis, systemic lupus erythematosus, and systemic sclerosis), but

now is thought to be more appropriate for diseases associated with defects in collagen, which is a component of the connective tissue. [NIH]

Collapse: 1. A state of extreme prostration and depression, with failure of circulation. 2. Abnormal falling in of the walls of any part of organ. [EU]

Colloidal: Of the nature of a colloid. [EU]

Colonoscopy: Endoscopic examination, therapy or surgery of the luminal surface of the colon. [NIH]

Colorectal: Having to do with the colon or the rectum. [NIH]

Colorectal Cancer: Cancer that occurs in the colon (large intestine) or the rectum (the end of the large intestine). A number of digestive diseases may increase a person's risk of colorectal cancer, including polyposis and Zollinger-Ellison Syndrome. [NIH]

Combination Therapy: Association of 3 drugs to treat AIDS (AZT + DDC or DDI + protease inhibitor). [NIH]

Common Bile Duct: The largest biliary duct. It is formed by the junction of the cystic duct and the hepatic duct. [NIH]

Complement: A term originally used to refer to the heat-labile factor in serum that causes immune cytolysis, the lysis of antibody-coated cells, and now referring to the entire functionally related system comprising at least 20 distinct serum proteins that is the effector not only of immune cytolysis but also of other biologic functions. Complement activation occurs by two different sequences, the classic and alternative pathways. The proteins of the classic pathway are termed 'components of complement' and are designated by the symbols C1 through C9. C1 is a calcium-dependent complex of three distinct proteins C1q, C1r and C1s. The proteins of the alternative pathway (collectively referred to as the properdin system) and complement regulatory proteins are known by semisystematic or trivial names. Fragments resulting from proteolytic cleavage of complement proteins are designated with lower-case letter suffixes, e.g., C3a. Inactivated fragments may be designated with the suffix 'i', e.g. C3bi. Activated components or complexes with biological activity are designated by a bar over the symbol e.g. C1 or C4b,2a. The classic pathway is activated by the binding of C1 to classic pathway activators, primarily antigen-antibody complexes containing IgM, IgG1, IgG3; C1q binds to a single IgM molecule or two adjacent IgG molecules. The alternative pathway can be activated by IgA immune complexes and also by nonimmunologic materials including bacterial endotoxins, microbial polysaccharides, and cell walls. Activation of the classic pathway triggers an enzymatic cascade involving C1, C4, C2 and C3; activation of the alternative pathway triggers a cascade involving C3 and factors B, D and P. Both result in the cleavage of C5 and the formation of the membrane attack complex. Complement activation also results in the formation of many biologically active complement fragments that act as anaphylatoxins, opsonins, or chemotactic factors. [EU]

Complementary and alternative medicine: CAM. Forms of treatment that are used in addition to (complementary) or instead of (alternative) standard treatments. These practices are not considered standard medical approaches. CAM includes dietary supplements, megadose vitamins, herbal preparations, special teas, massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complementary medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used to enhance or complement the standard treatments. Complementary medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complete remission: The disappearance of all signs of cancer. Also called a complete

response. [NIH]

Compress: A plug used to occludate an orifice in the control of bleeding, or to mop up secretions; an absorbent pad. [NIH]

Computational Biology: A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. [NIH]

Computed tomography: CT scan. A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized tomography and computerized axial tomography (CAT) scan. [NIH]

Computerized axial tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called CAT scan, computed tomography (CT scan), or computerized tomography. [NIH]

Computerized tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized axial tomography (CAT) scan and computed tomography (CT scan). [NIH]

Conception: The onset of pregnancy, marked by implantation of the blastocyst; the formation of a viable zygote. [EU]

Concomitant: Accompanying; accessory; joined with another. [EU]

Cones: One type of specialized light-sensitive cells (photoreceptors) in the retina that provide sharp central vision and color vision. [NIH]

Confidence Intervals: A range of values for a variable of interest, e.g., a rate, constructed so that this range has a specified probability of including the true value of the variable. [NIH]

Confounding: Extraneous variables resulting in outcome effects that obscure or exaggerate the "true" effect of an intervention. [NIH]

Congestive heart failure: Weakness of the heart muscle that leads to a buildup of fluid in body tissues. [NIH]

Conjugated: Acting or operating as if joined; simultaneous. [EU]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Conscious Sedation: An alternative to general anesthesia in patients for whom general anesthesia is refused or considered inadvisable. It involves the administering of an antianxiety drug (minor tranquilizer) and an analgesic or local anesthetic. This renders the patient free of anxiety and pain while allowing the patient to remain in verbal contact with the physician or dentist. [NIH]

Consciousness: Sense of awareness of self and of the environment. [NIH]

Constipation: Infrequent or difficult evacuation of feces. [NIH]

Constriction: The act of constricting. [NIH]

Constriction, Pathologic: The condition of an anatomical structure's being constricted beyond normal dimensions. [NIH]

Consumption: Pulmonary tuberculosis. [NIH]

Contraceptive: An agent that diminishes the likelihood of or prevents conception. [EU]

Contraindications: Any factor or sign that it is unwise to pursue a certain kind of action or treatment, e. g. giving a general anesthetic to a person with pneumonia. [NIH]

Control group: In a clinical trial, the group that does not receive the new treatment being studied. This group is compared to the group that receives the new treatment, to see if the new treatment works. [NIH]

Controlled clinical trial: A clinical study that includes a comparison (control) group. The comparison group receives a placebo, another treatment, or no treatment at all. [NIH]

Convulsions: A general term referring to sudden and often violent motor activity of cerebral or brainstem origin. Convulsions may also occur in the absence of an electrical cerebral discharge (e.g., in response to hypotension). [NIH]

Coordination: Muscular or motor regulation or the harmonious cooperation of muscles or groups of muscles, in a complex action or series of actions. [NIH]

Cor: The muscular organ that maintains the circulation of the blood. c. adiposum a heart that has undergone fatty degeneration or that has an accumulation of fat around it; called also fat or fatty, heart. c. arteriosum the left side of the heart, so called because it contains oxygenated (arterial) blood. c. biloculare a congenital anomaly characterized by failure of formation of the atrial and ventricular septums, the heart having only two chambers, a single atrium and a single ventricle, and a common atrioventricular valve. c. bovinum (L. 'ox heart') a greatly enlarged heart due to a hypertrophied left ventricle; called also c. taurinum and bucardia. c. dextrum (L. 'right heart') the right atrium and ventricle. c. hirsutum, c. villosum. c. mobile (obs.) an abnormally movable heart. c. pendulum a heart so movable that it seems to be hanging by the great blood vessels. c. pseudotriloculare biatriatum a congenital cardiac anomaly in which the heart functions as a three-chambered heart because of tricuspid atresia, the right ventricle being extremely small or rudimentary and the right atrium greatly dilated. Blood passes from the right to the left atrium and thence disease due to pulmonary hypertension secondary to disease of the lung, or its blood vessels, with hypertrophy of the right ventricle. [EU]

Coronary: Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

Coronary Disease: Disorder of cardiac function due to an imbalance between myocardial function and the capacity of the coronary vessels to supply sufficient flow for normal function. It is a form of myocardial ischemia (insufficient blood supply to the heart muscle) caused by a decreased capacity of the coronary vessels. [NIH]

Coronary heart disease: A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

Coronary Thrombosis: Presence of a thrombus in a coronary artery, often causing a myocardial infarction. [NIH]

Coronary Vessels: The veins and arteries of the heart. [NIH]

Corpus: The body of the uterus. [NIH]

Corpus Luteum: The yellow glandular mass formed in the ovary by an ovarian follicle that has ruptured and discharged its ovum. [NIH]

Cortex: The outer layer of an organ or other body structure, as distinguished from the internal substance. [EU]

Cortical: Pertaining to or of the nature of a cortex or bark. [EU]

Corticosteroids: Hormones that have antitumor activity in lymphomas and lymphoid leukemias; in addition, corticosteroids (steroids) may be used for hormone replacement and for the management of some of the complications of cancer and its treatment. [NIH]

Cortisol: A steroid hormone secreted by the adrenal cortex as part of the body's response to stress. [NIH]

C-Peptide: A 31-amino acid peptide which connects the A and B chains of proinsulin. The exact composition of the peptide is species dependent. In beta cells proinsulin is enzymatically converted to insulin with the liberation of the C-peptide. An immunoassay has been developed for assessing pancreatic beta cell secretory function in diabetic patients in whom circulating insulin antibodies and exogenous insulin interfere with insulin immunoassay. [NIH]

Cranial: Pertaining to the cranium, or to the anterior (in animals) or superior (in humans) end of the body. [EU]

Craniocerebral Trauma: Traumatic injuries involving the cranium and intracranial structures (i.e., brain; cranial nerves; meninges; and other structures). Injuries may be classified by whether or not the skull is penetrated (i.e., penetrating vs. nonpenetrating) or whether there is an associated hemorrhage. [NIH]

Creatinine: A compound that is excreted from the body in urine. Creatinine levels are measured to monitor kidney function. [NIH]

Crossing-over: The exchange of corresponding segments between chromatids of homologous chromosomes during meiosia, forming a chiasma. [NIH]

Cultured cells: Animal or human cells that are grown in the laboratory. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Curettage: Removal of tissue with a curette, a spoon-shaped instrument with a sharp edge. [NIH]

Cutaneous: Having to do with the skin. [NIH]

Cyclic: Pertaining to or occurring in a cycle or cycles; the term is applied to chemical compounds that contain a ring of atoms in the nucleus. [EU]

Cyproheptadine: A serotonin antagonist and a histamine H1 blocker used as antipruritic, appetite stimulant, antiallergic, and for the post-gastrectomy dumping syndrome, etc. [NIH]

Cystathionine beta-Synthase: A multifunctional pyridoxal phosphate enzyme. In the second stage of cysteine biosynthesis it catalyzes the reaction of homocysteine with serine to form cystathionine with the elimination of water. Deficiency of this enzyme leads to hyperhomocysteinemia and homocystinuria. EC 4.2.1.22. [NIH]

Cysteine: A thiol-containing non-essential amino acid that is oxidized to form cystine. [NIH]

Cystic Duct: The tube that carries bile from the gallbladder into the common bile duct and the small intestine. [NIH]

Cystine: A covalently linked dimeric nonessential amino acid formed by the oxidation of cysteine. Two molecules of cysteine are joined together by a disulfide bridge to form cystine. [NIH]

Cytochrome: Any electron transfer hemoprotein having a mode of action in which the transfer of a single electron is effected by a reversible valence change of the central iron atom of the heme prosthetic group between the +2 and +3 oxidation states; classified as

cytochromes a in which the heme contains a formyl side chain, cytochromes b, which contain protoheme or a closely similar heme that is not covalently bound to the protein, cytochromes c in which protoheme or other heme is covalently bound to the protein, and cytochromes d in which the iron-tetrapyrrole has fewer conjugated double bonds than the hemes have. Well-known cytochromes have been numbered consecutively within groups and are designated by subscripts (beginning with no subscript), e.g. cytochromes c, c1, C2, . New cytochromes are named according to the wavelength in nanometres of the absorption maximum of the a-band of the iron (II) form in pyridine, e.g., c-555. [EU]

Cytokine: Small but highly potent protein that modulates the activity of many cell types, including T and B cells. [NIH]

Cytoplasm: The protoplasm of a cell exclusive of that of the nucleus; it consists of a continuous aqueous solution (cytosol) and the organelles and inclusions suspended in it (phaneroplasm), and is the site of most of the chemical activities of the cell. [EU]

Cytotoxic: Cell-killing. [NIH]

Daclizumab: A monoclonal antibody that is being studied for treatment of adult T-cell leukemia. Also called dacliximab. Monoclonal antibodies are laboratory-produced substances that can locate and bind to cancer cells. [NIH]

Dairy Products: Raw and processed or manufactured milk and milk-derived products. These are usually from cows (bovine) but are also from goats, sheep, reindeer, and water buffalo. [NIH]

Data Collection: Systematic gathering of data for a particular purpose from various sources, including questionnaires, interviews, observation, existing records, and electronic devices. The process is usually preliminary to statistical analysis of the data. [NIH]

Databases, Bibliographic: Extensive collections, reputedly complete, of references and citations to books, articles, publications, etc., generally on a single subject or specialized subject area. Databases can operate through automated files, libraries, or computer disks. The concept should be differentiated from factual databases which is used for collections of data and facts apart from bibliographic references to them. [NIH]

De novo: In cancer, the first occurrence of cancer in the body. [NIH]

Deamination: The removal of an amino group (NH2) from a chemical compound. [NIH]

Death Certificates: Official records of individual deaths including the cause of death certified by a physician, and any other required identifying information. [NIH]

Decidua: The epithelial lining of the endometrium that is formed before the fertilized ovum reaches the uterus. The fertilized ovum embeds in the decidua. If the ovum is not fertilized, the decidua is shed during menstruation. [NIH]

Decompensation: Failure of compensation; cardiac decompensation is marked by dyspnea, venous engorgement, and edema. [EU]

Defense Mechanisms: Unconscious process used by an individual or a group of individuals in order to cope with impulses, feelings or ideas which are not acceptable at their conscious level; various types include reaction formation, projection and self reversal. [NIH]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Dehydration: The condition that results from excessive loss of body water. [NIH]

Dehydroepiandrosterone: DHEA. A substance that is being studied as a cancer prevention drug. It belongs to the family of drugs called steroids. [NIH]

Deletion: A genetic rearrangement through loss of segments of DNA (chromosomes),

bringing sequences, which are normally separated, into close proximity. [NIH]

Dementia: An acquired organic mental disorder with loss of intellectual abilities of sufficient severity to interfere with social or occupational functioning. The dysfunction is multifaceted and involves memory, behavior, personality, judgment, attention, spatial relations, language, abstract thought, and other executive functions. The intellectual decline is usually progressive, and initially spares the level of consciousness. [NIH]

Dendrites: Extensions of the nerve cell body. They are short and branched and receive stimuli from other neurons. [NIH]

Dendritic: 1. Branched like a tree. 2. Pertaining to or possessing dendrites. [EU]

Density: The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

Dental Caries: Localized destruction of the tooth surface initiated by decalcification of the enamel followed by enzymatic lysis of organic structures and leading to cavity formation. If left unchecked, the cavity may penetrate the enamel and dentin and reach the pulp. The three most prominent theories used to explain the etiology of the disase are that acids produced by bacteria lead to decalcification; that micro-organisms destroy the enamel protein; or that keratolytic micro-organisms produce chelates that lead to decalcification. [NIH]

Deprivation: Loss or absence of parts, organs, powers, or things that are needed. [EU]

Desensitization: The prevention or reduction of immediate hypersensitivity reactions by administration of graded doses of allergen; called also hyposensitization and immunotherapy. [EU]

Detoxification: Treatment designed to free an addict from his drug habit. [EU]

Deuterium: Deuterium. The stable isotope of hydrogen. It has one neutron and one proton in the nucleus. [NIH]

Diabetes Insipidus: A metabolic disorder due to disorders in the production or release of vasopressin. It is characterized by the chronic excretion of large amounts of low specific gravity urine and great thirst. [NIH]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

Diabetic Foot: Ulcers of the foot as a complication of diabetes. Diabetic foot, often with infection, is a common serious complication of diabetes and may require hospitalization and disfiguring surgery. The foot ulcers are probably secondary to neuropathies and vascular problems. [NIH]

Diabetic Ketoacidosis: Complication of diabetes resulting from severe insulin deficiency coupled with an absolute or relative increase in glucagon concentration. The metabolic acidosis is caused by the breakdown of adipose stores and resulting increased levels of free fatty acids. Glucagon accelerates the oxidation of the free fatty acids producing excess ketone bodies (ketosis). [NIH]

Diagnostic procedure: A method used to identify a disease. [NIH]

Dialysate: A cleansing liquid used in the two major forms of dialysis--hemodialysis and peritoneal dialysis. [NIH]

Dialyzer: A part of the hemodialysis machine. (See hemodialysis under dialysis.) The dialyzer has two sections separated by a membrane. One section holds dialysate. The other holds the patient's blood. [NIH]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Diarrhoea: Abnormal frequency and liquidity of faecal discharges. [EU]

Diastole: Period of relaxation of the heart, especially the ventricles. [NIH]

Diastolic: Of or pertaining to the diastole. [EU]

Diastolic pressure: The lowest pressure to which blood pressure falls between contractions of the ventricles. [NIH]

Diencephalon: The paired caudal parts of the prosencephalon from which the thalamus, hypothalamus, epithalamus, and subthalamus are derived. [NIH]

Dietary Fats: Fats present in food, especially in animal products such as meat, meat products, butter, ghee. They are present in lower amounts in nuts, seeds, and avocados. [NIH]

Dietary Proteins: Proteins obtained from foods. They are the main source of the essential amino acids. [NIH]

Dietetics: The study and regulation of the diet. [NIH]

Diffusion: The tendency of a gas or solute to pass from a point of higher pressure or concentration to a point of lower pressure or concentration and to distribute itself throughout the available space; a major mechanism of biological transport. [NIH]

Digestion: The process of breakdown of food for metabolism and use by the body. [NIH]

Digestive system: The organs that take in food and turn it into products that the body can use to stay healthy. Waste products the body cannot use leave the body through bowel movements. The digestive system includes the salivary glands, mouth, esophagus, stomach, liver, pancreas, gallbladder, small and large intestines, and rectum. [NIH]

Digestive tract: The organs through which food passes when food is eaten. These organs are the mouth, esophagus, stomach, small and large intestines, and rectum. [NIH]

Dihydrotestosterone: Anabolic agent. [NIH]

Dihydroxyacetone: A ketotriose compound. Its addition to blood preservation solutions results in better maintenance of 2,3-diphosphoglycerate levels during storage. It is readily phosphorylated to dihydroxyacetone phosphate by triokinase in erythrocytes. In combination with naphthoquinones it acts as a sunscreening agent. [NIH]

Dihydroxyacetone Phosphate: An important intermediate in lipid biosynthesis and in glycolysis. [NIH]

Dilatation: The act of dilating. [NIH]

Dilution: A diluted or attenuated medicine; in homeopathy, the diffusion of a given quantity of a medicinal agent in ten or one hundred times the same quantity of water. [NIH]

Dimerization: The process by which two molecules of the same chemical composition form a condensation product or polymer. [NIH]

Diploid: Having two sets of chromosomes. [NIH]

Direct: 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

Disease Progression: The worsening of a disease over time. This concept is most often used for chronic and incurable diseases where the stage of the disease is an important determinant of therapy and prognosis. [NIH]

Disinfectant: An agent that disinfects; applied particularly to agents used on inanimate objects. [EU]

Disparity: Failure of the two retinal images of an object to fall on corresponding retinal points. [NIH]

Dissection: Cutting up of an organism for study. [NIH]

Distal: Remote; farther from any point of reference; opposed to proximal. In dentistry, used to designate a position on the dental arch farther from the median line of the jaw. [EU]

Distention: The state of being distended or enlarged; the act of distending. [EU]

Diuresis: Increased excretion of urine. [EU]

Diuretic: A drug that increases the production of urine. [NIH]

Diurnal: Occurring during the day. [EU]

Dopamine: An endogenous catecholamine and prominent neurotransmitter in several systems of the brain. In the synthesis of catecholamines from tyrosine, it is the immediate precursor to norepinephrine and epinephrine. Dopamine is a major transmitter in the extrapyramidal system of the brain, and important in regulating movement. A family of dopaminergic receptor subtypes mediate its action. Dopamine is used pharmacologically for its direct (beta adrenergic agonist) and indirect (adrenergic releasing) sympathomimetic effects including its actions as an inotropic agent and as a renal vasodilator. [NIH]

Dose-dependent: Refers to the effects of treatment with a drug. If the effects change when the dose of the drug is changed, the effects are said to be dose dependent. [NIH]

Doxazosin: A selective alpha-1-adrenergic blocker that lowers serum cholesterol. It is also effective in the treatment of hypertension. [NIH]

Drive: A state of internal activity of an organism that is a necessary condition before a given stimulus will elicit a class of responses; e.g., a certain level of hunger (drive) must be present before food will elicit an eating response. [NIH]

Drug Interactions: The action of a drug that may affect the activity, metabolism, or toxicity of another drug. [NIH]

Drug Tolerance: Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

Duct: A tube through which body fluids pass. [NIH]

Dumping Syndrome: Gastrointestinal symptoms resulting from an absent or nonfunctioning pylorus. [NIH]

Duodenum: The first part of the small intestine. [NIH]

Dyes: Chemical substances that are used to stain and color other materials. The coloring may or may not be permanent. Dyes can also be used as therapeutic agents and test reagents in medicine and scientific research. [NIH]

Dyslipidemia: Disorders in the lipoprotein metabolism; classified as hypercholesterolemia, hypertriglyceridemia, combined hyperlipidemia, and low levels of high-density lipoprotein (HDL) cholesterol. All of the dyslipidemias can be primary or secondary. Both elevated levels of low-density lipoprotein (LDL) cholesterol and low levels of HDL cholesterol predispose to premature atherosclerosis. [NIH]

Dyspareunia: Painful sexual intercourse. [NIH]

Dyspepsia: Impaired digestion, especially after eating. [NIH]

Dysplasia: Cells that look abnormal under a microscope but are not cancer. [NIH]

Dyspnea: Difficult or labored breathing. [NIH]

Dystrophy: Any disorder arising from defective or faulty nutrition, especially the muscular dystrophies. [EU]

Eating Disorders: A group of disorders characterized by physiological and psychological disturbances in appetite or food intake. [NIH]

Eclampsia: Onset of convulsions or coma in a previously diagnosed pre-eclamptic patient. [NIH]

Edema: Excessive amount of watery fluid accumulated in the intercellular spaces, most commonly present in subcutaneous tissue. [NIH]

Effector: It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [NIH]

Efficacy: The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions. Ideally, the determination of efficacy is based on the results of a randomized control trial. [NIH]

Elasticity: Resistance and recovery from distortion of shape. [NIH]

Elastin: The protein that gives flexibility to tissues. [NIH]

Elective: Subject to the choice or decision of the patient or physician; applied to procedures that are advantageous to the patient but not urgent. [EU]

Electrocoagulation: Electrosurgical procedures used to treat hemorrhage (e.g., bleeding ulcers) and to ablate tumors, mucosal lesions, and refractory arrhythmias. [NIH]

Electrolyte: A substance that dissociates into ions when fused or in solution, and thus becomes capable of conducting electricity; an ionic solute. [EU]

Electrons: Stable elementary particles having the smallest known negative charge, present in all elements; also called negatrons. Positively charged electrons are called positrons. The numbers, energies and arrangement of electrons around atomic nuclei determine the chemical identities of elements. Beams of electrons are called cathode rays or beta rays, the latter being a high-energy biproduct of nuclear decay. [NIH]

Electroporation: A technique in which electric pulses of intensity in kilovolts per centimeter and of microsecond-to-millisecond duration cause a temporary loss of the semipermeability of cell membranes, thus leading to ion leakage, escape of metabolites, and increased uptake by cells of drugs, molecular probes, and DNA. Some applications of electroporation include introduction of plasmids or foreign DNA into living cells for transfection, fusion of cells to prepare hybridomas, and insertion of proteins into cell membranes. [NIH]

Embryo: The prenatal stage of mammalian development characterized by rapid morphological changes and the differentiation of basic structures. [NIH]

Embryo Transfer: Removal of a mammalian embryo from one environment and replacement in the same or a new environment. The embryo is usually in the pre-nidation phase, i.e., a blastocyst. The process includes embryo or blastocyst transplantation or transfer after in vitro fertilization and transfer of the inner cell mass of the blastocyst. It is not used for transfer of differentiated embryonic tissue, e.g., germ layer cells. [NIH]

Emergency Treatment: First aid or other immediate intervention for accidents or medical conditions requiring immediate care and treatment before definitive medical and surgical management can be procured. [NIH]

Emollient: Softening or soothing; called also malactic. [EU]

Enamel: A very hard whitish substance which covers the dentine of the anatomical crown of a tooth. [NIH]

Endemic: Present or usually prevalent in a population or geographical area at all times; said of a disease or agent. Called also endemial. [EU]

Endocrine System: The system of glands that release their secretions (hormones) directly

into the circulatory system. In addition to the endocrine glands, included are the chromaffin system and the neurosecretory systems. [NIH]

Endocrinologist: A doctor that specializes in diagnosing and treating hormone disorders. [NIH]

Endometrial: Having to do with the endometrium (the layer of tissue that lines the uterus). [NIH]

Endometrium: The layer of tissue that lines the uterus. [NIH]

Endorphins: One of the three major groups of endogenous opioid peptides. They are large peptides derived from the pro-opiomelanocortin precursor. The known members of this group are alpha-, beta-, and gamma-endorphin. The term endorphin is also sometimes used to refer to all opioid peptides, but the narrower sense is used here; opioid peptides is used for the broader group. [NIH]

Endoscope: A thin, lighted tube used to look at tissues inside the body. [NIH]

Endoscopic: A technique where a lateral-view endoscope is passed orally to the duodenum for visualization of the ampulla of Vater. [NIH]

Endoscopic retrograde cholangiopancreatography: ERCP. A procedure to x-ray the pancreatic duct, hepatic duct, common bile duct, duodenal papilla, and gallbladder. In this procedure, a thin, lighted tube (endoscope) is passed through the mouth and down into the first part of the small intestine (duodenum). A smaller tube (catheter) is then inserted through the endoscope into the bile and pancreatic ducts. A dye is injected through the catheter into the ducts, and an x-ray is taken. [NIH]

Endoscopy: Endoscopic examination, therapy or surgery performed on interior parts of the body. [NIH]

Endothelial cell: The main type of cell found in the inside lining of blood vessels, lymph vessels, and the heart. [NIH]

Endothelium: A layer of epithelium that lines the heart, blood vessels (endothelium, vascular), lymph vessels (endothelium, lymphatic), and the serous cavities of the body. [NIH]

Endothelium, Lymphatic: Unbroken cellular lining (intima) of the lymph vessels (e.g., the high endothelial lymphatic venules). It is more permeable than vascular endothelium, lacking selective absorption and functioning mainly to remove plasma proteins that have filtered through the capillaries into the tissue spaces. [NIH]

Endothelium, Vascular: Single pavement layer of cells which line the luminal surface of the entire vascular system and regulate the transport of macromolecules and blood components from interstitium to lumen; this function has been most intensively studied in the blood capillaries. [NIH]

Endothelium-derived: Small molecule that diffuses to the adjacent muscle layer and relaxes it. [NIH]

Endotoxic: Of, relating to, or acting as an endotoxin (= a heat-stable toxin, associated with the outer membranes of certain gram-negative bacteria. Endotoxins are not secreted and are released only when the cells are disrupted). [EU]

Endotoxin: Toxin from cell walls of bacteria. [NIH]

End-stage renal: Total chronic kidney failure. When the kidneys fail, the body retains fluid and harmful wastes build up. A person with ESRD needs treatment to replace the work of the failed kidneys. [NIH]

Energy balance: Energy is the capacity of a body or a physical system for doing work. Energy balance is the state in which the total energy intake equals total energy needs. [NIH]

Energy Intake: Total number of calories taken in daily whether ingested or by parenteral routes. [NIH]

Enhancer: Transcriptional element in the virus genome. [NIH]

Enkephalin: A natural opiate painkiller, in the hypothalamus. [NIH]

Enterocytes: Terminally differentiated cells comprising the majority of the external surface of the intestinal epithelium (see intestinal mucosa). Unlike goblet cells, they do not produce or secrete mucins, nor do they secrete cryptdins as do the paneth cells. [NIH]

Environmental Exposure: The exposure to potentially harmful chemical, physical, or biological agents in the environment or to environmental factors that may include ionizing radiation, pathogenic organisms, or toxic chemicals. [NIH]

Environmental Health: The science of controlling or modifying those conditions, influences, or forces surrounding man which relate to promoting, establishing, and maintaining health. [NIH]

Enzymatic: Phase where enzyme cuts the precursor protein. [NIH]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

Enzyme Inhibitors: Compounds or agents that combine with an enzyme in such a manner as to prevent the normal substrate-enzyme combination and the catalytic reaction. [NIH]

Eosinophils: Granular leukocytes with a nucleus that usually has two lobes connected by a slender thread of chromatin, and cytoplasm containing coarse, round granules that are uniform in size and stainable by eosin. [NIH]

Ependyma: A thin membrane that lines the ventricles of the brain and the central canal of the spinal cord. [NIH]

Epidemic: Occurring suddenly in numbers clearly in excess of normal expectancy; said especially of infectious diseases but applied also to any disease, injury, or other health-related event occurring in such outbreaks. [EU]

Epidemiological: Relating to, or involving epidemiology. [EU]

Epidermal: Pertaining to or resembling epidermis. Called also epidermic or epidermoid. [EU]

Epidermal Growth Factor: A 6 kD polypeptide growth factor initially discovered in mouse submaxillary glands. Human epidermal growth factor was originally isolated from urine based on its ability to inhibit gastric secretion and called urogastrone. epidermal growth factor exerts a wide variety of biological effects including the promotion of proliferation and differentiation of mesenchymal and epithelial cells. [NIH]

Epidermis: Nonvascular layer of the skin. It is made up, from within outward, of five layers: 1) basal layer (stratum basale epidermidis); 2) spinous layer (stratum spinosum epidermidis); 3) granular layer (stratum granulosum epidermidis); 4) clear layer (stratum lucidum epidermidis); and 5) horny layer (stratum corneum epidermidis). [NIH]

Epigastric: Having to do with the upper middle area of the abdomen. [NIH]

Epinephrine: The active sympathomimetic hormone from the adrenal medulla in most species. It stimulates both the alpha- and beta- adrenergic systems, causes systemic vasoconstriction and gastrointestinal relaxation, stimulates the heart, and dilates bronchi and cerebral vessels. It is used in asthma and cardiac failure and to delay absorption of local anesthetics. [NIH]

Epithelial: Refers to the cells that line the internal and external surfaces of the body. [NIH]

Epithelial Cells: Cells that line the inner and outer surfaces of the body. [NIH]

Epithelium: One or more layers of epithelial cells, supported by the basal lamina, which

covers the inner or outer surfaces of the body. [NIH]

Epitope: A molecule or portion of a molecule capable of binding to the combining site of an antibody. For every given antigenic determinant, the body can construct a variety of antibody-combining sites, some of which fit almost perfectly, and others which barely fit. [NIH]

Erectile: The inability to get or maintain an erection for satisfactory sexual intercourse. Also called impotence. [NIH]

Erection: The condition of being made rigid and elevated; as erectile tissue when filled with blood. [EU]

Erythrocyte Indices: Quantification of size and cell hemoglobin content or concentration of the erythrocyte, usually derived from erythrocyte count, blood hemoglobin concentration, and hematocrit. Includes the mean cell volume (MCV), mean cell hemoglobin (MCH), and mean cell hemoglobin concentration (MCHC). Use also for cell diameter and thickness. [NIH]

Erythrocytes: Red blood cells. Mature erythrocytes are non-nucleated, biconcave disks containing hemoglobin whose function is to transport oxygen. [NIH]

Erythromycin: A bacteriostatic antibiotic substance produced by Streptomyces erythreus. Erythromycin A is considered its major active component. In sensitive organisms, it inhibits protein synthesis by binding to 50S ribosomal subunits. This binding process inhibits peptidyl transferase activity and interferes with translocation of amino acids during translation and assembly of proteins. [NIH]

Esophageal: Having to do with the esophagus, the muscular tube through which food passes from the throat to the stomach. [NIH]

Esophagitis: Inflammation, acute or chronic, of the esophagus caused by bacteria, chemicals, or trauma. [NIH]

Esophagogastroduodenoscopy: Exam of the upper digestive tract using an endoscope. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [NIH]

Essential Tremor: A rhythmic, involuntary, purposeless, oscillating movement resulting from the alternate contraction and relaxation of opposing groups of muscles. [NIH]

Esterification: The process of converting an acid into an alkyl or aryl derivative. Most frequently the process consists of the reaction of an acid with an alcohol in the presence of a trace of mineral acid as catalyst or the reaction of an acyl chloride with an alcohol. Esterification can also be accomplished by enzymatic processes. [NIH]

Estrogen: One of the two female sex hormones. [NIH]

Estrogen receptor: ER. Protein found on some cancer cells to which estrogen will attach. [NIH]

Estrogen Replacement Therapy: The use of hormonal agents with estrogen-like activity in postmenopausal or other estrogen-deficient women to alleviate effects of hormone deficiency, such as vasomotor symptoms, dyspareunia, and progressive development of osteoporosis. This may also include the use of progestational agents in combination therapy. [NIH]

Ethanol: A clear, colorless liquid rapidly absorbed from the gastrointestinal tract and distributed throughout the body. It has bactericidal activity and is used often as a topical disinfectant. It is widely used as a solvent and preservative in pharmaceutical preparations as well as serving as the primary ingredient in alcoholic beverages. [NIH]

Ether: One of a class of organic compounds in which any two organic radicals are attached directly to a single oxygen atom. [NIH]

Ethnic Groups: A group of people with a common cultural heritage that sets them apart from others in a variety of social relationships. [NIH]

Eukaryotic Cells: Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

Evacuation: An emptying, as of the bowels. [EU]

Evoke: The electric response recorded from the cerebral cortex after stimulation of a peripheral sense organ. [NIH]

Excipients: Usually inert substances added to a prescription in order to provide suitable consistency to the dosage form; a binder, matrix, base or diluent in pills, tablets, creams, salves, etc. [NIH]

Excrete: To get rid of waste from the body. [NIH]

Exhaustion: The feeling of weariness of mind and body. [NIH]

Exocrine: Secreting outwardly, via a duct. [EU]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

Exons: Coding regions of messenger RNA included in the genetic transcript which survive the processing of RNA in cell nuclei to become part of a spliced messenger of structural RNA in the cytoplasm. They include joining and diversity exons of immunoglobulin genes. [NIH]

Expiration: The act of breathing out, or expelling air from the lungs. [EU]

Extensor: A muscle whose contraction tends to straighten a limb; the antagonist of a flexor. [NIH]

External-beam radiation: Radiation therapy that uses a machine to aim high-energy rays at the cancer. Also called external radiation. [NIH]

Extracellular: Outside a cell or cells. [EU]

Extracellular Space: Interstitial space between cells, occupied by fluid as well as amorphous and fibrous substances. [NIH]

Extracorporeal: Situated or occurring outside the body. [EU]

Extraction: The process or act of pulling or drawing out. [EU]

Extremity: A limb; an arm or leg (membrum); sometimes applied specifically to a hand or foot. [EU]

Fallopian Tubes: Two long muscular tubes that transport ova from the ovaries to the uterus. They extend from the horn of the uterus to the ovaries and consist of an ampulla, an infundibulum, an isthmus, two ostia, and a pars uterina. The walls of the tubes are composed of three layers: mucosal, muscular, and serosal. [NIH]

Family Planning: Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Fat: Total lipids including phospholipids. [NIH]

Fatigue: The state of weariness following a period of exertion, mental or physical, characterized by a decreased capacity for work and reduced efficiency to respond to stimuli. [NIH]

Fatty acids: A major component of fats that are used by the body for energy and tissue development. [NIH]

Fatty Liver: The buildup of fat in liver cells. The most common cause is alcoholism. Other causes include obesity, diabetes, and pregnancy. Also called steatosis. [NIH]

Feces: The excrement discharged from the intestines, consisting of bacteria, cells exfoliated

from the intestines, secretions, chiefly of the liver, and a small amount of food residue. [EU]

Feeding Behavior: Behavioral responses or sequences associated with eating including modes of feeding, rhythmic patterns of eating, and time intervals. [NIH]

Femoral: Pertaining to the femur, or to the thigh. [EU]

Femur: The longest and largest bone of the skeleton, it is situated between the hip and the knee. [NIH]

Fertilization in Vitro: Fertilization of an egg outside the body when the egg is normally fertilized in the body. [NIH]

Fetal Blood: Blood of the fetus. Exchange of nutrients and waste between the fetal and maternal blood occurs via the placenta. The cord blood is blood contained in the umbilical vessels at the time of delivery. [NIH]

Fetoprotein: Transabdominal aspiration of fluid from the amniotic sac with a view to detecting increases of alpha-fetoprotein in maternal blood during pregnancy, as this is an important indicator of open neural tube defects in the fetus. [NIH]

Fetus: The developing offspring from 7 to 8 weeks after conception until birth. [NIH]

Fibrin: A protein derived from fibrinogen in the presence of thrombin, which forms part of the blood clot. [NIH]

Fibrinogen: Plasma glycoprotein clotted by thrombin, composed of a dimer of three non-identical pairs of polypeptide chains (alpha, beta, gamma) held together by disulfide bonds. Fibrinogen clotting is a sol-gel change involving complex molecular arrangements: whereas fibrinogen is cleaved by thrombin to form polypeptides A and B, the proteolytic action of other enzymes yields different fibrinogen degradation products. [NIH]

Fibrinolysis: The natural enzymatic dissolution of fibrin. [NIH]

Fibroblast Growth Factor: Peptide isolated from the pituitary gland and from the brain. It is a potent mitogen which stimulates growth of a variety of mesodermal cells including chondrocytes, granulosa, and endothelial cells. The peptide may be active in wound healing and animal limb regeneration. [NIH]

Fibroblasts: Connective tissue cells which secrete an extracellular matrix rich in collagen and other macromolecules. [NIH]

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

Fistula: Abnormal communication most commonly seen between two internal organs, or between an internal organ and the surface of the body. [NIH]

Flatulence: Production or presence of gas in the gastrointestinal tract which may be expelled through the anus. [NIH]

Flatus: Gas passed through the rectum. [NIH]

Fluoridation: The addition of fluorine usually as a fluoride to something, as the adding of a fluoride to drinking water or public water supplies for prevention of tooth decay in children. [NIH]

Fluorine: A nonmetallic, diatomic gas that is a trace element and member of the halogen family. It is used in dentistry as flouride to prevent dental caries. [NIH]

Foam Cells: Lipid-laden macrophages originating from monocytes or from smooth muscle cells. [NIH]

Folate: A B-complex vitamin that is being studied as a cancer prevention agent. Also called folic acid. [NIH]

Fold: A plication or doubling of various parts of the body. [NIH]

Folic Acid: N-(4-(((2-Amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl)amino)benzoyl)-L-glutamic acid. A member of the vitamin B family that stimulates the hematopoietic system. It is present in the liver and kidney and is found in mushrooms, spinach, yeast, green leaves, and grasses. Folic acid is used in the treatment and prevention of folate deficiencies and megaloblastic anemia. [NIH]

Food Deprivation: The withholding of food in a structured experimental situation. [NIH]

Foot Ulcer: Lesion on the surface of the skin of the foot, usually accompanied by inflammation. The lesion may become infected or necrotic and is frequently associated with diabetes or leprosy. [NIH]

Forearm: The part between the elbow and the wrist. [NIH]

Fractionation: Dividing the total dose of radiation therapy into several smaller, equal doses delivered over a period of several days. [NIH]

Fructosamine: An amino sugar formed when glucose non-enzymatically reacts with the N-terminal amino group of proteins. The fructose moiety is dervied from glucose by the "classical" Amadori rearrangement. [NIH]

Fructose: A type of sugar found in many fruits and vegetables and in honey. Fructose is used to sweeten some diet foods. It is considered a nutritive sweetener because it has calories. [NIH]

Fungi: A kingdom of eukaryotic, heterotrophic organisms that live as saprobes or parasites, including mushrooms, yeasts, smuts, molds, etc. They reproduce either sexually or asexually, and have life cycles that range from simple to complex. Filamentous fungi refer to those that grow as multicelluar colonies (mushrooms and molds). [NIH]

Galactosides: Glycosides formed by the reaction of the hydroxyl group on the anomeric carbon atom of galactose with an alcohol to form an acetal. They include both alpha- and beta-galactosides. [NIH]

Gallbladder: The pear-shaped organ that sits below the liver. Bile is concentrated and stored in the gallbladder. [NIH]

Gallstones: The solid masses or stones made of cholesterol or bilirubin that form in the gallbladder or bile ducts. [NIH]

Gamma-Glutamyltransferase: An enzyme that catalyzes reversibly the transfer of a glutamyl group from a glutamyl-peptide and an amino acid to a peptide and a glutamyl-amino acid. EC 2.3.2.2. [NIH]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Gas: Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

Gas exchange: Primary function of the lungs; transfer of oxygen from inhaled air into the blood and of carbon dioxide from the blood into the lungs. [NIH]

Gastrectomy: An operation to remove all or part of the stomach. [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastric Bypass: Surgical procedure in which the stomach is transected high on the body. The resulting proximal remnant is joined to a loop of the jejunum in an end-to-side anastomosis. This procedure is used frequently in the treatment of morbid obesity. [NIH]

Gastric Emptying: The evacuation of food from the stomach into the duodenum. [NIH]

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

Gastroenteritis: An acute inflammation of the lining of the stomach and intestines, characterized by anorexia, nausea, diarrhoea, abdominal pain, and weakness, which has various causes, including food poisoning due to infection with such organisms as Escherichia coli, Staphylococcus aureus, and Salmonella species; consumption of irritating food or drink; or psychological factors such as anger, stress, and fear. Called also enterogastritis. [EU]

Gastroesophageal Reflux: Reflux of gastric juice and/or duodenal contents (bile acids, pancreatic juice) into the distal esophagus, commonly due to incompetence of the lower esophageal sphincter. Gastric regurgitation is an extension of this process with entry of fluid into the pharynx or mouth. [NIH]

Gastroesophageal Reflux Disease: Flow of the stomach's contents back up into the esophagus. Happens when the muscle between the esophagus and the stomach (the lower esophageal sphincter) is weak or relaxes when it shouldn't. May cause esophagitis. Also called esophageal reflux or reflux esophagitis. [NIH]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [NIH]

Gelatin: A product formed from skin, white connective tissue, or bone collagen. It is used as a protein food adjuvant, plasma substitute, hemostatic, suspending agent in pharmaceutical preparations, and in the manufacturing of capsules and suppositories. [NIH]

Gemfibrozil: A lipid-regulating agent that lowers elevated serum lipids primarily by decreasing serum triglycerides with a variable reduction in total cholesterol. These decreases occur primarily in the VLDL fraction and less frequently in the LDL fraction. Gemfibrozil increases HDL subfractions HDL2 and HDL3 as well as apolipoproteins A-I and A-II. Its mechanism of action has not been definitely established. [NIH]

Gene: The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein. [NIH]

Gene Dosage: The number of copies of a given gene present in a cell or nucleus. An increase in gene dosage can result in the formation of higher levels of gene product, provided that the gene is not subject to autogenous regulation. [NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

Genetic Code: The specifications for how information, stored in nucleic acid sequence (base sequence), is translated into protein sequence (amino acid sequence). The start, stop, and order of amino acids of a protein is specified by consecutive triplets of nucleotides called codons (codon). [NIH]

Genetics: The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genital: Pertaining to the genitalia. [EU]

Genitourinary: Pertaining to the genital and urinary organs; urogenital; urinosexual. [EU]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Geriatric: Pertaining to the treatment of the aged. [EU]

Gestation: The period of development of the young in viviparous animals, from the time of fertilization of the ovum until birth. [EU]

Gestational: Psychosis attributable to or occurring during pregnancy. [NIH]

Gestational Age: Age of the conceptus. In humans, this may be assessed by medical history, physical examination, early immunologic pregnancy tests, radiography, ultrasonography, and amniotic fluid analysis. [NIH]

Ginseng: An araliaceous genus of plants that contains a number of pharmacologically active agents used as stimulants, sedatives, and tonics, especially in traditional medicine. [NIH]

Gland: An organ that produces and releases one or more substances for use in the body. Some glands produce fluids that affect tissues or organs. Others produce hormones or participate in blood production. [NIH]

Glomerular: Pertaining to or of the nature of a glomerulus, especially a renal glomerulus. [EU]

Glomerular Filtration Rate: The volume of water filtered out of plasma through glomerular capillary walls into Bowman's capsules per unit of time. It is considered to be equivalent to inulin clearance. [NIH]

Glomeruli: Plural of glomerulus. [NIH]

Glomerulosclerosis: Scarring of the glomeruli. It may result from diabetes mellitus (diabetic glomerulosclerosis) or from deposits in parts of the glomerulus (focal segmental glomerulosclerosis). The most common signs of glomerulosclerosis are proteinuria and kidney failure. [NIH]

Glomerulus: A tiny set of looping blood vessels in the nephron where blood is filtered in the kidney. [NIH]

Glucocorticoid: A compound that belongs to the family of compounds called corticosteroids (steroids). Glucocorticoids affect metabolism and have anti-inflammatory and immunosuppressive effects. They may be naturally produced (hormones) or synthetic (drugs). [NIH]

Gluconeogenesis: The process by which glucose is formed from a non-carbohydrate source. [NIH]

Glucose: D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

Glucose Intolerance: A pathological state in which the fasting plasma glucose level is less than 140 mg per deciliter and the 30-, 60-, or 90-minute plasma glucose concentration following a glucose tolerance test exceeds 200 mg per deciliter. This condition is seen frequently in diabetes mellitus but also occurs with other diseases. [NIH]

Glucose tolerance: The power of the normal liver to absorb and store large quantities of glucose and the effectiveness of intestinal absorption of glucose. The glucose tolerance test is a metabolic test of carbohydrate tolerance that measures active insulin, a hepatic function based on the ability of the liver to absorb glucose. The test consists of ingesting 100 grams of glucose into a fasting stomach; blood sugar should return to normal in 2 to 21 hours after ingestion. [NIH]

Glucose Tolerance Test: Determination of whole blood or plasma sugar in a fasting state before and at prescribed intervals (usually 1/2 hr, 1 hr, 3 hr, 4 hr) after taking a specified amount (usually 100 gm orally) of glucose. [NIH]

Glucose-6-Phosphatase: An enzyme that catalyzes the conversion of D-glucose 6-phosphate and water to D-glucose and orthophosphate. EC 3.1.3.9. [NIH]

Glucuronic Acid: Derivatives of uronic acid found throughout the plant and animal kingdoms. They detoxify drugs and toxins by conjugating with them to form glucuronides

in the liver which are more water-soluble metabolites that can be easily eliminated from the body. [NIH]

Glutamate: Excitatory neurotransmitter of the brain. [NIH]

Glutamic Acid: A non-essential amino acid naturally occurring in the L-form. Glutamic acid (glutamate) is the most common excitatory neurotransmitter in the central nervous system. [NIH]

Glutamine: A non-essential amino acid present abundantly throught the body and is involved in many metabolic processes. It is synthesized from glutamic acid and ammonia. It is the principal carrier of nitrogen in the body and is an important energy source for many cells. [NIH]

Glutathione Peroxidase: An enzyme catalyzing the oxidation of 2 moles of glutathione in the presence of hydrogen peroxide to yield oxidized glutathione and water. EC 1.11.1.9. [NIH]

Glyburide: An antidiabetic sulfonylurea derivative with actions similar to those of chlorpropamide. [NIH]

Glycerol: A trihydroxy sugar alcohol that is an intermediate in carbohydrate and lipid metabolism. It is used as a solvent, emollient, pharmaceutical agent, and sweetening agent. [NIH]

Glycerophospholipids: Derivatives of phosphatidic acid in which the hydrophobic regions are composed of two fatty acids and a polar alcohol is joined to the C-3 position of glycerol through a phosphodiester bond. They are named according to their polar head groups, such as phosphatidylcholine and phosphatidylethanolamine. [NIH]

Glycine: A non-essential amino acid. It is found primarily in gelatin and silk fibroin and used therapeutically as a nutrient. It is also a fast inhibitory neurotransmitter. [NIH]

Glycogen: A sugar stored in the liver and muscles. It releases glucose into the blood when cells need it for energy. Glycogen is the chief source of stored fuel in the body. [NIH]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Glycosidic: Formed by elimination of water between the anomeric hydroxyl of one sugar and a hydroxyl of another sugar molecule. [NIH]

Goats: Any of numerous agile, hollow-horned ruminants of the genus Capra, closely related to the sheep. [NIH]

Goblet Cells: Cells of the epithelial lining that produce and secrete mucins. [NIH]

Gonad: A sex organ, such as an ovary or a testicle, which produces the gametes in most multicellular animals. [NIH]

Gonadal: Pertaining to a gonad. [EU]

Gonadotropin: The water-soluble follicle stimulating substance, by some believed to originate in chorionic tissue, obtained from the serum of pregnant mares. It is used to supplement the action of estrogens. [NIH]

Governing Board: The group in which legal authority is vested for the control of health-related institutions and organizations. [NIH]

Gp120: 120-kD HIV envelope glycoprotein which is involved in the binding of the virus to its membrane receptor, the CD4 molecule, found on the surface of certain cells in the body. [NIH]

Grade: The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

Graft: Healthy skin, bone, or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body. [NIH]

Grafting: The operation of transfer of tissue from one site to another. [NIH]

Graft-versus-host disease: GVHD. A reaction of donated bone marrow or peripheral stem cells against a person's tissue. [NIH]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Grasses: A large family, Gramineae, of narrow-leaved herbaceous monocots. Many grasses produce highly allergenic pollens and are hosts to cattle parasites and toxic fungi. [NIH]

Growth: The progressive development of a living being or part of an organism from its earliest stage to maturity. [NIH]

Growth factors: Substances made by the body that function to regulate cell division and cell survival. Some growth factors are also produced in the laboratory and used in biological therapy. [NIH]

Guanylate Cyclase: An enzyme that catalyzes the conversion of GTP to 3',5'-cyclic GMP and pyrophosphate. It also acts on ITP and dGTP. (From Enzyme Nomenclature, 1992) EC 4.6.1.2. [NIH]

Habitual: Of the nature of a habit; according to habit; established by or repeated by force of habit, customary. [EU]

Half-Life: The time it takes for a substance (drug, radioactive nuclide, or other) to lose half of its pharmacologic, physiologic, or radiologic activity. [NIH]

Haploid: An organism with one basic chromosome set, symbolized by n; the normal condition of gametes in diploids. [NIH]

Happiness: Highly pleasant emotion characterized by outward manifestations of gratification; joy. [NIH]

Haptens: Small antigenic determinants capable of eliciting an immune response only when coupled to a carrier. Haptens bind to antibodies but by themselves cannot elicit an antibody response. [NIH]

Headache: Pain in the cranial region that may occur as an isolated and benign symptom or as a manifestation of a wide variety of conditions including subarachnoid hemorrhage; craniocerebral trauma; central nervous system infections; intracranial hypertension; and other disorders. In general, recurrent headaches that are not associated with a primary disease process are referred to as headache disorders (e.g., migraine). [NIH]

Headache Disorders: Common conditions characterized by persistent or recurrent headaches. Headache syndrome classification systems may be based on etiology (e.g., vascular headache, post-traumatic headaches, etc.), temporal pattern (e.g., cluster headache, paroxysmal hemicrania, etc.), and precipitating factors (e.g., cough headache). [NIH]

Health Behavior: Behaviors expressed by individuals to protect, maintain or promote their health status. For example, proper diet, and appropriate exercise are activities perceived to influence health status. Life style is closely associated with health behavior and factors influencing life style are socioeconomic, educational, and cultural. [NIH]

Health Education: Education that increases the awareness and favorably influences the attitudes and knowledge relating to the improvement of health on a personal or community basis. [NIH]

Health Status: The level of health of the individual, group, or population as subjectively assessed by the individual or by more objective measures. [NIH]

Heart attack: A seizure of weak or abnormal functioning of the heart. [NIH]

Heart failure: Loss of pumping ability by the heart, often accompanied by fatigue, breathlessness, and excess fluid accumulation in body tissues. [NIH]

Heartbeat: One complete contraction of the heart. [NIH]

Heartburn: Substernal pain or burning sensation, usually associated with regurgitation of gastric juice into the esophagus. [NIH]

Hematocrit: Measurement of the volume of packed red cells in a blood specimen by centrifugation. The procedure is performed using a tube with graduated markings or with automated blood cell counters. It is used as an indicator of erythrocyte status in disease. For example, anemia shows a low hematocrit, polycythemia, high values. [NIH]

Hematoma: An extravasation of blood localized in an organ, space, or tissue. [NIH]

Heme: The color-furnishing portion of hemoglobin. It is found free in tissues and as the prosthetic group in many hemeproteins. [NIH]

Hemodialysis: The use of a machine to clean wastes from the blood after the kidneys have failed. The blood travels through tubes to a dialyzer, which removes wastes and extra fluid. The cleaned blood then flows through another set of tubes back into the body. [NIH]

Hemodilution: Reduction of blood viscosity usually by the addition of cell free solutions. Used clinically l) in states of impaired microcirculation, 2) for replacement of intraoperative blood loss without homologous blood transfusion, and 3) in cardiopulmonary bypass and hypothermia. [NIH]

Hemodynamics: The movements of the blood and the forces involved in systemic or regional blood circulation. [NIH]

Hemoglobin: One of the fractions of glycosylated hemoglobin A1c. Glycosylated hemoglobin is formed when linkages of glucose and related monosaccharides bind to hemoglobin A and its concentration represents the average blood glucose level over the previous several weeks. HbA1c levels are used as a measure of long-term control of plasma glucose (normal, 4 to 6 percent). In controlled diabetes mellitus, the concentration of glycosylated hemoglobin A is within the normal range, but in uncontrolled cases the level may be 3 to 4 times the normal conentration. Generally, complications are substantially lower among patients with Hb levels of 7 percent or less than in patients with HbA1c levels of 9 percent or more. [NIH]

Hemoglobin A: Normal adult human hemoglobin. The globin moiety consists of two alpha and two beta chains. [NIH]

Hemoglobinuria: The presence of free hemoglobin in the urine. [NIH]

Hemolysis: The destruction of erythrocytes by many different causal agents such as antibodies, bacteria, chemicals, temperature, and changes in tonicity. [NIH]

Hemolytic: A disease that affects the blood and blood vessels. It destroys red blood cells, cells that cause the blood to clot, and the lining of blood vessels. HUS is often caused by the Escherichia coli bacterium in contaminated food. People with HUS may develop acute renal failure. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Hemorrhagic stroke: A disorder involving bleeding within ischemic brain tissue. Hemorrhagic stroke occurs when blood vessels that are damaged or dead from lack of blood supply (infarcted), located within an area of infarcted brain tissue, rupture and transform an "ischemic" stroke into a hemorrhagic stroke. Ischemia is inadequate tissue oxygenation caused by reduced blood flow; infarction is tissue death resulting from ischemia. Bleeding

irritates the brain tissues, causing swelling (cerebral edema). Blood collects into a mass (hematoma). Both swelling and hematoma will compress and displace brain tissue. [NIH]

Hemostasis: The process which spontaneously arrests the flow of blood from vessels carrying blood under pressure. It is accomplished by contraction of the vessels, adhesion and aggregation of formed blood elements, and the process of blood or plasma coagulation. [NIH]

Heparan Sulfate Proteoglycan: A substance released by astrocytes, which is critical in stopping nervous fibers in their tracks. [NIH]

Heparin: Heparinic acid. A highly acidic mucopolysaccharide formed of equal parts of sulfated D-glucosamine and D-glucuronic acid with sulfaminic bridges. The molecular weight ranges from six to twenty thousand. Heparin occurs in and is obtained from liver, lung, mast cells, etc., of vertebrates. Its function is unknown, but it is used to prevent blood clotting in vivo and vitro, in the form of many different salts. [NIH]

Hepatic: Refers to the liver. [NIH]

Hepatic Duct, Common: Predominantly extrahepatic bile duct which is formed by the junction of the right and left hepatic ducts, which are predominantly intrahepatic, and, in turn, joins the cystic duct to form the common bile duct. [NIH]

Hepatitis: Inflammation of the liver and liver disease involving degenerative or necrotic alterations of hepatocytes. [NIH]

Hepatobiliary: Pertaining to the liver and the bile or the biliary ducts. [EU]

Hepatocyte: A liver cell. [NIH]

Hepatocyte Growth Factor: Multifunctional growth factor which regulates both cell growth and cell motility. It exerts a strong mitogenic effect on hepatocytes and primary epithelial cells. Its receptor is proto-oncogene protein C-met. [NIH]

Hepatoma: A liver tumor. [NIH]

Hereditary: Of, relating to, or denoting factors that can be transmitted genetically from one generation to another. [NIH]

Heredity: 1. The genetic transmission of a particular quality or trait from parent to offspring. 2. The genetic constitution of an individual. [EU]

Heritability: The proportion of observed variation in a particular trait that can be attributed to inherited genetic factors in contrast to environmental ones. [NIH]

Heterogeneity: The property of one or more samples or populations which implies that they are not identical in respect of some or all of their parameters, e. g. heterogeneity of variance. [NIH]

Heterozygote: An individual having different alleles at one or more loci in homologous chromosome segments. [NIH]

Hibernation: The dormant state in which some animal species pass the winter. It is characterized by narcosis and by sharp reduction in body temperature and metabolic activity and by a depression of vital signs. It is a natural physiological process in many warm-blooded animals. [NIH]

Histamine: 1H-Imidazole-4-ethanamine. A depressor amine derived by enzymatic decarboxylation of histidine. It is a powerful stimulant of gastric secretion, a constrictor of bronchial smooth muscle, a vasodilator, and also a centrally acting neurotransmitter. [NIH]

Histidine: An essential amino acid important in a number of metabolic processes. It is required for the production of histamine. [NIH]

Histology: The study of tissues and cells under a microscope. [NIH]

Homeostasis: The processes whereby the internal environment of an organism tends to remain balanced and stable. [NIH]

Homogeneous: Consisting of or composed of similar elements or ingredients; of a uniform quality throughout. [EU]

Homologous: Corresponding in structure, position, origin, etc., as (a) the feathers of a bird and the scales of a fish, (b) antigen and its specific antibody, (c) allelic chromosomes. [EU]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormone: A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

Hormone Replacement Therapy: Therapeutic use of hormones to alleviate the effects of hormone deficiency. [NIH]

Hospital Records: Compilations of data on hospital activities and programs; excludes patient medical records. [NIH]

Hybrid: Cross fertilization between two varieties or, more usually, two species of vines, see also crossing. [NIH]

Hybridomas: Cells artificially created by fusion of activated lymphocytes with neoplastic cells. The resulting hybrid cells are cloned and produce pure or "monoclonal" antibodies or T-cell products, identical to those produced by the immunologically competent parent, and continually grow and divide as the neoplastic parent. [NIH]

Hydrocortisone: The main glucocorticoid secreted by the adrenal cortex. Its synthetic counterpart is used, either as an injection or topically, in the treatment of inflammation, allergy, collagen diseases, asthma, adrenocortical deficiency, shock, and some neoplastic conditions. [NIH]

Hydrogen: The first chemical element in the periodic table. It has the atomic symbol H, atomic number 1, and atomic weight 1. It exists, under normal conditions, as a colorless, odorless, tasteless, diatomic gas. Hydrogen ions are protons. Besides the common H1 isotope, hydrogen exists as the stable isotope deuterium and the unstable, radioactive isotope tritium. [NIH]

Hydrogen Peroxide: A strong oxidizing agent used in aqueous solution as a ripening agent, bleach, and topical anti-infective. It is relatively unstable and solutions deteriorate over time unless stabilized by the addition of acetanilide or similar organic materials. [NIH]

Hydrolysis: The process of cleaving a chemical compound by the addition of a molecule of water. [NIH]

Hydrophobic: Not readily absorbing water, or being adversely affected by water, as a hydrophobic colloid. [EU]

Hydroxylysine: A hydroxylated derivative of the amino acid lysine that is present in certain collagens. [NIH]

Hydroxyproline: A hydroxylated form of the imino acid proline. A deficiency in ascorbic acid can result in impaired hydroxyproline formation. [NIH]

Hypercholesterolemia: Abnormally high levels of cholesterol in the blood. [NIH]

Hyperglycemia: Abnormally high blood sugar. [NIH]

Hyperhomocysteinemia: An inborn error of methionone metabolism which produces an excess of homocysteine in the blood. It is often caused by a deficiency of cystathionine beta-synthase and is a risk factor for coronary vascular disease. [NIH]

Hyperlipidemia: An excess of lipids in the blood. [NIH]

Hyperlipoproteinemia: Metabolic disease characterized by elevated plasma cholesterol and/or triglyceride levels. The inherited form is attributed to a single gene mechanism. [NIH]

Hyperphagia: Ingestion of a greater than optimal quantity of food. [NIH]

Hyperplasia: An increase in the number of cells in a tissue or organ, not due to tumor formation. It differs from hypertrophy, which is an increase in bulk without an increase in the number of cells. [NIH]

Hypersensitivity: Altered reactivity to an antigen, which can result in pathologic reactions upon subsequent exposure to that particular antigen. [NIH]

Hypertension: Persistently high arterial blood pressure. Currently accepted threshold levels are 140 mm Hg systolic and 90 mm Hg diastolic pressure. [NIH]

Hypertriglyceridemia: Condition of elevated triglyceride concentration in the blood; an inherited form occurs in familial hyperlipoproteinemia IIb and hyperlipoproteinemia type IV. It has been linked to higher risk of heart disease and arteriosclerosis. [NIH]

Hypertrophy: General increase in bulk of a part or organ, not due to tumor formation, nor to an increase in the number of cells. [NIH]

Hypoglycemia: Abnormally low blood sugar [NIH]

Hypoglycemic: An orally active drug that produces a fall in blood glucose concentration. [NIH]

Hypoglycemic Agents: Agents which lower the blood glucose level. [NIH]

Hypotension: Abnormally low blood pressure. [NIH]

Hypotensive: Characterized by or causing diminished tension or pressure, as abnormally low blood pressure. [EU]

Hypothalamic: Of or involving the hypothalamus. [EU]

Hypothalamus: Ventral part of the diencephalon extending from the region of the optic chiasm to the caudal border of the mammillary bodies and forming the inferior and lateral walls of the third ventricle. [NIH]

Hypothermia: Lower than normal body temperature, especially in warm-blooded animals; in man usually accidental or unintentional. [NIH]

Ibuprofen: A nonsteroidal anti-inflammatory agent with analgesic properties used in the therapy of rheumatism and arthritis. [NIH]

Id: The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

Ileal: Related to the ileum, the lowest end of the small intestine. [NIH]

Ileum: The lower end of the small intestine. [NIH]

Immune function: Production and action of cells that fight disease or infection. [NIH]

Immune response: The activity of the immune system against foreign substances (antigens). [NIH]

Immune system: The organs, cells, and molecules responsible for the recognition and disposal of foreign ("non-self") material which enters the body. [NIH]

Immunity: Nonsusceptibility to the invasive or pathogenic effects of foreign microorganisms or to the toxic effect of antigenic substances. [NIH]

Immunization: Deliberate stimulation of the host's immune response. Active immunization involves administration of antigens or immunologic adjuvants. Passive immunization involves administration of immune sera or lymphocytes or their extracts (e.g., transfer factor, immune RNA) or transplantation of immunocompetent cell producing tissue

(thymus or bone marrow). [NIH]

Immunoassay: Immunochemical assay or detection of a substance by serologic or immunologic methods. Usually the substance being studied serves as antigen both in antibody production and in measurement of antibody by the test substance. [NIH]

Immunoblotting: Immunologic methods for isolating and quantitatively measuring immunoreactive substances. When used with immune reagents such as monoclonal antibodies, the process is known generically as western blot analysis (blotting, western). [NIH]

Immunodeficiency: The decreased ability of the body to fight infection and disease. [NIH]

Immunoelectrophoresis: A technique that combines protein electrophoresis and double immunodiffusion. In this procedure proteins are first separated by gel electrophoresis (usually agarose), then made visible by immunodiffusion of specific antibodies. A distinct elliptical precipitin arc results for each protein detectable by the antisera. [NIH]

Immunogenic: Producing immunity; evoking an immune response. [EU]

Immunoglobulin: A protein that acts as an antibody. [NIH]

Immunologic: The ability of the antibody-forming system to recall a previous experience with an antigen and to respond to a second exposure with the prompt production of large amounts of antibody. [NIH]

Immunosuppressive: Describes the ability to lower immune system responses. [NIH]

Immunosuppressive Agents: Agents that suppress immune function by one of several mechanisms of action. Classical cytotoxic immunosuppressants act by inhibiting DNA synthesis. Others may act through activation of suppressor T-cell populations or by inhibiting the activation of helper cells. While immunosuppression has been brought about in the past primarily to prevent rejection of transplanted organs, new applications involving mediation of the effects of interleukins and other cytokines are emerging. [NIH]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

Implant radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called [NIH]

Implantation: The insertion or grafting into the body of biological, living, inert, or radioactive material. [EU]

Impotence: The inability to perform sexual intercourse. [NIH]

In situ: In the natural or normal place; confined to the site of origin without invasion of neighbouring tissues. [EU]

In Situ Hybridization: A technique that localizes specific nucleic acid sequences within intact chromosomes, eukaryotic cells, or bacterial cells through the use of specific nucleic acid-labeled probes. [NIH]

In vitro: In the laboratory (outside the body). The opposite of in vivo (in the body). [NIH]

In vivo: In the body. The opposite of in vitro (outside the body or in the laboratory). [NIH]

Incision: A cut made in the body during surgery. [NIH]

Incompetence: Physical or mental inadequacy or insufficiency. [EU]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Infancy: The period of complete dependency prior to the acquisition of competence in walking, talking, and self-feeding. [NIH]

Infarction: A pathological process consisting of a sudden insufficient blood supply to an area, which results in necrosis of that area. It is usually caused by a thrombus, an embolus, or a vascular torsion. [NIH]

Infection: 1. Invasion and multiplication of microorganisms in body tissues, which may be clinically unapparent or result in local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. The infection may remain localized, subclinical, and temporary if the body's defensive mechanisms are effective. A local infection may persist and spread by extension to become an acute, subacute, or chronic clinical infection or disease state. A local infection may also become systemic when the microorganisms gain access to the lymphatic or vascular system. 2. An infectious disease. [EU]

Infertility: The diminished or absent ability to conceive or produce an offspring while sterility is the complete inability to conceive or produce an offspring. [NIH]

Inflammation: A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

Inflammatory bowel disease: A general term that refers to the inflammation of the colon and rectum. Inflammatory bowel disease includes ulcerative colitis and Crohn's disease. [NIH]

Infusion: A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion. [NIH]

Ingestion: Taking into the body by mouth [NIH]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a step in a carcinogenic process. [NIH]

Inlay: In dentistry, a filling first made to correspond with the form of a dental cavity and then cemented into the cavity. [NIH]

Innervation: 1. The distribution or supply of nerves to a part. 2. The supply of nervous energy or of nerve stimulus sent to a part. [EU]

Inositol: An isomer of glucose that has traditionally been considered to be a B vitamin although it has an uncertain status as a vitamin and a deficiency syndrome has not been identified in man. (From Martindale, The Extra Pharmacopoeia, 30th ed, p1379) Inositol phospholipids are important in signal transduction. [NIH]

Insecticides: Pesticides designed to control insects that are harmful to man. The insects may be directly harmful, as those acting as disease vectors, or indirectly harmful, as destroyers of crops, food products, or textile fabrics. [NIH]

Insight: The capacity to understand one's own motives, to be aware of one's own psychodynamics, to appreciate the meaning of symbolic behavior. [NIH]

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

Insulin-dependent diabetes mellitus: A disease characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both. Autoimmune, genetic, and environmental factors are involved in the development of type I diabetes. [NIH]

Insulin-like: Muscular growth factor. [NIH]

Interferon: A biological response modifier (a substance that can improve the body's natural response to disease). Interferons interfere with the division of cancer cells and can slow tumor growth. There are several types of interferons, including interferon-alpha, -beta, and -gamma. These substances are normally produced by the body. They are also made in the laboratory for use in treating cancer and other diseases. [NIH]

Interferon-alpha: One of the type I interferons produced by peripheral blood leukocytes or lymphoblastoid cells when exposed to live or inactivated virus, double-stranded RNA, or bacterial products. It is the major interferon produced by virus-induced leukocyte cultures and, in addition to its pronounced antiviral activity, it causes activation of NK cells. [NIH]

Interleukin-6: Factor that stimulates the growth and differentiation of human B-cells and is also a growth factor for hybridomas and plasmacytomas. It is produced by many different cells including T-cells, monocytes, and fibroblasts. [NIH]

Interleukins: Soluble factors which stimulate growth-related activities of leukocytes as well as other cell types. They enhance cell proliferation and differentiation, DNA synthesis, secretion of other biologically active molecules and responses to immune and inflammatory stimuli. [NIH]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

Internal Medicine: A medical specialty concerned with the diagnosis and treatment of diseases of the internal organ systems of adults. [NIH]

Internal radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called brachytherapy, implant radiation, or interstitial radiation therapy. [NIH]

Interstitial: Pertaining to or situated between parts or in the interspaces of a tissue. [EU]

Intervention Studies: Epidemiologic investigations designed to test a hypothesized cause-effect relation by modifying the supposed causal factor(s) in the study population. [NIH]

Intestinal: Having to do with the intestines. [NIH]

Intestine: A long, tube-shaped organ in the abdomen that completes the process of digestion. There is both a large intestine and a small intestine. Also called the bowel. [NIH]

Intoxication: Poisoning, the state of being poisoned. [EU]

Intracellular: Inside a cell. [NIH]

Intracellular Membranes: Membranes of subcellular structures. [NIH]

Intramuscular: IM. Within or into muscle. [NIH]

Intravenous: IV. Into a vein. [NIH]

Introns: Non-coding, intervening sequences of DNA that are transcribed, but are removed from within the primary gene transcript and rapidly degraded during maturation of messenger RNA. Most genes in the nuclei of eukaryotes contain introns, as do mitochondrial and chloroplast genes. [NIH]

Intubation: Introduction of a tube into a hollow organ to restore or maintain patency if obstructed. It is differentiated from catheterization in that the insertion of a catheter is usually performed for the introducing or withdrawing of fluids from the body. [NIH]

Invasive: 1. Having the quality of invasiveness. 2. Involving puncture or incision of the skin

or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Involuntary: Reaction occurring without intention or volition. [NIH]

Ionizing: Radiation comprising charged particles, e. g. electrons, protons, alpha-particles, etc., having sufficient kinetic energy to produce ionization by collision. [NIH]

Ions: An atom or group of atoms that have a positive or negative electric charge due to a gain (negative charge) or loss (positive charge) of one or more electrons. Atoms with a positive charge are known as cations; those with a negative charge are anions. [NIH]

Irradiation: The use of high-energy radiation from x-rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Irradiation is also called radiation therapy, radiotherapy, and x-ray therapy. [NIH]

Irrigation: The washing of a body cavity or surface by flowing solution which is inserted and then removed. Any drug in the irrigation solution may be absorbed. [NIH]

Ischemia: Deficiency of blood in a part, due to functional constriction or actual obstruction of a blood vessel. [EU]

Ischemic stroke: A condition in which the blood supply to part of the brain is cut off. Also called "plug-type" strokes. Blocked arteries starve areas of the brain controlling sight, speech, sensation, and movement so that these functions are partially or completely lost. Ischemic stroke is the most common type of stroke, accounting for 80 percent of all strokes. Most ischemic strokes are caused by a blood clot called a thrombus, which blocks blood flow in the arteries feeding the brain, usually the carotid artery in the neck, the major vessel bringing blood to the brain. When it becomes blocked, the risk of stroke is very high. [NIH]

Islet: Cell producing insulin in pancreas. [NIH]

Isoleucine: An essential branched-chain amino acid found in many proteins. It is an isomer of LEUCINE. It is important in hemoglobin synthesis and regulation of blood sugar and energy levels. [NIH]

Isothiocyanates: Organic compounds with the general formula R-NCS. [NIH]

Jejunum: That portion of the small intestine which extends from the duodenum to the ileum; called also intestinum jejunum. [EU]

Joint: The point of contact between elements of an animal skeleton with the parts that surround and support it. [NIH]

Kb: A measure of the length of DNA fragments, 1 Kb = 1000 base pairs. The largest DNA fragments are up to 50 kilobases long. [NIH]

Keratinocyte growth factor: A substance that stimulates the growth of epithelial cells that line the surface of the mouth and intestinal tract. [NIH]

Keratolytic: An agent that promotes keratolysis. [EU]

Keto: It consists of 8 carbon atoms and within the endotoxins, it connects poysaccharide and lipid A. [NIH]

Ketone Bodies: Chemicals that the body makes when there is not enough insulin in the blood and it must break down fat for its energy. Ketone bodies can poison and even kill body cells. When the body does not have the help of insulin, the ketones build up in the

blood and then "spill" over into the urine so that the body can get rid of them. The body can also rid itself of one type of ketone, called acetone, through the lungs. This gives the breath a fruity odor. Ketones that build up in the body for a long time lead to serious illness and coma. [NIH]

Ketosis: A condition of having ketone bodies build up in body tissues and fluids. The signs of ketosis are nausea, vomiting, and stomach pain. Ketosis can lead to ketoacidosis. [NIH]

Kidney Disease: Any one of several chronic conditions that are caused by damage to the cells of the kidney. People who have had diabetes for a long time may have kidney damage. Also called nephropathy. [NIH]

Kidney Failure: The inability of a kidney to excrete metabolites at normal plasma levels under conditions of normal loading, or the inability to retain electrolytes under conditions of normal intake. In the acute form (kidney failure, acute), it is marked by uremia and usually by oliguria or anuria, with hyperkalemia and pulmonary edema. The chronic form (kidney failure, chronic) is irreversible and requires hemodialysis. [NIH]

Kidney Failure, Acute: A clinical syndrome characterized by a sudden decrease in glomerular filtration rate, often to values of less than 1 to 2 ml per minute. It is usually associated with oliguria (urine volumes of less than 400 ml per day) and is always associated with biochemical consequences of the reduction in glomerular filtration rate such as a rise in blood urea nitrogen (BUN) and serum creatinine concentrations. [NIH]

Kidney Failure, Chronic: An irreversible and usually progressive reduction in renal function in which both kidneys have been damaged by a variety of diseases to the extent that they are unable to adequately remove the metabolic products from the blood and regulate the body's electrolyte composition and acid-base balance. Chronic kidney failure requires hemodialysis or surgery, usually kidney transplantation. [NIH]

Kinetic: Pertaining to or producing motion. [EU]

Labyrinth: The internal ear; the essential part of the organ of hearing. It consists of an osseous and a membranous portion. [NIH]

Lactation: The period of the secretion of milk. [EU]

Laparoscopy: Examination, therapy or surgery of the abdomen's interior by means of a laparoscope. [NIH]

Large Intestine: The part of the intestine that goes from the cecum to the rectum. The large intestine absorbs water from stool and changes it from a liquid to a solid form. The large intestine is 5 feet long and includes the appendix, cecum, colon, and rectum. Also called colon. [NIH]

Laryngeal: Having to do with the larynx. [NIH]

Larynx: An irregularly shaped, musculocartilaginous tubular structure, lined with mucous membrane, located at the top of the trachea and below the root of the tongue and the hyoid bone. It is the essential sphincter guarding the entrance into the trachea and functioning secondarily as the organ of voice. [NIH]

Latent: Phoria which occurs at one distance or another and which usually has no troublesome effect. [NIH]

Laxative: An agent that acts to promote evacuation of the bowel; a cathartic or purgative. [EU]

Least-Squares Analysis: A principle of estimation in which the estimates of a set of parameters in a statistical model are those quantities minimizing the sum of squared differences between the observed values of a dependent variable and the values predicted by the model. [NIH]

Leprosy: A chronic granulomatous infection caused by Mycobacterium leprae. The granulomatous lesions are manifested in the skin, the mucous membranes, and the peripheral nerves. Two polar or principal types are lepromatous and tuberculoid. [NIH]

Leptin: A 16-kD peptide hormone secreted from white adipocytes and implicated in the regulation of food intake and energy balance. Leptin provides the key afferent signal from fat cells in the feedback system that controls body fat stores. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Lethargy: Abnormal drowsiness or stupor; a condition of indifference. [EU]

Leucine: An essential branched-chain amino acid important for hemoglobin formation. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Leukocytes: White blood cells. These include granular leukocytes (basophils, eosinophils, and neutrophils) as well as non-granular leukocytes (lymphocytes and monocytes). [NIH]

Library Services: Services offered to the library user. They include reference and circulation. [NIH]

Ligament: A band of fibrous tissue that connects bones or cartilages, serving to support and strengthen joints. [EU]

Likelihood Functions: Functions constructed from a statistical model and a set of observed data which give the probability of that data for various values of the unknown model parameters. Those parameter values that maximize the probability are the maximum likelihood estimates of the parameters. [NIH]

Linear Models: Statistical models in which the value of a parameter for a given value of a factor is assumed to be equal to a + bx, where a and b are constants. The models predict a linear regression. [NIH]

Linkage: The tendency of two or more genes in the same chromosome to remain together from one generation to the next more frequently than expected according to the law of independent assortment. [NIH]

Lipase: An enzyme of the hydrolase class that catalyzes the reaction of triacylglycerol and water to yield diacylglycerol and a fatty acid anion. It is produced by glands on the tongue and by the pancreas and initiates the digestion of dietary fats. (From Dorland, 27th ed) EC 3.1.1.3. [NIH]

Lipid: Fat. [NIH]

Lipid A: Lipid A is the biologically active component of lipopolysaccharides. It shows strong endotoxic activity and exhibits immunogenic properties. [NIH]

Lipid Peroxidation: Peroxidase catalyzed oxidation of lipids using hydrogen peroxide as an electron acceptor. [NIH]

Lipolysis: The hydrolysis of lipids. [NIH]

Lipopolysaccharide: Substance consisting of polysaccaride and lipid. [NIH]

Lipoprotein: Any of the lipid-protein complexes in which lipids are transported in the blood; lipoprotein particles consist of a spherical hydrophobic core of triglycerides or cholesterol esters surrounded by an amphipathic monolayer of phospholipids, cholesterol, and apolipoproteins; the four principal classes are high-density, low-density, and very-low-density lipoproteins and chylomicrons. [EU]

Lipoprotein Lipase: An enzyme of the hydrolase class that catalyzes the reaction of triacylglycerol and water to yield diacylglycerol and a fatty acid anion. The enzyme hydrolyzes triacylglycerols in chylomicrons, very-low-density lipoproteins, low-density lipoproteins, and diacylglycerols. It occurs on capillary endothelial surfaces, especially in

mammary, muscle, and adipose tissue. Genetic deficiency of the enzyme causes familial hyperlipoproteinemia Type I. (Dorland, 27th ed) EC 3.1.1.34. [NIH]

Lipoprotein(a): A family of lipoprotein particles varying in density and size depending on the protein-lipid ratio and the protein composition. These particles consist of apolipoprotein B-100 covalently linked to apolipoprotein-a by one or two disulfide bonds. There is a correlation between high plasma levels of this lipoprotein and increased risk for atherosclerotic cardiovascular disease. [NIH]

Lithotripsy: The destruction of a calculus of the kidney, ureter, bladder, or gallbladder by physical forces, including crushing with a lithotriptor through a catheter. Focused percutaneous ultrasound and focused hydraulic shock waves may be used without surgery. Lithotripsy does not include the dissolving of stones by acids or litholysis. Lithotripsy by laser is laser lithotripsy. [NIH]

Liver: A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

Liver Cirrhosis: Liver disease in which the normal microcirculation, the gross vascular anatomy, and the hepatic architecture have been variably destroyed and altered with fibrous septa surrounding regenerated or regenerating parenchymal nodules. [NIH]

Liver scan: An image of the liver created on a computer screen or on film. A radioactive substance is injected into a blood vessel and travels through the bloodstream. It collects in the liver, especially in abnormal areas, and can be detected by the scanner. [NIH]

Liver Transplantation: The transference of a part of or an entire liver from one human or animal to another. [NIH]

Lobe: A portion of an organ such as the liver, lung, breast, or brain. [NIH]

Localization: The process of determining or marking the location or site of a lesion or disease. May also refer to the process of keeping a lesion or disease in a specific location or site. [NIH]

Localized: Cancer which has not metastasized yet. [NIH]

Locomotion: Movement or the ability to move from one place or another. It can refer to humans, vertebrate or invertebrate animals, and microorganisms. [NIH]

Locomotor: Of or pertaining to locomotion; pertaining to or affecting the locomotive apparatus of the body. [EU]

Logistic Models: Statistical models which describe the relationship between a qualitative dependent variable (that is, one which can take only certain discrete values, such as the presence or absence of a disease) and an independent variable. A common application is in epidemiology for estimating an individual's risk (probability of a disease) as a function of a given risk factor. [NIH]

Longitudinal Studies: Studies in which variables relating to an individual or group of individuals are assessed over a period of time. [NIH]

Longitudinal study: Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups that differ in exposure levels. [NIH]

Loop: A wire usually of platinum bent at one end into a small loop (usually 4 mm inside diameter) and used in transferring microorganisms. [NIH]

Lovastatin: A fungal metabolite isolated from cultures of Aspergillus terreus. The compound is a potent anticholesteremic agent. It inhibits 3-hydroxy-3-methylglutaryl coenzyme A reductase (hydroxymethylglutaryl CoA reductases), which is the rate-limiting enzyme in cholesterol biosynthesis. It also stimulates the production of low-density lipoprotein receptors in the liver. [NIH]

Low-calorie diet: Caloric restriction of about 800 to 1,500 calories (approximately 12 to 15 kcal/kg of body weight) per day. [NIH]

Low-density lipoprotein: Lipoprotein that contains most of the cholesterol in the blood. LDL carries cholesterol to the tissues of the body, including the arteries. A high level of LDL increases the risk of heart disease. LDL typically contains 60 to 70 percent of the total serum cholesterol and both are directly correlated with CHD risk. [NIH]

Lower Esophageal Sphincter: The muscle between the esophagus and stomach. When a person swallows, this muscle relaxes to let food pass from the esophagus to the stomach. It stays closed at other times to keep stomach contents from flowing back into the esophagus. [NIH]

Lubricants: Oily or slippery substances. [NIH]

Lumen: The cavity or channel within a tube or tubular organ. [EU]

Lupus: A form of cutaneous tuberculosis. It is seen predominantly in women and typically involves the nasal, buccal, and conjunctival mucosa. [NIH]

Lymph: The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease. [NIH]

Lymph node: A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Also known as a lymph gland. Lymph nodes are spread out along lymphatic vessels and contain many lymphocytes, which filter the lymphatic fluid (lymph). [NIH]

Lymphatic: The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

Lymphatic system: The tissues and organs that produce, store, and carry white blood cells that fight infection and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and a network of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body. [NIH]

Lymphocyte: A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and diseases. [NIH]

Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Lymphoma: A general term for various neoplastic diseases of the lymphoid tissue. [NIH]

Lysine: An essential amino acid. It is often added to animal feed. [NIH]

Lytic: 1. Pertaining to lysis or to a lysin. 2. Producing lysis. [EU]

Macronutrients: Nutrients in the diet that are the key sources of energy, namely protein, fat, and carbohydrates. [NIH]

Macrophage: A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells. [NIH]

Magnetic Resonance Imaging: Non-invasive method of demonstrating internal anatomy based on the principle that atomic nuclei in a strong magnetic field absorb pulses of radiofrequency energy and emit them as radiowaves which can be reconstructed into

computerized images. The concept includes proton spin tomographic techniques. [NIH]

Malabsorption: Impaired intestinal absorption of nutrients. [EU]

Malignancy: A cancerous tumor that can invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malnutrition: A condition caused by not eating enough food or not eating a balanced diet. [NIH]

Mammary: Pertaining to the mamma, or breast. [EU]

Mammogram: An x-ray of the breast. [NIH]

Manifest: Being the part or aspect of a phenomenon that is directly observable : concretely expressed in behaviour. [EU]

Mannitol: A diuretic and renal diagnostic aid related to sorbitol. It has little significant energy value as it is largely eliminated from the body before any metabolism can take place. It can be used to treat oliguria associated with kidney failure or other manifestations of inadequate renal function and has been used for determination of glomerular filtration rate. Mannitol is also commonly used as a research tool in cell biological studies, usually to control osmolarity. [NIH]

Manometry: Tests that measure muscle pressure and movements in the GI tract. [NIH]

Mean blood pressure: The average blood pressure, taking account of the rise and fall that occurs with each heartbeat. It is often estimated by multiplying the diastolic pressure by two, adding the systolic pressure, and then dividing this sum by three. [NIH]

Meat: The edible portions of any animal used for food including domestic mammals (the major ones being cattle, swine, and sheep) along with poultry, fish, shellfish, and game. [NIH]

Medial: Lying near the midsaggital plane of the body; opposed to lateral. [NIH]

Mediate: Indirect; accomplished by the aid of an intervening medium. [EU]

Mediator: An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

Medical Records: Recording of pertinent information concerning patient's illness or illnesses. [NIH]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

Megaloblastic: A large abnormal red blood cell appearing in the blood in pernicious anaemia. [EU]

Melanin: The substance that gives the skin its color. [NIH]

Melanocytes: Epidermal dendritic pigment cells which control long-term morphological color changes by alteration in their number or in the amount of pigment they produce and store in the pigment containing organelles called melanosomes. Melanophores are larger cells which do not exist in mammals. [NIH]

Melanoma: A form of skin cancer that arises in melanocytes, the cells that produce pigment. Melanoma usually begins in a mole. [NIH]

Melanosis: Disorders of increased melanin pigmentation that develop without preceding inflammatory disease. [NIH]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

Memory: Complex mental function having four distinct phases: (1) memorizing or learning, (2) retention, (3) recall, and (4) recognition. Clinically, it is usually subdivided into immediate, recent, and remote memory. [NIH]

Meninges: The three membranes that cover and protect the brain and spinal cord. [NIH]

Menopause: Permanent cessation of menstruation. [NIH]

Menstrual Cycle: The period of the regularly recurring physiologic changes in the endometrium occurring during the reproductive period in human females and some primates and culminating in partial sloughing of the endometrium (menstruation). [NIH]

Menstruation: The normal physiologic discharge through the vagina of blood and mucosal tissues from the nonpregnant uterus. [NIH]

Mental Health: The state wherein the person is well adjusted. [NIH]

Mentors: Senior professionals who provide guidance, direction and support to those persons desirous of improvement in academic positions, administrative positions or other career development situations. [NIH]

Mesenchymal: Refers to cells that develop into connective tissue, blood vessels, and lymphatic tissue. [NIH]

Mesenteric: Pertaining to the mesentery : a membranous fold attaching various organs to the body wall. [EU]

Metabolic disorder: A condition in which normal metabolic processes are disrupted, usually because of a missing enzyme. [NIH]

Methionine: A sulfur containing essential amino acid that is important in many body functions. It is a chelating agent for heavy metals. [NIH]

Methylcellulose: Methylester of cellulose. Methylcellulose is used as an emulsifying and suspending agent in cosmetics, pharmaceutics and the chemical industry. It is used therapeutically as a bulk laxative. [NIH]

MI: Myocardial infarction. Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Microbe: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

Microcirculation: The vascular network lying between the arterioles and venules; includes capillaries, metarterioles and arteriovenous anastomoses. Also, the flow of blood through this network. [NIH]

Microdialysis: A technique for measuring extracellular concentrations of substances in tissues, usually in vivo, by means of a small probe equipped with a semipermeable membrane. Substances may also be introduced into the extracellular space through the membrane. [NIH]

Microorganism: An organism that can be seen only through a microscope. Microorganisms include bacteria, protozoa, algae, and fungi. Although viruses are not considered living organisms, they are sometimes classified as microorganisms. [NIH]

Micro-organism: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microscopy: The application of microscope magnification to the study of materials that cannot be properly seen by the unaided eye. [NIH]

Midaxillary line: An imaginary vertical line that passes midway between the anterior and posterior axillary (armpit) folds. [NIH]

Milligram: A measure of weight. A milligram is approximately 450,000-times smaller than a pound and 28,000-times smaller than an ounce. [NIH]

Milliliter: A measure of volume for a liquid. A milliliter is approximately 950-times smaller than a quart and 30-times smaller than a fluid ounce. A milliliter of liquid and a cubic centimeter (cc) of liquid are the same. [NIH]

Millimeter: A measure of length. A millimeter is approximately 26-times smaller than an inch. [NIH]

Mitochondrial Swelling: Increase in volume of mitochondria due to an influx of fluid; it occurs in hypotonic solutions due to osmotic pressure and in isotonic solutions as a result of altered permeability of the membranes of respiring mitochondria. [NIH]

Mitosis: A method of indirect cell division by means of which the two daughter nuclei normally receive identical complements of the number of chromosomes of the somatic cells of the species. [NIH]

Mobility: Capability of movement, of being moved, or of flowing freely. [EU]

Mobilization: The process of making a fixed part or stored substance mobile, as by separating a part from surrounding structures to make it accessible for an operative procedure or by causing release into the circulation for body use of a substance stored in the body. [EU]

Modeling: A treatment procedure whereby the therapist presents the target behavior which the learner is to imitate and make part of his repertoire. [NIH]

Modification: A change in an organism, or in a process in an organism, that is acquired from its own activity or environment. [NIH]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Molecular Probes: A group of atoms or molecules attached to other molecules or cellular structures and used in studying the properties of these molecules and structures. Radioactive DNA or RNA sequences are used in molecular genetics to detect the presence of a complementary sequence by molecular hybridization. [NIH]

Molecule: A chemical made up of two or more atoms. The atoms in a molecule can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms. [NIH]

Monitor: An apparatus which automatically records such physiological signs as respiration, pulse, and blood pressure in an anesthetized patient or one undergoing surgical or other procedures. [NIH]

Monoclonal: An antibody produced by culturing a single type of cell. It therefore consists of a single species of immunoglobulin molecules. [NIH]

Monoclonal antibodies: Laboratory-produced substances that can locate and bind to cancer cells wherever they are in the body. Many monoclonal antibodies are used in cancer detection or therapy; each one recognizes a different protein on certain cancer cells. Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or

radioactive material directly to a tumor. [NIH]

Monocytes: Large, phagocytic mononuclear leukocytes produced in the vertebrate bone marrow and released into the blood; contain a large, oval or somewhat indented nucleus surrounded by voluminous cytoplasm and numerous organelles. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

Monotherapy: A therapy which uses only one drug. [EU]

Monounsaturated fat: An unsaturated fat that is found primarily in plant foods, including olive and canola oils. [NIH]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

Motility: The ability to move spontaneously. [EU]

Motion Sickness: Sickness caused by motion, as sea sickness, train sickness, car sickness, and air sickness. [NIH]

Motor Activity: The physical activity of an organism as a behavioral phenomenon. [NIH]

Mucins: A secretion containing mucopolysaccharides and protein that is the chief constituent of mucus. [NIH]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Muscle Contraction: A process leading to shortening and/or development of tension in muscle tissue. Muscle contraction occurs by a sliding filament mechanism whereby actin filaments slide inward among the myosin filaments. [NIH]

Muscle Fibers: Large single cells, either cylindrical or prismatic in shape, that form the basic unit of muscle tissue. They consist of a soft contractile substance enclosed in a tubular sheath. [NIH]

Muscular Atrophy: Derangement in size and number of muscle fibers occurring with aging, reduction in blood supply, or following immobilization, prolonged weightlessness, malnutrition, and particularly in denervation. [NIH]

Muscular Dystrophies: A general term for a group of inherited disorders which are characterized by progressive degeneration of skeletal muscles. [NIH]

Mycophenolate mofetil: A drug that is being studied for its effectiveness in preventing graft-versus-host disease and autoimmune disorders. [NIH]

Mycotoxins: Toxins derived from bacteria or fungi. [NIH]

Myocardial infarction: Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Myocardial Ischemia: A disorder of cardiac function caused by insufficient blood flow to the muscle tissue of the heart. The decreased blood flow may be due to narrowing of the coronary arteries (coronary arteriosclerosis), to obstruction by a thrombus (coronary thrombosis), or less commonly, to diffuse narrowing of arterioles and other small vessels within the heart. Severe interruption of the blood supply to the myocardial tissue may result in necrosis of cardiac muscle (myocardial infarction). [NIH]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Myosin: Chief protein in muscle and the main constituent of the thick filaments of muscle fibers. In conjunction with actin, it is responsible for the contraction and relaxation of muscles. [NIH]

Myotonic Dystrophy: A condition presenting muscle weakness and wasting which may be

progressive. [NIH]

Naive: Used to describe an individual who has never taken a certain drug or class of drugs (e. g., AZT-naive, antiretroviral-naive), or to refer to an undifferentiated immune system cell. [NIH]

Naphthoquinones: Naphthalene rings which contain two ketone moieties in any position. They can be substituted in any position except at the ketone groups. [NIH]

Narcosis: A general and nonspecific reversible depression of neuronal excitability, produced by a number of physical and chemical aspects, usually resulting in stupor. [NIH]

Natural selection: A part of the evolutionary process resulting in the survival and reproduction of the best adapted individuals. [NIH]

Nausea: An unpleasant sensation in the stomach usually accompanied by the urge to vomit. Common causes are early pregnancy, sea and motion sickness, emotional stress, intense pain, food poisoning, and various enteroviruses. [NIH]

NCI: National Cancer Institute. NCI, part of the National Institutes of Health of the United States Department of Health and Human Services, is the federal government's principal agency for cancer research. NCI conducts, coordinates, and funds cancer research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer. Access the NCI Web site at http://cancer.gov. [NIH]

Necrosis: A pathological process caused by the progressive degradative action of enzymes that is generally associated with severe cellular trauma. It is characterized by mitochondrial swelling, nuclear flocculation, uncontrolled cell lysis, and ultimately cell death. [NIH]

Need: A state of tension or dissatisfaction felt by an individual that impels him to action toward a goal he believes will satisfy the impulse. [NIH]

Neonatal: Pertaining to the first four weeks after birth. [EU]

Neoplasia: Abnormal and uncontrolled cell growth. [NIH]

Neoplasms: New abnormal growth of tissue. Malignant neoplasms show a greater degree of anaplasia and have the properties of invasion and metastasis, compared to benign neoplasms. [NIH]

Neoplastic: Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining to neoplasia (= the formation of a neoplasm). [EU]

Nephropathy: Disease of the kidneys. [EU]

Nerve: A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

Nervous System: The entire nerve apparatus composed of the brain, spinal cord, nerves and ganglia. [NIH]

Neural: 1. Pertaining to a nerve or to the nerves. 2. Situated in the region of the spinal axis, as the neutral arch. [EU]

Neural tube defects: These defects include problems stemming from fetal development of the spinal cord, spine, brain, and skull, and include birth defects such as spina bifida, anencephaly, and encephalocele. Neural tube defects occur early in pregnancy at about 4 to 6 weeks, usually before a woman knows she is pregnant. Many babies with neural tube defects have difficulty walking and with bladder and bowel control. [NIH]

Neuroendocrine: Having to do with the interactions between the nervous system and the endocrine system. Describes certain cells that release hormones into the blood in response to stimulation of the nervous system. [NIH]

Neurologic: Having to do with nerves or the nervous system. [NIH]

Neuronal: Pertaining to a neuron or neurons (= conducting cells of the nervous system). [EU]

Neurons: The basic cellular units of nervous tissue. Each neuron consists of a body, an axon, and dendrites. Their purpose is to receive, conduct, and transmit impulses in the nervous system. [NIH]

Neuropathy: A problem in any part of the nervous system except the brain and spinal cord. Neuropathies can be caused by infection, toxic substances, or disease. [NIH]

Neuropeptide: A member of a class of protein-like molecules made in the brain. Neuropeptides consist of short chains of amino acids, with some functioning as neurotransmitters and some functioning as hormones. [NIH]

Neurotransmitters: Endogenous signaling molecules that alter the behavior of neurons or effector cells. Neurotransmitter is used here in its most general sense, including not only messengers that act directly to regulate ion channels, but also those that act through second messenger systems, and those that act at a distance from their site of release. Included are neuromodulators, neuroregulators, neuromediators, and neurohumors, whether or not acting at synapses. [NIH]

Neutrons: Electrically neutral elementary particles found in all atomic nuclei except light hydrogen; the mass is equal to that of the proton and electron combined and they are unstable when isolated from the nucleus, undergoing beta decay. Slow, thermal, epithermal, and fast neutrons refer to the energy levels with which the neutrons are ejected from heavier nuclei during their decay. [NIH]

Neutrophils: Granular leukocytes having a nucleus with three to five lobes connected by slender threads of chromatin, and cytoplasm containing fine inconspicuous granules and stainable by neutral dyes. [NIH]

Niacin: Water-soluble vitamin of the B complex occurring in various animal and plant tissues. Required by the body for the formation of coenzymes NAD and NADP. Has pellagra-curative, vasodilating, and antilipemic properties. [NIH]

Nidation: Implantation of the conceptus in the endometrium. [EU]

Nitric Oxide: A free radical gas produced endogenously by a variety of mammalian cells. It is synthesized from arginine by a complex reaction, catalyzed by nitric oxide synthase. Nitric oxide is endothelium-derived relaxing factor. It is released by the vascular endothelium and mediates the relaxation induced by some vasodilators such as acetylcholine and bradykinin. It also inhibits platelet aggregation, induces disaggregation of aggregated platelets, and inhibits platelet adhesion to the vascular endothelium. Nitric oxide activates cytosolic guanylate cyclase and thus elevates intracellular levels of cyclic GMP. [NIH]

Nitrogen: An element with the atomic symbol N, atomic number 7, and atomic weight 14. Nitrogen exists as a diatomic gas and makes up about 78% of the earth's atmosphere by volume. It is a constituent of proteins and nucleic acids and found in all living cells. [NIH]

Norepinephrine: Precursor of epinephrine that is secreted by the adrenal medulla and is a widespread central and autonomic neurotransmitter. Norepinephrine is the principal transmitter of most postganglionic sympathetic fibers and of the diffuse projection system in the brain arising from the locus ceruleus. It is also found in plants and is used pharmacologically as a sympathomimetic. [NIH]

Normotensive: 1. Characterized by normal tone, tension, or pressure, as by normal blood pressure. 2. A person with normal blood pressure. [EU]

Nuclear: A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [NIH]

Nuclei: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nucleic acid: Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nutrition Assessment: Evaluation and measurement of nutritional variables in order to assess the level of nutrition or the nutritional status of the individual. Nutrition surveys may be used in making the assessment. [NIH]

Nutritional Status: State of the body in relation to the consumption and utilization of nutrients. [NIH]

Observational study: An epidemiologic study that does not involve any intervention, experimental or otherwise. Such a study may be one in which nature is allowed to take its course, with changes in one characteristic being studied in relation to changes in other characteristics. Analytical epidemiologic methods, such as case-control and cohort study designs, are properly called observational epidemiology because the investigator is observing without intervention other than to record, classify, count, and statistically analyze results. [NIH]

Octreotide: A potent, long-acting somatostatin octapeptide analog which has a wide range of physiological actions. It inhibits growth hormone secretion, is effective in the treatment of hormone-secreting tumors from various organs, and has beneficial effects in the management of many pathological states including diabetes mellitus, orthostatic hypertension, hyperinsulinism, hypergastrinemia, and small bowel fistula. [NIH]

Ocular: 1. Of, pertaining to, or affecting the eye. 2. Eyepiece. [EU]

Ointments: Semisolid preparations used topically for protective emollient effects or as a vehicle for local administration of medications. Ointment bases are various mixtures of fats, waxes, animal and plant oils and solid and liquid hydrocarbons. [NIH]

Oligosaccharides: Carbohydrates consisting of between two and ten monosaccharides connected by either an alpha- or beta-glycosidic link. They are found throughout nature in both the free and bound form. [NIH]

Oliguria: Clinical manifestation of the urinary system consisting of a decrease in the amount of urine secreted. [NIH]

Oncogene: A gene that normally directs cell growth. If altered, an oncogene can promote or allow the uncontrolled growth of cancer. Alterations can be inherited or caused by an environmental exposure to carcinogens. [NIH]

Opacity: Degree of density (area most dense taken for reading). [NIH]

Opsin: A visual pigment protein found in the retinal rods. It combines with retinaldehyde to form rhodopsin. [NIH]

Optic Chiasm: The X-shaped structure formed by the meeting of the two optic nerves. At the optic chiasm the fibers from the medial part of each retina cross to project to the other side of the brain while the lateral retinal fibers continue on the same side. As a result each half of the brain receives information about the contralateral visual field from both eyes. [NIH]

Organelles: Specific particles of membrane-bound organized living substances present in eukaryotic cells, such as the mitochondria; the golgi apparatus; endoplasmic reticulum;

lysomomes; plastids; and vacuoles. [NIH]

Orthostatic: Pertaining to or caused by standing erect. [EU]

Osmolarity: The concentration of osmotically active particles expressed in terms of osmoles of solute per litre of solution. [EU]

Osmotic: Pertaining to or of the nature of osmosis (= the passage of pure solvent from a solution of lesser to one of greater solute concentration when the two solutions are separated by a membrane which selectively prevents the passage of solute molecules, but is permeable to the solvent). [EU]

Ossicles: The hammer, anvil and stirrup, the small bones of the middle ear, which transmit the vibrations from the tympanic membrane to the oval window. [NIH]

Osteoporosis: Reduction of bone mass without alteration in the composition of bone, leading to fractures. Primary osteoporosis can be of two major types: postmenopausal osteoporosis and age-related (or senile) osteoporosis. [NIH]

Otosclerosis: The formation of spongy bone in the labyrinth capsule. The ossicles can become fixed and unable to transmit sound vibrations, thereby causing deafness. [NIH]

Outpatient: A patient who is not an inmate of a hospital but receives diagnosis or treatment in a clinic or dispensary connected with the hospital. [NIH]

Ovaries: The pair of female reproductive glands in which the ova, or eggs, are formed. The ovaries are located in the pelvis, one on each side of the uterus. [NIH]

Overweight: An excess of body weight but not necessarily body fat; a body mass index of 25 to 29.9 kg/m2. [NIH]

Ovulation: The discharge of a secondary oocyte from a ruptured graafian follicle. [NIH]

Ovum: A female germ cell extruded from the ovary at ovulation. [NIH]

Oxidants: Oxidizing agents or electron-accepting molecules in chemical reactions in which electrons are transferred from one molecule to another (oxidation-reduction). In vivo, it appears that phagocyte-generated oxidants function as tumor promoters or cocarcinogens rather than as complete carcinogens perhaps because of the high levels of endogenous antioxidant defenses. It is also thought that oxidative damage in joints may trigger the autoimmune response that characterizes the persistence of the rheumatoid disease process. [NIH]

Oxidation: The act of oxidizing or state of being oxidized. Chemically it consists in the increase of positive charges on an atom or the loss of negative charges. Most biological oxidations are accomplished by the removal of a pair of hydrogen atoms (dehydrogenation) from a molecule. Such oxidations must be accompanied by reduction of an acceptor molecule. Univalent o. indicates loss of one electron; divalent o., the loss of two electrons. [EU]

Oxidation-Reduction: A chemical reaction in which an electron is transferred from one molecule to another. The electron-donating molecule is the reducing agent or reductant; the electron-accepting molecule is the oxidizing agent or oxidant. Reducing and oxidizing agents function as conjugate reductant-oxidant pairs or redox pairs (Lehninger, Principles of Biochemistry, 1982, p471). [NIH]

Oxidative Phosphorylation: Electron transfer through the cytochrome system liberating free energy which is transformed into high-energy phosphate bonds. [NIH]

Oxidative Stress: A disturbance in the prooxidant-antioxidant balance in favor of the former, leading to potential damage. Indicators of oxidative stress include damaged DNA bases, protein oxidation products, and lipid peroxidation products (Sies, Oxidative Stress, 1991, pxv-xvi). [NIH]

Oxygen Consumption: The oxygen consumption is determined by calculating the difference between the amount of oxygen inhaled and exhaled. [NIH]

Oxygenation: The process of supplying, treating, or mixing with oxygen. No:1245 - oxygenation the process of supplying, treating, or mixing with oxygen. [EU]

Palate: The structure that forms the roof of the mouth. It consists of the anterior hard palate and the posterior soft palate. [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

Palmitic Acid: A common saturated fatty acid found in fats and waxes including olive oil, palm oil, and body lipids. [NIH]

Pancreas: A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the Islets of Langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Pancreatic: Having to do with the pancreas. [NIH]

Pancreatic cancer: Cancer of the pancreas, a salivary gland of the abdomen. [NIH]

Pancreatic Ducts: Ducts that collect pancreatic juice from the pancreas and supply it to the duodenum. [NIH]

Pancreatic Juice: The fluid containing digestive enzymes secreted by the pancreas in response to food in the duodenum. [NIH]

Pancreatitis: Acute or chronic inflammation of the pancreas, which may be asymptomatic or symptomatic, and which is due to autodigestion of a pancreatic tissue by its own enzymes. It is caused most often by alcoholism or biliary tract disease; less commonly it may be associated with hyperlipaemia, hyperparathyroidism, abdominal trauma (accidental or operative injury), vasculitis, or uraemia. [EU]

Paneth Cells: Epithelial cells found in the basal part of the intestinal glands (crypts of Lieberkuhn). Paneth cells synthesize and secrete lysozyme and cryptdins. [NIH]

Papilla: A small nipple-shaped elevation. [NIH]

Paraffin: A mixture of solid hydrocarbons obtained from petroleum. It has a wide range of uses including as a stiffening agent in ointments, as a lubricant, and as a topical anti-inflammatory. It is also commonly used as an embedding material in histology. [NIH]

Parenteral: Not through the alimentary canal but rather by injection through some other route, as subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, etc. [EU]

Parenteral Nutrition: The administering of nutrients for assimilation and utilization by a patient who cannot maintain adequate nutrition by enteral feeding alone. Nutrients are administered by a route other than the alimentary canal (e.g., intravenously, subcutaneously). [NIH]

Paroxysmal: Recurring in paroxysms (= spasms or seizures). [EU]

Partial remission: The shrinking, but not complete disappearance, of a tumor in response to therapy. Also called partial response. [NIH]

Particle: A tiny mass of material. [EU]

Pathogenesis: The cellular events and reactions that occur in the development of disease. [NIH]

Pathologic: 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural

and functional changes in tissues and organs of the body caused by the disease). [EU]

Pathologic Processes: The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

Pathophysiology: Altered functions in an individual or an organ due to disease. [NIH]

Patient Compliance: Voluntary cooperation of the patient in following a prescribed regimen. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs. [NIH]

Patient Selection: Criteria and standards used for the determination of the appropriateness of the inclusion of patients with specific conditions in proposed treatment plans and the criteria used for the inclusion of subjects in various clinical trials and other research protocols. [NIH]

Pedigree: A record of one's ancestors, offspring, siblings, and their offspring that may be used to determine the pattern of certain genes or disease inheritance within a family. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

Penicillin: An antibiotic drug used to treat infection. [NIH]

Penis: The external reproductive organ of males. It is composed of a mass of erectile tissue enclosed in three cylindrical fibrous compartments. Two of the three compartments, the corpus cavernosa, are placed side-by-side along the upper part of the organ. The third compartment below, the corpus spongiosum, houses the urethra. [NIH]

Pentosephosphate Pathway: A pathway of hexose oxidation in which glucose-6-phosphate undergoes two successive oxidations by NADP, the final one being an oxidative decarboxylation to form a pentose phosphate. [NIH]

Pepsin: An enzyme made in the stomach that breaks down proteins. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Peptide T: N-(N-(N(2)-(N-(N-(N-(N-D-Alanyl L-seryl)-L-threonyl)-L-threonyl) L-threonyl)-L-asparaginyl)-L-tyrosyl) L-threonine. Octapeptide sharing sequence homology with HIV envelope protein gp120. It is potentially useful as antiviral agent in AIDS therapy. The core pentapeptide sequence, TTNYT, consisting of amino acids 4-8 in peptide T, is the HIV envelope sequence required for attachment to the CD4 receptor. [NIH]

Percutaneous: Performed through the skin, as injection of radiopacque material in radiological examination, or the removal of tissue for biopsy accomplished by a needle. [EU]

Perfusion: Bathing an organ or tissue with a fluid. In regional perfusion, a specific area of the body (usually an arm or a leg) receives high doses of anticancer drugs through a blood vessel. Such a procedure is performed to treat cancer that has not spread. [NIH]

Pericardium: The fibroserous sac surrounding the heart and the roots of the great vessels. [NIH]

Perinatal: Pertaining to or occurring in the period shortly before and after birth; variously defined as beginning with completion of the twentieth to twenty-eighth week of gestation and ending 7 to 28 days after birth. [EU]

Periodontal disease: Disease involving the supporting structures of the teeth (as the gums and periodontal membranes). [NIH]

Periodontitis: Inflammation of the periodontal membrane; also called periodontitis simplex. [NIH]

Perioperative: Around the time of surgery; usually lasts from the time of going into the

hospital or doctor's office for surgery until the time the patient goes home. [NIH]

Peripheral blood: Blood circulating throughout the body. [NIH]

Peripheral Nervous System: The nervous system outside of the brain and spinal cord. The peripheral nervous system has autonomic and somatic divisions. The autonomic nervous system includes the enteric, parasympathetic, and sympathetic subdivisions. The somatic nervous system includes the cranial and spinal nerves and their ganglia and the peripheral sensory receptors. [NIH]

Peripheral Neuropathy: Nerve damage, usually affecting the feet and legs; causing pain, numbness, or a tingling feeling. Also called "somatic neuropathy" or "distal sensory polyneuropathy." [NIH]

Peripheral Vascular Disease: Disease in the large blood vessels of the arms, legs, and feet. People who have had diabetes for a long time may get this because major blood vessels in their arms, legs, and feet are blocked and these limbs do not receive enough blood. The signs of PVD are aching pains in the arms, legs, and feet (especially when walking) and foot sores that heal slowly. Although people with diabetes cannot always avoid PVD, doctors say they have a better chance of avoiding it if they take good care of their feet, do not smoke, and keep both their blood pressure and diabetes under good control. [NIH]

Peritoneal: Having to do with the peritoneum (the tissue that lines the abdominal wall and covers most of the organs in the abdomen). [NIH]

Peritoneal Dialysis: Dialysis fluid being introduced into and removed from the peritoneal cavity as either a continuous or an intermittent procedure. [NIH]

Peritoneum: Endothelial lining of the abdominal cavity, the parietal peritoneum covering the inside of the abdominal wall and the visceral peritoneum covering the bowel, the mesentery, and certain of the organs. The portion that covers the bowel becomes the serosal layer of the bowel wall. [NIH]

Pesticides: Chemicals used to destroy pests of any sort. The concept includes fungicides (industrial fungicides), insecticides, rodenticides, etc. [NIH]

Petroleum: Naturally occurring complex liquid hydrocarbons which, after distillation, yield combustible fuels, petrochemicals, and lubricants. [NIH]

PH: The symbol relating the hydrogen ion (H+) concentration or activity of a solution to that of a given standard solution. Numerically the pH is approximately equal to the negative logarithm of H+ concentration expressed in molarity. pH 7 is neutral; above it alkalinity increases and below it acidity increases. [EU]

Phagocyte: An immune system cell that can surround and kill microorganisms and remove dead cells. Phagocytes include macrophages. [NIH]

Pharmaceutical Preparations: Drugs intended for human or veterinary use, presented in their finished dosage form. Included here are materials used in the preparation and/or formulation of the finished dosage form. [NIH]

Pharmacodynamics: The study of the biochemical and physiological effects of drugs and the mechanisms of their actions, including the correlation of actions and effects of drugs with their chemical structure; also, such effects on the actions of a particular drug or drugs. [EU]

Pharmacokinetic: The mathematical analysis of the time courses of absorption, distribution, and elimination of drugs. [NIH]

Pharmacologic: Pertaining to pharmacology or to the properties and reactions of drugs. [EU]

Pharmacotherapy: A regimen of using appetite suppressant medications to manage obesity by decreasing appetite or increasing the feeling of satiety. These medications decrease

appetite by increasing serotonin or catecholamine—two brain chemicals that affect mood and appetite. [NIH]

Pharynx: The hollow tube about 5 inches long that starts behind the nose and ends at the top of the trachea (windpipe) and esophagus (the tube that goes to the stomach). [NIH]

Phenotype: The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of yeasts. [NIH]

Phenylalanine: An aromatic amino acid that is essential in the animal diet. It is a precursor of melanin, dopamine, noradrenalin, and thyroxine. [NIH]

Phospholipids: Lipids containing one or more phosphate groups, particularly those derived from either glycerol (phosphoglycerides; glycerophospholipids) or sphingosine (sphingolipids). They are polar lipids that are of great importance for the structure and function of cell membranes and are the most abundant of membrane lipids, although not stored in large amounts in the system. [NIH]

Phosphorus: A non-metallic element that is found in the blood, muscles, nevers, bones, and teeth, and is a component of adenosine triphosphate (ATP; the primary energy source for the body's cells.) [NIH]

Phosphorylase: An enzyme of the transferase class that catalyzes the phosphorylysis of a terminal alpha-1,4-glycosidic bond at the non-reducing end of a glycogen molecule, releasing a glucose 1-phosphate residue. Phosphorylase should be qualified by the natural substance acted upon. EC 2.4.1.1. [NIH]

Phosphorylated: Attached to a phosphate group. [NIH]

Phosphorylation: The introduction of a phosphoryl group into a compound through the formation of an ester bond between the compound and a phosphorus moiety. [NIH]

Photocoagulation: Using a special strong beam of light (laser) to seal off bleeding blood vessels such as in the eye. The laser can also burn away blood vessels that should not have grown in the eye. This is the main treatment for diabetic retinopathy. [NIH]

Physical Examination: Systematic and thorough inspection of the patient for physical signs of disease or abnormality. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Physiology: The science that deals with the life processes and functions of organismus, their cells, tissues, and organs. [NIH]

Pigment: A substance that gives color to tissue. Pigments are responsible for the color of skin, eyes, and hair. [NIH]

Pilot study: The initial study examining a new method or treatment. [NIH]

Pituitary Gland: A small, unpaired gland situated in the sella turcica tissue. It is connected to the hypothalamus by a short stalk. [NIH]

Placenta: A highly vascular fetal organ through which the fetus absorbs oxygen and other nutrients and excretes carbon dioxide and other wastes. It begins to form about the eighth day of gestation when the blastocyst adheres to the decidua. [NIH]

Placental tissue: The tissue intervening between fetal blood and maternal blood in the placenta; it acts as a selective membrane regulating the passage of substances from the maternal to the fetal blood. [NIH]

Plants: Multicellular, eukaryotic life forms of the kingdom Plantae. They are characterized

by a mainly photosynthetic mode of nutrition; essentially unlimited growth at localized regions of cell divisions (meristems); cellulose within cells providing rigidity; the absence of organs of locomotion; absense of nervous and sensory systems; and an alteration of haploid and diploid generations. [NIH]

Plaque: A clear zone in a bacterial culture grown on an agar plate caused by localized destruction of bacterial cells by a bacteriophage. The concentration of infective virus in a fluid can be estimated by applying the fluid to a culture and counting the number of. [NIH]

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plasma cells: A type of white blood cell that produces antibodies. [NIH]

Plasma protein: One of the hundreds of different proteins present in blood plasma, including carrier proteins (such albumin, transferrin, and haptoglobin), fibrinogen and other coagulation factors, complement components, immunoglobulins, enzyme inhibitors, precursors of substances such as angiotension and bradykinin, and many other types of proteins. [EU]

Plasmids: Any extrachromosomal hereditary determinant. Plasmids are self-replicating circular molecules of DNA that are found in a variety of bacterial, archaeal, fungal, algal, and plant species. [NIH]

Plasmin: A product of the lysis of plasminogen (profibrinolysin) by plasminogen activators. It is composed of two polypeptide chains, light (B) and heavy (A), with a molecular weight of 75,000. It is the major proteolytic enzyme involved in blood clot retraction or the lysis of fibrin and quickly inactivated by antiplasmins. EC 3.4.21.7. [NIH]

Plasminogen: Precursor of fibrinolysin (plasmin). It is a single-chain beta-globulin of molecular weight 80-90,000 found mostly in association with fibrinogen in plasma; plasminogen activators change it to fibrinolysin. It is used in wound debriding and has been investigated as a thrombolytic agent. [NIH]

Plasminogen Activators: A heterogeneous group of proteolytic enzymes that convert plasminogen to plasmin. They are concentrated in the lysosomes of most cells and in the vascular endothelium, particularly in the vessels of the microcirculation. EC 3.4.21.-. [NIH]

Plasticizers: Materials incorporated mechanically in plastics (usually PVC) to increase flexibility, workability or distensibility; due to the non-chemical inclusion, plasticizers leach out from the plastic and are found in body fluids and the general environment. [NIH]

Platelet Aggregation: The attachment of platelets to one another. This clumping together can be induced by a number of agents (e.g., thrombin, collagen) and is part of the mechanism leading to the formation of a thrombus. [NIH]

Platelets: A type of blood cell that helps prevent bleeding by causing blood clots to form. Also called thrombocytes. [NIH]

Platinum: Platinum. A heavy, soft, whitish metal, resembling tin, atomic number 78, atomic weight 195.09, symbol Pt. (From Dorland, 28th ed) It is used in manufacturing equipment for laboratory and industrial use. It occurs as a black powder (platinum black) and as a spongy substance (spongy platinum) and may have been known in Pliny's time as "alutiae". [NIH]

Pleated: Particular three-dimensional pattern of amyloidoses. [NIH]

Plethysmography: Recording of change in the size of a part as modified by the circulation in it. [NIH]

Ploidy: The number of sets of chromosomes in a cell or an organism. For example, haploid means one set and diploid means two sets. [NIH]

Poisoning: A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

Polycystic: An inherited disorder characterized by many grape-like clusters of fluid-filled cysts that make both kidneys larger over time. These cysts take over and destroy working kidney tissue. PKD may cause chronic renal failure and end-stage renal disease. [NIH]

Polydipsia: Chronic excessive thirst, as in diabetes mellitus or diabetes insipidus. [EU]

Polymers: Compounds formed by the joining of smaller, usually repeating, units linked by covalent bonds. These compounds often form large macromolecules (e.g., polypeptides, proteins, plastics). [NIH]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

Polymorphism: The occurrence together of two or more distinct forms in the same population. [NIH]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Polyposis: The development of numerous polyps (growths that protrude from a mucous membrane). [NIH]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Polyunsaturated fat: An unsaturated fat found in greatest amounts in foods derived from plants, including safflower, sunflower, corn, and soybean oils. [NIH]

Polyuria: Urination of a large volume of urine with an increase in urinary frequency, commonly seen in diabetes. [NIH]

Portal Vein: A short thick vein formed by union of the superior mesenteric vein and the splenic vein. [NIH]

Posterior: Situated in back of, or in the back part of, or affecting the back or dorsal surface of the body. In lower animals, it refers to the caudal end of the body. [EU]

Postmenopausal: Refers to the time after menopause. Menopause is the time in a woman's life when menstrual periods stop permanently; also called "change of life." [NIH]

Postnatal: Occurring after birth, with reference to the newborn. [EU]

Postoperative: After surgery. [NIH]

Postprandial: Occurring after dinner, or after a meal; postcibal. [EU]

Post-translational: The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

Potentiate: A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [NIH]

Practice Guidelines: Directions or principles presenting current or future rules of policy for the health care practitioner to assist him in patient care decisions regarding diagnosis, therapy, or related clinical circumstances. The guidelines may be developed by government agencies at any level, institutions, professional societies, governing boards, or by the convening of expert panels. The guidelines form a basis for the evaluation of all aspects of health care and delivery. [NIH]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Predisposition: A latent susceptibility to disease which may be activated under certain conditions, as by stress. [EU]

Preeclampsia: A toxaemia of late pregnancy characterized by hypertension, edema, and proteinuria, when convulsions and coma are associated, it is called eclampsia. [EU]

Pregnancy Outcome: Results of conception and ensuing pregnancy, including live birth, stillbirth, spontaneous abortion, induced abortion. The outcome may follow natural or artificial insemination or any of the various reproduction techniques, such as embryo transfer or fertilization in vitro. [NIH]

Pregnancy Tests: Tests to determine whether or not an individual is pregnant. [NIH]

Pregnenolone: Steroid hormone. [NIH]

Premenopausal: Refers to the time before menopause. Menopause is the time of life when a women's menstrual periods stop permanently; also called "change of life." [NIH]

Prenatal: Existing or occurring before birth, with reference to the fetus. [EU]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Primary endpoint: The main result that is measured at the end of a study to see if a given treatment worked (e.g., the number of deaths or the difference in survival between the treatment group and the control group). What the primary endpoint will be is decided before the study begins. [NIH]

Probe: An instrument used in exploring cavities, or in the detection and dilatation of strictures, or in demonstrating the potency of channels; an elongated instrument for exploring or sounding body cavities. [NIH]

Progesterone: Pregn-4-ene-3,20-dione. The principal progestational hormone of the body, secreted by the corpus luteum, adrenal cortex, and placenta. Its chief function is to prepare the uterus for the reception and development of the fertilized ovum. It acts as an antiovulatory agent when administered on days 5-25 of the menstrual cycle. [NIH]

Progression: Increase in the size of a tumor or spread of cancer in the body. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Proinsulin: The substance made first in the pancreas that is then made into insulin. When insulin is purified from the pancreas of pork or beef, all the proinsulin is not fully removed. When some people use these insulins, the proinsulin can cause the body to react with a rash, to resist the insulin, or even to make dents or lumps in the skin at the place where the insulin is injected. The purified insulins have less proinsulin and other impurities than the other types of insulins. [NIH]

Projection: A defense mechanism, operating unconsciously, whereby that which is emotionally unacceptable in the self is rejected and attributed (projected) to others. [NIH]

Proline: A non-essential amino acid that is synthesized from glutamic acid. It is an essential component of collagen and is important for proper functioning of joints and tendons. [NIH]

Promoter: A chemical substance that increases the activity of a carcinogenic process. [NIH]

Promotor: In an operon, a nucleotide sequence located at the operator end which contains all the signals for the correct initiation of genetic transcription by the RNA polymerase holoenzyme and determines the maximal rate of RNA synthesis. [NIH]

Prone: Having the front portion of the body downwards. [NIH]

Pro-Opiomelanocortin: A precursor protein, MW 30,000, synthesized mainly in the anterior

pituitary gland but also found in the hypothalamus, brain, and several peripheral tissues. It incorporates the amino acid sequences of ACTH and beta-lipotropin. These two hormones, in turn, contain the biologically active peptides MSH, corticotropin-like intermediate lobe peptide, alpha-lipotropin, endorphins, and methionine enkephalin. [NIH]

Proportional: Being in proportion : corresponding in size, degree, or intensity, having the same or a constant ratio; of, relating to, or used in determining proportions. [EU]

Prospective Studies: Observation of a population for a sufficient number of persons over a sufficient number of years to generate incidence or mortality rates subsequent to the selection of the study group. [NIH]

Prospective study: An epidemiologic study in which a group of individuals (a cohort), all free of a particular disease and varying in their exposure to a possible risk factor, is followed over a specific amount of time to determine the incidence rates of the disease in the exposed and unexposed groups. [NIH]

Prostaglandin: Any of a group of components derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway that are extremely potent mediators of a diverse group of physiologic processes. The abbreviation for prostaglandin is PG; specific compounds are designated by adding one of the letters A through I to indicate the type of substituents found on the hydrocarbon skeleton and a subscript (1, 2 or 3) to indicate the number of double bonds in the hydrocarbon skeleton e.g., PGE2. The predominant naturally occurring prostaglandins all have two double bonds and are synthesized from arachidonic acid (5,8,11,14-eicosatetraenoic acid) by the pathway shown in the illustration. The 1 series and 3 series are produced by the same pathway with fatty acids having one fewer double bond (8,11,14-eicosatrienoic acid or one more double bond (5,8,11,14,17-eicosapentaenoic acid) than arachidonic acid. The subscript a or ß indicates the configuration at C-9 (a denotes a substituent below the plane of the ring, ß, above the plane). The naturally occurring PGF's have the a configuration, e.g., PGF2a. All of the prostaglandins act by binding to specific cell-surface receptors causing an increase in the level of the intracellular second messenger cyclic AMP (and in some cases cyclic GMP also). The effect produced by the cyclic AMP increase depends on the specific cell type. In some cases there is also a positive feedback effect. Increased cyclic AMP increases prostaglandin synthesis leading to further increases in cyclic AMP. [EU]

Prostate: A gland in males that surrounds the neck of the bladder and the urethra. It secretes a substance that liquifies coagulated semen. It is situated in the pelvic cavity behind the lower part of the pubic symphysis, above the deep layer of the triangular ligament, and rests upon the rectum. [NIH]

Prostate gland: A gland in the male reproductive system just below the bladder. It surrounds part of the urethra, the canal that empties the bladder, and produces a fluid that forms part of semen. [NIH]

Prostatic Hyperplasia: Enlargement or overgrowth of the prostate gland as a result of an increase in the number of its constituent cells. [NIH]

Protease: Proteinase (= any enzyme that catalyses the splitting of interior peptide bonds in a protein). [EU]

Protein C: A vitamin-K dependent zymogen present in the blood, which, upon activation by thrombin and thrombomodulin exerts anticoagulant properties by inactivating factors Va and VIIIa at the rate-limiting steps of thrombin formation. [NIH]

Protein S: The vitamin K-dependent cofactor of activated protein C. Together with protein C, it inhibits the action of factors VIIIa and Va. A deficiency in protein S can lead to recurrent venous and arterial thrombosis. [NIH]

Protein-Energy Malnutrition: The lack of sufficient energy or protein to meet the body's metabolic demands, as a result of either an inadequate dietary intake of protein, intake of poor quality dietary protein, increased demands due to disease, or increased nutrient losses. [NIH]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

Proteinuria: The presence of protein in the urine, indicating that the kidneys are not working properly. [NIH]

Proteoglycans: Glycoproteins which have a very high polysaccharide content. [NIH]

Proteolytic: 1. Pertaining to, characterized by, or promoting proteolysis. 2. An enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Prothrombin: A plasma protein that is the inactive precursor of thrombin. It is converted to thrombin by a prothrombin activator complex consisting of factor Xa, factor V, phospholipid, and calcium ions. Deficiency of prothrombin leads to hypoprothrombinemia. [NIH]

Protocol: The detailed plan for a clinical trial that states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate, and other aspects of trial design. [NIH]

Protons: Stable elementary particles having the smallest known positive charge, found in the nuclei of all elements. The proton mass is less than that of a neutron. A proton is the nucleus of the light hydrogen atom, i.e., the hydrogen ion. [NIH]

Proximal: Nearest; closer to any point of reference; opposed to distal. [EU]

Proximate cause: The abnormal event in a causal chain lying closest to an accidental event. [NIH]

Psoriasis: A common genetically determined, chronic, inflammatory skin disease characterized by rounded erythematous, dry, scaling patches. The lesions have a predilection for nails, scalp, genitalia, extensor surfaces, and the lumbosacral region. Accelerated epidermopoiesis is considered to be the fundamental pathologic feature in psoriasis. [NIH]

Psychiatry: The medical science that deals with the origin, diagnosis, prevention, and treatment of mental disorders. [NIH]

Psychic: Pertaining to the psyche or to the mind; mental. [EU]

Psyllium: Dried, ripe seeds of Plantago psyllium, P. indica, and P. ovata (Plantaginaceae). Plantain seeds swell in water and are used as demulcents and bulk laxatives. [NIH]

Puberty: The period during which the secondary sex characteristics begin to develop and the capability of sexual reproduction is attained. [EU]

Public Health: Branch of medicine concerned with the prevention and control of disease and disability, and the promotion of physical and mental health of the population on the international, national, state, or municipal level. [NIH]

Public Policy: A course or method of action selected, usually by a government, from among alternatives to guide and determine present and future decisions. [NIH]

Publishing: "The business or profession of the commercial production and issuance of literature" (Webster's 3d). It includes the publisher, publication processes, editing and editors. Production may be by conventional printing methods or by electronic publishing. [NIH]

Pulmonary: Relating to the lungs. [NIH]

Pulmonary Artery: The short wide vessel arising from the conus arteriosus of the right ventricle and conveying unaerated blood to the lungs. [NIH]

Pulmonary Edema: An accumulation of an excessive amount of watery fluid in the lungs, may be caused by acute exposure to dangerous concentrations of irritant gasses. [NIH]

Pulmonary Fibrosis: Chronic inflammation and progressive fibrosis of the pulmonary alveolar walls, with steadily progressive dyspnea, resulting finally in death from oxygen lack or right heart failure. [NIH]

Pulmonary hypertension: Abnormally high blood pressure in the arteries of the lungs. [NIH]

Pulse: The rhythmical expansion and contraction of an artery produced by waves of pressure caused by the ejection of blood from the left ventricle of the heart as it contracts. [NIH]

Purified Insulins: Insulins with much less of the impure proinsulin. It is thought that the use of purified insulins may help avoid or reduce some of the problems of people with diabetes such as allergic reactions. [NIH]

Pyridoxal: 3-Hydroxy-5-(hydroxymethyl)-2-methyl-4- pyridinecarboxaldehyde. [NIH]

Quality of Life: A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral and social environment. [NIH]

Race: A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

Radiation: Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

Radiation therapy: The use of high-energy radiation from x-rays, gamma rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body in the area near cancer cells (internal radiation therapy, implant radiation, or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy. [NIH]

Radioactive: Giving off radiation. [NIH]

Radiography: Examination of any part of the body for diagnostic purposes by means of roentgen rays, recording the image on a sensitized surface (such as photographic film). [NIH]

Radioimmunoassay: Classic quantitative assay for detection of antigen-antibody reactions using a radioactively labeled substance (radioligand) either directly or indirectly to measure the binding of the unlabeled substance to a specific antibody or other receptor system. Non-immunogenic substances (e.g., haptens) can be measured if coupled to larger carrier proteins (e.g., bovine gamma-globulin or human serum albumin) capable of inducing antibody formation. [NIH]

Radiolabeled: Any compound that has been joined with a radioactive substance. [NIH]

Radiological: Pertaining to radiodiagnostic and radiotherapeutic procedures, and interventional radiology or other planning and guiding medical radiology. [NIH]

Radiotherapy: The use of ionizing radiation to treat malignant neoplasms and other benign conditions. The most common forms of ionizing radiation used as therapy are x-rays, gamma rays, and electrons. A special form of radiotherapy, targeted radiotherapy, links a cytotoxic radionuclide to a molecule that targets the tumor. When this molecule is an antibody or other immunologic molecule, the technique is called radioimmunotherapy. [NIH]

Random Allocation: A process involving chance used in therapeutic trials or other research endeavor for allocating experimental subjects, human or animal, between treatment and control groups, or among treatment groups. It may also apply to experiments on inanimate objects. [NIH]

Randomization: Also called random allocation. Is allocation of individuals to groups, e.g., for experimental and control regimens, by chance. Within the limits of chance variation, random allocation should make the control and experimental groups similar at the start of an investigation and ensure that personal judgment and prejudices of the investigator do not influence allocation. [NIH]

Randomized: Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

Randomized clinical trial: A study in which the participants are assigned by chance to separate groups that compare different treatments; neither the researchers nor the participants can choose which group. Using chance to assign people to groups means that the groups will be similar and that the treatments they receive can be compared objectively. At the time of the trial, it is not known which treatment is best. It is the patient's choice to be in a randomized trial. [NIH]

Rationalize: To attribute one's actions to rational and creditable motives without adequate analysis of the true and unconscious motives. [NIH]

Reactive Oxygen Species: Reactive intermediate oxygen species including both radicals and non-radicals. These substances are constantly formed in the human body and have been shown to kill bacteria and inactivate proteins, and have been implicated in a number of diseases. Scientific data exist that link the reactive oxygen species produced by inflammatory phagocytes to cancer development. [NIH]

Receptor: A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell. [NIH]

Receptors, Serotonin: Cell-surface proteins that bind serotonin and trigger intracellular changes which influence the behavior of cells. Several types of serotonin receptors have been recognized which differ in their pharmacology, molecular biology, and mode of action. [NIH]

Recombinant: A cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

Recombination: The formation of new combinations of genes as a result of segregation in crosses between genetically different parents; also the rearrangement of linked genes due to crossing-over. [NIH]

Rectum: The last 8 to 10 inches of the large intestine. [NIH]

Red blood cells: RBCs. Cells that carry oxygen to all parts of the body. Also called erythrocytes. [NIH]

Red Nucleus: A pinkish-yellow portion of the midbrain situated in the rostral mesencephalic tegmentum. It receives a large projection from the contralateral half of the cerebellum via the superior cerebellar peduncle and a projection from the ipsilateral motor cortex. [NIH]

Reductase: Enzyme converting testosterone to dihydrotestosterone. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

Reflex: An involuntary movement or exercise of function in a part, excited in response to a stimulus applied to the periphery and transmitted to the brain or spinal cord. [NIH]

Reflux: The term used when liquid backs up into the esophagus from the stomach. [NIH]

Refraction: A test to determine the best eyeglasses or contact lenses to correct a refractive error (myopia, hyperopia, or astigmatism). [NIH]

Refractory: Not readily yielding to treatment. [EU]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Regression Analysis: Procedures for finding the mathematical function which best describes the relationship between a dependent variable and one or more independent variables. In linear regression (see linear models) the relationship is constrained to be a straight line and least-squares analysis is used to determine the best fit. In logistic regression (see logistic models) the dependent variable is qualitative rather than continuously variable and likelihood functions are used to find the best relationship. In multiple regression the dependent variable is considered to depend on more than a single independent variable. [NIH]

Regurgitation: A backward flowing, as the casting up of undigested food, or the backward flowing of blood into the heart, or between the chambers of the heart when a valve is incompetent. [EU]

Remission: A decrease in or disappearance of signs and symptoms of cancer. In partial remission, some, but not all, signs and symptoms of cancer have disappeared. In complete remission, all signs and symptoms of cancer have disappeared, although there still may be cancer in the body. [NIH]

Reproduction Techniques: Methods pertaining to the generation of new individuals. [NIH]

Reproductive system: In women, this system includes the ovaries, the fallopian tubes, the uterus (womb), the cervix, and the vagina (birth canal). The reproductive system in men includes the prostate, the testes, and the penis. [NIH]

Resection: Removal of tissue or part or all of an organ by surgery. [NIH]

Respiration: The act of breathing with the lungs, consisting of inspiration, or the taking into the lungs of the ambient air, and of expiration, or the expelling of the modified air which contains more carbon dioxide than the air taken in (Blakiston's Gould Medical Dictionary, 4th ed.). This does not include tissue respiration (= oxygen consumption) or cell respiration (= cell respiration). [NIH]

Respirator: A mechanical device that helps a patient breathe; a mechanical ventilator. [NIH]

Respiratory failure: Inability of the lungs to conduct gas exchange. [NIH]

Respiratory Physiology: Functions and activities of the respiratory tract as a whole or of any of its parts. [NIH]

Response Elements: Nucleotide sequences, usually upstream, which are recognized by specific regulatory transcription factors, thereby causing gene response to various regulatory agents. These elements may be found in both promotor and enhancer regions. [NIH]

Resting metabolic rate: RMR accounts for 65 to 75 percent of daily energy expenditure and represents the minimum energy needed to maintain all physiological cell functions in the resting state. The principal determinant of RMR is lean body mass (LBM). Obese subjects have a higher RMR in absolute terms than lean individuals, an equivalent RMR when corrected for LBM and per unit surface area, and a lower RMR when expressed per kilogram of body weight. Obese persons require more energy for any given activity because of a larger mass, but they tend to be more sedentary than lean subjects. [NIH]

Restoration: Broad term applied to any inlay, crown, bridge or complete denture which

restores or replaces loss of teeth or oral tissues. [NIH]

Reticular: Coarse-fibered, netlike dermis layer. [NIH]

Retina: The ten-layered nervous tissue membrane of the eye. It is continuous with the optic nerve and receives images of external objects and transmits visual impulses to the brain. Its outer surface is in contact with the choroid and the inner surface with the vitreous body. The outer-most layer is pigmented, whereas the inner nine layers are transparent. [NIH]

Retinal: 1. Pertaining to the retina. 2. The aldehyde of retinol, derived by the oxidative enzymatic splitting of absorbed dietary carotene, and having vitamin A activity. In the retina, retinal combines with opsins to form visual pigments. One isomer, 11-cis retinal combines with opsin in the rods (scotopsin) to form rhodopsin, or visual purple. Another, all-trans retinal (trans-r.); visual yellow; xanthopsin) results from the bleaching of rhodopsin by light, in which the 11-cis form is converted to the all-trans form. Retinal also combines with opsins in the cones (photopsins) to form the three pigments responsible for colour vision. Called also retinal, and retinene1. [EU]

Retinoblastoma: An eye cancer that most often occurs in children younger than 5 years. It occurs in hereditary and nonhereditary (sporadic) forms. [NIH]

Retinoids: Derivatives of vitamin A. Used clinically in the treatment of severe cystic acne, psoriasis, and other disorders of keratinization. Their possible use in the prophylaxis and treatment of cancer is being actively explored. [NIH]

Retinol: Vitamin A. It is essential for proper vision and healthy skin and mucous membranes. Retinol is being studied for cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Retinopathy: 1. Retinitis (= inflammation of the retina). 2. Retinosis (= degenerative, noninflammatory condition of the retina). [EU]

Retinyl palmitate: A drug being studied in cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Retrograde: 1. Moving backward or against the usual direction of flow. 2. Degenerating, deteriorating, or catabolic. [EU]

Retrospective: Looking back at events that have already taken place. [NIH]

Rheumatism: A group of disorders marked by inflammation or pain in the connective tissue structures of the body. These structures include bone, cartilage, and fat. [NIH]

Rheumatoid: Resembling rheumatism. [EU]

Rheumatoid arthritis: A form of arthritis, the cause of which is unknown, although infection, hypersensitivity, hormone imbalance and psychologic stress have been suggested as possible causes. [NIH]

Rheumatology: A subspecialty of internal medicine concerned with the study of inflammatory or degenerative processes and metabolic derangement of connective tissue structures which pertain to a variety of musculoskeletal disorders, such as arthritis. [NIH]

Riboflavin: Nutritional factor found in milk, eggs, malted barley, liver, kidney, heart, and leafy vegetables. The richest natural source is yeast. It occurs in the free form only in the retina of the eye, in whey, and in urine; its principal forms in tissues and cells are as FMN and FAD. [NIH]

Ribonuclease: RNA-digesting enzyme. [NIH]

Rickets: A condition caused by deficiency of vitamin D, especially in infancy and childhood, with disturbance of normal ossification. The disease is marked by bending and distortion of the bones under muscular action, by the formation of nodular enlargements on the ends and

sides of the bones, by delayed closure of the fontanelles, pain in the muscles, and sweating of the head. Vitamin D and sunlight together with an adequate diet are curative, provided that the parathyroid glands are functioning properly. [EU]

Risk factor: A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Rod: A reception for vision, located in the retina. [NIH]

Rodenticides: Substances used to destroy or inhibit the action of rats, mice, or other rodents. [NIH]

Root Planing: A procedure for smoothing of the roughened root surface or cementum of a tooth after subgingival curettage or scaling, as part of periodontal therapy. [NIH]

Rosiglitazone: A drug taken to help reduce the amount of sugar in the blood. Rosiglitazone helps make insulin more effective and improves regulation of blood sugar. It belongs to the family of drugs called thiazolidinediones. [NIH]

Rural Population: The inhabitants of rural areas or of small towns classified as rural. [NIH]

Sagittal: The line of direction passing through the body from back to front, or any vertical plane parallel to the medial plane of the body and inclusive of that plane; often restricted to the medial plane, the plane of the sagittal suture. [NIH]

Salicylate: Non-steroidal anti-inflammatory drugs. [NIH]

Salicylic: A tuberculosis drug. [NIH]

Salicylic Acids: Derivatives and salts of salicylic acid. [NIH]

Saline: A solution of salt and water. [NIH]

Saliva: The clear, viscous fluid secreted by the salivary glands and mucous glands of the mouth. It contains mucins, water, organic salts, and ptylin. [NIH]

Salivary: The duct that convey saliva to the mouth. [NIH]

Salivary glands: Glands in the mouth that produce saliva. [NIH]

Sarcosine: Methylamino-acetic acid. [NIH]

Satiation: Full gratification of a need or desire followed by a state of relative insensitivity to that particular need or desire. [NIH]

Saturated fat: A type of fat found in greatest amounts in foods from animals, such as fatty cuts of meat, poultry with the skin, whole-milk dairy products, lard, and in some vegetable oils, including coconut, palm kernel, and palm oils. Saturated fat raises blood cholesterol more than anything else eaten. On a Step I Diet, no more than 8 to 10 percent of total calories should come from saturated fat, and in the Step II Diet, less than 7 percent of the day's total calories should come from saturated fat. [NIH]

Scans: Pictures of structures inside the body. Scans often used in diagnosing, staging, and monitoring disease include liver scans, bone scans, and computed tomography (CT) or computerized axial tomography (CAT) scans and magnetic resonance imaging (MRI) scans. In liver scanning and bone scanning, radioactive substances that are injected into the bloodstream collect in these organs. A scanner that detects the radiation is used to create pictures. In CT scanning, an x-ray machine linked to a computer is used to produce detailed pictures of organs inside the body. MRI scans use a large magnet connected to a computer to create pictures of areas inside the body. [NIH]

Schizoid: Having qualities resembling those found in greater degree in schizophrenics; a person of schizoid personality. [NIH]

Schizophrenia: A mental disorder characterized by a special type of disintegration of the

personality. [NIH]

Schizotypal Personality Disorder: A personality disorder in which there are oddities of thought (magical thinking, paranoid ideation, suspiciousness), perception (illusions, depersonalization), speech (digressive, vague, overelaborate), and behavior (inappropriate affect in social interactions, frequently social isolation) that are not severe enough to characterize schizophrenia. [NIH]

Sclerosis: A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Scurvy: A deficiency disease due to lack of vitamin C in the diet. [NIH]

Secretin: A hormone made in the duodenum. Causes the stomach to make pepsin, the liver to make bile, and the pancreas to make a digestive juice. [NIH]

Secretion: 1. The process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. Any substance produced by secretion. [EU]

Secretory: Secreting; relating to or influencing secretion or the secretions. [NIH]

Sedative: 1. Allaying activity and excitement. 2. An agent that allays excitement. [EU]

Sedentary: 1. Sitting habitually; of inactive habits. 2. Pertaining to a sitting posture. [EU]

Segmental: Describing or pertaining to a structure which is repeated in similar form in successive segments of an organism, or which is undergoing segmentation. [NIH]

Segregation: The separation in meiotic cell division of homologous chromosome pairs and their contained allelomorphic gene pairs. [NIH]

Seizures: Clinical or subclinical disturbances of cortical function due to a sudden, abnormal, excessive, and disorganized discharge of brain cells. Clinical manifestations include abnormal motor, sensory and psychic phenomena. Recurrent seizures are usually referred to as epilepsy or "seizure disorder." [NIH]

Selenocysteine: A naturally occurring amino acid in both eukaryotic and prokaryotic organisms. It is found in tRNAs and in the catalytic site of some enzymes. The genes for glutathione peroxidase and formate dehydrogenase contain the TGA codon, which codes for this amino acid. [NIH]

Semen: The thick, yellowish-white, viscid fluid secretion of male reproductive organs discharged upon ejaculation. In addition to reproductive organ secretions, it contains spermatozoa and their nutrient plasma. [NIH]

Seminal vesicles: Glands that help produce semen. [NIH]

Senile: Relating or belonging to old age; characteristic of old age; resulting from infirmity of old age. [NIH]

Sepsis: The presence of bacteria in the bloodstream. [NIH]

Sequence Homology: The degree of similarity between sequences. Studies of amino acid and nucleotide sequences provide useful information about the genetic relatedness of certain species. [NIH]

Serine: A non-essential amino acid occurring in natural form as the L-isomer. It is synthesized from glycine or threonine. It is involved in the biosynthesis of purines, pyrimidines, and other amino acids. [NIH]

Seroconversion: The change of a serologic test from negative to positive, indicating the development of antibodies in response to infection or immunization. [EU]

Serologic: Analysis of a person's serum, especially specific immune or lytic serums. [NIH]

Serotonin: A biochemical messenger and regulator, synthesized from the essential amino acid L-tryptophan. In humans it is found primarily in the central nervous system, gastrointestinal tract, and blood platelets. Serotonin mediates several important physiological functions including neurotransmission, gastrointestinal motility, hemostasis, and cardiovascular integrity. Multiple receptor families (receptors, serotonin) explain the broad physiological actions and distribution of this biochemical mediator. [NIH]

Serous: Having to do with serum, the clear liquid part of blood. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Serum Albumin: A major plasma protein that serves in maintaining the plasma colloidal osmotic pressure and transporting large organic anions. [NIH]

Sex Characteristics: Those characteristics that distinguish one sex from the other. The primary sex characteristics are the ovaries and testes and their related hormones. Secondary sex characteristics are those which are masculine or feminine but not directly related to reproduction. [NIH]

Sex Determination: The biological characteristics which distinguish human beings as female or male. [NIH]

Shivering: Involuntary contraction or twitching of the muscles. It is a physiologic method of heat production in man and other mammals. [NIH]

Shock: The general bodily disturbance following a severe injury; an emotional or moral upset occasioned by some disturbing or unexpected experience; disruption of the circulation, which can upset all body functions: sometimes referred to as circulatory shock. [NIH]

Side effect: A consequence other than the one(s) for which an agent or measure is used, as the adverse effects produced by a drug, especially on a tissue or organ system other than the one sought to be benefited by its administration. [EU]

Sigmoid: 1. Shaped like the letter S or the letter C. 2. The sigmoid colon. [EU]

Sigmoidoscopy: Endoscopic examination, therapy or surgery of the sigmoid flexure. [NIH]

Signal Transduction: The intercellular or intracellular transfer of information (biological activation/inhibition) through a signal pathway. In each signal transduction system, an activation/inhibition signal from a biologically active molecule (hormone, neurotransmitter) is mediated via the coupling of a receptor/enzyme to a second messenger system or to an ion channel. Signal transduction plays an important role in activating cellular functions, cell differentiation, and cell proliferation. Examples of signal transduction systems are the GABA-postsynaptic receptor-calcium ion channel system, the receptor-mediated T-cell activation pathway, and the receptor-mediated activation of phospholipases. Those coupled to membrane depolarization or intracellular release of calcium include the receptor-mediated activation of cytotoxic functions in granulocytes and the synaptic potentiation of protein kinase activation. Some signal transduction pathways may be part of larger signal transduction pathways; for example, protein kinase activation is part of the platelet activation signal pathway. [NIH]

Signs and Symptoms: Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient. [NIH]

Simvastatin: A derivative of lovastatin and potent competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase (hydroxymethylglutaryl CoA reductases), which is the rate-limiting enzyme in cholesterol biosynthesis. It may also interfere with steroid

hormone production. Due to the induction of hepatic LDL receptors, it increases breakdown of LDL-cholesterol (lipoproteins, LDL cholesterol). [NIH]

Skeletal: Having to do with the skeleton (boney part of the body). [NIH]

Skeleton: The framework that supports the soft tissues of vertebrate animals and protects many of their internal organs. The skeletons of vertebrates are made of bone and/or cartilage. [NIH]

Skull: The skeleton of the head including the bones of the face and the bones enclosing the brain. [NIH]

Sludge: A clump of agglutinated red blood cells. [NIH]

Small intestine: The part of the digestive tract that is located between the stomach and the large intestine. [NIH]

Smooth muscle: Muscle that performs automatic tasks, such as constricting blood vessels. [NIH]

Social Environment: The aggregate of social and cultural institutions, forms, patterns, and processes that influence the life of an individual or community. [NIH]

Sodium: An element that is a member of the alkali group of metals. It has the atomic symbol Na, atomic number 11, and atomic weight 23. With a valence of 1, it has a strong affinity for oxygen and other nonmetallic elements. Sodium provides the chief cation of the extracellular body fluids. Its salts are the most widely used in medicine. (From Dorland, 27th ed) Physiologically the sodium ion plays a major role in blood pressure regulation, maintenance of fluid volume, and electrolyte balance. [NIH]

Soft tissue: Refers to muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body. [NIH]

Solvent: 1. Dissolving; effecting a solution. 2. A liquid that dissolves or that is capable of dissolving; the component of a solution that is present in greater amount. [EU]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

Somatostatin: A polypeptide hormone produced in the hypothalamus, and other tissues and organs. It inhibits the release of human growth hormone, and also modulates important physiological functions of the kidney, pancreas, and gastrointestinal tract. Somatostatin receptors are widely expressed throughout the body. Somatostatin also acts as a neurotransmitter in the central and peripheral nervous systems. [NIH]

Sorbitol: A polyhydric alcohol with about half the sweetness of sucrose. Sorbitol occurs naturally and is also produced synthetically from glucose. It was formerly used as a diuretic and may still be used as a laxative and in irrigating solutions for some surgical procedures. It is also used in many manufacturing processes, as a pharmaceutical aid, and in several research applications. [NIH]

Sound wave: An alteration of properties of an elastic medium, such as pressure, particle displacement, or density, that propagates through the medium, or a superposition of such alterations. [NIH]

Soybean Oil: Oil from soybean or soybean plant. [NIH]

Specialist: In medicine, one who concentrates on 1 special branch of medical science. [NIH]

Species: A taxonomic category subordinate to a genus (or subgenus) and superior to a subspecies or variety, composed of individuals possessing common characters distinguishing them from other categories of individuals of the same taxonomic level. In taxonomic nomenclature, species are designated by the genus name followed by a Latin or

Latinized adjective or noun. [EU]

Specificity: Degree of selectivity shown by an antibody with respect to the number and types of antigens with which the antibody combines, as well as with respect to the rates and the extents of these reactions. [NIH]

Spectrometer: An apparatus for determining spectra; measures quantities such as wavelengths and relative amplitudes of components. [NIH]

Spectrum: A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of a disease. [EU]

Sperm: The fecundating fluid of the male. [NIH]

Spike: The activation of synapses causes changes in the permeability of the dendritic membrane leading to changes in the membrane potential. This difference of the potential travels along the axon of the neuron and is called spike. [NIH]

Spinal cord: The main trunk or bundle of nerves running down the spine through holes in the spinal bone (the vertebrae) from the brain to the level of the lower back. [NIH]

Spleen: An organ that is part of the lymphatic system. The spleen produces lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach. [NIH]

Splenic Vein: Vein formed by the union (at the hilus of the spleen) of several small veins from the stomach, pancreas, spleen and mesentery. [NIH]

Spontaneous Abortion: The non-induced birth of an embryo or of fetus prior to the stage of viability at about 20 weeks of gestation. [NIH]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

Staging: Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

Stasis: A word termination indicating the maintenance of (or maintaining) a constant level; preventing increase or multiplication. [EU]

Statistically significant: Describes a mathematical measure of difference between groups. The difference is said to be statistically significant if it is greater than what might be expected to happen by chance alone. [NIH]

Steatosis: Fatty degeneration. [EU]

Steel: A tough, malleable, iron-based alloy containing up to, but no more than, two percent carbon and often other metals. It is used in medicine and dentistry in implants and instrumentation. [NIH]

Stent: A device placed in a body structure (such as a blood vessel or the gastrointestinal tract) to provide support and keep the structure open. [NIH]

Sterility: 1. The inability to produce offspring, i.e., the inability to conceive (female s.) or to induce conception (male s.). 2. The state of being aseptic, or free from microorganisms. [EU]

Steroid: A group name for lipids that contain a hydrogenated cyclopentanoperhydrophenanthrene ring system. Some of the substances included in this group are progesterone, adrenocortical hormones, the gonadal hormones, cardiac aglycones, bile acids, sterols (such as cholesterol), toad poisons, saponins, and some of the carcinogenic hydrocarbons. [EU]

Stillbirth: The birth of a dead fetus or baby. [NIH]

Stimulant: 1. Producing stimulation; especially producing stimulation by causing tension on muscle fibre through the nervous tissue. 2. An agent or remedy that produces stimulation. [EU]

Stimulus: That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

Stoma: A surgically created opening from an area inside the body to the outside. [NIH]

Stomach: An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

Stool: The waste matter discharged in a bowel movement; feces. [NIH]

Stress: Forcibly exerted influence; pressure. Any condition or situation that causes strain or tension. Stress may be either physical or psychologic, or both. [NIH]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

Stroke Volume: The amount of blood pumped out of the heart per beat not to be confused with cardiac output (volume/time). [NIH]

Stupor: Partial or nearly complete unconsciousness, manifested by the subject's responding only to vigorous stimulation. Also, in psychiatry, a disorder marked by reduced responsiveness. [EU]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subarachnoid: Situated or occurring between the arachnoid and the pia mater. [EU]

Subclinical: Without clinical manifestations; said of the early stage(s) of an infection or other disease or abnormality before symptoms and signs become apparent or detectable by clinical examination or laboratory tests, or of a very mild form of an infection or other disease or abnormality. [EU]

Subcutaneous: Beneath the skin. [NIH]

Submaxillary: Four to six lymph glands, located between the lower jaw and the submandibular salivary gland. [NIH]

Subspecies: A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

Substance P: An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

Substrate: A substance upon which an enzyme acts. [EU]

Sulfur: An element that is a member of the chalcogen family. It has an atomic symbol S, atomic number 16, and atomic weight 32.066. It is found in the amino acids cysteine and methionine. [NIH]

Superoxide: Derivative of molecular oxygen that can damage cells. [NIH]

Superoxide Dismutase: An oxidoreductase that catalyzes the reaction between superoxide anions and hydrogen to yield molecular oxygen and hydrogen peroxide. The enzyme protects the cell against dangerous levels of superoxide. EC 1.15.1.1. [NIH]

Supine: Having the front portion of the body upwards. [NIH]

Supplementation: Adding nutrients to the diet. [NIH]

Suppositories: A small cone-shaped medicament having cocoa butter or gelatin at its basis and usually intended for the treatment of local conditions in the rectum. [NIH]

Suppression: A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

Surfactant: A fat-containing protein in the respiratory passages which reduces the surface tension of pulmonary fluids and contributes to the elastic properties of pulmonary tissue. [NIH]

Survival Rate: The proportion of survivors in a group, e.g., of patients, studied and followed over a period, or the proportion of persons in a specified group alive at the beginning of a time interval who survive to the end of the interval. It is often studied using life table methods. [NIH]

Sympathomimetic: 1. Mimicking the effects of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. 2. An agent that produces effects similar to those of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. Called also adrenergic. [EU]

Symphysis: A secondary cartilaginous joint. [NIH]

Symptomatic: Having to do with symptoms, which are signs of a condition or disease. [NIH]

Synapses: Specialized junctions at which a neuron communicates with a target cell. At classical synapses, a neuron's presynaptic terminal releases a chemical transmitter stored in synaptic vesicles which diffuses across a narrow synaptic cleft and activates receptors on the postsynaptic membrane of the target cell. The target may be a dendrite, cell body, or axon of another neuron, or a specialized region of a muscle or secretory cell. Neurons may also communicate through direct electrical connections which are sometimes called electrical synapses; these are not included here but rather in gap junctions. [NIH]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Systemic: Affecting the entire body. [NIH]

Systemic lupus erythematosus: SLE. A chronic inflammatory connective tissue disease marked by skin rashes, joint pain and swelling, inflammation of the kidneys, inflammation of the fibrous tissue surrounding the heart (i.e., the pericardium), as well as other problems. Not all affected individuals display all of these problems. May be referred to as lupus. [NIH]

Systolic: Indicating the maximum arterial pressure during contraction of the left ventricle of the heart. [EU]

Systolic blood pressure: The maximum pressure in the artery produced as the heart contracts and blood begins to flow. [NIH]

Systolic pressure: The highest pressure to which blood pressure rises with the contraction of the ventricles. [NIH]

Tachycardia: Excessive rapidity in the action of the heart, usually with a heart rate above 100 beats per minute. [NIH]

Telangiectasia: The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [NIH]

Temporal: One of the two irregular bones forming part of the lateral surfaces and base of the skull, and containing the organs of hearing. [NIH]

Testicular: Pertaining to a testis. [EU]

Testis: Either of the paired male reproductive glands that produce the male germ cells and the male hormones. [NIH]

Testosterone: A hormone that promotes the development and maintenance of male sex

characteristics. [NIH]

Tetracycline: An antibiotic originally produced by Streptomyces viridifaciens, but used mostly in synthetic form. It is an inhibitor of aminoacyl-tRNA binding during protein synthesis. [NIH]

Thalamic: Cell that reaches the lateral nucleus of amygdala. [NIH]

Thalamic Diseases: Disorders of the centrally located thalamus, which integrates a wide range of cortical and subcortical information. Manifestations include sensory loss, movement disorders; ataxia, pain syndromes, visual disorders, a variety of neuropsychological conditions, and coma. Relatively common etiologies include cerebrovascular disorders; craniocerebral trauma; brain neoplasms; brain hypoxia; intracranial hemorrhages; and infectious processes. [NIH]

Thalassemia: A group of hereditary hemolytic anemias in which there is decreased synthesis of one or more hemoglobin polypeptide chains. There are several genetic types with clinical pictures ranging from barely detectable hematologic abnormality to severe and fatal anemia. [NIH]

Theophylline: Alkaloid obtained from Thea sinensis (tea) and others. It stimulates the heart and central nervous system, dilates bronchi and blood vessels, and causes diuresis. The drug is used mainly in bronchial asthma and for myocardial stimulation. Among its more prominent cellular effects are inhibition of cyclic nucleotide phosphodiesterases and antagonism of adenosine receptors. [NIH]

Therapeutics: The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thermal: Pertaining to or characterized by heat. [EU]

Thermogenesis: The generation of heat in order to maintain body temperature. The uncoupled oxidation of fatty acids contained within brown adipose tissue and shivering are examples of thermogenesis in mammals. [NIH]

Thigh: A leg; in anatomy, any elongated process or part of a structure more or less comparable to a leg. [NIH]

Thinness: A state of insufficient flesh on the body usually defined as having a body weight less than skeletal and physical standards. [NIH]

Third Ventricle: A narrow cleft inferior to the corpus callosum, within the diencephalon, between the paired thalami. Its floor is formed by the hypothalamus, its anterior wall by the lamina terminalis, and its roof by ependyma. It communicates with the fourth ventricle by the cerebral aqueduct, and with the lateral ventricles by the interventricular foramina. [NIH]

Thorax: A part of the trunk between the neck and the abdomen; the chest. [NIH]

Threonine: An essential amino acid occurring naturally in the L-form, which is the active form. It is found in eggs, milk, gelatin, and other proteins. [NIH]

Threshold: For a specified sensory modality (e. g. light, sound, vibration), the lowest level (absolute threshold) or smallest difference (difference threshold, difference limen) or intensity of the stimulus discernible in prescribed conditions of stimulation. [NIH]

Thrombin: An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

Thrombocytes: Blood cells that help prevent bleeding by causing blood clots to form. Also called platelets. [NIH]

Thrombolytic: 1. Dissolving or splitting up a thrombus. 2. A thrombolytic agent. [EU]

Thrombomodulin: A cell surface glycoprotein of endothelial cells that binds thrombin and

serves as a cofactor in the activation of protein C and its regulation of blood coagulation. [NIH]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

Thrombus: An aggregation of blood factors, primarily platelets and fibrin with entrapment of cellular elements, frequently causing vascular obstruction at the point of its formation. Some authorities thus differentiate thrombus formation from simple coagulation or clot formation. [EU]

Thyroid: A gland located near the windpipe (trachea) that produces thyroid hormone, which helps regulate growth and metabolism. [NIH]

Thyroid Gland: A highly vascular endocrine gland consisting of two lobes, one on either side of the trachea, joined by a narrow isthmus; it produces the thyroid hormones which are concerned in regulating the metabolic rate of the body. [NIH]

Thyroid Hormones: Hormones secreted by the thyroid gland. [NIH]

Thyroiditis: Inflammation of the thyroid gland. [NIH]

Thyrotropin: A peptide hormone secreted by the anterior pituitary. It promotes the growth of the thyroid gland and stimulates the synthesis of thyroid hormones and the release of thyroxine by the thyroid gland. [NIH]

Thyroxine: An amino acid of the thyroid gland which exerts a stimulating effect on thyroid metabolism. [NIH]

Tin: A trace element that is required in bone formation. It has the atomic symbol Sn, atomic number 50, and atomic weight 118.71. [NIH]

Tissue: A group or layer of cells that are alike in type and work together to perform a specific function. [NIH]

Tissue Plasminogen Activator: A proteolytic enzyme in the serine protease family found in many tissues which converts plasminogen to plasmin. It has fibrin-binding activity and is immunologically different from urinary plasminogen activator. The primary sequence, composed of 527 amino acids, is identical in both the naturally occurring and synthetic proteases. EC 3.4.21.68. [NIH]

Tolerance: 1. The ability to endure unusually large doses of a drug or toxin. 2. Acquired drug tolerance; a decreasing response to repeated constant doses of a drug or the need for increasing doses to maintain a constant response. [EU]

Tomography: Imaging methods that result in sharp images of objects located on a chosen plane and blurred images located above or below the plane. [NIH]

Tonicity: The normal state of muscular tension. [NIH]

Tonsil: A round-to-oval mass of lymphoid tissue embedded in the lateral wall of the pharynx situated on each side of the fauces, between the anterior and posterior pillars of the soft palate. [NIH]

Tooth Preparation: Procedures carried out with regard to the teeth or tooth structures preparatory to specified dental therapeutic and surgical measures. [NIH]

Topical: On the surface of the body. [NIH]

Torsades de Pointes: A ventricular tachycardia characterized by periodic twisting of the points of the QRS complexes and rates between 200 and 250 beats per minute. It may be self-limited or may progress to ventricular fibrillation. [NIH]

Toxaemia: 1. The condition resulting from the spread of bacterial products (toxins) by the bloodstream. 2. A condition resulting from metabolic disturbances, e.g. toxaemia of pregnancy. [EU]

Toxic: Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Toxicology: The science concerned with the detection, chemical composition, and pharmacologic action of toxic substances or poisons and the treatment and prevention of toxic manifestations. [NIH]

Toxins: Specific, characterizable, poisonous chemicals, often proteins, with specific biological properties, including immunogenicity, produced by microbes, higher plants, or animals. [NIH]

Trace element: Substance or element essential to plant or animal life, but present in extremely small amounts. [NIH]

Trachea: The cartilaginous and membranous tube descending from the larynx and branching into the right and left main bronchi. [NIH]

Tracheostomy: Surgical formation of an opening into the trachea through the neck, or the opening so created. [NIH]

Tracheostomy tube: A 2-inch- to 3-inch-long curved metal or plastic tube placed in a surgically created opening (tracheostomy) in the windpipe to keep it open. Also called a trach ("trake") tube. [NIH]

Traction: The act of pulling. [NIH]

Tractus: A part of some structure, usually that part along which something passes. [NIH]

Transaldolase: An enzyme of the transferase class that catalyzes the reaction sedoheptulose 7-phosphate and D-glyceraldehyde 3-phosphate to yield D-erythrose 4-phosphate and D-fructose phosphate in the pentosephosphate pathway. (Dorland, 27th ed) EC 2.2.1.2. [NIH]

Transaminase: Aminotransferase (= a subclass of enzymes of the transferase class that catalyse the transfer of an amino group from a donor (generally an amino acid) to an acceptor (generally 2-keto acid). Most of these enzymes are pyridoxal-phosphate-proteins. [EU]

Transcription Factors: Endogenous substances, usually proteins, which are effective in the initiation, stimulation, or termination of the genetic transcription process. [NIH]

Transduction: The transfer of genes from one cell to another by means of a viral (in the case of bacteria, a bacteriophage) vector or a vector which is similar to a virus particle (pseudovirion). [NIH]

Transfection: The uptake of naked or purified DNA into cells, usually eukaryotic. It is analogous to bacterial transformation. [NIH]

Transient Ischemic Attacks: Focal neurologic abnormalities of sudden onset and brief duration that reflect dysfunction in the distribution of the internal carotid-middle cerebral or the vertebrobasilar arterial system. [NIH]

Translation: The process whereby the genetic information present in the linear sequence of ribonucleotides in mRNA is converted into a corresponding sequence of amino acids in a protein. It occurs on the ribosome and is unidirectional. [NIH]

Translational: The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

Translocation: The movement of material in solution inside the body of the plant. [NIH]

Transmitter: A chemical substance which effects the passage of nerve impulses from one cell to the other at the synapse. [NIH]

Transplantation: Transference of a tissue or organ, alive or dead, within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Trauma: Any injury, wound, or shock, must frequently physical or structural shock, producing a disturbance. [NIH]

Trauma Centers: Specialized hospital facilities which provide diagnostic and therapeutic services for trauma patients. [NIH]

Tricuspid Atresia: Absence of the orifice between the right atrium and ventricle, with the presence of an atrial defect through which all the systemic venous return reaches the left heart. As a result, there is left ventricular hypertrophy because the right ventricle is absent or not functional. [NIH]

Triglyceride: A lipid carried through the blood stream to tissues. Most of the body's fat tissue is in the form of triglycerides, stored for use as energy. Triglycerides are obtained primarily from fat in foods. [NIH]

Trivalent: Having a valence of three. [EU]

Troglitazone: A drug used in diabetes treatment that is being studied for its effect on reducing the risk of cancer cell growth in fat tissue. [NIH]

Trophic: Of or pertaining to nutrition. [EU]

Truncal: The bilateral dissection of the abdominal branches of the vagus nerve. [NIH]

Tryptophan: An essential amino acid that is necessary for normal growth in infants and for nitrogen balance in adults. It is a precursor serotonin and niacin. [NIH]

Tuberculosis: Any of the infectious diseases of man and other animals caused by species of Mycobacterium. [NIH]

Tuberous Sclerosis: A rare congenital disease in which the essential pathology is the appearance of multiple tumors in the cerebrum and in other organs, such as the heart or kidneys. [NIH]

Tumor marker: A substance sometimes found in an increased amount in the blood, other body fluids, or tissues and which may mean that a certain type of cancer is in the body. Examples of tumor markers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and gastrointestinal tract cancers), and PSA (prostate cancer). Also called biomarker. [NIH]

Tumor suppressor gene: Genes in the body that can suppress or block the development of cancer. [NIH]

Tumor-derived: Taken from an individual's own tumor tissue; may be used in the development of a vaccine that enhances the body's ability to build an immune response to the tumor. [NIH]

Type 2 diabetes: Usually characterized by a gradual onset with minimal or no symptoms of metabolic disturbance and no requirement for exogenous insulin. The peak age of onset is 50 to 60 years. Obesity and possibly a genetic factor are usually present. [NIH]

Tyrosine: A non-essential amino acid. In animals it is synthesized from phenylalanine. It is also the precursor of epinephrine, thyroid hormones, and melanin. [NIH]

Ubiquitin: A highly conserved 76 amino acid-protein found in all eukaryotic cells. [NIH]

Ulcer: A localized necrotic lesion of the skin or a mucous surface. [NIH]

Ulceration: 1. The formation or development of an ulcer. 2. An ulcer. [EU]

Ultrasonography: The visualization of deep structures of the body by recording the reflections of echoes of pulses of ultrasonic waves directed into the tissues. Use of

ultrasound for imaging or diagnostic purposes employs frequencies ranging from 1.6 to 10 megahertz. [NIH]

Unconscious: Experience which was once conscious, but was subsequently rejected, as the "personal unconscious". [NIH]

Unsaturated Fats: A type of fat. [NIH]

Uraemia: 1. An excess in the blood of urea, creatinine, and other nitrogenous end products of protein and amino acids metabolism; more correctly referred to as azotemia. 2. In current usage the entire constellation of signs and symptoms of chronic renal failure, including nausea, vomiting anorexia, a metallic taste in the mouth, a uraemic odour of the breath, pruritus, uraemic frost on the skin, neuromuscular disorders, pain and twitching in the muscles, hypertension, edema, mental confusion, and acid-base and electrolyte imbalances. [EU]

Urea: A compound (CO(NH2)2), formed in the liver from ammonia produced by the deamination of amino acids. It is the principal end product of protein catabolism and constitutes about one half of the total urinary solids. [NIH]

Uremia: The illness associated with the buildup of urea in the blood because the kidneys are not working effectively. Symptoms include nausea, vomiting, loss of appetite, weakness, and mental confusion. [NIH]

Ureter: One of a pair of thick-walled tubes that transports urine from the kidney pelvis to the bladder. [NIH]

Urethra: The tube through which urine leaves the body. It empties urine from the bladder. [NIH]

Urinary: Having to do with urine or the organs of the body that produce and get rid of urine. [NIH]

Urinary Plasminogen Activator: A proteolytic enzyme that converts plasminogen to plasmin where the preferential cleavage is between arginine and valine. It was isolated originally from human urine, but is found in most tissues of most vertebrates. EC 3.4.21.73. [NIH]

Urine: Fluid containing water and waste products. Urine is made by the kidneys, stored in the bladder, and leaves the body through the urethra. [NIH]

Urogenital: Pertaining to the urinary and genital apparatus; genitourinary. [EU]

Urogenital System: All the organs involved in reproduction and the formation and release of urine. It includes the kidneys, ureters, bladder, urethra, and the organs of reproduction - ovaries, uterus, fallopian tubes, vagina, and clitoris in women and the testes, seminal vesicles, prostate, seminal ducts, and penis in men. [NIH]

Uterus: The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a fetus develops. Also called the womb. [NIH]

Vaccine: A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. [NIH]

Vagina: The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal. [NIH]

Vaginal: Of or having to do with the vagina, the birth canal. [NIH]

Vaginosis: A condition caused by the overgrowth of anaerobic bacteria (e. g., Gardnerella vaginalis), resulting in vaginal irritation and discharge. [NIH]

Vagus Nerve: The 10th cranial nerve. The vagus is a mixed nerve which contains somatic afferents (from skin in back of the ear and the external auditory meatus), visceral afferents

(from the pharynx, larynx, thorax, and abdomen), parasympathetic efferents (to the thorax and abdomen), and efferents to striated muscle (of the larynx and pharynx). [NIH]

Valine: A branched-chain essential amino acid that has stimulant activity. It promotes muscle growth and tissue repair. It is a precursor in the penicillin biosynthetic pathway. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

Vascular Resistance: An expression of the resistance offered by the systemic arterioles, and to a lesser extent by the capillaries, to the flow of blood. [NIH]

Vasculitis: Inflammation of a blood vessel. [NIH]

Vasoconstriction: Narrowing of the blood vessels without anatomic change, for which constriction, pathologic is used. [NIH]

Vasodilators: Any nerve or agent which induces dilatation of the blood vessels. [NIH]

Vasomotor: 1. Affecting the calibre of a vessel, especially of a blood vessel. 2. Any element or agent that effects the calibre of a blood vessel. [EU]

Vector: Plasmid or other self-replicating DNA molecule that transfers DNA between cells in nature or in recombinant DNA technology. [NIH]

Vein: Vessel-carrying blood from various parts of the body to the heart. [NIH]

Venous: Of or pertaining to the veins. [EU]

Venous blood: Blood that has given up its oxygen to the tissues and carries carbon dioxide back for gas exchange. [NIH]

Ventilation: 1. In respiratory physiology, the process of exchange of air between the lungs and the ambient air. Pulmonary ventilation (usually measured in litres per minute) refers to the total exchange, whereas alveolar ventilation refers to the effective ventilation of the alveoli, in which gas exchange with the blood takes place. 2. In psychiatry, verbalization of one's emotional problems. [EU]

Ventilator: A breathing machine that is used to treat respiratory failure by promoting ventilation; also called a respirator. [NIH]

Ventral: 1. Pertaining to the belly or to any venter. 2. Denoting a position more toward the belly surface than some other object of reference; same as anterior in human anatomy. [EU]

Ventricle: One of the two pumping chambers of the heart. The right ventricle receives oxygen-poor blood from the right atrium and pumps it to the lungs through the pulmonary artery. The left ventricle receives oxygen-rich blood from the left atrium and pumps it to the body through the aorta. [NIH]

Ventricular: Pertaining to a ventricle. [EU]

Ventricular fibrillation: Rapid, irregular quivering of the heart's ventricles, with no effective heartbeat. [NIH]

Venules: The minute vessels that collect blood from the capillary plexuses and join together to form veins. [NIH]

Veterinary Medicine: The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [NIH]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

Viral Load: The quantity of measurable virus in the blood. Change in viral load, measured in plasma, is used as a surrogate marker in HIV disease progression. [NIH]

Virulence: The degree of pathogenicity within a group or species of microorganisms or viruses as indicated by case fatality rates and/or the ability of the organism to invade the

tissues of the host. [NIH]

Virus: Submicroscopic organism that causes infectious disease. In cancer therapy, some viruses may be made into vaccines that help the body build an immune response to, and kill, tumor cells. [NIH]

Visceral: , from viscus a viscus) pertaining to a viscus. [EU]

Visceral fat: One of the three compartments of abdominal fat. Retroperitoneal and subcutaneous are the other two compartments. [NIH]

Vitamin A: A substance used in cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Vitamin D: The vitamin that mediates intestinal calcium absorption, bone calcium metabolism, and probably muscle activity. It usually acts as a hormone precursor, requiring 2 stages of metabolism before reaching actual hormonal form. It is isolated from fish liver oils and used in the treatment and prevention of rickets. [NIH]

Vitro: Descriptive of an event or enzyme reaction under experimental investigation occurring outside a living organism. Parts of an organism or microorganism are used together with artificial substrates and/or conditions. [NIH]

Vivo: Outside of or removed from the body of a living organism. [NIH]

Volition: Voluntary activity without external compulsion. [NIH]

Waist circumference: To define the level at which the waist circumference is measured, a bony landmark is first located and marked. The subject stands, and the technician, positioned to the right of the subject, palpates the upper hip bone to locate the right ileum. Just above the uppermost lateral border of the right ileum, a horizontal mark is drawn and then crossed with a vertical mark on the midaxillary line. The measuring tape is then placed around the trunk, at the level of the mark on the right side, making sure that it is on a level horizontal plane on all sides. The tape is then tightened slightly without compressing the skin and underlying subcutaneous tissues. The measure is recorded in centimeters to the nearest millimeter. [NIH]

Watchful waiting: Closely monitoring a patient's condition but withholding treatment until symptoms appear or change. Also called observation. [NIH]

Water Deprivation: The withholding of water in a structured experimental situation. [NIH]

Weight Gain: Increase in body weight over existing weight. [NIH]

White blood cell: A type of cell in the immune system that helps the body fight infection and disease. White blood cells include lymphocytes, granulocytes, macrophages, and others. [NIH]

Windpipe: A rigid tube, 10 cm long, extending from the cricoid cartilage to the upper border of the fifth thoracic vertebra. [NIH]

Withdrawal: 1. A pathological retreat from interpersonal contact and social involvement, as may occur in schizophrenia, depression, or schizoid avoidant and schizotypal personality disorders. 2. (DSM III-R) A substance-specific organic brain syndrome that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce a state of intoxication. [EU]

Womb: A hollow, thick-walled, muscular organ in which the impregnated ovum is developed into a child. [NIH]

Wound Healing: Restoration of integrity to traumatized tissue. [NIH]

Wound Infection: Invasion of the site of trauma by pathogenic microorganisms. [NIH]

Xenograft: The cells of one species transplanted to another species. [NIH]

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer. [NIH]

X-ray therapy: The use of high-energy radiation from x-rays to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. X-ray therapy is also called radiation therapy, radiotherapy, and irradiation. [NIH]

Yeasts: A general term for single-celled rounded fungi that reproduce by budding. Brewers' and bakers' yeasts are Saccharomyces cerevisiae; therapeutic dried yeast is dried yeast. [NIH]

Zona Fasciculata: The wide middle zone of the adrenal cortex. This zone consists of large lipid-laden cells radially arranged in parallel cords. It converts pregnenolone to cortisol by a series of enzymatically regulated steps. A small amount of corticosterone is formed as a by-product of cortisol synthesis. [NIH]

Zymogen: Inactive form of an enzyme which can then be converted to the active form, usually by excision of a polypeptide, e. g. trypsinogen is the zymogen of trypsin. [NIH]

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