THE ENZYME TREATMENT OF CANCER AND ITS SCIENTIFIC BASIS

BEING COLLECTED PAPERS DEALING WITH THE ORIGIN, NATURE, AND SCIENTIFIC TREATMENT OF THE NATURAL PHENOMENON KNOWN AS MALIGNANT DISEASE.

BY

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"When, from a correct General Principle, one develops the conclusions in special cases of its application, new surprises, for which one was not previously prepared, always make their appearance. And, since the conclusions unfold, not according to the author's caprice, but after their own laws, it has often made the impression upon me that really it was not my own work which I wrote down, but merely the work of another.

Hermann Von Helmholtz

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PREFACE

"Man," writes the learned and genial Carl Ernst von Baer, "considers himself just as necessarily in the centre of his mental horizon as of his mathematical one." When, in the closing hours of the last day of the nineteenth century, I wrote this citation in the original German, as the opening words of the preface of the first of a series of memoirs upon the history of the germ-cells, I little reckoned that the controversy regarding their story, which was the final link in the general principle of an antithetic alternation of generations, would be carried on around the side-issue—the special case in von Helmholtz's sense—of the origin, nature, and scientific treatment of cancer. All. Of these are concerns of embryology, for they are problems of reproduction, growth, and there stereo-chemical processes of life. In the discussion of a similar problem of embryology—that of parthenogenesis (pFdogenesis) or virgin reproduction in fly-maggots (*Ceidomya*) –von Baer used the above words. His account of this discovery of Wagner's has its special interest in connection with the present work.

Carl Ernst von Baer writes: * "that at first the dis-

*Baer, Carl Ernst von: "Über Prof. Nic. Wagner's Entdeckung von Larven, die sich fortpflanzen, Herrn Ganin's verwandte und engänzende Beobachtungen und über die Paedogenesis überhaupt," in *Mélanges Biologiques,* v., 1865*,* pp. 203-308; loc. cit., pp 241-243.

covery appears to be received with doubt" –that even the well-known worker on the parthenogenesis of bees, von Siebold, expressly said that it appeared to him to be incredible—"only shows how unexpected it was and how little one was prepared for it. It is thus a testimony of its importance, and, so to speak, a compliment for it. I should like to recall an expression of Wilhelm von Humboldt's who, when someone criticized one of his earlier philological works adversely, in a reply expressed himself somewhat as follows: 'A book which immediately on its first appearance finds general approval really does not deserve to be printed at all, for it contains only that which in the convictions of all is completely accepted, or at lease for which they were entirely prepared.' That is very true, for the really new, when it is far-reaching and thorough, can only gradually find an entrance, because numerous convictions must be altered in order to make its proper place for the new-comer. That the corals were inhabited by animals was first discovered by the naval surgeon Peyssonel, in the years 1723-1725, and it was no less a man than the great Réaumur who rejected the discovery as an absurdity in 1727, when Peyssonel had communicated his finds to him. These researches had been carried on for several years, and they were indeed numerous and careful, for Peyssonel says: 'In the tubes of *Tubipora* there sit animals, what one believes to be flowers in the noble corals'" (*Corallium rubrum,* the red coral of commerce) " 'are also animals; for they occur at all seasons of the year, they retract themselves when they are touched, and when one lifts the corals out of water, in the Madreporarian corals the animals resemble the sea-anemones; the skeleton of the coral on decomposing gives off an animals odour, and even the chemical investigation proves the presence of animal substances.'

All these grounds Réaumur mentions, but concludes that the corals are plants which excrete a stony substance, and that if one sees animals in them these must be parasites which have wandered into them. He finds it quite out of question , as one sees, to imagine the existence of branched animals. Out of consid-eration for the individual, he does not mention the name of him who had asserted such remarkable things, In this way Peyssonel remained quite unknown and unrecognized. But when, later on, Trembley made known his observations on the fresh-water polypes, and in the buds of these one had before his eyes a branched, animal, Réaumur asked the botanist, Bernard de Jussieu, who was going to the seaside, to examine what connection this had with the corals. When, then, De Jussieu expressed himself in favour of their animal nature, Réaumur at last believed it himself, and withdrew his former judgment. Peyssonel, who learnt in the West Indies that Réaumur had not published the memoir sent to him, but that later on the correctness of his discovery had been recognized, in 1751 sent a new memoir, not to Paris, but to London, where in appeared in 1753 in the Philosophical Transactions. Thus, thirty years passed before he succeeded in publishing his discovery, and five years more before, by the publication of the tenth edition of Linnæus's "Systema Naturæ' (1758), it gained general acceptance. How many and angry writings did there not appear against Harvey's account of the circulation of the blood, because it was not known what to do with the air or the spirits (*Archæi)* which were supposed to reside in the arteries, and when Harvey died, twenty years after the publication of his discovery, it had not yet become generally accepted. Much longer still was it before the discovery of Copernicus found general acceptance, and

the earth had to describe its path round the sun many times before the Holy Chair allowed it to be spoken of publicly."

At that time, in view of the history of science, it was quite anticipated, that the new facts concerning the history and continuity of the germ-cells from generation to generation would obtain a hostile welcome and reception, and that their discoverer would undoubtedly win a reward for all his patient labours similar to the recompenses meted out in past times to all those pioneers, termed by Robert Browning, "God's elect," from Khalif Al-Mamun, who dared to measure the earth and to describe it as a globe, down to Pasteur, who in our own day, among other brilliant deeds, caused "chemistry to take possession of medicine" (Duclaux). But the anathema did not come then; it was reserved for another occasion, and one of far greater import for human welfare and hopes. On the one hand, some of the germ-cell finds could be annexed—apparently—by others; on the other, they seemed to fit in so well with Weismann's conceptions of a hypothetical germ-plasm – a thing non-existent—that to many it appeared possible to incorporate them with the doctrines of this distinguished zoologist. To another, again, they looked like furnishing in fact a confirmation of the vague speculations of Richard Owen, and this has led to the assignment of the actual work and discoveries to him, who actually never did any investigations at all into the history of the germ-cells. In fine, in one way or another, the germ-cell finds wee disposed of and dispersed. Some of them—some of the more fundamental points—were cast aside and ignored; others, the more obvious, were annexed or parcelled out, and ascribed to this, that, or the other embryologist or zoologist, and practically nothing at all was left over to

the credit of the original observer, who, indeed, ought to have congratulated himself on the –for his welfare—fortunate turn of events. All this has reference to Great Britain and America.

Then came the time, the "divisions" and "brigades" being complete and ready, and eager to take the field, when the general principle of an antithetic alternation of generations, with an actual tangible continuity of germ-cells from generation to generation, had to be applied to the special case of cancer or malignant disease. Since it has long been one of my maxims in research to reap and garner the harvest completely, leaving as little gleanings as possible for others, this application of the general principle could not be left undone. Cancer stood defiantly in the way, and an immediate decisive campaign against it was inevitable.

New conclusions were reached, one after the other, and in due course these were published. Mankind in general , and medical mankind in particular, wee supposed to be waiting the advent of some new scientific discovery concerning the nature of cancer, in the hope that this would lead ultimately to success in its non-operative medical treatment. The reception give to the new conclusions in Great Britain was hardly in accord with that which, in a scientific era, might have been foreseen. The scientific investigator might have been attacking some of the most sacred and deeply rooted religious and moral convictions of mankind concerning cancer or malignant disease. The physical martyrdom was lacking; but there are, as I can testify from experience, many more ways than one of burning a scientific man at the stake.

Two of the discoveries referred to by von Baer—those of Copernicus and Harvey—had this feature in common:

that, at the time they were published, it was not, and could not be, foreseen that they possessed intrinsic vital importance for mankind. None the less, they were denounced, and their authors along with them. Did the histories of the discoveries of Morton, Simpson, Semmelweis, Lister, and—last and greatest—Pasteur not prove the contrary, one might have concluded that the main reasons for the opposition to, and the denouncement of, Copernicus and Harvey, for example, were that these discoveries had no apparent bearing on the physical welfare of humanity. If so, mankind would welcome eagerly any discoveries

relating to the scientific nature and treatment of cancer, even though, as an old and very wise friend remarks, they were made by a chimney-sweep.

Actual experiences have not tallied with these anticipations. Whether it would have been otherwise had the discoveries been made and published twenty-five or thirty years earlier –for instance, in my student days, or at the time when the late Sir James Paget concluded (1887), that operative interference with can-cer was not advisable, --is a moot question. In the light of actual events, since the scientific man especially learns from experience, I have surmised, perhaps rightly, that all these denunciations of scientific discoveries and of their authors –the latter including among many other Khalif Al-Mamun, Servetus, Copernicus, Giordana Bruno, Galileo, Vesalius,*

* "In the same year (1543, when appeared the treatise of Copernicus on the 'Revolutions of the Heavenly Bodies'), Vesalius, a young Belgian anatomist, published his "Structure of the Human Body,' a volume rich in facts ascertained by dis-section. Some of these facts were held to contradict the teaching of Galen. Next year Vesalius was driven by the hostility of the medical profession to burn his manuscripts and relinquish original work; he was not yet thirty years of age" (L. C. Miall, 'History of Biology,' 1911, p. 20).

De Dominis, Harvey, Buffon, Morton, Simpson, Semmelweis, Lister, and Pasteur, etc.—have been due, not so much to religious motives and the *odium theologicum,* as to the innate constitution of human nature and its intolerance of the new and the strange, even though this be calculated to be of surpassing benefit to humanity.

As to the particular instance dealt with in this book I have nothing at all to retract—even at the stake—concerning my scientific conclusions as to the origin, nature, and rational treatment of the natural phenomenon known as cancer or malignant disease. The words of Galileo, *Eppur si muove,* were a definite enough statement on his position. Pasteur told his opponents that he lived in a realm of which they knew nothing and into which they had no entry. These words of his also I adopt. Cancer is a natural phenomenon, germinal in origin and asexual (trophoblastic) in nature, and it is one which, by the laws of Nature, must yield to the magic influences of the all-powerful ferments, trypsin and amylopsin. Of these, trypsin has been described—rightly—by a scientific man, Dr. Emil Westergaard, as far "more powerful than dynamite."

Those who think differently, or think they think differently, or who don't think at all, and who without adducing any but negative finds without value in science, persist in denying the scientific research nugatory, all scientific evidences in utter disregard of truth itself, are endeavouring, possibly without even knowing it, to render all scientific research nugatory, all scientific progress an impossibility. The logical sequel to all such futile and vain opposition to scientific truth and progress would be, not the creation and lavish endowment of institutes for cancer research, but the foundation of societies for the prevention of cruelty to cancer.

No apology is offered for the very frequent use of the

term "science" and its variations in the present writing. The writer is actuated solely by his deep reverence for the truths of Nature: her facts and truths are to him everything, and human "authority" nothing. Neither praise nor blame, nor even abuse nor ridicule, is asked for, sought after, or desired. The actual discoveries entailed in the finding out of Nature's remedies for malignant disease possibly are, be it admitted, trifling; perhaps, too, they deserve no human praise, much less do they call for ridicule. The long years spent in daily and nightly labours in the search after the general principle of an antithetic alternation of generations as the basis of the life-cycle of all the higher animals, including man, were something different, and the results were their own and only reward. Why the publication of true facts of Nature—such as are recorded in this book—should earn for their author the recompense of ridicule I

know not. Baseless assertions—such as that "trypsin" is without action upon living cancer-cells—are not evidences, and in no civilized court of justice would they be admitted as such. One thing is now clear, and the whole world may be challenged to contradict it: this is, that if it be asserted—as it has been more than once publicly by British official researchers—that trypsin is devoid of action upon living cancer-cells, then this same "trypsin" would also be found by an physiological chemist to be destitute of action upon all other albuminous substances in this universe. A "trypsin" devoid of action upon cancer-cells can also have no action at all upon milk, and yet it is mainly by its action upon milk that trypsin is usually estimated by chemists and by manufacturers of ferment preparations. Since a strong solution of trypsin, when injected daily hypodermically, has been known to liquefy a large living recurrent epithelioma or skin-cancer in less

than fourteen days, it follows, that those who assert, that "trypsin" is devoid of action upon living cancer-cells, might state with equal truth, that the "trypsin" they used had also no action at all upon anything else-
that is, was quite inert.

Looking back over the history of the ferment, trypsin, in science, though really discovered, but not named, by Baron Corvisart in 1857, it was for some ten years in danger of being forgotten. Then, in 1867, Professor W. Kühne took it up for research purposes, and in 1876 he gave it the name it bears of "trypsin," from T*púXw*, "I wear away." That is, it took Kühne nine years to establish this ferment securely as a possession of science. Why should I expect to be more fortunate than he? If nine years were required to set at rest the question of the mere actual existence of such a ferment as trypsin, it is perhaps quite out of question to say how many times the earth will have to describe its path round the sun -—n conformity with the doctrine of Coperniucus—before mankind will admit the truth of my discoveries concerning Nature's uses of trypsin and its complement, amylopsin. It may be that they, including many surgeons, would rather themselves die of cancer than admit the truth. Like the other happenings in the history of the reception of my cancer studies, this would not be at all a new attitude, for, according to Brewster, "a protégé of Kepler's, of the name of Horky, wrote a volume against Galileo's discovery" of the satellites of Jupiter, "after having declared 'that he would never concede his four new planets to that Italian from Padua, even if he should die for it.'" But sooner or later, if not now –possibly in the far-off future, when the inertia of the past two thousand years shall have ceased to be, and a new advance of the human intellect shall commence –it will be recognized

that, while the ferments of cancer came into existence in the dim and distant past in an ascending series of complexity, for the purpose of building-up asexual generation, trypsin and its modification, amylopsin, were evolved millions of years ago as things even more powerful than the ferments of cancer, and for the primary purpose of pulling down asexual generation, in order that something new –a sexual generation—might arise, blossom, and people the earth. That these latter ferments have also a very great digestive import, and are, therefore –to man, as the centre of the universe—of personal and even great commercial value, happens to be a corallary to what was their original use, and to the uses which they are still first of all given by Nature in every normal development.

Each one of us human beings, in the course of the gestation in which he or she arose, as a prime condition of his or her existence and persistence, was compelled by the iron necessity of Nature to destroy a natural phenomenon of the same nature as cancer –to wit, the trophoblast or asexual generation of normal development—and by no other means than the secretion of pancreatic ferments. This is the reason which confers a lasting truth on the words which I wrote down on December 8, 1904, and which, almost

immediately, gave the solution of the problem of cancer—"The mammalian embryo solved the problem of cancer ages ago." "Still it moves," commented Galileo. If the enzyme treatment of cancer be abandoned for the next century—if trypsin and amylopsin be maligned as "useless" or "futile" in cancer—all the same every human being who comes into this world in that time will never omit to employ his own pancreatic ferments in his development—never fail, since failure means death, to the pancreatic or enzyme

treatment of cancer in his own gestation—for the suppression of normal trophoblast or asexual generation. For otherwise this, as the most deadly form of cancer known—chiro-epithelioma—would inevitably destroy him—and his parent. In normal development, trypsin and amylopsin, unheeding human medical and surgical perversity, intolerance, and ignorance, will continue to destroy cancer, or trophoblast, or asexual generation, as in the past has happened for untold millions of years, for long ages before man was evolved.

For this is one of Nature's fundamental postulates, one of her inexorable laws for the continued existence of a race of human beings to people the earth, and without its strict and unbending observance there would be no living human beings upon the earth, no surgeons, no "cancer experts," loudly parading and proclaiming publicly their ignorance of the origin and nature of cancer, and –no problems of cancer.

* * * * *

It is a pleasant duty to put on record here how much in recent years the writer owes to the help of Messrs. Fairchild Brothers and Foster, of New York City, to Mr. B. T. Fairchild, and to their European manager, Mr. A. E. Holden. On all occasions the latter never failed to find some way of meeting my demands upon him. Like his chief, Mr. B. T. Fairchild, he has helped the humane and scientific work in every way in his power. What the debt is which the world owes to Mr. B. T. Fairchild himself, to his deep interest in the enzyme treatment of cancer, and to his scientific powers and knowledge, I will not attempt to determine. A later generation may be better able to estimate it. I know that from his heart not so long ago he sent the message that, except myself,

no man on earth could have a greater satisfaction than he in seeing this enzyme treatment succeed.

Of the portions of the book which have been published previously, Chapters I., III. and IV. are republished from the *Lancet*, and Chapters V. and VI. from the *Medical Record*, by permission of the editors and proprietors of those journals; and the usual acknowledgments and thanks are tendered herewith. Chapters II., III. And IV. may be taken to represent the results of work undertaken with the aid of research grants from the Carnegie Trust of the Scottish Universities, amounting in all to the sum of £70. Most of the pioneer work of the earlier years was carried out without the aid of grants from any source.

8, Barnton Terrace,
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October 12, 1911.

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INTRODUCTION

Some years ago a former fellow-student—M.D. (Lond.), Fellow of the Royal College of Physicians, London, physician to a large hospital in London – remarked that a single case of cure of undoubted cancer would establish the truth of the writer's published statements, and bring the whole world to his feet. Not long after then, here and there cures were published; but to these I will not refer; for, unlike those of the York case, the scientific proofs of them are not in my possession, and in one way or another it may be said of many of them, that the evidences in their favour were incomplete or inconclusive, which latter was, indeed, the verdict pronounced, without adducing scientific evidences, upon "trypsin" by Sir Henry Morris, Bart., late President of the Royal College of Surgeons, London, as recently as 1908. To a profession such as the medical one, which does not yet grasp the nature of the scientific evidences, the results of the pancreatic or enzyme treatment, even in the most favourable cases, might easily have been taken to be "inconclusive." The scientific facts that certain tumours had yielded to the stereo-chemical test—the highest court of appeal—and thereby had shown their malignant

nature, were not evidences to those, who knew nothing at all of modern embryology or of stereo-chemistry, and who relied implicitly upon the microscopical examination and appearances of a portion of the growth taken before or after operation. Then there were the countless failures,* many of them due, as I am now convinced, to faulty preparations, or to injections which were very much too weak for their work. In this way great difficulties had to be surmounted, quite apart from what has been termed the "conservatism" of the medical profession. Apart from the latter, these difficulties seem now to have been removed. Definite statements can be made concerning the requirements of really efficacious preparations for the treatment, and a successful case of cure, not standing isolated, can be, and is, produced in the present writing.

*For the sake of the scientific truth, the published opinion of Professor F. Blumenthal, of the University of Berlin—certainly a competent judge—regarding these should be noted. The vast majority of the cases hitherto treated (usually with very weak injections and with small does of these) were in an advanced phase of cancer. Oftener than not they were some of the failures of surgery. Professor Blumenthal remarks—rightly and scientifically—that the cases as yet handed over for medical treatment, as opposed to surgical, wee nearly all such that no possible treatment could have saved them. Lest this should be supposed to be exaggerated, Professor Blumenthal's actual words may be cited. He writes: "Die innere Behandlung des Carcinoms ist heute lediglich beschränkt auf die verzweifelten, nicht operablen Fälle. Wir haven jetzt daran festzhalten, dass jede bösartige Geschwulst, so lange sie operabel ist, auch durch Operation entfernt werden muss. Es handelt sich also für die innere Behandlung um eine Kategorie von Krankheitsfällen, welche vergleichbar sind mit verallgemeinerter Tuberculose, disseminierter Eiterung. Man stellt an die innere Therapie die Anforderung, nicht die beginnenden Fälle zu heilen, sondern überlässt ihr fast nur solche Fälle, die wohl niemals gerettet werden könnten, auch wenn es eiene innere Methode gäbe." Ferdinand Blumenthal, "innere Behandlung und Fürsorge bei Krebskranken," in *Zeitschrift f. Krebs forschung*, vol. X., pp. 134-148 (1910); loc. Cit., p. 134.

In the eighth section of "The Belfast Address" the physicist, Professor John Tyndall, wrote: "But there is in the true man of science a desire stronger than the wish to have his beliefs upheld—namely, the desire to have them true. And this stronger wish causes him to reject the most plausible support if he has reason to suspect that it is vitiated by error." That is the writer's position to-day. Six years ago he stated publicly that, in the secretion of that important digestive gland, the pancreas, Nature had furnished a potent means of coping with cancer. Even though there had been no other successes at the hands of Captain Lambelle, R.A.M.C. or of other, the successful issue of the case of the York ex-drummer, described in Chapter VIII., demonstrates for all time the scientific truth of the foregoing conclusion. The army surgeon who treated the patient, and the writer of these lines, both invite the fullest investigation of this case. The tumour was recurrent immediately after two operations upon it, and it had become inoperable. The diagnosis was confirmed by microscopical examination of a portion of the tumour-mass removed at the second operation by a pathologist of the Royal Army Medical College. A section which he made is in the writer's possession, and from an examination of it he is able to say that the diagnosis given is not open to the slightest question. The patient is alive and well, free from recurrence, and his address is written across the copy of the ten charts of the case, all certified and signed by the surgeon, and which, like the photographic negatives, copies of the official documents, and all other particulars, I owe to my friend, Captain F. W. Lambelle, M. D., R.A. M.C., now stationed in Central India. All the evidences are open to the most searching investigation, and this in the interest of scientific truth as well as in those of humanity, is invited.

A surgeon, who published as a "scientific report" an account of the failure of the enzyme treatment at his hands in a large series of (mostly very advanced) cases, remarked to the writer not long ago that a single case of success would not prove his thesis. The exact opposite of this assertion has been maintained quite recently by the Moseley Professor Surgery in Harvard University, Boston, Dr. Maurice H. Richardson. In the *Journal of the American Medical Association,* February 4, 1911, in an article upon "The Operative Treatment of Cancer of the Breast" (p. 315), he write: "And yet I am full of enthusiasm in the hope that the near future or the next method will solve the problem. One single total disappearance of undoubted breast cancer under any form of non-operative treatment will presage success, just as surely as a successful man-flight presaged aviation." A little further on he adds: "One varies, perhaps, in the positiveness of one's opinion. One's diagnosis may be an absolute conviction. I have often said—and I here repeat—that the diagnosis of cancer by gross appearance, plus the history, made by an experienced man is more worthy of credence in some cases than the microscopic examination alone." Everything of import here named by Professor Richardson has been fulfilled to the letter. In 1908 Captain Lambelle gave the enzyme treatment, as laid down by him further on in this book, in a case of "encephaloid"* cancer of the breast The patient was a Yorkshire lady of social position. The diagnosis was made by "experienced men," as well as by Lambelle himself. There was no operation and no microscopical examination. In his last letter to me, dated December 1,

*"Encephaloid cancer," a term used by pathologists to define soft cancer from hard cancer, or scirrhus. Encephaloid cancer is so termed because of its brain-like softness. It is described as quick-growing and rapidly fatal (see Appendix L).

1910, he writes concerning this case: "By the way, that case of encephaloid breast cancer is alive and free from recurrence—diagnosed October, 1908. I saw her on November 29, as near as mortal man can say 'cured.'" Further comment on the above is not needed.

I was well aware, as any scientific man is, that negative results in scientific experiments never proved anything at all in science, but was also under the impression that very many scientific discoveries of great moment had been the outcome of single successful experiments. The fall of an apple from a tree revealed the law of universal gravitation to Newton. In our own day a single photographic impression of some keys, etc., led the physicist Röntgen, in 1895, to the discovery of the Röntgen, or X rays; and, strange to say, the find of a few stray ganglion cells in the development of an American lake-fish in 1888 led the writer ultimately to the discovery of the nature of cancer, and of much besides. The scientific investigator knows, even if some surgeons be ignorant of it, that very many discoveries in science are the outcome of what at first were of the nature of single successful experiments. Even the cures* of cancer by

*Looking at the matter from the point of view of practical embryology, the so-called "cures" of cancer by surgical operation are probably in all cases without exception examples of the "cure" of a benign tumour, a more or less reduced "embryoma." Naturally benign tumours are of common occurrence, and whether diagnosed by microscopical examination or only clinically , the diagnosis of cancer is not one which can be regarded as conforming to a scientific criterion. When one thinks of the extraordinary frequency of recurrence after surgical operation, one can only conclude that, in the absence of the crucial stereo-chemical tests, either of adequate injections of sufficiently potent preparations of trypsin and amylopsin, or of examination of the tumour albumins by means of the polarimeter, at present there is no valid evidence extant that operation has ever cured a single case of malignant disease, though it may quite well have induced it, as the X rays have often done. Sir James Paget. A scientific

surgical operation are not in blocks of certain dimension; but assuming that surgery ever does cure even a single case of cancer—a very big assumption which, as a scientific man, I make only for the sake of argument—each case of cure would be of the nature of a single successful experiment. I do not for a moment deny that surgery does, and has done, many very wonderful thing, but to assert that it ever knowingly cures a single case of cancer is a scientific absurdity.

If ten, a hundred, a thousand, or ten thousand cases of cure be required—by the surgeons, not by science—to establish truth of the scientific foundations of the pancreatic or enzyme treatment of cancer, then from the particulars furnished in later chapters of this book, any of these numbers can be obtained, always provided, as the lawyers say, that properly and scientifically standardized and guaranteed preparations be employed and the treatment be carried out in the scientific fashion—letter and spirit—laid down here by Captain Lambelle and the writer. Since the medical profession of Great Britain has, through some of its members, been most careful to guard that the writer, who is a mere scientific man, and "not even a medical practitioner," should treat no cases at all—cancer being a natural phenomenon, not "an incurable disease"—more than this single demonstration cannot be asked from me. There is, sad enough to say, no dearth of cases, for in England and Wales alone annually nearly 40,000 people, some of them surgeons, die from malignant disease.

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man of high standing because of the extent and nature of his investigations, doubted whether operation was ever advisable in case of cancer, and on the evening of my Liverpool lecture of 1905, I heard a prominent surgeon declare that he would not be willing, even in the most favourable case of cancer in which he had operated, to stake a sovereign against its recurrence.

It behooves me to add a few words of explanation of Captain Lambelle's connection with the work. In his address, "Science and Immortality" (London, 1904), Sir William Osler, in the finest written compliment any of my researches had ever received, described (p.58) "the patiently worked-out story of

the morphological continuity of the germ-plasm" *(i.e.,* the germ-cells) as "one of the fairy-tales of science." Shortly after then their author was to have an unexpected and much greater compliment, because of a practical kind, paid to these investigations. As a scientific man the writer places his trust, in true military fashion, in "divisions" and "brigades," represented by the published records of observation and experiment, and not in "fairy-tales of science." The investigation, one of the most powerful of my "divisions," which immediately preceded the cancer work was into the history of the germ-cells, the forerunners of eggs and sperms, from generation to generation. Some of the published results of these researches found their way as far as China, where, in Hong-Kong, a Captain of the British Royal Army Medical Corps happened to be stationed. These finds interested him so much that he endeavoured, on human embryos, to make independent observations.

In the first instance these failed, as any experienced practical embryologist would have foretold. This officer, Captain F. W. Lambelle, M.D., was shortly afterwards ordered home again, and, on reporting himself to the Director-General at the War Office, he related the foregoing facts and his deep interest in my scientific researches. This led the Director-General to station Captain Lambelle with the 2nd Light Dragoons (The Royal Scots Greys), at that time in garrison in Edinburgh, so that he might learn more of my work. From the day when, un-

announced, Captain Lambelle entered my little room in full uniform, and saluting, introduced himself, we have been close friends. He worked for himself over much my material—a collection also, like the Scots Greys, "Second to None!"—and he read all my published papers, which, unlike some scientific people, he thoroughly understood and appreciated; in fact, he evinced the deepest interest in all the problems and their solutions which had occupied my leisure hours during many years. At that time I happened to be, *noiens velens*, in the thick on the cancer-business, and he often expressed his regrets that the nature of his work, with young healthy soldiers, gave him no chances of looking into cancer-matters practically for himself. Subsequently, his appointment as operating surgeon of the Military Hospital, York—the hospital of the Northern Command—placed, one after the other, four cases of cancer in his way, and of these he cured three, the fourth dying from hæmorrhage as the treated dead sloughing tumour came away. One of these cases fully recorded in this book. The other two successful cases are not laid stress upon by him, simply because, although the clinical diagnoses of cancer were ample, the microscopical evidences, upon which scientifically I personally lay no stres at all, were lacking.* In order to say the surgeons who have set up this arbitrary stand of the microscopical appearances of cancer as a criterior—often a very deceptive one—the requisite slides of sections of the tumour have to be produced as completing the surgical diagnosis.

In his last letter to me before sailing to India, Captain Lambelle stated that the total number of injections given in latest case was 120. Apparently, from the charts, the ferments exhibited March to July, 1909, did not

*Compare Professor Richardson's opinion as cited on p. 4.

amount to more than 60,000 tryptic units and 120,000 amylolytic ones. That is to say, for his last published case the strengths and doses of injections employed during the vital period of the treatment can be stated. This can be said also only of the report of Messrs. Ball and Thomas. Dr. Bainbridge, according to his own statement, used injections of five strengths of trypsin, but in his report he does not discriminate among these, or give figures, from which even approximate calculations, or any at all; can be made. All of those in this country, or elsewhere, who, publicly or privately, have condemned the treatment, with the single exception mentioned above, whatever its scientific value, have furnished no particulars of strengths

or doses and of the total number of injections exhibited; in fact, not one of them has given a scientific verdict, for not one of them has produced any evidences that he ever employed any ferments whatever. In 1906 and 1907 the statement was often made by several very prominent London surgeons to private patients that they had "tried" trypsin in cancer, but had found it "useless." They themselvew knew nothing at all about the preparations used, but actually this adverse verdict was given after the employment of preparations containing at that time less than 10 tryptic units per cubic centimetre or ampoule.* This should be

*The first injections of "trypsin" employed in 1906 were all, or nearly all, made up from Fairchild Brothers and Foster's "trypsin in powder." This, which is no longer on sale anywhere, was a very potent preparation, and it had been on the market for many years. At the beginning of April, 1906, the manufacturers of this "trypsin in powder," as they announced by advertisements in the chief British medical and chemical newspapers, withdrew it from sale. Tis step placed others makers of "trypsin injections" upon their own resources, or very largely so. There was already a "famine in the land" as regards "trypsin," so much of one that I heard through friends of several cancer patients who were being treated with raw sweetbreads,

compared with Captain Lambelle's usual dose of one thousand (1,000) tryptic units plus two thousand (2,000) amylolytic units, 1 ampoule or 1 c.c. of each.

A University Professor of Surgery, in support of his public statement of 1910, that the pancreatic ferments were "futile" in cancer, recently sent me copies of Bainbridge's report, and an author's copy of a paper by Sir Henry Morris, read before the Surgical Congress, Brussels, September 21 to 25, 1908. In the latter it is written: "He noted the reports on the use of the latter "'trypsin'), and the fact that the evidences in its favour could not be considered conclusive." Trypsin alone, a most deadly remedy for cancer if employed without abundant amylopsin, is mentioned. Nothing whatever is said about the conclusive or non-conclusive character of the failing evidences, that adequate strengths and doses of trypsin, and any at all of amylopsin, had been employed. No doubt the preparations wee said to be "potent." Possibly to-day Sir Henry Morris could no more produce any scientific evidences concerning the strengths and compositions of the injections he was referring to in 1908 than the University Professor, mentioned above, did do or could do when I asked him politely for some particulars as scientific evidences of the truth of his published statement. It ought not to be necessary, but—*leider!*--it is, to remind surgeons that in science it is a rule—as it also is in courts of justice—that no

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or pancreas glands. I have always considered the withdrawal of this "trypsin in powder" as a very wise step, but one of its direct consequences would appear to have been the extensive employment, especially in and about London, of a "trypsin" injection possession at that time rather less than ten units of tryptic strength. The eminent surgeons mentioned above had not, as a matter of fact, a ghost of an idea of the potencies of the injections they so glibly condemned—the boxes of ampoules were labelled with the magic word "trypsin."

assertion shall be made without at the same time the production of the evidences for it.

Of course, "trypsin" is not a cure for cancer, a fact stated by the writer in *Nature* four years ago. The evidences for this, it may be added, are forthcoming in abundance whenever asked for. What has destroyed cancer without injury to the patient in cases not too far advanced, and what will do the like again and again, is the use of properly prepared injections of trypsin of a strength of at least a thousand Roberts tryptic units of activity plus equal amounts of amylopsin of two thousand to two thousand four hundred (2,000 to 2,400) Roberts amylolytic units of strength per cubic centimetre, and the doses of injections and their frequency must be adapted to the needs of the particular case under treatment.

As “failure is easier of attainment than success in anything,” it would be possible to the end of time for some surgeon, or official cancer researcher, to declare that trypsin and amylopsin were “useless,” or “futile,” in the particular cases treated by him, and used as he employed them. Scientifically, all such verdicts are worthless, unless the evidences for them be produced in full; and these must include the previous history of the case, the duration of the treatment, the preparations used, definite statements as to their purity, all necessary details as to their quantitative values, their doses, and the number of these. Science, as a mistress, makes exacting demands upon the observer, and the mere designation of a document as a “scientific report” does not alone confer any scientific value upon its contents.

The view generally accepted by mankind, even by all medical men, has long been that cancer is “an incurable disease.” How often have I not heard this expression, even from very prominent surgeons! Not only was

cancer incurable, but it was a disease of the nature and origin of which the whole of the medical profession, by its own confession, often proclaimed by leading surgeons in public orations, knew nothing at all about. Under such circumstances it could hardly be strange that it should not be in conformity with the generally accepted, when a scientific man, who knew very well what he was speaking about, and who, like Pasteur, had earned the right to an opinion by his investigations of many long year, announced that cancer was not a disease, but a natural phenomenon, that it was germinal in origin and asexual (trophoblastic) in nature. This was all something new, which had never been said before by anyone, living or dead. As at the present time we were supposed, but possibly erroneously, to have outlived the Dark Ages, and as, at all events, those who made me, the scientific Germans, who have advanced far beyond the Dark Ages, had long advocated and practised “the freedom of science in the modern state,” it was something to be examined scientifically. It is interesting to see how this was realized in Germany.

A recent part of the German *Journal of Cancer Investigation* (vol. x., part 1) contains the report of a special Cancer Congress, held in May, 1910. Here Professor C. Neuber, well known for his researches into the chemistry of cancer, writes on p. 70 regarding the position of chemistry in cancer research in words which recall Duclaux’s declaration concerning chemistry and medicine. Neuberg affirms that where the problems of the nature of tumours are in question, chemistry will never retreat from the field of conflict. Duclaux said: “With Pasteur chemistry took possession of medicine. It is easy to foresee that she will never loosen her hold upon it."” As a study of

the following pages will show, my fundamental discoveries of the nature of cancer, and of the places of the two all-powerful ferments, trypsin and amylopsin, in the treatment of this natural phenomenon, not disease, were founded in the first instance in the science of embryology. This is as true for the separate reasons advanced for the employment of trypsin and of amylopsin as it is for those urged in 1902 as demonstrating the asexual (trophoblastic) nature of cancer.* Afterwards, from 1906, the chemical evidences—the stereo-chemical ones—began to reveal themselves to the observer, who was not like that genius Pasteur, “a mere chemist,” but a practical embryologist, who had chanced to have some sort of elementary chemical education at the hands of Sir Henry Roscoe and of that pioneer of comparative physiological chemistry, the late Professor C. F. W.

**Sexual and Asexual, Sexual Generation and Asexual Generation.*—In animals and in plants two modes of reproduction are recognized, the sexual one, by means of germ-cells, eggs, and sperms, and the asexual by budding, which is really a process of continuous indefinite cell-division, with no eggs or sperms. In an animal or plant a sexual generation is one which bears reproductive organs, in which eggs or sperms, or both, arise. On the other hand, an asexual generation of an animal or plant is one which never bears reproductive organs, eggs or sperms, or

both, but which reproduces in the way indicated above, really by cell-division. In plants the asexual generation is the flowering plant, which is capable of indefinite unrestricted increase, as, for example, a *Gloire de Dijon* rose or the fine white chrysanthemum, *Niveus*. Origianlly there was but one plant of each of these. The sexual generation of a flowering plant is a small microscopic entity contained with the flower. In animals all the individuals which bear sexual organs belong to the sexual generation, which the asexual generation are represented in various ways. Thus, in the sea-ploypes, by the colony of polypes, while here the medusæ or "jelly-fish" are sexual; in worms, starfish, etc., but what are known as larvæ, while here the wor, starfish, etc., are sexual; and lastly, in the highest animals or mammals the asexual generation is present only during uterine life, as what Hubrecht termed the trophoblast. This latter used to be regarded as one of the "fœtal membranes" under the name of chorion.

Krukenberg. Thus it came about that, while the line of first advance was purely embryological, later a junction could be effected with the science of stereo-chemistry, and a further base for operations obtained in the fundamental discoveries of Pasteur on the asymmetry of naturally occurring organic compounds.

The following remarks* (literally translated), by Professor F. Blumenthal, of Berlin, concerning "trypsin" and cancer are of interest: "For a long time the trypsin-therapy of Beard awakened greater hope. This depends upon the quick digestion of the cancerous tumour by trypsin. If trypsin or pancreatin be injected into a cancer, one notes a fairly quick softening of the same, leading to a liquefaction, which is aseptic, not made up of pus. In some cases it appears that in small and readily accessible tumours it has been possible with the help of trypsin to cause the tumour to disappear. I will recall only the case in the aural clinic of Munich. In larger tumours, especially with metastates, I have only had failures. Successes also seem to be lacking in mouse-tumours, as Bashford reported. † In the treatment with

* Blumenthal, F., "Innere Behandlung und Fürsorge bei Krebskranken," in *Zeitschr. F. Krebsforschung*, 1910, vol. X., pp. 137-138.

† It would appear not to have occurred to Professor Blumenthal that this statement might have reference to inert ferments. Since the experiments, which must be supposed to have led to this erroneous conclusion, have never yet been published, and since they are, indeed, not mentioned in a single word in the Third Scientific Report of the Imperial Cancer Research Fund, published in 1908, and, lastly, since there are no scientific or other evidences extant to show that ferments of any kind or sort had ever been employed in these unpublished experiments, I feel bound to ask Professor Blumenthal to explain, as a scientific man, why he cites these unpublished experiments, and non-existent evidences? It is common enough to note in scientific publications that published experiments or evidences have been ignored by the author, but it is something quite new to find unpublished experiments and mythical evidences cited in a

trypsin I have also noticed a disagreeable complication, which consists in this, that often the digestive power of the trypsin passed over also to sound tissue, and a disagreeable destruction of this came to pass. Recently Sticker and Falk have improved the trypsin-therapy in that they have united the action to trypsin to charcoal, by which means, after a single injection, this action persists much longer, since this carbenzyme is not so quickly used up as ordinary trypsin."

Regarding the foregoing, only a few words need be added. It will be noted that Blumenthal also confirms the "liquefying" action of trypsin on cancer. This has now happened in London, Berlin, New York, and elsewhere. The researcher of the Imperial Cancer Research Fund denied some years ago that trypsin had any action at all upon cancer-cells. Looked at scientifically, either trypsin acts upon living cancer-cells, and

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scientific paper. Moreover, as Professor Blumenthal is quite aware, the results of his own experiments with "tryspin" are in direct contradiction with the verdict pronounced, without the production of any evidences, by officials of this cancer research. It reminds one of the reception accorded to von Siebold's discovery of two sorts of

spermatozoa in a fresh-water diœcious snail, *Paludina vivipara*, in 1836. Within an easy walk of Würzburg, this snail is readily found in great numbers, and the first time that these two sorts of sperms were seen by me was in 1882, in living material obtained not far from Würzburg. None the less, when von Siebold published his find, the professor of Anatomy in the University of Würzburg, the celebrated anatomist and embryologist, Alber von Kölliker, interposed the weight of his authority, and, without taking the trouble to examine the facts for himself in the animal concerned, disposed of von Siebold's finds…simply by denying the correctness of his observations. Since that time an extensive literature has sprung up concerning twofold sperms in *Paludina* and many other animals, including man, and the well-known cytologist, F. Meves, has published a minute account of the development and histology of these two sperms of this snail, the wormlike and the hairlike forms.

ultimately, if used in solutions of sufficient strength, liquefies them, as maintained by myself, Blumenthal, and—"in some cases"—by Bainbridge, or it has no action upon them, as stated in 1906, and again in 1907 by official researchers. One or other of these statements must be false. The official assertion was unsupported by the production of any evidences whatever, the former rests upon the independent testimony of four* different observers, situated as widely apart as London, Edinburgh, Berlin, and New York. The official statement is untrue. Already, in *Nature* (January 10,1907), I called upon the executive of the Imperial Cancer Research Fund to substantiate the assertions made under their auspices, or to withdraw them. I now repeat this unsatisfied demand, merely adding that, if they wish their finds still to stand, they must complete the statements scientifically by the addition that inert trypsin† had been employed, and that the assertions challenged related to such inert trypsin, and not to trypsin in an active form.

In the later pages of this book I have explained why it comes about that in some cases trypsin may act upon

* As I recognize, while finally reading through this manuscript before sending it to press, a fifth observer of the formation of "liquid cancer" can be cited. From the charts of Captain Lambelle's case of sarcoma, and from his description on a subsequent page of the course of his case of lympho-sarcoma, it is clear that in what he speaks of as "sero-purulent fluid" in the one case, and "purulent fluid" in the other, he was really dealing with liquefied cancer.

† The General Superintendent of this cancer research himself writes as follows: "It is surprising how many people are unconvinced that the scientific examination of such claims presupposes exact knowledge of the ingredients of the remedy. In the absence of this knowledge, negative conclusions could always be ascribed to error" (*British Medical Journal,* May, 27, 1911, p. 1221). One wonders whether he knew this when the unpublished experiments with "trypsin" were carried out, if so, why he failed to act upon it.

"normal" somatic tissues. It is in very advanced cancer cases, where the tissues have been much acted upon by the ferments and toxic products of cancer, and have thereby been injured. In this connection the finds of Yoshimoto and Neuberg concerning the auto-digestion of cancerous liver, and of portions bordering upon the cancer, are of much import.

As to the improvements in the treatment brought about by Sticker and Falk, I content myself with the record of them, and make no comment beyond saying that, in my opinion, no "trypsin-therapy" which is unaccompanied by abundant animal amylopsin will be, or can be, satisfactory in the long run.

In the long, interesting article, summing up what he considers to be our present knowledge of the chemistry of cancer, published in the "Ergebnisse der Physiologie" (1910), Professor F. Blumenthal, of Berlin, has a reference to "trypsin" in cancer. Recalling his own investigations with Wolff, published in 1905 (*Med. Klinik,* No. 5), he states that (in the test-tube!) all the tumours, five in number, wee very easily attacked and pulled down by trypsin, and in a footnote he adds: "These finds were the basis of the

trypsin-therapy of cancer." In a more recent publication (German *Journal of Cancer Investigation,* vol. X., p. 137), he makes a similar statement in these words: "For a long time the trypsin-therapy of Beard awakened greater hope. This depends upon the fact that the cancerous tumour is quickly digessted by trypsin" (in the test-tube!). On the other hand, the writer of the brief article upon cancer in the new eleventh edition* of the "Enclopædia Britannica" assigns as

*The prospectus states that "this new edition represents the results of a fresh survey, undertaken in every department of knowledge by the most eminent authorities, up to the year 1910."

the reason of my advocacy of trypsin in cancer that the pancreas-gland was believed to be a t fault in cancer patients. Versions of the reasons similar to these two have been given in other places—thus, in the *Münchener Medizinische Wochenschrift*. They are both quite incorrect. My only connection with the first was in publishing in the *Lancet* of April 29, 1905, a summary and translation of some recent German cancer work, including that of Blumenthal and Wolff upon the chemistry of cancer, and the citation of this relation of trypsin to the cancer-cell as a certain support of my views. As to the second reason, neither the writer of the article in the "Enclopædia Britannica" nor anyone else can find in any of my published writings even a hint of this statement. Moreover, it has been supposed that my affirmation of the germinal origin of cancer meant that it was embryonic or somatic, and my name has been quoted as that of a supporter and advocate of "embryonic theories," such as the Remak-Cohnheim one of "embryonic rests." In the first article referred to ("Ergebnisse der Physiologie") Blumenthal considers these embryonic theories as refuted from the chemical side by the chemical fact mentioned in his paper, such as the discovery by Abderhalden and Pincussohn that the ferments contained in extracts of mouse-tumours pull down silk peptones and polypetids atypically. With this conclusion I agree absolutely, and would add that ever since 1902, and before then, I have been an opponent of the Remak-Cohnheim theory of "embryonic rests" upon grounds of embryological observation, leading to the conclusion that these "rests" are mere figments of the imagination. The Remak-Cohnheim theory of embryonic rests is, therefore, now untenable on decisive chemical and embryological grounds, and must be abandoned.

My theories of cancer, its origin and nature, differ *toto cælo* from those advanced by any other observer, living or dead. The theory of the germinal origin of cancer, which says that a cancer arises primarily from a latent germ-cell, does not mean that cancer is embryonic in origin or character. Germ-cells, such as fertilized eggs, give rise to something else than embryo or soma: they produce on occasion trophoblast (asexual generation). I know that some embryologist, for whom chemistry and physiology have no existence in their researches, describe the trophoblast of Hubrecht as merely another name for what they term "extra-embryonic epiblast." To use the latter term does not signify anything more than where in normal development the supposed portion of epiblast lies—i.e., beyond the embryo. I do not agree with them that trophoblast is epiblastic (embryonic skin) in character, or that their description of it as "extra-embryonic epiblast" in any way defines it embryologically. Their account is merely descriptive, and it gives no information whatever concerning the chemical, physical, or physiological characters of this "extra-embryonic epiblast" or trophoblast, which, quite unlike ordinary epiblast or embryonic skin, eats and erodes the maternal tissues.

In very simple words I will now endeavour to summarize what is meant by the germinal origin and the asexual or trophoblastic nature of cancer. To these shall be added brief accounts of the reasons advanced six years ago for employing "the secretion of that important digestive gland, the pancreas," including the two ferments, trypsin and amylopsin, in the scientific treatment of cancer. It is appropriate

that this should be written down on January 20, 1911, the sixth anniversary of the scientific lecture in Liverpool, in which the more important of these reasons were first announced publicly.

One of the most remarkable of the many brilliant things done by the illustrious French chemist, Louis Pasteur, was the giving of two public scientific lectures, in 1860, "On the Asymmetry of Naturally Occurring Organic Compounds," which include the albumins, sugars, starches, etc., found or formed in animals or plants. In a scientific instrument, known as a polarimeter, these compounds always rotate the plane of polarized light to the right or to the left. Therefore, by chemists they are described briefly as dextro- or lævo- (d- or l-) compounds—for example, dextrose, or d-sugar, and lævulose or 1-sugar. That is, as they occur in living nature, animals or plants, they are never "compensated mixtures" of both stereo-isomers—never, for instance, of dextrose, and lævulose—and in such "compensated mixtures" all rotation is absent, because the one compound twists the plane of polarized light as much to the right as the other does to the left. When the chemist is able to manufacture any of these compounds in the laboratory, he has never been able to make the one compound, the 1- one, without an equal amount of the other, the d-one. To get them separated he has had to employ expedients, such as fermentation by yeast, etc., when one of the two might be attacked and pulled down, but not the other. The fact that all living organisms, whether animal or plant, manufacture or contain invariably only the one stereo-isomer, and not the other, has often been commented upon. Thus, by Professor W. J. Pope, who writes that while d-glucose (d-sugar) is a valuable foodstuff, we should be unable to digest its opposite or anithesis, 1-glucose, although they have the same chemical composition—that is, are isomers or stereo-isomers. Humanity is, therefore, according to him, composed of dextro-men and dextro-women; and, putting his words, which will

be found in Chapter VI., in simpler language, just as we ourselves should probably starve if provided with food of organic compounds the opposites in light-rotation of those to which we are accustomed, so our opposites, the lævo-men, if they were to come among us now, when we have not yet succeeded in manufacturing the more important foodstuffs artificially, would find our food, even our bodies, not suitable for their nourishment. That is, these foodstuffs would require to be changed, or "inverted." If we our-selves had to digest compensated mixtures, we should need a double digestive apparatus. He supposes that in course of time the one set of compounds as articles of food has vanished. If it were scientifically true, as well as "generally accepted," that the fertilized egg gave rise directly to an embryo or individual, then one of the sets would have vanished from the nutrition of all higher animals. Now, one of my discoveries has been that Pope's hypothetical lævo-men do exist, and that they are represented by, among other things, the cancers. In this way the second set of nutritive compounds has not vanished, but at its basis the antithesis of two sets of things—compounds of carbon, defined by Pasteur—is the same antithesis as that of two sets of living things, asexual and sexual respectively, discovered and in the researches of more than twenty years described by me as occurring in the cycle of life of a fish, a frog, or a man, etc.

The fertilized egg, and any of the (primary) germ-cells which arise later on, possess the intrinsic property (potentiality) of developing in the one direction or the other; in the asexual, with the cleavage of the fertilized egg, when trophoblast first raises, as in every normal development; in the sexual, when a primary germ-cell, which itself is

derived ultimately from the fertilized egg, unfolds as an embryo or individual. What I found was that Nature employed this peculiarity of the antithetic or opposite character of certain naturally occurring compounds, all containing carbon, and many of them also nitrogen, as the chemical basis of the cycle of animal life. She did not attempt to unite both sets of the compounds, the 1- ones and the d- ones, in any one form, animal or plant; neither did she dispense with one of the sets. Had she done either of these things, had she been able to do it, she would have carried out the "generally accepted" view of direct development, egg leading directly to embryo. Then the egg would produce the hen, and the hen the egg, and so on *ad infinitum*. On the contrary, in order to get back to the fertilized egg again, Nature had found it necessary to separate the "compensated mixtures" into their components, to use at one time the one set, made up of certain 1- and other d- compounds, and then to use the other set, made up of the opposite ones; that is, she swings the pendulum of life first in the one direction, and then in the other, and in this way brings it back again to the starting-point—the fertilized egg.

As pointed out in Chapter VI., in connection with the account of Professor Pope's lecture, by means of two generations, asexual and sexual, which alternate in the life-cycle from egg to egg. Nature not only utilizes two of the apparent possibilities afforded by the existence of stereo-isomeric compounds, but also she is thereby enabled to bring round again and again the cycle of life to its starting-point. Under the orthodox and "generally accepted" view of direct development these things have not been explained, but they have simply been ignored. The like orthodox views have also, notoriously, been

impotent to elucidate cancer, and the reasons for this failure lie on the surface.

Normally, in development, the fertilized egg, by forming trophoblast (asexual generation), swings the pendulum in the direction of dextro-albumins, lævo-starches, and 1- sugars, etc., and later the primary germ-cell, by unfolding as a sexual individual or embryo (sexual generation), in which new eggs or sperms arise, reverses the swing of the pendulum in the direction of the formation of lævo-albumins, dextro-sugars, d-starches, etc. Abnormally, some primary germ-cell, originally destined to give rise to a twin identical with the individual harbouring it, either, *ab origine*, does this by producing a monstrosity, or a benign tumour—an "embryoma"—or, remaining latent, anon it swings the pendulum in the opposite direction, and produces a cancer, which is trophoblastic (asexual) in nature—that is, is the same product as would arise normally from a fertilized egg. A cancer thus is not somatic, not embryonic, not "gametoid tissue" (Farmer, Moore, and Walker), not derived from an "embryonic rest" (Remak-Cohnheim), but it is trophoblast (asexual generation), the very antithesis or opposite of embryo or soma (sexual generation), embryologically and chemically.

When Professor Pope spoke of dextro men and women, he would, in my opinion, have done better to have used the terms "lævo-men" and "lævo-women." For while the sugars and starches of our foodstuffs are d-compounds, the nitrogenous or albuminous constituents are 1-compounds. This leads one also to point out to the non-chemical reader that the one generation—say the sexual one, man—does not use exclusively compounds of one rotation, 1- or d-ones, but these stereo-isomeric compounds form series, some of them being 1-compounds,

others d-compounds. The like is true of the ferments, which certain of the albumins give rise to as modifications of themselves. Trypsin is like the albumin from which it is derived lævo-rotatory; it converts d-starches into d-sugars, among other things, but not 1-ones, and thus not the 1-glycogen or animal starch of cancer. It acts upon and pulls down certain d-compounds of cancer. On the other hand, the proteolytic or albumin-attacking ferment of cancer is a dextro-rotatory body, like the (dextro-rotatory)

of cancer, from which it is derived. It attacks and pulls down, not the living dextro-totatory albumins of cancer, but the living lævo-rotatory albumins of the human body.

The conception I have formed of one action of amylopsin in the enzyme treatment of cancer is briefly as follows: Acting upon the living d-albumins of cancer, trypsin pulls them down in the chemical scale a certain distance, but not into simple harmless products. On the contrary, some of the products of its action are very poisonous, and to all appearance these are dextro-rotatory, like cancer albumin. As compounds of this rotation they can be acted upon and reduced to simple harmless compounds by the ferment amylopsin, owing to its configuration, its lævo-rotatory character. †

* For an opportunity of determining these facts concerning the rotations of trypsin and amylopsin I am indebted to Mr. P. W. Squire, London. At my request he kindly sent me freshly prepared and strong solutions of both trypsin and amylopsin, as well as a bottle of the "menstruum" in which they were dissolved. In my polarimeter the latter showed no rotation at all, while both tyrpsin and amylopsin were strong lævo-rotatory.
It was not my purpose to calculate their "specific rotations."

† The following natural question was recently put to the writer by a surgeon keenly interested in these matters: "If

The first and only reasons advanced by me publicly at Liverpool, now six years ago to the day, for the use of pancreatic ferments in cancer, were that at a certain period of development every normal embryo, or soma, or sexual individual, commenced to suppress the trophoblast or asexual generation of normal development. This came to pass by the initiation of the functioning of the sweetbread or pancreas-gland, with its powerful ferments, the two chief of which are trypsin and amylopsin.

Some imaginary relation of diabetes to cancer, or some suspected failure or "fault" on the part of the sweetbread or pancreas gland, had nothing at all to do with the reason—as little as had the discovery a little later on, by Blumenthal and Wolff, that trypsin easily digests

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(continued from page 24 footnotes)
trypsin acts upon dextro-albumins, of what use is it in the ordinary adult body, seeing that the albumins of human food are lævo-albumins?" No more than Nature does would I separate amylopsin in its action from trypsin, for, like Nature, we must associate the two ferments. Trypsin and amylopsin, acting upon the dead lævo-albumins of our food-stuffs: Trypsin only pulls these down to a limited extent, converting them into substances capable of absorption, and on these amylopsin has no action. These are built up again into living lævo-albumins by cell ferments in the body-cells. Trypsin and amylopsin acting upon the living dextro-rotatory albumins of asexual generation or cancer: Trypsin at once attacks these, and pulls them down into quite other bodies than those which its forms from dead lævo-albumins. These bodies, or some of them, are rank poisons to the human body, but, as they are further acted upon amylopsin, and by it pulled down into simple, harmless products, the two ferments, trypsin and amylopsin, acting here together, pull down the cancer-albumins, these products of the action of trypsin are chemically relatively highly organized and can be used as food by the cells of the body. This not the case with the products, to which the action of trypsin and amylopsin on cancer-albumins, living or dead, gives rise. He who doubts the truth of the above had better, before publishing his doubts, study the recent work of Professor Abderhalden and his pupils.

cancer cells (in the test-tube). Nor have I ever held, as some have done, that because they supposed, erroneously, that trypsin had some action in "splitting up" glycogen or animal starch, that it "dissolved" glycogen, therefore it should be used in cancer cases. From the start I wished all the ferments—trypsin, amylopsin, and steapsin—of the pancreas gland to be used in the injections employed.* The import of trypsin was, of course, clear, for it was known, since the work of Corvisart and Kühne, to attack and pull down dead l-albumins, and I anticipated—rightly, in spite of all the contradictions extant, which are false—that it would, and scientifically regarded must, pull down the living d-albumins of cancer or

trophoblast. † The special reasons for the employment of very potent injections of amylopsin, which normally converts starch into a d-sugar, termed "glucose," came later on. It was found that the injections first used, which were very deficient in amylopsin, being sometimes, indeed, almost chemically pure trypsin, produced after some six to eight weeks, according to the strengths employed, very bad symptoms. These were first reported to me by French and Italian physicians, and I told them that, as this treatment followed the lines of what happened in a normal human gestation from the seventh week onwards, they

* For evidence of this, reference need only be made to the following fact: Early in 1906, when the London representative of a well-known firm of manufacturing chemists, specialist in the ferments, called upon me, I requested him to inform his firm that in my opinion the injections for use in cancer ought to contain all the ferments.

† The evidences of the truth of this will be found in the text under the description of the course of the York case. The like facts wee also witnessed in the very similar course of the Naples case, and these scientific finds are confirmed up to the hilt by the facts concerning the "liquefaction of cancer" in the living human body, as detailed subsequently.

should treat these symptoms as they would the vomiting of pregnancy. I then found that for this and for the covulsive illness sometimes happening in pregnancy, and known as "eclampsia," there was no rational treatment extant in medicine. So once again a new problem had to be solved embryologically. It was, What induced these bad symptoms in pregnancy, leading up to eclampsia, and in cancer ending with the continued injected of trypsin, in something identical with eclampsia? With continued improvements in the treatment, especially in the preparation of the injections, when put up scientifically, these bad symptoms do not now arise to anything like the extent that they die in 1906, for example. They were, in an ascending sereies, nausea, vomiting, pain in the back, "sleeping in any position," drowsiness, mental and physical torpor, high arterial tension, and albuminuria, culminating on occasion in convulsions, lasting several hours, with complete unconsciousness (coma). Only one case of the latter (mentioned farther on) was ever reported to me. It happened that there was an extensive experimental study of eclampsia in one of the German medical journals for 1905 by Professor Zweifel, as well as the report of a lecture by him in the Munich *Medizinische Wochenschrift* (February 13, 1906). He concluded that eclampsia was due to sarco-lactic acid in the fœtal blood and placenta, but the conclusions appeared to rest upon thin ice, and there may well have been other substances. Professor Zweifel's name awakened recollections of a former discovery of his, to the effect that amylopsin was not produced in the human pancreas gland until some months after birth. I had never before had occasion to consider the import of this fact embryologically, although I had worked over the whole course of gestation, studied its span, the cause of birth, the

milk nutrition, etc., from the standpoint of the embryologist. Certain of my researches, published some ten years earlier, when applied to the problem, furnished the solution with ease. One German medical man has described the following advocacy of amylopsin in cancer as "fantastic," which is merely a pious "opinion," not a scientific argument; but I am willing to admit that sometimes Nature may do things which to some people, like a certain King of Spain, may appear to be "fantastic." Whether it be a "fantastic" fact or not, genuine amylopsin always does its work in the scientific treatment of cancer.

In the days of long ago, in our ancestry, as in that of all mammals, and as now happens in most marsupials, like the kangaroo, opossum, etc., birth took place at what I have termed the "critical period." This is the moment in development when the embryo is first complete in all its parts. In a rabbit it is after some fifteen days out of a total gestation of thirty; in a human being in the seventh week of pregnancy, out of the total of nine months. With birth at this period the milk-nutrition was initiated. In this amylopsin is not of any use, and can be dispensed with. When, as she did, Nature prolonged the

gestation, in order to bring the young into the world in a more perfect form, she deferred in so doing more and more the start of the milk-nutrition. In prolonging the gestation, she forgot, or omitted to introduce, amylopsin at an earlier period and not the "unconscious memory" remained that it was not needed until the milk-period had passed. Consequently there is an absence of amylopsin during all fœtal life. Usually the difficulties caused by this can be surmounted if the mother produce sufficient amylopsin, but from the seventh week of gestation pregnancy is a sorry business, owing to

This absence of amylopsin in the fœtus. To this day, to my knowledge, such is the "conservatism" of the medical profession, amylopsin has not been employed as an injection in any case of threatened eclampsia.* But in cancer it has for some years past been used along with trypsin, and it has never failed to perform its task of removing the bad symptoms. The first case in which it was injected, in 1906, was that of a very distinguished artist and art-critic, who was suffering from an advanced cancer, recurrent after three operations. I had previously told his physician—a London one of high standing—when, almost to the day, his patient would develop the bad symptoms. The first intimation was in a friendly letter written from the patient's club by himself, in the course of which he complained of being drowsy, and said finally that he could hardly hole his pen for this reason. Then his physician wrote that the patient showed high arterial tension and albuninuria, and that he was about to inject amylopsin. Under the influence of this ferment all the symptoms vanished in two days. Had trypsin been as successful hitherto as amylopsin in its mission in the treatment of cancer, very many who are now dead would still be among us.

How the term "tryspin treatment" came to find its

*This is a very remarkable fact. To many physicians of both sexes the writer has explained the scientific reasons for concluding that the source of eclampsia was to be sought and found in an absence or deficiency of amylopsin in the maternal blood, to be remedied, of course, by hypodermic or intramuscular injections of genuine amylopsin of 2,000 units of activity per cubic centimetre. So far as he is aware, though more than one of these has expressed intentions of "trying" this scientific remedy, there is no single case of actual or threatened eclampsia, in which such injections were made. Instead thereof, the barbarous remedy of stripping the capsules of the kidneys is still often resorted to, and only recently a new device has been sug-gested seriously—to wit, amputation of the breasts.

way into general use is still a mystery to me. It was, I believe, first employed by an anonymous writer—still quite unknown to me—in the *Daily Mail*, somewhere about the end of January, 1906. It caught on, and nothing I could do ever altered the name of the treatment. But with certain other happenings this use of the term "trypsin treatment" was a disastrous occurrence. Since early in 1906 I have always used the designation of "the pancreatic or enzyme treatment." An "enzyme" is another name for a ferment. Again and again I have insisted upon the fact that a "trypsin treatment" of cancer was about the most deadly remedy which could be devised. It is impossible to estimate how many treated cases all over the world have failed from toxæmia owing directly to this use of trypsin without abundant amylopsin.

Particular attention may be directed to the following: The scientific treatment of cancer or malignant disease advocated by me is not, and it never was, a "trypsin treatment." From the days of its first annunciation—December 13,1904, and January 20,1905—it was meant to be of injections of "the secretion of that important digestive gland, the pancreas"—that is to say, of pancreatic ferments, including both trypsin and amylopsin. I lay no claim what ever to have "discovered" such a scientific absurdity as "that tryspin dissolved glycogen"—as water also does—or the equally ridiculous one that it was a "property [of trypsin] without doubt of breaking up glycogen in living tissues" (*The Hospital*, January 26, 1907, p. 297). I do not and have not,

"suggested" the use of secretin, or erepsin, or enterokinase, alon with one or both of the pancreatic ferments mentioned above, just as little as that of soap or chian trupentine. I deal in science, not in domestic commodities. None of these

things are in conformity with the enzyme treatment of cancer.

Moreover, it is not suggested in this book that the injection of 60,000 genuine tryptic units and 120,000 amylolytic units in the space of four months will cause any and every malignant tumour to shell out or encapsulate. At times a cancer may shell out on less, as happened, for exaple, in the Naples case of inoperable cancer of the tongue. In others, again, a much more vigorous treatment, for all I know, may be needed. Thus, the case in which, to my knowledge, the greatest number of tryptic units was ever injected in a given time was one of multiple scarcoma. In this case, in eight weeks, according to my calculations, 84,000 tryptic units, and only about 16,800 amylolytic units, of the strongest injections then on sale, wee given. Several of the tumours did, indeed, disappear, but, so far as I am aware, the patient was not cured of sarcoma. Attention may be directed to the comparatively small amount of amylopsin employed, and it is my suspicion that the case failed from toxæmia, due to this lack of amylopsin. This case was treated in the early1907, and at that time the very great importance of large injections of amylopsin had not been recognized. The trypsin injection used in this case of multiple sarcoma contained 500 tryptic and 100 amylolytic units per cubic centimetre or ampoule. Owing to these facts, the course of treatment, doses, etc., cannot be compared with that adopted by Captain Lambelle which such conspicuous success. At all events, genuine trypsin was injected, and Dr. H.O.S. did not condemn the treatment. If a malignant tumour posses an enzyme (ferment) totally different from that (trypsin) widely present, according to Vernon, in traces in normal tissues, surely that is a fact of supreme significance and import. Since

1904 one of my main theses has been that, just as in normal development there was an antithesis or opposite character, of two generations—sexual and asexual respectively—so the like antithesis obtained, of necessity, in the ferments employed by these for their nutrition. The ferments of the asexual generation or trophoblast were therefore the antitheses or opposites of the pancreatic ferments, trypsin and amylopsin; and as cancer was in nature asexual generation (trophoblast), so its ferments mush be identical with those employed by the trophoblast of normal development. All life-processes take place through the action of ferments, and without these there would be no life, such as we know it. It follows from this that the action of cancer ferments upon substances on which trypsin and amylopsin, or normal cell-ferments, will also act, cannot be the same as that of the latter; that is, the products of the fermentation must be different when used upon the same sub-stratum. The proof of this, and the answer in the affirmative to the above question, has really been furnished quite recently by German scientific chemists. In the paper by Professor Neuberg, already cited (p. 12), he writes that "Comprehensive investigations into unusual ferment phenomena of tumours have been made by E. Abderhalden, with P. Rona, A.H. Koelker, F. Medigreceanu, and L. Pincussohn. They showed that often, but not constantly in human and animal tumours enzymes can be detected which split up polypeptids and peptones quicker than normal cell-ferments do. In addition, it was established that extracts of caner (die Krebssäfte) split up polypeptids in entirely atypical fashion. While, for example, normally cell-ferments hydrolize d-alanyl-glycyl-glycin to d-alanin and glycyl-glycyl, tumour fluid splits it into glycocoll and d-alanyl-glycin. The pulling

down (Abbau) of cancer (carcinoma) takes place thus at quite other points (Stellen) of the animo-acid compounds that those at which all other peptolytic ferments attack." All this is in complete accord with the scientific foundations of the enzyme treatment of cancer, and it is exactly what one might expect under the view of the trophoblastic or asexual nature of cancer, advocated by me. As Blumenthal urges, it alone, apart from all other considerations, is sufficient to refute and render untenable the "embryonic views," such as the Remak-Cohnheim one. Professor Abderhalden, in speaking of the foregoing finds, remarks that it is improbable that the atypical pulling-down of the silk peptone is accidental, and he describes the enzymes concerned in this al "atypical ferments of tumours." Again, Yosimoto found that the proteolytic autolysis (albuminous self-digestion) of cancerous liver was much increased over the normal, not only in the tumour portion, but in those free from tumour. Neuberg, studying the like self-digestion of liver-cancer, discovered a characteristic produce—fiz., reducing pentose, which in the self-digestion of normal liver is not produced.

In the Third (and latest) Report of the Imperial Cancer Research Fund (1908) the word "ferment" occurs but twice in its 440 pages. Dr. W. Cramer writes (p. 433): "The effect which a growing tumour produces on a normal organism* is a problem of nutrition similar to the growth of a fœtus in a pregnant animal. It cannot be explained by attributing to a cancer-cell the formation of pathogenic substances of a hypothetical nature, such as a 'cancer ferment,' or a 'cancer toxin.'" The reader will not how this is rendered in the Introduction to the Report by the Editor: "Dr. Cramer's paper shows how

*A "normal position" is here understood to mean a rat inoculated with a malignant tumour.

precise bio-chemical methods can now be applied to the study of the growth of cancer, and brings new and exact information as to the nature of the relations existing between the tumour and the animal bearing it. The effect which a growing tumour produces upon a normal organism is the problem of nutrition similar to the growth of a fœtus in a pregnant animal; *it cannot be explained by assuming the formation of pathogenic 'cancer ferments' or 'cancer toxins."*" In the foregoing the italics are mine, and they are introduced to draw attention to the method of citing the "new and exact information."

As demonstrating the exact opposite of this information, one may cite the following recent words of Blumenthal and Neuberg: "Moreover, we consider the question of the abnormal enzymatic (ferment) processes in tumours as completely cleared up, since it has also been answered in a positive sense by Abderhalden and his colleagues, working with quite other methods." The original German of this passage will be found in a short article by Blumenthal and Neuberg on "Proteolytische Fermente der Krebszelle," in 1909; also to the same author, in *Zeitschr. F. Kresborchung,* vol. X., 1910; and to Blumenthal, "Ergebnisse der Physiologie," "Die chemische Vorgäange bei der Krebskrankeit," pp. 363-428, 1910; separate edition of the memoir (Asher-Spiro, Berlin), 1910.

In a review of Bainbridge's report, the *Lancet* (October 9, 1909, p. 1079) states: "A negative result of this kind has the great value we have indicated, in that the medical profession have before them chapter and verse

for their placing no faith in trypsin, and none in persons who persist in advocating its use by repeating stories of alleged 'cures' when, as a matter of fact, the patients referred to have been proved to have died from the disease." Scientifically, it is not necessary to do more than insist on the fallacy of lying any stress at all upon "a negative result," and in the present instance this happens to be specially true, for "the medical profession," if it were "placing faith" in the evidences furnished by Bainbridge's report, would find it now difficult, but impossible, to cite from it any real scientific grounds for this. The "chapter" may be found easily, for the "scientific report" has been scattered broadcast, but the "verse" is a present blank. In the chemical experiment the observer must satisfy, not only himself concerning his reagents, but also the requirements of science.

As Bainbridge employed five different strengths of trypsin injections, of which the strongest is stated to have been six time the strength of the weakest, and as he furnished no particulars to show in which cases each of these injections had been employed, or the total number and sizes of the doses in a given time, the "chapter and verse" of his evidence can carry no sort of conviction to any logical mind. The reference to patients "proved to have died from the disease" in the citation above is, of course, to the single case of Miss K. H., which has never once been cited by me as a "cure," or even believed for a moment to have been "cured." This case (No. 7 of Bainbridge's report) furnishes a far more useful and instructive object-lesson of the value of surgery in cancer than of trypsin and amylopsin.

The following is the history of this case as give on pp. 20 and 21 of Bainbridge's report: "Duration of disease previous to enzyme treatment: about three

years. Previous treatment: removal of growth from left breast, June 4, 1904 (Dr. Edward W. Peet); radical operation refused. About one year later thirty-two X-ray treatments (Dr. William J. Morton); trypsin, 5 to 10 minim doses, April 27, to October 31, 1906 (Dr. Morton). Radical operation, November 3, 1906 (Bainbridge). Removal of enlarge nodules and secondary deposits in skin, January 22, 1907 (Bainbridge). Condition when enzyme treatment was begun: full enzyme treatment instituted twenty-four days after radical operation. Recurrent, irremovable cancer of left side of chest and glands of neck; liver enlarge, probably cancerous; general condition poor." This is a fair sample of what surgically is understood by "a thorough, scientific test." According to the above the cancer of the breast had existed for not far short of three years, and the case had failed twice surgically before a real enzyme treatment was, as a last resort, undertaken.

Dr. Morton's treatment with 5 to 10 minims of "trypsin" thrice weekly during some six months in 1906 may be dismissed as no treatment at all. I doubt whether with the strengths then on sale, which no endeavours of mine could persuade manufacturers to increase, the patient received in all more than one of the doses mentioned in this book—viz., 1,000 tryptic units. According to Bainbridge's report, and its author, as the surgeon concerned, perhaps knows the facts better than any anonymous critic, the order of events was the very opposite of that usually assumed. The knife failed twice before Bainbridge evoked the ferments. There might, indeed, be some point, if little truth, in the statement here referred to, had the patient derived any benefit at all from "submission to the knife."

Looking back over the field of my researches since the

summer of 1888, twenty-three years ago, at various phases of the journey, it was all a lonely pilgrimage

"Towards the unknown region,
Where neither ground is for the feet,
Nor any path to follow."

WHITTIER

New problems, entailing fresh, patient labours, constantly arose, and the solutions of these brought, invariable, new surprise in their train. The start of the work was the discovery of a transient nervous apparatus in the development of a fish; this was the one end of the slender thread. Its unravelling was always intensely interesting and absorbing to the observer, and the thread went on, and on, and on, always continuously, unlike any other thread of research known to me in the whole history of embryology. Then, at last, the other end came in sight, twenty-five years after the observer first began, in Semper's old research institute in the ancient University of Würzburg, to learn from the master how research problems were to be approached, dealt with, and solved. The story of this is told in Chapter VI.

The first piece of work upon the thread occupied some five or six years; for that time was required to work out, night after night, and put together the results, which are recorded, with eight plates, in the memoir upon "The History of a Transient Nervous Apparatus" (1896). This was clearly an asexual structure, the work upon it a prelude to the cancer investigations. There are, indeed, published researches extant, such as Professor A. Goette's immense monograph upon the development of a toad, *Bombinator,* which took a longer time; but, so far as I know the literature of embryology, there is no other embryological monograph which covers so long a period of development, or span of time, some seventeen

months, as this. It is nearly twice the length of time of a human pregnancy from conception to birth.

But this is not the place to write a history of a quarter of a century's researches in embryology. Suffice it to say that the chain of researches is now a complete one, every link has been tested, and no flaw discovered. As one outcome of this systematic investigation, a single case of successful cure of malignant disease, quite apart from others recorded in the published literature, is brought before the whole work, and the invitation is give that any test of its truth be applied to it. All the methods employed are published in full. The remedies suggested and the modes of using them may be rejected or ignored; but the truth, if scientific truth have any place at all in this world, must be admitted. The facts are: that in a case of malignant disease, termed by the pathologists a "round-celled sarcoma"—named by me, scientifically, irresponsible trophoblast or asexual generation—which was recurrent and inoperable after two extensive surgical operations upon it; the remains of the tumour, under the influence of the all-powerful ferments, trypsin and amylopsin, finally shelled out, leaving the patient free from all trace of malignant disease, and, in fact, "cured." I ask that these scientific fact, which cannot be denied, be admitted, and that with this the tardy acknowledgment be made, that when, on January 20,1905, a scientific man, whose sole object was the revelation of the truths of Nature, stated publicly that "in the secretion of that important digestive gland, the pancreas," Nature had provided a potent remedy for cancer: what he then said was nothing more than scientific truth, which is the greatest of all truth.

This, Nature's remedy, may be taken or left; but the truth may be denied no longer. It is beyond my power

to prevent mankind, in happy ignorance of what the cycle of life really is, from awaiting some other solution of the problems. In doing this futile thing mankind may watch, and hope, and pray, until the crack of doom; but all in vain. Even if the scientific solution were to dawn upon official research, it could—in this universe, at all events, and as it is constituted—be none other than that offered by Nature! No denial can any longer have the smallest value against the supreme truth, that when properly—that is scientifically-applied, the pancreatic ferments, trypsin and amylopsin, being the most powder things in the whole range of organic nature, are efficacious agents against cancer.

At the present time science and scientific research are not things to be made light of, to be scoffed at and jeered at in the market-place, or to be ignored. With the publication of the facts contained in this book, the responsibility is shifted to other shoulders than those of the scientific observer. All I ask is, that these truths of Nature, which she has given as a revelation of boundless and priceless import to a world which was not ready for them—that these shall not be denied, but be received reverently as what they are—true facts of Nature. Cancer is a natural phenomenon, not a disease; although it may bring disease in its train. Its treatment—that of a natural phenomenon—has been committed legally, logically, rationally, and scientifically not to the hands of the scientific observer, who has discovered its origin and nature. It is the business of the scientific observer, not that of the medical man or surgeon, to study and elucidate natural phenomena. Let the truth be acknowledged

for its own sake. As the writer is "not even a medical practitioner," the adoption of the treatment in all or any cases of cancer is not compulsory; but it may not for a moment be imagined that scientifically it is intended to make good the failures of surgery.*

The statement made in this book that cancer is a natural phenomenon, not a disease is unassailable. It rests upon scientific evidences, which are impregnable against all attacks; but it may be questioned whether civilized mankind as a whole has any real conceptions of the nature of natural phenomena in general. Some are beneficent. The sun rises, and its heat and light render this earth habitable to man. Owing to natural phenomena, the seasons return in orderly fashion, bringing, among other things, spring, with its fresh, new green; summer, with its wealth of flower; and autumn, with its harvest of fruit and grain. Other natural phenomenon are maleficent—malignant. The volcano, also a natural phenomenon, has in the past buried or destroyed countless cities; and even in our own day this has happened. Some naturalists have been of opinion that the fossil remains of innumerable animals, now extinct—often found in great multitudes heaped together-owed their present existence, as imperfect records of past events, to catastrophes which were also

*While for the sake of humanity the enzyme treatment may be refused to no case of cancer, recurrent after one or more operation, if such cases fail, from the point of view of pure science, they may not be regarded and cited as "test cases"; for in them there always lies the possible source of error of experiment of previous operative interference. With a positive result, as in the York case, such a case becomes, on the other hand, a test one of the severest description; for in it success has been obtained, in spite of the existence of the possible source of error.

natural phenomena. Last, cancer, with all its malignancy—a thing which laughs to scorn the impotence of the surgeon's knife, which yearly claims its thousands upon thousands of human

victims *--is at its scientific basis only a maleficent natural phenomenon, such as these. We come into being and exist as human beings because of beneficent natural phenomena, and as human beings we continue, for a span of time, to subsist, in spite of maleficent natural phenomena. The course of some natural phenomena is unalterable by human agency; others, again, by a knowledge of the working of Nature, of science, can have their maleficent action stemmed and averted; and, as a scientific man, I affirm that cancer belongs to the category of these.

To those, surgeons and others, who have not, like the writer, foolishly devoted their lives to scientific research and experiment, but wisely to more mundane pursuits—such as the acquirement of wealth—let the following warnings be uttered: "If you wish to set up what you term 'test cases,' pray let them be such as shall fulfil in every way the requirements of science. Do not vitiate your experiments from the very start, as has happened, by choosing some 66 per cent. Of the cases, in which there lay the pernicious 'error of experiment' of previous surgical operation, once or several times over. Remember also that if your cases be chosen rightly—that is, scientifically—even then there remain the reagents employed, and how used. Do not forget that in this, as in every scientific chemical experiment, the observer must not only satisfy himself regarding his reagents, but be prepared,

*On the basis of the present population of the United Kingdom of Great Britain and Ireland (45,000,000), the tribute exacted by malignant disease in a single century would be not less than 3,875,000 human lives, or over 100 daily; for India 27 millions.

if called upon to do so, to produce scientific evidences concerning their nature and composition.* Above all, do not for a moment imagine that you 'have tried trypsin in cancer, and have found it useless,' when to all intents and purposes you might just as well have been testing the effects of a solution of glycerine and water. Do not think it is 'science' to perform mere elementary qualitative experiments upon your injections, showing that they have some action upon starch and upon white of egg. Lastly, under the erroneous idea that it thereby makes the thing a scientific document, do not publish any account of your negative experiments with trypsin and amylopsin with the sub-title, "A Scientific Report,' unless the document in question fulfil, like my scientific memoirs and like this book, in all respects the requirements of science."

The greatest exaction of science is truth. This is why the expression, "scientific truth," is so far-reaching and invincible. In the opening passages of this Introduction two points were referred to, and to them at its close I return. "There is," said Tyndall, in somewhat different words, "in the true scientific man a desire far greater than to have his conclusions 'generally accepted': it is the ardent wish to see them verified in fact." Again, it was pointed out that the problems of the origin, nature, etc., of cancer formed but a special case, a side-issue, of the application of a general principle. This general principle, revealed by my researches of more than twenty years, was of an antithetic alternation of generations with a continuity of germ-cells from generation to generation as the basis of the cycle of life. This, *the law* of animal development, waw what during many years of research Carl Ernst von Baer groped for, but in vain. In this

*Apparently this rule of science has no applications in official cancer research.

connection a confession on p. 451 of von Baer's "Autobiography" (second edition, 1886) is of great interest. Here, in a review of his own published embryological researches, he writes: "Und der Generations-Weschsel schleuderte mich ganz zurück" (And the alternation of generations threw me right back). As the reader will find a subsequent chapter, there are grounds for

supposing that the like difficulties connected with alternation of generations interfered with the researches of another great embryologist, Johannes Müller. It required, in fact, the later botanical investigations of Hofmeister and others to furnish a new basis for attacking this fundamental problem of alternation of generations in animals. Sixty years after von Baer published his investigations I began mine—in the summer of 1888. These researches certainly lasted far longer than his, and their completion only came nearly twenty years later, with the final overthrow and rout of cancer. This latter, including the physical fact of the actual liquefaction of living cancer in the living human body, and embracing the true cure of malignant disease in the single case—a test one for all time—of Lambelle's ex-drummer in York has a far wider import and deeper bearing than its applications in medicine, and for the welfare of humanity. The scientific investigator is bound, on occasion, to divest himself of his humanity, and to look at his problems and their solutions in cold-blooded fashion. He must draw the conclusions, even though the heavens fall. This I shall now proceed to do in brief, reserving a fuller treatment for some other place and occasion.

For the past century, to go no farther back innumerable attempts have been made—all in vain—to solve the problems of cancer, or malignant disease. In Dr. Jacob Wolff's monumental work, "Die Lehre

von der Krebskrankheir," vol. i., the list of investigators given includes more than a thousand names—to be exact 1,004. Why, of these, did 1,003 fail, and but a single on succeed? The answer to this is not far to seek, and, indeed, it is contained in the true solution which is detailed in the following pages. All scientific research, to be successful in the end and enduring, must start in correct principles, or, at any rate, not in false ones. Until in recent years a practical embryologist of long-working experience applied the general principle of an antithetic alternation of generations to the problem of cancer, it had always been attacked from the standpoints of three embryological dogmas, which have this in common—that they are false, though "generally accepted." These are epigenesis, or direct building-up of the embryo from the products of the fertilized egg (Harvey and Wolff); somatic origin of germ-cells, as "chips" of the "old block" (Huxley); and recapitulation in development, as maintained by Haeckel and his followers. If these doctrines, which are pretty "generally accepted," were true, if they contained a particle of truth, the solutions of the problems of cancer would follow inevitably out of them. If they were false, as they are, their applications to cancer could but lead to failure, and this has been the case. Years ago, as opposed to these dogmas and as scientifically true, I set up, on grounds of observation, the three doctrines of evolution with predestination (Weismann anticipating me in this), a morphological continuity of germ-cells, and an antithetic alternation of generations.

This trilogy of doctrines is in reality one and indivisible. If this trilogy were scientifically correct, its application to the problems of cancer must end in their resolution, and this has, in fact, happened. It would not have

taken place under any constitution of the visible universe other than the one which includes this general principle of an antithetic alternation of generations as the basis of the cycle of life of animals and plants. It would have been lacking, were this general principle untrue, had my researches since 1888 been false as well as "heterodox." Were direct development or epigenesis, somatic origin of germ-cells, etc. Nature's method, cancer would not, could not, have been liquefied by injections of pancreatic ferments in London, New York, Berlin, and York; no malignant tumours at all would have disappeared under the influence of injections of pancreatic

ferments; and Lambelle's ex-pensioned drummer would long ago have perished miserably from the ravages of malignant disease, as countless other cases still do every day, week, and year all over this earth. It follows that the current dogmas of direct development or epigenesis, set up in the eighteenth century by the researches of Harvey and Caspar Friedrich Wolff, somatic origin of germ-cells, and recapitulation in development which are taught in all, or almost all, the Universities of the civilized world, and which are supposed to underlie the sciences of embryology, zoology, and anatomy, not to mention physiology and pathology, etc.—that these are false, even though they be "orthodox." Therefore, the general principle of an antithetic alternation of generations has not only resulted in the overthrow and rout of cancer, but its decisive success in this has demonstrated how necessary it is, in the interest of truth itself, that without further delay—unless scientific truth have ceased to be a requirement of science—the scientific house be put in order, the false dogmas be cast out and rejected as worthless, and the Golden Rule of an antithetic alternation of generations be set up as a fundamental scientific general principle of the sciences of

life—embryology, biology, etc. Orthodoxy will not in science render false doctrines true, and Tyndall's words become a mere mockery and delusion unless they apply to the embryologist and biologist, as well as to the physicist and chemist.

Twenty years ago my general principle—an antithetic alternation of generations with a continuity of germ-cells from generation to generation as the basis of the cycle of life—was almost within my grasp; that is, had almost been established by facts of observation. After a few more years of patient research this was so—at last. Those, and those only, who know and appreciate the history of the growth of human scientific knowledge—"The Growth of Truth" (Osler) can realize the true import of this. Two of the greatest scientific investigators of the nineteenth century were Hermann von Helmholtz and Louis Pasteur. As investigator they were incomparable, beyond comparison with others or with each other. What the latter thought about general principles in scientific research is cited, else in this book, and it may be found in full in his live, "La Vie de Pasteur," written by Vallery-Radot. The illustrious physicist and physiologist, Hermann von Helmholtz, wrote his view in the following beautiful lines: "When, from a correct general principle, one develops the conclusions in special case of its application, new surprises, for which one was not previously prepared, always make their appearance. And since the conclusions unfold, not according to the author's caprice, but after their own laws, it has been made the impression upon me that really it was not my own work which I wrote down, but merely the work of another."*

* "Wenn man aus einem richtigen Allgemeinen Principe die Folgerungen in den einzelnen Fällen seiner Anwendung für sich entwickelt, so kommen immer neue Überraschungen zum Vor-

The general principle of an antithetic alternation of generations has now been applied to the special case of the natural phenomenon knows as "cancer," or "malignant disease." Even though this had been in the York case alone, at the hands of Captain Lambelle, it has proved itself to be capable of solving the enigmas of cancer, of explaining it scientifically, and of coping with it successfully. Not only so, but in the sequel it has turned out—and it is no accident—that at its basis this general principle merges into a certain other one, laid bare by the researches of "Pasteur, van t'Hoff, and Le Bel. This, which relates to the asymmetry of naturally occurring organic compounds, rests upon a foundation-stone of the visible universe, the asymmetrical

carbon atom. It is this which is the true and only scientific basis of the science of stereo-chemistry, and, as my researches have shown for all time, of the sciences of life, embryology and biology. The problems of cancer were vulnerable along two different lines of attack—embryology and stereo-chemistry. While official cancer research has failed hitherto to follow up either line of attack, the writer, in his private cancer studies, has developed both of these—the only possible points of attack—and along both the "divisions" and "brigades" have achieved the complete overthrow and decisive rout of *Cancer*.

(footnotes from page 46)
schein, auf die man vorher nicht gefasst war. Und da sich die Folgerungen nicht nach der Willkür des Autor, sondern nach ihren eigenen Gesetze entwickeln, so hat es mir oft den Eindruck gemacht, als wäre es gar nicht meine eigene Arbeit, die ich niederschreibe, sondern als ob ich nur die Arbeit eines Anderen neiderschriebe" (From a letter written to Sir William Thomson [Lord Kelvin] in 1860).

PART 1

THE PROBLEMS OF CANCER

CHAPTER 1

EMBRYOLOGICAL ASPECTS AND ETIOLOGY OF CARCINOMA*

At a time when so much is being attempted in the investigation of the problem of the nature of cancer, it may appear presumptuous on the part of an embryologist to express opinions and conclusions regarding this grave question. It has long been a subject of earnest research by physicians and pathologists, who naturally are familiar with actual facts and finds concerning carcinoma, foreign to the embryologist. But hitherto the physician and the surgeon, the pathologist and the gynæcologist, have failed utterly to establish anything concerning the etiology of cancer, and without the intervention of the embryologist success may be as distant in the future as in the past.

As indicated by the above title, the present chapter is intended to deal with aspects of carcinoma as they strike an embryologist, and not every embryologist, but one particular investigator. At the outset it may be asked, "Is the etiology of carcinoma an embryological problem?" As the thing itself and its manifestations demonstrably fall within the province of the surgeon and the pathologist, for it confronts them almost daily, it is possibly not

*The *Lancet*, June 21, 1902.

very clear why the problem of the nature of cancer should be an embryological one at all. It is a disease carrying with it death and destruction. On the other hand, the problems of the embryologist, as generally understood, treat not of disease, but of the blossoming-forth of life itself—of the phenomena which culminate in the appearance of new living beings. Death and decay would seem to be things of which, from his researches, the embryologist might be expected to obtain no practical knowledge. He is supposed to be concerned with "das Werden," while das Vergehen" is beyond the scope of his researches. Would that it were so! Unless he shut his eyes to plain facts, "das Vergehen" in the midst of das Werden"—death in budding life itself—is continually before him.

The conviction impressed upon the writer's mind from many years devoted to the study of the mode of the development of the higher animals, the vertebrata, is that everywhere and at

any point atrophy and death and degeneration of cell, of organs, of organism, of embryos themselves, are among the commonest phenomena under the eyes of the embryologist. His textbooks, even his published researches, may be silent of these; for, as a rule, he believes himself to be concerned solely with the coming-into-being; and the opposite aspect, the decline of life, he leaves severely alone. It is not, in his tacit opinion, a theme of the science of embryology. This view of the problems of the science has for many years failed to commend itself to the writer, and in his own researches he has endeavoured to take account of everything happening and capable of being observed during the developmental cycle, whether progressive or retrogressive.

The manifestations of life present themselves under the headings of either form and structure, or function. Embryological research deals largely with form and structure, or, more exactly, with the coming about of these. And as, according to the testimony of pathologist, cancer, when it appears, is something new to the organism,--a neoplasm, a foreign thing, not growing and functioning after the manner of the individual containing it, increasing by cell-division after unknown laws, which appear to defy all law, carrying with it widespread eroding destruction, only comparable to that dealt out by some parasites—the phenomena of cancer would have analogies at least to many such lying within the domain of the embryologist. Cancer is something with a beginning; it increases like a developing embryonic germ by cell-division; it invades territory at first foreign to it, and it differs only from a parasitic organism in the fact that its mode of reproduction is what may be defined as asexual. And thus, while as a rule its cycle is limited to the individual harbouring it, carcinoma is something with for itself an indefinite life-cycle, which is only bounded by the life of its host, but which cannot be carried directly over, by germs or fertilized gametes, to another organism.* That the resemblance between the life-cycle of a cancer and that of a higher animal should be incomplete is natural; for the former is an abnormal product, and it is in the nature of such to differ in some or other important details from the typical or normal.

The problem of the nature of cancer has long been before the writer in his investigations; in fact, ever since

*It has, however, been shown by Hanau and Wehr to be possible to transplant cancer from one individual—e.g., the dog—to another.

he learnt, from the researches of Welms* and other, that it had been encountered occasionally along with those curious tumours, the "dermoid cysts" of ovary or testis—the "embryomata," or rudimentary embryos of Wilms. The latter speaks of this occasional connection † of the two—it had in 1902, according to Wilms, been observed some nine times—as a remarkable fact (p. 86), in that, in an organism of one or two years of age, the development of carcinoma can happen. As this relates to the presumed age of the embryoma, and not to that of the individual harbouring the latter, the validity of the conclusion is not apparent. On his part the writer must reject it. For the past two year, from time to time, in researches upon the germ-cells, observations have been made which appeared to have bearings upon the nature of carcinoma. ‡ This period may not seem a long one; but beyond it life the investigations of other twelve years, without which the standpoint of to-day would be an impossibility. If, therefore, no study of cancers underlie the present chapter, the approach of the problem is not a sudden one; but it as been preceded by prolonged observation, and, moreover, animal life is the same whether it be that of a hyroid polype upon a shell of the seashore, or that of a cancer within an individual of the human race.

The immediate cause of the present writing was as follows: In a recent paper, dealing with the understudy theory of heredity, in an altogether different connection,

* Wilms, Max, "Über die Dermoidcysten und Teratome," etc. in *Deutsches Archiv f. klin. Med.,* v. 55,1895, pp. 1-108, Pl. 3; also Martin, "die Krankheiten des Eierstockes," etc., Leppzic, 1899, pp. 576-614.

† Chorio-epithelioma, even in the male, and usually in the testis, has, of recent years, turned out to be not uncommon.

‡ Some years ago, at Liverpool, Mr. H. J. Styles, F.R.C.S., published figures of all the supposed "cancer-parasites," and showed what they really wee. All of these have been seen by the writer in degenerating germ-cells of development.

a few comments had been written down upon the mode of growth exhibited by certain organisms, and a comparison drawn between this and the pernicious growth of the human chorion in certain cases.* And it was not until long after the proof had been returned that is was seen how in this comparison the key to the problem of the nature of cancer had been given away. If the pernicious growth of the chorion be really carcinomatous—and it is recognized † as such by pathologists under the names of malignant placentoma, deciduoma, chorio-epithelioma or destructive placental ploype ‡--the nature of cancer is clear as the light of day. And it has seemed desirable to offer the present essay, in order that at least a warning note might thereby be uttered, and an earnest attempt made to point to the futility of investigation in the direction of a cul-de-sac, such as the probable one of cancer, as due to unicellular organisms.

In the following, the facts concerning carcinoma, as

*The passage in question is as follows: "It should be mentioned that De Vries and Weismöö
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öööööööööööööööööööööööööööööööööw the mammals;* the animal lowest in the scale in which it has been recored being the short-headed phalanger (*Belideus breviceps*).† The disease is a corollary to uterine gestation.

If the cycle of development of the higher animals really be that concluded by the writer, if his interpretation of the phenomena of mammalian development—which are not in the least based upon facts or factors noted in cancer, but upon normal development here—if these be correct, the nature of carcinoma is not hypothetical at all, but is actually known. More than one font cannot be assumed, and it one fountain-head be shown, all other

* See. However, the closing lines of this chapter.

† Bland-Sutton. J.: "Evolution and Disease," London, 1890, p. 247, Fig. 123. The case is one of cancer in the marsupial pouch.

explanations become superfluous. In certain cases in human development, where either no embryo arises within the chorion, or when the embryo becomes aborted or dies prior to the suppression of the asexual generation, the latter—the chorion—may go on gowing indefinitely, and may give rise to what pathologists and gynæcologists recognize to be a form of cancer, placentoma, or chorio-epithelioma (Marchand). For years now I have recognized, and, in homologizing this structure with the larval skin of an amphibian, Hubrecht has gone a long way in the like direction, that the human chorion represents the main portion or whole of the asexual generation here. In certain cases, therefore, we here witness the conversion of the chorion—i.e., of the asexual generation—into a malignant tumour, a carcinoma.

What other proof could be asked for? That this proof of the nature of cancer is not in agreement with accepted views of normal development cannot be set down to the fault of the writer. He holds, and has long maintained, such views to be false and unfounded in fact, and moreover, it has been attempted to indicate the right way. The arguments and conclusions have been neither refuted nor confirmed, but they have been ignored. But embryologists, are living, and have long been existing therein, in a mental universe, where but a tithe of the facts observed are explicable under their views. Under the conception of development as an antithetic alternation of generations—especially as laid down in "Hereditary and the Epicycle of the Germ-Cells" *--all the known facts of development fit in, all are capable of easy and natural explanation. And the elucidation of the etiology of carcinoma follows as a natural corollary to the law of the

*Bilogisches Centralblatt, 1902, vol. xxii., pp. 321-328, 353-360, and 398-408.

development cycle. The embryologist and pathologist may ignore and neglect the plain and palpable fact, but on no theory of direct development—a thing only existing for the higher animals in the human imagination—can any explanation whatever of the nature of carcinoma be advanced. This would have been recognized clearly long ago had some embryologist taken the trouble, as the writer has done since 1888, to trace out in full the details of the life-cycle of one of the higher animals from egg to egg. The idea of direct development, accepted without examination of the evidences, and the erroneous belief in the somatic (body) origin of germ-cells, have retarded the advance of knowledge to an extent difficult to estimate.

The nature of the argument employed in the present writing may be summarized as follows: Granted the facts of the origin, migrations, and history of the germ-cells of vertebrates, and assuming the course of the life-cycle to be that previously indicated, by hypothesis cancer is derived from vagrant primary germ-cells, which, instead of forming a more or less complete embryo or embryoma, skip this, and give rise to an asexual generation of indefinite unrestricted powers of growth. This is, of course, purely hypothetical, but it becomes the true explanation by the following facts: On the one hand, as my researches have shown, the hypothetical *verirrte Keime*, or "lost germs," of pathologists not only exist, but they are numerously represented, and by things capable of abnormal development—the vagrant primary germ-cells. On the other hand, the carcinomatous nature of such an abnormal growth of an asexual generation has been demonstrated abundantly by Marchand for the instances of the pernicious growth of the chorion, chorio-epithelioma. If such a chorion, or trophoblast, the representative more

or less complete of the asexual generation, when robbed of its embryo, or when it fail to form such, can—and this is established—give origin to a malignant carcinomatous tumour, the nature of cancer is clear. The vagrant primary germ-cell is the seed, while its fruit, sometimes represented by an embryoma, may, on occasion, take the form of a carcinoma.

In the foregoing pages, written in 1902, cancer is spoken of as "a disease," for not until the researches had advanced much farther did it become clear that cancer was a natural phenomenon. The origin of a cancer from "a vagrant germ-cell" is urged; but on grounds, given later, it soon became necessary to restrict this power of independent development to some few only of the vagrant germ-cells. Its asexual nature is clearly defined in the foregoing, and while at that time its restriction to mammals seemed clear (although in 1895 its occurrence in some other vertebrates had been recorded, as I found later on), below the mammals it is still anything but common. Even now (1911) no case is known in reptiles, and but a few instances have been found in birds, while in many thousands of frogs examined the writer has only encountered on undoubted case of epithelioma. Considering its frequency in mammals, especially in man, the statement made above of its connection with uterine gestation would still appear to have a basis of fact under-lying it. The adaptation of the asexual generation (trophoblast) to uterine life, shown by the occurrence of uterine gestation, favours its abnormal development in mammals as a parasitic cancer, as in no other class of back-boned animals. In the following chapter an attempt will be made to show how the tumours are related among themselves, and to the individual harbouring such a new formation.

CHAPTER ll

THE EMBRYOLOGY AND ETIOLOGY OF TUMOURS

A. THE EMBRYOLOGY OF TUMOURS.

The etiology of tumours is one of the darkest regions of pathology. This is by no means due to lack of hypotheses, rather to the absence of material basis for any of those current. It cannot fall within the scope of the work to treat of anything like all the different ideas at some time or other maintained.*

The writer's purpose will be served best by referring only to views as to the nature of pathological growths, based in some form or other upon embryology. † One cannot read the writings of the pathologists of the twenty-five years without being struck by the un-

* For these, and their name is legion, see Wolff, Jacob: "Die Lehre von der Krebskrankheit," Jena, Gustav Fisher, part i., 1907, and part ii., 1911.

† To account for tumours the two views most advocated at present appear to be that of "embryonic rests" or displacements, and that of metaplasy. Under "metaplasy" pathologists understand change in the character of tissue-cells, even in later life. Both are purely hypothetical, and each of them, has been described as savouring of the miraculous. From the modern embryological standpoint both of them may be said to be impossibilities. Regarding "metaplasy," as little as a man can return to his childhood, so little an any of the cells of his body take on embryonic characters, or change their nature. If any one small part of the body can do this, why not grant the same superhuman power to the whole?

doubted tendency on the part of, at any rate, many of them to assign some sort or other of embryo-logical basis to very many, if not all, tumours. I should be the last person in the world to deprecate this, convinced as I am that far more tumours than almost any pathologist now living possibly imagines to be explicable embryologically have such a basis. I only differ from many pathologist in regarding these neoplasms from an embryological standpoint which is as strange to them as it is to the majority of embryologists. The pathologist who is an exponent of a developmental etiology of tumours naturally endeavors to bring them under the laws of embryology, as given in current textbooks. Since my work of many years past has clearly brought home to me the erroneous, baseless, and impossible nature of many of the tenets and doctrines of modern embryology—e.g., direct development, somatic origin of germ-cells, and epigenesis—it must, of course, be equally clear than an "embryology of tumours" founded on these can only be fallacious.

A tumour, whether simple or complex, is a living thing, and, like everything living, it comes gradually into being, it unfolds and manifests itself, and in this way it has its own developmental history. This statement may appear somewhat metaphorical, but its meaning is clear enough if it be said that very many tumours, from the most complicated teratomata down to cancer (carcinoma and sarcoma), are but bizarre manifestations of some portion of an animal life-cycle. The truth of this could not become apparent hitherto for two reasons: on the one hand, the views maintained as to the normal cycle of development were erroneous; and, on the other, the true science of embryology is as yet almost a *terra incognita* to pathologists. But, just as there is a science of normal

development waiting for recognition in our Universities, *--one whose continued neglect and exclusion will continue to revenge itself upon mankind, as it has already done in the past, by a corresponding retardation of priceless knowledge—so there is also (a branch of the foregoing, and only to be understood in the light of it) an important field of abnormal embryology, largely represented by the tumours and their problems—a knowledge of which can only be advance by aiding and fostering the former.

In his magnificent monograph upon tumours Borst writes eloquently of this pathological embryology as a large and interesting region of knowledge, through whose mystical portals we penetrate at the moment with feebly burning torches of comprehension (Erkenntniss), but with the highest expectations. The torches here spoken of may be identified as those of the science of normal embryology, than which there is possibly no department of knowledge of more moment to mankind, and by whose light alone these dark, but to mankind gravely important, regions can be illumined adequately.

In studying the views presently advocated as to the etiology of tumours, the following points are apparent to the embryologist. In their basis, so far as this is embryological, they are but modification of the Remak-

*The writer seeks no such post, although aware that in the last two years of his life the creation of such a University Chair in London for him was the cherished wish of the late George Bond Howes, Professor of Zoology in the Royal College of Science, South Kensington. But it may be pointed out that, unlike Germany and the United States, Great Britain has to-day not a single University Chair of Embryology. Had such posts been as common for the last fifty years as those in many other subjects of infinitely less important to mankind and to medicine, the problems of cancer might have been solved long ago, and possibly thousands of human beings saved from the torments of malignant disease.

Cohnheim theory of embryonic rests,* and the descriptions and classifications of the tumours usually adopted have no embryological groundwork whatever, proceeding, as they do, from the simple to the complex, instead of from the most complicated teratomata—the embryomata of Wilms—to the simple tumours represented by but one tissue—a "connective tissue" or an epithelium. †

The "rest-theory" of Remak-Cohnheim, and their followers is a natural corollary of epigenesis as the mode of the development; and so little as the possibility of this mode of development can be admitted, as little can the existence of such rest of embryonic tissues, organs, or structures, be allowed. ‡ With the rejection of the Remak-Cohnheim theory, the modification suggested by Ribbert also falls to the ground. If the embryo be not gradually built up from a pile of material, as a house is erected, there can be no superfluous bricks or other structures to ball back upon as the seed of later tumours. Even were the development epigenetic—and this is certainly not the case—the actual existence of such rests has never yet been demonstrated; nor is it shown by the occasional appearance of a supernumerary or accessory organ or structure, such as an extra kidney, thymus,

* The theory of "embryonic rests" as the source of tumours is almost invariably attributed to the pathologist Cohnheim. As shown in another chapter, it was first enunciated by the embryologist Remak, and for this reason and for clearness it will be referred to in these pages as the "Remak-Cohnheim" theory.

† To his knowledge Wilms and C. P. White are the only authors who, like the writer, regard the neoplasms in this "inverted" fashion. It may help to support their attitude in this

important matter to add that the writer arrived at the conclusion that, as a rule, the tumours were approached in the wrong order, before seeing their writings.

‡ The recognition of the impossibility of epigenesis as the mode of the development was first made by Weismann in his "Germplasm" (1893).

adrenal, ovary, or spleen. In no embryological sense can such be considered to represent the missing hypothetical rests. Such structures have not been known to give rise to tumours.

Perhaps the theory of embryonic rests has undergone its most important and most scientific alterations at the hands of Wilms,* of whose views—to some extent, at the least—Borst† is also an exponent. Of Wilms's researches on tumours, and especially of the facts laid bare by them, it is not too much to say that they are epoch-making. But of his embryological conclusions it must be added that they are necessarily false, because based on the premisses of an impossible embryology.

The lost germs or rest of Remak-Cohnheim are replaced by Wilms by what he terms "germinal shuntings" (Keimausschaltungen). Essentially, Wilm's theory is almost as simple as that to be here advocated, and, like the later, the hypothesis of germ-shuntings will readily explain many tumours. The germ-shuntings of Wilms are conceived as follows: At various periods of the development, from the earliest to undefined later ones, prior to the completion of the parts of the embryo, there are single cells or little groups of such, set apart to furnish some structure of the embryo. These are often serially repeated (metameric segmentation) in great numbers. Some on or more of these may be shunted out of the normal connection (? by what) at almost any period of the devlopment. According to Wilms, this shunting is not to be regarded as a displacement, for the thing shunted actually remains in the organ to which it really

*Wilms, Max: "Die Mischgeschwülste," Leipzic, 1899-1903, 3 Hefte.

`† Borst, Max: "Die Lehre von den Geschwülsten," Wiesbaden, 1902, 2 vols.

belongs.* If this hypothetical shunting—which, to may mind, in a normal development is physically impossible without disaster to the developing embryo—happen in the earliest periods, it will be in connection with cells of the cleavage, and one or more of these may become the abnormally placed seeds of a tumour or tumours. As an example, to be commented upon later in its true bearings, Wilms himself found in one case not less than five embryomata or rudimentary embryos in one ovary! These represent under Wilms's views five blastomeres of the cleavage. I do not know whether or not there be any upholder of epigenetic development who is prepared to grant the subtraction of this number of cleavage-products without utter disaster to the further development. As will be seen anon, the experimental researches of Driesch, Herbst, and other—Bonnet notwithstanding—do not in the least support Wilms and Bonnet in their extravagant suppositions. Again, according to Wilms, if the happening be at a later period, it may concern, for instance, a part of one or more mesoblastic somites, and, as we know the fate of these, the structure of a tumour arising subsequently can be foretold. Thus a tumour in the region of the vertebral may be made up of "embryonic mesenchyme," or formative tissue, cartilage, and bone; or of the first, or of the first and second of these. Such a tumour Wilms derives from a "shunted" mesoblastic somite, because such a somite gives rise normally to these tissues. Now that, for example,

*On closer examination, contradictions in Wilm's statements may be found. Thus, to account for some tumours, or parts of such, Wilms requires "germs" from mesoblastic somites, and these may, according to him, be displaced physically into—for example—the kidney or uterus. In this way Wilms's theory is seen to have very much in common with the earlier one of Remak-Cohnheim.

somites may be shunted, actually or but physiologically, from the normal connection is purely hypothetical, and nothing of the kind has ever been witnessed. Rudimentary somites occur even in the trunk region in some animals, but these are rudimentary, and probably always disappear.

Wilms regards his germs as things destined in reality to form parts of "the embryo," and therefore as belonging to this.* Under his views cases of five embryomata in one ovary require the shunting into this of five blastomeres during the early development; that is to say, in this instance the original fertilized egg must have been divided up in some way or other into at least six portions, one of which formed a normal embryo, while the remaining five retained at lease the potentialities of each becoming an abnormal embryo or embryoma. It is open to doubt whether any upholder of epigenesis will admit the possibility of the course of events happening in this way. As it would seem a new hypothesis is needed to account for each of the five embryomata, with an additional one to explain the continued normal character of the development after such a shaking and shunting.

Equally formidable difficulties are furnished by the well-known instances of multiple tumours, of various kinds, in one individual. Indeed, the doctrine of epigenesis as the mode of the development labours under quite sufficient insuperable intrinsic difficulties without having to bear the burdens imposed upon it by such

* As decisive against the origin of tumours from cells, or tissues, of the individual in which they develop, may be cited the facts that very many of them are encapsulated from the surroundings—thus, tumours of the kidneys, breast, and parotid; and that various observers—thus, Wilms and Borst—deny any passage or transition of normal tissues into them. The encapsulation of many tumours is of embryological interest, because many of the aberrant germ-cells exhibit this feature.

serious tamperings with the development , as Wilms's theories demand. Nor should it be forgotten that, while on the one hand Wilms speaks of an embryonic "over-production" (!), he states that the germs of his tumours develop in exactly those organs to whose edifice under normal circumstances they ought to have contributed.

Underlying the doctrine of the shunted germs are the dogmas of epigenesis and somatic origin of germ-cells. The latter is an absolute necessity to the former. Since the founder of this (Professor Waldeyer) has seen reason to reject his former conclusions in favour of a morphological continuity of germ-cells, the greatest stronghold of epigenesis has fallen.* Brilliant as are Wilms's actual investigations of the tumours, when regarded from the objective embryological standpoint, the "shunted germs," evoked to account for the facts, are just as hypothetical and chimerical as any other "lost germs" ever conceived of by pathologists.

Wilms's theory, ingenious, and enticing though it be, is but a clearer defined modification of that of embryonic rests. As with the latter, epigenesis and hypothesis are its main bases; and as to the Remak-Cohnheim theory, the objection can be urged that it is an unnecessary

multiplication of causes. This is well illustrated by Wilms's and Borst's distinctions of monogerminal and bigerminal tumours. Double monsters and certain teratomata are regarded as bigerminal, and, placed in contrast

*See Waldeyer, W." "Die Geschlechtszellen," Abdruck aus dem "Handbuch der vergleichenden und experimentellen Entwickelungsgeschichte der Wirbeltiere," von Dr. Oscar Hertwig, vol. i., 1903, pp. 404-405. With the "prevision," of which Pasteur so often spoke, on p. 405 Waldeyer writes: Die" Folgerungen aus dieser Lehre von der Kontinuität der Geschlechtszellen sind fast unbsehbar für die gesamte Biologie" (The consequences of this doctrine of the continuity of germ-cells are almost incalculable for every branch of Biology).

with the remaining complicated "three-layered" tumours, which, as due to developmental abnormalities of a single embryo, are stated to be monogerminal. As, according to Wilms, all possible transition between the most complicated embryomata and the simpler tumours exist, there would appear to be no grounds for this and similar increases in the hypotheses.

Apart from its entirely hypothetical character, its lack of support in facts of embryology, and its continual and unnecessary multiplication of causes, the theory of germ-shuntings labours under other difficulties. It is not easy to conceive any adequate cause for such shuntings during development, and the difficulty is greatly increased when cases of multiple tumours in very different parts of the body, each of which requiring one or more shuntings at some period or other, are taken account of; for with them a normal development would appear to be quite out of question. But, granted the possibility of such shuntings, the real difficulties begin. What causes such a shunted germ, ignoring all laws of differentiation, to embark upon a career of damage, riot, and destruction of its own? To take an instance from Wilms, typical of many such: the germ of an osteo-sarcoma will be a cell or germs of the periosteum of some bone. Normally, like its fellows, it ought to have contributed to the formation of that bone. Instead, thereof, at some period or other, after lying dormant, it breaks all bounds, and proceeds on a line of development of its own. This is such that, unless brought to a stop by some extrinsic cause or other (operation or death of the host), it may be the parent-cell of more progeny than all the other bone-producing cells in the body! In find, Wilms ascribes to his shunted germs far greater embryological potentialities than Nature ever endowed them with. On the other

hand, some of the aberrant and vagrant germ-cells described by the writer undoubtedly possess, as was once remarked to the writer by a human anatomist, far greater potentialities for mischief than any germs ever conceived of by pathologists.

Not only the embryonic rests and the germinal shuntings, but a host of subsidiary hypotheses—among others, those of Borst, relating to the tumours of the sacral and cerebral regions—become superfluous in the light of the much simpler theory of tumour-formation as due to—(1) the abnormal development of a persistent primary germ-cell, and (2) the bizarre pathological manifestation by this of some greater or less portion of a life-cycle. Under this view most, if not all, tumours receive a simple explanation, and under it, also, it must be manifest that previous attempts—that of Wilms excepted—to explain the tumours, in taking the simpler ones as the starting points, have really begun at the wrong end of the scale. Neither in theory nor in practice can the degree in greatest possible reduction of an embryoma or rudimentary embryo be

defined, and, in fact, in actual practice and theory a simple tumour will represent a low degree of such reduction.

Certainly, regarded as pathological manifestations of some greater or less portion of a life-cycle, all the peculiarities of very many tumours are fully explained. A germ-cell, developing abnormally, may after its developmental unfolding has begun, undergo degenerative changes of various kinds and degrees as to greater and smaller portions of its parts, or some foundations may remain latent, wholly or in part; and in this way a single cell, or a larger or smaller group of such, endowed with certain well-defined potentialities, may be left as the actual seed, as the origin, of the tumour thereby arising

Matters would appear to be complicated in some cases by the existence of two well-marked portions in a normal life-cycle: the asexual one, represented by the chorion (trophoblast); and the sexual one, taken up by an embryo, or Metazoon. Some tumours—some ovarial teratomata, described by Wilms—exhibit attempts to include the whole life-cycle, in that, along with a pathological bizarre embryo, cancer, representing the asexual generation, is encountered. In other tumours, again, there would appear to be nothing of the asexual generation; and still others, the malignant cancers, confine themselves entirely to being abnormal manifestations of the asexual portion—the first part of the life-cycle.

The comparative embryology of tumours may now be considered more in detail. The see or seeds of tumours are unquestionably some or other of the vagrant (or if in ovary or testis, persistent) primary germ-cells, treated of at greater length in the writer's works upon the germ-cells. So far (1911) they have only been found from fishes to reptiles; but from various considerations it is not open to doubt that they occur even in the highest vertebrates, and in man himself. Apparently they have been noted by Roux and Barfurth in the frog, and by me in the salamander (*S. maculosa*). In all the embryos yet studied by me under a certain age—i.e., with the limits during which germ-cells are easily found in embryos—no single embryo examined has been devoid of them.

The mode of the development and the life-cycle, in practically all its details, are the same in mammals as in fishes, and unquestionably the whole organization and development of man follow closely along, but along higher lines than, those of a fish. It is therefore concluded that, could one but hit upon some easy method of distinguishing germ-cells during the early development of man and

mammals, the occurrence of vagrant ones in various parts of the body, skin, pericardium, pylorus, rectum, liver, kidney, etc., would be as common a phenomenon here as in the fishes.

The germ-cells of vertebrates generally are, since 1900, beginning to be regarded as undoubted products of the egg-cleavage.* Since Wilms, Bonnet, Marchand, and Borst consider certain teratomata, at any rate, to be the offspring of cleavage-products, there would appear to be an identity between their conclusions and my own in this respect. Nothing could well be farther from the true facts. Taking Wilms as the leading exponent of the one side, the divergences between the two views work out as follows;

By Wilms and other certain tumours, not by any means all, are referred to cleavage-cells, not identified as germ-cells, but really destined to form some part of the embryonic body. These cleave-cells are "shunted" from the normal connection at some very early, but not defined, period

of the development. As so derived, they are parts of the organism in which they occur. Against the above, the writer's conceptions may be stated in the following:

Most, if not all, true tumours are pathological manifestations of some portion of a life-cycle, and they are due to abnormal attempts at development on the part of aberrant germ-cells, derivatives of the cleavage, and destined, not for the embryonic body, but for future generations. Such vagrant or persistent germ-cells are the sister-cells of the one by whose unfolding the "embryo" or individual arose, and, developing pathologically alongside and within another (sister) form,

*Compare the recent monographic works on Embryology by Korschelt und Heider, and by Waldeyer.

with degeneration of some of their products, they leave as the basis of a tumour a greater or less number of cells, endowed with more or fewer potentialities. As so derived, they are not parts of the organism, but are its sisters or brothers, identical with it in ultimate characters.

As indicating the amount of agreement between my conclusions and those of Wilms, and the extent to which I have adopted his views, except in so far as these are embryological, the following passage from his latest work (1903) may be cited: "The groups of tumours are of equal value in their etiology; they differ among themselves only in that the one groups arises from cells of the earliest period of development—the time of the cleavage; the other, from cells of somewhat later time—the period of the formation of the germinal layers" (p. 270). This I would amend as follows: "In their etiology the tumours are of equal value, and they are the results of pathological bizarre attempts at development on the part of aberrant primary germ-cells, originally identical, in characters, and, in fine, in all respects, with that primary germ-cell, by whose unfolding the individual harbouring such a tumour arose. As the offspring of primary germ-cells, they may be referred to cells of the cleavage, but not to such appertaining to the embryo. They never arise from cells of the period of embryo-formation (Zeit der Keimblattbildung).

The comparison sufficiently emphasizes the divergences, and, be it added, the existence of ovarial and testicular embryomata is decisive against their derivation from cleavage-cells in the sense of Wilms and Bonnet; for none such appertaining to the embryo can find their way into these organs, but instead thereof there are germ-cells, which originally go back to the cleavage. In passing, Wilms's denial of the possible origin of an embry-

oma from a germ-cell of the testis may be cited as an instance of a refusal to recognize the plain and simple facts of the writer's researches upon the germ-cells.

As further evidence for the origin of embryomata from cleavage-cells (of the embryo), Wilms refers to the unilateral nature of many of them. This is supposed to indicate something corresponding to the results of Roux's well-known experiments upon the egg-cleavage of he frog, which many years ago were believed to demonstrate the "prospective destinies" of, say, the first four products of the cleavage. It must always be difficult to determine what the researches into so-called "experimental embryology" really demonstrate, more especially in view of the discrepancies in the results of the different observers; but to most of them it would probably be more correct to apply the term "experimental pathology," for the finds border on pathology rtather than upon embryology. Normal larvæ of reduced size may have been obtained by such experiments; normal embryos—Roux's "hemi-embryods" are not such—have never been a result. Roux's particular finds probably ensued not because he had experimentally halved the cleaving

germ, but because in trying to do this he had induced pathological changes. If the hem-embryomata referred to by Wilms be hem-embryos in Roux's sense, this ought also to apply to the individual harbouring them. As a matter of fact, it is a pathological change in the embryomata which induces the halving, as evidenced by several pathological skate embryos, described by me, in nearly all of which there were marked reductions, either in the head-end or on one side of the body.

Marchand and (formerly) Wilms have been disposed to derive the embryomata from fertilized polar bodies. The writer must emphatically reject this view. Wilms

relinquished it, because in one instance he found not less than five embryomata in a single ovary, and, of course, this number of polar bodies has been met with nowhere in the animal kingdon. Even two embryomata, a tera-toid in the cranial cavity and an ovarian embryoma—a condition recorded—suffice to negative the possibility; for it has been pointed out to me that nowadays it would appear to be the rule in mammals that only one polar body should be formed.*

Wilms (*loc. Cit.,* p. 250) sums up his ideas pretty clearly in the following: "In other words, double monstrosities, fœtal inclusions, and embryomata are all, indeed, to be referred back to an over-production (!) in the early development, but only in the double formations (Bildungen) do the cleavage-cells (Furchungskuglen) and the formation proceeding from them develop at the same time; in the other cases the one of the two only attains development at a later period."

Before treating of the comparative embryology of the tumours at length, one or two other things call for notice. Marchand, and finally Wilms, consider all the teratomata as of equal value morphologically. With this I would express cordial agreement. A vagrant germ-cell, developing pathologically in pericardium, abdomen, sacral region, or elsewhere, to form a more or less rudimentary embryo, in doing this is giving rise to something exactly comparable to an embryoma of ovary or testis. On p. 251 of "Die Mischgeschwülste," Wilms writers: "A series of sacral teratomata is remarkably completely developed. An embryo *en miniature* in the most exquisitve fashion may be developed." He goes on to say that he himself possesses

*This was written in 1903, but now (1911) more recent researches of Sobotta, Burckhard, van der Stricht, Lams, Doorme, and J.P. Hill, have shown that in certain mammals the first polar body is formed in the ovary, and afterwards disappears.

microscopical preparations of a sacral teratoma from the Giessen collection, with brain, mouth, trachea, œsophagus, stomach, gut, and large pancreas gland present. The teratomata or embryomata undoubtedly pass gradually over into the teratoids of the sexual organs, in which, according to Wilms, along with more or less normal development of embryonic organs, one encounters in other parts of the tumour riotous pathological growth. While, on the one hand, the teratoid tumours pass gradually into the highly organized embryomata, on the other hand, according to Wilms, "we have certainly also in the testis, as I have already sufficiently emphasized for the mixed tumours of the kidney and the parotid, all possible transitions, from the most complicated embryoid forms down to the simple ones."

The mixed tumours here referred to by Wilms—the tumours into whose nature and characters he has carried out such brilliant observations—furnish the key to the general problem of the etiology of the tumours in general. Wilms's writings upon the mixed tumours of the

kidney, vagina, uterus, mammary gland, and parotid, are of intense interest, even to the embryologist. To my mind they justify completely his conclusion that they and the embryomata are of like etiology (*loc. Cit.,* p. 279). In his further attempts to trace their embryological history one cannot agree with him; for, just as he derives the embryomata from blastomeres (of the embryo), and not from vagrant germ-cells, so he assigns as the origin of the mixed tumours "shunted germs" of later and later periods. Certain of the vagrant germ-cells, defined later on, amply suffice to account for the mixed tumours also; indeed, the basis for these and other tumours may be found in (1) the actual existence of vagrant and aberrant germ-cells, and (2) the embryological fact that

each and every primary germ-cell (those of the ovary and testis, of course, included) possesses the faculty of that primary germ-cell, which unfolded as an embryo, of doing likewise.

Of great significance with reference to the question of the germ-cell origin of tumours are the comparatively frequent instances of tumours arising in multiple centres. Some of the recorded cases may be cited from Borst (Iloc. Cit., *p. 57, A,* et seq.*)*. In the same individual, tumours have been found in liver, uterus, ovary, kidney, skin, etc.; or, again, in the paired organs of the two sides. Babesiu found in the uterus, in the middle of a myoma, a columnar eqpithelial cancer, and Niebergall recorded a complicated uterine tumour of myoma, polypes, sarcoma, and cancer. Equally important and significant to the embryologist are the facts relating to the occasional presence of different tumours at the same time in different parts of the body. Borst (*loc. Cit.,* p. 58) gives the following instances:

1. Cancer of the stomach with ovarial cystoma and fibroma of uterus.

2. Cancer of skin and of rectum.

3. A teratoid of the cranial cavity and an ovarian embryoma.

4. Uterine myoma, lipoma of kidney, enchondroma of lung.

5. Cancer of the thyroid, and multiple fibromata of kidney and uterus, with large papillomata of skin.

Borst looks upon all these and other recorded cases as accidental! They are interesting, however, in the light of—(1) the hypothetical germ-shunts; (2) the various places in which vagrant germ-cells, may be found, and (3) the probably necessity of a certain physiological condition or nidus for the development and growth of a tumour of a certain character.

In the comparative account of the tumours I shall follow the lines laid down by Wilms, and, therefore, it is his summary of them, not mine. His account of their comparative anatomy appears to me to be logical and convincing; and in giving his results in tabular form I should like to say with what intense interest and instruction I have studied his writing. As elsewhere stated, the highest and most complicated tumours—the cystic embryomata of ovary and testis (Wilms)—are at the basis instances of identical twins with one abnormal embryo, the enbryoma. If nothing else would account for their pathological development, the circumstance that neither they nor any of the less complicated tumours can, from their mode of origin, contain sexual organs might suffice. They are, therefore, sterile embryos; and in other directions my researches have convinced me that embryonic sterility may be the source of pathological changes.

From the facts established concerning the tumours by pathologists, it is clear to the comparative anatomist and embryologist that in certain respect they present certain analogies to instances of parasitism among animals. They differ, however, markedly in being, from the mode of their development, sterile organism, even in the best-developed cases. The resemblances between tumours and parasitic Metazoa or higher animals may be exemplified by a short account of certain snails parasitic upon Echioderms (starfish and the like). The series is derivable from free-living *Eulima* species. It may be taken as beginning with *Mucronalia eburnea,* which is an external parasite, and possesses the full organization of a snail. *Stylifer linckiæ* is also an ecto-parasite, but it is partially encapsulated upon the host. In this case the foot is rudimentary, and the radula is absent.

Through other species of *Styifer, Entocolax ludwigii* is reached. This is parasitic in the body-cavity of a seacucumber (a Holothurian), and with the endoparasitism the shell, mantle, gills, and sense organs disappear. The series culminates in *Entoconcha mirabilis*, parasitic in the sexual organs of a sea-cucumber (*Synapta digitata*). This is nothing but a worm-like sac, containing (hermaphrodite) sexual organs. In its organization there is nothing whatever of molluscan characters, and its true nature can only be made out in one or other of two ways: by the comparative anatomy of the series of such parasitic mollusca, which reveals all the stages from highly organized forms down to absolute reduction of most or all of the organs, or by the study of the development; for, as Johannes Müller showed in one of his classic works, *Entoconcha* is a true gasteropod, with shell and other organs.

As it is impossible to follow the whole development of a tumour from its first start, and as many of them attain only a very low degree of embryonic differentiation, the series of forms in them, leading from the highest to the lowest, from the most organized to the simple onles, can only be followed after the method of comparative anatomy, and this is the plan adopted by Wilms in his researches. From the results of a study of tumours made in this way, and with the facts established by the writer's researches upon the germ-cells, and the course of the cycle of development of the higher animals, the following conception* of the true nature of a neoplasm or tumour is obtained.

A tumour is a more or less reduced, more or less incom-

*It should be specially noted that in this definition *malignant* tumours (carcinoma and sarcoma) are excluded—only tumours representing the *sexual* generation are included.

pletely differentiated sterile Metzaoan or higher animal organism, which, starting by the abnormal development of a vagrant primary germ-cell, and growing under conditions unfavourable to the complete and normal differentiation of all its parts, unfolds and develops those things, for whose growth the nidus is suitable, the rest degenerating. And, exactly as identical twins are the offspring of two sister or brother germ-cells, identical in ancestry from the same primitive germ-cell, and identical in all ultimate characters, so also any higher animal, and a tumour within it, stand in the same relations of ancestry from one primitive germ-cell, have the like ultimate characters (identity) at the starting-point of their development; but, unlike fully-developed identical twins, the individual and its tumour develop in different directions: the one upwards along the track of higher and higher organization, the other downwards, along the roadway of abnormality, of degeneration, of arrest, even at times—when the asexual generation is represented—of riot, destruction, and disaster.

The highest tumours, then, are (1) the cystic embryomata. On these follow (2) the solid embryoid or teratoid tumours of the ovary, containing skin, gut, and "mesoderm" and derivatives of these. (3) The less highly developed ones of the testis. Like the foregoing, these are "three-layered," the skin is scanty, they contain gut and trachea, the head-region is rudimentary, and their growth is unlimited. Borst has recorded in them ganglion cells and sympathetic ganglia. (4)Teratoid tumours, where the "embryonic" tissue is mainly sarcomatous (cancer or asexual generation). (5)Teratoid tumours of the testis with the epidermal layer lacking. (two-layered tumours of Wilms). There teratoids lead to (6) the more complicated sacral and parotid tumours, and

as in them, there are, according to Wilms, all transitions down to the simplest, these latter being sarcoma (cancer, or asexual generation). (7) Mixed tumours of the breast, kidney, cervix, uterus, vagina, and parotid. These are sometimes, not often, two-layered (epidermis), and they are usually made up of tissues, which can best be described as sarcamatous (cancer, or asexual generation).

B. THE ETIOLOGY OF TUMOURS.

The foregoing really forms a continuation of extension of the section on "Dermoid Cysts and Teratomata," in a memoir* published by me some years ago. On p. 671 it was written, "How, it may be asked, shall one limit the possible reduction of an embryoma? Where shall the line be drawn?" The present chapter offers an answer to that question. As the writer suspected in 1900, no line can be drawn between an embryoma and a simple tumours. In this connection, apart from the references to the writings of Wilms, it may be of interest to quote from another writer and able pathologist, L. Pick. † On p. 1193, in discussing the bearings of his finds, Pick writes: "As I have already shown elsewhere, it would be false to identify in an embryoma that which, of sorts of tissue or organs, is finally preserved with that which was originally laid down in it in the germ. We know that here occasionally only a certain kind of tissue attains development, that alongside this all other tissues wither in their development—indeed, completely vanish—or by the one-sided tumour-like growth

*Beard, J.: "The Germs Cells," part. I., *Raja batis,*, in *Zool. Jahrb*., *Anat. Abteil.,* 1902, vol. xvi., pp. 615-702; *loc. Cit*., p. 669.

† Pick, L.: "Zur Kenntniss der Teratome: Blasenmolenartige Wucherung in einer "Dermoidcyste" des Eierstocks," in *Berliner klin. Wochenshr.,m* Dec. 22, 1902, pp. 1189-1193.

of the one sort of tissue may be actually destroyed, or 'suffocated." In this way at one time a true embryoma may be found in the curious form of an isolated tooth, at another time, perhaps, as a sort of glioma, or as an ovarian true thyroid-struma, or, again, as a chorio-epithelioma with metastases."

In other respects Pick's communication is of great interest. His researches have established for, at any rate some, ovarial teratomata, as Schlagenhaufer's* had already done for the like tumours of the testis, the occurrence of a choiron or trophoblase—in the instance recorded in a more or less degenerate condition. Their finds throw a considerable amount of welcome light upon the (according to Wilms†) frequently malignant character of the testicular embryomata, and the cases—some nine in 1902, to which Pick's instance furnished a tenth—other the occurrence of cancer in connection with an ovarian embryoma. As in the ordinary chorio-epithelioma of gestation, in embryomata of ovary and testis, carcinomatous growth, when present, is now (1903) recognizable as having arisen from the asexual generation (chorion or trophoblast). These words were actually read to a large audience, as occurring in a paper on "The Embryology of Tumours," by me, on February 16, 1903. Before the Royal Society, Edinburgh. This was the last occasion on which I communicated anything of my researches to the learned society. Practically the whole of that paper is given in this book as it was originally written. Publication of it was refused by the Royal Society, Edinburgh. Shortly afterwards I made a full abstract of it in English,

*Schlangenhaufer, Fr.: "Über das Vorkommen chorio-epithelioma and traubenartiger Wucherunger in Teratomen," in *Wiener klin. Wochenshr*., 1902, Nos. 22-23.

†Wilms, M.: "Die mischgeschwülste," 1902, iii., p. 242.

and this included the above words, and sent it to the editor of *Ziegler's Beiträge*, and of the *Centralblatt für allgemeine Pathologie,* the celebrated pathologist and man of science, the late Geheimrat Dr. Ernst von Ziegler, Professor in Ordinary of Pathology in the University of Freidburg in Breisgau, with the request that he would publish it in the latter scientific journal. He replied that not only would he do so, but that he would have it translated into German, so that more people might read it. It appeared in full in vol. xiv., pp. 513-520, 1903. In March, 1905, some two years later, a discussion took place in Berlin upon cancer. This is reported in the *Berliner klin. Wochenschrift,* 1905, No. 13. The same number contains the brilliant speech contributed to the discussion by Dr. L. Pick.* In the course of this Pick proved, step by step, in actualy instances and on actual specimens, the scientific truth of the statement that an ordinary cancer (carcinoma) may, on occasion, arise from the chorion or trophoblast, that at times this

exhibits the structural appearance of chorio-epithelioma, at others of ordinary cancer—"das gewöhnliche Carcinom." In this place I cite the opinion of Dr. L. Pick as that of one fully competent, not only to give a judgment of a great scientific value on this question, but to defend it.

Embryologists and pathologists might have been expected to have taken the following words † by the late

*For a summary and translation of this, see Appendix B.

†Giacomini, C.: "Probleme aus Entwickelungsanomalien d. menschlichen Embryo," in *Ergebn. Anat. U. Entwickelungsgesch,* in 1894, vol. iv., pp. 615-649; *loc. Cit*., p. 640. The actuall words are: "Das Chorion ist von allen Bildungen des Eies diejenige, welche vor jeder anderen entsteht, sich bald von den anderen Teilen unabhängig macht, und indem es frühzeitig seine Zellen entwickelt, in den Stand gesetzt wird, zu leben und zu entwickeln, auch wenn alle anderen Teile des Eies durch irgend welchen Umstand aufgehört haven, zu existieren."

Professor C. Giacomini seriously to heart, instead of ignoring them: "Of all the structures of the egg, the chorion is that which arises before every other, quickly makes itself independent of the others, and, by the quick development of its cells, is placed in a position to live and to develop even when all other parts of the egg, through some cause or other, have ceased to exist."

In recent years the writer has urged again and again that in researches upon animal development two things must be kept sharply separate: the embryo or sexual form and the asexual foundation—in human development the chorion or trophoblast—upon which it arises. According to orthodox embryology this chorion or trophoblast is a part of the embryo, although it is invariably present before any part of an embryo; although it may persist after the complete disappearance of the embryo; although it is never formed from or by an embryo; and although ultimately it never makes any part of the embryonic body! Logically, how can it be maintained that a structure which arises before an embryo, and out of no part of it, and which never goes to form any part of any organ of the body, is embryonic or fœtal in nature? What is there to prevent, as Pick suggest, the total disappearance of all parts of an ovarian or testicular embryoma except the (pathological) chorion or trophoblast? The persistence and further growth of this would but, and does, result in cancer (carcinoma). He who doubts this had better read the facts as they were described in 1905 by Dr. L. Pick and as they are given in abstract in the Appendix. As the chorion is always present before an embryo, nothing in the abnormal development of a vagrant or aberrant germ-cell would appear to forbid the arrest of this prior to the appearance of any trace of an "embryoma," with the natural sequel—a carcinoma.

But, surely, now, the etiology of cancer is as clear as that of the tumours in general!

Very shortly after the date of writing the above, a little further light was obtained in another direction. It is a natural question to ask, "Can any and every primary germ-cell undergo

abnormal development, or is this power limited to certain of them?" A full reply to this would entail prolonged investigation into the developmental problems of identical twins, triplets, etc. For a long time now (1911) this matter has engaged the writer's attention more or less, but though some landmarks can be recognized, the end is not yet in sight. So far as I can see, the whole doctrine of the tumours and cancer centres in the problems of identical twins, triplets, etc.—in fine, in the question of the number of embryos which may arise from one egg, and therefore be contained in one chorion or trophoblast.

A full discussion of identical twins, etc., must be reserved for another occasion, in a projected book upon heredity. Here it need only be stated that their occurrence is probably more frequent than has been supposed hitherto. By competent authorities it has been estimated that in man identical twins form 25 per cent. of all twins. Their comparative frequency alone is against the idea of their occurrence being due to, say, a chance division of the developing egg. The absurd supposition of their etiology by "the splitting of a germ" was exposed by me in a letter in the *Lancet*, January 7, 1905, p. 56. Extremely improbably, if not impossible, is the origin of one of them from a fertilized polar body. As little can hold this as accept the idea of "chance" in the development. In some other mammals identical twins would appear to be very common. Thus, in the sheep, where the total number of young is usually two or three,

the writer has several times come across them *in utero*. There exists, however, a case in literature of embryology, published in three different scientific journals of high standing—that of an armadillo, the "tatu" (*Prapus hybirdus*) where, according to von Jhering,* from seven to twelve young are formed within one chorion—that is, as products of one egg. The observation tallies with, and is allied to, that already recorded by A. von Kölliker † in 1879, of four fœtuses within one chorion in a related species, *Dasypus* (*Prapous*) *novemcinctus* (the nine-banded armadillo). Not long after the above was written, aided by a small grant from the Carnegie Trust, I was able, with the kind assistance of Professor von Jhering, to obtain from Brazil two small sending of pregnant uteri of both of these species. An examination of some of the material amply confirms the statements of both von Jhering and von Kölliker. As von Jering remarks, the observation shows how little reason there is for the common belief that it is an invariable rule, or even law, for only one embryo to arise from a single egg. The occurrence and comparative frequency of identical twins, triplets, etc., in man, taken along with the above observations and other considerations, point to a former multiplicity of embryos, formed as the progeny of one egg, even in the ancestry of man.

A further step may now be taken, and it may be insisted that the tumours, including cancer, date back to this condition as their source. In the course of ages, one or more of the former identical twins, triplets, etc., has become rudimentary; but it, or they, may reappear

*von Jhering, H.: "Über 'Generationswecjsel' bei Säugetieren," in *Biol. Centralblatt,* in 1886, vol. vi., pp. 532-539; also in *Berliner Sitzungsberichte* and *Arch. F. Physiologie*, 1886.

† von Kölliker, A.: "Entwicklungsgeschichte des Menschen," II. Augl., 1879, p. 362.

in the form of embryomata, finally of tumours, even of cancer. In this way it comes to be recognized that there must be a vast difference among the various vagrant and aberrant germ-cells in potentialities for mischief. Some few, and not all—how many in each case it is at the moment impossible to say, and it may never be determined—possess the potentiality of developing like the embryo containing them. If they do this normally, identical twins, triplets, etc., may result. If they do not degenerate, and degeneration is probably often their fate, they may come to lie somewhere or other in the embryo, even in its sexual organs. Here they may be encapsulated for a longer or shorter time, and, finally, one or more of them may commence (abnormal) development, and form an embryoma, or other tumour even, by attempting to begin the whole cycle anew, with arrest in the embryonic portion—a cancer.* Vagrant germ-cells in development are, I imagine, far too numerous for anything like all to be required to account for the tumours and for cancer. Probably it may be regarded as sufficient if there be in every development at least one, three, or seven such, which, if they do not degenerate, may become the seed of later tumours. To the embryologist it is of great interest to establish that, as in the upward direction the embryomata pass step by step into identical twins, triplets, etc., so as gradually in the downward one

*It should be mentioned that pure embryomata, as true, benign tumours, are probably in all cases congenital—that is, commencing their development at the same time as the individual harbouring them. Apparently, this does not invariably exclude the appearance of malignancy in some of them at a later time. On the other hand, malignant disease (carcinoma and sarcoma) is not congenital, but the seed of such a tumour is to be found in certain of the latent germ-cells, as described in the text. Of course, cancer is hereditary, no matter what all the official cancer-researchers in the world may say. The true nature of heredity is as far from their thoughts as the principles of modern embryology.

they merge into the simple tumours, and that any portion of the life-cycle of normal development may manifest itself as a tumour.

From the above it may have become manifest that for the elucidation of the nature of the tumours two things are needed: pathology, a much fêted and daily more and more endowed branch of learning; and embryology, the science of the coming-into-being of life, at present the handmaid of many sciences, and almost without a habitation to call its own.* This despised and rejected branch of human knowledge, whose task it is to treat of the "Werden und Vergehen" of living things, is in importance second to none. Without its light, much possible knowledge in other sciences is enshrouded in thick pitchy darkness; without it one branch of pathology at least could have no real scientific existence. In certain direction we may turn to pathology for the collection of the facts, but to embryology for their explanation. The pathologist may know the facts, but that knowledge gives him no key to their solution; for this lies in the study of the normal development of living things—embryology.

*Eighteen years ago there died an English embryologist, a wealthy man, who had for years devoted some of his means towards the advancement of science. In the medical faculty, in which he taught, embryology was lectured upon by five different medical professors to large classes of students, while he, a specialist, had practically no students. His course was not prescribed in the regulations. Embryology is to-day (1911) in Great Britain not one of the courses laid down in the curriculum for medical students. In scientific Germany it is otherwise,

and in my own University of Freiburg-in-B., although the medical faculty contains fewer students than in more than one British medical school, my old friend Professor Franz Keibel has as many as 150 medical students every summer in his lectures upon comparative embryology. His laboratory for practical embryology is so crowded with medical students that a year ago, when visiting Freiburg, I was informed that he was at his wits' end what to do with them.

CHAPTER III

THE PROBLEMS OF CANCER*

Under this title the following remarks were published in the *Lancet* in 1904 as a summary of a University lecture. The objects in view were to throw some embryological light on the possible lack of import of a practical kind attaching to certain recently published observations on so-called "heterotypic" mitoses or cell-divisions in cancer-cells; to point to the futility of regarding carcinoma as due in origin to some sort of "conjugation" of leucocytes of the body; and, lastly, while insisting upon the fundamental identity of carcinoma and sarcoma, to indicate how the problems of cancer finally ended embryologically in those identical twins and their origin. The import, or absence of import, of the first two—the "heterotype" mitoses and the supposed "conjugation"—has now been generally recognized, and the original position taken up regarding these has been abandoned by official cancer research in Great Britain. As pointed out by Dr. Jacob Wolff ("Die Lehre von der Krebskrankheit," vol. i., p. 438), this view of the "conjugation of resting nuclei"—one of them that of a leucocyte—was enunciated originally by Auerbach in 1890, but this fact escaped the notice of the official researchers.

*The *Lancet*, October, 29, 1904.

The fundamental problem, the very basis of embryology, is the course of the life-cycle in the higher animals, including man. This question of the mode of the development far exceeds in import all other problems of pure embryology. It touches upon, without at present offering any explanation of, the nature of life itself. But while the latter is now beyond human grasp, and may elude it for ever, the solution of the great problem of the life-cycle, seemingly so complex, albeit so simple, furnishes results of overwhelming import for all the sciences of life. The history of embryology tells us how for centuries the fight, whether epigenesis or preformation, went on; how, on the one side, the development was regarded as analogous to the building of a house, "part being added to part," and how, on the other, men like Haller denied any coming into being, the embryo being preformed in all its parts. So slow is real progress in a science like embryology, and so greedily receptive of error is the human mind, that in our day we hardly dare hope to see the last of the two rival erroneous doctrines of epigenesis and preformation. Like the chameleon of the story, "the creature's neither one no t'other." Underlying the phenomena of development in the higher animals there are an antithetic alternation of asexual and sexual generations, a morphological continuity of germ-cells, which, paraphrasing Robinson's eloquent words, go back to a beginning so remote as to be utterly beyond our knowledge, and pass to a future of which we can form no conception whatever. Under the phenomena presented by the germ-cells in their cycle direct development and epigenesis can find no places. Looked at in the light of the facts, they are impossibilities

and, like the recapitulation theory, merely illusions of the human imagination. An antithetic alternation is seen to be an iron necessity of the development as soon as it is perceived that an organism, an asexual one, must develop upon which germ-cells can arise; while the sexual generation, "the embryo" of embryologists, is called forth from one of these germ-cells to contain and to nourish the rest for a certain brief span of time. Moreover, the facts of development, which to some extent have been unearthed during the past fifteen years within this city, throw a flood of new light upon the crude materialism of modern embryological textbooks. The biophores of Weismann and the pangens of De Vries become shadowy entities of the real existences of which there are no evidences. And while with humility admitting that to say it is to furnish no explanation of the riddle of life, it must be recognized that the characters or qualities of animals or plants are certainly not present in the germ in the shape of ultra-microscopic particles of chromatin, the pangens or biophores, but that all the wonderful and infinite variety of animate nature has its fount in unconscious memories of germ-cells.*

Modern embryology, not to be confused with that extant in textbooks, claims as its own two vastly important regions of human knowledge. These are the facts and nature of heredity and genetic variation and

*For a fuller account of the theory of heredity based in the unconscious memories of germ-cells, set up by Professor Ewald Hering, now Director of the Physiological Institute in the University of Leipzic, in 1870, see Beard, J.: "Philosophical Biology," in Ainsworth Davis's "Science of To-Day," vol. ii., 1909, pp. 37-64, with list of literature, which should also include Samuel Butler's "Unconscious Memory," first edition, 1880, revised edition, 1910 (Fifield, London), and the presidential address to the British Association for the Advancement of Science, 1908, by Professor Francis Darwin.

that portion of pathology treating of the tumours or neoplasms, benign and malignant. The phenomena termed "heredity" are germinal in nature, and in this way they fall within the province of the embryologist, not in that of the mathematician. But at first sight it is, perhaps, not so clear that neoplasms—living things possessing simple or complicated structures, but devoid of any useful functions—should be entities about whose nature the embryologist need concern himself at all. As recently as four years ago—that is, in 1900—but few of the higher teratomata were recognized as embryonic in nature. Now almost the other extreme has been reached, and possibly there are few tumours, benign or malignant, the embryonic nature of which has not been advocated by some observer or other, usually a pathologist. By embryonic is meant that their tissues would be identical with—even, according to some observers, derived from—some of those making up an embryonic body, that they would be, in the word employed by Wilms, "embryomata." As to their origin, apart from the so-called "parasitic theories," which are more remarkable for the things they leave untouched than for the "facts" they explain, for benign or malignant tumours, or for both, certain erroneous views, not really based in embryology, have within the last year been advocated at home and abroad. Malignant neo-plasms, such as cancer, have been supposed to arise from somatic cells of the individual, either with or without a conjugation of such. To my mind there is a little evidence—and that is none at all—to show that somatic cells could, or do, conjugate with their fellows or with other cells, such as leucocytes. Indeed, the appearances described and figured as conjugation in a cancer are capable of other and simple explanations. Certainly, if

they represent a real conjugation, the preparation ought to carry conviction to the minds of embryologists and cytologists, such as, to name three Würzburg ones, Stöhr, Schultze, and Sobotta. This is improbable, for the true nature of the preparations shown last July* at Oxford appears to me to be fairly clear.

Very common among pathologists is a modification of the Remak-Cohnheim theory of embryonic rests as the basis of neoplasms. This doctrine of "shunted germs," only possible under the erroneous dogma of epigenesis, has many followers, especially in Germany. The apparent manifold variety of the malignant tumours, which fortunately is not real, led to the conclusion that they were made of a embryonic or somatic cells; that, for example, a primary cancer of the liver or kidney was composed of liver or kidney cells, and so on. The embryological conclusions to be advanced here, and which are based on research, do not permit of that explanation. A malignant tumour is such in virtue of the facts, among others, that its cells are *not* embryonic (though they may mimic such, or even resemble no other cells in the human body), and, that, like cells of the trophoblast or chorion of normal that, like cells of the trophoblast or chorion of normal development, the neoplasm eats or erodes its way through other structures, even through living bone. On the other hand, a benign tumour does consist solely of somatic or embryonic cells. Its tissues are normal in structure, for it is a true embryoma, or more or less rudimentary embryo, in Wilms's sense. A neoplasm is, in short, a futile attempt to repeat a greater or less portion of the cycle of normal development. A true embryoma recites merely some greater or less piece of the embryonic portion; a pure cancer or sarcoma—for these are one and the same thing under different disguises—may attempt

*1904.

to produce the whole life-cycle, with the exception of the embryonic part. In an unmixed cancer or sarcoma there is absolutely nothing whatever of an embryo; there is not a vestige of a somatic cell.

To reinforce their attitude several supporters of the doctrine of shunted germs have invoked the aid of fertilized polar bodies. Every elementary student knows these, and is aware that nowhere in the animal kingdom have they ever been known to exhibit any potentialities worth of the least notice. To the embryologist versed in recent advances the theory of fertilized polar bodies, with its allied assumptions of all sorts of embryonic rests or germinal shunts, must seem to be one of the most absurd ideas ever enunciated in science. Like the somatic origin and the supposed "conjugation," this must be rejected. Fortunately or unfortunately, the number of polar bodies formed by the mammalian egg is far too limited to permit of their introduction into the question. No mammal is known in which more than one polar body* arises; while, for example, Wilms found as many as five embryomata in one ovary, and Baart de la Faille † recorded a case of quadruplets where three of the fœtuses hung as more or less incomplete parasites from the palate of the fourth. On the present occasion a few words more must suffice regarding the manifold embryological aspects

* 1911. No mammal is known in which more than one persistent polar body is formed.

† *Vide* Schatz: "Klinische Beiträge zur Physiologie des Fœtus," *Archiv für Gynäkologie*, 1900. The original paper, by Baart de la Faille, is said to be very rare. The specimen is described (p. 252) with some others by E. Schwalbe in Ziegler's "Beiträge zur Pathologischen Anatomie," 1904, vol. xxxvi., pp. 242-272, "Der Epignathus und seine Genese." This case is illustrated by an excellent figure in Schwalbe's "Die Morphologie der Missbildungen des Menschen und der Tiere," part ii., Jena, Gustav Fischer, 1907, p. 147, Fig. 139, and p. 325, Fig. 356.

of neoplasms. They form, and this requires emphasis, only one set of many degenerative and retrogressive phenomena encountered at all sorts of stages of the cycle in comparative embryology. Truly, in dealing practically with embryology, "in the midst of life we are in death." "Das Werden" is ever accompanied by "das Vergehen."

The whole doctrine of the tumours centres in the problems of identical twins. Than these latter there is nothing more replete with interest in embryology. Of vast import is the recognition of the existence of two kinds of these. There are identical twins, which come as it were out of the same mould, and there is a second and rarer kind—the "looking-glass-image" twins.* The occurrence of the latter throws welcome light upon various zoological and anatomical questions—on the right-handed and left-handed snails, fishes, etc.—as well as upon the phenomena of reversed viscera. Ion other direction identical twins pass gradually into double monsters, and these in their turn into the higher tumours or teratomata. At the basis of the tumours is the fact that from one fertilized egg a multiplicity of embryos may arise, just as from one such in a sea-polype a legion of jelly-fish may take their birth. As in the polar bodies of oögenesis (egg-formation) we have rudimentary or abortive gametes (conjugating-cells), so in the development of the higher animals we meet with rudimentary or

*These looking-glass image twins are the greatest wonder in animate nature. Along with Captain Lambelle and a former pupil, Dr. M. M. Morrison, a few years ago the writer had a unique opportunity of examining and photographing two of these (twin boys) in the south of Scotland. Both were very degenerate, and both suffered from club-foot. The deformities in the right foot of the one were in the left foot of the other, and so on. One of the two exhibited the phenomena of reversed viscera, with right aortic arch, stomach and spleen transposed, etc. The actual finds and photographs will be published elsewhere.

abortive germ-cells, originally really destined to form embryos. In other words, in the history of the race there has been a reduction in the number of actual normal embryos arising, but with the persistence of such "embryonic" germ-cells (embryonic in destiny) and the retention by these of more or less of the "memories" needed to unfold an individual of the species. As shown two years ago in the *Lancet*,* a malignant tumour—and this is true of both cancer and sarcoma—is nothing more than an irresponsible trophoblast or chorion, the asexual generation, which in every normal development is the forerunner of an embryo. Though not recognized, or, at all events, not stated by them, the researches of Farmer, Moore, and Walker, † as well as those of Bashford and Murray,‡ have confirmed the truth of this view, and to the hilt. For it is an inalienable property of the trophoblast of normal development that upon it germ-cells arise. Once these have come into existence, it is but a

**Lancet*, June 21, 1902, p. 1758.

† Farmer, Moore, and Walker: "Resemblances Exhibited by the Cells of Malignant Growths in Man and those of Normal Reproductive Tissue," *Lancet*, December 26, 1903, p. 1830.

‡ "The Zoological Distribution, the Limitations in the Transmissibility, and the Comparative Histological and Cytological Characters of Malignant New Growths" (Scientific Reports of the Imperial Cancer Research Fund, No. l, London, 1904). First of all, cancer was "embryonic," and then it was not; it arose, for the second or third time in history, from a "conjugation" of body-cells, and then it did not; the "infective venereal tumour of bull-dogs" was an infective granuloma, and then, on the very same evidences, it was a true sarcoma, because like the writer, Mr. Shattock said it was. It is given to official research to change its opinions as often

as it sees fit. The above paper was put out with a great flourish as a confirmation of the work of Farmer, Moore, and Walker, and I was assured that the original discovery could have been made by official research. Then at a later period this confirmation was withdrawn, for which see the Proceedings of the Royal Society, London, B, vol. lxxvi., 1906.

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question of a certain limited number of cell divisions before they present the phenomena associated by many embryologists with the reduction of chromosomes. In short, the proof furnished by the researches of Farmer, Moore, and Walker, of the occurrence of divisions in cancer and sarcoma cells usually associated with the maturation of germ-cells, was the one thing lacking to establish beyond question the true nature of a malignant tumour as the pre-embryonic portion of the life-cycle, the asexual generation. While at present it would be wrong to assume that such cell divisions must of necessity occur at some time or other in all malignant tumours—for even a malignant tumour may conceivably be so reduced or retrograded as to be unable to repeat the whole cycle of the germ-cells, just as no tumour is known to form actual sperms—it is now beyond doubt that the occurrence of such division in certain cases proves a malignant neoplasm to be the pre-embryonic portion of the life-cycle. It is a life-cycle with the embryo omitted. Germ-cells never do arise, and never could have arisen, from somatic or embryonic cells or tissues.

The true science of the tumours, then, has its embryological basis in the facts and phenomena of identical twins, triplets, etc. The facts of normal development, as seen in identical twins, as well as in certain armadillos, many sheep, etc., demand that we should recognize that just prior to the unfolding of an embryo there are "n" divisions of germ-cells, resulting usually in one embryonic cell and a certain as yet undefined number of retrograde or rudimentary gametes, these have now lost to a greater or less degree—this varying in different cases—their powers of undergoing a completely normal development. They are not to be confused with those

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germ-cells destined for the sexual organs of the individual. A malignant neoplasm, due to the spontaneous development of such a retrograde germ-cell, which in the days of long ago would have given rise to an identical twin, has lost to a greater or less degree those potentialities, those unconscious memories, which would have permitted it to complete the full life-cycle of normal development, ending in the formation of a normal embryo. The memories which it retains condition the character of the tumour to which it will give rise, and it is these rudimentary memories, stimulated by its environment in some particular organ, which result now in a sarcoma, now in a carcinoma, mimicking the structure in which it lies. This explains why in one development a certain germ-cell will produce an identical twin, while the corresponding germ-cell in another instance develops into a monster, or into an embryoma, or into such with a malignant tumour, or into a mixed and malignant neoplasm, or, lastly, into a simple sarcoma or carcinoma. All depends upon the amount of unconscious memory retained by those retrogressive germ-cells, which formerly gave birth to normal embryos, identical twins, triplets, etc. Nay, one may safely take a further step in the like direction. Chorio-epithelioma, a deadly form of cancer in pregnancy, usually rises in instances where either no embryo has been formed (hydatid mole), or it has been aborted at the critical period* as a monstrosity. Is it at all unlikely that here, for some reason or other, either the wrong germ-cell had developed, or, at any rate, that such a one had early usurped the place of the developing

*For a full account of the "critical period" and its peculiarities see J. Beard, "Certain Problems of Vertebrate Embryology," 1896, and "The Span of Gestation and the Cause of Birth," 1897, both published by Gustav Fischer, Jena.

one? This would be one the memories of which could but result in a malignant tumour—that is to say, one mimicking the structure of correct chorion. If this be true, we have in chorio-epithelioma merely a form of cancer arising very early in the life of the individual, and invading a new host, the unfortunate mother.

The things that we have been dealing with are startling enough, and it may be asked. What steps are being taken to apply them in practice and to carry our embryological knowledge of the malignant neoplasms still further? Practically none. Beyond the boundaries of Edinburgh, I am not aware that at the present time the embryological aspects of the malignant tumours (in the sense of my conceptions of that science as opposed to the utterly erroneous fairy-tales of the textbooks) are receiving any particular attention. Abroad, for example, the leading investigators appear to be hopelessly at sea.* In cancer research, momentous as it is for human welfare and hopes, there is far, far too much industrious but futile digging in culs-de-sac. But there is a gleam of hope for the immediate future. Authorities connected with a great institution which is distinguished for its rapid and wonderful advances in scientific research have for some little time been considering and elaborating a scheme by which cancer research within its walls may be placed shortly under the direction of an able embryologist. † If this be done, the first important step in Great Britain will have been taken towards the proper recognition and

*Judging by the recent investigations of Abderhalden and his pupils, and those of Blumenthal and Neuberg, as described in the Introduction, this is now (1911) not the case. As it has turned out in the sequel, cancer was vulnerable along at least two lines of attack, the embryological one, and the stereo-chemical one. It is really along the latter that the above observers are, slowly but surely, advancing.

† This did not take place.

independent establishment of a science of the utmost moment to mankind—the true science of life, embryology. In these condition, and given abundant material of the right sort, we may hope to witness soon advances in our knowledge of the malignant neoplasms of which we can now form no conception, and the vast importance of which it is impossible to gauge.

The three most important points in the above chapter appear to be the recognition that the problems of cancer finally merge into those of identical twins, triplets, etc., of the fundamental identity of sarcoma and carcinoma, and the mimicry of the tumours. The latter, of course, was not new, but it was a revival of a doctrine enunciated early in the nineteenth century by Fleischmann, and later on advocated by the late Sir James Paget. At the time this chapter was written down (October, 1904) the writer was deeply engrossed in the microscopical study of malignant tumours. This work was interrupted by a controversy with Mr. Roger Williams, F.R.C.S., which was started by the latter in the *Lancet*, and the letters of both sides will be found in that journal of the closing months of 1904 and early in 1905.

In the course of this, in a reply to my opponent, I wrote down the words: "The mammalian embryo solved the problem of cancer ages ago." After writing this, I looked at it, and said to myself, "Yes, it is quite true, but—how?" Then the thought came, Why are you bothering

about the microsocical details of these tumours? You ought to be working at the things which occupied you ten years ago. Without further loss of time I got out all my material relating to the critical period, and the two papers, "On Certain Problems," etc., and "The Span of Gestation," which

I had published on these problems, and sat down again to study all. Then—at once—it was seen that the problem of the "how" had been solved ten years earlier, but that no great stress had been laid upon the solution—the commencing activities of the pancreas gland at the critical period. This was the starting-point of Chapter IV., dealing with the chief problem of cancer.

CHAPTER IV

THE CANCER PROBLEM*

In the following simple story the correctness will be assumed of all the conclusions as to the etiology and nature of cancer which were advanced in, for example, the abstract of my lecture on the "Problems of Cancer," published in the *Lancet* of October 29, 1904. The appended classification of neoplasms—an extension and inclusion of the "embryomata" of Wilms—may serve to make clear here what a malignant tumour is defined to be.

1. *Enbryomata* (benign neoplasms). –Pathological manifestations of some greater or less portion of an embryo. They are composed of real tissues—that is, normal or somatic ("embryonic") cells or tissues. At its basis each is a greater or less portion of a twin, triplet, quadruplet, etc., identical with the individual containing it. They are not endowed with indefinite powers of growth, and they nourish themselves like other normal tissues.
2. *Amphimyxomata* (malignant neoplasms). –Combinations of embryomata and trophoblastomata. Pathological manifestations or attempts to reproduce the whole life-cycle, including trophoblast and embryo. They are transitional forms. (The mixed tumours of Wilms are not all malignant, some being merely embryomata.)
3. *Trophoblastomata* (malignant neoplasms). Pathological manifestations of the asexual portion (trophoblast) of the life-cycle and sometimes—whether or not always is not at present known—attempting to repeat the germ-cell portion of the life-cycle, as shown by the researches of Farmer, Moore, and Walker. They are not known to differentiate actual functional gametes, eggs or sperms. They never include or repeat any part of an embryo. They are never composed of somatic ("embryonic") cells, though they may mimic such or even resemble no other cells in the body. As Sir James Paget pointed out long ago,* they are "imitation tissues." They exhibit powers of unlimited growth and increase, and they nourish themselves by eroding and destroying normal cells and tissues in a manner exactly like that of the trophoblast of normal development.

To illustrate the points to be considered, I have put out

*The designation of a malignant neoplasms as an "imitation tissue" was first used by the writer about a year ago (1903) in an address to the Edinburgh pathological Club. The clear recognition of the existence of such "imitation tissues," as well as of the close resemblance, amounting to identity, of benign tumours to normal tissues, will, however, be found in Sir James Paget's classic work, "Lectures of Surgical Pathology," 1870, third edition, pp. 382 and 387. This book is a veritable treasure-house of valuable information. History does indeed repeat itself, and, according to Virchow, in 1815 Fleischmann explained that the tumours were "only copies of normal organic parts of the very same body in which they arise and subsist." The authority of J. F. Meckel, according to Virchow, prevented the acceptance of this most important conclusion; indeed, this anathema has persisted or been renewed since that time, for to-day (1905) the condlusion, rightly drawn by Fleischmann ninety (!) years ago, is not accepted, so far as I am aware, by any living pathologist. *Eppur si muove!*

certain microscopical preparations of transient ganglion cells, parts of the asexual generation of a dogfish. These may be taken to typify the trophoblast of a mammal or the cells of a malignant tumour. The preparations show: (a) cells in full functional activity prior to the critical period, and (b) cells which, with the passing of the critical phase, have entered upon their long, slow course of degeneration by simple atrophy. It would have been preferable to exhibit preparations of trophoblast, but those made after this method some years ago are now faded. The facts in the two cases, the mammal (sheep, pig, and others) and the fish (*Scyllium, Raja,* and others), are, however, quite similar. There is, indeed, only one mode of development in vertebrate animals. Freshly made preparations of human trophoblast of, say, the fifth and ninth weeks of gestation would display the like bloom on the one side of the critical period and the same decay on the other. Such figures of mammalian trophoblast have, indeed, been published already in the writings of my friend Dr. J. P. Hill.

The question which I wish to discuss is one which interested me exceedingly some years ago, long before its significant bearings upon the cancer problem were obvious. In a nutshell it is this: Why do these and certain other cells of a fish development, like those of the mammalian trophoblast, go on flourishing for a certain definite portion of the early development, whilst the parts of the sexual generation, "the embryo," are unfolding, and then with an almost tragic suddenness commence to degenerate and die? What brings this remarkable change to pass, one which in human development is lacking, if "the embryo" be absent or very abnormal?

Cancer is an irresponsible trophoblast. The unfolding

of an embryo would stay its growth just as the formation of the sexual generation ends the growth of a shoot of a flowering plant. How does "the embryo" bring about this result? It does not devour the trophoblast, but it must produce something which, as was pointed out two years ago,* brings the degeneration to pass. Only in ordinary chorio-epithelioma is the malignant neoplasm a persisting portion and derivative of the trophoblast of the immediately previous gestation. Any ordinary cancer or sarcoma is anew development of trophoblast, due to the attempt of a germ-cell to start the cycle anew. Except in mode of nutrition, this irresponsible trophoblast does not resemble normal trophoblast, but it often mimics the structure in which it lies or it is like no other organ or tissue in the body. In any and every higher mammalian (Eutherian) development there is the potentiality of a malignant tumour, † chorio-epithelioma, and this danger exists until the

degeneration of the trophoblast is an assured but not completed fact. As researches made some years ago, but never published, demonstrated,

* The *Lancet*, June 21, 1902, p. 1758.

† So far as is at present known, chorio-epithelioma does not occur in any mammal except man. The multiplicity of embryos in most other cases is against its happening. In almost every gestation in the pig, and often in the rabbit, there are abortive embryos, from the trophoblast of which a malignant tumour might arise but for the presence and influence of the other embryos. In the course of the discussion the case of a full-time anencephalic (headless) human fœtus was cited as against the validity of the conclusions advanced. In this the entire alimentary canal and pancreas were absent. A little cross-examination elicited the information that nothing was known as to its fœtal membranes, and that it was one of twins. The latter point is decisive in explaining how this monster had escaped the weeding-out of the critical period. Had it been a single embryo, not a twin, it would undoubtedly have been aborted at the critical period, and, moreover, hydatid mole or chorio-epithelioma would very possible have followed.

in the pre-critical period the staining of the trophoblast cells resembled that of the function transient ganglion cells-with methyl-blue eosin they took on an exquisite blue stain. With the passing of the critical period the cells of the trophoblast, as Hill has shown for the bandicoot (*Perameles*), no longer took on the blue stain, but absorbed ever more and more the red eosin. The like change will be noticed in the transient ganglion cells of the fish; it is also seen in the merocytes* of the yolk.

Rather less than two years ago I really commenced to work at the problems of malignant neoplasms from their embryological aspects. The starting-point for research here was obtained from certain results of prolonged investigations into the mode of vertebrate development. From these it had been established beyond question that in the normal life-cycle of development in any of the higher animals there were two generations—an asexual one, the "larva," or phorozoon, and a sexual one, "the embryo"—that the former was mainly, if not entirely, represented in mammalian development by the trophoblast, and that in every normal development the trophoblast was suppressed by the sexual generation, its de-generation commencing at the critical period with the completion of all the parts of the embryo. For the past eight years it had been recognized that at the critical period a change in nutrition always occurred. In 1902† the conclusion was advanced that cancer was an irresponsible trophoblast, the continued and unbounded

*"Merocytes" are certain curious nuclei, or, perhaps cells, with no particular cell-substance around them as a rule, which occur in the yolk-sac of many fishes. Often they are much elongated and branched, due to incomplete cell-division (pluiripolar mitoses). Apparently they are asexual structures. The writer has, as yet, not published all his observations upon these merocytes.

† The *Lancet*, June 21, 1902, p. 1758.

growth of which was favoured by the absence of an "embryo" or sexual generation.

At that time there appeared to be one hopeful outlook for cancer research along the lines of embryology. It was that in every normal development the trophoblast, which in the absence of a completed embryo might become a malignant tumour, chorio-epithelioma, was invariably suppressed and degenerated. The task was to find out how this came about; for there appeared to

be good reason for the hope, if not for the sure belief, that the factor or factors which brought about this result in normal development might also be potent when directed against an irresponsible trophoblast or cancer. To find these factors would be the solution of a general scientific problem of which apparently cancer was but a special case. These factors have now been found, and in consequence cancer ceases to be a problem for the embryologist. A scientific solution of a certain problem has been obtained; whether or not this be at the same time a solution of the cancer problem in its medical aspects would not be for the embryologist to predict. He can only guarantee the truth of the embryological findings and conclusions, and maintain that these would remain, even though they should fail utterly when applied in the treatment of malignant tumours.

The change in nutrition initiated at the critical period in vertebrate animals, from fishes to man, is based in the commencing functional activities of the pancreas-gland or sweetbread. This introduces an alkaline digestion by means of the pancreatic juice with its various ferments. But what of the pre-critical nutrition? There are many ways in which this might be investigated. One might examine normal trophoblast, cancer or sarcoma, blastoderm of a fish—such as the skate—cleaved eggs of an amphibian, or

blastoderm of a bird, all these being in the main homologous structures or asexual generations. What is found to obtains in the one must hold good in the others, for there is but one mode of vertebrate development. In this direction, when dealing with the yolk and merocytes or fish-development and with the mammalian trophoblast in past years, some results had already been obtained; and in taking up the thread anew one's thoughts reverted naturally to the chick and frog. In a recent publication Professor M. M. Hartog* writes (p. 587): "One thing is clear as the result of this: all probability henceforward is in favour of the view that in the animal, as in the plant, a cell can only utilize its reserves secondarily and mediately—by the internal secretion of an enzyme." The author commences his paper by commenting upon the known facts that it has been shown in every case examined that in the utilization of reserves in plants a ferment or enzyme is always present, which in suitable circumstances can effect *in vitro* the same process—usually of hydrolysis—which the living organism performs. He next proceeds to demonstrate that in the early development of animals, in the cells of the frog's egg, in which cleavage is ended, but no embryo yet present, and in the blastoderm of the three or four day's chick, there is a proteolytic ferment present. Under proper precautions, this in acidulated solution (from 003 to 007 per cent hydrochloric acid) gives the biuret reaction showing the presence of peptone. The reaction is absent in neutral or slightly alkaline solution.

*Hartog, M. M.: "Some Problems of Reproduction—II.," *Quarterly Journal of Microscopical Science*, 1904, vol. xlvii., pp. 583-608.

On p. 587 he arrives at the important conclusion that the digestion in the frog's egg (prior to the appearance of an embryo) and in the blastoderm of the chick (with the embryo removed) must be a purely intracellular acid one.* For comparative and other reasons I now apply this conclusion to the trophoblast of a mammal and to the cells of a malignant neoplasm. No more than those of the trophoblast do the cells of a cancer contain yolk. None the less, in both the digestion must be the "ancestral" acid "peptic" (intracellular) one, characteristic of the asexual generation of a vertebrate, for this has been handed down as an unconscious memory from the time when the

mammalian yolk-sac contained food material. Recent researches, especially those of Vernon, have revealed the presence of traces of trypsin in many organs of the body. But this enzyme has never be4n, and cannot be, demonstrated in any malignant tumour. On the contrary, the work of Petry † on many carcinomata and sarcomata has proved the occurrence in these of a proteolytic ferment. ion exception of pepsin; but the peptic digestion of the stomach, although important in its action upon fibrous tissue, thus loosening such things as muscle-fibres (flesh), can on occasion (after removal of the entire stomach by operation) be dispersed with. For shortness and clearness, when this chapter was first published, I spoke of "acid-ferments" and "alkaline-ferments," meaning thereby ferments or enzymes acting respectively in acid and alkaline media. A certain anonymous critic might note this, and in future be mindful of the maxim, "Teach not a parent's mother to extract the embryo juices of the egg by suction," etc.

† petry, Eugen: "Ein Beitrag zur Chemie maligner Geschwüste," *Zeitschrift für Physiologische Chemie*, 1899, vol. xxvii., p. 398.

researches, this is evidently of an (? Intracellular) acid nature, like that recorded by Hartog for the chick blastoder, etc. Petry's work is cited in the latest edition (1903) of Hoppe-Seyler's "Handbuch der Chemicschen Analyse" 9p. 387) as proving the presence of enzymes in malignant tumours.

In this connection it would be of interest to cite some of the discussions upon "Extrazelluläre und Intrazelluläre Verdauung" and upon the enzymes or ferments in Verworn's "Allegemeine Physiologie" (pp. 161 *et seq.)* In studying the history of the yolk-sack of fishes I made many observations upon this question some years ago. At times one meets with cases in the yolk sac which are more "extracellular" than "intracellular." Ultimately, indeed, the latter passes into the former. In the sequel therefore, the term "intracellular" will be used within brackets to indicate not so much its actual nature nowadays as its origin in past times from a real intracellular digestion occurring in the presence of yolk. In the chick or skate the yolk is contained in a yolk-sac; in a frog, within the cells of the cleavage. None the less, the ferment is the like one.* The trophoblast of normal

*It should not be forgotten that, as Verworn remarks (op. Cit., p. 171,) there exists a "quite overwhelming abundance of ferments." Hartog would seem to assume that the one discovered by him in the cleaved frog's egg and in the blastoderm of the chick, which must be common to the asexual generations of vertebrates, is the same as, for example, the enzyme of the mammalian stomach.. For present purposes it is not needful to insist upon this. Here it will be maintained that this enzyme of the blastoderm trophoblast, or malignant tumour can only act in a slightly acid medium, and that in all probability it is a much weaker one than that characteristic of then the pancreas. The existence of the asexual enzyme and of the sexual one may account for the necessary existence of a gastric and an intestinal digestion. The sexual generation is of later origin in time than the asexual one, and its evolution has been bound up with that of a new digestive gland and enzyme, the pancreas, etc.

development, like the trophoblastoma of chorio-epithelioma, nourishes itself by an (intracellular) acid digestion. A malignant tumour, a cancer or sarcoma, nourishes itself in exactly the like manner. Like the trophoblast, it eats and erodes its way, destroying tissues by an (intracellular) acid digestion. Only by such could a cancer erode bone.* To describe in detail what should follow would be to recite much of two papers † published long ago as well as some other points

noted since that time. The solution of the question is possibly the resolution of the problem of cancer. The mammalian embryo solved this ages ago; indeed, it "inherited" the solution from "ancestors" much lower down in the scale. The very existence of "the embryo" throughout the higher animals is dependent upon the suppression, the degeneration and death, of the asexual foundation upon which it came into being. In many invertebrata the sexual generation eats up "often by phagocytes or wandering cells" the asexual foundation or "larva"; and it must be recognized that in the higher forms it practically digests it. On the present occasion no account of the work required to establish it need be given; much, not all, of it is contained in my published memoirs. The fact may be stated briefly that in fish and mammal alike it is the

*This remark about the power of cancer to erode living bone was a trap for the unwary, deliberately set by the writer. As had before happened, it caught its victim with certainty; for at once it was asserted, as I had often before heard it, that the wall of an aneurysm could erode bone also—thus, the vertebral column—and did I therefore mean to suggest that this was an acid-erosion, etc.? The reply to this is, that the pressure of the aneurysm here kills the bone, and that the dead, not living, bone is then removed by the agency of some enzyme of the leucocytes or white blood cells.

† Beard, J.: "Certain Problems of Vertebrate Development," 1896, and the "Span of Gestation and the Cause of Birth," 1897, both published by Dr. Gustav Fischer, Jena.

commencing functional activity of the pancreas which initiates the degenerative changes in the asexual generation. At this epoch, the critical period, the fish commences to feed itself on yolk, not by an (intracellular) acid "peptic" digestion, but by an alkaline pancreatic one. In some of the textbooks of physiology stands the statement that the human pancreas at birth "contains tryspin and the fat-decomposing ferment, but not the diastatic one"* (Zweifel); but, as I know from my comparative observations of years past, its activities really commence at the time the anus is formed, early in the seventh week of gestation, at a period when in the days of long the organism would have begun to digest the yolk of its now empty yolk-sac. The pancreas functions throughout fœtal life in a mammal, though it has nothing to digest except the trophoblast.

During fœtal life the pancreas gland is pouring out its secretion into an intestine which at the present day contains no food to be digested, for the food of the fœtus has been prepared by the pancreatic digestion of the mother. To the fœtus *in utero* this alkaline digestion is of no direct use, but it has an indirect import in acting upon trophoblast. The commencing activities of the pancreas during fœtal life initiate an alkaline digestion by means of the most powerful and important of all the digestive juices. To which of its ferments the observed results be due does not concern us. † If the secretion be

* The diastatic ferment is, of course, amylopsin. Here, therefore, on the first appearance in a medical journal of an advocacy of pancreatic, ferments in cancer, amylopsin is noted, and its absence at birth mentioned along with the name of Zweifel as the discoverer of this fact.

† The writer had intended, in correcting the proof for the *Lancet*, to insert the following note, which was actually spoken at Liverpool on January 20, 1905: "As my work of past years has revealed, at the critical period the embryo, complete in all

absent, neither the asexual structures of a fish development nor the cells of chorio-epithelioma do, or can, degenerate.

Under the conclusion already advanced regarding the nature of cancer as an irresponsible trophoblast, in consideration of the facts regarding the acid and eroding action of the trophoblast and of carcinoma, and in respect of the fact that in the absence of a completed embryo or fœtus and its pancreatic secretion the trophoblast may become one of the most deadly of malignant tumours—chorio-epithelioma—it must be clear that nature itself has possibly provided a remedy for cancer and the pernicious (intracellular) cancerous digestion of the trophoblast in the secretion of that important digestive gland, the pancreas. This structure, I understand, is very rarely the seat of a primary carcinoma, and almost never of a sarcoma.* Moreover, it is very important

continued from page 118

its parts, begins to nourish itself by an alkaline pancreatic digestion, and with a ferment known as trypsin. If this latter be wanting, the asexual generation, the trophoblast, may become a malignant tumour of the deadliest description; in its presence it becomes harmless and slowly degenerates. Clearly, then, since cancer is an irresponsible trophoblast, the ferment, which brings about the degeneration of this in normal development ought to possess potency when directed against the cells of a malignant tumour." For reasons of scientific priority, which also led me to read to the audience the abstract of Liverpool lecture, published next day in full in the *Liverpool Daily Post and Mercury*, it seems desirable to draw attention to this matter here also.

* Two recently recorded cases of tumours of the pancreas may be cited. In the *Berliner klinische Wochenschrift,* 1904, p. 479, Herr Ury, "Berichtet über einen Fall von Pancreas-carcinom mit Fett - Stühlen, wlche, durch Darrichung von Pancreon wesentlich gebessert wurden," and in the *Journal of Medical Research*, Boston, 1902, vol. viii., pp. 385-395, A. G. Nicholls records a "simple adenoma of the pancreas." The first shows that the pancreas was not properly functioning, while the second in which the tumour was not larger than a marrowfat pea, illustrates the difficulties encountered by tumours in this organ.

to note, that just as cancer is found everywhere in the vertebrata, just as there is one mode and one only of vertebrate development, so the pancreas gland and its secretion are a common heritage of vertebrate animals.

Briefly, as I conceive it, in normal development and in a malignant tumour the matter is simply a question of the victory of a stronger enzyme over a weaker one. In view of all this, the events in a malignant tumour—such as, for example, the "heterotype" mitoses—lose much of their importance. They may still possess an interest for the cytologist and embryologist, and even a passing one for the pathologist. But to the physician and surgeon these abortive attempts to form gametes cease in treatment to have any import whatsoever.

Practically all that was sought after from my own researches regarding cancer has now come to light. Embryologically, the problem of cancer has been to discover the antithesis of two enzymes and in particular to find out the enzyme capacity of destroying a weaker one, and thus of leading to the degeneration of the tumour by simple atrophy. The whole story is but another example of that antithetic alternation which underlies all the phenomena of living things. The solution of the problem of the functional relation of embryo and trophoblast—how the latter nourishes itself by an (intracellular) acid "peptic" digestion and degenerates slowly by a pancreatic digestion—becomes at the same time the embryological, if not the medical, resolution of the problems of malignant neoplasms, as well as of chorio-epithelioma. As an embryologist, who is not a physician or surgeon, my task is ended. The further applications of the scientific and theoretical solution of the problem may safely be left in the hands of those who know far better how to employ it. But they may not forget that in nature the degenera-

tion and disappearance of these asexual structures, sometimes quick are often exceedingly slow, though sure. Not that it is likely that the surgeon has removed his last malignant tumour, but that, as one of the results of the work* begun more than sixteen years ago, they physician has possibly had forged for him a light and not dangerous weapon, only second, if not equal, in potency to the surgeon's knife. †

*Most of the work has been carried out in Edinburgh, latterly with grants from the Moray Research Fund and Carnegie Trustees.

† As later events have proved, this estimate—with deference to certain transparently anonymous critics—was much too modest. The pancreatic ferments, trypsin and amylopsin, when direct *scientifically* against the living cells of cancer or sarcoma, are infinitely more potent than the knife of any surgeon!

CHAPTER V

THE INTERLUDE OF CANCER*

"In preda al duol non mi lasciar!"

MAZZONI: *Cavalleria Rusticana.*

With the results of the preceding chapter, the writer regarded the problem as no longer one for the embryologist. It seemed to him that any further problems of cancer were rather for comparative physiological chemistry than for such a branch of science as embryology. This has, indeed, turned out to be correct. As appeared in the sequel, cancer was vulnerable by two lines of attack—embryology and stereo-chemistry. At the present time (1911) the scientific Germans—wuch as Abderhalden, Blumenthal, Neuber, and others—are advancing slowly, but surely, along the line of stereo-chemistry. That they have been anticipated in this advance is shown in the following chapters of this book, as well as in the introduction. In the present chapter, therefore, there is presented a connected account not merely of what is given in preceding pages, but also of many things worked out in years now long past. The following lines contain an attempt to show how various purely embryological problems and their solutions bear upon the problems of cancer.

*From the *Medical Record*

The embryologist never tells the story of his work in the order of his researches. He cannot; for in these he pushes his way little by little, step by step, from the known to the unknown, and at any given time he may be working in two directions—upwards from the starting-point of the fertilized egg, and downwards from the finished embryo. Thus it happened, that what, logically regarded, should have been the first investigation in 1888—the history of the germ-cells—was actually the last, as it was also the coping-stone which crowned the work, and made it lasting.

The actual cancer researches have been a mere interlude in the whole—an *intermezzo*. "The prey of pain let me not be!" The solution of the problems of cancer was but a corollary of what had gone before, and it followed naturally and irresistibly out of the germ-cell results, the

course of the life-cycle, and the conclusions as to the germinal continuity and heredity. Since the embryological theories of the textbooks are, to apply the words of Pasteur, a mass of baseless hypotheses, it follows that the solution of the problems of cancer can be grasped properly only by a comprehension of the course of the cycle of life from generation to generation, as my researches of past years have revealed it.

The starting-point of a new cycle is the fertilization of an egg, and the outline history of the cycle is not complete until we have shown how new eggs, new reproductive elements, arise; and until we have reached the point at which these are ready for fertilization, to start the cycle anew. An egg is fertilized and development begins by its cleavage; an ever-increasing number of cells is formed in this way, and anon we reach a point, at which the orthodox embryologist says that the egg-cleavage is finished. What has then come into being? The usual

reply is, " A new organism, an embryo." No such thing! At the close of cleavage, in none of the higher animals is any trace of an embryo present. Something is there, but not an embryo. I will ask the reader to regard this developing egg from the start of cleavage as a living organism, but not an embryo.

The criterion of anything in embryology is the fate or destination of the cells. In a worm's egg, which has cleaved five times, giving 32 cells, or in a skate's egg, which has undergone ten division, resulting in 1,024 cells, there is not a single cell present which is embryonic in destiny. Nearly all the cells are predestined to form portions of an asexual foundation or larva, termed by me the "phorozoon," or bearing animal. This is a transient organism; for, as a rule, its life is very brief. It has a part to play in the cycle, and, like the Moor, when it has done its appointed task, it can go. The results upon which, generally speaking, my conclusions are founded have been obtained by what my late friend and teacher—Professor George Bond Howes, Huxley's assistant and successor—was wont to term the comparative morphological (and physiological) method. Under it there is but one mode of development for all the higher animals: in essentials the life-cycle is always similar, not only from fishes to man, but from worms and even lower forms to fishes. These "phorozoa," or asexual generations of various marine organisms, have long been known. Often, and until a connection therewith was established, they received names distinct from those of the sexual generations. Thus, the larva, "phorozoon," or asexual generation of a brittle star, is still known as a *Pluteus*, and so on.

The late Professor N. Kleinenberg first set up (1886) the doctrine of development by substitution of organs. Under this, every organ of the larva (asexual generation)

FIGURE 5 (two pages) GO HERE!!

was ultimately replaced by a corresponding, but differently developed, organ of the adult form (sexual generation). For a variety of reason, into which space forbids entry here, it soon became clear to the writer that Kleinenberg's doctrine was inadequate, and that, instead of a substitution of organs, there was in development in reality a substitution of organisms. The sexual organism replaced the asexual one. This was seen to be an alternation of generation, and as there was no homology or close likeness between the asexual form or its organs, it was an antithetic alternation of generations.*

Now that we have the mention of the word "antithetic," it may be permitted in passing to point out how Pasteur's researches started in the antithesis of the two sorts of tartrate crystals: mine in that of two nervous systems in the life-history of a fish. Here we are dealing with anatomical antithesis; later we shall come to recognize physiological antithesis—that of two ferments.

The tracing of the asexual generation in the backboned animals or vertebrata, from fishes to man, was not without its own special difficulties. These were due rather to expecting too much, and to failing at first to realize that the higher one ascended in the scale of life, the greater became the organization of the sexual form or generation, and the more insignificant the asexual one, until in the highest animals, the mammals and man, the asexual generation became reduced to the almost structureless chorion or trophoblast, as Professor A. W. Hubrecht named it in 1889. Many people, quite ignorant of all the embryological advances of recent years, appear to imagine that I not only introduced the

*See Appendix C, "The netazoan Life-Cycle and Alternation of Generation."

name "trophoblast," but also invented the thing, to which it is applied in embryology. These things are not true. The name was invented for a thing defined by Hubrecht in 1889, and the thing itself has existed for untold millions of years!

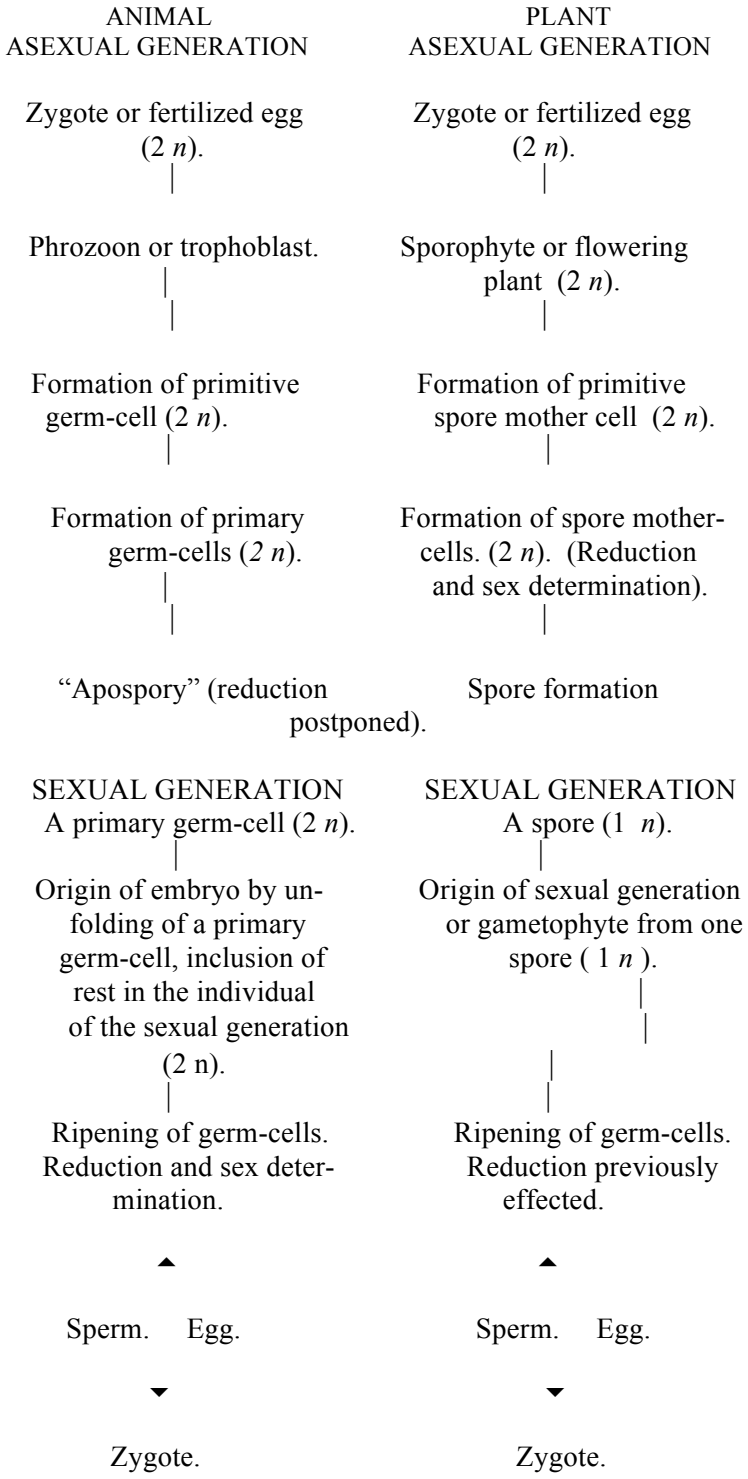
In 1895 the standpoint had been attained that in every life-cycle of a higher animal, such as man, there were two generations: an asexual one—the trophoblast, and a sexual one—the metazoan individual or person. The puzzle was not how the first of these arose, for clearly it could be demonstrated any day in the week that it was the direct product of the cleaved or segmented egg (*vide* Fig. 5, phorozoon or larva). Somehow or other there arose gradually upon it the sexual generation by a process of evolution or unfolding.

How! Something resembling the spore mother cells of plants was required. That was very apparent. (See the table of Revised Comparison.) It was not until towards the close of 1900, when the firstharvest of the germ-cell researches had been reaped, that the problem was cleared up. The germ-cell researches had been reaped, that the problem was cleared up. The germ-cells arose before the embryo, as products of a single cell, the primitive germ-cell (U.K.Z. of the diagram, Fig. 5), in a direct line from the fertilized egg. They came into being upon the asexual generation or trophoblast. To contain and to nourish these germ-cells for a brief span of time another organism was need, a sexual one, endowed with sexual organs.

How was the sexual organism obtained? In embryology things do not come into existence out of nothing! True, there are embryologists who look upon holes or cavities as the sources of important organs, but the writer at all events is not a "hole-morphologist"!*

*Any more than the author of this expression, the late Professor N. Kleinenberg, was.

TABLE OF REVISED COMPARION OF ANIMAL AND PLANT LIFE-CYCLES.



In the above table *n* equals the reduced number of chromosomes, and 1 *n* signifies the emancipated cell, 2 *n* the duplicated or conjugated cell, the "conjugation" or joining together being carried out at fertilization. The "reduction" is the undoing of the previous duplication effected at conjugation.

The unit from which anything arises is the single cell. There was only one source from which such a sexual generation could arise: this was by the evolution or unfolding—the sacrifice—of one germ-cell for the well-being of the rest, and to contain. At the epoch of the formation of the primary germ-cells all were alike in origin and potentialities. All were so many potential individuals of the species. If two developed independently, the result would be identical twins; if three, triplets, and so on.

Reviewing matters, starting with the fertilized egg, this gives rise to an asexual generation—the trophoblast, upon which there arises an "apical cell"—the primitive germ-cell. This latter divides a certain limited number of times, this number being a fixed one for the species; but while it is *n* in the male, it is *n* plus *1* in the female. The products are 2, 4, 8, 16, 32, 64, 128, 256, 512, etc. In the diagram it is depicted as 128. These 128 germ-cells are the primary germ-cells. It is they which enter the embryonic body (Fig. 4) when this arises, and it is some of them which come to occupy all sorts of abnormal position. But all the line of primary germ-cells are not destined for future generations. Some few of them, 1, 2, 4, or 8, are embryonic in destiny. At least one of these must unfold to form an embryo. If any of the others do so, the result is identical twins, triplets, etc. If any of these "embryonic" germ-cells lie dormant within the developed embryo, they may become the seed of future tumours, as will appear later on. The line of heredity, so far revealed, leads from fertilized egg to the primary germ-cells, and thence through all the history of the germ-cells within the "reproductive glands" to new eggs and sperms; that is, all things considered, the cycle is one of unicellular organism, the germ-cells, in

the history of which the sexual generation or individual is but an incident.

Another important question to be solved some fifteen years ago was the how and the when of the suppression of the asexual generation. This latter, whether represented by the transient nervous apparatus and other structures of a fish, or by the trophoblast of a mammal, went on flourishing for a certain—not very long—space of time, and then, quite suddenly, all growth was stopped, and its degeneration was initiated. In years long gone by how often have I not watched these asexual structures under the microscope, seen them flourish and blossom, and then—subito, as the Italians say—begin to fade away, as though blighted! The correlation of phenomena is often of the greatest importance to the embryologist in his work; and when this sudden fading away was first established, it was also noted that the commencing formation of the posterior fissure of the spinal cord was a concomitant phenomenon. This led to one of the many little research excursions I have made right up the back-boned series to the mammals, and to the study of human embryos themselves. A whole array of interesting and connected events was soon unearthed, and the putting together of these culminated in the discovery of the critical period—one of the most momentous finds ever made!

"There is a period in the development of every vertebrate embryo, during which, and only then, it resembles the embryo of any other vertebrate in a corresponding phase in certain general features. But while it thus agrees exactly with any other embryo of this period in characters, which are common to all vertebrate animals it differs from the embryo of any other class in certain special class features, and also from any other embryo 9

of the same class, but of a different order in other and ordinal characters. Immediately before this period is reached it begins to put on generic and specific characters, and thus it then begins to differ from all other embryos in these." In other words, the embryo then first asserts its presence, announces its own individuality. It is then first present as a complete thing. It then first begins to use its own digestive apparatus, especially its pancreas gland, and in a higher mammal to feed itself by means of the allantoic placenta. This critical period is common to all back-boned animals in their development. At this period the average marsupial is born into the world, and then it first begins its long mammary nutrition.. In so great a hurry is it to get into the world that it forms its anus in the act of being born. The human embryo does the same at the like period, in the seventh week of gestation, as though it were a marsupial, although it has no use for this aperture for many months to come. Then the allantoic placenta—an organ of the embryo or sexual generation, like the pancreas gland—first begins to function, and then normally the trophoblast begins to function, and then normally the trophoblast begins to fade, to be suppressed, and to degenerate.

Though ferments first made their appearance in my published writings in 1892—for I pride myself on having been one of the very few pupils the late Professor C. F. W. Krukenberg ever had—it was not until 1904 that their all-important bearings upon the critical period were evident. In human gestation, if at the critical period the embryo be wanting or very abnormal (a very abnormal human embryo can only persist as one of identical twins), the phenomena of the critical period are lacking, and the normal trophoblast, which always begins its life by eroding the uterine epithelium and wall, may go on with this process, exhibit indefinite powers of growth, and eat

its way through uterus and other organs, finally blocking the lungs and brain of the mother. This is chorio-epithelioma, recognized to be a form of cancer by Professor F. Marchand in 1895. This is without doubt the most deadly form of cancer. Here the sexual generation being unable to suppress the asexual one or trophoblast, the latter exhibits the characteristics of asexual generations, the powers of indefinite growth and increase. Pathologists at present distinguish wrongly between two forms of chorio-epithelioma, a malignant one and a benign one. The latter has no real existence, for in it the trophoblast cells are all dead and undergoing the characteristic degeneration due to the action of pancreatic ferments. A "benign" chorio-epithelioma, as Professor Schmorl found, may happen in any gestation, for the trophoblast cells of the pre-critical periods, which have invaded the maternal organs—even the lungs—are normally also brought to commencing degeneration at the critical period.

In 1902 the conclusion was reached that cancer was asexual generation or irresponsible trophoblast, and in these words for the first time in human history the nature of cancer was laid bare.

Its origin was not at first so clear, but by the year 1904 it was recognized that the problems of like or identical twins, upon which the writer was then and since engaged, threw light upon its origin. Owing to their extra-embryonic origin aberrant germ-cells are quite common, and they may be met with anywhere in the embryonic body. The ordinary aberrant germ-cells, which usually degenerate, were much too abundant a source to furnish the origin of a cancer. *Entia non sunt multiplicanda*. The etiology of double monsters and of malignant tumours was traceable to the phenomena of

like twins. The facts concerning these, as well as those relating to Hermann von Jhering's finds in the armadillo (*Praopus hybridus*), which my work has fully confirmed, furnished the key. This armadillo, the "tatu," produces all its young in one chorion or trophoblast, and therefore they are all indentical, of the like sex, and all products of one egg. The whol doctrine of the tumours, benign and malignant, centres in the phenomena of like twins—that is, in a former multiplicity of embryos, all products of one egg. To-day the "tatu" (*P. hybridus*) produces seven to twelve such, all derived from a single egg, all of the like sex, and some of them more or less rudimentary!

These latter tell a very significant story* to the embryo-

*Because hypothetical, the following may find a place as a foot-note. From the consideration comparatively of a variety of embryological phenomena, well known to the investigator, it is obvious that the procedure, where only a single embryo is going to arise from one of the primary germ-cells, will not be quite the same when two or more embryos are destined to unfold. The setting apart of one cell will be preceded by one or two divisions, giving one functional cell and possibly three abortive ones. But if the development shall result in, say, triplets, there will be, not merely two division, but at least three, if not four. Of the products, which are all primary germ-cells, three will unfold as embryos, three may be abortive or rudimentary, and, if there be eight all told, two will remain as "embryonic cells," which later on, in some or other of the individuals arising, may become the seed of tumours, benign or malignant. But these cell division have a curious tendency to be in twos or pairs, or even in threes; so that in the formation of triplets, instead of eight cells, there may be sixteen concerned. How many of these will be abortive, and how many "embryonic" in potentialities, is at present impossible to say. The armadillo, *Praopus hybridus*, with its seven to twelve young in one chorion or trophoblast, affords an instance where at least sixteen cells must originally in every case have arisen at the line of primary germ-cells and in addition to those cells destined to become the sexual products. Of these sixteen cells, seven normally give rise to fully-developed embryos, five to more or less rudimentary ones, and there still remain four, which—as cancer, is not known here—may be abortive.

ologist. They recall to him other similar phenomena in embryology. Reductions in numbers of units (cells), formerly of importance, but which now persist, not because they are really required, but because their existence and persistence are parts of an old scheme of the cycle of animal life.

The writer has had abundant opportunities of noting the liability of identical twins to cancer, but to state the matter in this way is misleading. Those individuals who develop malignant growths are as liable to such as are identical twins to cancer, but to state the matter in this way is misleading. Those individuals who develop malignant growths are as liable to such as are identical twins, and for the same reasons. Without doubt cancer is hereditary. This is abundantly borne out by clinical histories in my possession. There are records where both parents died of it, where even one or other grandparent developed cancer, and it is only too commonly told the writer that in some particular case the father or the mother was a victim of cancer. The most remarkable example known to me at present is in the family of a master-carpenter in Edinburgh. His mother died of uterine cancer, and he has lost all his brothers and sisters, seven in number, by some form or other of malignant disease. Embryologically regarded, persons suffer from cancer because they are at the basis members of a group of identical twins or triplets. It is, therefore, not from any and every aberrant germ-cells that a cancer takes its start, but from one or other of some few germ-cells, embryonic in destiny, cells which should have given rise to twins, triplets, etc., identical with the embryo, which arose in any particular gestation.

footnotes continued from page 132

But if the number of young here arising at every gestation were much reduced, while all the preliminaries were retained, what a rich harvest of tumours might be the result! In a case of identical triplets, cited by Professor H. H. Wilder, at least two of the sisters died of cancer.

The line of primary germ-cells of the diagram (Fig. 5) is not made up of one only, destined to form an embryo, and of *n*-1, destined for a future generation, but it is composed of a limited number, 2 or 4 or 8, often not so many, embryonic in destiny, of which as a rule one only becomes a normal embryo, and *n*-2, or *n*-4, etc., are set apart to provide for the cycle of unicellular organisms or germ-cells. Such a persistent embryonic germ-cells, encapsulated within the individual, may at any time, by illness, injury, irritation, or other cause—such as declining years—weakening the system, be awakened into activity. The "age incidence" of cancer is scientific nonsense, for it is only relative. Whenever this happens—the time is long past when it should have unfolded as an embryo, it attempts to resume the cycle, and its "unconscious memories" only enable it to try to repeat the asexual portion of the cycle. Such an encapsulated germ-cells can only do one or other of two things in the end—and live. It may develop, and it only does this congenitally with the developing individual, or it may attempt to go on with the life-cycle—trophoblast.* In this way it becomes an irresponsible trophoblast, and it may imitate or mimic anything in its environment. Whatever it mimic—something existent or non-existent—it is always an "imitation tissue," and behind the domino or mask an irresponsible trophoblast.

In nearly all the foregoing, morphological aspects have been under consideration. It now behooves us to take account of the physiological and functional ones. The

* This is more fully shown in the Introduction (p.23) and in the later chapters.

critical period in a fish or mammal or man is that at which the embryonic organs as a whole first begin to function. The fish begins to feed itself, digesting the yolk by intestinal digestion. The mammal or human embryo begins to do the like (in the absence of food-yolk) by means of the commencing functional activities of the allantoic placenta. At this epoch in the fish the pancreas gland manifests its activities by the presence of abundant zymogen granules in the cytoplasm of its cells, That these result in the secretion of pancreatic ferments is shown by the digestion of yolk within the gut. Owing to this digestion, the fish, like the mammal, gets ever bigger and bigger. None of the yolk enters its stomach, for this has then as little functional activity as the stomach of a mammal has during fœtal life. An internal yolk-sac is formed for the reception of the yolk from the external one, and the yolk-duct opens into the duodenum. This fact alone indicates to the embryologist that the pancreas gland is functioning. In an average marsupial at the critical period this gland certainly begins its functional activities, for the animal is then born, begins its mammary nutrition, and digests the milk. If a certain thing happen at the critical period of a fish, or a marsupial, I know from experience that something corresponding to it will take place at the like period in a higher mammal or a man. A fish forms its anus at this period, so does a marsupial, while in the act of being born, and so does a man, although he does not need it for some seven months more. As the pancreas gland begins its functions in a fish or an average marsupial, so it must do in the development of a man. Otherwise there would be no essential unity in the mode of the development. Undoubtedly, under the action of the pancreatic ferments, the asexual structures of a fish development begin

to degenerate, and, as represented by the trophoblast, they do the like in a mammal or a man.

This leads to an inquiry as to modes of nutrition, regarding which the reader may find much interesting information in Verworn's "General Physiology," and still more in Otto von Fürth's "vergleichende chemische Physiologie der niederen Tiere," Jena, 1903. The unicellular organisms or protozoa, all asexual generation of animals—such as invertebrate larvæ, fish blastoderm and mammalian trophoblast, not forgetting cancer-cells—nourish themselves intracellularly and by means of a ferment acting in slightly acid medium. On the other hand, an extracellular digestion, by means or ferments, pancreatic enzymes, acting in slightly acid, neutral, or alkaline media, is restricted to the sexual generations or individuals of the higher animals (Metazoa) and man. In the former the ferment is possibly always the like one, and it would possible by, to my mind, identical with the cancer-ferment, discovered by Eugene Petry in 1899, and which I have named "malignin." The ferments of the sexual generations being much more powerful than the intracellular one found in the forms referred to above—being, indeed, the most powerful things in the whole range of organic nature—it would follow that just as these higher ferments destroy in life the living cells of malignant tumours, pulling down their albumins, so also they must destroy the organisms—usually asexual generations, of tuberculosis, sleeping-sickness, malaria, yellow fever, etc.—when injected into the blood by means of hypdermal medication.* Regarded from the strictly scientific standpoint of the embryologist, who is "Not

* Now (1911) the writer would desire to call special attention to these words, written and published more than fours years ago, but hitherto unheeded.

even a medical man," the tubercle bacillus, like the trypanosome, or the organism of yellow fever, or that of malaria, etc., can no more live in the presence of these higher ferments than the cancer-cell can. This has been shown apparently, in one case at lease, clinically and pathologically for the tubercle bacillus, by my friend Dr. Margaret A. Cleaves,* of New York City. The first case of cancer which it fell to her able brain and skilled hands to treat by means of injections of pancreatic ferments was also complicated by tuberculosis of the bowel. When, in August, 1906, the first communications passed between us, I informed Dr. Cleaves that, in my scientific opinion, whatever happened to the large masses of rectal cancer present, which appeared too great to leave room for hope of their entire removal, the tubercle bacilli would be bound to go. They disappeared, and after amylopsin had been injected for some little time the pathologists failed to find a single tubercle bacillus in the discharge, where previously they had been abundant. In our joint opinion, the result was due rather to amylopsin than to trypsin, for the former is the medium of all others in which the leucocytes can act. As in the treatment of cancer, the injection used against any of the above human inflictions should be an extract, freshly prepared from the pancreas gland direct, and containing all the ferments, especially the one in the presence of which the leucocytes act—amylopsin. †

* Cleaves, M. A." "The Physiological Action of the Pancreatic Enzymes, with Special Reference to Hematology, Urinology, and Clinical Pathology," *Medical Record*, June 1, 1907.

† Now (1911) for tuberculosis, malaria, sleeping-sickness, yellow fever, etc., I would advise the use of injections of 500 tryptic units per ampoule, plus 1,000 to 2,000 amylolytic units per amploule (*vide* Appendix F). Compare also Bätzner, Wilhelm: "Trypsinbehandlung d. Chir. Tuberculose," in *Arch. Klin, Chir*., vol. xcv., Heft 1, 1911.

Of the ferments of the sexual generations, by far the most important is that first discovered by the Court physician, Baron Corvisart, and to which afterwards Professor W. Kühne gave the name of "trypsin." It is this enormously powerful ferment, trypsin, upon which Nature relies for the suppression of trophoblast in normal mammalian gestation. Lower down in the scale than the mammals she associates with it its complement, amylopsin. Fœtal blood of a mammal does not contain this latter, and the fœtal pancreas gland does not produce it. In the human pancreas gland amylopsin is not formed until some few months after birth. The reason of this is not far to seek. When in the ancestral mammals uterine development was initiated, along with it and following its close there was evolved the mammary nutrition. In this amylopsin is not needed, and its production by the pancreas gland was postponed until the milk nutrition was done with. The mammary nutrition is (on the testimony of more than one embryologist: thus, on that of my friend J. P. Hill, as well as on my own) older in time than the allantoic placenta. The latter was introduced to defer the birth period, and by prolonging the gestation, as detailed in my "Span of Gestation," to bring the young into the world in a more perfect state. In prolonging the gestation, the mammary nutrition was postponed, and in this way the appearance of amylopsin upon the scene put off to an even later period. This has led to grave difficulties and dangers in human gestation, for there is no such thing in nature as a ferment possessing both proteolytic and amylolytic powers.*

The proper scientific treatment of cancer is the enzyme or pancreatic one. If trypsin alone be used, bad symp-

*Although *a ferment*, possessing such powers, has been advertised in medical newspapers.

toms very soon arise, all of which recall the vomiting of pregnancy and eclampsia. Trypsin alone is a very deadly remedy for cancer, the reason being that in killing the cancer albumins this enzyme does not split them up to harmless simple products. What the products of the action of trypsin alone are it is impossible to say, for they may quite conceivably vary with the amount of the injection, its strength, and with the size of the tumour. Anyway, some of them are rank poisons to the organism, and they lead to nausea, vomiting, pain in the back, drowsiness, high arterial tension, albuminuria, œdema, etc., and even to convulsions, lasting several hours. The cause of such symptoms and of the eclampsia of pregnancy did not long puzzle the embryologist, who perceived that it was the absence of the complementary ferment, amylopsin, which induced them. Nature had committed a grave error in omitting amylopsin from fœtal blood, and in relying solely on trypsin. In normal gestation, if anything went wrong with the maternal pancreas gland, and if the maternal supply of amylopsin became diminished or ceased, then serious symptoms were bound to follow. To my knowledge, at the moment of writing, injection of amylopsin have not yet been given in any case of eclampsia, but they have, whenever used in cases of cancer, removed all the bad symptoms named.

The preparations employed in the enzyme treatment of cancer should be like those first used in America—the Fairchild preparations; that is to say, they must be potent extracts, scientifically prepared from the fresh gland direct. The trypsin injection must be especially rich in trypsin. The injection of amylopsin must have great amylolytic potency, and it is also to be used at all times to meet and remove all bad symptoms, and in the later periods of treatment, when all the cancer albumin

has been destroyed It must be an extract of the pancreas gland as free as possible from trypsin. (Compare Chapter VII.)

This treatment is not intended for use against benign tumours, which are composed of real or somatic tissues, and which are not killed or broken up by trypsin. Owing to this, the injections furnish a chemical test of the true nature of a tumour, whether it be benign or malignant. Thus, some pathologists look upon adenomata as benign, or at all events as only potentially malignant. To my mind, there are "imitation tissues," and I should anticipate that any and every adenoma would yield to the chemical test.

Owing to the circumstance that the cycle of life is really a continuous procession and succession of unicellular organisms, germ-cells, from which there arise asexual generation or trophoblast, and embryo or sexual generation, the tumours can be classified into three groups, as follows:

1. *Embryomata* (benign neoplasms).—Pathological manifestations of some greater or less portion of the sexual generation—"the embryo." They are composed of real tissues—that is, normal or somatic ("embryonic") cells or tissues. At its basis each is greater or less portion of a twin, triplet, etc., identical with the individual containing it. They are not endowed with indefinite powers of growth, and they nourish themselves like other normal tissues.
2. *Amphimyxomata* (malignant neoplasms).—Combinations of embryomata and trophoblatomata. Pathological manifestations or attempts to reproduce the whole life-cycle-including trophoblast and embryo. They are transitional forms. (The mixed tumours of Wilms are not all malignant, some being merely embryomata.)
3. *Trophoblastomata*: *Cancer and Sarcoma* (malignant neoplasms).—Pathological manifestations of the asexual portion (trophoblast) of the life-cycle. They are not known to differentiate functional gametes, eggs or sperms. They never include or repeat any part of an embryo. They are never composed of somatic ("embryonic") cells, though they may mimic such, or even resemble no other cells in the body. As Fleischmann, Paget, and Bland-Sutton pointed out, they are "imitation tissues." They exhibit powers of unlimited growth and increase, and they nourish themselves by eroding and destroying normal cells and tissues in a manner exactly like that of the trophoblast of normal gestation, and by means of a ferment acting intracellularly—viz., malignin.

As the two latter divisions are made up of malignant tumours, it is for them, and not for the members of the first group, that the enzyme treatment is intended.

In the foregoing simple story I have endeavoured to the best of my ability to give in outline some idea of the course and nature of my scientific work and conclusions since the days of May-June, 188, when I worked on the shores of Black Lake, New York. Much has happened since then, not only in my own little field of work, but outside of it. It is since that time—that is, in 1889—that Hubrecht set up the name "trophoblast" to replace with a different significance the older term "chorion." Long after then came the period of my germ-cells researches, not yet completed. These have, however, extended so far that they are revolutionizing embryology. In the light they throw on phenomena, the old Wolffian idea of epigenesis, and the allied Remak-Cohnheim hypothesis of embryonic "rests" as the sources of tumours, along with many other things, become memories of the past in science. The night is far spent;

a new sun is rising. Epigenesis, somatic origin of germ-cells, and recapitulation in development, are fading away into thin air before the mighty powers of Evolution with predestination

(Weismann), an actual tangible continuity of germ-cells from generation to generation, and an antithetic alternation of generations as the mode—the only possible one—of animal development.

The suspicion entertained at Liverpoole in 1905, then expressed to two Professors of the University of Liverpool, and which is somewhat reinforced by the references to the work of Pasteur in the present chapter, that the problems of cancer had been lifted into the field of chemistry, soon showed itself to be a reality. Not only were the questions still pending chemical ones, but they belonged to a branch of chemistry with which the name of Pasteur will ever be associated as its founder—stereo-chemistry. This is more clearly revealed in the following chapter.

CHAPTER VI

THE ASYMMETRY OF THE CYCLE OF LIFE, BEING
"THE END OF THE THREAD." *

In past years every new unravelling of the thread led to new problems. But no matter how many side branches or collateral issues came up, the main course of the thread was continuous, and the observer's senses were concentrated upon it, to the exclusion of all else. Among other things the thread passed through the problems of heredity and genetic variation, the determination of sex, the continuity of germ-cells, the problems of identical twins, and by reason of these, as well as from the nature of the cycle of life, through the embryology of neoplasms, and of cancer itself. For a long time I had imagined the cancer studies to have been an interlude in the work, but no, the thread of research passed directly through the problems of cancer. And now, quite unexpectedly, the end of the thread has been reached, because portions of it had been unravelled by some of the greatest workers in science, because Louis Pasteur, one of the greatest investigators who ever lived, van't Hoff, Le Bel, and Wislicenus had lived and laboured, because their researches had founded stereo-chemistry, or chemistry, in space.

The present chapter is simply "The End of the Thread."

*From the *Medical Record.*

Like my fellow-workers, I had been taught to regard the development of any of the higher animals as "direct"; that is to say, from the fertilized egg a new sexual organism, a worm or a fish, a bird or a man, arose directly. From the tissues or soma of this sexual organism new reproductive products, eggs or sperms, sprang. In this way the simple cycle of "egg-sexual organism, egg-sexual organism" repeated itself *ad infinitum*. Under this, still generally accepted, conception of development the germ-cells were somatic in origin, and the gradual building up (epigenesis) of a new sexual organism happened directly, when such an egg had been fertilized. Such, briefly, was the simple embryological creed which my teachers, Milnes Marshall, Huxley, and Carl Semper, taught. During some eight or ten of the early years of my original work this was my embryological faith, if an investigator may have any scientific creed.

Epigenesis, direct development, and a somatic origin of germ-cells, have now long been associated with another embryological dogma, the capitulation theory, according to which any higher animal "climbs its own genealogical tree in the course of its development." To what

lengths and depths of scientific error this latter doctrine can lead, see the fifth revised of Haeckel's "Evolution of Man."

My embryological faith was perfectly orthodox when, on June 14, 1888, I left the shores of Black Lake, New York, with an extensive assortment of preserved material of fish development. One of the earliest finds made after the return to the Anatomical Institute of the University of Freiburg in Breisgau was of the existence of two distinct and separate nervous systems in the life history of the bill-fish, *Lepidosteus osseus.* About a year later the like find of a twofold nervous apparatus was

made in some other fishes and amphibians, and especially in the smooth skate, *Raja batis*.* The transient nervous apparatus of ganglion cells and nerve fibres in the skate development functioned for a time, for about three months from the start out the total of *circa* seventeen, and then quite suddenly began to fade away, and to undergo a slow but sure degeneration.

The two nervous systems crop up again and again in my published writings since 1888, and, as indicating the import long attached to this antithesis, I find myself writing in 1905 a paper, "The Cancer Problem," † opening with a recital of some of the facts in the history of the transient ganglion cells. All my original work, from 1888 down to to-day, is impregnated with facts concerning the two nervous systems, and the antithesis underlying them. The discovery of that antithesis has impelled and influenced all my work since that time.

With the termination of the period of research marked by the publication of "The Interlude of Cancer," I recognized that my original work was approaching and tending to converge to the work of Pasteur. The researches had led finally into problems of the chemistry of the ferments, and especially of the extracellular enzymes, trypsin and amylopsin. It is not too much to say that Pasteur had founded a science of the ferments. True, he laboured for many years at the problems of intracellular enzymes, such as the yeast organism, the mould, *Penicillium*, etc., and the enzymes trypsin and

*Beard, J. : "The Early Development of *Lepidosteus osseus*,." Proc. Roy. Soc. Lond., 1889, vol. xlvi., p. 108-118. *Ibid*: Ichtyopsida : An Account of the Development and Degeneration of Ganglion Cells and Nerve Fibres, Part I., *Raja batis*," *Zool. Jahrb. Morph. Abteil*., 1896,, vol. viii., pp. 1-106, 8 plates.

† *Ibid*: "The Cancer Problem," *Lancet,* February 4, 1905.

amylopsin, for a knowledge of which the world is so greatly indebted to Corvisart* and Kühne † never entered into the sphere of Pasteur's researches.

The interesting thing is, according to his own testimony, ‡ that Pasteur's work, like mine since 1888, centred in the fundamental discovery of an antithesis. Some medical men of Pasteur's day denied the truth of his conclusions, either on flimsy evidences or on none at all—just as happens to-day. Equally they sought to deny the scientific investigator the right to any opinion on a question regarded by them as medical, but which was really scientific. "What!" cried Pasteur, "I have been engaged for twenty years in research on a subject, and have no right to an opinion? And the right of verifying, controlling, discussing, and questioning belongs more especially to him who has done nothing to clear up the matter, to one who has just read more or less attentively my works with his feet on the fender! You say, my dear colleague, that in the actual state of science it is better to have no opinion. Ah, well! I, even I, have one, and no of sentiment, but of reason, for I have acquired the right by twenty years of assiduous work. My

opinion, or better, my conviction is, that in the actual state of science of which you speak spontaneous generation, is a chimæra, for my experiences are complete, and they all prove that spontaneous generation *is* a chimæra. As to my opponents, proof in hand I have contradicted every one of their assertions, and they have never dared

*Corvisart, Lucien: "Sur une Fonction peu connue du Pancreas," Paris, 1857,58, pp. 1-123.

† Kühne, Wilhelm: "Ueber das Verhalten verschiedener organisirter und sog. Ungeformter Fermente," and "Über das Trypsin (Enzym des Pandreas)," *Verhandl. Des. Heidelb. Naturhist. Med. Vereins*. N. s., I., No. 3, 1876, pp. 1-10.

‡ Vallery-Radot, René: "La Vie de Pasteur," Paris, 1901.

seriously contradict one of mine." In passing, be it remarked that every work=d of this passage might be applied to happenings at the present time regarding the problems of cancer. Then Pasteur explained how the whole series of his marvellous discoveries, chemical, bacteriological, or medical, hung together and formed a complete chain—*e.g*., anthrax, the pure fermentation of beer, the acetification of vinegar, the diseases of vines, the means of preventing them, and, lastly, going back seventeen years, the first link in the chain of discoveries, that of the double tartrate crystals, and the facts concerning their dimorphism.* "The best proof that an observer is right is the uninterrupted fruitfulness of his work." †

Pasteur worked for seventeen years at his chain of discoveries; it was in 1907 nineteen years since the first link of my chain was forged. The thread each of us obtained at the start was the discovery of the antithesis of two things: he, the two kinds of tartrate crystals; I, the two distinct and separate nervous systems in the life-cycle of a fish.

Why should all this be? What connection was there between the two facts, which, apparently, were as wide apart as the poles? The evident fact has already been referred to, that in 1904 the two independent lines of work were converging, but it was more than this. It was a union. The thing which impelled Pasteur's work incited mine also. The antithesis he discovered was in

*Pasteur, Louis: "De la Dissymmétrie Moléculaire des Produits Organiques Naturels." Lecom professée devant la Société Chimique, 1860.

† This chain-like character of Pasteur's researches has been commented upon by others—thus by Miall ("History of Biology," 1911)—but I doubt whether any of the commentators have grasped the true significance of Pasteur's meaning.

reality that also found by me. The asymmetry of the naturally occurring organic compounds, like that of the tartrate crystals, was the same asymmetry as that of the two nervous systems, and the facts of both observers were based in the fundamental verity of the asymmetrical carbon atom, first stated by van'g Hoff and Le Bel.* Therefore, the researches and discoveries of Pasteur and the writer, as fundamentally classified, are chapters, long or short, in the science of stereo-chemistry. Behind the work, which culminated in and formed the real scientific basis for my publication on "The Interlude of Cancer," there are the researches in stereo-chemistry of Pasteur, van't Hoff, Le Bel, and Wislicenus, and the eternal truth of the asymmetrical carbon atom.

It is not fitting on this occasion to write a treatise on the science of stereo-chemistry or chemistry in space. It has long been recognized by chemists—though this fundamental scientific truth would appear to have had as little influence on physiology as upon medicine—that because

the carbon atom is asymmetrical, like the pentavalent nitrogen one, † isomeric compounds may be built up in more than one direction. To take a comparatively simple instance of these isomeric compounds, the tartrate crystals of Pasteur's researches, the one is the looking-glass image in crystalline form of the other. The one in solution turns the plane of polarized light to the right, is dextro-rotatory; the other to the left, is lævo-rotatory. The ferment of the yeast organism acts upon the lævo-tartrate; that of the mould, *Penicillium*, upon the dextro-tartrate. On the other hand, the yeast

*Richardson, G. M.: "The Foundations of Stereo-Chemistry" Memoirs by Pasteur, van't Hoff, Le Bel, and Wislicenus. Translated and edited. New York, 1901.

† Wedekind, Edgar: "Zur Stereochemie des füunfwertigen Stickstoffes," Leipzig, 1890.

organism is without action on the dextro-tartrate; the *Penicillium* leaves the lævo-tartrate untouched. This, as Pasteur demonstrated, is one method of separating the two in a mixture. Now, it is a remarkable fact that when any of these isomeric compounds are manufactured in the laboratory, equal amount of the dextro- and of the lævo- compounds make their appearance in the mixture. Pasteur first noted the fact that all the artificial products of the laboratories and all the sorts of minerals encountered in nature are without action on polarized light, unlike all the naturally occurring organic compounds. This has only altered since 1860, according to Duclaux, in that, while chemists can manufacture certain of these compounds in mixtures of equal amounts of the isomers, they can also be separated by the action of ferments, which are specific in this direction. For other alterations see the works of Pope and van't Hoff.* In the two lectures Pasteur demonstrated that the naturally occurring organic compounds rotate the plane of polarized light to the right or to the left, and in this way are dextro- or lævo- rotatory. As Duclaux writes, "Nature alone knows how to manufacture the one isomer without producing the other." "A living cell is a laboratory of dissymmetrical forces, or a dissymmetrical protoplasm, acting under the influence of the sun."

In his "Chemical Statics and Dynamics," Dr. J. W. Mellor † writes as follows: "It is interesting to observe that only the dextro-sugars occur in Nature(?), and that these are the only sugars which can be assimilated as foodstuffs by the yeast-plant. No organism capable of

*van't Hoff, J. H.: "Stereo-Chemie nach van't Hoff's Dix Années dans l'Histoire d'une Theorie, neu bearbeitet von W. Meyerhoffer," 1892.

† Mellor, J. W. : "Chemical Statics and Dynamics," London, 1904.

digesting artificially synthesized lævo-sugars is known." He then quotes from Professor W. J. Pope.* "It would seem to follow, as a legitimate conclusion, that while *d*-glucose is a valuable foodstuff, we should be incapable of digesting its enantiomorphously related isomeride *l*-glucose. Humanity is, therefore, composed of dextro-men and dextro-women. And just as we ourselves would probably starve if provided with food enantiomorphously related to that to which we are accustomed, so, if our enantiomorphously related isomerides, the lævo-men, were to come among us now, at a time when we have not yet succeeded in preparing synthetically the more important foodstuffs, we should be unable to provide them with the food necessary to keep them alive." The term "enantiomorphism," to describe the properties of the isomeric compounds, was coined by Pasteur.

In Richardson's translation of "Pasteur's two lectures one may read (p. 27): "Perhaps this will disclose a new world to us. Who can foresee the organization that living matter would

assume, if cellulose were lævo-rotatory instead of being dextro-rotatory, or if the lævo-rotatory albumins of the blood were to be replaced by dextro-rotatory bodies?" With the exception of this passage, the citation from Professor Pope is the sole chemical one I have encountered, in which the possible existence of an antithetic generation is indicated. One may put his words differently, that in order to exist the "lævo-men" would need to be able, by means of ferments, to pull down all our food substances and to rebuild in the opposite, or enantiomorphously related, or antithetic direction. As will appear presently, unfortunately, the hypothetical "lævo-men" do exist

*Pope, William J.: "Recent Advances in Stereo-Chemistry," *Nature*, 1903, vol. lxviii., pp. 280-283.

among us, and they do pull down and build up again in the opposite direction, for the "lævo-men" are the cancers.

In the light of the antithetic alternation of generations and of the natural antithesis of the compounds arising in the two generations, the following passage from Professor Pope's address (p. 283) is of interest. It is also instructive, because of the generally accepted but false views of the question: "Again, suppose that at its origin life were carried on non-enantiomorphously, and that it involved the consumption and the production only of non-enantiomorphous substances and of compensated mixtures, it may well be foreseen that a stage in development might arise when each individual, in view of the increasing complexity of his vital processes, would have to decide to use only the one enantiomorphous component of his compensated food, and so evade an otherwise necessary duplication of his digestive apparatus. Acting intelligently or fortuitously, one half of the individuals would become dextro-beings, while the other halve would become lævo-individuals; the succeeding generations would thus be of two enantiomorphously related configuarations." He then goes on to express his own opinion that in course of time one configuration, the weaker one, would disappear permanently. But in this opinion the facts of botanical and embryological science are not taken into account. It is, however, only necessary to make the "succeeding generations," spoken of, alternate in order to meet the scientific requirements of Nature, and so to make the passage absolutely true as a statement of scientific fact. This is done by inserting in the closing passage the word "alternating," when it would read: "the succeeding generations alternating would thus be of two enantiomorphously related configurations."

Pasteur did, indeed, foresee that in his finds there was given the basis of a science of comparative physiology. It is sad to reflect that in 1860 he wrote as follows, and that in all the intervening years his weighty words have been ignored by physiologists and physicians alike: "I have, in fact, set up a theory of molecular asymmetry, one of the most important and wholly surprising chapters of science, which opens up a new, distant, but definite horizon, for physiology." Before the present writing was penned, this horizon for physiology seemed as distant as in 1860, for as a general rule the facts concerning the asymmetrical carbon atom and the naturally occurring organic compounds find no mention in current textbooks of modern physiology.

"Who can foresee the organization that living matter would assume, if cellulose were lævo-rotatory, instead of being dextro-rotatory?" Pasteur was a" a mere chemist," and "not evena a medical man." He was not a biologist, though most of his researches were biological, and he was not an embryologist. Had he been well versed in the biology of his own day, the suggestion

of a hypothetical lævo-cellulose might have opened up an immense field to his further researches. At the time he wrote, Hofmeister's researches* on the life-histories of various plants, with the main facts concerning the alternation of generations therein observed, were already the possession of science. † If there be a dextro-

*Hofmeister, Wilhelm: "Vergleichende Untersuchungen," 1850.

† In his "History of Botany" the late Professor Julius von Sachs writes in terms of eloquence and amiration of Hofmeister's researches: "The result of these 'Comparative Investigations, 1851,' was of such grandeur as in the realm of descriptive botany has not since happened a second time." He speaks of "the brilliance of the grand sum total, 'alternation of generations' had proved itself to be the highest law of development in plants,

cellulose, or a lævo-albumin, or a dextro-sugar, or a dextro-glycogen, stereo-chemistry asserts the possibility, or the necessity, of the occurrence of a lævo-cellulose, a dextro-albumin, a lævo-sugar, a lævo-glycogen. This the reader will find laid down on p. 14 of Meyerhoffer's German translation of van't Hoff's work. Duclaux* rightly observes that to obtain the change from the on direction of asymmetry to the other, it is necessary to back to the "germ." Like the cellulose of a flowering plant, a rose or an oak-tree, that of the fern-plant is dextro-cellulose. But in the life-cycle of the fern, as in that of the flowering plant, there are two generations, the asexual one, or fern-plant, and the sexual one, the small and insignificant prothallus. As the cellulose of the fern is dextro-cellulose, so that of the latter must be lævo-cellulose, and so with the other naturally occurring organic compounds. None such found naturally in an asexual generation of a plant, or in a sexual generation of an animal, will be met with in the corresponding sexual generation of a plant or asexual generation of an animal; but, it occurring at all, it will be represented by a compound with the opposite rotation. The reason is because (like the pentavalent nitrogen one) there is an asymmetrical carbon atom.

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governing the whole long series." He dilates on "the grand picture which Hofmeister had drawn up of the genetic connections of the members of the Plant Kingdom." What the zoologists wee to experience fifty years later—viz., an antithetic alternation of generations in animals as *the law* of their developmental cycles, was unravelled for plants by Wilhelm Hofmeister, nine years before Pasteur gave the two lectures "On the Asymmetry of the Naturally Occurring organic Compounds," and before he uttered the prophetic words, "Who can foresee the organization that living matter would assume, if cellulose were lævo-rotatory instead of being dextro-rotatory?"

*Duclaux, E.: "Pasteur, Histoire d'un Espirit," Paris, 1896, pp. I-vii and 1-393.

The cycle of life, animal or vegetable, is asymmetrical, because the antithetic alternation of generations underlying it is founded on the asymmetry of these atoms. The generations, sexual or asexual, alternate according as the compounds are built up in the one direction or the other, for at its basis development is the building-up of naturally occurring compounds. In both animals and plants enzymes or ferments are the chief actors in this. The new organism, whether animal or plant, destroys that upon which it arose, and builds up in the opposite direction. The birth of the new fern-plant implies the destruction of the prothallus. The embryo or sexual generation of a mammal, or a man, destroys the asexual generation, the trophoblast, or chorion, upon which it arose, and builds up its compounds in the opposite direction to that employed by the latter. So also the cancer. This irresponsible trophoblast or asexual generation destroys the naturally

occurring organic compounds and the sexual organism upon which it arose, and builds up in the opposite direction.

The action of a ferment is always a specific one. It fits the substance upon which it acts, "as a key fits a lock" (Emil Fischer). Other substances it leaves untouched, even isomeric compounds having an opposite rotation. As Dr. Margaret A. Cleaves* wrote in the *Medical Record* of June 1, 2907: "It is probably that enzymes are of stereo-chemical configuration in their construction; that is, that they are built upon a central element having a definite valence, and hence, that all enzymes are capable of entering into chemical action

*Cleaves, M. A.: "The Physiological Action of the Pancreatic Enzymes, with Special Reference to Hematology, Urinology, and Clinical Pathology," *Medical Record*, June, 1, 1907, New York.

with only those substances that attract and have an opposite isomeric form." Confining one's attention to cancer, the cancer-ferment malignin acts upon and pulls down the lævo-albumins of the living human body. As I have stated with von Leyden,* Blumenthal, † and Bergell, ‡ and more recently this was confirmed by Neuberg and Ascher, the action of trypsin on the living albumin of cancer is specific. Quoting further from Dr. Cleaves, "The only possible explanation of the effect of trypsin on pathological conditions capable of giving a tryptic reaction must be that certain proteid molecules—*e.g.*., in cancerous conditions—are capable of being attacked by trypsin, because of their special configuration." In other words, the conclusion (foreseen by Dr. Cleaves also) may be drawn, that the albumin or albumins of cancer are dextro-rotatory. All this has been denied, without evidences beyond bald assertion, by various "authorities," official researchers and medical journalists. As the lævo-albumins of the healthy living human body are not acted upon by trypsin, whereas the albumins of a living cancer are, it follows, as day succeeds night, that the latter must be dextro-albumins. No amount of contradiction in official reports, or in medical newspapers, can ever alter the truth of this fact, for "all enzymes are capable of entering into chemical action with only those substances which attract and have the opposite isomeric form."

Much has been written about glycogen in tumours.

*Leycen, E. von, and Bergell, P.: "Ueber die Therapeutische Anwendung von Pancreatin in Carcinoma," *Zeitschr. F. klin. Med.*., 1907, vol. lxi., pp. 360-365.

† Blumenthal, V.: "Die Chemische Abartung der Zellen beim Kreb," *Zeitschr. F. Krebsforschung*, 1907, vol. v., pp. 182-189; "Die Chemische Vorgänge bei der Krebskrankheit," *Ergbn. D. Exper. Path. U. Therap.,* 1907, vol. i., pp. 65-104.

‡ Bergell, P.: "Zur Chemie der Krebsgeschwülste," *Zeitschr. F. Krebsforschung*, 1907, vol. v., pp. 204-208.

Brault thought that the malignancy of a tumour varied directly as its richness in glycogen. Another medical man, impressed with this view, sought some substance which would "break up" this glycogen of a tumour, and hit upon trypsin. But the curious thing is that not only, of course, has trypsin no action upon the glycogen of a cancer, but the like is true of amylopsin. The latter at once converts the dextro-glycogen of the liver, but as Dr. Cleaves has shown in her paper already cited, amylopsin has no action upon the glycogen occurring naturally in a cancer. The reason is because the latter glycogen is a lævo-one. The interpretation to be placed upon the leucocytic phenomena of the Cleaves "trypto-glycogenic reaction" (the enormous increase of the

eosinophile leucocytes under the enzyme treatment of cancer and their attraction by the glycogen of the tumour) is that amylopsin leaves the glycogen of a cancer untouched, but that it stimulates the leucocytes to seize it and to invert it. Just as isomeric compounds in the form of starches occur in both generations of plants, so also isomeric compounds of glycogen or animal starch are found in sexual and asexual generations of animals, including cancer. But, if the dextro-compound occur naturally in the one generation, the lævo-sugar in "the allantois." According to him, (p. 398) it disappears towards the fifth or sixth month of

*Bernard, Claude: "Lecon de Physiologie Expérimental,' Paris, 1855, vol. i.

intra-uterine life of the calf, a fact which goes to show the lævo-sugar to be formed in the trophoblast, and not in the allantois. Doubtless, its disappearance coincides with the development of large numbers of leucocytes in the fœtus. To my knowledge this lævo-sugar has more recently been rediscovered " in the placenta," but I am not aware that the fact has been republished. Of course, the "allantois" and the "placenta" are synonymous, but the real source of the lævulose in both instances was asexual generation or trophoblast.

The asymmetrical carbon atom, like its colleague, the pentavalent nitrogen one, has hitherto found as little place or mention in medicine or in physiology as has an antithetic alternation of generations. Man has thus found it possible to dispense with things and phenomena indispensable to Nature, and but for which he would have no existence! Whatever matter may be, whatever the nature of what we term "living matter," at the basis of life lie the fundamental facts of the asymmetrical carbon atom and the isomeric compounds. At the base of all animal or plant life, too, because of these facts, there rests the antithetic alternation of generations. With the start of the asexual or the sexual phase of the cycle, the naturally occurring compounds are built up in the one direction or in the other. With the beginning of the next phase of the cycle, the alternate one, sexual or asexual, the swing of the pendulum about the asymmetrical carbon atom is on the other side, and the naturally occurring organic compounds are built up in the opposite direction. In animal life, that of the higher animals, the compounds are built up after the fertilization of the egg, and in the life-period of the asexual generation in the direction of lævo-sugar, lævo-glycogen, and dextro albumins. This evolution of compounds is the antithesis

of that which obtains with the unfolding of the sexual generation, "the embryo" or individual. Here the naturally occurring organic compounds are evolved in the direction of dextro-sugars, dextro-glycogen, and lævo-albumins. It is of great interest to compare together animals and plants in this connection. As I wrote some years ago; "the plan carried out in animals has been such as to favour the ever greater and greater amplification of the sexual generation. In plants, as elsewhere already insisted, the reverse is the case. Here the asexual generation has undergone increased amplification without ever being able to attain to any very high degree of histological differentiation. The sexual generation of plants is at the best a miserable failure from the morphological point of view, and this must be set down to the factors indicated, and still more to others yet to be described. The higher one ascends, the smaller it becomes, until, in the highest flowering plants, it has almost reached the vanishing point, without, however, being able to disappear entirely. In animals it is the phorozoon or asexual generation which makes the bravest show in the lower metazoa; but even here it is usually overshadowed in degree of morphological differentiation by the embryo or sexual generation. In the higher forms it becomes reduced; but, like the rudimentary sexual generation of the higher plants, it cannot vanish, for it also has its

assigned task in the reproductive round." The scientific investigator does not, of course, deal in *a priori* agruments. Were he to do so, he would expect to find the condition exactly the same in plants as in animals. For is it not "generally held," and for this reason scientifically correct, that animals and plants have a common ancestry? Do not zoologists and botanists agree that at the bottom of the scale animals

and plants merge together, and that some of the lower organisms may be described equally well as animals or as plants? The scientific truth of the matter is that there is no merging together of the two kingdoms. Such a blending is impossible, because of the asymmetrical carbon atom. None the less, the asymmetrical carbon atom vouches the unity of organic nature.

It is clear that, if in any group of organisms, animals, plants, bacteria, fungi, etc., there be two phases of the life-cycle, asexual and sexual, there are for any given case two directions in which the naturally occurring organic compounds can be built up. But it should not be forgotten that the number of possible isomeric compounds increases with their complexity. The sexual generation of animals is characterized by dextro-sugars, dextro-glycogen, and lævo-albumins. In the corresponding sexual generation of plants, such as the fern prothallus, these are absent, being replaced by enantiomorphous compounds with the opposite rotations. It is the asexual generation of plants, the flowering plant, and not the sexual generation, which possess dextro-sugar, destro-starch, and lævo-albumins. The harmony of this is twofold. It realizes the apparent possibilities, and from the point of view of animal life it is of overwhelming important that it should be so. Ultimately, of course, all animals are dependent on plants for their foodstuffs. Were the sexual generations of plants the producers of the foodstuffs of animals, the latter, owing to the insignificance of the former, would find existence a very serious problem. The sexual generations of plants form substances resembling those fabricated by the asexual generations of animals, trophoblast, or cancer. Even if obtainable in sufficiently large quantities, the substances found naturally in a cancer would not be suitable as the

foodstuffs of an animal—a man, for example. But, as the asexual mode of reproduction, whether of a plant or of a cancer, is the more prolific one, there has been, hitherto at all events, no failure of the part of the asexual generation of plants to furnish ultimately the foodstuffs of animals. The conditions met with in animals are reversed in plants. Here a lævo-cellulose, a lævo-sugar, a lævo-starch, and one or more dextro-albumins must be sought for, not in the asexual generation as in animals, but in the sexual one, as represented by, for example, the fern prothallus. "Science is prevision," said Pasteur. Because of the truth of this one is able to set up the following table of comparisons:

Animal.

Sexual generation or individual.	Asexual generation, trophoblast or cancer
Lævo-albumins, not acted upon when living by trypsin and amylopsin, but attacked in life and pulled down by the cancer-ferment, malignin.	Dextro-albumins, not acted upon when living by their own intracellular ferment, malignin, but attacked in life by trypsin and amylopsin.
Dextro-sugars.	Lævo- sugar.
Dextro-glycogen.	Lævo-glycogen.
Pigment melanin.	Pigment not melanin (in melanosarcoma),

Blumenthal.

Plant.

Asexual generation (flowering plant or fern).	Sexual generation (fern prothallus).
	Dextro-albumin.
Lævo-albumins.	Lævo-starch.
Dextro-starch.	Lævo-sugars.
Dextro-sugars.	

It would be interesting, were sufficient information available, to inquire into the conditions met with in bacteria and fungi. These are fundamentally neither animals nor plants. So far as the facts are known regarding their compounds and their ferments, some of them

seem to resemble the asexual generation of animals, rather than that of plants. In given circumstances many of them can attack the living compounds of the sexual generations of animals, or of the asexual generations of plants, pulling them down and building up in an opposite direction. As the plants and the animals are not genetically connected, so also, in all probability, the bacteria and the fungi have no genetic relationships with each other, or with the animals or the plants. Like the two latter, they are separate evolutions.

In 1889, in his study of the placentation of the hedgehog, *Erinaceus europæus,* Professor A. A. W. Hubrecht* set up the term "trophoblast" (p. 298), at the same time assigning to it, as the name implies, a nutritive significance. The nutritive import of the trophoblast of normal mammalian gestation has since that time been confirmed by many other embryologists, notably by Professor E. van Beneden and M. Duval, and it has been "generally accepted." In the light of our present knowledge, a significance different from that seen in it by Professor Hubrecht must be recognized in "trophoblast." Trophoblast has, and can have, no nutritive import for the developing embryo. This is quite obvious, once it is noted that the natural compounds formed in it are built up in the wrong direction to be useful as food for the developing sexual organism. The term, therefore, cannot be employed in future in a physiological sense. As Duclaux said: "Nature alone knows how to manufacture the one isomer without producing the other." The chemist in the laboratory manufactures equal amounts of both isomers. May one deny Nature the power to do the like

*Hubrecht, A. A. W.: "The Placentation of *Erinaceus europæus," Quart. Journ. Micros. Sci.,* 1889, vol. xxx., pp. 283-404, 13 plates.

on occasion? Certainly not. It must be concluded, that in the fertilized egg she can build up in both directions. By the first few cleavages of the egg—usually the first three to five—she can separate off portions as cells, endowed solely with the powers of producing the isomeric compounds of trophoblast, while retaining for the cell in the line of heredity the property of forming both. With the start of the evolution of an embryonic body, again by cell-division, she can separate off one or more original embryonic cells with powers the opposites of those possessed by trophoblast, all this taking place before any extra-cellular enzymes, such as trypsin and amylopsin, are formed. Full agreement, therefore (in a sense), may be expressed with the conclusion of Duclaux, that "to introduce in a cell principles immediately different, and the inverse of those which existed there, it is necessary to act upon it at the moment when it is most

plastic, to take the cell of the germ and try to modify it" (p. 66). But, as Duclaux also observes, this cell has an heredity, and this determines not only its being, but what it shall become.

As may be gathered from the foregoing, the enzyme treatment of cancer professes to be, as is, a scientific one. Mankind in general, and surgeons in particular, have long looked for a cure for cancer. Presumably, this was to replace the knife. Now, at last, science and scientific research have offered not a cure, but the scientific treatment of and *the cure* of cancer. At once the surgical demand was altered into the request for a cure after the fact of operation on the living cancer. Scientifically, this demand cannot be met. Cancer is a natural phenomenon, not a disease. To "operate" upon living asexual generation is unnatural. As a scientific remedy, the enzyme treatment of cancer makes no claim to be the cure for cancer after it has been interfered with opera-

tively once or oftener. As a natural treatment, it is not intended for post-operative "inoperable" recurrent cases. Did surgeons know that cancer was in its nature asexual generation, they would never touch a living cancer with the knife. For it is the property of asexual generation, animal or vegetable, that it can be subdivided indefinitely. In evidence of this fact one need only refer to all the inoculations of cancer which, starting from one original mouse-tumour, have been made into other mice. But on may also cite the very numerous observations made in recent years in what has been termed "experimental embryology," but which would be designated more correctly "experimental pathology." Very numerous observations in this unnatural subject will be found in the many volumes of the *Archiv für Entwicklungsmechanik,* in the *Journal of Experimental Zoology,* and elsewhere. Many of the observations were made upon fertilized eggs in cleavage, and the experiments were almost as successful in subdividing the asexual generation represented by an egg in cleavage as are the gardener's proceedings in making and rooting cuttings from a chrysanthemum plant. The student of all these published experiments will notice, that the organisms experimented upon never reverted to the normal. These experiments proclaim the truth of the statement, that by operation a living cancer may be, and usually is, subdivided indefinitely. Moreover, let the words of the late Professor of Medicine in the University of Berlin, E. von Leyden, be recalled: A cancer reacts by increased growth to any injury, mechanical, chemical, or thermal." As a rule, not free from exceptions, in my experience, while absolutely unoperated cases, if not too advanced, invariably do well under the treatment, cases where there was previously operative interference cannot be guaranteed, and by me are not endorsed as likely to

be successful. Nature does not "operate" upon living asexual generation, and perhaps for this reason she has not evolved an infallible mode of treating scientifically the failures of surgical operation. Dr. Rice's case* of laryngeal cancer may be cited as an instance of the successful treatment of an unoperated tumour, as also the Naples case of inoperable cancer of the tongue. † Within the past few days (1907) another case of the like kind has been reported privately as cured. Here, in October, 1906, on operation a leading London surgeon found an inoperable cancer of the cæcum. ‡ He made no attempt to remove it. In December the enzyme treatment was commenced, and continued until April, when on examination this surgeon pronounced it "almost a cure." Now, in August, the cancer has quite disappeared. This unreported case is paralleled by one in the *British Medical Journal* of August 31, 1907, p. 541. The like history is true of many other cases. But with post-operative recurrent cases, while there may be success, as

in Dr. Wiggin's case, § since certified as cured, the cancer is more likely to "run its parabola" than to yield to a scientific treatment.

When official researchers are heard proclaiming to mankind that the enzymes, trypsin and amylopsin, have no action upon living cancer-cells, this is not merely a denial of the truth and validity of all my embryological work of the past nineteen years. (That is nothing new.

*Rice, Clarence C.: "Treatment of Cancer of the Larynx by Subcutaneous Injection of pancreatic Extract (Trypsin)," *Medical Record*, November 24, 1906, pp. 812-816, New York.

† Beard, J.: "The Scientific Criterion of a Malignant Tumour," *Medical Record*, January 5, 1907, New York. See also Appendix D.

‡ See Appendix G, No. 3.

§ Wiggin, F. H.: "Case of Multiple Fibro-Sarcoma of the Tongue," *Journ. Amer. Med. Assoc.,* December 15, 1906. Pp. 2003-2008.

Were it to-day a new scientific discovery that "two and two make four," its truth would be challenged!) But by such negations the fundamental truths of the science of stereo-chemistry are also impugned, as well as the asymmetrical carbon atom. In short, when the efficacy of the enzyme treatment of cancer is question or denied, the constitution of the visible universe is condemned.

"Sooner or later a conviction may dawn upon investigators that the laws governing animal development lie deep, and that to discover them we must also take wider and more comprehensive views of our problems. Moreover, it should not be forgotten that little things, like a few stray ganglion cells, may hide an all-important story, and that here, as elsewhere, in the apparent exception itself the key to the mystery often lies concealed."

PART 11
THE PANCREATIC OR ENZYME TREATMENT OF CANCER

RETROSPECT

About three years ago a medical correspondent in New York suggested to the writer that in a year or two he would perhaps review the history of the enzyme or pancreatic treatment of cancer during the years from 1906, pointing out the mistakes he and others had made, and withdrawing those things in his scientific conclusion which had not stood the test of time and experiment. The reply then made was: "When that time comes, I shall have nothing to retract." This is true to-day, and nothing in the first "Scientific Report"* issued by the New York Skin and Cancer Hospital alters its truth in the least. When, in 1903, the writer laid aside other scientific work on the germ-cells, heredity and variation, he was well aware that the impending campaign would be a deadly one, and that if victory did—as scientifically it must—result, the field of conflict would be as thickly strew with the victims of cancer as any of the bloodiest battle-grounds of human history. Six years ago, when,

*Bainbridge, William Seaman, A.M., Sc.D., M.D.: "The Enzyme Treatment for Cancer" (Scientific Report on Investigations with Reference to the Treatment of Cancer, No. 1, 1909, New York, pp. 1-34.

on January 20, 1905, in a public lecture in Liverpool, "the secretion of that important digestive gland, the pancreas," was clearly indicated as the scientific means of routing cancer, nothing at all was known as to doses and strengths of pancreatic injections, or even as to the proper modes of making up potent and keeping solutions of trypsin and amylopsin. Failures galore must have resulted, even if medical men had given the treatment to their best, instead of to their very worst, cases—as a rule, to advanced inoperable, or to post-operative recurrent inoperable, cases. There have, indeed, been many failures, even without the list published by Dr. Bainbridge, but—there have also been some successes. In the face of any successes, of Dr. Bainbridge's own words (p. 32), "That *injecto trypsini*, in some cases, seems to cause more rapid disintegration of" (to 'liquefy' according to Beard) "cancerous tissue," and "that *injectio amylopsini* seems to diminish cachexia in some cases, in accordance with the claims of Beard and other," of what value are the failure—what do they prove in science? There are few—indeed, there are no—scientific discoveries of import to man which escape the like fate, if others attempt to confirm them, or if, and more usually (such is human nature), others seek to refute them. To take an instance suggested by a medical friend with reference to this report, how many of those, who in one way or another, with weak or with inert injections, or with minimal doses, or single injections, or with none at all, have sought to test my conclusions, could confirm the scientific researches of Starling on secretin? *Not one*! From some knowledge of the history of science, and of the receptions accorded by mankind to many scientific discoveries of import to the human race, and from a close knowledge and experience of the medical profession

--for have not several thousand medical men now in practice passed through my hands as pupils?--what else could be expected, than that witha very little knowledge, or with none at all, adverse verdicts should be pronounced upon the thing without any delay to examine the scientific evidences?

So little scientific care is, as a rule, bestowed upon the publication of the results of the enzyme treatment that, notwithstanding the publication of semi-polar accounts of my work in the *Lancet* and the *Medical Record*, I never yet read an accurate description* of the scientific basis of the matter from a medical pen in the pages of any medical newspaper. Most of the medical writers appeared not even to know what trophoblast was. It would be an easy, not to add an instructive, task to show that my work on the germinal origin and trophoblastic nature of cancer, with all its consequences (trypsin and amylopsin), differed in no way in the reception it encountered at the hands of the medical profession from previous discoveries recorded in the history of medicine. Have the names and labours of Pasteur, Lister, Morton, and Corvisart—to name but a few—been forgotten?

Scientific objections, which might have been raised, but which were never produced until it was too late, have been noted by others. Here I will add anew one. According to my finds, in any normal human gestation, Nature only allows the equivalent of cancer—trophoblast—to grow for a little less than seven weeks before she introduces the suppressing and destroying ferment or ferments. This is a point which should be borne in mine,

*There is one surgical exception to this. In the Appendix of his book, "The Control of a Scourge" (pp. 293 *et seq*.), Mr. C. P. Childe, B.A., F.R.C.S., gives a correct scientific account of the "pre-embryonic or trophoblastic theory" of cancer.

but which hitherto has usually been ignored, in attempting to remove by ferments an "inoperable," usually recurrent cancer of two years' or more standing, or in a laboratory vainly trying, aided by weak, or even inert, ferments, to cure a moust of a tumour "about as big as itself." The processes employed by Nature in destroying asexual generation (trophoblast) are probably, like so many of her methods, self-regulating, and in view of this one might not be so sanguine of imitating her successfully, had not undoubted success been obtained.

More than once official cancer researchers have publicly described the pancreatic ferments, usually through other spokesmen, as devoid of action upon living cancer-cells, but in not one of the three "Scientific Reports" of the Imperial Cancer Research Fund are any evidences at all for this untrue assertion to be found. The photographs contained in this book, as well as the evidences concerning the liquefaction of cancer, amply refute this false and erroneous conclusion. Of course, the probability—nay, certainty—is that inert ferment-jpreparations had been employed in the unpublished experiments relied upon. Such official researchers may be asked to note that I have never urged the use of inert ferments in cancer, and have never supposed that such would have any action upon cancer-cells—or upon any proteid or other substance whatever, for that matter.

Four years ago a medical correspondent, Captain in the Indian Medical Service, wrote from Bushire, making the pertinent remark: "It is a pity that your opponents do not try to meet your 'facts,' instead of taking their stand upon their 'opinions,'" The reply to this was not difficult to find. As Dr. Bainbridge sagely remarks on p. 4 of his "Scientific Report": "The irresponsible trophoblast does not concern us here." The reasons

and evidences for my conclusions as to the nature of cancer and its treatment on natural or scientific lines were beyond them. "Was der Bauer nit kennt, das frisst er nit." What the leader-writer or ex-cancer researcher never learnt, that he is not likely to try and refute. Even "mecial science" would tilt in vain against the organization of the visible universe, though it has often made the essay, as witness Pasteur's experiences.

In his essay "on Liberty," which as a weighty, scientific document may be recommended to the attion of those who write on and of "medical science," John Stuart Mill says: "The dictum that truth always triumphs over persecution is one of those pleasant falsehoods which men repeat after one another till they pass into commonplaces, but which all experience refutes."

The passage cited was laid down by Mill in 1878, and possibly human nature has changed since then. The reader will note that all experience refutes the dictum. Medicine, which includes, or should include, the applications of certain sciences to human needs, has its own history in this respect. It is much simpler, and requires infinitely less knowledge, a modicum of crass ignorance often sufficing, to stifle a truth in its birth than to refute it on scientific grounds. To attempt to do the latter, moreover, entails the observance of certain canons of science, one of these being that no assertion shall be made without the production of the evidences. This is, perhaps, the real reason why the evidences for the asexual (trophoblastic) nature of cancer, etc., have never been attacked on scientific grounds.

The numerous "negative results" obtained by Dr. Bainbridge and by many other medical men are not scientific evidences against the truth of my conclusions.

They only prove that in certain cases, where as a rule the pancreatic ferments were administered as an alternative to the Last Sacrament, these ferments, as there exhibited, did not cure cancer, in the New York Skin and Cancer Hospital; though on the testimony of others they did cure it in Naples, in York and in other places.

On reading the thirty theses, advanced as conclusions, mostly without the evidences, by Dr. Bainbridge, I am reminded of another phase of this cancer problem. Some years ago two graduates of Edinburgh decided to test the asexual (trophoblastic) nature and the germinal origin of cancer in a crucial fashion, by transplanting living ovaries and living trophoblast into other individuals (rabbits) of the same species. At that time I was wont to discuss these cancer problems with a scientific man, a human anatomist, since deceased. Occasion was taken to describe the results of these "crucial experiments." "They published no details of the experiments," I said, "so that it was not possible to inquire into the reasons for the failures; but they concluded that, because trophoblast and ovary were not transplanted successfully and brought to grow in a new individual of the species, therefore, cancer was not germinal in origin or trophoblastic in nature." The words were hardly uttered when my departed friend, the professor anatomy, sprang up. "No, no!" he cried, "that will not do. A negative result of that sort never proves anything in science."* It remains to add that a few years later living ovaries were transplanted successfully in the rabbit by Dr. F. H. A. Marshall and W. A. Jolly †, and others, and

**Vide* Appendix H.

† Marshall, Francis H. A., and Jolly, William A.: "Results of Removal and Transplantation of Ovaries," in Trans. Roy. Soc. Edinburgh, 1907, vol. xv., with two plates; also "The Nature of the Ovarian Influence upon the Uterus as illustrated

to-day the sole impediment in the way of the successful transplantation of living trophoblast is the Act of Parliament relating to vivisection.

When Mr. Walter Ball and Mr. E. F. Thomas saw fit to publish an account of how they tried "the trypsin treatment," to their credit be it said, they did give particulars, as will appear anon, such that a good insight could be obtained into, and an estimate made of what they had really done. The like cannot be said of Dr. Bainbridge's report. It winds up with thirty theses or conclusions, but the evidences establishing the truth of these are not to be found in the text. This is as true of the favourable points as of the unfavourable ones. The references to the liquefying action of trypsin on cancer-cells, and to the beneficial effects of amylopsin, might seem to refute this, but no evidences of these are adduced anywhere in this "scientific report," and certainly the writer would feel inclined to doubt them, had he not witnessed them elsewhere again and again.

The liquefaction of cancer, by adequate injections of trypsin, which was first seen by me in actual liquid cancer, taken from living patients by a prominent consulting physician in London, and which I first brought to Dr. Bainbridge's notice in microscopical preparations of such liquid cancer, is a matter of supreme importance, worth of much more length reference than the two lines accorded to it in Bainbridge's report. The facts were first seen on February 26, 1907, and afterwards confirmed in the same case and in another. Since it is quite four years ago that the discovery was made, in the interests

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footnotes continued from page 171

by the Effects of Excision and Grafting of Ovaries," in Coll. Rep. Univ. Edin., Physiol. Dept., 1907-08, No. ii; and "Results of Ovarian Transplantation," in Seventeenth Internate. Congress Physiol., Heidelberg, 1907.

of science and of scientific truth I feel it my duty to record them. The first intimation was in these words under the above date: "A pensioned fireman had a cancer of the tongue and jaw removed at King's College Hospital. It recurred as a mass the size of my two fists. The case was desperate, and I treated him at once with my strongest stuff. Five days ago a soft place appeared, which I thought was an abscess, but I could get out no pus. The softness* is increasing, and yesterday I put in a needle and drew out some fluid, which I am sending you in a bottle. You shall see what you shall see. To my eyes it is already dead broken-down cancer tissue, and that in less than a fortnight." The fluid could not be filtered down, and resort was made to a centrifuge. This furnished a small amount of solid matter, and sufficient to make up about ten microscopical slides. The examination of these enabled the certain diagnosis of epthelioma or skin cancer to be made. In this first bottle there were some remains of epithelial cells, as well as the characteristic "pearls" of epithelioma. In another bottle, obtained two days later, the "pearls" were the sole

*The mention of this softness is very interesting in connection with the happenings of the York case, described in a subsequent chapter. The photographic figures (6and 7) were taken on July 15. In the charts one may read: "July 15, photographs taken, slough removed, a ragged hole left, but no bleeding; granulations hard and firm." Prior to this time the charts contain the following: "June 14, the growth is beginning to separate in the cheek, a little depression is visible, and on palpation only the thickness of the skin intervenes between the finger and the mouth. July 6, face very swollen, red margin or demarcation round tumour. July 9, a small vesicle has formed on the cheek. July 10, vesicle grows rapidly. July 11, vesicle has burst, and a profuse sero-purulent discharge pours from the cheek; a pultaceous slough is disclosed. July 13, the slough increases in size." Probably the phenomena noted in the two cases were identical up to a point. The profuse "sero-purulent discharge" mentioned by Captain Lambelle, may be identified as liquid cancer.

evidences, and they were not at all numerous. The opinion then formed was, that, in the course of two or three days more, even these evidences of epithelioma would have vanished. Very shortly afterwards the same hospital physician had a similar result in an American patient suffering from cancer of the tongue.

This liquefaction of cancer, which, it may be added, can only be carried out safely in the presence of large quantities of amylopsin, is, of course, a stereo-chemical reaction. Now, Dr. Bainbridge admits (p. 32) that it occurs "in some case" and not in others; why there was an apparent exception to this chemical reaction. The reason, of course, was, that in many of the very advanced cases experimented upon the strengths and doses of the injections were inadequate to perform this chemical reaction. But this obvious explanation seems never to have occurred to the author.

Regarded from the point of view of science, this liquefaction of a living malignant tumour by means of adequate injections of trypsin and amylopsin is seen to be of momentous importance. It stamps the treatment, when scientifically given, as one continuous and sustained stereo-chemical reaction. Obviously, the liquefaction of the tumour and of any metastases is the aim of the treatment. To the writer it does not seem that great difficulties will usually be encountered with glandular metastases or again and again he has known these to disappear, even when the main tumour continued its career of growth and destruction. But in two ways at least the matter has great practical import. Since the liquefaction is the goal to be aimed at, and since all toxic

effects produced by the action of trypsin upon the tumour-cells can be averted by sufficiently powerful injections of genuine amylopsin of great strength, made along with those of trypsin, in all probability in the long run a considerable shortening of the vital and crucial period of the treatment can be, and will be, obtained. Again, the resulting liquefaction may be looked upon as being in essence a separation of the tumour into two main portions,--a liquid one, which either must be got rid of as a "sero-purulent" discharge, or, getting into the blood, must be excreted by the skin and kidneys; and a more solid portion, the skeleton or framework of the tumour-cells, which, it near the surface, may be sloughed out; if deeper, then encapsulated. In many cases it may be desirable once the phenomena of liquefaction have been induced, to remove the dead tumour by operation, and, so it appears to me, it is at such a time, when every tumour-cell has ben killed and its albumins liquefied, that surgical intervention is called for, if at all.

The eighth thesis (p. 32) must be specially noted and challenged. It reads: "That because of the tendency of *injectio trypsini* to disintegrate the tissues, it may to a direct menace to life—(a) by eroding large blood-vessels(when the disease is contiguous to these structures, as when deep in the neck or in the ;elvis), thus causing death by hæmorrhage; (b) when given in large doses, over considerable periods of time, by overwhelming the system with toxic products (tumour toxins), thus, in some cases, hastening death." Regarding (a), I deny flatly that trypsin has any such action on normal somatic tissues as that attributed to it by Bainbridge. His conclusion is not in accord with the tenets of stereo-chemistry. The statement is a new answer to the old riddle: "Why do the stomach and intestines not digest

themselves in life?" The reply here given is tantamount to saying, "Because they do." The scientific answer to the conundrum is, that those ferments, such as trypsin and amylopsin, which build up the somatic albumins in life, do not pull them down in the living state, but that the antitheses of these ferments, their stereo-isomers, the ferments of cancer, do attack and pull down such albumins in life. In the cases mentioned by Bainbridge it is the fault of the tumour—that is, of its ferments, not that of the "trypsin" injection, and in such cases as much danger at least attaches to any possible treatment, even to surgery. The erosion of a "large vessel" is caused by the tumour, and not be the "trypsin." The flimsy inaccuracy of the statement (a) is shown by the following considerations: Wherever the cancer may be, the injections are never made into it, but hypodermically, or deep into the muscles, at some distance from it. Owing to Harvey's discovery of the circulation of the blood, it is clear that in this treatment the ferments circulate in the blood to reach the tumour. Therefore, in all cases they course through all the "large vessels," but in Bainbridge's report there is no suggestion that these ferments ever "erode" the "large blood-vessels, unless these be contiguous to the tumour. In the case of the York ex-pensioner the tumour was not many millimetres away from the carotid artery, but even the injection of 60,000 units of trypsin (in four months) caused no damage to this vital structure. As to (b), this was a discovery of mine in 1906, and not of Dr. Bainbridge's. it is quite true, if nothing but trypsin be administered, provided that the trypsin injection be strong. Not only did I discover this fact, but my scientific knowledge also furnished, in amylopsin, the remedy. I well recollect that this latter find had to be

made against time, in order to save the life of a very distinguished man, a brilliant artist and art-critic. The New York surgeon forgets the great feature of the enzyme treatment of cancer, amylopsin. Since June, 1906 (*Medical Record*, June 23, 1906, p. 1020), the writer has never recommended the use of trypsin without amylopsin, sufficient to counteract the formation of the toxic products, of which Dr. Bainbridge writes. When he put down this paragraph, he must surely have forgotten that he ever heard from me of certain uses of amylopsin. Finally, both of his objections are proved to be absurd from Captain Lambelle's procedure and results. In the case, cited anon, in the period from march 8 to July 15 (four months), Captain Lambells injected somewhere about 60,000 tryptic units, an amount possibly much greater than Dr. Bainbridge ever injected in a single case. But Captain Lambelle did not experience either (a) or (b), and his observations are opposed diametrically to both of those conclusions, which can only be described as "errors of experiment." Taken alon with thesis 9, "that the injections are often painful," the two things together read like an attempt to create a prejudice against the treatment. Scientifically, it is not easy to decide which of the two paragraphs is the more trivial.

In certain cases, and in these only, there are two dangers inherent in the enzyme treatment. These are (a) perforation, due to shrinkage of the tumour under the action of the ferments, as in œsophageal and gastric cancer; and (b) hæmorrhage, really due to the like cause, as in uterine and some pelvic cases. The physician should, however, note that these dangers are present in such cases, whatever treatment be adopted, or even if the cancer be allowed to pursue its course merrily; and that

they do not arise always, though threatening to do so, as in the Uppingham case of cancer of the stomach and liver.

In his report Dr. Bainbridge does not conceal a tendency to belittle the experiences of other physicians. Some of "the earlier claims of cures" were not so "absurd" as he imagines, and the "strange symptoms" and "terrific" results from small doses were, in my opinion, correct. The author overlooks the circumstance that he was not using the same injections as these observers, that he had profited by the increased experiences of the makers. Looked at scientifically, the writer would anticipate "terrific" results, even serious ones, from the use of small doses of trypsin in certain cases of cancer, where the tumour was large and the antitryptic power of the blood small. His remarks upon this and other matters only reveal to the scientific observer a lack of scientific imagination and of the capacity to adapt means to ends, which is so important in scientific experiment. If an injection be deficient in amylopsin, as also if it be not properly freed from poisonous peptones, even the use of no more than 1 c.c. daily may, as I have known to happen, be attended by serious consequences. Like the literature in general, the experimental results of Dr. S. Pinkus* receive no notice in this "scientific report." This investigator found the following things after injecting certain unnamed sterile solutions of "pancreatin preparations" in dogs and guinea-pigs: "Here one or two injections sufficed to raise the temperature from 1° to 18° permanently; in all cases there was a strong local reaction, invariably leading to further necroses. Five cavies and the dog No. 4 died in eight to ten days." It is also added that

Pinkuss, A., and Pinkus, S.: "Die Krebskrankheit und ihre therapeutische Beeinflussung durch Fermente," Sonderabdruck aus der *Medizinische Klinik*, 1907, Nos. 28 and 29; 15 pages.

all the disturbances subsided when an injection of genuine amylopsin was substituted.

The thirtieth and final thesis of Bainbridge's report reads that the enzyme treatment "does not cure cancer." At the time this verdict was published, Captain Lambelle had reported his latest case of success to the War Office of Great Britain, and this report is given *verbatim* on a succeeding page. Even though there had been no others, even though Rice, Golley, Wiggin, Campbell, Goeth, Cutfield, Guarracino, and others, had had no successful cases, even if the remains of the cancer of the tongue in the Naples case had not been seen by two of the leading physicians of Naples (*vide* Appendix D) to shell out, "like the kernel of a nut," I am prepared to take my stand, and now do so, upon the result of the published case of the recurrent sarcoma in York alone, to maintain that it has established the truth of my theses, and to declare that with this result all the essential portions of the problem, regarded scientifically, are solved once and for all. Bainbridge's thirtieth thesis is false. He, who would set up the frivolous objection that the York case was one of malignant sarcoma, not of cancer, and that sarcoma does "not come within the definition of cancer," may be invited to study the eleventh chapter of the present writing, and before urging this multiplication of causes scientifically to make for himself the crucial tests with the polarimeter to prove that cancer and sarcoma are not identical. In the cycle of animal life, as also in the visible universe, there is not room for two fundamentally different malignant tumours, cancer and sarcoma. The embryological evidences upon which this distinction has been founded, like those of this science underlying all current pathological classifications of malignant tumours, are absurd and unscientific.

When Captain Lambelle first sent me the three original photographs of his case, he remarked that the outcome was "just as in the Naples case." The Naples case was described briefly by me in the *Medical Record* for January 5, 1907 (see Appendix D). Here, in a case of inoperable epithelioma (skin cancer) of the tongue, the remains of the tumour finally shelled out "like the kernel of a nut." Referring, finally, to my abortive experiments,* which from circumstances beyond my control were never completed, in the preliminary report it was written that "it appeared probably to us that at the time we killed it, its 'cure' (*i.e*., that of the "trypsin" mouse) from cancer was not far distant, and the microscopical examination confirmed this opinion. Even without further treatment the tumour would in all probability have been absorbed shortly, or its remains cast out." What was here foretold happened in fact in an epithelioma in Naples and in a sarcoma in York. It is on positive results such as these that the edifice of science is built up; not upon negative finds, such as those recorded without the scientific evidences by Dr. Bainbridge.

As to the "thorough scientific test" of which the author writes on p. 3, I demur to this, just as I question the accuracy of the statement on p. 5, that "at all times during the trial of the enzyme treatment I (Dr. Bainbridge) have been in close touch with Dr. Beard." † Since I first met Dr. Bainbridge, in September, 1906, with the single exception of Case 7, I have been entirely

*Beard, J. : "The Action of Trypsin unpon the Living Cells of Jensen's Mouse-Tumour," in *British Medical Journal*, January 20, 1906.

† Compare also the *Lancet* (October 9, 1909, p. 1079): "We would point out, as a proof of the straightforward character of the inquiry, that throughout touch seems to have been kept with Dr. Beard." In the sense understood by the *Lancet* this is incorrect.

ignorant of his doing. No information was at any time vouchsafed to me. Of the 100 cases, one (No. 49) was not cancer, sixty-six were post-operative failures, and eighteen were "inoperable," making eighty-nine out of the 100. Of the remaining eleven, four are described as "lost sight of" and three as "alive." Of the class of case which a scientific test demands—viz., an absolutely unoperated one-the100 cases include seven, as against sixty-six recurrent cases after one or several operations. Of these seven cases, three were "lost sight of," three were "alive," and one was dead. Five of the cases at least were syphilitic, and my experience hitherto has been that no good results can be hoped for in cases suffering from such a complication as syphilis. Ten of them had been treated with the X rays, which, looked at scientifically, must be regarded as one of the best stimulants of cancer ever discovered. How far the eighteen inoperable cases wee suitable ones for the treatment it is impossible to say. Here, as in all other respects, Dr. Bainbridge was his own judge, jury, prosecuting advocate, etc., and all the scientific man need say to sum up shortly what the report is, apart from all other considerations, there are in it no evidences at all to show that Dr. Bainbfidge ever considered, much less sought to eliminate, all or any possible sources of error in his experiments.

On the fifth line of his "scientific report" the author refers to the determination he had expressed in 1907 to give the enzyme treatment "a thorough, scientific test." A study of his report reveals that (1) five strengths of trypsin injections were used, of which the strongest is stated to have had six times the potency of the weakest; but no attempt is made in the report to discriminated between these five injections, or the cases in which each

was employed, and there are no records of the doses or their number in a given time. (2) One case (No. 49) was "goitre," not cancer; of the remaining ninety-nine, sixty-six were post-operative failures; that is, in a test assumed by the author to have been "a thorough, scientific test," two out of every three cases contained the pernicious source of error of previous operation. (3) Lambelle's results show—and this I have always maintained—that a treatment of less than three months cannot be considered adequate; I would even add an additional month, and regard 120 days as a general minimum, not maximum. Therefore (4) the hundred cases treated by Bainbridge may be summed up as follows:

	Per Cent.
(a) Exclude from the result, because no injections were given, Nos. 35,49,52,&92	= 4
(b) Exclude, because no real treatment was given, or because "lost sight of," or ceased treatment. Nos. 11,31,37,38,39,40,41,43,44,45,47,48,57,58,63,70,75,86,88,89,94 97, and 99	=23
(c) Exclude No. 7 (Miss K.H.), for obvious reasons	= 1
(d) According to the report, there was "improvement," or prolongation of life, in Nos.	

5,6,8,14,16,17,18,19,20,22,26,28,34,42,46,50,60,72,78,80,and 100 =21

(e) Treated for more than ninety days, Nos. 3,12,23,32,51,66,76,79,81,82,84,98 =12

(f) Exclude, because treated for less than ninety days, with an average treatment of forty-six days, or six weeks four days, Nos. 1,2,4,9,10,13,15,21,24,25,27,29,30, 33,36,53,54,55,56,59,61,62,64,65,67,68,69m71,73,74,77,83,85,87,90,91,93,95&96=39

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100

But of those under (e) we are bound to exclude from a "scientific test"—

(1) The post-operative failures, Nos. 23, 76,79,82,and 84 = 5

(2) Owing to previous X-ray treatment, Nos. 3, 51 and 66 = 3

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8

leaving under the heading (e) 4 per cent.

The sum of these numbers, 4, 23, 1, 21, 12, and 39 makes up the total of 100. Of the four cases remaining under (e), No. 12 was a surgical failure after the enzyme treatment, and the remaining three were evidently very advanced and malignant cases. The lack of anything more than "improvement" and "prolongation of life" in the twenty-one cases under (d), and the failure of the four cases under (e) might conceivably be due to injections too weak or doses too small, or to both, for those particular cases. I am, however, reminded of Blumenthal's opinion (2), and the possibility or probability must not be overlooked that they may have been so advanced and hopeless that no possible treatment could have saved them. The like probably held the nine "test" cases treated by Messrs. Ball and Thomas.

The impression made upon the mind of another, who more than once has had success* withthe enzyme treatment, and who understands and fully appreciates its scientific foundations—I mean Captain F. W. Lambelle, M.D., R.A.M.C., lately operating surgeon of the Military Hospital, York—may be cited.

*In all four cases, treated as described in the present writing. They were (1) chondro-sarcoma of ribs; (2) encephaloid carcinoma of breast; (3) lympho-sarcoma, induced by X-ray treatment for carotid aneurysm by another medical man; and (4) round-celled sarcoma of jaw. The fate of the third is described in the present writing. The other three are, I believe, alive and well. Concerning (2) see Appendix L.

Regarding the case of lympho-sarcoma, it may be mentioned, as showing the true inwardness orf th pathological distinction of sarcoma and carcinoma, that in the microscopical examination of sections of the treated tumour after death the keratinous remains of tumour-cells were "mistaken" for epithelial cells by an official pathologist, and the diagnosis of "epithelioma" was given. I do not term this a mistake, for it was clear evidence of as little, "epithelial cells" as those of epithelioma or of trophoblast.

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He writes: "In reading Dr. W. Seaman Bainbridge's report one is struck by two repeated phrases, which seem to dominate his whole theme—(1) the patient 'died' within a few months of treatment by ferments have been undertaken; (2) the treatment was 'negative in all respects.' Though Dr. Bainbridge's report is lacking in many details, which would have greatly helped in establishing its value as a scientific report, it is evident from (1) that the great majority of the cases which came under treatment were in an advanced stage of the disease. What does failure in such cases mean? Does Dr. Bainbridge as a surgeon condemn the operation for strangulated hernia simply because in a strangulated hernia case of five days' duration the patient's chances of recovery are one in ten or less? With regard to (2), the treatment was "negative"; it is also stated that 'the control cases did as well with injections of glycerin and sterile water, or sterile water alone plus the régime, as did the others with the full enzyme treatment.' These statements may be capable of some other interpretation than that which Dr. Bainbridge gives. Dr. Bainbridge has only shown that in his hands the treatment of cancer by ferments has been a failure, and it has yet to be shown wherein lay the cause of the want of success, remembering that failure is always easier of attainment than success in anything, and that on the frontiers of science still more so is this the case. Nor is that failure surprising to me, when I read how little Dr. Bainbridge has understood of the enzyme treatment, for in his summary he says, 'that aiding digestion, increasing elimination, and decreasing local absorption are the most important features of the treatment' Dr. Bainbridge's report may be 'negative in all respects,' for paragraph 7 of his summary is proof that Dr. Bainbridge has never seen the effects of trypsin upon a malignant growth. He says 'that, while it may accelerate the breaking down in the centre of the tumour mass, the periphery is found to be actively growing.'

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Herein he describes the normal life-history of an unchecked cancerous growth—the growth goes on its own course merrily, without restraint from the enzyme treatment exhibited.*

"In the four years a fair amount of pathological evidence has been acquired, which is not in accordance with Dr. Bainbridge's experience; and, without going minutely into details, let me cite two cases which seem to me to indicate (1) that trypsin does attack cancerous growths; (2) that trypsin can destroy cancerous growths:

"Case 1.—Male, 51. Lympho-sarcoma. Superficial cervical glands. Died from hæmmorhage from separating sloughing tumour. Naked-eye inspection of the tumour showed no gland-tissue whatever-it was a dense fibrous stroma pent up with purulent fluid. Microscopically, all that remained of the malignant cells were keratinous masses, in which the individual cells were unrecognizable. The treatment had exerted a selective action on the malignant cells, had

destroyed them almost entirely, and their necrotic remains were in process of removal by leucocytes.

"Case 2.—Male, 25. Round-celled sarcoma of upper jaw. Primary growth removed by operation…recurrence in all the glands of the left side of the face. Treatment begun March 8, 1909. Tumour removed entire as one large slough on July 15, 1909, patient making an excellent recovery.

"What happened in both these cases was that under the action of trypsin the tumour became gangreous.

*If the account be taken of the "heterolytic" cancer-ferment termed by me "malignin," and of the antitryptic properties of the blood in most, if not all, cancer cases, it must be clear that Dr. Bainbridge produces no evidence at all that he has ever had free pancreatic ferments in the blood of any of his unsuccessful cases. Nay, in view of Captain Lambelle's apt criticism concerning the natural course of cancer, described by Dr. Bainbridge in his report, it is quite palpable that Dr. Bainbridge, in any of these unsuccessful cases, had never exhibited sufficient trypsin and amylopsin to neutralize the cancer ferment or ferments present.

The periphery of the growth in each case was marked out be a red line—an 'area of demarcation' as plain as in a gangrenous limb. In Case 1—a failure just short of success—we can see the process set forth, the influence of the trypsin upon the peripheral portions of the growth being to stem the invasion of the malignant cells, and to rouse the adjacent somatic tissues to that process of repair pathology calls inflammation. In Case 2 the gangrene of the tumour became complete, and the sloughing tumour was lifted from its bed without leaving one bleeding-point, nor so much as an oozing granulation."

It will be demonstrated presently that from a knowledge of ferment powers (in the tryptic and amylotytic units set up by the late Sir William Roberts, M.D. F.R.S., Professor of Medicine in the Owens College, Manchester), and from the details furnished by the authors themselves, a fairly accurate estimate may be made for each individual case of the actual amount of trypsin and of amylopsin exhibited in the cases reported by Messrs. Ball and Thomas. In leaving the report under notice it may be remarked, with some emphasis upon its scientific value, that a similar estimate can be made in not a single on the cases described by Dr. Bainbridge. In view of more recent clinical work of others, it may be stated that the amylopsin injections employed by Dr. Bainbridge were very much too weak; that his four weaker trypsin injections. All of which I have more than once tested, were in strength quite inadequate for their work; and that regarding the fifth and strongest trypsin injection, the "special quadruple X," which to my knowledge has never been sent to Great Britain, and possibly never furnished to anyone except Dr. Bainbridge, I can say nothing, beyond that I doubt whether it possesses more than 750 Roberts

tryptic units, whereas it should have 1,000 such at least.

One criticism, if it can be called such, has been made to the effect that the theoretical basis on which "the trypsin treatment of cancer" is built contains too many unknown factors to be accepted as sound. There is a learned ring about this empty statement, but it lacks all evidences. I suppose that, as the factors are unknown, they cannot be named. One might as well say, "The theoretical basis upon which Newton's conception of universal gravitation is built contains too many unknown factors to be accepted as sound." Certainly, one could not name these! I seem to read once more the remark made by a pathologist, who was one of the first to whom I told by letter my conclusions as to the import of the pancreatic enzymes in cancer in 1904. It was that there were "difficulties." He never named them, then or later. It was a strange and weird remark to make to a man who had spent his life overcoming and trying to overcome and trying to overcome scientific "difficulties." There is also the fallacy of speaking of "the trypsin treatment," which I agree is thoroughly unsound.

As to the researches of Achalme, von Bergmann, Guleke, and Bamberg, cited sometimes as proving "that injections of trypsin are immediately followed by the production anytitrypsin, so that an effect opposite to that aimed at is produced," the marvel is that this statement should be made seriously. The reason is passed over in silence that this result was due to organic impurities in the preparations used.

CHAPTER VII

GENERAL DIRECTIONS FOR THE PANCREATIC OR ENZYME TREATMENT OF CANCER IN ITS VARIOUS FORMS

When, in January, 1906, trypsin began to be employed in the treatment of cancer in many places, Fairchild's "trypsin in powder," and Merck's trypsin, were the best-known preparations of this enzyme upon the market. Fairchild's "trypsin in powder" was a very potent substance, prepared by this firm for "dissolving diphtheritic membrane," and, so I understand, long used successfully for this purpose. In recent years it had been superseded by Behring's "antidiptheritic serum," a substance the nature of which is still unknown. Regarded scientifically, the innovation cannot be described as an advance. The sole mistake made by Messrs. Fairchild Brothers was in advocating its use as a powder, and not in the form of a hypodermic injection of trypsin (and amylopsin). There is no doubt in my mind to-day that certain of the injections of trypsin and of amylopsin, in combination, would with certainty and without any of the dangerous complications (serum-anaphylaxis) attaching to the usage of a "serum" dissolve this membrane, and cure diphtheria. But, of course, at present the medical profession is wedded to "sera," which may be described briefly as unknown substances of uncertain action. So much for the preparations of "trypsin"

obtainable some years ago. When injections for use in cancer were first on sale, none of the makers did, or could, furnish any general direction as to how they should be employed. Many were the letters received by the writer, especially from French and Italian physicians and surgeons, asking for some directions as to the procedure to be adopted. These requests led to the first "general directions" from my pen. These latter were constantly being altered in accordance with the reports received and the knowledge gained. Even in their final formed, as printed for my convenience in 1907, they professed to lay down no strict course applicable to all cases. It was written: "The question of proper dosage is not yet decided finally, and it will probably be found to vary with different cancer." Many of his friends and correspondents will, if need be, confirm the

statement that all along the writer's chief concern has been to impress upon physicians and chemists the urgent necessity of seeing that every dose of trypsin was accompanied by an adequate amount of amylopsin. The one injection was termed, unfortunately, *injectio trypsini* by the makers, but those with which I was in any way concerned always contained some amylopsin, a quantity which I could never get made large enough for the requirements. As will be seen, this has now been brought about in another way.

Even now it is not for me to lay down any fixed limit of size of tumour, or of time for the previous growth of the tumour, beyond which success cannot be hoped for; but it must be insisted, and emphasis laid upon the point, that no treatment can be considered adequate, unless it be such as will more than overcome, more than negative, the antitryptic (toxic) properties of the cancer ferment, malignin. To find in very bad cases, as some

have done, trypsin in the urine* is not enough; it must be shown that this is not antitrypsin (*vide* Bainbridge's Report, p. 14: "The above experiments showed the presence in the urine in cases on the trypsin treatment, in non-cancerous patients, and in patients with cancer who had not been treated by trypsin, of an enzyme possessing properties of digestion similar to trypsin").

This is cited as one instance where the actual ferment present was not determine. In the same way, if sugar be noted in the urine, it must be determined that it is not lævulose.

Dr. Bainbridge and others have, of their own initiative, set up what they term "test cases." In a scientific sense no case can be regarded as a test one, where any other treatment had been employed previously, or where the conditions of the "test," like the Ball and Thomas ones, and those of Dr. Bainbridge, had been laid own by the authors themselves without the agreement of the investigator, and without the scientific observance of the rules relating to "errors of experiment." As will later on be done with one series of these "test," so any other "scientific tests" shall be placed in their proper scientific aspects, including all the cases published by Dr. Bainbridge, when the authors see fit to reveal in scientific fashion what they have really done in the process of carrying out their "scientific experiments."

Then there are the preparations and the dosage. Scores,

*Similarly, in the first of the cases recorded by Dr. A. Pinkuss, in the paper already cited (p.12), it is stated that trypsin was first detect in the urine after forty-eight injections, and from thence onwards it remained mostly positive. Considering the strengths of injections used, it appears more likely that antitrypsin from the cancer was mistaken for trypsin, and this surmise is rather confirmed by the statement that a rigor was only observable on the forty-third day or treatment.

if not hundreds, of those in this country who, if asked, would give an adverse opinion of the pancreatic enzymes in cancer have never even employed them.. This may be illustrated.

A former pupil, a physician in this city, has urged that the medical man is bound to trust to chemists for his drugs, etc., and as an instance he cited digitalis. To which the reply was obvious. If a physician, using digitalis, did not get the reaction he anticipated, he would naturally suspect the preparation, and would inquire as to its true chemical character, but he would not, in the absence of the expected reaction, condemn the use of digitalis. This, however, has been done again and again with preparations of trypsin (and amylopsin), in the absence of any proof or knowledge that the preparations used contained any enzymes whatever. It is illogical and absurd

to condemn a scientific treatment, as some eminent surgeons in London have done, when it was the preparations employed by them which needed their censure.

Early in July, 1909, I spent several hours in the society of a well-known Glasgow operation surgeon, who volunteered the information that he had used "trypsin" in cancer, but had gathered a poor opinion of it. "It all depends upon what you used," I said. He named certain preparations at one time much advertised. "Well," I answered, "as to those preparations, in 1906-07, when quite fresh, if they contained any active ferments at all it was only pure trypsin, and they were so made up that a box of them would be inert in fourteen days or less; indeed, they had no keeping properties at all. At times, as I had to know, they were exported to the Cape, but it is inconceivable that they could have been in the least active by the time they crossed the Equator."

In certain independent laboratory estimations of these preparations, made by a fully competent chemist and physician in February, 1907, the tryptic power per ampoule of these preparations was found to be 9·6 Roberts tryptic units. That is to say, if preparations of such a strength of trypsin (9·6 units), and of the very slight amylolytic power of 0·37 amylolytic units, were now used for what Captain Lambelle and I regard as full normal doses, given daily or every other day, the following would be the procedure: The full daily dose of 1,000 tryptic units would require the use of quite 100 ampoules of 9·6 units, and the full dose of amylopsin could be obtained from more than 5,000 ampoules of the strength of 0·37 unit, ore more than five litres. I commend these figures to certain transparently anonymous scribes, cancer researchers and ex-researchers, in the English medical press.

It has been pointed out that little or no evidences of the value of pancreatic ferments in malignant disease have been published in France or Germany. With out present knowledge of the requirements of the treatment, it would be surprising to find any positive evidence in the medical publications of either country. This lack of evidences is easily explicable. From Germany the total number of applications for general directions or for preparations to date (June, 1911) is two, all told, and doubtless most of the cases there treated received the German preparations mentioned by Dr. P.T.Hald (*LancetI,* November 16, 1907, pp. 1371-1375)k, and to his article the reader may be referred for information as to their strength (*vide* Appendix M).

The writer has not a single record of a request for injections as strong as 250 or 500 tryptic units from any French physician. Some French and Italian cases were

treated with the first Fairchild injections, which have long been recognized as far too weak, and which are not now on sale anywhere. In France and Italy, whence came the first rush of request in 1906, a very large number of cases in 1906 received injections, which at that time were found to possess a tryptic power of 9·6 tryptic units.

Before me lies a "list of doctors and hospitals" in Great Britain which were supplied with certain active preparations of trypsin and amylopsin. The list was compiled for the information of Dr. Bainbridge. The trypsin injections include the "regular," or 125 units, and the "extra special," or 500 units. The amylopsin injection had presumably 100 units of strength. The total number of physicians is 126, of hospitals 43. Of the former, 96 used trypsin of 125 units, and 30 of 500 units. Amylopsin, as a separate injection (100 units of activity), was order by 74 of the 126 physicians, and by 16 of the 42 hospitals. That is to say, 77 per cent. of the physicians and 79 per cent. of the hospitals never had a stronger injection of trypsin than 125 units, and amylopsin was employed by about 59 per cent. of the physicians, and by 37 per cent. of the hospitals. Some of

the latter were large London hospitals, others special hospitals for the treatment of cancer. These are some of the "fair trials" given to this scientific treatment. As the strengths of the preparations employed wee entirely in the hands of the physicians and surgeons concerned, for the makers resolved to be guided by them, it is clear that the trial of the enzymes in Great Britain was little, if anything, better than the von Leyden experiments with very weak trypsin in Germany. None the less, Professor von Leyden wrote (German *Journal of Clinical Medicine*, vol. lxi., pp. 360-365): "In the therapy of the experiment there lies a new experience established.

For we have never seen that a tumour which was circumscriptly brought to a dissolution of its cells by a tryptic ferment, reacted by increased growth to this procedure, either locally or generally." According to my calculations, based upon Table V. of Dr. Hald's paper, to be cited presently, the "trypsin" employed in the Berlin experiments varied in strength downwards from a maximum of about 125 units (see Appendix M). There is no mention of the employment of amylopsin in any of the Berlin work. It is easy to recognize that had von Leyden and his colleagues made use of injections of 1,000 units of tryptic strength, plus similar ones of 2,000 units of amylolytic activity, and in the doses given in more than one case by Captain Lambelle, he would, in all probability, have expressed the opinion, later on give by Professor F. Blumenthal, and quoted in the *British Medical Journal* of January 11, 1908, that "the treatment by a ferment which destroys the cancer cell has a great future before it." It is not a new opinion of the writer's that, with the exceptions of those of Captain Lambelle and a very few others, the injections given, especially in the years 1906-1909, were in the inverse proportion to the results vainly expected.

Hitherto in his publications the writer has not committed himself to definite statements as to the actual and relative strengths of the injections of enzymes, or their amount. The actual treatment of every single case, the writer being "not even a medical practitioner," exactly as Pasteur was "not even a medical man," was absolutely in the hands of the physician concerned. But I doubt whether any physician or surgeon can say truthfully that I ever told him that he was giving too large or too strong injections of trypsin and amylopsin. Again, the manufacturers placed on sale just such preparations as

they deemed suitable, and with one exception none of them ever asked a scientific opinion from me as to their procedure. More than once the one firm with whom, through their European manager, I was long in constant communication, declined to put out still stronger injections, until some physician should ask for them. That is to say, like the writer, they preferred to place the responsibility upon the shoulders of the physicians in charge. When, therefore, for example, Dr. P. Tetens Hald,* referring to one of the Fairchild preparations, says, "This solution is of the same strength as the 'special injection' recommended by Beard," this "recommendation" must be understood as given because the high reputation of the firm of Fairchild Brothers and Foster was a guarantee that all their preparations were reliable and scientifically prepared, and not because, in my scientific opinion, they wee at that time the best possible preparations ideally for use in either absolute or relative strengths. I knew of no better ones on the market—indeed, for a very long time, of none as good; and, in addition to other advantages, they had for my purposes the very great recommendation that through agents they could be obtained in almost every part of the world, at the Cape, in Australia, India, Italy, Spain, etc. Thus, no single correspondent had to be told that reliable injections of trypsin and of amylopsin were out of his reach. Moreover, these

injections had active ferment powers in whatever part of the world they happened to be purchased, a thing which cannot be said of certain other injections.

The time has now arrived when it is the writer's duty

*Hale, P. Teten: "Comparative Researches on the Tryptic Strengths of Different Trypsin Preparations, and on their Action on the Human Body," in the *Lancet* (November 16, 1907, pp. 1371-1375).

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as a scientific investigator bound to publish the truth for its own sake, no matter what the cost may be, to state in brief terms the conclusions which he has formed from his studies, from results obtained by others, and from various information. Many physicians and surgeons have "tried the treatment" with either (1) injections so weak or inert as to be no better than glycerine and water, or (2) weak injections of almost pure trypsin, fortunately as a rule in very small doses.* For, as I have more than once warned the medical profession, trypsin alone is about the most deadly remedy for cancer which could possibly be devised. Again, in Germany especially, preparations of "trypsin" have been used which were not free from poisonous peptones, and such may still be in use there, for aught I know. Again, trypsin with no amylopsin has been used (London), and amylopsin alone (Geneva and Paris), and pepsin alone (Glasgow), and lastly, anything with the label "trypsin," the medical men concerned not knowing or troubling to find out whether they were using trypsin, or amylopsin, or both, or something else, or neither the one nor the other. At times, as I found, the general directions for the use of genuine preparations of trypsin and amylopsin were being employed with preparations which would have been quite useless even as a cure for corns.

In venturing to lay down a course of treatment for average cases of cancer (carcinoma and sarcoma) certain conditions must be mentioned and insisted upon. More-

*There was once case reported to me out in the far West of the United States, in which, as no other preparations could be obtained, an apparently strong injection of pure trypsin, made up on the spot, was employed. The patient developed quickly those symptoms of eclampsia which at one time were the rule from the sixth to the eighth weeks of treatment, and in addition he was seized with convulsions lasting several hours, with complete unconsciousness (coma).

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over, it must be understood distinctly, that if "test cases" are to be treated, after the lines of Messrs. Ball and Thomas and Dr. W. S. Bainbridge, certain other scientific stipulations must be made, and in scientific fashion "the test" must be carried out under rules of procedure agreed upon between the testing surgeon and the scientific investigator. In other words, all apertures for the creeping in of "errors of experiment" must be closed up. Above all, cases such as post-operative recurrent ones, in which any other treatment had been employed previously, cannot be used and cited as failures in any test claiming to be scientific.

1. From Captain Lambelle's results, published and unpublished, and from the outcome of the Uppingham case, the treatment appears to be applicable to inoperable, recurrent, and primary cases; but in taking up treatment the physician is urged to bear in mind all along the size and extent of the tumour and the previous history in fixing upon strengths and doses. On occasion much larger doses might probably be injected with safety, provided that for every increased of trypsin an adequate amount of amylopsin be injected at the same time; or under the system of Roberts units advocated, for every tryptic unit let there be *at least* two amyloytic ones.

2. The injections should be freshly made, and when ever possible not many days old. All boxes should bear the date of manufacture.
3. On no account may the injections be made up from commercial "trypsin in powder" or similar things.

Great stress must be laid upon both of these points. Obviously injections containing peptones are unfit for use, though in some instances the treatment has been condemned after the employment of such. A special reason for the use of freshly-made-up injections lies in

the facts concerning the conversion of amylopsin into trypsin in solutions of the pancreas gland, which have stood for some time.

4. Nothing less strong than the injections and doses to be mentioned presently can be relied upon, judging by past experiences, as adequate. The remark about "toxins and antitoxins" in the "General Directions," drawn up by me in 1907, may be recalled. "While the tumour is alive, and for some little time after, it may be taken that the cancer ferment, malignin, and the pancreatic ferments, especially trypsin, act towards each other, somewhat like toxin and antitoxin." There is in my mind no doubt that the strengths hitherto used have, except in a few cases, been quite inadequate to over the antitryptic properties of the blood in cancer patients, and unless this be done it is useless to expect the usual results of ferment action—*i.e.*, that a ferment present itself in a very small amount produces a great output of work.
5. The actual position of affairs in the past few years can be best described by quoting the impartial opinion of a competent author. On p. 340 of "E. Merck's Annual Report of Recent Advances in Pharmaceutical Chemistry and Therapeutics" (Darmstadt, vol. xxii., August, 1909) on may read regarding trypsin: "The mode of action and the value of pancreas preparations in cancer has not yet received a wholly reliable explanation. Great difficulties are encountered because the preparations used by the various investigators differ greatly in respect to their chemical properties, their purity, and in the amount of active substances they contain, and often these factors are not fully known to the student of the literature, or to the physician who has used them and describes their action. Further difficulties arise

5. (cont'd) when pancreatin and trypsin are described as substances of equal value, and how shall we gauge the action of pancreatin and trypsin ampullæ whose mode of preparation and whose composition is not mentioned in the original paper, neither is there any mention made of their sterility of the method by which they have been sterilized? We need not wonder, then, to find that one author has never seen local inflammation follow the injection, while another reports severe local irritant effects. So long as the solutions of pancreatin and trypsin are treated as secret remedies no one will be able to form a clear picture of the value of trypsin treatment from the many publications which have appeared."
6. If the foregoing citation be read carefully, and its meaning appreciated, the reader will be prepared for what follows. The writer has never made up, or offered for sale, injections of either trypsin and amylopsin. In laying down, as I am about to do, certain strengths and doses of trypsin and of amylopsin as normal ones, which

in the discretion of the physician may be exceed on occasion, if used in the same invariable proportions, I also state how, in my scientific opinion, these should be assayed—that is, "standardized." The physician must satisfy himself that all this has been done, and he must not ask any guarantee from the scientific investigator for any preparation to which he has not placed his name as a pledge of its true character. If the physician should

*The following passage occurs in a recent letter from one who knows thoroughly what he is writing about: "Even at this day, by the way, there is a 'trypsin' (so labelled) on the market which is practically identical with the products sold as pancreatin from the same source; the only way they differ is in the name—the label. Equally, there are products sold as amylopsin which differ from the preparations sold as pancreatin only in name."

publish "test cases," apart form other conditions of a scientific test, he must be prepared to produce scientific evidences that the preparations he employed were what they pretended to be. As I have no preparations upon the martket, the onus is upon him, and it will not suffice as a scientific test of any value at all if he produce, as Messrs. Ball and Thomas did, mere elementary qualitative evidences that "in each stance the solutions were found to be potent" (Reports of the Middlesex Hospital, 1907, No. 6, p. 19).

7. Again, a South American physician once informed the writer that in South America all sorts of things had been offered for sale and used under the name of "trypsin," some of them possibly with the writer's name attached to them, as did indeed happen, without his consent or knowledge, in Italy. I do not suppose that matters wee on the whole much better in the Old World Among other happenings a preparation was advertised as "a proteolytic and amylolytic ferment"—that is to say, as a ferment possessing both proteolytic and amylolytic powers.
8. It has been pointed out recently to the writer by a medical friend, that in every disease there is a period beyond which success in treatment cannot be hoped for or expected, and the like is true of cancer. It is, therefore, in the highest interests of the patient that, for example, there should be no delay for futile operations. During such times the mischief is progressing, possibly slowly but surely, and the above period is getting nearer and nearer. When the pancreatic enzymes, trypsin and amylopsin, will act upon so-called "normal tissues" (Bainbridge and Blumenthal), this period has been reached or passed. Though for the sake of humanity the treatment may be give in such cases, it is not, scientifically regarded, intended for these cases. As

Dr. Cleaves first insisted, and Captain Lambelle has urged it too, during the treatment scientific blood-examinations are of very great importance. This again points to the treatment of cases in sanatoria.

The system of units of tryptic and amylolytic activity adopted by Sir W. Roberts, M.D., F.R.S., is an empirical one, but it possesses certain advantages over some of the methods employed in scientific laboratories for estimating, for example, tryptic activity. Unlike, for instance, the accurate scientific methods advocated by Dr. Emil Westergasard and Dr. Tetens

Hald (*Lancet*, November 16, 1907, p. 1371 *et seq*.), it does not require a fully, equipped laboratory for its accomplishment, and often I have used it in my own house. With a little practice and after the careful study of Sir W. Roberts' papers, any physician ought to be able to use these excellent methods for himself with very simple apparatus, which can be put together almost anywhere. The apparatus should include a racing stop-watch. It may be that in course of time some more severly scientific methods of estimating the activity of trypsin, and amylopsin too, may, with great advantage, be employed, such as, for example, the tryptic assay, advocated and discovered by Emil Abderhalden (*Zeitschrift physiol. Chemie*, 1907, vol. li.). In the meantime the writer is content to suggest, as at present sufficiently accurate and scientific for all practical purposes, the tryptic and amylolytic methods discovered by Sir William Roberts, and published by him in the Proceeding of the Royal Society, London, as well as in a special book.*

*Roberts, William: "On the Estimation of the Amylolytic and Proteolytic Activity of Pancreatic Extracts," in Proc. Roy. Soc. London, 1881, vol. xxxii., pp. 145-161; and "Digestion and Diet," London, 1891, Smith, Elder and Co.

The test for trypsin was named by Roberts "the meta-casein

Because to do so would take up much space, I refrain from giving an account of the Roberts methods and their results. Possibly in the interest of science—not "medical science"—some of the medical journals may see fit to republish his Royal Society paper. If not, one prominent consulting physician, who has made still further investigations into these matters, may deem it expedient to publish the memoir, which, I believe, he wrote down a few years ago. Briefly, it may be stated that Roberts set up certain tryptic and amylolytic units, in terms of which preparations or injections might be designated. Thus, of the injections used in 1907, practically all those sold by two firms, the one in London, the other in New York, had no greater tryptic strength than 500 Roberts units, while as a rule their amylolytic activities were considerably under 500 units. Some of the injections had not more than 100 units of strength, and the German injections were excessively weak in such units of tryptic strength and possessed no amylolytic powers worth mentioning. Under the newer procedure it has been found best to put up the two ferments, trypsin and amylopsin, in separate ampoules, which I would suggest should be differently coloured. The trypsin injection thus prepared should be as free as possible of amylopsin, and the amylopsin injection should be to all intents free from trypsin. The ampoule of 1 c.c. should contain in this bulk 1,000 units of tryptic activity, and the ampoule of amylopsin should have per ampoule at least 2,000 units of amylolytic activity. Personally, I do not believe that reliance can be placed upon injections containing respec-

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(footnotes from page 201)

test," and it depends upon the time required by milk to reach the coagulation point. It is, in my experience, an extremely delicate test, and free from the objections attaching to the "bitter taste" test employed in America.

tively per c.c. less than 1,000 units of tryptic strength and 2,000 units of amylolytic power. It must be specially noted that on no account whatever should the trypsin injection be used without the amylopsin one. The rule is for every ampoule of 1 c.c. of trypsin (1,000 units) on injection a corresponding amount, 1 ampoule of 1 c.c. of amylopsin (2,000 to 2,400 units), must be employed. The two injections should be mixed together in the syringe. What, for want of a better term, may be described as the normal daily dose is 1 ampoule, or 1 c.c. of trypsin (1,000) plus 1

ampoule, or 1 c.c. of amylopsin (2,000 to 2,400 units). If a less dose be deemed necessary, the contents of the ampoule can be diluted or less used. But the one injection should never be used without the other, and in the proportion named. On occasion I see no objections to the use of still stronger injections, but I understand that 1,300 tryptic units per 1 c.c. represents about the maximum strength at present obtainable. As a scientific man, I do not believe than an injection of , say, 124 tryptic units or less is of any real value.

It may be stated here than even with the large amount of amylopsin injected by Captain Lambelle in the york case the patient exhibited unfavourable symptoms of drowsiness, nausea, and vomiting in June, 1909. These may be explained in one of two ways: Either the amylopsin injection was breaking up into trypsin, or sufficient amylopsin was not being used, in spite of the large or strong doses being given. After much consideration of the matter, the writer urges strongly the two following things. All amylopsin injections employed should have the maximum strength possible of amylopsin—which, I believe, about 2,400 units per cubic centimetre or ampoule. As shown in Chapter IX., to all appear-

ances it is impossible with present methods to avoid the presence of some trypsin in every amylopsin injection. A careful watch should be kept on this, that it is as little as possible—from 10 to 20 units. But even this is not sufficient. The injections used should be as freshly made up as possible, for, as will be seen, amylopsin may be some means be broken up into trypsin, and at present the conditions under which this happens are not known. It may, of course, be a change due to temperature.

In the past few years the injections have been given hypodermically, but the great advantages of the procedure adopted by Captain Lambelle, and give in his own words on a succeeding page, may be insisted upon; that is, the injections should be given "intramuscularly deeply into the muscles of the buttock, or about the iliac crest, or in the flank." To my mind it is as unnecessarily painful procedure to give them hypodermically into the abdominal wall.

It is of the utmost importance to avoid any suspension of treatment, especially during the first four months, or until the tumour has liquefied, and its remains have shelled out or become encapsulated. There are two reasons for this. In the first place, if there be still any living portions of the tumour, even a few single cells, these may thereby have time to adapt themselves to their ferment environment, and by increased secretion of antitryptic bodies (? intracellular ferments) sicceed in neutralizing the pancreatic enzymes injected. This is in complete accordance with the finding of stereo-chemistry, for when present in equal amounts, the dextro- and lævo- stereo-isomers neutralize each other, and the mixture has no action upon polarized light (Pasteur). Secondly, under such circumstances there is great danger of toxæmia, from the formation of poisonous substances

from the degenerating tumour, or from the portion in degeneration. In my experiences cases have occurred where the physician, being convinced that the tumour was dead, and that the remains might best be left "to come away of themselves," has permitted the patient to remove himself far from all medical supervision, with the inevitable result that a fatal toxæmia has ended the case.

Assuming the treatment to be continued for at least four full months, or 120 days, in this rigorous fashion—a thing which experience in York and elsewhere has proved possible—then it can be stated that the patient received in this time at least 1,000 x 60 to 1,000 x 120 tryptic units, and 2,000 x 60 to 2,000 x 120 amylolytic units, or in all 60,000 to 12,000 tryptic units and 120,000 to 240,000 amylolytic units—in words, from sixty to one hundred and twenty thousand tryptic units, and from one hundred and twenty thousand to two hundred and forty thousand

amylolytic units. As one instance, the case described by Captain Lambelle received in 120 days about 60,000 tryptic units, according to calculations made from the charts.

In the Uppingham case of cancer of the stomach and liver, the physician did not allow me to make the requisite calculations from the charts taken; but from other sources the amount of trypsin injected would appear to have been 63,00 units, and of amylopsin 94,000 units. As will be seen, this amount much exceeds the total injected by Messrs. Ball and Thomas, not in one, but in nine "test" cases: trypsin, 63,000 units against 30,000 units; and amylopsin, 94,000 units against the miserable total of 16,00 units in these experiments. It may be added that certain hospitals which "tested" the treatment, with weak trypsin injections in small doses, never obtained

any amylopsin at all, and therefore never used amylopsin injections.

All injections which are not standardized after the above fashion, or at all events not guaranteed at least equal in tryptic or amylolytic potency to any injections so standardized, and all which contain less tryptic and amylolytic strengths than those indicated, are not, in my scientific opinion, suitable for use in the treatment of cancer, and not in conformity with the enzyme treatment of cancer.

All weaker injections, say, 500, 250, 125, or even 10 tryptic units, should be refused, and none of those with less than 2,000 amylolytic units are to be employed. If smaller or weaker doses be deemed desirable, less of the injections should be used. The amylopsin injection may be given without the trypsin one, not to "cure" the cancer, or to "digest" it, but to remove any of the bad symptoms. The trypsin injection, on the contrary, may never be employed without at the same time at least as much of the amylopsin injection; in other words, for every trypsin unit at least 2 amylopsin units must be injected. The ideal place for the treatment is in a sanatorium under constant medical and nursing supervision, and in good hygienic surroundings. The patient should be kept as quiet as possible, a diet as laid down by Captain Lambelle in this book be given, and the patient should refrain from any exertions of a bodily kind which could be avoided, even though he or she might feel fit to carry such out.

A special warning must be made against the all too common practice of sending cancer patients to the seaside. Again and again I have known it to happen that in the course of this enzyme treatment the physician has, on his own responsibility, stopped the treatment for a time in

order to allow the patient to enjoy the benefits of a stay by the sea. There is, however, nothing, except possibly the X or Röntgen rays, which is so favourable to the rapid growth and increase of cancer-cells as sea air. As asexual generation—the equivalent of cancer—first arose in the sea, the possible reason of this may be ovbious.

Finally, the writer begs to intimate to possible correspondents that he does not undertake to guarantee any particular preparations of pancreatic ferments. It has indeed been suggested that the writer should "hold himself responsible for the ferments being rightly furnished" to physicians who wish to "try" the enzyme treatment. The guarantees must be sought from the manufacturers, and not from one whose object in publishing these facts is merely to demonstrate beyond contradiction, that the words he said, regarding the uses Nature made of the secretion of the pancreas gland, at Liverpool on January 20, 1905, were true. Moreover, the writer holds strongly, that it is the duty of the State to provide and guarantee suitable injections of trypsin and of amylopsin, properly standardized, and in this way not allow these to be exploited at times by persons incompetent to make up scientifically standardized injections of the kinds demanded by

the treatment. Any work with the pancreatic enzymes, even the making-up of ampoules of injections, calls for great scientific knowledge, skill, and accuracy. As is well known to some, the enzymes are extremely delicate bodies, and often, when the inexperienced experimenter thinks he has got trypsin or amylopsin safely bottled and hermetically sealed up, all traces of it as an active agent have vanished.

On any point of difficulty arising out of the contents of this book, or in the scientific treatment of cancer cases, he is prepared to reply, as in the past, to all letters of a

genuine character (“ plants” have not been lacking), provided that sufficient stamps, or, if from abroad, an international reply-coupon be enclosed. Cables and telegrams, if replies be desired, must have such replies prepaid. The writer does no treat any cancer cases himself, and in past years also he has not done so.

CHAPTER VIII
TWO RECENT CASES

The York case of recurrent sarcoma was published in a scientific and medical journal, which is not readily accessible. To the editor of the *Journal of the Royal Army Medical Corps,* Major W. H. Horrocks, R. A. M.C., I am indebted for permission to republish Captain F. W. Lambelle’s report to the War Office, and my acknowledgments and thanks to him and to my friend Captain F. W. Lambelle, R. A. M. C., may be expressed here for their consent to the republication with the original photographs. The report, which speaks for itself, was published, with three photographs, by the War Office of Great Britain in the *Journal of the Royal Army Medical Corps,* No. 3, vol. xiv., March, 1910, pp. 316-318. It is as follows:

> A.—A FURTHER REPORT OF THE CASE OF PENSIONER W. DU T., LATE DRUMMER, NO. 5669, PERMANENT STAFF, 4TH BATTALION WEST YORKSHIRE REGIMENT, BY CAPTAIN F. W. LAMBELLE, ROYAL ARMY MEDICAL CORPS, WITH THREE PHOTOGRAPHS.

Admitted to Military Hospital, York, on January 11, 1909, suffering from sarcoma of left upper jaw

Operations for the removal of the growth were performed on January 12, 1909, and on March 2, 1909.

Section l* of the growth submitted to the Royal Army

*Scientific accuracy demands a correction here. In the copies of the official documents relating to the case, on March 2, 1909, Captain Lambelle writes of sending “ a pathological specimen”—

Medical College on March 2, 1909, was found to be round-celled sarcoma.

Recurrence occurred soon after the second operation, infiltrating the lymphatic glands of the face, and extending by continuity of periosteum to opposite alveolar process and along orbital plate and nasal process of same side, when further operative treatment became impracticable.

After special request Squire's trypsin and amylopsin were supplied for the treatment of the case. On July 15, 1909, all the recurrent growths were necrotic, and were in process of being cast off, firm, healthy granulations being left behind. The treatment has been continued until September 15, 1909, on which date the patient showed no sign whatever of malignant growth. All the necrotic tumour has been cast off; the mouth is clean and healed. The patient's general condition has also greatly improved, though he is still debilitated from his long illness, and requires hospital treatment. A small plastic operation may be necessary to close the sinus in the cheek; this, with nutritious dieting and massage, will, I believe, complete the cure.

F. W. Lambelle, Captain, R. A. M.C.

York,
September 27, 1909.

The writer feels called upon to say that the permission to republish this report is dated July 30, 1910, and that at this date, more than a year after the slough of the dead tumour was lifted out of its bed, the patient was still free from any trace of malignant disease.

A later letter from Captain Lambelle, dated October 17, 1910, with two further photographs, describes the patient as quite well, free from malignant disease, and "cured."

(footnotes from page 209)
" a portion of a tumour of the superior maxillary bone." Under date March 6, 1909, the diagnosis of round-celled sarcoma is given by the official pathologist of the Royal Army Medical College, and the words are added: "A stained specimen is sent by this post."

The last photographs were taken on October 15, 1910.

From the copies of the ten charts of this case kindly given me by Captain Lambelle, I take the following notes: "Treatment began, March 8, 1909; stopped, September 17, 1909; recommenced, January 14, 1910; finally stopped, March 24, 1910; 120 injections in all given. August 9, 1909, small slough removed from floor of orbit. August 12, 1909, a large slough removed from the mouth from situation of tuberosity of maxilla. August 24, 1909, mouth now clear of sloughs, is quite clean, and healing rapidly. On October 28, 1909, plastic operation to close small aperture in face." Captain Lambelle last wrote to the writer regarding this case under date November 23, 1910: "I saw du T. on Saturday morning last [November 19], alive and well—'Never better in his life,' he said—for he had come to bid me good-bye on my leaving the hospital at York." In view of the publication of this book, the writer wrote to the patient referred to above, under date September 11, 1911. The reply came with the date September 14, 1911, from the patient himself, and on this date he was alive, well, and not suffering from sarcoma of the jaw. The six photographic illustrations (Figs. 6 to 11) relate to this case.

Captain Lambelle's success in three out of his four cases to date was due, in my opinion, not at all to any help of mine, for as a fact I knew nothing of his cases until the treatment in each had done its work, but to the circumstance that he had studied the matter theoretically and practically. He knew from his own observations on my material, as well as from the study of my scientific memoirs, all about "the irresponsible trophoblast. "Unlike Bainbridge, it never occurred to him to say: "The irresponsible trophoblast does not concern us here."

Were he asked, he would undoubtedly say: "On the contrary, since cancer is asexual generation or trophoblast, in its treatment, all question concerning the irresponsible trophoblast do concern

us." To this I would add, to a far greater degree than the use of the knife upon a living "irresponsible trophoblast" or cancer. The critics have, by common consent, been silent all along concerning the scientific grounds of the enzyme treatment of cancer. But to the scientific man first and foremost comes the question: "What is your attitude towards scientific general principles?"

It is really remarkable with what persistence the identity of sarcoma and carcinoma is denied by the medical profession—almost without exception. Since the writing of this book was finished this supposed "fact" of the absence of identity has been affirmed from the medical side. Doubtless the writer will hear again and again the old, old fable, that sarcoma and carcinoma are very different things, and that the York case was *only* one of sarcoma—of a very malignant type.* In anticipation, it may be pointed out that, apart from other considerations, † the course and outcome of the York case were exactly in parallel with those of the Naples case of inoperable carcinoma (epithelioma) of the tongue, for among other things, here as there, the remains of the tumour finally shelled out "like the kernel of a nut." The like is true of Lambelle's unreported case

*The charts demonstrate this abundantly. Professor Friedrich Henke describes the "small-celled round-celled" sarcoma as one of the most malignant of the sarcomata (*Mikroscopisch Geschwulstdiagnostik,* Jena, 1907, p. 107).

† As long ago as 1904, I detected under the microscope the "epithelial cell" among the tumour-cells of several slides of sarcomata, purchased from two Leipzic dealers. This find was one of the things which led me to the conclusions of the mimicry of the malignant tumours, and of the fundamental identity of carcinoma and sarcoma.

of "encephaloid" cancer of the breast, except that here the remains of the tumour, being more deeply seated, did not shell out, but presumably became encapsulate (see Appendix L). The only real differences between these two successful cases and the recurrent "round-celled" sarcoma in York were that in them there was no microscopical diagnosis; but in fact something of infinitely greater scientific moment was present—a stereo-chemical diagnosis. The art—not science—of modern medicine would be no more rational than the "medicine" of Macbeth or Romeo and Juliet, unless it were based in such sciences as chemistry, embryology, etc.

B.—THE UPPINGHAM CASE OF CANCER OF THE STOMACH, WITH EXTENSIONS TO THE LIVER.

This Case is a present unpublished, and, therefore, I do not propose to do more than give the briefest account of it, and only in order to use the figures concerning the injections employed. The physician informed me some time ago that he intended to publish it in due course. At the same time he did not allow me to examine the charts again, though I had often seen these. They were asked for in order to compute from them the number of units of trypsin and amylopsin injected, but the figures of these were obtained actually from other and reliable sources. This case of cancer in a man of middle age was diagnosed surgically as inoperable, presumably because of the involvement of the liver after an exploratory laparotomy by one of the chief surgeons at St. Thomas's Hospital, London about the end of July, 1908. The man was sent home to die. Apparently in November, 1908, the treatment was commenced. The charts taken regularly were sent to me from time to time, and I may mention that for a long time they showed a temperature reaction after the

injections. From time to time information as to the procedure employed by Captain Lambelle was furnished for use in this case. Beginning November 11, 1908, the injections of trypsin and amylopsin were continued until August 18, 1909, and they were then stopped, not having been resumed since. In this period there were injected at least 63,000 tryptic units and 94,000 amylolytic ones. This amount is similar to that used in the case of the York pensioned soldier, and it much exceeds the total employed at the Middlesex Hospital, not in one, but in nine cases. Under the date August 5, 1910, there came the intimation, from a friend who had just visited him, that the patient was still alive, and that on the above date it was "now exactly two years and one week since the abdominal incision was made, and the case pronounced by Mr. Battle as one of inperable carcinoma of the stomach." Looking back over the history of this case, I feel bound to say, that while the numbers of unites of trypsin and of amylopsin were such as might be considered adequate, the administration of the amount was spread over far too great an interval of time (nine month).

The above opinion was written in August, 1910. Soon afterwards the patient developed a more extensive albuminuria, which had troubled him for some little time. He died about the end of September, 1910. Another physician called in diagnosed "Bright's disesase," which was the scientific opinion I had formed independently, but on his return home his own physician declared the mischief to be cancer. There was, so I understand, no post-mortem, the symptoms in the latter months were not those usually associated with cancer of the stomach and liver, but of Bright's disease. It is now an old opinion of the writer's, frequently stated to

medical correspondents, that many cancer patients, even if cured of cancer, would sooner or later fall victims to diabetes or Bright's disease. In my scientific opinion these are both diseases of the liver, and for diabetes the illustrious physiologist, Claude Bernard, published this conclusion more than fifth years ago.*

It has been written: "We do not underestimate the value of temporary relief; but even accepting all the statements of its advocates as absolutely trust worthy, it is still conspicuously inferior in this respect to surgery." This is, presumably, a reference to the enzyme treatment of cancer, which in years now past, on the testimony, published and unpublished, of numerous physicians in all parts of the world, has given great and continued relief from pain and suffering to the victims of cancer in cases where every device of surgery had failed. If any man living know the equal of adequate injections of trypsin and amylopsin in this respect, let him produce it. These ferments, trypsin and amylopsin, have not—at least in the visible universe—their superiors, or even their equals, as means of relief in cancer. Regarding the above citation, the matter can be carried a little further. Surgery has never once succeeded where trypsin and amylopsin had failed. On the other hand, as witness the published York case, trypsin and amylopsin have succeeded where surgery failed—as it die twice in this case.

CAPTAIN LAMBELL'S COURSE OF TREATMENT.

1. *Diet*.—Avoid acid-forming foods. No beef, no wine, no common salt, no vinegar. Stimulants, when necessary, brandy or whisky. Reduce nitrogenous food

*For some of the other reported successful case *vide* Appendix G, 273.

to a minimum consistent with keeping up the bodily strength. Diet recommended: milk, fresh vegetables, bread, butter, cheese, with eggs, chicken, and the lighter sot of fish in moderate

amount. The idea being to keep an excess of alkalies in the blood—the internal administration of calcium lactate aids the above diet in this respect.

2. *Oral Administration*.—I give no ferment preparation by the mouth at all. Calcium lactate is the only drug necessary.
3. *General Management*.—As usual in hospital.
4. *Local Treatment*.—None, unless there be an inflamed or ulcerating skin area or opening. Hot boric fomentation, changed four hourly. Irrigation with potassium permanganate lotion or weak iodine lotion, where there is foul discharge. Strong antiseptics—*e. g.,* mercuric salts and carbolic acid, etc.—are to be avoided, as interfering with the - action of the ferments. On no account may the case be subjected to treatment with radium or Röntgen rays.
5. *Hypodermic Treatment*.—This is the essential part. Injections used are trypsin of 1,000 units of tryptic activity per cubic centimetre, and amylopsin of 2,000 units of amylolytic activity per cubic centimetre.. The injections should be given daily, if possible. The injection must not be made into the cancer itself. The injections are given intramuscularly, deeply into the muscles of the buttock, or about the iliac crest or in the flank. Abscess frequently follows injections into the subcutaneous tissues. In some hundreds of injections I have never once had an abscess. I always give equal quantities of the above two preparations. I never give the trypsin without adding more amylopsin. The full dose has been 1 ampoule of trypsin, or 1 c.c. + 1 ampoule of amylopsin, or 1 c.c. In units of activity, 1,000 units of tryptic activity + 2,000 units of amylolytic power. After an injection I always massage the part for one minute, so that the injection does not lie in a pool, or abscess may follow. A local analgesic is unnecessary. Cleanse the part before injection with spirit solution of biniodide of mercury, 1 in 1,000, and seal the puncture with rubber plaster.

The foregoing directions for treatment have my full approval. One or two things may be added to them. With slight alterations, the "General Directions," drawn up by the writer, and amended from time to time in 1906-07, in most respects still hold good. While never regarding the oral treatment as more than an adjunct to the patient's digestion—but a valuable one without the slightest influence upon the cancer—I see no objections at all—but advantages—in the use of calcium lactate, suggested by Captain Lambelle. It has been my opinion now for more than four years that it was of the utmost importance that each and every trypsin injection should contain much amylopsin. It seems best to follow the procedure adopted by Captain Lambelle, and to use two separate injections of trypsin and amylopsin. These should never be of less potency than 1,000 units of tryptic activity, and 2,000 units of amylolytic power. The trypsin injection should never be given without at the same time a corresponding amount of amylopsin; and, if this be done, the necessity of using amylopsin alone will, I imagine, disappear. On occasion the full dose of 1,000 tryptic and 2,000 to 2,400 amylolytic units may, in the judgment of the physician, be increased, provided that the rule of two amylolytic units for each tryptic unit be followed strictly.

The injection of amylopsin (2,000 to 2,400 units per cubic centimetre) may, in the judgment of the physician, be given without the injection of trypsin, for it is only the use of trypsin alone which causes bad symptoms. It must be stated distinctly that the dose of 1,000 units of

trypsin + 2,000 to 2,400 units of amylopsin is not to be understood as one which will suffice for all cases. In very malignant cancers and sarcomata, more especially in recurrent cases, it may be necessary to exceed, even to doubt it. This may be expressed briefly in the words, "Give the most you can give, and as often as you can give it, with due regard to the constitutional effects produced. Do not, however, rely upon preparations, which are not guaranteed to possess a tryptic strength of 1,000 units per cubic centimetre, or an amylolytic power of at least 2,000 units per cubic centimetre. In the eyes of its discoverer, the enzyme treatment of cancer does not consist in the use of preparations of less guaranteed strengths than these." Judging by the charts of Captain Lambelle's latest case, it is not necessary in all cases to give daily injections for long period, for in the first four months of treatment the total number of injections did not exceed sixty, within sixteen more from the middle of July to September 17.

There are certain points in the treatment which call for special notice. The injections, hypodermic or intramuscular, are the essential items. The chief—possibly the only—uses of oral preparations in the treatment are the improvement of the patient's digestion and metabolism. It must be recalled that Dr. S. Pinkus, in his experiments of introducing large doses of pancreatic ferments into the blood of a healthy dog, could note, as the sole visible effect, increase in weight on the part of the animal. In treating cases of cancer the physician should not forget this fact. As I and others have noted again and again—and the like observation has been made by Captain Lambelle—it is one thing to introduce pancreatic ferments into the blood of a healthy man, and quite another to do the like in such a person, afflicted with

malignant disease. In the first instance, always provided that scientifically prepared and pure ferment preparations were used, there would be no obvious reactions, no rigors, and no rises of temperature. At most there would increase in weight, due to increased and improved metabolism, and a sense of well-being on the part of the "patient." But, again, what enormous differences occur when the patient is suffering from cancer! Reactions, obvious ones, may then be looked for with certainty, and these alone would, in my opinion, be a sufficient diagnosis of cancer, if such complications as tuberculosis could be excluded. Let it be repeated, and with emphasis, that small and weak doses of injections are useless. Even as I write these line there comes a report of violent reactions from even the injection of five drops of strong trypsin* in a case where large masses of cancer were present. The small, almost insignificant, amount of trypsin in use here was attempting a task beyond its powers-to wit, the complete breaking up of the cancer-substance it had attacked. With a much large dose, given along with an equal amount of strong genuine amylopsin, there would be present sufficient of each of the ferments—trypsin and amylopsin—to break up the portions of cancer attacked completely into simple harmless products, and such violent effects would not, in my opinion, be encountered.

I have always maintained that, were I treating cases, my own treatment would commence with the injection of, say, 1,000 units of trypsin and 2,000 units of amylopsin,

*An interesting commentary upon Bainbridge's statement in his report (p.7): "From this it will be seen how absurd were some of the earlier claims of "cures," as well as the strange symptoms and "terrific" results from the small doses employed." In this case, in Chicago, one of the strong Fairchild injections employed by Bainbridge was in use on August 12,1911.

mixed on injection; that is, I should employ Captain Lambelle's usual procedure from the start. I should not willingly reduce the dose of trypsin, but rather, if bad effects were noted, increased the amount of amylopsin, even double it. With such doses as these not many injections—not half a dozen—would be exhibited before the injection would be followed shortly by a rigor, which soon passes off, if the patient be in bed. Later in the day—in my experience from 6 p.m. to 9 p.m.—there would be a marked temperature reaction up to 103ºF., or even sometimes higher. The patient will demand, and should have at all times, abundant water, or barley-water, to drink. The curious feature of this rise in temperature, as I have seen it, is that the skin is dry, and not bathed in perspiration. Of course, the pulse along with it is very much quickened. In fact, this treatment would appear to place great demands upon the heart, and it is my own opinion that wherever possible the patient should receive the injections in bed, should be kept there during such temperature-reaction, and as before stated at all times be kept as quiet as possible, refraining from all avoidable physical exertions. In Captain Lambelle's cases it was noted by him that the effects of the injections—*i.e.,* the constitutional symptoms—lasted from eighteen to twenty-four hours. On the average he gave injections every other day. At times the amount of injection, the number of units, was decreased to one-half or one-quarter of the usual amount of 1,000 tryptic and 2,000 amylolytic units. Also, as I conceive it, the injections should, if the patient can stand such a course, be exhibited oftener than every other day—as often as four,

five, or six times a week—if such "heroic" treatment be demanded by the case under treatment. Probably the case—a very desperate one—of the pensioned fireman, described in connection with the "liquefaction of cancer," failed, not on account of the large amount of tryptic units given daily (to wit, 2,000), but because along with these at least 4,00 amylolytic units were called for, but not exhibited. From the phenomena noted in this case and in two of those treated by Captain Lambelle, it would appear that the objective to be aimed at in the enzyme treatment of cancer is the liquefaction of the main tumour or tumours. With this in view, it should be the purpose of the physician to give as large and as strong injections of the two ferments in the proper proportions as the patient can endure. As Captain Lambelle remarks in one of his letter: "Give the most you can, and as often as you can, with regard to the constitutional effects produced." The self-evident fact that very strong injections should be used has been stated already by Dr. P. Tetens Hald in the *Lancet* as long ago as 1907.

There remains another serious problem which, I confess, it is beyond my feeble powers to solve. It is this: "How shall the physician be provided with only the preparations upon which on all occasions he can rely?" I have known my own printed "General Directions" to be used along with preparations, which in my own experiences, as well as in those of others, had no action worth speaking of upon milk, and which did not at that time contain an appreciable amount of amylopsin. There was no excuse for this, as these directions not only gave full particulars concerning genuine preparations of trypsin, amylopsin, etc., but also a list of places and addresses throughout the world where these could be obtained. These—the Fairchild Preparations—were absolutely genuine; but—

as now recognized by me, as a rule not free from exception—they were not in former years strong enough for their work. In various quarters of the world worthless preparations of trypsin and amylopsin have been offered for sale, at times extensively advertised, and employed in cases of cancer, to the serious detriment of the scientific enzyme treatment of cancer. The problem is—

and it is not one for the scientific investigator as such—How shall this sort of happening be prevented in the future? It is an extremely grave matter, for human lives are at stake in this treatment. One of the chief medical newspapers in Great Britain, the *Lancet*, has as one of its features—and a most excellent one it is—a laboratory for the making of scientific examinations and the drawing up and publication of reports upon pharmaceutical products offered for sale and for use in medicine. To my knowledge, none of the injections employed hitherto in the treatment of cancer have been reported upon by this laboratory, and in default of State control and State monopoly the sooner and the oftener such examination and report upon various pancreatic preparations be made the better for mankind and for science.

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CHAPTER IX

ON THE RELATIONS OF TRYPSIN AND AMYLOPSIN

When one reads some of the things which have been written concerning trypsin in some medical journals, as well as in American daily newspapers, one might think that our present knowledge of this and other ferments dated back to the time of Moses, or that was embraced among the laws of the Medes and Persians. Actually, of course, a knowledge of any real functions of the pancreas gland is not yet sixty years old, and the name "trypsin" goes no further back than 1876, when it was bestowed finally on one of the pancreatic ferments by the investigator, Wilhelm Kühne, of Heidelberg. The name "amylopsin" is of still more recent origin (Wingrave, "Amylolytic Ferments," *Lancet*, 1898, i., p. 1251). The latest phase of our knowledge will be found in the third edition of Oppenheimer's book, "Die Fermente," in which there is a table classifying ferments into tryptases, amylases, etc. Reference should also be made to the circumstances that some investigators have been of opinion that trypsin was not a single ferment, and that a "vegetable trypsin" had also been recognized. Now, it has long been the writer's experience that no useful end was served in scientific research by diving and subdividing things, so as to increase their number; on the contrary, that the unity or organic nature was always

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to be aimed at, and that, as William of Occcam long ago laid down, *Entia non sunt multiplicanda.*

In the following lines something must be said of two aspects of the writer's studies of pancreatic ferments and their uses. There are not many things in my research career which fill me with greater satisfaction than the line of reasoning and the conclusions as to the place of amylopsin in the enzyme treatment of cancer. Amylopsin itself, no matter what the doses be, will not cure cancer; but it cannot be dispensed with when pancreatic ferments, such as trypsin, are employed against malignant disease. If trypsin had been as successful hitherto in its mission in the treatment of cancer as amylopsin, there would be many living who are now departed, and the literature of medicine would contain fewer "scientific" leaders upon "cancer booms" Amylopsin was introduced into the enzyme treatment, not because of the discovery of any action upon cancer cells, and no because it was "thought 'to digest' the dead cancer cells" (Bainbridge's Report, p. 6),but because the conclusion was reached, upon purely embryological grounds, that sufficiently potent injections of amylopsin would remove all the bad symptoms leading up to something identical with "the vomiting of pregnancy" and with eclampsia itself, which had arisen in very many cases in England, Italy, France, and elsewhere. In the very first case in which it was "tried," as also in countless cases since that time, amylopsin always removed these symptoms. But it is a

curious commentary upon what has been termed the "conservatism" of the medical profession, that although injections of this enzyme were recommended for the treatment of eclampsia, not a single case is known at present to the writer where this was employed. So much for the place of science in "medical science."

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When, in the early days of December, 1904, the writer first came to recognize the import of "the secretion of that important digestive gland, the pancreas," in the medical treatment of cancer, at once he became alive to the necessity of keeping a scientific eye upon all the four supposed ferments described in its secretion. The import of trypsin was quite clear from the first moment. Not many months elapsed before the place of amylopsin could be assigned to it, and on scientific grounds, which have never been impugned. Rightly or wrongly, but in accordance with the scientific plan of avoiding all unnecessary multiplication of causes, the separate existence of a milk-curdling ferment in the pancreas gland was rejected. Finally, no function in the treatment could be found for a fat-emulsifying enzyme. It may have its uses, but certain discoveries known to me on this point were the work of another, and not of myself, and they are still unpublished.

Now, from the start it appeared very unlikely that a gland, like the pancreas gland, should secret four fundamentally different ferments. It was known, moreover, that the relative amounts of these depended largely upon the kind of food upon which the animal was fed. Nitrogenous foods led to the production of much trypsin; a starchy diet increased the relative amount of amylopsin. These considerations, along with the chemical facts concerning the action of amylopsin upon starches, led the writer, in the closing months of 1906, to certain conclusions as to the relations of trypsin and amylopsin. They were not published, because during that and the preceding year the writer had furnished the transparently anonymous scribes of certain arguments and criticisms—there never were any such—but for their "opinions" and powers 15

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of ridicule. However, on January 18, 1907, the writer, in a letter to an old fellow-student, a consulting and hospital physician in London, wrote as follows: "As to trypsin and amylopsin, this is private, lest….The real original ferment of the pancreas gland, in my opinion, is trypsin. Amylopsin is a modification of trypsin. The latter probably acts by adding 2 molecules of hydorxyl, the other 6. Assuming T (trypsin) to be the substratum, to which these molecules are attached, the two things would be like this (here there was a rough diagram in the letter). How the tryspin molecules get slung together to form amylopsin is more than I can say; but it does not seem to me *a priori* probable that a gland should form four fundamentally different ferments." At the time, although, since "science is prevision," so much could be foreseen, the steps needed to establish this in fact were not obvious. Later on, from the avidity with which the leucocytes appeared to seize upon amylopsin, some further slight evidence seemed to be presenting itself, but the mystery did not clear up. Then came the paper by Dr. P. Teten Hald,* and this contained some surprising things concerning the two amylopsin injections on sale. It may be stated here, that the reason why the writer had insisted that the amylopsin injection should be free from trypsin was, because it had been found impossible to persuade the manufacturers to increase the amylolytic strength of their trypsin injections without diminishing the strength of trypsin. Owing to this, it appeared that after some weeks of treatment any injection of trypsin was not as well borne as previous.y Dr. Hald tested two of

*Hald, P. Tetens: "Comparative Researches on the Tryptic Strength of Different Trypsin Preparations, and on their Action on the Human Body," in the *Lancet*, November 16, 1907,.pp. 1371-1372.

the amylopsin injections as to their supposed freedom from trypsin, and found that in fact they both, from different makers, showed pronounced tryptic activities. On p. 1375 he writes:

"The two amylopsin preparations which I examined were stated to be free from trypsin. They behaved, however, with respect to the second phase, just as if they were genuine strong trypsin preparations, as they brought about a very pronounced decomposition of the glutin into lower nitrogenous compounds. The doubt that was aroused by the surprising result of the gelatin experiments was therefore solved. Unquestionably, the amylopsin preparations contained abundant quantities of trypsin, and their importance for the treatment could not, if they really have any such importance, be due to their freedom from trypsin."

While accepting Dr. Hald's facts, at that time the writer could not account for them, any more than he could then explain certain happenings in New York with some of the first-made injections of amylopsin. Here the physician had found that the injection amylopsin intensified the very symptoms which it was supposed to counteract. The only supposition then possible was that he had by mistake injected trypsin instead of amylopsin, the tubes and boxes then in use being alike.*

For the sake of accuracy, it should be added that long before the publication of Dr. Hald's paper the writer had from time to time tested the injection of amylopsin sent out from New York as to the existence of tryptic powers in it, but invariably with negative results. The number of tests carried out by Dr. Hald, and the period of time over which these extended, were not sufficient

*To avoid such mistakes, it is most important that the two injections should be put up in differently coloured ampoules.

to warrant the conclusion that all the ampoules of amylopsin at that time sent out as "free from trypsin" did, in fact, contain much trypsin. As a fact—so I am informed—the amylopsin injections now on sale cannot be free with certainty of all traces of trypsin.

In March, 1910, in the course of a correspondence with Mr. P. W. Squire, of Messrs. Squire and Sons, chemists on the establishment of the King, certain facts transpired which, by the kindness of Mr. Squire, Iam permitted to publish in his own words. He wrote: "With regard to mentioning my name in your paper, I have no objection to this, providing you confine yourself to a question of fact, and you must not commit me to any theoretical view of the subject. The facts as I have them are as follows: Sterilettes amylopsin (Squire) were being prepared, and a batch of the liquid was examined for its tryptic and amylolytic values, which were respectively found to be—trypsin=500; amylopsin-2,400. This was on July 28, 1909. On January 30, 1910, the liquid was again examined; the tryptic value then equalled 1,250, and the amylolytic value 1,200." It may be added that Mr. Squire's figures relate to the units of tryptic and amyloytic activity set up by the late Sir William Roberts.

I regard these facts as a scientific proof of the truth of my conclusion of January, 1907, that "amylopsin is a modification of trypsin." The facts recorded seem to indicate a decomposition of some portion of the amylopsin of July, 1909,. into trypsin by by January 30,

1910. Any mistake in the assays does not appear possible. The find also throws the needed light upon the discovery by Dr. Hald of trypsin in two different amylopsin prepara-

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tions, sent out as pure amylopsin. Of course, it has still other bearings; upon the specificity of ferments, for instance, and upon the relations between the leucocytes and amylopsin in the enzyme treatment of cancer and tuberculosis. Amylopsin might be regarded as the ferment-food of the leucocytes, in extension of the view previously expressed by the writer in the *Medical Record* that amylopsin was the medium in which the leucocytes acted. By the use of the scientific imagination possessed by the writer, and of which professor Leo Loeb recently wrote in the *Medical Record* (June 25, 1910, p. 1086; see Appendix E, p. 267), he considers that it is highly probably, not only that the leucocytes can convert amylopsin into an intracellular tryptic ferment, but that they can transform it into an inverting enzyme. The interesting subject may be left with the remark that once again it is a confirmation of the scientific truth of the words of Pasteur, that "Science is Prevision."

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CHAPTER X

A PUBLISHED TEST OF "THE TRYPSIN TREATMENT OF CANCER"

Like the publication by Dr. Bainbridge, the contribution* of Messrs.. Ball and Thomas professes to be a "scientific report." As already stated, unlike the former document, the publication of the latter does give information—such that a searching scientific investigation can be made into the details of the procedure adopted. It must be recalled that, in the words of this report, "Two cases of carcinoma were placed on trypsin treatment in My, 1906, in the Cancer Wards of the Middlesex Hospital, but with negative result, there being no improvement in the patients, nor was the progress of the growth influenced by the trypsin injections." Here the authors omitted to notice two significant facts: of these cases, one had a single injection, and the preparation used had at that time been found to be inert in ferment powers by others as well as by myself. These cases are Nos. 1 and 2 of the report. It is possible—though I should not care to guarantee it scientifically—that in Case 1 as much as 100 Roberts tryptic units were in all exhibited, and in Case 2 certainly not more than ten such. There is no mention of any employment of

*Ball, Walter, and Thomas, E. Fairfield: "The Trypsin Treatment of Cancer," in *Archives of the Middlesex Hospital*, Sixth Report from the cancer Research Laboratories, London, May, 1907, pp. 18-34.

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amylopsin, active or inert. The other nine cases were treated with the Fairchild injections, and every ampoule of trypsin and of amylopsin was tested qualitatively, not quantitatively, before use. It was found that each and every ampoule had some strength—how much, apparently, being regarded as a detail of minor importance. Quinine is said to cure malaria, but to-day no physician or surgeon would anticipate any "improvement" from the use of preparations containing a small amount of active quinine, irrespective of the amount per cubic centimetre and of the dosage. I

pass over the previous histories of the cases, for the good reason that the report is practically silent upon these points. One remark on p. 33 may be noted, viz., that—

"The length of time during which the patient were under observation previous to the commencement of treatment is of importance. For in large measure a prolonged period before commencement of treatment signifies an acclimatization of the patient to hospital surroundings, and a greater equanimity towards the possible value of any particular treatment in view of the many failures with which the 'patient's lengthened stay in hospital has made him acquainted."

The enzyme treatment is a stereo-chemical—not a hypnotic one! This argument, if of any scientific value at all, would apply to the surgical dictum of "early operation" in cancer also, Moreover, it ignores the fact that the cancer also "acclimatizes" itself, not to add that it grows.

The injections used had per ampoule, without any loss for qualitative tests, the following values: Trypsin "regular," 125 units; trypsin "special," 250 units; and amylopsin, 100 units. The maximum dose given in most cases was 15 minims, or ¾ ampoule; never 40 minims, as mentioned as the general dose then in use in the "Direc-

tions," which (?) "were rigorously carried out" (p. 18). The strongest dose of trypsin given, and but for a part of the time, was 188 units—of amylopsin, 75 units. Had the "General Directions" been followed, the average dose would have been : trypsin, 500 units; amylopsin, 200 units. That is to say, the dose was never even half enough of either injection, according what was them known. In the light of Captain Lambelle's results, the dose of 15 minims of trypsin was less than one-fifth of what it should have been, and the amylopsin, which should have been given along with the trypsin, was one-twenty-sixth of the normal. In other words, if the "special trypsin" had been in use all the time, the present daily dose of trypsin would have been reached in the injections of more than five days together, and the amylopsin daily dose in some twenty-six days. In the following an estimate is made of the number of units of trypsin and of amylopsin injected in each case, the figures of the report being used for the calculations.

TABLE 1

Case.	Days treated.	Units Trypsin.	Units Amylopsin.
III.*	24	938	625
IV.	40	2,500	20
V.	68	3,750	1,200
VI.	26	1,000	600
VII.	71	3,575	1,700
VIII.	71	2,250	1,600
IX.	122	7,625	4,500
X.	77	4,000	2,050
IX.	118	9,250	2,150

*Case III. Is stated to have been a "carcinoma of the Kidney," and after death the tumour was found to weigh 70 ounces—that is 4 pounds 6 ounces—the size of a respectable joint of beef. Could it be regarded as a scientific experiment, seriously

In Table 2 the number of doses given in each of the nine cases during the whole period of treatment is given. These doses are, of course, those which at the present time have been given in York Uppingham, London, and possible elsewhere.

TABLE 2.—SUMMARY OF DOSES OF 1,000 UNITS TRYPSIN AND 2,000 UNITS AMYLOPSIN GIVEN IN THE NINE CASES.

Case.	Trypsin.	Amylopsin.
III.	minus 1	1/3
IV.	2½	1/100
V.	nearly 4	3/5
VI.	1	1/3
VII.	3 ½	minus 1
VIII.	2 ¼	minus 1
IX.	8	2 ¼
X.	4	1
XI.	9 ¼	1 1/8

Taken together, the nine cases received about thirty-six doses of trypsin and about eight of amylopsin. On an average adequate treatment extending over 120 days, the total trypsin injected would be at least 1,000 x 60 units, or 60,000 units; of amylopsin, 2,000 x 60 units, or 120,000 units. In the nine cases the total number of tryptic units injected, as far as can be determined, was 36,000 units; of amylopsin, 16,000 units. To have made success more certain there should have been injected—of trypsin, 720,000 units; of amylopsin, 1,440,000 units. The

(footnotes continued from page 232)
undertaken, to attempt to digest and liquefy a joint of beef of these dimensions, in twenty-four days or in a blue month, with the minute quantity of 938 tryptic units, which could easily be compressed into a bulk of 1 c.c., or less than twenty drops of water?

points are summarized in the statement that on the average each patient received about one-tenth of the trypsin, and one twenty-second of the amylopsin, which under the directions (which "were rigorously carried out") he should have received. In the newer light of to-day, on an average, the trypsin for each case was on-seventeenth, and the amylopsin one seventy-seventy (1/77), of the amount it should have been. The only scientific facts proved in these experiments on "the trypsin treatment of cancer" were that, examined qualitatively by their actions* on white of egg and on starch, the Fairchild preparations then on sale "were found to be potent."

*Regarding this "test" for trypsin, one who has devoted very many years of his life to the study of the ferments, writes me recently: "Dr. X., for instance, has given wide publicity to a test by which trypsin is condemned or approved by its action upon coagulated egg-albumin, when it is a fact, known to everyone familiar with the chemistry of the enzymes, that trypsin is of feeble action upon boiled egg-albumin, and, indeed, it may be said naturally characteristically so. The enzymes act upon the substances, upon which they are naturally engaged, and native coagulated albumin, which has never received any preliminary or initial conversion by gastric juice, is a proteid which trypsin has never learned to act upon."

CHAPTER XI

THE CRUCIAL TEST OF THE NATURE OF CANCER

In AN ARTICLE UPON CANCER (*Medical Record*, December 4, 1909, p. 940), Dr. Jabez N. Jackson writes of the spending of millions of dollars on laboratories for cancer research, and opines "that the entire lives of many of the ablest and most scientific investigators in our [that is, the medical] profession have been devoted exclusively to this problem." It should have been added, not in such laboratories, or as paid researchers. It so happens that most of my own private cancer studies cover approximately the period of this official investigation of cancer—*i.e*., from 1903 to the present time. Voluminous official reports and statistics have been published in this period, but for all the funds expended upon large salaries and petty researches, amounting to thousands of pounds sterling yearly, no strikingly important fact or suggestion bearing in the least upon the origin, the nature, or the scientific treatment of cancer has come to light.* It was, indeed, recognition of this happening, and of its probable continued occurrence in the near future, owing to entire lack of scientific general principles † in official

*Even the conclusion, based in research, that "carcinoma is common to all vertebrates" forms no exception, for it was enunciated by another investigator in 1895, years before official research commenced.

† According to Sir Robert Finlay, MP., K.C., the celebrated Edinburgh surgeon, Sime, said, in answer to one of his assistants, Annandale, who had asked for a particular direction, instead of

research, which led the writer to throw aside absorbing work on the problems of Heredity and Germinal Continuity, and take up on branch of his studies—cancer, or asexual generation, or trophoblast.

Whether the sum be millions of dollars or not, unquestionably very large amounts—thousand of pounds sterling yearly—have been expended in recent years on cancer research in England alone.* And the result of eight years' of work and "research"? *Chi lo sa!* True, the official researchers and others often speak or write about the "cause" of cancer, as if the "cause" were a legitimate object of their quest, and—in ignorance of the teachings of Carl Ernst von Baer, Emil du Bois-Reymond, and other great investigators—that "causes" are beyond the range of scientific research. †

(footnotes from page 235)

a general principle, " You are wrong. If you get a general principle you can keep right on the whole, and supplement your information as you go along. If you get a particular direction, and take a single turning you are done for ever."

*It should not be forgotten that the cancer researches recorded in this book cost the Carnegie Trust (Universities of Scotland) Research Fund the sum of seventy pounds sterling (£70). Ofthis sum, fifty shillings, the price paid for a certain dog, was lost, owing to the then ignorance of myself and of an Edinburgh surgeon that chloroform is fatal to dogs. Fifty pounds was expended in the wages of a youth being trained to do microscopical work (preparation and staing of section) for me. When trained, he had to accept another situation! So that the actual balance-sheet of these researches upon cancer works out to the magnificent sum of seventeen pounds ten shillings.

† The latest pronouncement of official cancer research is contained in ""The Ingleby Lectures on Advances in Knowledge of Cancer" (the *LancetI,* June 10, 1911, pp. 1596-1597). It concludes as follows: "What had to be found was, how to imitate the process of natural healing, and how not to hunt on false tracks after curative sera on the analogies of diphtheria antitoxin or cytotoxic sera; till then the surgical treatment must remain a rational and the only treatment; but

in the end it ought not to be beyond human ingenuity to find out and imitate the mechanism of the natural healing of cancer." This latter

The true author of the theory of "embryonic rests" as the source of tumours, malignant and benign, was the embryologist Remak.* Later on his views were adopted by the pathologist Cohnheim, and t0-day the theory is invariably, but erroneously, attributed to the latter, under the name of "Cohnheim's theory." Following in his footsteps, some researches at times regard cancer-cells of this, that, or the other organ, skin, mammary gland, liver, etc., therby implying, if not stating, their somatic nature. Well and good. If cancer-cells be "embryonic" or somatic in nature—if they be skin-cells, or liver-cells, or breast-cells, † etc.—then it follows that their albumins must be of the same nature as those of the normal somatic or embryonic cells from which presumably they arose. This I deny point-blank, and, as the scientific man is bound to do, I will shortly give some of the reasons. In passing, be it remarked, nothing

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(footnotes from page 236)

is exactly what the enzyme treatment of cancer or malignant disease professes to do, neither more nor less. If words have meaning, "natural healing" signifies nature's method, which is all the scientific investigator is concerned with. The mere denial of this, or the use of inert trypsin to test its truth, is not scientific evidence.

*Remak, Robert: "Ein Beitrag zur Entwickelungsgeschichte der krebshaften Geschwülste," in *Deutsche Klinik*, 1854, vol. vi., p. 170.

† My old opponent, Mr. W. Roger Williams, F.R.C.S., is one of these. In the *Medical Record* of February 9, 1907, (p. 237), he implied that the cells of a malignant tumour of the pancreas gland could secrete, not merely trypsin, but also amylopsin and lipase. On which I suggested that in a universe in which this could happen it would not be surprising to learn "that some cancer-cells produce bile or excrete urea, or that in cancer of the breast the tumour-cells, true to their (supposed) origin from mammary-cells—the mythical 'tumour germs' of my opponent—actually go the length of secreting—milk!"

could reveal more distinctly the fundamental divergence between "Cohnheim's theory" of neoplasms and embryonic rest—mythical structures which the practical embryologist never sees—and my theories of the origin and nature of cancer.

"If a doctrine be challenged," said Pasteur, "it happens seldom that its truth or falsehood cannot be established by some crucial test. Even a single experiment will often suffice either to refute or to consolidate the doctrine." By " a single experiment" Pasteur meant a single scientific experiment. A hundred experiments—or even a hundred thousand—of the sorts given by Dr. Bainbridge (First Scientific Report) would not be crucial in any sense to a Pasteur.

Now, the doctrine of the asexual (trophoblastic) nature of cancer has been challenged, although no scientific evidences of any kind have ever been adduced against its truth by official cancer researcher, ex-researchers, anonymous leader-writers, newspaper scribes, or medical men. Of course, the non-existent evidences against its truth cannot be produced, no matter how often or how urgently they be demanded. This doctrine of the asexual (trophoblastic) nature of cancer, however, as a scientific one, falls into line with those referred to by Pasteur; for it happens that its truth or falsehood can be established by "some crucial test"—by a crucial test of the severest scientific character. This natural test has not as yet been applied to this doctrine of the nature of cancer, even by the writer, who with Pasteur believes that "science is prevision." He has never yet

seen with his own eyes that which he now challenges the whole array or researchers and writers—the pathologist, the official researchers, and the Executive of the Imperial cancer Research, London—to refute. If, after due

scientific investigation, published, unlike many other things, with the scientific experiments and evidences—if after this any many deny the truth of what is about to be affirmed on the word of a scientific investigator of nearly twenty-nine years' standing, then it will be the time for the writer to make for himself the crucial test; and this shall be done, and the results published, as soon as the necessary material has been obtained.

In Pasteur's lectures* one may read:

"How can one avoid, for example the assumption that corresponding to a dextro-rotatory body there must be a lævo-rotatory body, now that we know the cause of the dextro- and lævo-rotatory character? That would be to doubt that an irregular tetrahedron had an enantiomorphous image, or that for a right-handed screw there could be a corresponding left-handed screw, or that a right hand was matched by a left hand. Therefore the elementary constituents of all living matter will assume one or the other of the opposite asymmetries, according as the mysterious life-force which causes asymmetry in natural bodies acts in one direction or the other. Perhaps this will disclose a new world to us. Who can foresee the organization that living matter would assume, if cellulose were lævo-rotatory instead of being dextro-rotatory, or if the lævo-rotatory albumins of the blood were to be replaced by dextro-rotatory bodies? These are mysteries which call for an immense amount of work in the future, and to-day (1860) bespeak consideration in science."

(1) It is, of course, a truism to state that the normal or somatic albumins are lævo-rotatory. (2) In the pancreas gland they form for themselves the wonderful

*Pasteur, Louis: "On the Asymmetry of Naturally Occurring Organic Compounds,: in G. M. Richardson's "The Foundations of Stereo-Chemistry," *loc. Cit.,* p. 27. New York, American Book Company (no date).

enzymes or ferments, trypsin and amylopsin, which help the intracellular enzymes to build them up. (3)Cancer-cells attack and pull down the living lævo-rotatory albumins. (4) As racemic acid is a mixture of dextro- and lævo-tartrates, which are attacked respectively by the mould (*Penicillium*) and by yeast (*Torula*), and are separable by them—or, more strictly, by the ferments they produce—so also a living human being, suffering from the natural phenomenon, not disease, known as cancer, is in a sense a mixture of two sorts of albumins—the lævo-rotatory albumins of the body, and the dextro-rotatory ones of cancer. (5) As *Torula* (yeast) attacks the lævo-tartrate, so cancer-cells attack and pull down the lævo-rotatory albumins of the body; and as the mould (*Pencicillium)* acts upon dextro-tartrates, so, when administered in adequate doses, and such as are more than sufficient to neutralize the antitryptic ferments of cancer, trypsin and amylopsin, the powerful pancreatic enzymes, attack in life and pull down the dextro-rotatory albumins of cancer. (6) The albumins of cancer are stereo-isomers of those of the body, and the antithesis of these; and as the latter are lævo-rotatory, the albumins of cancer are dextro-rotatary. (7) The crucial test of the true nature of the albumins of cancer may be made by submitting a solution of them to an examination in the polarimeter, when this solution will be found to rotate the plane of polarized light to—the right!

The reader may not cherish the fond delusion that as yet there are no evidences of an observational kind supporting the thesis that the albumins of cancer are dextro-bodies. There are, and these are of a decisive nature, although not to be found in the published researches of any official cancer research body. As the chemist Emil Fischer remarked, a ferment fits the sub-

stance upon which it acts "as a key fits a lock." Now, on a previous page, reference has been made to the "liquefaction of cancer" by means of potent hypodermic injections of trypsin. This has been seen more than once by a London consulting physician, who sent me several tubes of such liquid cancer from two patients suffering from epithelioma (skin-cancer). As already stated, the accuracy of this observation has been confirmed by Professor F. Blumenthal, of Berlin, and by the observation made by Captain Lambelle in the treatment of the two cases of lympho-sasrcoma and sarcoma.* Since no observation refuting this has ever been published, it stands as a discovery doubly confirmed by observation. As hundred of medical men have found, trypsin does not "liquefy" the normal somatic lævo-rotatory albumins of the body and blood, although in some very advanced cancer cases, where they have been much injured by the action of the cancer, it may not be without some action upon them. ‡ It follows from all this that, even without the use of the polarimeter, the scientific

*Bainbridge's sixth thesis on p. 32 of his "Scientific Report" reads: "That *injectio trypsini*, in some cases, seems to cause more rapid disintegration of (to 'liquefy,' according to Beard) cancerous tissue." Since to this author it only "seems to do this, and since his report does not contain a particle of evidence of the fact, I do not here cite—because there are none to quote—any observations of his as confirming this undoubted fact. It suffices that Professor Blumenthal and Captain Lambelle have witnessed it, the latter in two case. Possible, Dr. Bainbridge never saw it at all, except in the microsocpical preparation, or preparations, which I sent him in 1907.

‡ Such cases are probably much too advanced for success to be possible. A medical friend has recently written to me that in every disease there is a point beyond which the case is hopeless, and that blood-examinations in cancer cases under treatment were very desirable. In my opinion, this again indicates the folly of operation on living cancer, for this does but stimulate its growth and increase, until anon this point is reached. Then it is too late for any treatment to be successful.

conclusion is warranted that the albumins of cancer, because liquefied in the living state by adequate injections of trypsin, are dextro-bodies. This conclusion was, indeed, clearly enunciated in the pages of the *Medical Record* of October 19, 1907, by the writer (compare Chapter VI.). It has not been "generally accepted," nor has it been refuted, but it has been ignored. Facts, however, are awkward things, which in the long run cannot be set aside systematically, especially by those who are supposed to be searchers after the truths of Nature.

CHAPTER XII
"SCIENCE IS PREVISION"

The science of stereo-chemistry, or chemistry in space was founded by Pasteur in 1860, He it was who then set up what he termed "enantiomorphism" to describe the peculiarities of the isomeric naturally occurring organic compounds. As every teacher in any medical school is well aware, the science of chemistry plays too unimportant a part in the education of the medical student. Therefore it is not strange that the stereo-chemistry of naturally occurring organic compounds should have been so neglected in the practice of medicine, in what is wrongly designated "medical science." If the neglect be excusable in medicine, the like may not be siad for natural science. Leaving physiology aside, for all the use hitherto made of its findings in zoology and embryology, in animal biology in a wide sense, stereo-chemistry might never have had any existence. For instance, practically all the beliefs—superstitions one might truly term them—of embryologists, such as the germ-layer theory, the recapitulation theory, epigenesis or direct development, etc., date back to a time when there was no known science of stereo-chemistry. Except by the writer, no attempt has ever been made by any other embryology—least of all by Hackel or Weismann—to bring the doctrines of embryology into line with the

canons of stereo-chemistry. But it may be taken as an axiom not open to ridicule that what Nature cannot dispense with, that the scientific investigator may not ignore.

Now, in the course of my research career it has never been a maxim of mine to leave unto others what I could do myself, and the like is true of the present situation also. Much more than the asexual (trophoblastic) theory of cancer depends upon this crucial test. It is the ultimate basis of the law and mode of animal development. By the canons of stereo-chemistry, no less than by those of embryology, trophoblast and cancer must be made up of dextro-rotatory albumins—that is, in simple words, these albumins in solution must in the polarimeter rotate the plane of polarized light to the right, not to the left.

The foregoing theses are set up to define the position now, and the prophecy is made that, when submitted to the polarimeter under strictly scientific conditions, it will be seen that the albumins of cancer and of trophoblast rotate the plane of polarized light to the right, and not to the left. The natural—that is, the scientific—means of destroying these dextro-rotatory albumins in the living condition are sufficiently potent injections of trypsin and amylopsin.

A great investigator and thinker, August Weismann, once said that the investigator should never forget that he stood upon his predecessors' shoulders. Possibly the scoffers and the anonymous writers stand upon nothing less substantial than a soap-bubble! They have kept concealed carefully the foundations upon which their feet might be supposed to rest. Let them not forget that my feet rest upon the mighty shoulders of Pasteur, and that, in their turn, his were fixed firmly upon foundation-stones of the visible universe.

"I have, in fact," said this genius, "set up a theory of molecular asymmetry—one of the most important and wholly surprising chapters of science—which opens up a new, distant, but definite, horizon for physiology."

Again, Pasteur wrote:

"The characteristic of erroneous theories is that they are never able to present new facts; and every time a fact of this nature is discovered, in order to take it into account, they are obliged to graft a new hypothesis upon the old ones. The characteristic of true theories, on the contrary, is of being the expression of the facts themselves, of being commanded and dominated by them, of

being able to foresee new facts certainly, because these by their nature are linked up with the former—in a word, the characteristic of these theories is focundity."*

As a "crucial test" of the true nature of a supposed malignant tumour it is inconceivable that anything should be named beside the stereo-chemical one. To carry it out in some of the many wealthy official cancer research laboratories would be a matter of ease for any stereo-chemist. It would not be a serious drain on the vast funds of many of them to engage the services of a trained stereo-chemist to do the work. The cost could hardly equal—certainly not exceed—that of the publication of a single "scientific report." The results obtained by a properly qualified man—a scientific investigator in the true spirit as well as in the letter—would at all events tend to close for ever one pathway leading to error (Huxley); and I venture to think—whether it be a hanging matter or not—that it might open the eyes of the medical profession to the roadway leading to scientific

*Vallery-Radot, René: "La Vie de Pasteur," Paris, 1901, p. 352. What Pasteur termed "a true theory" I identify as "a general principle."

truth. After all, the naturally occurring organic compounds, as is now well known, except in orthodox embryology, zoology, and pathology, are either lævo- or dextro-rotatory. If the albumins of cancer be lævo-rotatory, and not, as I affirm, dextro-rotatory, then embryology as a science, as the absorbing passion of a life of investigation, is in vain. Then trypsin and amylopsin open left-handed locks. Then—but then only—there is some contradiction in the constitution of the visible universe, as it has been determined by scientific men, who have worked for the love of the labour. But if the albumins of cancer be dextro-rotatory, and its glycogen lævo-rotatory, then let the scoffers hide their diminished heads.

Let trypsin and amylopsin be recognized to be what they are—the most powerful things in the whole range of organic nature.

It can add nothing of import to what the writer has endured during a research life of nearly twenty-nine years for daring to proclaim new truths of science without fear or favour, to take this further decisive step, which must either damn his labours of the past twenty-three years, or crown them with unfading glory; for it is my scientific conviction that that septuagenarian army surgeon of the American Civil War, who had had the enzyme treatment for cancer himself some four or five years ago (1906-07)spoke truly, when (December, 1908) he wrote words to the effect that the treatment of cancer by the ferments trypsin and amylopsin would in the end replace the knife—that this scientific treatment would go on, and be ever more developed, after he and I had done our labours and were at rest.

APPENDIX A
THE LIVERPOOL LECTURE:* GERM CELLS AND THE CANCER PROBLEM

Last evening Dr. John Beard, University Lecturer on Comparative Embryology, Edinburgh, delivered an address at the Liverpool University Anatomical Society upon "Germ-Cells in Relation to Malignant Disease." In the opening statement reference was made to the supposed cancer parasite, and the curative serum recently brought forward by Doyen, of Paris; to the secret treatment now being used by Professor Opitz, of Marburg; and to the recently issued pessimistic report of the American Cancer Commission. There was, of course, remarked the speaker, no cancer parasite; but did such a thing exist, the Parisian one could not be the real article, for a well-

known pathologist was about to publish an account of what he (the pathologist) held to be the only true cancer parasite. Thus one advocate of the parasitic theory refuted another, and the American Cancer Commission denied, with the great majority of pathologists, the existence of any cancer parasite. In the telegraphic summary of the American report there were only three statements not open to challenge. These were that the best remedy was early operation, that cancer was not due to any parasite, but that it was probably connected with errors of development. Notwithstanding all that

*From the *Liverpool Daily Post and Mercury*, January 21, 1905.

The American Commission might say, the nature of cancer as an irresponsible asexual generation or trophoblast had been known for two and a half years. The speaker proceeded to give an account of his own work upon the history and origin of the germ-cells, from which it had been established beyond question that these were pre-embryonic in origin, arising upon an asexual foundation or trophoblast, and that by the self-sacrifice of one an embryo was unfolded to contain and to nourish the other germ-cells for a certain brief span of time. In every case examined it had been found that a varying percentage of the germ-cells failed to reach the right place in the body, and these might be found in almost any organ or position. At first sight it had seemed that any of these might later on give rise to a tumour, benign or malignant, for they represented, in fact, the "lost germs" of the pathologists. The speaker's earlier work upon the life-cycle, published between 1894 and 1898, was next briefly described. These researches had established that, prior to the appearance of an embryo or sexual form, there arose an asexual foundation—the trophoblast—upon which the germ-cells and embryo came into being. In any normal case, at a certain definite period, the embryo was able to suppress the asexual foundation, and the latter slowly degenerated. If however, the embryo were absent or very abnormal, the trophoblast might, and often did, become a very deadly form of cancer—chorio-epithelioma. The two generations had different nutritions—a fact of extreme importance—and the "digestion" of a cancer resembled that of the trophoblast of normal development. An account was then given of the speaker's conclusions as to the origin of tumours, and their relation to identical twins, triplet, etc. It was shown that each such identical twin, triplet, etc., was due to the independent development of a single germ-cell, and not, as was commonly held,