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PREFACE

This volume opens with a comprehensive review of Cryptosporidiosis in Southeast Asia by Yvonne Lim of the University of Malaya and colleagues. Although well understood in high-income nations, the epidemiology and socioeconomic impact of these enteric diseases in Southeast Asia is not so well appreciated. The authors succeed in highlighting the scale of the problem with a penetrating review of the regional literature, from which they also highlight some of the key operational and research challenges that will need to be overcome to effectively control Cryptosporidiosis in the region.

The second chapter by Hélène Moné based at the University of Perpignan and colleagues is a detailed overview of the epidemiology and control of schistosomiasis in the Economic Community of West African States (ECOWAS). Given that ECOWAS represents 15 countries and around 30% of the total population of the African continent, there is a considerable wealth of literature relating to schistosomiasis and transmission across diverse ecological landscapes. Control activities are progressing at different rates in the member countries and this detailed analysis of the situation will provide an excellent foundation on which to build further integrated control efforts. The authors stress the need for greater interaction between engineers, health experts and educationalists as countries move towards sustainable control of schistosomiasis.

We are very pleased to include the final chapter by Ton Polderman of the Leiden University Medical Centre and colleagues on human infections of *Oesophagostomum.* This contribution provides a fascinating account of an unusual intestinal parasite and the consequences of infection in man, paying particular attention to studies in Ghana and Togo. Over the last 20 years or so, various clinical, epidemiological and molecular studies have helped to unravel the biology of this intriguing helminth parasite and the pathology caused by infection. Successful control is possible and for the time being it seems that transmission in northern Ghana may have ceased.

D. ROLLINSON AND S. I. HAY

CHAPTER 1

Cryptosporidiosis in Southeast Asia: What's out There?

Yvonne A.L. Lim,* **Aaron R. Jex,†** **Huw V. Smith,‡** and **Robin B. Gasser†**

Contents

Abstract

Cryptosporidiosis is a socioeconomically important, enteric disease caused by a group of protozoan parasites of the genus *Cryptosporidium*. The significant morbidity and mortality in animals and humans caused by this disease as well as its considerable impact on the water industry have made its prevention and control a global challenge, particularly given that there are presently no widespread, affordable or effective treatment or vaccination

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strategies. Although much is known about *Cryptosporidium* and the impact of cryptosporidiosis and other diarrhoeal diseases in developed countries, this is not the case for many developing countries in Africa, South America and Asia. In Southeast Asia, which represents an epicentre for emerging infectious diseases, cryptosporidiosis has been reported in countries, such as Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand and Vietnam. In most of these countries, the likely predisposing factors for cryptosporidiosis include rapid population growth and expanding urbanisation (which are often linked to inadequate municipal water supplies and poorly managed refuse disposal) as well as the tropical climate and the increasing prevalence of HIV/AIDS and other infectious diseases. Given the close proximity of these countries and the extent of migration within and among them, cryptosporidiosis can be difficult to control. National and regional surveillance is central to preventing and controlling cryptosporidiosis. To date, most studies of cryptosporidiosis in Southeast Asia have focus on estimating the prevalence of infection in humans and animals using conventional diagnostic techniques. Future investigations using reliable molecular tools should enable improved insights into the epidemiology, systematics and population genetics of *Cryptosporidium* in this region. An enhanced understanding of the transmission of cryptosporidial infections and the significance of environmental contamination will require a multidisciplinary approach, built on shared resources. Such an integrated approach would underpin stable and powerful partnerships in efforts to prevent and control this disease. The purpose of the present chapter is to review available data and information on cryptosporidiosis in Southeast Asia and to provide recommendations in the pursuit of a better understanding of *Cryptosporidium* in this region, in order to facilitate the development of effective multidisciplinary interventions to control cryptosporidiosis.

1.1. INTRODUCTION

Cryptosporidiosis is a socioeconomically important, enteric disease of humans and other animals, caused by a group of protozoan parasites of the genus *Cryptosporidium*. This disease is transmitted *via* the faecal–oral route (e.g. *via* food, water or direct contact) (Cacciò, 2005; Cacciò and Pozio, 2006). In addition to infection by direct transmission, cycles of autoinfection within a host can cause chronic cryptosporidiosis, particularly in immunodeficient patients (Current and Garcia, 1991). Clinical cryptosporidiosis usually establishes rapidly within days to weeks (prepatent period is usually ~7–21 days; Ramirez et al., 2004). Symptoms include nausea, vomiting, severe abdominal cramping and diarrhoea

(Chen et al., 2002; Kosek et al., 2001), which often resolve in immunocompetent hosts (Fayer and Ungar, 1986); however, cryptosporidiosis can persist in malnourished and/or immunocompromised individuals, leading to a fatal syndrome characterised by chronic diarrhoea, substantial weight loss and wasting (Tzipori and Widmer, 2008). Clinical intervention is challenging because most of the chemotherapeutic drugs (such as paromomycin, azithromycin and nitazoxanide) used and the vaccines developed (Kosek et al., 2001; Riggs, 2002) are not highly effective or available for widespread use at low cost in most countries.

Currently, cryptosporidiosis of humans is known to be associated primarily with *Cryptosporidium hominis* and *C. parvum* (see Cacciò, 2005; Cacciò and Pozio, 2006). However, other species and/or genotypes do occur occasionally (Chalmers et al., 2002; Xiao et al., 2001) and often infect people with congenital or acquired immunodeficiency (e.g. HIV/AIDS) or immunosuppression (Cama et al., 2003, 2006; Gatei et al., 2002a). The epidemiology of human cryptosporidiosis and associated species of *Cryptosporidium* can be complex. *C. hominis* is hypothesised to be specific to humans and thus transmitted exclusively *via* anthroponotic pathways (Cacciò, 2005). In contrast, *C. parvum* appears to be capable of exploiting anthroponotic or zoonotic transmission routes, with infected cattle or small ruminants (sheep or goats) acting as reservoir hosts (Cacciò, 2005; Robertson, 2009; Thompson et al., 2008; Xiao and Feng, 2008). The substantial impact of water-borne cryptosporidiosis on human health is well documented, with *Cryptosporidium* being linked to more than half of the 325 outbreaks of water-borne protozoal disease documented globally to date (Karanis et al., 2007). Oocysts are often disseminated *en masse* through municipal drinking water systems (MacKenzie et al., 1994, 1995) or public swimming pools (Karanis et al., 2007) and thus have a major potential to result in a rapid spread of disease to large numbers of individuals. The specific detection of *Cryptosporidium* oocysts in the environment is critical to prevention and control. Given that the World Health Organization (WHO) has recognised *Cryptosporidium* as a 'reference pathogen' for determining water quality globally (Medema et al., 2006), monitoring the presence of *Cryptosporidium* oocysts in water is also important in relation to the transmission of other enteric pathogens. Although microscopic detection methods are commonly used, their sensitivity and/or specificity are/is often inadequate, such that the application of accurate molecular tools is essential to gain improved insights into the epidemiology of cryptosporidiosis and the genetics of *Cryptosporidium* populations, in order to underpin prevention and control strategies (Jex et al., 2008; Savioli et al., 2006).

Given its significant morbidity and mortality in humans and animals worldwide, cryptosporidiosis has become a global challenge, particularly considering the impact of the HIV/AIDS pandemic (Tzipori and Widmer, 2008).

The direct and rapid nature of disease transmission (CDC, 2008), the resilience of *Cryptosporidium* oocysts in the environment (King and Monis, 2007) and the lack of affordable, readily available chemotherapy or vaccines against cryptosporidiosis (Kosek et al., 2001; Riggs, 2002) are key factors that limit effective prevention and control. Therefore, the control of cryptosporidiosis is heavily reliant on a sound understanding of its epidemiology in humans and animals as well as knowledge of the genetic structures and species compositions of *Cryptosporidium* populations (acquired through the use of accurate analytical and diagnostic tools) (Jex et al., 2008). Although much is known about *Cryptosporidium*/cryptosporidiosis in developed countries, there is limited information and data for many developing countries, including those in Africa, South America and Asia. For instance, to date, there has been no systematic review of the literature for Southeast Asia, resulting in a lack of appreciation of the importance of cryptosporidiosis in this geographical region. Most of the available information is either published in national journals and/or languages other than English, thus reducing its accessibility to the global community. The purpose of the present chapter was to (i) provide a relevant background on Southeast Asia, (ii) review available data/information on *Cryptosporidium*/cryptosporidiosis in this region, (iii) identify knowledge gaps and (iv) provide recommendations in the pursuit of a better understanding of *Cryptosporidium*, cryptosporidiosis and its epidemiology in Southeast Asia, such that practical prevention and control strategies can be put in place in the near future.

1.2. BACKGROUND ON SOUTHEAST ASIA

Southeast Asia consists of 11 countries, including Brunei Darussalam, Cambodia, East Timor, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand and Vietnam, which cover an area of ~4 million km^2 and are inhabited by approximately one-twelfth (~554 million people) of the world's population. This region of Asia is located between India and China and has numerous natural resources and substantial commercial markets, with a steadily increasing 'purchasing power' (Anonymous, 2004). From an economic perspective, some Southeast Asian countries are 'developing', whilst others, such as Singapore, Malaysia, Thailand and Indonesia, are amongst the most dynamic economies in the world.

Southeast Asia is recognised as an 'epicentre' for emerging infectious diseases (Lam, 1998). Many of the countries in this region experience high population densities and rapid population expansion but, with limited available financial resources, urbanisation is often associated with substantially inadequate municipal water supply or refuse disposal. These factors, coupled with the HIV/AIDS pandemic and a tropical or

subtropical climate, which is conducive to the propagation of many protists, have contributed to a perpetual transmission of infectious diseases. Improved means of transport, increased inter- and intra-country migrations and a burgeoning tourism trade have also enhanced the potential for the spread of some infectious diseases (particularly those with direct modes of transmission), including cryptosporidiosis. Presently, a number of Southeast Asian countries face a severe, and likely underestimated, problem with HIV/AIDS, due to its high prevalence and rapid spread (Anonymous, 2008b). Individuals with HIV/AIDS are more susceptible to other opportunistic pathogens, including *Cryptosporidium* spp. (e.g. Tzipori and Widmer, 2008). For economical and political reasons, there is an increased migration of people within and among these countries (Martin et al., 2006), suggesting that the dissemination of cryptosporidiosis and other pathogens associated with people with HIV/AIDS could increase.

With a perspective on tackling diseases associated with poverty, the WHO included cryptosporidiosis in its 'Neglected Diseases Initiative' in 2005 (Savioli et al., 2006). In regions of the world for which substantial epidemiological data are available (e.g. Karanis et al., 2007; Leoni et al., 2006), *Cryptosporidium* is amongst the commonest causes of diarrhoea. Although recent data suggest that cryptosporidiosis may represent one of the most significant obstacles in the fight against poverty in some countries within Southeast Asia (Lim et al., 2008a; Savioli et al., 2006), there has been no systematic appraisal of the current state of knowledge for this geographical region. For this reason, we have undertaken a comprehensive review of all of the accessible information/data and publications ($n = 77$) for individual countries (see Table 1.1).

1.2.1. Cambodia

Cambodia is a small country with a population size of ~13.9 million (Anonymous, 2009). Cambodia's recovery from being ravaged by decades of civil war, genocide and the virtual elimination of its skilled workforce has been slow and by setbacks. However, with renewed political stability (i.e. new national elections in 1998 and the death of the leader of the Khmer Rouge, Pol Pot, in April 1998) the Cambodian economy is showing signs of recovery (Anonymous, 2007). For many years, the resettlement camps on the Thai–Cambodia border served as a separate or second 'Cambodia' during the tragic political upheaval, which began in the 1970s and ended in 1999. Public health concerns about cryptosporidiosis in these border camps were addressed in two studies. The first study showed that 2.4% of 85 samples from children with diarrhoea had cryptosporidiosis (Nordlander et al., 1990). Two years later, in another resettlement camp, faecal samples from 487 children (<5 years of age) with

TABLE 1.1 A summary of key epidemiological information and data on *Cryptosporidium*/cryptosporidiosis in humans, animals and the environment for individual Southeast Asian countries, except Brunei Darussalam and East Timor, for which no data are presently available

Country	Population/Source	Prevalence (%)	Sample size	Species/Genotypes	References
Cambodia	Children	2.4	85		Nordlander et al. (1990)
	Children refugees	7.4	487		Arthur et al. (1992)
	HIV-infected patients	45	80	*C. hominis* and *C. parvum*	Chhin et al. (2006)
	Water spinach	17	35		Vuong et al. (2007)
Indonesia	Premature baby	Not applicable	Not applicable		Katsumata et al. (1993)
	Hospital patients	2.1	1960		Katsumata et al. (1998)
	Community	1.1	4368		
	Cats	2.4	13		
	Healthy girls	Not applicable	2	Proposed to be *C. muris*	Katsumata et al. (2000)
	HIV-infected patients	4.9	318		Kurniawan et al. (2009)
Laos	Refugees	5	324		Taylor et al. (1988)
Malaysia	A young patient	Not applicable	Not applicable		Che Ghani et al. (1984)
	Paediatric patients	4.4	158		Mendez et al. (1988)
	Paediatric patients	4.3	836		Mat Ludin et al. (1991)
	Paediatric patients	11.4	131		Lai (1992)
	Children	10.6	47		
	Paediatric patients	2.1	192		Ng and Shekhar (1993)
	HIV-infected intravenous drug users	23	168		Kamel et al. (1994a)
	Orang Asli (Aborigines)	20.1	159		Kamel et al. (1994b)
	Orang Asli	5.5	127		Lim et al. (1997)
	Paediatric patients	2.0	237		Menon et al. (1999)

	Wild and domestic rats	4.1	49		Lim and Ahmad (2001)
	Paediatric patients	0.9	258		Menon et al. (2001)
	Cattle	25	96		Farizawati et al. (2005)
	HIV-infected patients	3	66		Lim et al. (2005)
	Birds	6	100		Rohela et al. (2005)
	Orang Asli	2.7	74		Hakim et al. (2007)
	Birds	3.4	116		Lim et al. (2007a)
	Bird handlers	12.5	8		
	Orang Asli	4.1	321		Mohammed Mahdy et al. (2007)
	Primates	14.1	99		Lim et al. (2008b)
	Ungulates	5.7	70		
	Feline	14.3	28		
	Calves	36	50	*C. parvum* and the 'deer-like' genotype of *Cryptosporidium*	Halim et al. (2008)
	River water	11.5	174		Lim et al. (2008a)
	Well water	7.1	28		
	Raw water from drinking water treatment plant	6.9	87		
	Backwashed water	100	2		
	Sewage treatment effluent	20	30		
	HIV-infected patients	18.6	59	*C. parvum*	Zaidah et al. (2008)
Myanmar	Infants	3.4	203		Aye et al. (1994)
	Pre-school children	3.4	472		Wongstitwilairoong et al. (2007)

(*continued*)

TABLE 1.1 (*continued*)

Country	Population/Source	Prevalence (%)	Sample size	Species/Genotypes	References
Philippines	Babies	2.6	735		Cross et al. (1985)
	Paediatric patients	8.5	823		Laxer et al. (1990)
	Paediatric patients	2.5	236		Paje-Villar et al. (1994)
	Cancer patients	28.3	53		Rivera et al. (2005)
	Hospital patients	1.9	3456		Natividad et al. (2008)
Singapore	A child with AIDS	Not applicable	Not applicable		Wu et al. (1994)
Thailand	Patients	0.5	1500		Thamlikitkul et al. (1987)
	Children in orphanage	8	205		Janoff et al. (1990)
	Children in orphanage	7.3	303		Jongwutiwes et al. (1990)
	Paediatric patients	1.3	387		Jirapinyo et al. (1993)
	HIV-infected patients	8.8	250		Moolasart et al. (1995)
	AIDS patients with chronic diarrhoea	13.3	45		Manatsathit et al. (1996)
	HIV-infected patients	9.1	22		Punpoowong et al. (1998)
	HIV-infected patients	5.7	122		Uga et al. (1998)
	HIV-infected patients	25.6	43		Wanke et al. (1999)
	Hospital patients	19.2	288		Waywa et al. (2001)
	HIV-infected patients	Not applicable	34	*C. hominis*, *C. meleagridis*, *C. parvum*, *C. felis* and *C. canis*	Gatei et al. (2002b)

	HIV-infected patients	12.8	156		Saksirisampant et al. (2002)
	HIV-infected patients	Not applicable	29	*C. hominis*, *C. meleagridis*, *C. muris* and *C. felis*	Tiangtip and Jongwutiwes (2002)
	HIV-seropositive patients	11.5	78		Pinlaor et al. (2005)
	HIV-seronegative patients	1	78		
	Raw water	35	20		Sutthikornchai et al. (2005)
	Holstein-Friesian dairy cows	9.4	363		Jittapalapong et al. (2006)
	HIV-infected patients	Not applicable	46	*C. parvum*	Nuchjangreed et al. (2008)
	Cattle	Not applicable	200	*C. parvum*	
Vietnam	HIV-infected patients	Not applicable	3	*C. hominis*	Gatei et al. (2003)
	Cattle	35.7	266	*C. parvum* (bovine type) and *C. andersoni*	Nguyen et al. (2007)

acute or chronic diarrhoea were examined using a conventional microscopic-staining method, and 7.4% of them were shown to be infected with *Cryptosporidium* (Arthur et al., 1992). Because enteric pathogens infecting children were frequently isolated from both the children's and their mothers' hands, the route of transmission of enteric pathogens was attributed to person-to-person contact. With the HIV epidemic on the rise, a study (Chhin et al., 2006) was initiated at the Infectious Disease Department of the Norodom Sihanouk Hospital in Phnom Penh, the largest referral centre for patients with HIV/AIDS in Cambodia. In total, 80 individuals were examined (40 individuals with HIV/AIDS whose median $CD4^+$ cell count was 11.5 cells/mm^3 and 40 HIV-negative individuals = control group). Overall, *Cryptosporidium* (detected in 45% of individuals tested) was the commonest protistan pathogen (Chhin et al., 2006). Interestingly, the percentage of *Cryptosporidium*-infected people was similar between the HIV/AIDS cohort and the control group (40% and 53%, respectively). Importantly, the prevalence of *Cryptosporidium* was high in both asymptomatic and symptomatic patients, suggesting an 'under-diagnosis' of sub-clinical cryptosporidial infections in HIV-infected patients in Cambodia. Confirmation of cryptosporidiosis with polymerase chain reaction-based restriction fragment length polymorphism (PCR-RFLP) indicated the presence of *C. hominis* in symptomatic patients, and both *C. hominis* and *C. parvum* in asymptomatic people (Chhin et al., 2006).

Some research on cryptosporidiosis in Cambodia has focused on the use of wastewater in the production or processing of food. Recent estimates indicate that as much as 20% of all food crops in peri-urban areas around Phnom Penh are grown using untreated wastewater (Muong, 2004). This practice represents a high risk for the transmission of enteric pathogens; however, peri-urban farms are an important source of food for Phnom Penh's citizens, and wastewater is an integral component of peri-urban farming in these regions. The monitoring of the concentrations of enteric pathogens in wastewater lakes and irrigation systems is thus a critical component of sustainable peri-urban farming. The WHO published guidelines for the use of wastewater and greywater in food production (Anonymous, 2006a,b), but it did not advise on the testing for pathogenic protists. Unfortunately, cost often prohibits preventative testing for such pathogens in many developing nations (Vuong et al., 2007).

As a component of a large research programme conducted in Southeast Asia (Production in Peri-Urban Systems in Southeast Asia, PAPUSSA), a recent study (Vuong et al., 2007) was undertaken to investigate the levels of faecal pathogens in Boeng Cheung Ek Lake, the main recipient of wastewater from the city of Phnom Penh. The major crop grown in this lake is water spinach (*Ipomoea aquatica*), a popular vegetable grown for both human consumption and animal feed. This vegetable is

rich in protein, has a short growth period and is resistant to common insect pests. *Cryptosporidium* oocysts were detected (by immunofluorescence microscopy) in 6 of 35 (17%) water spinach samples, with an average concentration of 0.5 oocyst per gram (wet weight) of plant (Vuong et al., 2007). Other parasites discovered included species of *Giardia* (56%; 6.6 cysts per gram) and *Cyclospora* (8%) as well as helminths (11%; 0.1 egg per gram). Although the *Cryptosporidium* oocysts detected in this study were not identified genetically, the presence of eggs of various helminths (*Trichuris*, *Ascaris* and hookworms), protists (*Giardia* and *Cyclospora*) and thermotolerant coliforms (10^5–10^7 per gram of spinach) suggested substantial human faecal contamination in wastewater and that the oocysts detected represented *C. parvum* and/or *C. hominis*. As water spinach is usually boiled or fried prior to consumption in Cambodia and elsewhere in Southeast Asia, the risk of food-borne transmission posed by these oocysts seems to be low. However, water spinach is only one of the vegetables grown in Cambodia using wastewater, and many of the other vegetables grown locally are consumed raw and thus could pose a significant risk for the transmission of enteric infectious diseases, including cryptosporidiosis. In addition, the health risks posed by occupational exposure of farmers during the harvest and subsequent handling and transport of vegetables from production sites to the markets (e.g. through the splashing of vegetables with contaminated water to keep them moist and fresh as well as through unhygienic practices linked to the reuse of contaminated containers or baskets) are expected to be high (see Vuong et al., 2007).

1.2.2. Indonesia

Indonesia, with a population of ~219 million, is the fourth most populous nation in the world and the largest archipelago bridging the Asian and Australian continents (Anonymous, 2009). More than two-thirds of the population resides in Java, the centre of the country's economic and political powers. The majority of studies of cryptosporidiosis/*Cryptosporidium* are from Surabaya, the capital of the province of East Java and the second most populous Indonesian city with ~3 million inhabitants.

Cryptosporidiosis was first detected in a premature baby (Katsumata et al., 1993). Subsequently, a study of hospital-based and community-based populations in Surabaya was conducted to assess the significance of cryptosporidiosis as a cause of acute diarrhoea in patients of various age groups (Katsumata et al., 1998). In the hospital cohort, approximately one-third of all cryptosporidial infections (2.1% of 1960 patients) were linked to asymptomatic individuals (0.8% of all patients). Children of less than 2 years of age were shown to be most susceptible to cryptosporidiosis and more likely to be symptomatic (1.8% of all patients tested and

85.4% of the 41 infected with *Cryptosporidium*). In the community-based group, the prevalence of *Cryptosporidium* was 1.1% (49 of 4368), with oocysts being detected frequently in diarrhoeic samples (8.2% of 257 people) during the rainy season (June to October). In the same study, *Cryptosporidium* oocysts were detected in 2.4% of 13 faecal samples from cats. However, no molecular data were provided regarding the specific identity of these oocysts and their potential to infect humans. This study (Katsumata et al., 1998) emphasised that high rainfall, flooding and crowded living conditions are significant risk factors for *Cryptosporidium* infections in Surabayan communities. Cats were also considered as a potential risk factor associated with the spread of cryptosporidiosis in Surabaya; however, considering the complex epidemiology and host-specificity of many *Cryptosporidium* species (Xiao et al., 2002, 2004), further studies are required to genetically characterise *Cryptosporidium* species and genotypes from cats and other animals utilising molecular tools and to assess their zoonotic potential. Recently, an evaluation of intestinal parasites in HIV/AIDS patients revealed that 4.9% ($n = 318$) have cryptosporidiosis and/or *Blastocystis hominis* infection (Kurniawan et al., 2009). Although assumed to be *C. parvum* in most studies in Indonesia, oocysts have been identified solely using morphological and/or morphometric methods. Nonetheless, Katsumata et al. (2000) reported *C. muris* oocysts in stool samples from two asymptomatic girls (4 and 5 years of age) using morphological and PCR approaches. However, the primers used in this study (Katsumata et al., 2000) were genus- rather than species-specific, raising questions as to the validity of the findings. Clearly, more emphasis should be placed on the use of advanced and effective molecular tools for the specific and genotypic identification of oocysts and the analysis of the genetics of *Cryptosporidium* populations in Indonesia.

1.2.3. Laos

Laos, with a population of ~5.9 million, is one of the least developed and most enigmatic of the three former French Indochinese states (i.e. Cambodia, Vietnam and Laos) in Southeast Asia (Anonymous, 2009). Its neighbouring country, Thailand, has a long history of providing sanctuary for Hmong hill-tribe refugees, who fled the political persecution following the Vietnam War in 1975. The Thailand–Laos refugee camps were finally closed in 1992. To date, the only study of *Cryptosporidium* from Laos (Taylor et al., 1988) examined Hmong and other Laotian hill-tribe refugees in the Ban Vinai camp (established in 1975), which is located on the Thailand–Laos border, 650 km north of Bangkok. This latter study detected cryptosporidial oocysts in 5% of 324 faecal samples tested and determined that *Cryptosporidium* ranked among the most

common enteric pathogens detected (along with *Escherichia coli*, *Campylobacter* and rotavirus) in young children (of <2 years of age) suffering from acute diarrhoeal disease (Taylor et al., 1988).

1.2.4. Malaysia

Malaysia is a multi-racial and multi-religious country with a population of ~25.6 million (Anonymous, 2009). It is a vibrant and economically thriving nation with two land masses, Peninsular Malaysia and Malaysia Borneo (i.e. Sarawak and Sabah). Some fundamental data on cryptosporidiosis in humans, animals and the environment in Malaysia are available (reviewed by Lim et al., 2008a).

In humans, the first reported case of cryptosporidiosis in Southeast Asia was recorded in Malaysia in a young man presenting with diarrhoea (Che Ghani et al., 1984). Subsequent studies concentrated on high-risk people, such as hospitalised children, HIV-infected patients and Orang Asli (aborigine) communities. Cryptosporidiosis was recorded in 1–11% of hospitalised children (Lai, 1992; Mat Ludin et al., 1991; Mendez et al., 1988; Menon et al., 2001; Ng and Shekhar, 1993), 2% ($n = 237$) of immunosuppressed children suffering from cancer and receiving chemotherapy (Menon et al., 1999) and 11% ($n = 47$) of diarrhoeic, young children in rural communities (Lai, 1992).

With the increasing numbers of HIV cases in Malaysia, *Cryptosporidium* is continually gaining importance as an opportunistic pathogen. From 1986 to 2008, ~96,000 HIV/AIDS cases (~0.4% of the Malaysian population) were identified, with an average of 10 new cases being detected each day, equating to one case every 144 min (Anonymous, 2008a). Intravenous drug users constitute the majority of HIV cases in Malaysia. In 1994, *Cryptosporidium* oocysts were detected in 23% of 168 asymptomatic, HIV-positive intravenous drug users (Kamel et al., 1994a) and, recently, a prevalence of 3% (2 cases with 1 mortality due to advanced AIDS) was determined in 66 hospitalised HIV-infected patients (Lim et al., 2005).

Cross-sectional studies of cryptosporidiosis in the Orang Asli communities in Malaysia have estimated various prevalence rates (2.7–20.1%), with most infections being asymptomatic (Hakim et al., 2007; Kamel et al., 1994b; Lim et al., 1997; Mohammed Mahdy et al., 2007). The repeated finding of asymptomatic patients highlights their significance as carriers of cryptosporidial infection and as sources for environmental contamination as well as accidental transmission to susceptible people in Malaysia. Despite the documented occurrence of *Cryptosporidium*, only recently have molecular tools been used to verify the specific and/or genotypic identity of *Cryptosporidium* oocysts (Zaidah et al., 2008). In this study (Zaidah et al., 2008), the authors compared the use of a microscopic, diagnostic technique (Ziehl–Neelsen staining) with a nested PCR

approach (targeting a region of the small subunit [SSU] of the nuclear ribosomal gene) for the detection of *Cryptosporidium* oocysts in faecal samples collected from 59 HIV patients from Kota Bharu. Eleven of these faecal samples tested positive for *Cryptosporidium*. However, of these 11 samples, 9 tested positive by nested PCR (and were identified as *C. parvum* based on sequencing), just three were identified by microscopy and only one sample was found to be positive using both microscopy and PCR. This study (Zaidah et al., 2008) highlighted the increased sensitivity and specificity (i.e. fewer false positives) of PCR-based tools, the need for the use of such tools in routine diagnostic testing and the likelihood that the incidence of cryptosporidial infections has been underestimated in Malaysia to date.

In livestock, epidemiological studies (Farizawati et al., 2005; Fatimah et al., 1995a,b; See, 1997) indicated a prevalence of 14.5–36% in goat kids, neonatal lambs and cattle. More recently, PCR-RFLP of SSU identified both *C. parvum* and *Cryptosporidium* 'deer-like' genotypes in cattle (Halim et al., 2008). Although zoonotic transmission has not yet been elucidated in detail in Malaysia, one study (Farizawati et al., 2005) has indicated the contribution of infected cattle to environmental contamination through the detection of *Cryptosporidium* oocysts (20–3100 per litre) in ''wastewater'' ponds on farms and in rivers receiving effluent from these wastewater ponds (3–240 oocysts per litre). Six species of birds (i.e. wrinkled hornbill, great argus pheasant, black swan, swan goose, marabou stork and moluccan cockatoo) displayed in different locations of a zoo were also found to excrete *Cryptosporidium* oocysts in the faeces (Rohela et al., 2005). Subsequently, cryptosporidiosis was detected both in birds (3.4% of 116) and in a bird handler at the same zoo (Lim et al., 2007a), which might indicate a local spread to other captive species in this setting, and possibly zoonotic transmission to bird handlers. However, molecular tools were not utilised to test this latter hypothesis. Importantly, *C. meleagridis* of birds (Morgan et al., 2001) is a known pathogen of humans (Leoni et al., 2006; Xiao et al., 2004), and, thus, transmission from birds to humans may be possible. A further study in the same zoo revealed 14.1% of 99 primates (7 species), 5.7% of 70 ungulates (3 species) and 14.3% of 28 felids (4 species) to be positive for *Cryptosporidium* oocysts (Lim et al., 2008b). *Cryptosporidium* oocysts were also detected in 4.1% of 49 rats (*Rattus exulans*) captured in an Orang Asli community (Lim and Ahmad, 2001). With rats being ubiquitous and found in close proximity to humans, livestock, food and water supplies, drainage and effluent routes, *Cryptosporidium*-infected rodents might represent a significant reservoir for transmission of cryptosporidiosis to humans and livestock due to their cohabitation and contamination of the environment. Here again, the application of molecular diagnostic tools (using suitable markers) would provide valuable insights.

In the environment, *Cryptosporidium* oocysts have been detected commonly in Malaysia (Lim et al., 2008a). For instance, in a study conducted in the northern state of Kelantan, where many households are dependent on well water for their daily chores and washing, 7.1% of 28 well-water samples were contaminated with *Cryptosporidium* oocysts (Lim et al., 2008a). An analysis of published studies indicated that 11.5% of 174 river water samples analysed contained *Cryptosporidium* oocysts (0.4–246 oocysts per litre). The quality of drinking water from eight treatment plants was also evaluated; *Cryptosporidium* oocysts were only found in the raw water (0.05–3 oocysts per litre) and backwash water (1200–1600 oocysts per litre) (Ahmad et al., 1997; Lim and Aahmad, 2004; Lim et al., 2008a; Tan, 1998). Sewage treatment works can also contribute *Cryptosporidium* oocysts to receiving waters used for the reclamation of drinking water, as demonstrated by two studies (Lim, 1996; Lim et al., 2007b) which showed that treated sewage effluent contained 20–80 *Cryptosporidium* oocysts per litre.

The occurrence of oocysts in soil within house compounds, particularly where children play regularly, should be of concern to public health officials, as *Cryptosporidium* oocysts have been detected in soil samples in Malaysia (Lim et al., 1999, 2008a). The viability of *Cryptosporidium* oocysts in water and soil in the Malaysian environment was assessed in two studies using fluorogenic vital dyes, 4′,6-diamidino-2-phenylindole (DAPI) and propidium iodide (PI). Both studies indicated that it takes 1–2 months for *Cryptosporidium* oocysts to become non-viable (Farizawati et al., 2005; Lim et al., 1999) in a tropical climate. It is likely that the high humidity and frequent rainfall contribute to prolonged viability of oocysts in the environment (particularly in soil or on exposed surfaces); oocysts are particularly susceptible to desiccation (Anderson, 1986; Nasser et al., 2007). However, fluorogenic dyes (and all other currently available viability assays, aside from experimental infection trials; Campbell et al., 1992; Mendez-Hermida et al., 2007) can provide a means of suggesting infectivity, but improved molecular tools are still required for assessing both viability and infectivity of cryptosporidial oocysts (cf. Jex et al., 2008).

1.2.5. Myanmar

Myanmar, one of the largest countries by geographical area on the mainland of Southeast Asia, is ruled by a military junta. It has an estimated population size of 48.3 million (Anonymous, 2009). Cryptosporidiosis was first detected in Myanmar in 1994 among infants (between 2 and 11 months of age) presenting with a mild, transient form of acute diarrhoea (Aye et al., 1994). Results from this study showed that 3.4% of 203 infants with diarrhoea were found to pass *Cryptosporidium* oocysts (Aye et al.,

1994). An investigation of intestinal parasites in 472 pre-school children (3 months to 5 years of age) conducted in Sangkhlaburi, a rural district in the western part of Thailand along the Thai–Myanmar border, which consists of Karen, Thai, Mon, and Burmese nationalities, identified cryptosporidiosis cases at an overall prevalence of 3.4%, with the highest percentage occurring during the rainy season (June to October) (Wongstitwilairoong et al., 2007). In consideration of the large proportion of asymptomatic carriers detected in other countries of Southeast Asia (Hakim et al., 2007; Janoff et al., 1990; Kamel et al., 1994b; Lim et al., 1997; Mohammed Mahdy et al., 2007; Wanke et al., 1999), it is highly probable that this prevalence of *Cryptosporidium* infections in humans in Myanmar is an underestimate.

1.2.6. The Philippines

The Philippines has a population size of ~85.5 million (Anonymous, 2009) and is made up of 7107 islands, with the main island groups consisting of Luzon, Visayas and Mindanao. The 'mixed economic system' (i.e. a private–public ownership) in the Philippines has contributed to it being one of the emerging market economies of the world. The first reported case of cryptosporidiosis in the Philippines was in 1985 in the San Lazaro Hospital in Manila, where 2.6% of 735 babies (6–20 months of age) were found (by coproscopic examination) to be passing *Cryptosporidium* oocysts (Cross et al., 1985). Such oocysts have also been detected in humans, cattle and carabao (i.e. water buffalo) faeces in a rural area in the Philippines (Laxer et al., 1988). Two other studies, using a serological approach, suggested a prevalence of 8.5% of *Cryptosporidium* infection in babies (1–24 months of age; $n = 823$) (Laxer et al., 1990) and 28.3% among 53 Filipino cancer patients (Rivera et al., 2005). In hospitalised Filipino children ($n = 236$), 2.5% tested positive for cryptosporidiosis (Paje-Villar et al., 1994). More recently, an extensive study involving 3456 diarrhoeic human patients throughout the Philippines showed a relatively low prevalence (1.9%) of cryptosporidiosis (Natividad et al., 2008). This disease was most prevalent in paediatric patients on Luzon Island during the rainy season (Natividad et al., 2008).

1.2.7. Singapore

With a population size of 4.3 million (Anonymous, 2009), Singapore is one of the smallest countries, but has one of the most robust and dynamic economies in Southeast Asia. Singapore is recognised as a country with a world renowned port, airport, airline and civil service. Surprisingly, despite Singapore's dependence on the importation of food and water from neighbouring countries, in particular Malaysia, there is no cohesive

baseline data on cryptosporidiosis in Singaporeans. To date, the only publicly available report of intestinal cryptosporidiosis in Singapore was from a single child with AIDS, who presented with profuse diarrhoea (up to 15 episodes a day) over a 1-week period (Wu et al., 1994). Recently, mainly due to Singapore's need to import drinking water, more emphasis has been placed on developing and enhancing detection methods for *Cryptosporidium* in water samples (Hu et al., 2004; Lee et al., 2004, 2008). With its huge monetary resources, molecular expertise and state-of-the-art infrastructure, Singapore is expected to be more active in the research of *Cryptosporidium* and cryptosporidiosis. The consolidation of the existing and development of new and innovative molecular diagnostic tools must be considered as a major goal in future research efforts.

1.2.8. Thailand

Thailand has a population size of ~65.9 million (Anonymous, 2009), and, like Singapore and Malaysia, the Thai economy is large (Morrison, 2003). Historically, Thailand has represented a relatively stable democracy (under the oversight of the Thai royal family). Cryptosporidiosis in humans is well documented in Thailand, mainly in children and HIV-infected people. Children were the main focus of early studies (Echeverria et al., 1989; Janoff et al., 1990; Jantanavivat et al., 1991; Jirapinyo et al., 1993; Jongwutiwes et al., 1990; Mungthin et al., 2001; Termmathurapoj et al., 2000; Thamlikitkul et al., 1987). For example, Thamlikitkul et al. (1987) reported a prevalence of 0.5% ($n = 1500$), highlighting *Cryptosporidium* as a common, non-viral cause of acute diarrhoea in young children. Other studies of cryptosporidiosis in Thai children recorded prevalences of 0.5–7.1% (Jantanavivat et al., 1991; Jirapinyo et al., 1993). The main clinical presentation in paediatric cases included acute or prolonged diarrhoea with fever (mean duration being 6.6 days) (Jantanavivat et al., 1991; Jirapinyo et al., 1993; Thamlikitkul et al., 1987). These studies emphasised the need for the differential diagnosis of infections caused by key pathogens (Jantanavivat et al., 1991; Jirapinyo et al., 1993; Thamlikitkul et al., 1987). The transmission of cryptosporidiosis in institutions, such as orphanages, appears to be significant in Thai children. For children living in orphanages, the prevalence of *Cryptosporidium* has been estimated at 7–12% (Janoff et al., 1990; Jongwutiwes et al., 1990; Mungthin et al., 2001; Termmathurapoj et al., 2000). In an early study, Janoff et al. (1990) highlighted an association between cryptosporidiosis and an acute, depressed nutritional status in orphans, which likely contributed to the relatively high prevalence of infection in the institutional setting. Interestingly, most children examined in Thai orphanages were asymptomatic (Janoff et al., 1990; Jongwutiwes et al., 1990; Mungthin et al., 2001;

Termmathurapoj et al., 2000), which emphasises their significance as 'carriers'; particularly under poor hygienic conditions (in such orphanages), there is a substantial risk of transmission of cryptosporidiosis to healthy children via direct person-to-person contact.

Since the HIV epidemic began in 1984, a significant number of studies of cryptosporidiosis in Thailand has focused on HIV-infected patients (Chokephaibulkit et al., 2001; Gatei et al., 2002b; Manatsathit et al., 1996; Moolasart et al., 1995; Nuchjangreed et al., 2008; Pinlaor et al., 2005; Punpoowong et al., 1998; Saksirisampant et al., 2002; Tiangtip and Jongwutiwes, 2002; Uga et al., 1998; Wanachiwanawin et al., 2002; Wanke et al., 1999; Waywa et al., 2001; Wiwanitkit, 2001). These studies have indicated a high prevalence (8.8–27%) of cryptosporidiosis among HIV-positive and/or HIV/AIDS patients, particularly those with CD4 counts of <100 cells/mm^3 (Pinlaor et al., 2005) and clinical signs, such as chronic, watery diarrhoea and weight loss (Chokephaibulkit et al., 2001; Moolasart et al., 1995; Wanke et al., 1999). These publications emphasised the need for the routine diagnosis of cryptosporidiosis, given its major clinical significance in HIV-infected patients (Chokephaibulkit et al., 2001; Wiwanitkit, 2001). Gatei et al. (2002b) investigated the molecular epidemiology of cryptosporidiosis in patients with advanced AIDS in Thailand. Employing PCR-RFLP analysis and DNA sequencing of partial SSU, these authors discovered that 50% of 34 isolates were associated with *C. hominis* (known previously as *C. parvum* type-1), 21% with *C. meleagridis*, 15% with *C. parvum* (previously *C. parvum* type-2), 9% with *C. felis* and 6% with *C. canis*. Using similar approaches, Tiangtip and Jongwutiwes (2002) tested 29 faecal samples from HIV patients in Thailand and found infections associated with *C. hominis* (82.8%), *C. meleagridis* (10.3%), *C. felis* (3.4%) or *C. muris* (3.4%).

Cattle farming is common in Thailand. Dairy herds are relatively widespread, with the Nong Pho (central Thailand) representing an area with a high density of farms. The shedding of human-infective oocysts by dairy cattle is well documented globally (Nolan et al., 2009; Santin et al., 2008; Smith et al., 2005; Xiao and Feng, 2008), but the prevalence of *Cryptosporidium* in developing countries is often unclear. A recent, broad survey of *Cryptosporidium* in Holstein-Friesian (dairy) cows from 108 farms (randomly selected from a total of 860 farms) was conducted in Nong Pho. In total, 363 cattle, varying from 6 months to 5 years of age, were tested (using conventional Ziehl–Neelsen staining/microscopy and an immunoassay). Oocysts were detected in 9.4% of the 363 cattle, with 31.5% of the farms having *Cryptosporidium*-infected cattle (Jittapalapong et al., 2006). Importantly, only two cattle were test-positive based on microscopy, whereas 34 were inferred to harbour *Cryptosporidium* based on a commercial immunoassay (ProSpecT, Alexon-Trend, Inc., Minnesota; specificity = 98.6%), suggesting significant limitations associated

with the use of microscopy alone. By age group, the prevalence estimate was highest (15.1%) in young animals and decreased with age (7.8% and 5.2% in cattle of <1 year and 1–5 years of age, respectively). Farm management was found to be a significant contributing factor to the prevalence/incidence of cryptosporidial infection. All 108 farms were rated as poorly ($n = 54$) or acceptably managed ($n = 54$) based on specific selection criteria, which included pen flooring and bedding type, cleaning practices and the storage of feed and bedding. Poorly managed farms were more likely, by a ratio of 4:1 ($n = 34$) to have cattle infected with *Cryptosporidium* (as determined by the immunoassay), emphasising the importance of farm management in the transmission of infectious diseases among animals and potentially to the wider human community (Jittapalapong et al., 2006). Although Jittapalapong et al. (2006) did not genetically characterise *Cryptosporidium* in their study, a subsequent investigation in Thailand (see Nuchjangreed et al., 2008) conducted using a nested-PCR approach (employing SSU) identified *C. parvum* in all *Cryptosporidium* test-positive samples ($n = 8$), suggesting the contribution of infected cattle to human cryptosporidiosis in Thailand.

In the environment, an extensive network of water canals in Thailand and the practice of disposing of domestic and commercial waste into these urban canal networks represent a substantial potential source of waterborne diseases. A recent study (Anceno et al., 2007) showed that the concentration of *Cryptosporidium* oocysts in two canals (i.e. Klong Neung and Klong Song) in Thailand was between 0 and 95 oocysts per litre and confirmed the specific identity of these oocysts as *C. parvum* by real-time PCR and sequencing of a region of the *Cryptosporidium* oocyst wall protein (*cowp*) gene. This study provided compelling evidence that the canal networks are likely to play a significant role in the dispersal of anthroponotic and zoonotic pathogens (Anceno et al., 2007). The findings from this study highlighted problems associated with the contamination with pathogens, including *Cryptosporidium*, through run-off from nearby streets and market places, and through the direct disposal of untreated household sewerage. The authors also conducted a risk assessment and concluded that the accidental ingestion of as little as 100 ml of untreated canal water represented a 'high probability of infection among exposed individuals', which peaked during the dry season (i.e. when canal water is shallow and most prone to turbulence). The authors also indicated that such risks could be reduced through the retention of canal water in stabilisation ponds, significantly reducing oocyst load presumably through settling, and oocyst viability presumably through prolonged exposure to sunlight (UV radiation). Importantly, Anceno et al. (2007) showed that oocyst concentrations could vary substantially from point-to-point along these canals, indicating the need for testing at multiple locations. Since water volumes ingested by humans and animals could be

small (e.g. 100 ml), the sensitivity and specificity of the test procedure were critical in reliably assessing risk levels. Clearly, future investigations should utilise advanced molecular techniques (e.g. PCR-based tools utilising suitable genetic markers; Jex et al., 2008) to infer the zoonotic potential of *Cryptosporidium* oocysts from any biological matrix and to compare against species/genotypes already known in the developed world (Jex and Gasser, 2009).

It has been demonstrated that contaminated water used in the food industry (e.g. for the washing and preparation of food) can represent a significant source of infection and can present a risk without the direct consumption of the water itself (Smith et al., 2007). Recently, Sutthikornchai et al. (2005) employed an immunological assay for the detection of *Cryptosporidium* oocyst contamination in bulk water used in the frozen food industry in Thailand (20 industrial sites). At these sites, water was sourced from underground aquifers and then treated (by sand filtration and chlorination) prior to direct use in food preparation. However, given that untreated water was often used for cleaning, oocyst levels were examined both in treated and untreated aquifer water samples. In total, *Cryptosporidium* oocysts were detected in untreated water samples from 6 (35%) of the 20 industrial sites at an average of 29 oocysts per 1000 litres (geometric mean: 27) (Sutthikornchai et al., 2005). Although there was no evidence that the treated water samples used directly for food preparation contained detectable oocyst levels, this study revealed a high prevalence and broad distribution of *Cryptosporidium* oocysts in underground aquifers and the environment. Although the specific identity of such oocysts should be determined in the future using molecular techniques, this study by Sutthikornchai et al. (2005) illustrated the potential for untreated water to contaminate food products and subsequently infect workers, particularly given that *Cryptosporidium* oocysts are at least partially resistant to freezing (Fayer and Nerad, 1996).

1.2.9. Vietnam

Vietnam, with a population size of 84 million (Anonymous, 2009), is one of the more flourishing of the war-ravaged countries in Southeast Asia. The extensive collaborative scientific research programmes instigated, since Vietnam embraced the open-market policy, have enabled some epidemiological investigations of *Cryptosporidium*/cryptosporidiosis. Molecular data were first reported for *Cryptosporidium* from humans in 2003. *Cryptosporidium hominis* was discovered in three isolates from HIV-infected adults (Gatei et al., 2003). More recently, a study investigating the prevalence and epidemiology of *Cryptosporidium* infection in cattle ($n = 266$) in the central region of Vietnam identified *C. parvum* (33.5%), *C. andersoni* (5.6%) and mixed infections (3.4%) of both species (Nguyen et al., 2007).

This study revealed that cryptosporidial infections showed an age-related pattern, with *C. parvum* being more prevalent in diarrhoeic calves of <6 months of age, and asymptomatic *C. andersoni* infection occurring in adult cattle (Nguyen et al., 2007). This age-affiliation was consistent with the results from two longitudinal studies of cryptosporidiosis in dairy cattle in the USA (Santin et al., 2004, 2008) and highlights the particular relevance of young calves as potential reservoirs of *C. parvum* for transmission to humans.

1.2.10. Brunei Darussalam and East Timor

Both Brunei Darussalam and East Timor have small populations; 0.4 and 1 million people, respectively (Anonymous, 2009). Brunei Darussalam is an oil-rich monarchy, whilst East Timor became a fully independent republic only in 2002. To date, no cryptosporidiosis cases have yet been reported from either country. Both countries represent interesting regions for research into *Cryptosporidium*/cryptosporidiosis, albeit for differing reasons. Brunei Darussalam is a wealthy island nation and has huge monetary resources. In contrast, East Timor still lacks a substantial amount of infrastructure (e.g. for provision of drinking water or sewage treatment) and is home to many remote communities in which cryptosporidiosis is predicted to be prevalent. There is substantial scope for future studies of the nature and extent of cryptosporidiosis in these countries.

1.3. CONCLUSIONS AND RECOMMENDATIONS

Cryptosporidiosis is a global disease which has been included in the 'Neglected Diseases Initiative' (Savioli et al., 2006), and *Cryptosporidium* has been defined as a 'reference pathogen' for assessing the quality of water (Medema et al., 2006). As *Cryptosporidium* is resistant to common water treatments and there is no affordable, highly effective therapeutic or vaccination intervention against cryptosporidiosis, prevention and control strategies must be underpinned by substantial epidemiological data obtained through the use of accurate molecular-diagnostic tools. However, despite the importance of diarrhoeal diseases globally and the major impact that cryptosporidiosis has on human and animal health (Tzipori and Widmer, 2008), there are still major gaps in the knowledge of the prevalence and distribution of *Cryptosporidium* species/genotypes in many areas of the world, including Southeast Asia.

The present chapter highlights that, although cryptosporidiosis is prevalent in many parts of Southeast Asia, very little is known about the epidemiology and health impacts of this disease in this part of the world. Key studies have targeted mostly high risk groups, such as HIV-infected

patients and children of <5 years of age, but, clearly, cross-sectional community studies are needed to (i) strengthen *Cryptosporidium* surveillance in the general population, (ii) identify asymptomatic carriers (Hakim et al., 2007; Janoff et al., 1990; Kamel et al., 1994b; Lim et al., 1997; Mohammed Mahdy et al., 2007; Wanke et al., 1999), (iii) determine the range of *Cryptosporidium* species/genotypes present and (iv) identify any geographical and seasonal trends in the transmission of cryptosporidiosis.

An assessment of the impact of cryptosporidiosis requires reliable epidemiological datasets, supported by informative, national and regional surveillance systems. With comprehensive information on the impact of diarrhoeal diseases, effective control measures can be implemented. In spite of some researchers stressing the major importance of *Cryptosporidium* as an intestinal protozoan in Southeast Asia since the early 1980s (Mendez et al., 1988; Thamlikitkul et al., 1987), surprisingly, faecal samples are usually not routinely examined for *Cryptosporidium* oocysts in diagnostic laboratories (Jantanavivat et al., 1991; Jirapinyo et al., 1993; Jongwutiwes et al., 1990; Lim et al., 2005, 2008a), and cryptosporidiosis is not a notifiable disease in most countries in this region. As a result, cryptosporidiosis remains under-diagnosed and a seriously neglected disease.

It is essential that routine diagnostic testing for *Cryptosporidium* is carried out on patients with gastrointestinal disease (with or without evidence of diarrhoea). In addition, large-scale surveys of domestic and wild animals (as potential reservoirs for human infection) and the environment are needed. Such epidemiological surveys should rely on the use of molecular-diagnostic tools that are sensitive, specific and cost-effective. Most epidemiological data for Southeast Asia have been based on the use of conventional microscopic methods of diagnosis. However, this phenetic approach is of limited utility, as neither oocyst morphology nor morphometry allow the specific identification of oocysts, and both lack diagnostic specificity and sensitivity (particularly for the examination of bulk water samples) (e.g. Fall et al., 2003; Jex et al., 2008). The application of molecular-diagnostic tools, particularly those based on PCR and employing multiple genetic markers, now underpins epidemiological investigations of *Cryptosporidium* and cryptosporidiosis, allowing specific and genotypic identification and differentiation of oocyst isolates from any source, with much greater sensitivity and specificity than achievable using conventional microscopic approaches (Jex et al., 2008; Smith et al., 2006). Molecular epidemiological data are essential in assessing the risk posed to the public by oocysts detected in biological or environmental samples, and could be used to aid health professionals in 'tracking' infection sources.

Advanced molecular-diagnostic and molecular-analytical approaches are utilised to yield vital DNA sequence data on genetic variation among

Cryptosporidium populations from various biological samples, facilitating the surveillance, tracking and control of cryptosporidiosis within and across national boundaries. Although some molecular methods can be expensive to perform, the costs can be kept low through the use of practical electrophoretic and other mutation scanning tools (Jex and Gasser, 2009; Jex et al., 2008). Clearly, in Southeast Asian countries, an improved diagnostic, prevention and control strategy will require a multidisciplinary and integrated scientific approach, built on a sustained sharing of skills, expertise and resources, and focused on improved legislation regarding communicable infectious diseases. With consolidated efforts in countries such as Malaysia, with centres of expertise in the epidemiology of water-borne cryptosporidiosis, Singapore, with strengths in the development of technology for the detection of oocysts in water, and Thailand and Vietnam, with progress in the molecular characterisation of *Cryptosporidium*, detailed insights into *Cryptosporidium*/cryptosporidiosis can be gained without Southeast Asian countries having to forsake research because of insufficient funding.

Given the complex geography and trans-national relationships within Southeast Asia, a workable strategy for reducing the burden of cryptosporidiosis would require both scientific and political solutions. In order to advance epidemiological surveillance and to understand the significance of cryptosporidiosis in this region, the following approaches are recommended:

- Establishing national surveillance systems for cryptosporidiosis, based on the use of standardised microscopic and molecular-diagnostic tools and reporting systems;
- Developing shared regional, epidemiological databases for the monitoring of geographical and seasonal variations in prevalence and intensity of cryptosporidial infections, aiding comparative investigations;
- Founding a regional *Cryptosporidium* repository to facilitate the exchange of oocyst isolates and/or DNA samples derived from them;
- Establishing centres or international consortia for diagnostic testing, to reduce redundancy in infrastructure and costs, and to maximise accessibility to equipment, information and expertise;
- Developing evidence-based research to assist policy makers, particularly to incorporate *Cryptosporidium* detection as a parameter in national drinking water quality standards;
- Establishing and utilising methods to assess the infectivity, viability and/or survival of oocysts in water destined for human consumption and the environment;

Adopting these advances or measures in Southeast Asia should assist in developing effective risk assessment, management and communication models.

Multidisciplinary intervention, including increased public awareness, advice on appropriate hygienic practices (e.g. for waste disposal, food handling and use of swimming facilities), the adoption of highly active anti-retroviral therapy (HAART) and the implementation of better water treatment and management strategies (US-EPA, 1996) have reduced the prevalence and impact of cryptosporidiosis in developed nations. The lessons learnt from these interventions should now be disseminated worldwide, particularly to developing regions, such as those in Southeast Asia, where cryptosporidiosis has a substantial adverse impact on human health. Considering the high human population densities in many developing nations, the limited or lack of access to safe drinking water, the pressures placed on water resources by accelerating climate change and the increase in prevalence of immunodeficiency as a result of the HIV/AIDS pandemic, diarrhoeal pathogens, *Cryptosporidium* in particular, represent major and emerging threats to the health and well-being of people in regions in which there are massive gaps in knowledge of infectious diseases. Closing these gaps in Southeast Asia will require substantial and sustained international efforts and investments. This focus has the potential to greatly aid in the prevention and control of neglected diseases, not only limited to cryptosporidiosis, but also including other infectious diarrhoeal diseases (e.g. giardiaisis and amoebic dysentery) as well as debilitating diseases caused by soil-transmitted helminths (Bethony et al., 2006). Such an approach would provide a model for the deployment of similar strategies in other developing regions around the world, represent an integral component of addressing global poverty and make a major contribution to developing the socioeconomic fabric of many nations.

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CHAPTER 2

Human Schistosomiasis in the Economic Community of West African States: Epidemiology and Control

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Contents

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Abstract The present study aims to report on the epidemiology and control of schistosomiasis in the Economic Community of West African States (ECOWAS), which represents 30% of the total population of the African continent. Fifteen states are included in ECOWAS, three of which were elected by the Schistosomiasis Control Initiative: Mali, Niger and Burkina Faso, the other 12 countries being Benin, Cape Verde, Côte d'Ivoire, The Gambia, Ghana, Guinea, Guinea Bissau, Liberia, Nigeria, Senegal, Sierra Leone and Togo. For each country we updated, according to the different administrative regions of the country, the epidemiological data concerning the prevalence of human schistosomiasis and the prevalence of snail schistosomiasis and the control programmes each country is developing. The study highlights the common data in ECOWAS regarding the status of the infected people, the causes of schistosomiasis infection, the epidemiology of *Schistosoma haematobium* and *Schistosoma mansoni* in relation to their respective snail intermediate hosts, *Bulinus* and *Biomphalaria*. The new epidemiological approaches generating maps of zones of disease risk will provide helpful tools for schistosomiasis control.

2.1. INTRODUCTION

Schistosomiasis is a water-borne human helminthiasis caused by blood flukes and occurs in approximately 76 countries around the world (Africa, South America, Middle East and the South Asian continent) (Engels et al., 2002). It is estimated that 779 million people are at risk of infection by schistosomes and 207 million people are infected, mostly in sub-Saharan Africa (97%) (Steinmann et al., 2006). Those most at risk are school-age children, women with their infants and pre-school children, and those involved in occupations such as irrigation, farming and fishing. The two major species of human schistosomes in Africa, *Schistosoma haematobium* and *Schistosoma mansoni*, make up 2 of the 13 neglected tropical diseases (NTDs) in this continent (Molyneux et al., 2005). Schistosomiasis is part of the seven most prevalent NTDs (Hotez et al., 2007a) and ranks as the second most prevalent NTD after hookworm infection in sub-Saharan Africa (Hotez and Kamath, 2009).

The life cycle of human schistosomes includes two obligatory hosts: the human host in which the adult male and female parasites sexually reproduce (dioecy) and a freshwater snail in which the parasite asexually

multiplies. The human-to-snail transmission is ensured by a swimming larval stage, the miracidium, hatching from the egg and which actively penetrates the snail. The snail to human transmission is ensured by the cercaria, a swimming larval stage produced by the intramolluscan larval stages, the sporocysts. Cercaria actively penetrates and migrates through the human skin, reaches the vascular system, travels to the liver where it grows to an adult worm. Here, male and female worms pair up and then live for many years in the blood vessels surrounding the bladder or intestine, feeding on the blood. Female worms lay eggs, many of which escape from the body during urination or defecation. In heavy infections, thousands of eggs escape from the body daily by rupturing capillary blood vessels causing blood loss. Those eggs which do not escape become trapped mainly in the liver, causing damage, and in extreme cases, eventually leading to death.

No country of the sub-Saharan African continent is safe from infection today and worse still is the development of water resources such as the construction of dams and irrigation schemes in order to face the growing demand of water, food and energy that often leads to an expansion of the habitats of intermediate host snails, enhancing the potential transmission sites for schistosomiasis and introducing schistosomiasis into new areas.

The Economic Community of West African States (ECOWAS) is the most populous regional economic community in Africa. It represents a West African common market of more than 280 million consumers, that is, around 30% of the total population of the African continent. It is a group of 15 countries, founded in 1975 and the member states include: Benin, Burkina Faso, Cape Verde, Côte d'Ivoire, The Gambia, Ghana, Guinea, Guinea Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone and Togo (Fig. 2.1). These countries offer a wide range of natural environments with four classes of ecoregion (land with the same characteristic plant succession), from North to South: the subtropical desert and semi-desert, the subtropical dry grassland, the tropical dry forest and savanna and the tropical wet forest (Fig. 2.1). The number of classes each country of ECOWAS is transected by goes from only one class for Cape Verde (subtropical dry grassland), The Gambia and Togo (subtropical dry forest and savanna) and Liberia (tropical wet forest) to three classes for Niger, Mali and Nigeria; the eight other countries are transected by two ecoregion classes.

ECOWAS aims to promote co-operation and integration programmes, projects and activities, particularly in food, agriculture and natural resources, industry, transport and communications, energy, trade, money and finance, taxation, economic reform policies, human resources, education, tourism, legal matters, information, culture, science, technology, services and health. A Specialised Agency of ECOWAS, called West African Health Organisation (WAHO), was formed in 1987. It merged

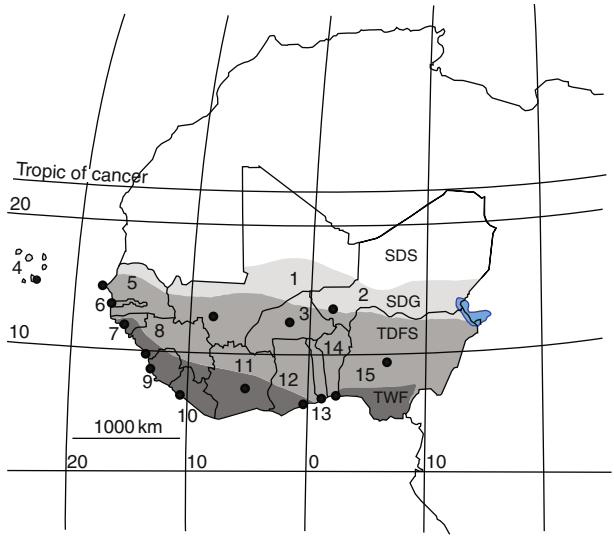

FIGURE 2.1 The 15 countries belonging to the Economic Community of West African States (ECOWAS) with the ecoregions that transect them: 1, Mali; 2, Niger; 3, Burkina Faso; 4, Cape Verde; 5, Senegal; 6, Gambia; 7, Guinea-Bissau; 8, Guinea; 9, Sierra Leone; 10, Liberia; 11, Côte d'Ivoire; 12, Ghana; 13, Togo; 14, Benin; 15, Nigeria; SDS, subtropical desert and semi-desert; SDG, subtropical dry grassland; TDFS, tropical dry forest and savanna; TWF, tropical wet forest. The black dots are the capitals.

with the Francophone 'Organisation de Coordination et de Coopération pour la Lutte Contre les Grandes Endémies' (OCCGE) and the Anglophone 'West African Health Community' (WAHC) and was committed to transcending linguistic borders to serve all 15 ECOWAS Member States. Its objectives are the following: ''. . . the attainment of the highest possible standard and protection of health of the peoples in the sub-region through the harmonisation of the policies of the Member States, pooling of resources, and cooperation with one another and with others for a collective and strategic combat against the health problems of the sub-region''.

The basic principle for ECOWAS is to raise the living standards of its peoples (around 7.5 million people (almost half being women), almost 3% of the regional population are considered migrants) and to remove, between Member States, the obstacles to the free movement of persons, goods, service and capital. However, this free movement of people, together with the large water network in ECOWAS, favours the expansion of the water-dependent parasitic endemic diseases, like malaria, onchocerciasis and schistosomiasis. Furthermore, the great majority of the countries in ECOWAS harbour 5 of the 13 NTDs of Africa and schistosomiasis in individuals is often associated with three different

soil-transmitted helminth (STH) infections (ascariasis, trichuriasis and hookworm infection) (Molyneux et al., 2005).

Schistosomiasis causes serious public health problems in this region of Africa, and epidemiological data on prevalence of infection in humans, associated or not with malacological surveys and schistosome prevalence in snails, are regularly published. However, the efforts towards a regular updating of the epidemiological data in order to follow the evolution of the disease are different depending on the countries it is associated with. Different also are the ways by which each country fights the disease. Indeed, ECOWAS countries may be separated into two groups: the first group includes the countries integrated in the Schistosomiasis Control Initiative (SCI) and the second group includes all the other countries. The two most important human schistosome species existing in ECOWAS are *S. haematobium* and *S. mansoni*. A third species, *Schistosoma guineensis* (Kane et al., 2003; Pagès et al., 2003), is also present, and originated from the division of *Schistosoma intercalatum* into two separate species, *S. intercalatum* in the Democratic Republic of the Congo and *S. guineensis* in the Lower Guinea region. Therefore, in the present chapter, we will consider rectal schistosomiasis in ECOWAS as being due to *S. guineensis* and not *S. intercalatum*.

The present study aims to update the more important and recent data on human schistosomiasis epidemiology in ECOWAS. The objectives are, for each of the ECOWAS country, to present the country with its ecoregions, hydrography and administrative divisions; to update the epidemiological data concerning prevalence of infection in both humans and snails and the control programmes that are being developed.

2.2. THE SCHISTOSOMIASIS CONTROL INITIATIVE

The Schistosomiasis Control Initiative (2008) was established at Imperial College London in June 2002 as a partnership that included the Bill and Melinda Gates Foundation, the World Health Organisation and the Harvard School of Public Health. The award has been directed to delivering treatment for schistosomiasis and STHs to millions of sub-Saharan Africans at high risk of this serious disease. Eight countries were selected by the SCI: five from East Africa (Burundi, Rwanda, Tanzania, Uganda and Zambia) and three are situated in the Central North of ECOWAS, Mali, Niger and Burkina Faso (Fig. 2.1). The last three countries are neighbours, share borders and are the only countries which do not have any access to the Atlantic Ocean. National control programmes were launched in 2004 for these three countries, and their evaluations are in process (Brooker et al., 2004). The national control programmes are supported by the US Agency for International Development (USAID)

Neglected Tropical Disease Control Program (Hotez et al., 2007a). Clements et al. (2008) produced maps using Bayesian geostatistical models for Mali and Niger in order to be integrated into the SCI-supported national intervention strategies.

2.2.1. Mali

2.2.1.1. Ecoregions, hydrography and administrative regions (Figs. 2.1 and 2.2)

Mali is transected by three ecoregions from North to South: the subtropical desert and semi-desert in the North of the country, which occupies the largest place, the subtropical dry grassland and the tropical dry forest and savanna. The country is drained by two major rivers and their tributaries, the Niger River in the Eastern (the third longest on the continent) and Southern parts and the Senegal River in the Western part. The Niger River flows on through 1700 km in Mali and the flood period reaches its peak in October/November producing an inland sea of 20,000–30,000 km^2. During the dry season, freshwater is distributed to numerous lakes and residual pools. Three major dams are situated on the Niger River and its

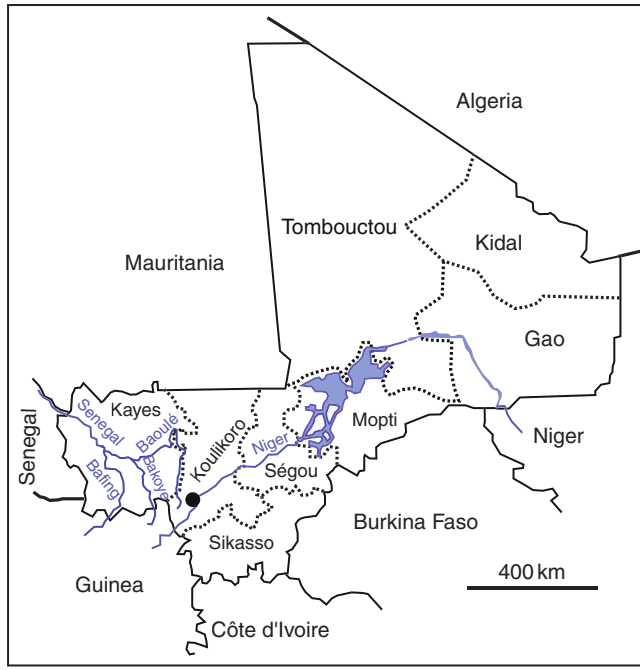

FIGURE 2.2 Mali, its water network and its eight regions. The black dot is the capital, Bamako.

tributaries: Markala dam in the Ségou region, Selingué dam in the Sikasso region and Sotuba dam near Bamako. They are associated with the development of irrigated areas. The Senegal River is situated in the Kayes region. It issues from the junction of the Baoulé, the Bakoye and the Bafing rivers and runs through 730 km in Mali. The Kayes region harbours two major dams: the Manantali dam in the Bafing basin and the Félou dam on the Senegal River. Mali is divided into eight regions: Gao, Kayes, Kidal, Koulikoro, Mopti, Ségou, Sikasso and Tombouctou. Its capital is Bamako.

2.2.1.2. Human schistosomiasis prevalence

Schistosomiasis in this country develops and spreads only South of the 17th N latitude.

2.2.1.2.1. Schistosoma haematobium This species has been found largely distributed in the different regions of Mali. However, four zones were particularly analysed: the urban and periurban area of Bamako (Koulikoro region), the Sélingué dam (Sikasso region), the rice irrigation scheme 'Office du Niger' (near the Markala dam in the Ségou region) and the touristic Dogon Plateau in the Mopti region. In Bamako district, the prevalence ranged from 1.2% to 98.3% (number of surveys = 84; 18 less than 10%) (Doumenge et al., 1987), and was 36.6% (Doumbo et al., 1992), 69.8% (Sangho et al., 2002), 46.7% and 80.7% (Dabo et al., 2003). The prevalence in the Sikasso region before the construction of the Sélingué dam ranged from 0% to 62% (number of surveys = 38; prevalence less than 10% in 26 and nil in 3) (Doumenge et al., 1987). After the construction of the dam, the fishermen who had migrated to the area near the dam had the highest prevalence (57.9%), compared to that from the resettled villages (20.9%) or that from the non-resettled villages (11.6%) (Traoré, 1989). In the zone of the rice irrigation scheme the prevalence ranged from 10.5% to 97% (number of surveys = 47) (Doumenge et al., 1987) and was 53.8% and 73.1% (Traoré et al., 1998). Furthermore, *S. haematobium* was found to be more prevalent in the areas with double cropping (67.3–96.2%; number of surveys = 5) compared to the areas with single cropping (28.4–52.5%; number of surveys = 5) (Coulibaly et al., 2004). These results are supported by those of Brinkmann et al. (1988a) who found that the risk of schistosomiasis infection was six times higher in irrigated areas than in savanna villages. In several villages of the touristic Dogon Plateau, prevalence ranged from 0.8% to 100% (number of surveys = 52; prevalence less than 10% in 5) (Doumenge et al., 1987), from 32.4% to 59.5% (number of surveys = 5) (de Clercq et al., 1994) and was 13.7% and 72.6% (Traoré et al., 1998). The epidemiological data available from the other regions of Mali showed that prevalence ranged from 4% to 86% in Kayes region (number of surveys = 22; prevalence less than 10% in 8) and from 4.7% to 41.2% in Tombouctou/Gao region

(number of surveys = 11; prevalence less than 10% in 2) (Doumenge et al., 1987).

2.2.1.2.2. Schistosoma mansoni *S. mansoni* has been found largely distributed in the different regions of Mali. The three zones already investigated for *S. haematobium* were more particularly followed up: the Bamako city and suburban areas, the rice irrigation scheme area and the Dogon Plateau. Contrasting results were obtained in Bamako zone where prevalence ranged from 0% to 92.7% (number of surveys = 73; prevalence less than 10% in 58 and nil in 40) (Doumenge et al. (1987), was low between 3.4% (Doumbo et al., 1992) and 8.7% (Sangho et al., 2002) or higher between 22.8% and 28.2% (Dabo et al., 2003). The rice irrigation scheme of the 'Office du Niger' showed higher prevalence, from 0% to 83.7% (number of surveys = 46; prevalence less than 10% in 7 and nil in 1) (Doumenge et al., 1987) and from 81.0% to 100% (number of surveys = 10) (Coulibaly et al., 2004). The Dogon Plateau harboured quite low prevalence, from 0% to 21.6% (number of surveys = 30; prevalence less than 10% in 25 and nil in 9) (Doumenge et al., 1987) and 0% to 26.8% (number of surveys = 5; prevalence less than 10% in 3 and nil in 1) (de Clercq et al., 1994). The other regions that harboured quite a low prevalence were Kayes from 0% to 39% (number of surveys = 21; prevalence less than 10% in 15 and nil in 7), Sikasso from 0% to 37.5% (number of surveys = 38; prevalence less than 10% in 34 and nil in 16) and Tombouctou from 0% to 3% (number of surveys = 4; prevalence less than 10% in 4 and nil in 2) (Doumenge et al., 1987), but a higher prevalence was reported from Central Mali (36–93%, Kardorff et al., 1994). The presence of both *S. haematobium* and *S. mansoni* was reported from the different regions (Coulibaly et al., 2004; Dabo et al., 2003; de Clercq et al., 1994; Doumbo et al., 1992; Doumenge et al., 1987; Sangho et al., 2002). The prevalence of *S. mansoni* was generally lower than that of *S. haematobium*, except in some areas around Bamako and in the Ségou region where both parasites showed a similar high prevalence.

2.2.1.2.3. Schistosoma guineensis The presence of *S. guineensis* in the Malian population has not been reported. However, its presence was detected in a group of travellers returning from the Dogon Plateau in the Mopti region (Corachan et al., 1992; Visser et al., 1995). The presence of *S. guineensis* in the Malian population still needs to be confirmed.

2.2.1.3. Snail intermediate hosts and their schistosome prevalence

Several snail intermediate hosts were found in Mali: *Bulinus globosus*, *B. forskalii*, *B. senegalensis*, *B. truncatus* and *B. umbilicatus* as hosts for *S. haematobium*, and *Biomphalaria pfeifferi* as the host for *S. mansoni* (Madsen et al., 1987). Four main zones were surveyed: the suburban

area of Bamako, the Sélingué Lake, the rice irrigation scheme area 'Office du Niger' and the Dogon Plateau. In Bamako, the *S. haematobium* prevalence was 20.6% for *B. truncatus* and 24.1% for *B. globosus* and the *S. mansoni* prevalence was 25–30% (Madsen et al., 1987) and 49.3% (Dabo et al., 2003) for *B. pfeifferi* which was very high. In Sikasso region, in the Sélingué Lake, *B. globosus*, *B. forskalii* and *B. truncatus* were found, the latter being widely distributed and naturally infected (12%); *B. pfeifferi* was also present (Madsen et al., 1987). In the 'Office du Niger', *B. forskalii*, *B. truncatus* and *B. pfeifferi* were found, but only the latter two were naturally infected: the infected snails were collected from the principal canals with a prevalence of 11% in *B. truncatus* and 27% in *B. pfeifferi* and were also found in smaller canals (Madsen et al., 1987). Another study showed that the snails were mainly from the tertiary canals and collected during the off-season (from January to May) when the prevalence was very high, 55.7% and 77.8% for *B. truncatus* and 75.6% and 96.9% for *B. pfeifferi* respectively (Coulibaly et al., 2004). In Dogon Plateau, all the *Bulinus* species, except *B. umbilicatus*, were found but none shed schistosome cercariae (Madsen et al., 1987). In another study, *B. truncatus* and *B. pfeifferi* were found in pools and some (data not shown) were naturally infected while non-infected *B. forskalii* were found in smaller numbers in brick pits (de Clercq et al., 1994). *B. senegalensis* was only found in Mopti and Ségou regions and *B. umbilicatus* was only found in Mopti region; they were never found naturally infected (Madsen et al., 1987).

2.2.1.4. Schistosomiasis control

A national programme of schistosomiasis control started in the Dogon Plateau in 1982, as a component of a dam-building project (Brinkmann et al., 1988b) and was active afterwards also in the 'Office du Niger' irrigation area, in the Baguineda irrigation area near Bamako and in the Sélingué dam zone. The control was mainly based on periodical mass chemotherapy of school-age children with high schistosome prevalence, by using praziquantel (Brinkmann et al., 1988b; Landouré et al., 2003), and also attention being paid to sanitation and health education. A new impulse in schistosomiasis control came in 2004, thanks to Schistosomiasis Control Initiative (2008) support (Fenwick et al., 2006; Garba et al., 2006), when the National Schistosomiasis Control Programme (PNLSG) was launched in the Ségou region. Almost 700,000 children and adults were treated in this region; the overall coverage rate was over 92%. In 2005, in the Dogon Plateau (Mopti region), more than 1 million individuals, all children aged 5–15, were targeted for treatment in 6 days. Prevalence has been reduced by approximately 50% in these two regions as also in Bamako area. Since 2005, Mali has expanded its National Schistosomiasis Control Programme and continues to treat the at-risk population once annually. Before large-scale administration of the

treatment, ultrasonography has been found to be a suitable and valid public health tool for urinary schistosomiasis for morbidity control programmes focused on children (Koukounari et al., 2006). In 2007, USAID awarded a grant to Mali in order to scale up its NTD programme to an Integrated NTD Control Programme. Furthermore, in order to provide a basis for local reorganisation and the strengthening of public health programmes, forecasts of *S. haematobium* have been generated in the region of Ségou (Niono area) from a data set 1996–2004 (Medina et al., 2008). Schistosomiasis remains a major health problem in Mali as *S. haematobium* and, to a lesser extent, *S. mansoni* were found at a higher prevalence in the urban zones and also near the waterbodies along the Niger River and its tributaries. Prevalence in snails was also found to be very high for these two schistosome species. The presence of *B. forskalii*, host for *S. guineensis*, should alert the authorities to the possible transmission of this schistosome in the country. The efforts that have already been made in Mali need to be continued in order to achieve long-term sustainable schistosomiasis control.

2.2.2. Niger

2.2.2.1. Ecoregions, hydrography and administrative regions (Figs. 2.1 and 2.3)

Niger is transected by three ecoregions from North to South: the subtropical desert and semi-desert in the North of the country, which occupies the largest place (Agadez region), the subtropical dry grassland forming a land band from West to East and a small part of the tropical dry forest and savanna beginning at the South limits of Niamey. Only two permanent waterbodies exist in Niger; they are situated in the West and East extreme South of the country: the Niger River in the South-West runs through 400 km from Mali to Benin, and crosses Tillabéri and Dosso regions and also Niamey city; Lake Chad (Diffa region) enters a small part of the South-East of Niger. The population of Niger is concentrated in the Niger River valley and all along the Nigerian border. Niger is divided into seven regions: Agadez, Diffa, Dosso, Maradi, Tahoua, Tillaberi and Zinder regions. Its capital is Niamey.

2.2.2.2. Human schistosomiasis prevalence

Schistosomiasis in Niger is found in areas under the 15th N latitude and also occurs in the Aïr plateau (altitude average between 500 and 900 m) in the North of Agadez city in the Agadez region.

2.2.2.2.1. Schistosoma haematobium The epidemiological studies were concentrated in the Tillabéri region, along the Niger River and in Niamey city. Distribution of *S. haematobium* was not homogeneous around the irrigated areas of the Niger River, and prevalence ranged from 3% to

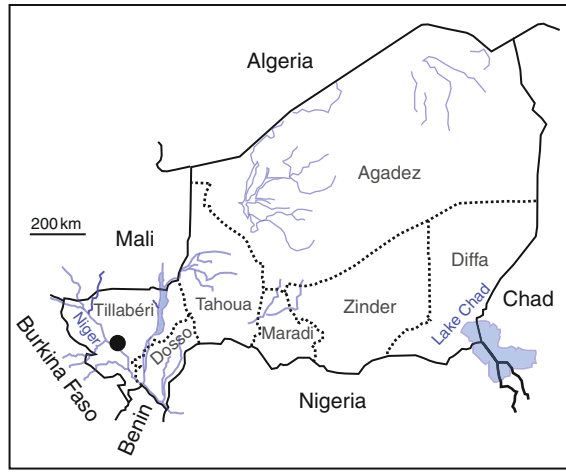

FIGURE 2.3 Niger, its water network and its seven regions. The black dot is the capital, Niamey.

96% (number of surveys = 57, prevalence less than 10% in 6) (Doumenge et al., 1987). Re-infections following treatment were higher in the villages close to the canals (27.6%, 28.6% and 28.8%) compared to those far from the transmission sites (4.5% and 9.1%) (Ernould et al., 2004). A very high prevalence (98%) was found in the Niger River valley and re-infection following treatment was high (32%) (Garba et al., 2001a). A high prevalence (77%) was found in a village located near a rice plantation irrigation scheme and nil prevalence in a village where water was supplied from wells (Bretagne et al., 1985). In Niamey city, the prevalence was lower in the urban zone (16%) compared to the periurban one (74%) (Ernould et al., 2003). In the schools of the urban zone in Niamey, prevalence ranged from 0% to 100% (number of surveys = 30; prevalence less than 10% in 18 and nil in 1) (Ernould et al., 2000). In the other regions of South Niger (Dosso, Maradi, Zinder and Diffa) prevalence was from 25% to 60% (Doumenge et al., 1987). In the Aïr plateau (Agadez region), prevalence of 24.1% and 43.5% was found in two villages in the North of Agadez (Mouchet et al., 1990).

2.2.2.2.2. Schistosoma mansoni This species was found primarily restricted to the far South of the country in the Dallol Foga valley at the confluence of both Benin and Nigeria borders, with prevalence from 18.5% to 48% (Mouchet et al., 1987a). However, it was found more recently in the Niger River valley with a prevalence that increased in 1 year from 5.9% to 19.5% (Garba et al., 2004).

2.2.2.3. Snail intermediate hosts and their schistosome prevalence

Several snail intermediate hosts of the genus *Bulinus* were found in Niger: *B. globosus*, *B. forskalii*, *B. senegalensis*, *B. truncatus* and *B. umbilicatus.* All of them were found in the extreme South of the Dosso region (Mouchet et al., 1987a). In the irrigation areas of Niamey, *B. truncatus* was often associated with *B. globosus* but *B. truncatus* was considered to be the most important intermediate host for *S. haematobium* with prevalence of 1.8%, 5.9% and 9.4% (Ernould et al., 2000; Labbo et al., 2003a), the presence of infected *B. truncatus* being observed in the irrigation canals but not on the edges of the river (Labbo et al., 2008). In the ponds, the four species of *Bulinus* were present, but only two species were found naturally infected: *B. truncatus* with a prevalence of 5.9% and *B. senegalensis* with a prevalence of 1% (Ernould et al., 2000; Labbo et al., 2003a). In some parts of the irrigated areas, *B. forskalii* was the predominant snail (Ernould et al., 2004) and was found naturally infected by *S. haematobium*, although with a low prevalence of 0.05% (Labbo et al., 2007). In the other regions of Niger, both *B. truncatus* and *B. senegalensis* were found in permanent pools in the desert zone of Agadez (Mouchet et al., 1990) and *B. umbilicatus* was found in the temporary pool foci of Eastern Niger (Chippaux et al., 1997). *B. pfeifferi* was the only snail host for *S. mansoni* in Niger and its distribution was enhancing since it was collected in the Dallol Foga valley in the extreme South of the Dosso region (Mouchet et al., 1987a) and then was found to spread into the Niger River valley (Labbo et al., 2003b).

2.2.2.4. Schistosomiasis control

The control of schistosomiasis in Niger has been principally made thanks to the 'Projet de Lutte contre la Bilharziose Urinaire' (PLBU) created in 1991 with a financial support from the European Union. This was coordinated by the 'Centre de Recherche sur les Méningites et les Schistosomoses' (CERMES) depending on a West African Organization for Public Health, the 'Organisation de Coordination et de Coopération pour la lutte contre les Grandes Endémies' (OCCGE) (Chippaux et al., 1997, 2000; Garba et al., 2001b). Control was based on chemotherapy, formation and an awareness campaign of the population. In 2004, a national control programme was launched in Niger with the support of the Bill and Melinda Gates Foundation through the SCI (Fenwick et al., 2006; Garba et al., 2006), adopting a rapid countrywide treatment strategy to ensure that all target groups were treated for schistosomiasis twice in 2 years. By 2007, over 6.2 million treatments had been delivered. The May 2008 mass treatment campaign successfully distributed treatment for lymphatic filariasis, trachoma, onchocerciasis, schistosomiasis and STHs to approximately 8 million people. A follow-up of school children took place in sentinel sites along the Niger River and in proximity to ponds and the

control permitted to reduce significantly the prevalence of infection by *S. haematobium* from 75.4% to 38% (Tohon et al., 2008). Schistosomiasis still remains a major health problem in Niger because *S. haematobium* prevalence is still high, because *S. mansoni* may spread due to the spreading of its snail host, *B. pfeifferi*, and because the Kandadji dam is under construction (2008–2013) on the Niger River in Tillabéri region and may enhance schistosomiasis transmission in the Niger River valley. Schistosomiasis control must be perpetuated in this country.

2.2.3. Burkina Faso

2.2.3.1. Ecoregions, hydrography and administrative regions (Figs. 2.1 and 2.4)

Burkina Faso is transected by two ecoregions: the subtropical dry grassland in the extreme North corresponding to the Sahel region and the tropical dry forest and savanna in all the other regions of the country. The hydrographic net is important with the Upper Volta basin draining four sub-basins, Mouhoun (Black Volta), Nazinon (Red Volta), Nakambé (White Volta) and Pendjari forming in Ghana the Lake Volta. Another basin, the Upper Comoé basin, drains the extreme South-West of the country. A lot of waterbodies such as rivers, lakes and ponds in Burkina

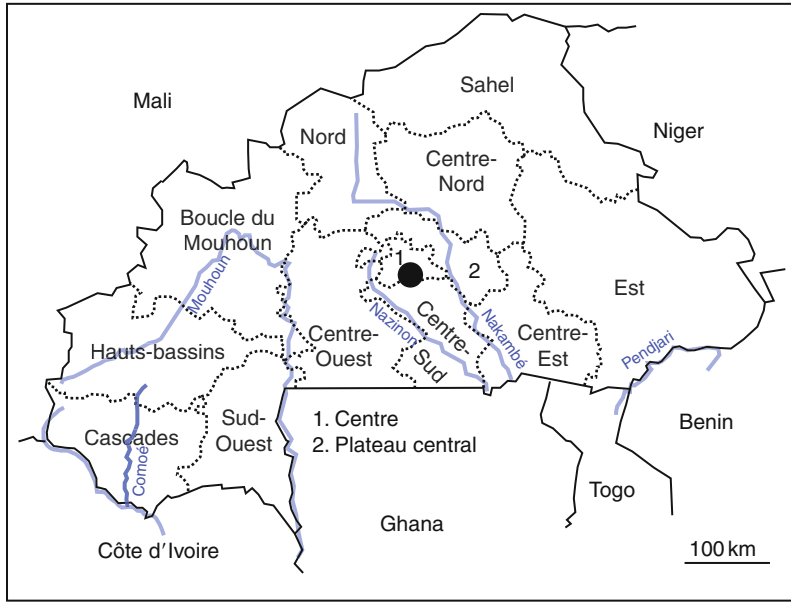

FIGURE 2.4 Burkina Faso, its water network and its 13 regions. The black dot is the capital, Ouagadougou.

Faso are non-permanent and depend largely on rainfall. Furthermore, many man-made waterbodies were constructed for agriculture. Burkina Faso is divided into 13 regions: Boucle du Mouhoun, Cascades, Centre, Centre-Est, Centre-Nord, Centre-Ouest, Centre-Sud, Est, Hauts-Bassins, Nord, Plateau-Central, Sahel and Sud-Ouest regions. Its capital is Ouagadougou.

2.2.3.2. Human schistosomiasis prevalence

2.2.3.2.1. Schistosoma haematobium This species is present in all the regions of Burkina Faso. Prevalence was generally high, with a diminishing trend from the North-East to the South-West and ranged from 0% to 100% (number of surveys = 183; prevalence less than 10% in 30 and nil in 2) (Doumenge et al., 1987) and from 0.9% to 100% (number of surveys not shown) (Poda et al., 2004a). This trend was also found in a smaller area of the Centre and Centre-Nord regions where 85%, 37.5% and 10.5% were found along a line of 150 km from North-East to South-West (Poda et al., 2001a). The Sahelian and Northern regions were the most heavily infected, due to the presence of water only in rare and temporal ponds around which populations are concentrated. For the Ziga dam on the Nakambé River (Centre-Nord region), the prevalence ranged from 26.1% to 75.9% (number of surveys = 5) (Garba et al., 1999) and in the Sourou zone (Boucle du Mouhoun region), prevalence ranged from 8.5% to 83.3% (number of surveys = 8, prevalence less than 10% in 1) (Poda et al., 2001b). In the other parts of the country, dam constructions constituted amplifying factors for schistosome transmission (Poda et al., 2004b). For example, in the Boucle du Mouhoun region (Sourou province), prevalence shifted from 19% to 70% and in the Hauts-Bassins region it turned from 14% to 80%. The same trend was observed for the Bagré dam on the Nakambé River in the Centre-Est region (Poda et al., 2003, 2004a). The Bagré dam has been newly renovated and expanded. These results showed that surveys before and after dam constructions are needed in order to quantify the impact of these man-made constructions on schistosomiasis transmission.

2.2.3.2.2. Schistosoma mansoni This species is less widely distributed than *S. haematobium* but its range appears to be expanding in the country. It is present mainly in the South-East of the country but several isolated foci were found in other regions. Prevalence ranged from 0% to 79% (number of surveys = 28; prevalence less than 10% in 17 and nil in 10) (Doumenge et al., 1987) and was 52.7% (Sorgho et al., 2005) in the South-West, whereas an absence of *S. mansoni* was shown in Ziga zone (Centre-Nord region) (Garba et al., 1999). Appearance and expansion of *S. mansoni* have been noticed in various areas in relation to the building of new water supplies. Prevalence enhanced from 1.1% to 5% and then to 7% in the years 1995, 1998 and 1999 in the Bagré zone (Centre-Est region) and from

1.3% to 45% between 1957 and 1987 in the Hauts-Bassins region (Poda et al., 2003, 2004a). In Sourou zone (Boucle de Mouhoun region), *S. mansoni* was absent until 1987 and spectacularly enhanced from 0%, 5.3%, 6.9% and 50.6% to 8.2%, 10.1%, 22.7% and 90.8%, respectively, in five villages situated along the Sourou River (Poda et al., 2004b).

2.2.3.3. Snail intermediate hosts and their schistosome prevalence

Five species of *Bulinus* were found in Burkina Faso: *B. globosus*, *B. forskalii*, *B. senegalensis*, *B. truncatus* and *B. umbilicatus.* Three species, *B. forskalii*, *B. senegalensis* and *B. truncatus*, occurred in all the regions, *B. umbilicatus* was only found in the extreme East of Burkina Faso and *B. globosus* was found only in the South of the 14th Northern parallel (Poda et al., 2003, 2004a). Each species has preference biotopes, *B. truncatus* the irrigation canals and the dams, *B. senegalensis* the ponds, *B. globosus* the waterbodies and *B. forskalii* both dams and waterbodies (Poda et al., 2004a). In Sourou zone particularly, *B. senegalensis* occurred in any type of biotope whereas *B. truncatus* preferentially occurred in the irrigation canals and the dams: the first one was found naturally infected (6.6%) and the second one was free of infection (Poda et al., 2001b, 2004b). Infection in *B. truncatus* has only been recorded in the North-East of the country (1.9%) (Poda et al., 2001a). *B. pfeifferi* was found only in the South of the 14th Northern parallel. Its distribution spread to new areas due to hydro-agricultural projects, as in the Sourou zone where it was first recorded in 1990 (Poda et al., 2004b) and consequently enhanced *S. mansoni* transmission in the area. *B. pfeifferi* was found in some areas of the Centre-Est region where *S. mansoni* has not yet been detected (Garba et al., 1999) and the appearance of the parasite in this zone is thus possible.

2.2.3.4. Schistosomiasis control

The National Schistosomiasis and Soil-transmitted helminthiasis Control programme (PNLC) was officially launched in 2004 thanks to the financial and technical support from the Bill and Melinda Gates Foundation through the SCI (Fenwick et al., 2006; Garba et al., 2006). A nationwide treatment campaign was implemented in 2004 and 2005 which targeted 3.6 million people (communities and schools) and the treated population was 3.3 million people (Gabrielli et al., 2006). The 1-year (Koukounari et al., 2007) and 2-year (Touré et al., 2008) impacts of single praziquantel treatment showed a significant reduction in *S. haematobium* prevalence from nearly 60% to less than 10%. Burkina Faso faces the expansion of both *S. haematobium* and *S. mansoni*. Control of these diseases requires continuous efforts and chemotherapy campaigns at regular intervals. In 2009, the Burkina Faso NTD Control Programme launched its third integrated mass drug administration in the North-Eastern district of Dori (Sahel region).

2.3. OTHER COUNTRIES

The 12 other countries belonging to ECOWAS will be analysed from West to East.

2.3.1. Cape Verde

2.3.1.1. Ecoregions, hydrography and islands

Cape Verde is an archipelagic nation located in the Macaronesia ecoregion of the North Atlantic Ocean, off the Western coast of Africa (Figs. 2.1 and 2.5). It belongs to the subtropical dry grassland ecoregion. The islands are divided into the Barlavento islands (Santo Antão, São Vicente, Santa Luzia, São Nicolau, Sal and Boa Vista) and the Sotavento islands (Maio, Santiago, Fogo and Brava). The largest island, both in size and population, is Santiago, where the capital of Praia is located.

2.3.1.2. Human schistosomiasis prevalence

Human schistosomiasis was never reported but bovine schistosomiasis is prevalent (Rosa and Simoes, 1998).

2.3.1.3. Snail intermediate hosts

The snail *B. forskalii* was reported in the Santiago Island (Rosa and Simoes, 1998).

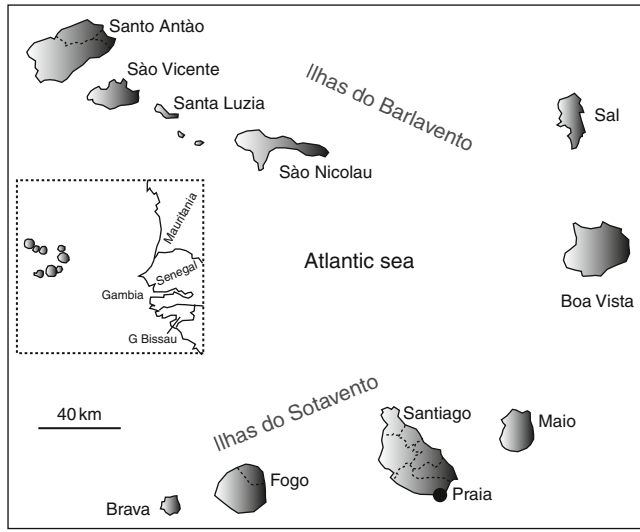

FIGURE 2.5 Cape Verde. The islands are divided into the Barlavento islands (Santo Antão, São Vicente, Santa Luzia, São Nicolau, Sal and Boa Vista) and the Sotavento islands (Maio, Santiago, Fogo and Brava). The black dot is the capital, Praia.

2.3.1.4. Control

In 2004 with funding from the Spanish Government, activities started with a focus on NTDs as a whole (schistosomiasis, STHs, lymphatic filariasis, trachoma and malaria). The programme concluded that schistosomiasis is not a public health problem for Cape Verde compared to STHs (Schools and Health, 2008).

2.3.2. Senegal

2.3.2.1. Ecoregions, hydrography and administrative regions (Figs. 2.1 and 2.6)

Senegal is transected by two ecoregions: the subtropical dry grassland in the northernmost third of the country (representing one-third of the surface of the country) and the tropical dry forest and savanna in the South. Senegal River runs in the North of the country all along the border with Mauritania. Many major irrigated schemes are located along the Senegal River basin (Diama dam, Richard Toll linked to the Lac de Guiers, Dagana, Matam and Bakel) and also along the Saloum and Casamance River basins for rice and sugar cane productions. Senegal is divided into 14 regions: Dakar, Diourbel, Fatick, Kaffrine, Kaolack, Kedougou, Kolda, Louga, Matam, Saint-Louis, Sédhiou, Tambacunda, Thiès and Ziguinchor regions. Its capital is Dakar.

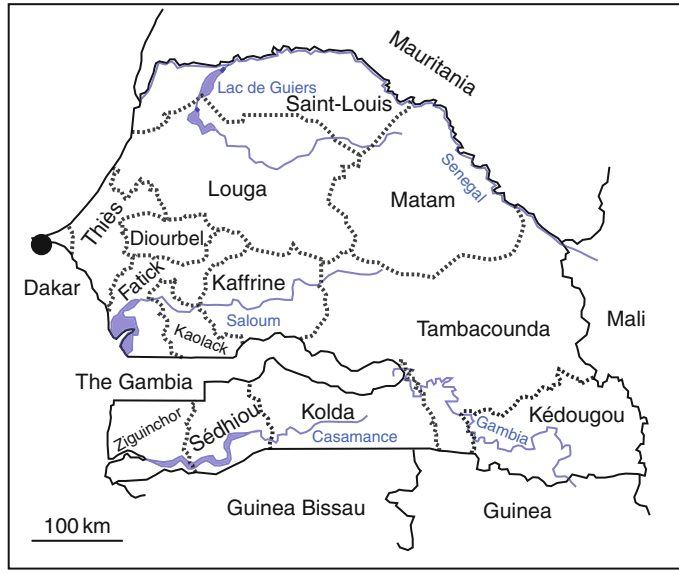

FIGURE 2.6 Senegal, its water network and its 14 regions. The black dot is the capital, Dakar.

2.3.2.2. Human schistosomiasis prevalence

Both *S. haematobium* and *S. mansoni* exist in Senegal and most of the recent studies have been made in the Senegal River Basin.

2.3.2.2.1. Schistosoma haematobium The Senegal River runs through three regions in Senegal: Tambacounda, Matam and Saint-Louis regions. Prevalence ranged from 5.5% to 44% (number of surveys = 17; prevalence less than 10% in 3) (Doumenge et al., 1987). The construction of the Diama dam (operational in 1986) has led to the creation of new foci for *S. haematobium* (Southgate et al., 2001). In the lower valley of the Senegal River basin, overall prevalence was 28% in 1994 (de Clercq et al., 1999) and ranged from 0.37% to 41.5% in 1995 (Picquet et al., 1996). Three years after the first cases of *S. haematobium* in a village of the delta, 87% of the population was found infected (Verlé et al., 1994). In the Middle valley, prevalence was 11.5% and 51.6% (Picquet et al., 1996). In the Middle and Upper valleys, prevalence (obtained from microhaematuria) ranged from 10% to 73% and increased in every age-group after treatment with praziquantel (de Clercq et al., 2000). Prevalence in the other regions of Senegal was 5.4%, 15%, 23% and 75.9% (Doumenge et al., 1987) and 30.2% (Seck et al., 2007) for the Fatick region, from 2.2% to 38.8% (number of surveys = 5; prevalence less than 10% in 3) for the Dakar region, from 0% to 65% (number of surveys = 29; prevalence less than 10% in 21) for the Thiès region, 2% and 32.1% for the Diourbel region, 25% and 34% for the Kaolack region, 35% for the Kaffrine region, 7%, 17% and 22% for the Tambacounda region and from 0% to 85% (number of surveys = 13; prevalence nil in 4) for the Casamance River basin (Ziguinchor, Sedhiou and Kolda regions) (Doumenge et al., 1987).

2.3.2.2.2. Schistosoma mansoni This species was not reported along the Senegal River basin by Doumenge et al. (1987). It arrived there (near the Lac de Guiers) a year and a half after the Diama dam construction and became the predominant schistosome species in the area, prevalence shifting from 1.9% in 1988 to 71.5% in 1989 (Talla et al., 1990), 60% in 1990 (Talla et al., 1992), 81.3% in 1995 (Picquet et al., 1996), 80% in 1997 (de Clercq et al., 1999) and 91% in 2006 (ten Hove et al., 2008). In this zone, this species is found together with *S. haematobium* and mixed infections were found in 21% and 23% (de Clercq et al., 1999) and in 56% of the studied population (ten Hove et al., 2008). The construction of the Diama dam in the Senegal River delta in order to prevent the intrusion of sea water enhanced the prevalence of *S. mansoni* in this zone (Southgate et al., 2001). Prevalence reached almost 100% after irrigation works in an area of the delta where this parasite was not present before (Stelma et al., 1993). In this region, the role of hygienic bathing after defecation (more than the

stool itself) on the transmission of *S. mansoni* was highlighted (Sow et al., 2008) since almost half of the population never used the latrines, even though they existed (Sow et al., 2003). In the other regions of Senegal, *S. mansoni* was found in geographically limited sites and prevalence was 47% in Thiès region, 3.9% in Fatick region, 5%, 18.5% and 30% in Kédougou region, on the Guinean border and 40% and 70% in Kolda city (Doumenge et al., 1987). Furthermore, rodents were found to participate in *S. mansoni* transmission along the Senegal River. Two species, *Arvicanthis niloticus* and *Mastomys huberti*, were found naturally infected by *S. mansoni* in Richard-Toll with a prevalence of 5.5% and 4.5%, respectively (Duplantier and Sène, 2000). In the lower valley of the Senegal River basin, overall prevalence of mixed *S. haematobium* and *S. mansoni* infections was 21% (de Clercq et al., 1999).

2.3.2.3. Snail intermediate hosts and their schistosome prevalence

Five species of *Bulinus* could be collected in Senegal: *B. globosus*, *B. senegalensis*, *B. truncatus*, *B. forskalii* and *B. umbilicatus* (Picquet et al., 1996; Vercruysse et al., 1994). The first four species were found in the Senegal River basin and the first three were found naturally infected (Chaine and Malek, 1983; Vercruysse et al., 1985). *B. globosus* acted as the main intermediate host in the Lower Senegal River valley (Picquet et al., 1996; Rollinson et al., 1997) while *B. senegalensis* and *B. umbilicatus* (Picquet et al., 1996) and *B. truncatus* (de Clercq et al., 2000) were involved in the transmission of *S. haematobium* in the middle valley. Prevalence of naturally infected *B. truncatus* was 0.5%, 10% and 25% (Sène et al., 2004). The snail *B. pfeifferi* was the only host species for *S. mansoni*. In the Senegal River basin, near the Lac de Guiers, prevalence of *S. mansoni* in these snails was 4.8% in the late 1980s (Talla et al., 1990), became high in the early 1990s (from 8.6% to 63.9%; number of surveys = 10; prevalence less than 10% in 1) (Diaw et al., 1991), and very high (77% and 85%) in the late 1990s (de Clercq et al., 1999). The dense snail population in this zone could be explained by changes in the freshwater habitats caused by the Diama dam construction and could explain the very high prevalence of *S. mansoni* observed in human populations (Diaw et al., 1990; Picquet et al., 1996). Seasonality in the *B. pfeifferi* populations (whether infected by *S. mansoni* or not) was found to peak in late 'spring' or early 'summer', just before the heat of the summer and 80% of the infected snails were found during this period (Sturrock et al., 2001).

2.3.2.4. Schistosomiasis control

Control of schistosomiasis was funded and implemented in the Saint-Louis region of Senegal by the European Development Fund from 1995 to 1999. Its research component was the ESPOIR project (European Special Programme for Operational and Integrated Research). Control was based

on chemotherapy on schoolchildren, vector control and promotion of safe water supply and sanitation. Four years after the beginning of the programme, a positive evaluation concluded that adequate and affordable diagnosis and treatment was provided for the majority of patients (van der Werf et al., 2002). A national survey has been carried out in 1996, and a national control programme, funded by the World Bank, was initiated in 1997 (World Health Organisation, 1999). Following the outbreak of *S. mansoni* in Northern Senegal, the development of resistance to praziquantel has been strongly suspected since cure rates were abnormally low with this drug compared to the cure rates obtained with another drug, oxamniquine (Stelma et al., 1997). The low cure rates with praziquantel were confirmed in the same area (Tchuem Tchuenté et al., 2001). Chemotherapy in Senegal in terms of praziquantel resistance was and is still debated and the use of combination chemotherapy or alternative drugs in such specific countries was proposed (Appleton and Mbaye, 2001; Cioli, 1998; Webster et al., 2008). An anti-malarial drug, artesunate, was recently positively evaluated in Northern Senegal since, when used for anti-malarial treatment, it had also an important impact on the level of infection with *S. haematobium* (Boulanger et al., 2007). Schistosomiasis control in this country is difficult, especially when done during a period of intense transmission (Ofoezie, 2000). Following a single treatment, re-infection was rapid with prevalence reaching pre-treatment levels within 7 months (de Clercq et al., 1999). Senegal needs permanent health care facilities, water supply and health education in order to teach the young population the life cycle of the parasite and to make them change their hygienic behaviour.

2.3.3. The Gambia

2.3.3.1. Ecoregions, hydrography and administrative divisions (Figs. 2.1 and 2.7)

The Gambia is the smallest country in mainland Africa. It belongs to the tropical dry forest and savanna ecoregion and is surrounded by Senegal. It is situated along the Gambia River (which has its source in Guinea) and consists of little more than the downstream half of this river and its two banks. The Gambia is divided into five divisions and one city. The divisions are Central River, Lower River, North Bank, Upper River and Western and the city, Banjul, which is the capital.

2.3.3.2. Human schistosomiasis prevalence

Both *S. haematobium* and *S. mansoni* were found in this country but few recent data are available.

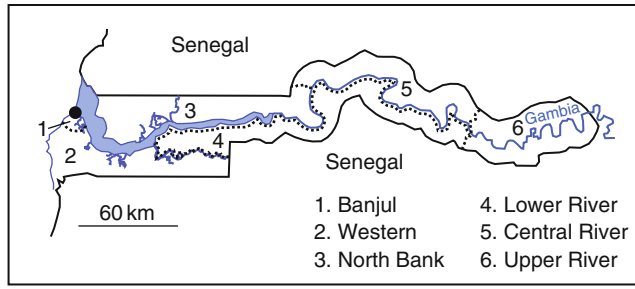

FIGURE 2.7 The Gambia, its water network and its five divisions. The black dot is the capital, Banjul.

2.3.3.2.1. Schistosoma haematobium Prevalence ranged from 12.4% to 72.7% (number of surveys = 6) (Doumenge et al., 1987) and from 26% to 78% (number of surveys = 14) (Wilkins et al., 1984) in the Central River division and a prevalence of 55% was obtained in the Western division (Doumenge et al., 1987).

2.3.3.2.2. Schistosoma mansoni This species was restricted to the Western division, near the capital Banjul, where prevalence ranged from 4.5% to 71.4% (number of surveys = 4) (Doumenge et al., 1987).

2.3.3.3. Snail intermediate hosts and their schistosome prevalence

B. globosus, *B. forskalii*, *B. truncatus*, *B. senegalensis* and *B. pfeifferi* were found in The Gambia (Doumenge et al., 1987; Sellin and Boudin, 1981) but no data are available on their schistosome prevalence.

2.3.3.4. Schistosomiasis control

Chemotherapy and molluscicide (Goll et al., 1984) were used as control measures against schistosomiasis in The Gambia. Recent epidemiological data are needed for this country.

2.3.4. Guinea-Bissau

2.3.4.1. Ecoregions, hydrography and administrative regions (Figs. 2.1 and 2.8)

This country is transected by two ecoregions: the tropical dry forest and savanna in the Northern and Eastern parts and the tropical wet forest in the Southern part of the country. Three rivers cross the country from East to West and form the Cacheu basin in the North, the Gêba basin in the Middle and the Corubal basin in the South of the country. Guinea-Bissau is divided into nine regions: Bafata, Biombo, Bissau, Bolama, Cacheu, Gabu, Oio, Quinara and Tombali regions. Its capital is Bissau.

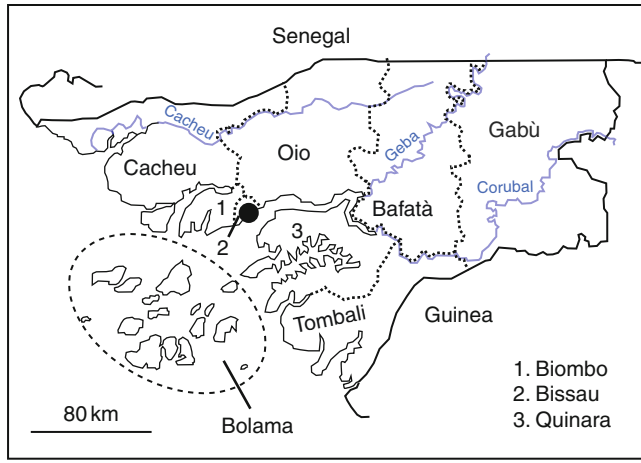

FIGURE 2.8 Guinea-Bissau, its water network and its nine regions. The black dot is the capital, Bissau.

2.3.4.2. Human schistosomiasis prevalence

Very few data are available regarding schistosome prevalence in humans and no data could be found on schistosomiasis control for this country. *S. haematobium* was present in the three basins with 13% along the Cacheu River, 34% along the Gêba River and 18% along the Corubal River. The regions infected by *S. haematobium* were the Cacheu region with prevalence ranging from 0% to 54% (number of surveys = 10; prevalence nil in 7), the Bafata region with 0% and 7% and the Gabu region with 0%, 20% and 26.7% (Doumenge et al., 1987). The Southern regions of Tombali, Quinara, Biombo, Bissau and Bolama and the Oio region were free of *S. haematobium* (Doumenge et al., 1987). The species *S. mansoni* was reported in Guinea-Bissau (World Health Organisation, 1985).

2.3.4.3. Snail intermediate hosts and their schistosome prevalence

B. globosus, *B. senegalensis* (Doumenge et al., 1987) and *B. pfeifferi* (Sellin and Boudin, 1981) were reported. However, no data on their schistosome prevalence are available. Recent epidemiological data are needed for this country.

2.3.5. Guinea

2.3.5.1. Ecoregions, hydrography and administrative regions (Figs. 2.1 and 2.9)

Two ecoregions occur in Guinea. The tropical dry forest and savanna in the major Eastern part of the country contains the Fouta Djalon Mountain (Labé and Mamou regions). The tropical wet forest in the extreme

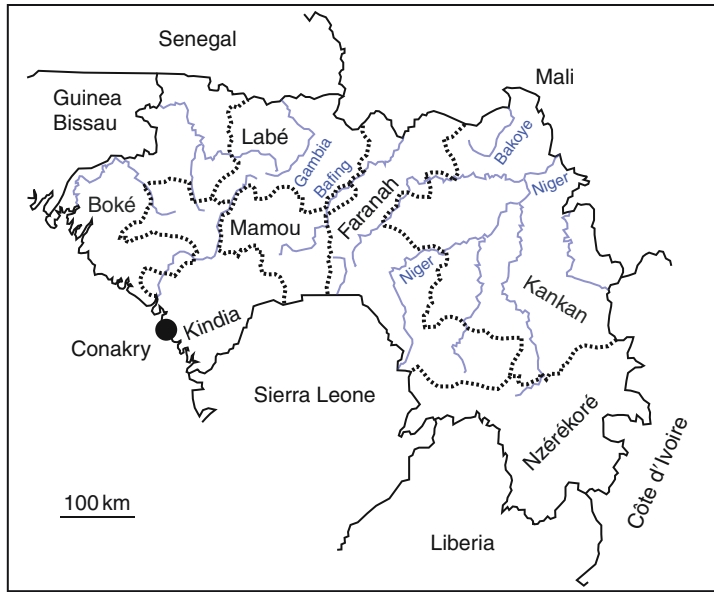

FIGURE 2.9 Guinea, its water network and its seven regions. The black dot is the capital, Conakry.

Western part of the country (Boké and Kindia regions and Conakry city) and in the extreme South of the Nzérékoré region contains the Nimba Mountain. From the Fouta Djalon Mountain to the West side, different rivers go down to the Western coastal region where salinity is high. From the Fouta Djalon to the East side, three major rivers have their sources, the Gambia River, the Bafing and Bakoye rivers (tributaries of the Senegal River) and the Niger River and some of its tributaries. Guinea is divided into seven regions and one city. The regions are Boké, Faranah, Kankan, Kindia, Labé, Mamou, Nzérékoré and the city, Conakry, is the capital.

2.3.5.2. Human schistosomiasis prevalence

Coastal Guinea is almost free of schistosome infection thanks to the high salinity unfavourable to the intermediate snail hosts. Unfortunately, the rest of the country harbours both *S. haematobium* and *S. mansoni*. For *S. haematobium*, prevalence was 32% and 40% in Nzérékoré region (Doumenge et al., 1987) and 19.9% for the whole country (Gyorkos et al., 1996). For *S. mansoni*, prevalence ranged from 13.8% to 57.9% (number of surveys = 6) in the Eastern regions (Doumenge et al., 1987), and was 25% (Gyorkos et al., 1996) and 9.1% (Montresor et al., 1997) for the whole country.

2.3.5.3. Snail intermediate hosts and their schistosome prevalence

B. globosus, *B. truncatus* and *B. pfeifferi* were found near the borders with Sierra Leone and Liberia in the South-East of the country (Sellin and Boudin, 1981) but no data on their schistosome prevalence were given.

2.3.5.4. Schistosomiasis control

A sectorial adjustment education programme was implemented in Guinea in 1995 by the Ministry of pre-university education. Recent epidemiological data are needed for this country.

2.3.6. Sierra Leone

2.3.6.1. Ecoregions, hydrography and administrative provinces (Figs. 2.1 and 2.10)

Sierra Leone is constituted for the major part by the tropical wet forest ecoregion, except in its extreme North-East where the tropical dry forest and savanna develops. The mountains of the Northern and Eastern provinces give rise to several rivers which go into the Atlantic Ocean through coastal plains. Sierra Leone is divided into three provinces (Eastern, Northern and Southern) and one Western area including the capital, Freetown.

2.3.6.2. Human schistosomiasis prevalence

Both *S. haematobium* and *S. mansoni* were found in Sierra Leone, but none was observed in the coastal plains (Western area and the biggest parts of the Northern and Southern provinces) due to the high salinity of the surface waters.

2.3.6.2.1. Schistosoma haematobium The Eastern province was the most heavily infected, especially along the border with Liberia, with prevalence ranging from 7.6% to 93% (number of surveys = 24; prevalence less than 10% in 3), the Northern and Southern provinces were less heavily infected with prevalence ranging from 2.3% to 40% (number of surveys = 8; prevalence less than 10% in 2) and from 0.6% to 64% (number of surveys = 8; prevalence less than 10% in 6), respectively (Doumenge et al., 1987). Rice swamps were not associated with an increase in the prevalence of *S. haematobium* since low prevalence was observed, 0.6% (Gbakima, 1994) and 8.2% (White et al., 1982). However, higher prevalence was found related to diamond mining, 16.3% (Gbakima et al., 1987) and 26.8% (White et al., 1989).

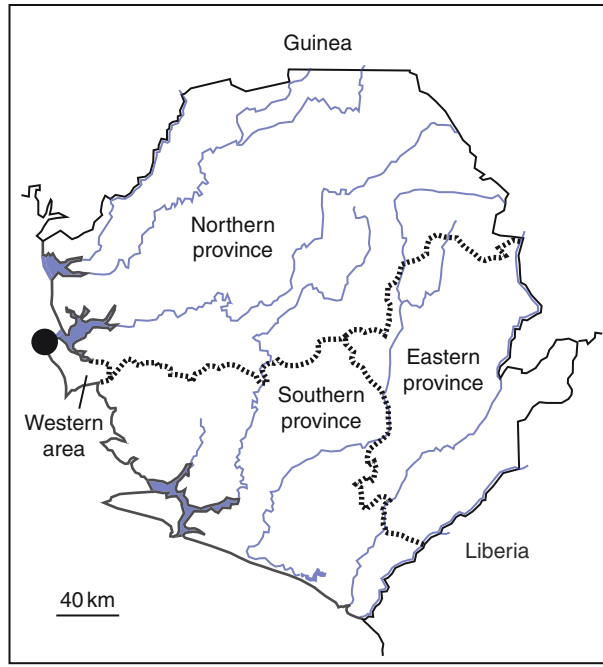

FIGURE 2.10 Sierra Leone, its water network and its three provinces and its Western area. The black dot is the capital, Freetown.

2.3.6.2.2. Schistosoma mansoni The distribution of *S. mansoni* is more restricted compared to that of *S. haematobium* and the prevalence much lower: from 0% to 12.6% in the Eastern province (number of surveys = 12; prevalence less than 10% in 10 and nil in 1), very low in the Southern province (from 0% to 1.1%; number of surveys = 5; prevalence nil in 3) and heterogeneous, 0.7%, 2.9%, 40% and 45.1% in the Northern province (Doumenge et al., 1987). All the *S. mansoni* foci also harboured *S. haematobium* and both infections in the same individual were detected (no data). *S. mansoni* seems to extend its range in the Southeast of the country due to the development of rice swamps, even though the prevalence was low, 2.5% (White et al., 1982) and 0.3% (Gbakima, 1994). However, diamond mining provided many breeding places for snails and prevalence was higher 22.3% (Gbakima et al., 1987) and 27.5% (White et al., 1989) and it was hypothesised that *S. mansoni* was imported from neighbouring countries since gold and diamond mining in Eastern, Northern and Southern provinces have attracted migrant workers including miners. Human migrations and displacements have also contributed to *S. mansoni* transmission: for example, prevalence was 16.7% in the Internally

Displaced Persons in the displacement Parade Ground Camp, Freetown, which was around 2000 (Gbakima et al., 2007).

2.3.6.3. Snail intermediate hosts and their schistosome prevalence

B. globosus, *B. forskalii* and *B. pfeifferi* are the snail intermediate hosts for schistosomiasis in the highlands of Sierra Leone (Doumenge et al., 1987; Sellin and Boudin, 1981).

2.3.6.4. Schistosomiasis control

The Ministry of Health and Sanitation of Sierra Leone are implementing a national plan of action for integrated control of onchocerciasis, schistosomiasis, STHs and elimination of lymphatic filariasis in Sierra Leone (2006–2010). A mapping of schistosomiasis is included in this programme. Sierra Leone may be faced with a possible enhancement of *S. haematobium* and *S. mansoni* transmission through improvement and spreading of rice swamps and also through human migrations. The national control programme currently existing will provide appropriate strategies for control and for targeting priority areas.

2.3.7. Liberia

2.3.7.1. Ecoregions, hydrography and administrative counties (Figs. 2.1 and 2.11)

The whole country is situated in the tropical wet forest ecoregion. The numerous rivers run parallel from the Northern and the Eastern parts of the country down to the Atlantic Ocean and cross the coastal plains. Liberia is divided into 15 counties: Boni, Bong, Gbarpolu, Gran Bassa, Grand Cape Mount, Grand Gedeh, Grand kru, Lofa, Margibi, Maryland, Montserrado, Nimba, River Cess, River Gee and Sinoe counties. Its capital is Monrovia.

2.3.7.2. Human schistosomiasis prevalence

Both *S. haematobium* and *S. mansoni* were found in Liberia, but only the three North-Eastern counties among the 15 were infected, the waterbodies of the coastal regions being too salty.

2.3.7.2.1. Schistosoma haematobium Prevalence ranged from 0% to 41.6% (number of surveys = 36; prevalence less than 10% in 18 and nil in 7) in Lofa county, near the Guinea border, and from 0% to 67.6% (number of surveys = 94; prevalence less than 10% in 23 and nil in 11) in Bong county. Nimba county harboured infected sites but no data were available (Doumenge et al., 1987). The impact of 6-year swamp rice farming was

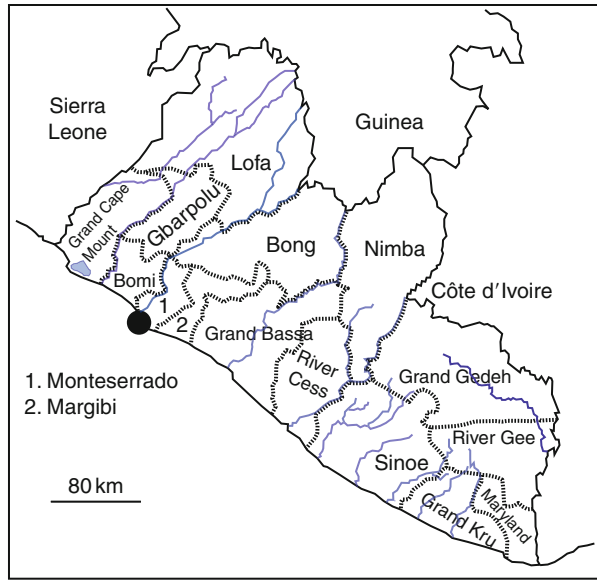

FIGURE 2.11 Liberia, its water network and its 15 counties. The black dot is the capital, Monrovia.

emphasised since prevalence was 42% in such a site compared to 11% in a village where rice farming had not yet been implemented (Kazura et al., 1985).

2.3.7.2.2. Schistosoma mansoni Prevalence ranged from 0% to 8% (except one prevalence at 30%) (number of surveys = 31; prevalence nil in 18) in Lofa county which was a low level of infection and from 0% to 79.4% (number of surveys = 84; prevalence less than 10% in 39 and nil in 18) in Bong county, the highest endemic region for this species. Nimba county harboured infected sites but no data were available (Doumenge et al., 1987). All the sites harbouring *S. mansoni* also harboured *S. haematobium*. The impact of 6-year swamp rice farming was also emphasised for this species with a prevalence being 87% in the area of the rice swamp and only 9% outside of this area (Kazura et al., 1985).

2.3.7.3. Snail intermediate hosts and their schistosome prevalence

B. globosus and *B. pfeifferi* were found to be the snail intermediate hosts for *S. haematobium* and *S. mansoni* in the Bong region, with a prevalence of 10.3% and 12.3%, respectively (Dennis et al., 1983). *B. senegalensis* was also reported in this country (Sellin and Boudin, 1981).

2.3.7.4. Schistosomiasis control

To our knowledge, no national schistosomiasis control programme has been implemented in Liberia and recent epidemiological data are needed.

2.3.8. Côte d'Ivoire

2.3.8.1. Ecoregions, hydrography and administrative regions (Figs. 2.1 and 2.12)

Côte d'Ivoire is transected by two ecoregions: in the Northern half, the tropical dry forest and savanna, and in the Southern half, the tropical wet forest. The rivers are numerous and all perpendicular to the Atlantic Ocean. Many of them have their source in the North of the country and then flow either to the North (Mali and Guinea) or, for the majority of

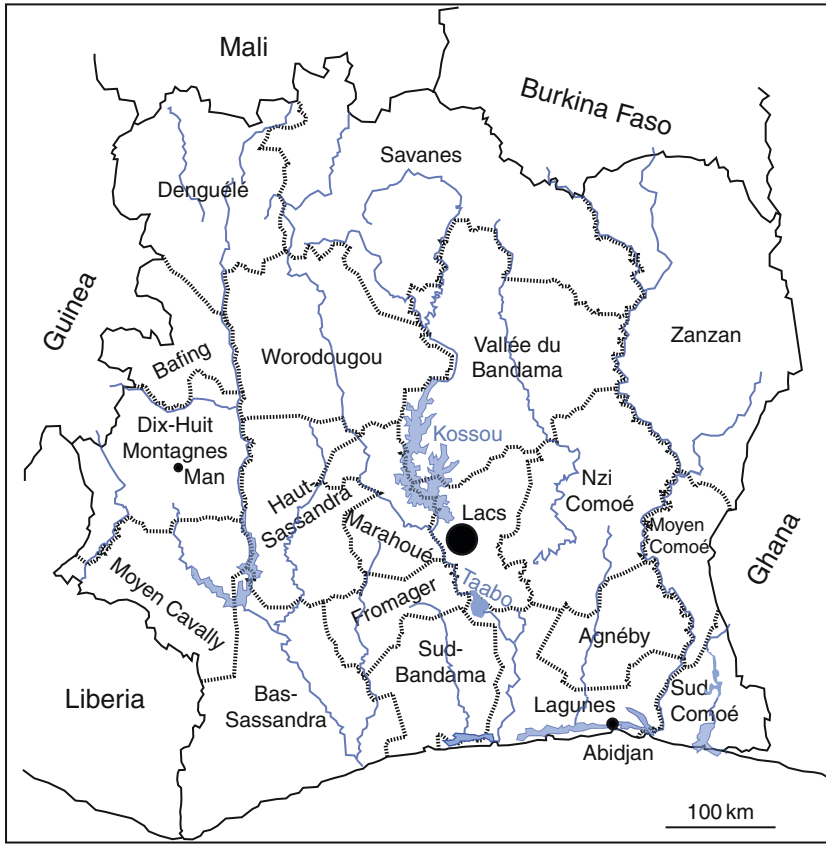

FIGURE 2.12 Côte d'Ivoire, its water network and its 19 regions. The large black dot is the capital, Yamoussoukro.

them, to the South. Some big lakes (like Kossou Lake in the centre of the country, near the capital, Yamoussoukro) are present in the Centre and South of the country. Dam constructions, irrigation schemes and artificial lakes are numerous along and near the main rivers. Côte d'Ivoire is divided into 19 regions: Agnéby, Bafing, Bas-Sassandra, Denguélé, Dix-Huit Montagnes, Fromager, Haut-Sassandra, Lacs, Lagunes, Marahoué, Moyen-Cavally, Moyen-Comoé, N'zi-Comoé, Savanes, Sud-Bandama, Sud-Comoé, Vallée du Bandama, Worodougou and Zanzan regions. Its capital is Yamoussoukro.

2.3.8.2. Human schistosomiasis prevalence

The two species *S. haematobium* and *S. mansoni* were found in Côte d'Ivoire.

2.3.8.2.1. Schistosoma haematobium Prevalence was below 7% in both the savanna (North) and the forest (West) parts of the country and was not related to the agro-ecosystems (absence of rice growing, single-cropping and double-cropping) (Yapi et al., 2005). This prevalence was lower than that indicated by Doumenge et al. (1987) for the savanna area (including the Bafing, Denguélé, Savanes and Worodougou regions) where prevalence ranged from 0.7% to 45.2% (number of surveys = 9; prevalence less than 10% in 4) and for the forest area (including the Dix-Huit Montagnes and the Moyen-Cavally regions) where prevalence ranged from 0% to 80% (number of surveys = 28; prevalence less than 10% in 12 and nil in 3). In the Centre and South-East (including five regions), overall prevalence was 18.6% (N'guessan et al., 2007). In the Centre, including the Lacs, Marahoué and Vallée du Bandama regions, a high prevalence was found and ranged from 1.7% to 92% (number of surveys = 44; prevalence less than 10% in 9) (Doumenge et al., 1987), with 88–94% near the man-made lake of Taabo (N'Goran et al., 2001). In the Agnéby region particularly, prevalence was high and ranged from 19.2% to 92% (number of surveys = 11) (Doumenge et al., 1987). In the South of the country, in Abidjan city (Lagunes region), prevalence was very low (0.8%) (Menan et al., 1997) from 0.1% to 27.6% (number of surveys = 5; prevalence less than 10% in 4) (Doumenge et al., 1987).

2.3.8.2.2. Schistosoma mansoni In the savanna part of the country (North), prevalence was 2.1%, 11.9% and 16.1% and in the forest part of the country (West), it was higher with 17.5%, 46.6% and 61.3%. This prevalence was related to the agro-ecosystems (absence of rice growing, single-cropping and double-cropping, respectively) (Yapi et al., 2005). These data are lower than those indicated by Doumenge et al. (1987) for the savanna area (including the Bafing, Denguélé, Savanes and Worodougou regions), where prevalence ranged from 1% to 53.3% (number of

surveys = 9; prevalence less than 10% in 2). However, they are similar to the prevalence indicated for the forest area (including the Dix-huit Montagnes and the Moyen-Cavally regions), where prevalence ranged from 0% to 82% (number of surveys = 24; prevalence less than 10% in 10 and nil in 4) (Doumenge et al., 1987). High prevalence was also found in the Western part, around the city of Man in the Dix-huit Montagnes region which benefited from numerous studies: 38% (Raso et al., 2005a,b), from 59.8% to 70.8% (Utzinger et al., 1998) and 80.4% (Utzinger et al., 2003) in rural areas and 50.1% (Matthys et al., 2007) in the urban area of Man. For the studies of Raso, Matthys and collaborators attempts were made to find the demographic, socioeconomic and environmental factors influencing prevalence. It was found that several factors, including age, sex, farming, toilet disposal, education level, proximity to water and water contact with irrigation wells and ponds had a strong influence on infection prevalence. In the Centre (Lacs and Marahoué regions) and South-East (Agnéby, Moyen-Comoé and Sud-Comoé regions), overall prevalence was 23.3% (N'guessan et al., 2007). In the Central part of the country, *S. mansoni* was found very focally with very low prevalence (Doumenge et al., 1987). In the Agnéby region (South-East) particularly, prevalence ranged from 1.9% to 75% (number of surveys = 10; prevalence less than 10% in 3) (Doumenge et al., 1987), was 10% (Agbaya et al., 2004) and 20.6% (Adoubryn et al., 2006). Mixed infections with *S. haematobium* and *S. mansoni* were observed in 3.2% of the screened schoolchildren (Adoubryn et al., 2006).

2.3.8.3. Snail intermediate hosts and their schistosome prevalence

B. globosus and *B. pfeifferi* were found all over the country, *B. truncatus* has been found mainly in the Central, Northern and North-Eastern parts of the country (Doumenge et al., 1987; Mouchet et al., 1987b). *B. forskalii* was also reported (Sellin and Boudin, 1981). No data are available regarding the schistosome prevalence in the snail intermediate hosts in Côte d'Ivoire.

2.3.8.4. Schistosomiasis control

In order to optimise schistosomiasis control, the identification of the high risk regions of schistosomiasis was ascertained in different ways. A questionnaire was used (presence of blood in urines and in stools) in schools of five regions: Lacs and Marahoué in the Centre of the country and Agnéby, Moyen-Ogoué and Sud-Oguoué in the South-East of the country (N'guessan et al., 2007). The results showed that Agnéby and Marahoué were the highest risk zones for both species of schistosomiasis and this result was related to the proximity with numerous waterbodies harbouring the snail intermediate hosts (N'guessan et al., 2007). Another questionnaire was used which focussed on water-contact patterns and

showed that an increasing level of *S. mansoni* infection was significantly associated to three behaviours: crossing rivers, swimming/bathing and fishing with nets (Utzinger et al., 2000). Schistosomiasis control in Côte d'Ivoire will also benefit from the studies which provided the risk mapping of schistosomiasis *mansoni* and models for epidemiology. Schistosomiasis mapping was made thanks to an integrated approach combining diverse data source, geographical information system (GIS) and remote sensing technologies, and Bayesian spatial statistics in the area of the city of Man in the Dix-huit Montagnes region (Beck-Wörner et al., 2007; Raso et al., 2005b, 2006). They found significant correlations between the infection prevalence of *S. mansoni* and stream order of the nearest river, water catchment area and altitude. A model for epidemiology was provided by the use of a Bayesian approach which permitted to estimate the age-specific prevalence of *S. mansoni* (Raso et al., 2007). Praziquantel was used as chemotherapy against *S. mansoni* and its efficacy was tested in a community in Western Côte d'Ivoire (Man area, Dix-huit Montagnes region), showing a low cure rate whose explanation may indicate intense disease transmission, concurrent infections with other parasites or tolerance or resistance to the drug (Raso et al., 2004b). Indeed, a significant positive association was found between *S. mansoni* and hookworm infections in this area (Keiser et al., 2002; Raso et al., 2004a). A high incidence of re-infection was also found in high endemic areas of *S. haematobium* after praziquantel treatment (N'Goran et al., 2001). To our knowledge, no national schistosomiasis control programme has been implemented in Côte d'Ivoire but control activities were achieved focally with support from various partners (Tchuenté and N'Goran, 2009). Despite the efforts made in Côte d'Ivoire in order to understand the epidemiology of schistosomiasis in humans, the studies mainly focused on a few regions of the country, such as the Man area (Dix-huit Montagnes region) for *S. mansoni*. Further work dedicated to understanding the epidemiology in both humans and snail hosts in all the regions of the country is needed, especially around the areas of man-made constructions (dams, irrigation schemes and artificial lakes). Schistosomiasis remains a severe public health problem in Côte d'Ivoire. The studies targeted on modelling and mapping schistosomiasis will provide a good help to optimise schistosomiasis control (Vounatsou et al., 2009).

2.3.9. Ghana

2.3.9.1. Ecoregions, hydrography and administrative regions (Figs. 2.1 and 2.13)

Ghana is part of the tropical dry forest and savanna ecoregion, except the South-West of the country which belongs to the tropical wet forest. In all the savanna part contains, from North to South, the Volta basins, the very

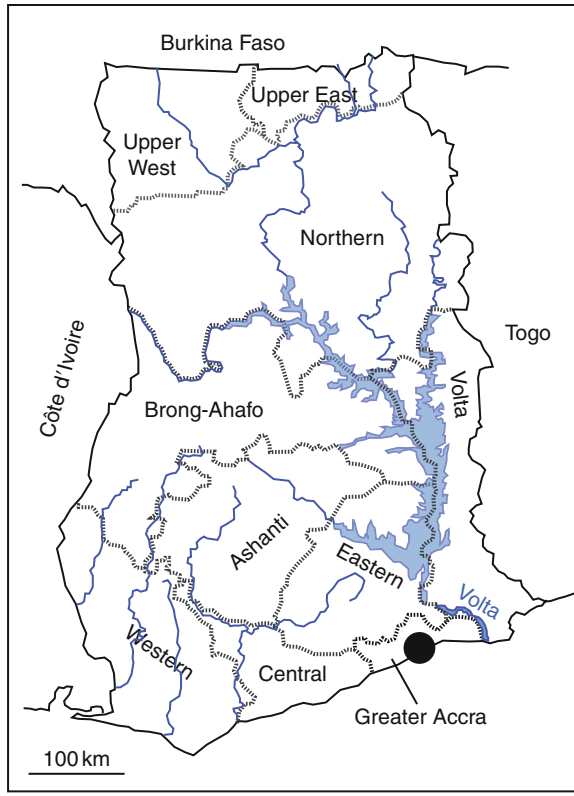

FIGURE 2.13 Ghana, its water network and its 10 regions. The black dot is the capital, Accra.

big Lake Volta with the Akosombo dam and the Volta delta. A lot of dams were constructed along the Volta River. The forest part of the country is separated from the savanna part by the Kwahu plateau (Ashanti and Eastern regions) from which several rivers flow to the Atlantic Ocean. Ghana is divided by 10 regions: Ashanti, Brong-Ahafo, Central, Eastern, Greater Accra, Northern, Upper East, Upper West, Volta and Western regions. Its capital is Accra.

2.3.9.2. Human schistosomiasis prevalence

S. haematobium was found in the whole country and *S. mansoni* distribution was more focal.

2.3.9.2.1. Schistosoma haematobium All the regions were found infected by *S. haematobium*. Prevalence was very variable and ranged from $<10\%$ to $>70\%$ (number of surveys $= 44$; prevalence less than 10% in 6) in the

two upper regions of the country, from 3% to 80.6% (number of surveys = 16; prevalence less than 10% in 1) in the Northern region, from 8% to 90% (number of surveys = 10; prevalence less than 10% in 1) in the Brong-Ahafo region, from 5.4% to 83.3% (number of surveys = 8; prevalence less than 10% in 3) in the Ashanti region, from 4.3% to 21.6% (number of surveys = 4; prevalence less than 10% in 3) in the Western region, from 13.3% to 99% (number of surveys = 27) in the Eastern region, from 0.8% to 98.5% (number of surveys = 65; prevalence less than 10% in 24) in the Volta region, from 0% to 85.3% (number of surveys = 14; prevalence less than 10% in 4) in the Greater Accra region and from 4.5% to 68% (number of surveys = 4; prevalence less than 10% in 2) in the Central region (Doumenge et al., 1987). All the regions were found heavily infected by *S. haematobium*, especially after the constructions of Lake Volta and other dams, while the Western and Central regions were the less heavily infected (Doumenge et al., 1987). A quite high prevalence (11.2%) was found in the Central region in infants (less than 5 years old) who were not visiting water contact sites (Bosompem et al., 2004). This indicated that transporting water home from transmission sites may play an important role in transmission of the disease. Continuing high levels of *S. haematobium* infections were found in the Upper Eastern region (Hunter, 2003). Indeed, this author showed that the prevalence shifted from 17% to 51% in 2 years after the constructions of 104 dams in the region (late 1950s). He highlighted that 40 years later, in 1997, there were still elevated levels of schistosomiasis (from 28% to 85%; number of surveys = 19) and that haematuria in this part of the country has even become a 'rite of passage' for young people. In a very focal place in this region, the Tono irrigation area, prevalence was very high, 67.7% (Amankwa et al., 1994). Near the capital Accra, in three rural areas, prevalence ranged between 50% and 60% and the study was intended to be the baseline for a schistosomiasis control programme (Aryeetey et al., 2000).

2.3.9.2.2. Schistosoma mansoni This species was found in the two Upper regions of the country with a low prevalence ranging from 0% to 10.2% (number of surveys = 40; prevalence less than 10% in 39 and nil in 3) (Doumenge et al., 1987). However, in the Tono area (Upper East region), where large reservoirs and rice irrigation projects were implemented, prevalence was 68.7% and mixed infections with *S. haematobium* were numerous (47.6%) (Amankwa et al., 1994). Very focal areas with very low prevalence of *S. mansoni* were found elsewhere in the country, except a prevalence of 52.4% in a village in the Volta region (Doumenge et al., 1987). In the Central region, particularly, prevalence was always zero (Bosompem et al., 2004; Doumenge et al., 1987).

2.3.9.3. Snail intermediate hosts and their schistosome prevalence

Very few data are available on the snail intermediate hosts in Ghana. In the Upper East region, *B. globosus* is the most important snail host for *S. haematobium*, less importantly *B. truncatus* is also found but both occur through the entire irrigation project. *B. pfeifferi* is the snail host for *S. mansoni* and is concentrated in the main canals (Amankwa et al., 1994). Near the Volta Lake, *B. truncatus* was found to proliferate (Doumenge et al., 1987).

2.3.9.4. Schistosomiasis control

Control of schistosomiasis in Ghana requires improvement in diagnosis, and availability and cost of treatment (van der Werf et al., 2003). The use of latent class (LC) modelling to address the problem of diagnosis has been addressed recently and clearly demonstrated that microscopic detection of parasite eggs in urine was the best currently available diagnostic tool for *S. haematobium* infection (Koukounari et al., 2009). Some regional control programmes using chemotherapy were followed and evaluated, as in the Greater Accra and Eastern regions of Ghana and it was established that an integrated approach for the control, including health education, should be used to support chemotherapy (Nsowah-Nuamah et al., 2004). Recently, the Ministry of Health of the Republic of Ghana implemented a 2-year strategic plan (2007 and 2008) for integrated NTD Control (Hotez et al., 2007a,b). During the second year of the programme, the NTD Control Programme supported a national mapping exercise in 77 districts for schistosomiasis prevalence and intensity with the technical assistance of the Schistosomiasis Control Initiative. In 2009, Ghana is undertaking its first nationwide distribution of Praziquantel, targeting more than 2 million school-age children in 45 districts. Schistosomiasis constitutes an important public health problem in Ghana. Some regions were understudied as the Western, Central and Brong-Ahafo regions. Malacological studies are lacking in order to map the potential transmitting zones for the disease. Schistosomiasis control in Ghana will now benefit from the national programme that is under way in this country.

2.3.10. Togo

2.3.10.1. Ecoregions, hydrography and administrative regions (Figs. 2.1 and 2.14)

Togo is situated in the Dahomey gap which refers to the portion of the tropical dry forest and savanna ecoregion that extends all the way to the coast in Togo, and also in Ghana and Benin. Togo is the only country in ECOWAS exclusively harbouring this ecoregion. Dahomey gap separates the Western tropical wet forest from the Eastern tropical wet forest. The climate is much drier than in the forest, consequently, an open savanna prevails adapted to the moderate rainfall and high evaporation

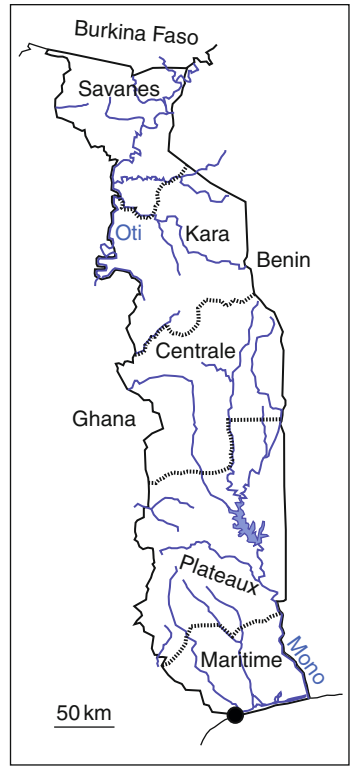

FIGURE 2.14 Togo, its water network and its five regions. The black dot is the capital, Lomé.

in the hot temperatures. All the main rivers of Togo flow towards the South. Parts of some of them constitute the borders with the neighbouring countries, like Oti in the North-West with Ghana, and Mono in the South-East with Benin. Man-made dams exist in Togo, with the large dam Nganbeto, along the Mono River. Togo is divided into five regions: Centrale, Kara, Maritime, Plateaux and Savanes regions. Its capital is Lomé.

2.3.10.2. Human schistosomiasis prevalence

S. haematobium was found in all the regions of the country and *S. mansoni* distribution was more focal.

2.3.10.2.1. Schistosoma haematobium Prevalence varied according to the regions; from 0% to 48% (number of surveys = 10; prevalence less than 10% in 6 and nil in 1) in the Savanes region, from 0% to 75.7% (number of surveys = 20; prevalence less than 10% in 8 and nil in 3) in the Kara region, from 3% to 53.7% (number of surveys = 5; prevalence less than

10% in 3) in the Centrale region, from 2% to 90% (Number of surveys = 11; prevalence less than 10% in 1) in the Plateau region and from 0% to 98% (number of surveys = 52; prevalence less than 10% in 24 and nil in 8) in the Maritime region (Doumenge et al., 1987). Prevalence was still high in the country in the late 1990s ranging from 0.6% to 72% (Agbo et al., 1999) and even more recently, in the Central region, prevalence was 41% (Hamm et al., 2009).

2.3.10.2.2. Schistosoma mansoni This species exists in all the regions of Togo but its distribution is much less important than that of *S. haematobium*. The prevalence was equal to zero in almost all the sites, except in very few sites from all the regions where prevalence ranged from 0.1% to 38.5% (number of surveys = 16; prevalence less than 10% in 9) (Agbéré et al., 1995; Doumenge et al., 1987) but reached very high levels with 51.5% (Lapierre et al., 1988) and even 79.6% (Lapierre et al., 1984) in the Kara region and 54.7% (Lapierre et al., 1984) in the Plateau region. In the late 1990s, prevalence was lower and ranged from 0.6% to 10% in the country (Agbo et al., 1999), recently reaching 15% in the Central region (Hamm et al., 2009).

2.3.10.3. Snail intermediate hosts and their schistosome prevalence

A malacological study was made before the construction of the Nangbeto dam in the different sites of the future lake (Plateau region) (Salami-Cadoux et al., 1990). *B. globosus* was found in both permanent and temporal sites and *B. pfeifferi* only in the permanent sites. *B. globosus* was found naturally infected with a prevalence of 10.2% but not *B. pfeifferi* (Salami-Cadoux et al., 1990). Both *B. globosus* and *B. pfeifferi* were found in the Kara region (Lapierre et al., 1984) and 3–15% of the *B. pfeifferi* were found naturally infected (Lapierre et al., 1992). *B. truncatus* and *B. forskalii* were also reported (Sellin and Boudin, 1981).

2.3.10.4. Schistosomiasis control

A programme is underway in Togo in order to integrate control activities for malaria, lymphatic filariasis, trachoma, schistosomiasis, onchocerciasis and STHs (Hotez et al., 2007b). Togo significantly lacks in recent data on schistosomiasis, and the programme which will be implemented will provide such data.

2.3.11. Benin

2.3.11.1. Ecoregions, hydrography and administrative departments (Figs. 2.1 and 2.15)

Benin belongs to the Dahomean gap, as do Togo and a part of Ghana, and is constituted by the tropical dry forest and savanna. A very small part of the country, the extreme South-East part, belongs to the tropical wet

FIGURE 2.15 Benin, its water network and its 12 departments. The large black dot is the capital, Porto-Novo.

forest and corresponds to the delta of the Ouémé and Zou rivers, near the city of Cotonou. The South hydrological basin contains two other main rivers, Couffo and Mono in the border with Togo. The hydrographical net in the North is constituted by tributaries of the Niger River in the North-East and the Pendjari River in the North-West on the border with Burkina Faso. This last river is a tributary of the Oti River, crossing Togo and joining the Volta Lake in Ghana. Benin is rich with natural lakes, lagoons and marshes near the coast. During the low water period, numerous pools remain all over the country. Man-made constructions were built for agricultural needs and water supply. Benin is divided into 12 departments: Alibori, Atacora, Atlantique, Borgou, Collines, Donga, Kouffo, Littoral, Mono, Ouémé, Plateau and Zou departments. Its capital is Porto-Novo.

2.3.11.2. Human schistosomiasis prevalence

The two species *S. haematobium* and *S. mansoni* were found in Benin, the first one being more largely distributed.

2.3.11.2.1. Schistosoma haematobium Prevalence varied according to the department and also within each department and ranged from 4% to 67.1% (number of surveys = 13; prevalence less than 10% in 2) in the Borgou department, from 5% to 60% (number of surveys = 8; prevalence less than 10% in 1) in the Atakora department, was 25% and 60% in the Zou department, ranged from 2.3% to 86% (number of surveys = 9; prevalence less than 10% in 2) in the Mono department and from 0% to 84.1% (number of surveys = 76; prevalence less than 10% in 21 and nil in 5) in the Ouémé department (Doumenge et al., 1987). In the Atacora department, a recent study showed a prevalence of 96% (Ibikounlé et al., 2009). In the Atlantique department, prevalence ranged from 6.9% to 42.9% (number of surveys = 5; prevalence less than 10% in 2) in villages situated around the Toho-Todougba Lake at 30 km West of Cotonou (Chippaux et al., 1990) and 57.1% and 100% (Ibikounlé et al., 2009). In the Kouffo department prevalence was 19.7% (Garba et al., 2000).

2.3.11.2.2. Schistosoma mansoni This species was totally absent in the Ouémé department with 52 surveys free of infection and almost absent in the Borgou department with 10 surveys free of infection and two surveys with a prevalence of 1% and 7.5% (Doumenge et al., 1987). In the Couffo department, prevalence was 3.9% (Garba et al., 2000). In the Atlantique department, prevalence was the highest ever found in the country and ranged from 4% to 32.4% (number of surveys = 5; prevalence less than 10% in 2) in villages situated around the Toho-Todougba Lake and 8.4% of the studied population was mixed infected by *S. haematobium* and *S. mansoni* (Chippaux et al., 1990). Recently, a prevalence of 74.3% was found in this area, with 45.7% of mixed infections with *S. haematobium* (Ibikounlé et al., 2009).

2.3.11.3. Snail intermediate hosts and their schistosome prevalence

B. globosus, *B. forskalii* and *B. pfeifferi* were found in the Atlantique department in South Benin (Chippaux et al., 1990) but their infection with schistosomes was not attended. *B. globosus* and *B. pfeifferi* were also found in the Couffo department in South Benin and none of the snails were found to be naturally infected (Garba et al., 2000). A large-scale study was conducted recently in Benin to assess the diversity in the human schistosome transmitting snails in 9 out of the 12 departments of the country (Ibikounlé et al., 2009). These authors showed that four intermediate snail hosts exist in Benin. *B. forskalii* and *B. globosus* were

the most widely distributed (in 8 out of the 9 departments) and had a preference for artificial sites; *B. truncatus* was only present in the Borgou department and preferred the artificial permanent sites. *B. pfeifferi* was found in three departments (Borgou, Mono and Atlantique) and was shown to prefer the sites with permanent water compared to temporary ones. Naturally infected snails were only observed in the Atlantique department, with a prevalence of 0.56%; in this department, the prevalence of *S. mansoni* was the highest (Chippaux et al., 1990).

2.3.11.4. Schistosomiasis control

Except for local treatments using chemotherapy, a national schistosomiasis control programme has not been implemented yet in Benin. The very recent data obtained in Benin are witness to the fact that both urinary and intestinal schistosomiasis constitute a growing serious public health problem in this country. The collaboration between French and Benin Universities, through the Cooperative Programme for Academic and Scientific Research (CORUS) developed by the Department for International Cooperation and Development of the French Ministry of Foreign and European Affairs, aims to provide the baseline for a national control programme.

2.3.12. Nigeria

2.3.12.1. Ecoregions, hydrography and administrative departments (Figs. 2.1 and 2.16)

Nigeria is transected by three ecoregions: the subtropical dry grassland forming a narrow band in the North, the tropical dry forest and savanna in the major part of the country and the tropical wet forest in the extreme South of the country. The hydrography is dominated by five zones. The first zone is the Niger River basin constituted by the Niger River, its tributaries (except the Benue River), the Kainji dam (the biggest in the country), the Jebba dam, marshy plains down South and the delta. The second zone is formed by the Benue basin with the Benue River and its tributaries. The third zone contains all the rivers and the marshy plains and lagoons that lie to the South-West of the country, on the Western side of the Niger River delta. The fourth zone contains all the rivers and the marshy plains and lagoons that lie to the South of the country, on the East side of the Niger River delta. Finally, the fifth zone is situated to the North-East of the country and is constituted by the Lake Chad and all the rivers and marshy plains that flow into it. Whatever the zone, natural ponds and swamps are very numerous and the construction of many water development projects in the country contribute to the transmission of schistosomiasis. Nigeria is divided by 36 states and one federal capital territory.

FIGURE 2.16 Nigeria, its water network and its 36 states. The large black dot is the capital, Abuja.

2.3.12.2. Human schistosomiasis prevalence

The two species *S. haematobium* and *S. mansoni* were found in Nigeria, the second one showing generally a lower prevalence. Nigeria hosts half of the population of the ECOWAS, and the data will be presented for each state and the states will be grouped according to the five hydrographical zones presented above (see Section 2.3.12.1.).

2.3.12.2.1. Schistosoma haematobium

Niger River basin Sokoto state: a high prevalence was found in this zone with 84 and more than 90% (Doumenge et al., 1987) and along the Bakalori dam, 42.1% (Umar and Parakoyi, 2005). Niger state: prevalence ranged from 0% to 60% (number of surveys = 7; prevalence nil in 1) (Doumenge et al., 1987). Kwara state: prevalence was high and ranged from 9% to 97% (number of surveys = 13; prevalence less than 10% in 1) (Doumenge et al., 1987) and was 45.4% (Bello and Edungbola, 1992). Anambra state: prevalence was high with 45.4% in one village (Ozumba et al., 1989) and from 5.6% to 96.4% (number of surveys = 15; prevalence

less than 10% in 1) in villages around Agulu Lake (Emejulu et al., 1994) and the intensity of infection and haematuria were positively associated in these two studies. Delta state: a high prevalence of 53.3% was found in an area where quarry mining pits were present, compared to a much lower prevalence of 13.9% in a zone with no quarry pits (Nduka et al., 2006). An outbreak of schistosomiasis occurred just after the construction of a massive road network and a bridge, and the prevalence shifted from 10% to 38.5% (number of surveys = 10) before these constructions and to 89.1–95.1% (number of surveys = 10) after the constructions (Nwabueze and Opara, 2007). River states: prevalence varied a lot with 57.8% (Agi, 1995), 83.3% (Agi and Okafor, 2005) and 20.7% (Agi, 2007). Prevalence was still quite high (19.8%) in children less than 5 years old (Opara et al., 2007).

Benue River basin Plateau state: prevalence was high and ranged from less than 1% to 52% (number of surveys = 7; prevalence less than 10% in 2) (Doumenge et al., 1987) and from 22.9% to 62.4% (number of surveys = 6) (Akufongwe et al., 1996). Adamawa state: prevalence was very high with 69% and 94% (Doumenge et al., 1987). Benue state: prevalence was 45.7% (Mbata et al., 2009).

West part of the delta Ogun state: prevalence ranged from 0% to 70% (number of surveys = 45; prevalence less than 10% in 17 and nil in 2) (Doumenge et al., 1987), was 80% and 82.4% (Ofoezie et al., 1991) and was 1.6% (Agbolade et al., 2007). In pre-school children (less than 5 years old), prevalence ranged from 65.2% to 77.6% (number of surveys = 3) (Mafiana et al., 2003) and was related to the mother's domestic and occupational activities; it was still very high in infants less than 1 year old (42.9%). It was estimated by the geographical information system that the high-risk areas (more than 50% prevalence) were in the North Western part of the state and that 99% of school-age children were at risk of infection (Ekpo et al., 2008). Oyo state: prevalence ranged from 6.5% to 73% (number of surveys = 20; prevalence less than 10% in 4) (Doumenge et al., 1987) and from 1.6% to 57.9% (number of surveys = 15; prevalence less than 10% in 6) (Okoli and Odaibo, 1999). Osun state: prevalence was 48.5% (Amole and Jinadu, 1994), 66.4%, 70.3% and 76.2% (Adewunmi et al., 1991), 43% and 52.5% (Oladejo and Ofoezie, 2006) and 46.3% and 56.2% (Ugbomoiko et al., 2009); transmission was seasonal and occurred during the dry season (Adewunmi et al., 1990). Edo state: prevalence was high with 43% and more than 50% (Doumenge et al., 1987), 35.2% (Ogbeide et al., 1994), 32.6% (Nmorsi et al., 2001a), 21.4% (Nmorsi et al., 2001b), 60% (Nmorsi et al., 2005) and 59.5% (Nmorsi et al., 2007). Ondo state: except one free infection, prevalence ranged from 50% to 93.9% (number of surveys = 11) (Doumenge et al., 1987). Lagos state:

prevalence ranged from less than 2.5% to 90.9% (number of surveys = 12; prevalence less than 10% in 3) (Doumenge et al., 1987).

East part of the delta Ebonyi state: prevalence ranged from 10.7% to 51.9% (number of surveys = 15) (Anosike et al., 2003) and from 20.1% to 24.7% (number of surveys = 10) (Anosike et al., 2006). Abia state: prevalence range from 25.5% to 52.3% (number of surveys = 11) (Nwosu et al., 2005). Cross River state: prevalence was high with 43.5% (Ejezie et al., 1991), 44% (Ekanem et al., 1994, 1995), from 10.4% to 38.9% (number of surveys = 4) (Okoli and Iwuala, 2004), 42.5% (Akeh et al., 2008), 51% (Eyong et al., 2008) and 38.5% (Inyang-Etoh et al., 2009). Imo state: prevalence was 30% (Doumenge et al., 1987) and ranged from 0% to 27.8% (number of surveys = 10; prevalence less than 10% in 1 and nil in 1) (Okoli et al., 2006).

Lake Chad zone Kano state: prevalence ranged from 6.1% to more than 90% (number of surveys = 16; prevalence less than 10% in 2) (Doumenge et al., 1987) and was 26.6% and 36.8% (Betterton et al., 1988). Bauchi state: prevalence was 53% (Doumenge et al., 1987) and 17.9% (Akogun, 1990). Borno state: prevalence ranged from 4.3% to 100% (number of surveys = 9; prevalence less than 10% in 3) (Doumenge et al., 1987) and was 6.2% (Chugh et al., 1986).

2.3.12.2.2. Schistosoma mansoni

Niger River basin Sokoto state: prevalence was 13% and 27% (Doumenge et al., 1987). Niger state: prevalence ranged from 0% to 23% (number of surveys = 7; prevalence less than 10% in 6 and nil in 1) (Doumenge et al., 1987). Kwara state: prevalence ranged from 0% to 78% (number of surveys = 6; prevalence less than 10% in 4 and nil in 1) (Doumenge et al., 1987). Anambra state: prevalence was either very low (0.4%) (Doumenge et al., 1987) or nil, despite the presence of the vector snail, *B. pfeifferi* (Ozumba et al., 1989).

Benue River basin Plateau state: prevalence ranged from less than 1% to 28% (number of surveys = 6; prevalence less than 10% in 4) (Doumenge et al., 1987). Adamawa state: prevalence was 39% (Doumenge et al., 1987).

West part of the delta Ogun state: prevalence ranged from 0% to 20.8% (number of surveys = 6; prevalence less than 10% in 5 and nil in 3) (Doumenge et al., 1987) and was 2.3% (Agbolade et al., 2007). Oyo state: prevalence ranged from 0% to 7.4% (number of surveys = 4; prevalence less than 10% in 4 and nil in 3) (Doumenge et al., 1987) and from 16.3% to 30.2% (number of surveys = 4) (Morenikeji et al., 2009). Osun state: transmission was demonstrated throughout the year (Adewunmi et al., 1990). Lagos state: prevalence was 0.2% and 1% (Doumenge et al., 1987).

Lake Chad zone Kano state: prevalence ranged from 1.7% to 14% (number of surveys = 9; prevalence less than 10% in 6) (Doumenge et al., 1987). Bauchi state: prevalence was 28% (Doumenge et al., 1987) and 10.8% (Akogun, 1990). Borno state: prevalence ranged from 0% to 15% (number of surveys = 8; prevalence less than 10% in 7 and nil in 3) (Doumenge et al., 1987).

2.3.12.2.3. Schistosoma guineensis This species was only reported in the River states in the Niger delta with low prevalence of 0.9% from faecal samples (Agi, 2007). An ectopic occurrence of *S. guineensis* was reported in the urine of some patients of Port Harcourt (prevalence from 1% to 9.8%), while, surprisingly, no eggs of this species were detected in the stools (Arene et al., 1989).

2.3.12.3. Snail intermediate hosts and their schistosome prevalence

2.3.12.3.1. Niger River basin Anambra state: *B. truncatus*, *B. globosus*, *B. forskalii* and *B. pfeifferi* were found. *B. truncatus* and *B. globosus* were the only snails found naturally infected, particularly in the lakes and their arms. For *B. truncatus*, prevalence could reach 40–50% (Ozumba et al., 1989) and ranged from 1.5% to 8.1% (number of surveys = 7) (Emejulu et al., 1994). For *B. globosus*, prevalence ranged from 3.6% to 8.9% (number of surveys = 7) (Emejulu et al., 1994). Delta state: *B. truncatus*, *B. globosus*, *B. forskalii* and *B. senegalensis* were found (Nduka et al., 2006; Nwabueze and Opara, 2007). Rivers state: *B. globosus* and *B. forskalii* were found and only the first one was naturally infected (Agi, 1995, 2007) and prevalence was 12.1% during the dry months (Agi and Hart, 2007).

2.3.12.3.2. Benue River basin *B. truncatus*, *B. globosus* and *B. pfeifferi* were found in the Plateau state, and *Bulinus* snails (species not given) were found naturally infected, around 10% during the wet season but from 10% up to 50% during the dry season (up to almost 50%) (Akufongwe et al., 1996).

2.3.12.3.3. West part of the delta Ogun state: *B. globosus* and *B. forskalii* were found in this state and *B. globosus* was found naturally infected with prevalence of 2.3% and 21% (Agbolade et al., 2004). *B. truncatus* was also found, together with *B. globosus* and *B. forskalii* and their relative proportions were 0.2%, 17.6% and 16.1%, respectively, the 66.1% left including other species of snails which are non-hosts for human schistosomes (Ofoezie, 1999). Oyo state: *B. globosus*, *B. forskalii*, *B. truncatus* and *B. pfeifferi* were the snail intermediate hosts found in this state (Okoli and Odaibo, 1999). *B. globosus* was the most abundant and it was found, together with *B. pfeifferi*, naturally infected (data on prevalence not available) (Okoli and Odaibo, 1999). Osun state: *B. globosus* was abundant and *B. pfeifferi* was also present (Adewunmi et al., 1991; Oladejo and Ofoezie, 2006).

2.3.12.3.4. East part of the delta Ebonyi state: *B. truncatus*, *B. globosus*, *B. senegalensis* and *B. pfeifferi* were found. *B. truncatus* and *B. globosus* were found naturally infected in rice swamps and ponds (data not available) (Anosike et al., 2003). *B. globosus* and *B. senegalensis* were found naturally infected with a prevalence of 31.2% and 10% (Anosike et al., 2006). Abia state: *B. globosus*, *B. truncatus*, *B. forskalii* and *B. pfeifferi* were found and only *B. globosus* shed schistosome cercariae (31.1%) (Nwosu et al., 2005).

2.3.12.3.5. Lake Chad zone *B. truncatus*, *B. globosus*, *B. senegalensis*, *B. forskalii* and *B. pfeifferi* were found in Kano state and *B. senegalensis* was the most widespread, preferring the shallow pools (Betterton et al., 1983, 1988).

2.3.12.4. Schistosomiasis control

A national plan of action for the control of schistosomiasis was drawn with the view to 'reduce the prevalence by 50% within 5 years in operational areas' (Anosike et al., 2003). The use of school questionnaires was recommended for rapid identification of communities at higher risk of urinary schistosomiasis since they could be validated by parasitological tests (Mafe et al., 2000). In order to help in developing a control programme, predictive risk maps of the probability of occurrence of the disease were generated and the risk for infection was quantified (Ekpo et al., 2008). These authors used questionnaires, geographical information system and remote sensing environmental data from Ogun state and demonstrated that land surface temperature was the only significant environmental variable in predicting the presence and absence of *S. haematobium*. In Nigeria, the World Health Organisation's rapid assessment method for urinary schistosomiasis (answer yes to the presence of haematuria) was validated and proposed as a useful alternative to the parasitological tests (Nduka and Nwosu, 2008). Chemotherapy and molluscicide were used in the Rivers state (Agi, 1995). In the Cross River state, the efficacy of praziquantel against *S. haematobium* was enhanced when combined with another drug, artesunate, a derivative of the antimalarial drug, artemisinin (Inyang-Etoh et al., 2009). Schistosomiasis is a serious public health problem in Nigeria and prevalence is still very high. The importance of dam constructions on the enhancing of schistosomiasis transmission was highlighted (Ofoezie, 2002). Even if much work has already been done in order to get baseline data, much work is still to be done to get more baseline data since the country is large and that data is lacking concerning some states. Control of schistosomiasis in this state is a huge task and needs a strong organisational implementation.

2.4. CONCLUSIONS AND PERSPECTIVE

In ECOWAS, infected people are a predominantly rural population whose water contact is linked to working activities, agriculture (rice crops), farming, fishing (even in a boat), watering of cattle, trading, crossing, quarry mining, to domestic activities (water collection, washing of utensils and clothes), to personal activities (fetching, bathing, religious behaviour), or to recreational activities (playing, swimming). Water-related activities (outside of the house) are necessary to the majority of the people living in ECOWAS but these outdoor water activities are the source of the schistosomiasis infection. At the same time, development of water resources is beneficial for providing hydro-electric power and enhancing agricultural production and freshwater fishing and thus for feeding the growing population. For these aims, hundreds of dams were constructed in ECOWAS countries during the last four decades. Unfortunately, the man-made constructions have adverse environmental effects. They are generating new foci for the expansion of the snail intermediate hosts and the establishment of water resource projects are associated with outbreaks of schistosomiasis. Very recent outbreaks of schistosomiasis are still observed following construction projects that enhanced the development of a large snail population. The enhancement of the prevalence due to dam constructions and agricultural purposes does not constitute only a temporary enhancement but a true permanent problem for the country because the solution to be addressed is then more important than before the constructions. Another important cause of infection is due to the enhancement of these water-related activities during the dry season, when water becomes more important for people due to its rareness. The problem is that the densities of the snail intermediate hosts, especially the naturally infected ones, are also substantial during the dry season. This increases the chances of cercariae–human contact. Other factors such as age (from 5 to 19 years old), sex (male, but not always, not under 5 years old), poor level of school attainment, occupation, source of water for domestic use, absence of latrines, small distance to the source of water have a significant association with the risk of being infected. Furthermore, in places where no safe water supply is available, infection may be acquired very early in life (less than 1 year old) when the infants accompany their mothers to their different water-related activities (Mafiana et al., 2003) as observed in Benin by the authors of the present chapter (H. Moné, M. Ibikounlé, A. Massougbodji and G. Mouahid).

Human schistosomiasis in ECOWAS countries is highly endemic and no country is about to eliminate the disease as it is feasible in Oman or in Morocco, for example. *S. haematobium* was reported in all the countries belonging to ECOWAS, except Cape Verde (Table 2.1). Prevalence was highly variable, generally reached very high levels and did not regress

TABLE 2.1 Epidemiology of human schistosomiasis in ECOWAS

Country[a]	*S. h.*	*B. g.*	*B. u.*	*B. f.*	*B. s.*	*B. t.*	*S. m.*	*B. p.*
Mali	P	P+	P	P	P	P+	P	P+
Niger	P	P	P	P+	P+	P+	P	P
Burkina Faso	P	P	P	P	P+	P+	P	P
Cape Verde	A	A	A	P	A	A	A	A
Senegal	P	P+	P	P	P+	P+	P	P+
The Gambia	P	P	A	P	P	P	P	P
Guinea-Bissau	P	P	A	A	P	A	P	P
Guinea	P	P	A	A	A	P	P	P
Sierra Leone	P	P	A	P	A	A	P	P
Liberia	P	P+	A	A	P	A	P	P+
Côte d'Ivoire	P	P	A	P	A	P	P	P
Ghana	P	P	A	A	A	P	P	P
Togo	P	P+	A	P	A	P	P	P+
Benin	P	P	A	P	A	P	P	P+
Nigeria	P	P+	A	P	P+	P+	P	P+

S. h., Schistosoma haematobium; B. g., Bulinus globosus; B. u., Bulinus umbilicatus; B. f., Bulinus forskalii; B. s., Bulinus senegalensis; B. t., Bulinus truncatus; S. m., Schistosoma mansoni; B. p., Biomphalaria pfeifferi; P, presence; A, absence; P+, presence of schistosome naturally infected snails.
[a] The countries were listed according to their rank in the text.

since 1960. The global trend is an enhancement of the prevalence as soon as man-made constructions are made. Regarding the snail intermediate hosts, five species of *Bulinus* were reported in ECOWAS (Table 2.1): *B. globosus*, *B. umbilicatus*, *B. forskalii*, *B. senegalensis* and *B. truncatus*. The five species split into three species groups of *Bulinus* (Brown, 1994; Kane et al., 2008): *B. africanus* group with *B. globosus* and *B. umbilicatus*, *B. forskalii* group with *B. forskalii* and *B. senegalensis*, *B. truncatus/tropicus* group with *B. truncatus*. *Bulinus globosus* was found in 14 among the 15 ECOWAS countries and was found naturally infected in only five countries (Table 2.1). It is often presented as the major host for *S. haematobium* and the presence of naturally infected snails in the other countries of ECOWAS should be surveyed. This snail is well adapted to various habitats but prefers seasonally rain-filled pools and habitats with well-developed aquatic vegetation and clear water. *B. umbilicatus* is present in the Northern part of ECOWAS only (Mali, Niger, Burkina Faso and Senegal) (Table 2.1). It was never found naturally infected by *S. haematobium* and its role as a natural snail intermediate host of *S. haematobium* is being questioned. It likes pools and can survive dry periods for several months. *B. forskalii* is present in 11 out of the 15 ECOWAS countries (Table 2.1). However, Guinea-Bissau, Guinea, Liberia and Ghana remain

potential countries to harbour *B. forskalii* since it has been found in all the bordering countries. It represents the only *Bulinus* reported in Cape Verde. Natural infection by *S. haematobium* was only reported in Niger. This snail prefers a permanent source of water such as irrigation canals. It is often found in mixed population with *B. senegalensis*. *B. senegalensis* is present in 8 out of the 15 ECOWAS countries (Table 2.1). However, the countries situated from Guinea to Benin could potentially harbour *B. senegalensis* since it has been found in all the bordering countries. *B. senegalensis* was found naturally infected in four countries: Niger, Burkina Faso, Senegal and Nigeria and acts as an important snail host in ECOWAS. It likes shallow pools, excavations, accepts highly turbid water and habitats devoid of aquatic vegetation. It is often found with *B. forskalii. B. truncatus* is present in 11 out of the 15 ECOWAS countries. However, Guinea-Bissau, Sierra Leone and Liberia remain potential countries and should be surveyed closely since all the neighbouring countries harbour it. Natural infection by *S. haematobium* was found in five countries: Mali, Niger, Burkina Faso, Senegal and Nigeria. This snail represents one of the three more important *Bulinus* host in ECOWAS. It is the dominant *Bulinus* species in man-made lakes and irrigation canals. Four countries harbour the five species of *Bulinus*: Mali, Niger, Burkina Faso and Senegal. Three countries harbour three different naturally infected snail intermediate hosts: Niger with *B. forskalii*, *B. senegalensis* and *B. truncatus*; Senegal and Nigeria with *B. globosus*, *B. senegalensis* and *B. truncatus*.

S. mansoni was reported in all the countries belonging to ECOWAS, except Cape Verde (Table 2.1). Its prevalence is generally low (even if some foci showed very high prevalence) and its distribution is generally patchy. Tendency for *S. mansoni* is to spread to new areas thanks to the spreading of its snail intermediate host, *B. pfeifferi*. This snail has exactly the same distribution as *S. mansoni* and constitutes the only snail intermediate host in ECOWAS (Table 2.1). All the ECOWAS countries should harbour naturally infected *B. pfeifferi* since autochthonous people are infected. At the moment, the naturally infected snails were only found in Mali, Senegal, Liberia, Togo, Benin and Nigeria.

Studies on mixed infections involving *S. haematobium* and *S. mansoni* are rare. They were reported only in three countries, Côte d'Ivoire with 3.2% (Adoubryn et al., 2006), Senegal with 21% (de Clercq et al., 1999) and Benin with 45.7% (Ibikounlé et al., 2009). More studies on polyparasitism are needed since the two species coexist in all the ECOWAS countries (except Cape Verde).

S. guineensis was only reported in two countries: Mali and Nigeria but its presence in these two countries needs to be confirmed by other data. Indeed, in Mali, autochthonous people were never found infected while infection was reported in tourists coming from the Dogon zone.

In Nigeria, *S. guineensis* was reported in stools with a very weak prevalence and in urine. Indeed, *S. guineensis* is unlikely to spread to areas where *S. haematobium* is already established because of the possible hybridisation between *S. haematobium* and *S. guineensis*, paired with the competitive mating interactions between these two species with the dominance of *S. haematobium* (Cosgrove and Southgate, 2003). The mechanism of the replacement of *S. guineensis* by *S. haematobium* is introgressive hybridisation; the use of molecular markers, as the single-stranded conformational polymorphism analysis, better than morphology, is necessary in order to ensure definitely the presence of *S. guineensis* (Mintsa Nguema et al., in press; Webster et al., 2005).

Baseline data are needed before control. Traditionally, epidemiological studies entailed the detection of parasite eggs in urines or stools by microscopy. They are very helpful for diagnosing, but they are time-consuming. This is why an alternative method of diagnosing was proposed in high endemic countries for *S. haematobium*, which is the case of the countries belonging to ECOWAS. It is based on the detection of visible haematuria in the urines directly by the health workers or by the use of questionnaires addressed to the people. This test is simple with a potentially low cost and it is also rapid if carried on by a good organisation. Geographical information systems and remote sensing may help to map the high-risk zones. Predictive risk model maps can be generated to delineate areas for intervention.

Organisation of the control is an important goal for all the countries in ECOWAS. An integrated approach is needed using different tools in order to control the disease and two rules must be followed at the same time: the reduction of the existing disease by the treatment of the population and the enhancement of the resources available for the prevention of the disease. Mass chemotherapy is used by all the countries affected by schistosomiasis and praziquantel is widely used. However, there is some evidence of praziquantel resistance in Senegal and new drugs or new drug combinations are searched for. The Schistosomiasis Control Initiative put in place in three countries in ECOWAS (Mali, Niger and Burkina Faso) demonstrated that schistosomiasis prevalence can be reduced efficiently with mass treatment of the population. Enhancing sustainability of these programmes is now a new challenge (Garba et al., 2009). Schistosomiasis Control Initiative constitutes a model of the organisational programmed control and can be emulated in other countries affected by this disease as in sub-Saharan Africa (Fenwick et al., 2009). Health education and community mobilisation is the most important tool since it will make people aware of the risks. It is necessary in ECOWAS countries because even when supplied with safe water, people were still using the reservoir water for recreational activities. Mothers also need to be educated about the risk when they expose their infants to the infection. Co-operation

is needed in each country between engineers, health experts and national education professionals and between the different countries of ECOWAS for a schistosomiasis sustainable control since they share a large water network and since the ECOWAS people travel all around the countries.

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CHAPTER 3

The Rise and Fall of Human Oesophagostomiasis

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Abstract Until recently, the infections of humans with representatives of the genus *Oesophagostomum* were thought to be rare and of zoonotic origin. In the 1980s, it was recognised that intense transmission associated with the disease was taking place in northern Togo and Ghana. Pathology can be severe and two clinical presentations, called 'Dapaong Tumour' and 'multinodular disease', have been described. Lesions can now be efficiently and specifically visualised by ultrasound. The prevalence of infection appeared to be high in many villages, although its distribution was limited and focal. Parasitological diagnosis has been based on the demonstration of third-stage larvae in stool cultures and more recently on PCR. Molecular and epidemiological evidence supports the proposal that *Oesophagostomum bifurcum* infections of humans in Ghana and Togo represent a distinct genotype from that of non-human

primates in the area. Mass treatment, using repeated doses of albendazole rapidly resulted in the effective elimination of human oesophagostomiasis in the affected areas.

This review takes a historic perspective on oesophagostomiasis of humans. This chapter discusses how the unexpected success of mass treatment together with aberrant pathogenesis, the severity of pathology in humans and the limited geographic distribution of the parasite all reflect a poor adaptation of the parasite to the human host.

''Dr Andrew Foy, of the West African Medical Staff, was good enough whilst home on leave recently, to present to the London School of Tropical Medicine a tube containing a considerable number of specimens of Necator americanus, passed by a patient at Ibi, Northern Nigeria. In the course of routine examination of individual specimens, I have been able to single out from the collection six examples of Oesophagostomum apiostomum, a parasite frequently producing serious intestinal lesions in monkeys but hitherto apparently unknown in man, unless, as will be discussed later, Oesophagostomum brumpti is to be regarded as the same species. The specimens resemble N. americanus very closely in size and in general appearance, and would probably have been overlooked, had they not been scrutinized with a hand lens...''

These are the opening sentences of Dr Leiper's brief report on 'The occurrence of *O. apiostomum* as an intestinal parasite of man in Nigeria', published in 1911 (Leiper, 1911). Several of the key features and questions were already addressed in this early paper. It was the first and, until the 1980s, and apart from two other early observations of Johnson (1913) and Henry and Joyeux (1920), the only report of finding adult *Oesophagostomum* worms in human stool samples. Moreover Leiper wondered whether the parasites found by him, those commonly found in monkeys and apes, those described by Railliet and Henry (1905) in a patient from the Omo Valley in Southern Ethiopia and found by Brumpt in 1902, were all the same, or should be considered as separate species (Railliet and Henry, 1905). This is, indeed, a very relevant question that will be addressed later.

From the first recognition of *Oesophagostomum* species in man by Brumpt in 1902/1905 until the early 1980s, when Dr Sénamé Baeta described 51 cases during his 4-year stay as a doctor/surgeon in the Regional Hospital of Dapaong in Northern Togo (Gigase, 2008; Gigase et al., 1987), only a few isolated clinical cases of human infection were seen in a number of different countries. Following Dr Baeta's report it was recognised that, in Northern Togo (and Ghana), *Oesophagostomum* infections in humans were not a rare condition but widely present, though easily overlooked, in the rural population.

The aim of this chapter is to provide an overview of what is now known of *Oesophagostomum* as a parasite of man. Special attention will be paid to the zoonotic characteristics of oesophagostomiasis since infection with the same or closely related species is a very common and sometimes serious infection in non-human primates. The focus of the overview will be on the natural history of the parasite and the fragility of the host–parasite relationship that became apparent in the severity of pathology and in the unexpected success of attempts to control the infection.

Some information comes from cases of clinical infection, mostly reported from surgical departments in 15 countries across Africa, Asia and South America. The other comes from a set of epidemiological studies carried out in what appeared to be the highly endemic area of northern Ghana and Togo. Much information has been published previously, but several aspects have only been recorded in PhD theses and some of the personal observations of the present authors are included as well.

3.1. OESOPHAGOSTOMES OF PIGS, RUMINANTS AND MONKEYS

The genus *Oesophagostomum* is now considered to comprise a number of subgenera, representatives of which all have a similar morphology and life cycle. The adult worms are roughly 1–2 cm long and inhabit the lumen of the caecum and colon of the definitive host. The life cycle is characterised by the occurrence of a tissue-dwelling larval stage, resulting in the formation of nodular abscesses of variable size in the intestinal wall, hence the popular name 'nodular worm'. The principal subgenera, the species as recognised by Lichtenfels (1980), and the hosts involved are summarised in Table 3.1. Infection by a species of *Oesophagostomum* in

TABLE 3.1 Subgenera, species and hosts commonly parasitized by *Oesophagostomum* spp.

Subgenus	Species	Host
Oesophagostomum	*dentatum*	Pig
	quadrispinulatum	Pig
Proteracrum	*columbianum*	Sheep, goat, wild antilopes
Hysteracrum	*venulosum*	Sheep, goat
Basicola	*radiatum*	Cattle, buffalo
Conoweberia	*aculeatum*	Primates, human
	bifurcum	Primates, human
Ihlea	*stephanostomum*	Primates, human

other than its natural host is considered to be rare (Glen and Brooks, 1985; Stewart and Gasbarre, 1989). The exception is *Oesophagostomum venulosum*, which has been reported in cattle in the United States, although it is mostly a parasite of sheep and wild ruminants. Before focusing on the species infecting non-human primates and man, some of the most relevant characteristics of the 'nodular worms' of veterinary importance need to be considered (Anderson, 1992).

3.1.1. *Oesophagostomum* in pigs and ruminants

Oesophagostomum dentatum is considered to be a phylogenetically old and well-established parasite of pigs (Glen and Brooks, 1985). The balanced host–parasite relationship is expressed in the comparatively benign pathology resulting from infection, which normally takes place orally (Anderson, 1992; Veglia, 1923) through ingestion of third-stage larvae. The larvae invade the mucosa and sub-mucosa of the caecum and colon and, by day 4, distinct nodules can be recognised. The third-stage larvae (L_3) moult by day 7–10 and a few days later the fourth-stage larvae (L_4) escape from their nodules to return to the intestinal lumen. The nodules have then attained their maximum size of about 8 mm. Following the release of the L_4 larvae into the gut lumen, the inflammatory tissue reaction resolves and 2 weeks later virtually no evidence of the parasite's histotropic phase can be found. Further development of the L_4 larvae into adult worms takes place in the lumen of the caecum and colon. Eggs are usually first found about 1 month post-infection (McCragen and Ross, 1970), but sometimes occur much earlier, at 17–19 days (Bjørn et al., 1990; Roepstorff et al., 1996). Most gross pathology is the result of heavy infection, with many adult worms. Reduced nutrient absorption and consequently reduced growth is the result.

Oesophagostomum quadrispinulatum, a related but less studied species, is commonly found together with *O. dentatum*. This species causes more severe tissue damage and larger nodules in the caecal and colonic mucosa are found (Christensen et al., 1996; Stockdale, 1970).

The life cycle of *Oesophagostomum radiatum* of cattle is quite similar. Andrews and Maldonado observed that 72 h after experimental infection all the larvae were found to be in the wall of the small intestine or caecum (Andrews and Maldonado, 1941, 1942). The third larval moult took place around day 8 or 9 post-infection (PI). By day 10 some L_4 larvae had already left the intestinal wall, ''and most of those remaining were apparently ready to return to the lumen of the intestine''. The first eggs were found 37–41 days PI.

In *Oesophagostomum venulosum*, a parasite of sheep and goats, the nodules are formed on day 2 or 3 PI; by day 4 most larvae have already left the nodules and the L_4 larvae are found in the lumen, in close

proximity to the wall. Thereafter the L_4s gradually move from the small intestine to the caecum and colon (Goldberg, 1951). By day 15 PI, many parasites are eliminated in the faeces, mostly as adult worms, but with a small percentage of L_4 larvae. Symptoms of infection are all due to the presence of the adult worms, not the encysted larval stages. At post-mortem, only a few remnants of nodules are found and in the rare cases where a nodule was found, it did not contain larvae (Goldberg, 1951).

In *Oesophagostomum columbianum*, a parasite of sheep, two distinct types of lesion occur: small granulomatous lesions formed around the histotropic stages in the small intestine and large caseous nodules in the large intestine. Dash (1973) showed that the majority of encysted third-stage larvae are found in the small intestine. Histotropic L_4 larvae are predominantly found in the wall of the large intestine, over a long period, between day 10 and day 66 PI. These histotropic L_4 larvae in the large intestine may be arrested at mid-fourth stage while L_4 larvae in the lumen continue to develop to the adult stage. The L_4-containing nodules contain greenish yellow pus around the larvae. These large intestinal lesions may be quite severe and may lead to perforation of the intestinal wall and peritonitis. In animals experimentally infected, cured and re-infected with *O. columbianum*, the number of larvae reaching adulthood was very low. Even 66 days after the second infection, less than 5% of the parasites recovered were adults and over 90% were histotropic L_4 larvae trapped in the large intestinal wall (Dash, 1973).

From Dash's experimental infection data, it is concluded that there are two separate histotropic phases: one covering no more than 5–10 days in the small intestine, and another in the large intestine occurring later and of longer duration. Dash concluded that ''the caseous nodule appears to be a characteristic reaction to the histotropic fourth-stage larva of *O. columbianum* in a host which is sensitised either by a previous infection or during the first histotropic phase of the same infection''. The fate of the fourth-stage histotropic larvae was not determined but ''it seems unlikely that they would have been able to penetrate the connective tissue capsule of the caseous nodule and it seems probable that eventually they would have been destroyed in the intestinal wall'' (Dash, 1973).

O. columbianum appears poorly adapted to its present host ('an example of a parasite in the wrong host') and the contrast with the host–parasite relationship in *O. venulosum* infections in the same host is impressive. Later, these conclusions are rephrased and made more specific: it is suggested that *O. columbianum* is normally a parasite of wild antelope that has only recently become adapted to sheep (Dash, 1982).

In the reports of experimental infections in sheep, cattle and goats, the regimen for infection appeared to be important. In some species, such as *O. venulosum*, trickle infections led to the establishment of fewer adult worms. This effect is attributed to the development of some level of

immunity (Anderson, 1992; Goldberg, 1952). Similarly, initial infections with *O. radiatum* in calves have been reported to be protective against re-infection (Roberts et al., 1962). Extensive experience with the effect of different dose levels and infection regimens have also been described for *O. dentatum* (Barnes, 1997; Christensen et al., 1995).

3.1.2. *Oesophagostomum* in monkeys

Oesophagostomum infections in monkeys and apes have been studied in descriptive, rather than in experimental, studies. The details of the parasite life history are therefore less well defined and more effort is required to understand the life cycle and consequent pathology. The species involved are *Oesophagostomum bifurcum* and the closely related *Oesophagostomum aculeatum*, found in a wide variety of species of Old World monkeys, and *Oesophagostomum stephanostomum*, mainly found in chimpanzees and gorillas. The taxonomy and nomenclature of primate *Oesophagostomum* species has been confused for many years. We now follow the classification used by Chabaud and Larivière (1958), largely based on Travassos and Vogelsang (1932). The old names *Oesophagostomum brumpti* and *O. apiostomum* have both been used to describe the species that is now called *O. bifurcum*.

In his overview of parasites of non-human primates transmissible to man, Orihel (1970) opens with the observation that oesophagostomes are among the most common and most injurious helminth parasites of monkeys and apes. Rousselot and Pellissier (1952) had already indicated that infection with *O. stephanostomum* was almost universal in wild gorillas. In Ruch's authoritative overview in *Diseases of Laboratory Primates*, it is concluded that sometimes, ''especially in an older animal having immunity to the worm'', the developing L_4 larvae are captured in a tissue reaction. This nodule, ''frequently caseous, may persist for long periods and be conspicuous at necropsy. In the non-immune animal the worms return to the lumen in 5–8 days and grow to maturity, completing the sexual life cycle'' (Ruch, 1959).

As early as 1906, Weinberg gave a detailed description of the pathology of *Oesophagostomum* species in monkeys and apes and 2 years later, in 1908, an extensive and much cited description of the pathological findings in two chimpanzees and 22 smaller monkeys was published (Weinberg, 1906, 1908). Weinberg was himself quite impressed that the lesions were so characteristic, and consistent, irrespective of the host, and the species of *Oesophagostomum*. The nodules described by Weinberg are most commonly found in the caecum and first part of the colon. Their size varies from the size of peas to small nuts. They always contain one juvenile worm, amidst caseous material and '*un magma sanguinolent*'. They are found in the sub-mucosa, sometimes slightly deeper in the

muscular layers. The nodules are some 5–9 mm in diameter and harbour a juvenile worm, not an L_4 larva. In a few rare cases only, smaller cysts are found in the muscular layer, containing small larval stages. Eggs are never found, either in the nodules, or in the intestinal lumen.

The most severe and heavy infections, often resulting in death of the monkeys or apes, were typically reported in situations where cross-infection could take place under insanitary, overcrowded shipping conditions (Ruch, 1959). Rousselot and Pellissier (1952) observed that 12 out of 14 newly captured gorillas were infected with *O. stephanostomum*. It was believed that, in the wild, these gorillas managed to keep the parasitism within bounds but among captives, the number of parasites rapidly increased to fatal levels. It is only in the colonic wall of these recently captured gorillas that large numbers of larvae were found in addition to the characteristic nodules containing a juvenile adult worm.

3.1.3. Concluding remarks

It is important to note that, in monkeys and apes, it is the adult worm that is normally found in the nodules. This is in marked contrast to ruminants and pigs, where L_4 and only very rarely older stages are found.

3.2. *OESOPHAGOSTOMUM* INFECTIONS IN MAN

Until the publication of the series of cases described by Gigase et al. (1987) and Storey et al. (2000), no more than 31 clinical cases of *Oesophagostomum* infections had been convincingly diagnosed and described, as summarised in Table 3.2. Several authors, however, expressed the view that many more had probably been missed. Anthony and McAdam (1972) for example described a series of 34 cases of 'helminthoma' in Uganda and indicated that *Oesophagostomum* species were the most common helminths involved (*Ternidens deminutus* and *Ancylostoma duodenale* were found less frequently), but definite proof of the presence of *Oesophagostomum* worms was provided in no more than three patients. Welchman (1966), also in Uganda, confirmed an *Oesophagostomum* infection in one patient and suspected it to be present in two others, although he did not actually find the worms.

3.2.1. Clinical infections in man

An early and very detailed description of the pathological findings in human infection was given in a 32-page paper by Wolferstan Thomas, who carefully illustrated with five full colour plates. Yet, the author apologises: ''unfortunately the case occurred at a time when there were

TABLE 3.2 The clinical cases published

Country	Year	Publication	Patients' details	*Oesophagostomum* species
'West Africa'	1944	Joyeux (1944)	No details	*???*
Senegal	1959	Baylet and Paillet (1959)	Young child	*O. stephanostomum*
Côte d'Ivoire	1975	Curan (1975)	Child, age 5	*O. stephanostomum*
Ghana	1964	Haaf and van Soest (1964)	4 children, 5 adults	*O. bifurcum*
Ghana	1978	Barrowclough and Crome (1979)	Girl, age 8	*Oesophagostomum species*
Ethiopia	1902	Railliet and Henry (1905)	Male, age 30	*O. brumpti*
Ethiopia	1977	Leoutsakos et al. (1977)	Male, age 29	*O. brumpti*
Kenya	1977	Kaminsky and Ndinya-Achola (1977)	Male, age 14	*Oesophagostomum species*
Sudan	1964	Jacques and Lynch (1964)	Male, age 20	*O. apiostomum*
Uganda	1953	Elmes and McAdam (1953)	Girl, 5[a]; girl ?; adult, 31[a]	*O. stephanostomum/O. brumpti/ Oesophagostomum species*
Uganda	1958	Lothe (1958)	Child, age 1½	*O. stephanostomum*
Uganda	1966	Welchman (1966)	Male, age 31[a]	*Oesophagostomum species*
Uganda	1967	Loeffler (1995)	Male, age 28	*Oesophagostomum species*
Uganda	1969	Marshall and Deneka (1966)	Boy, age 2½[a]	*Oesophagostomum species*
Uganda	1972	Anthony and McAdam (1972)	1 child, 2 adults[a]	*O. apiostomum*
Zimbabwe	1932	Blackie (1932)	No details	*O. bifurcum*
Zimbabwe	1969	Gordon et al. (1969)	Child 16	*Oesophagostomum species*
Brazil	1910	Thomas (1910)	Male	*O. stephanostomum*
Indonesia	1949	Joe (1949)	Male, age 45	*O. bifurcum*
Brunei	1989	Ross et al. (1989)	Male, age 18[a]	*Oesophagostomum species*
Malaysia	1992	Karim and Yang (1992)	Male, age 18	*O. apiostomum*

Note: The species *O. brumpti* and *O. apiostomum* are nowadays classified as *O. bifurcum*.
[a] The patients marked with an *a* were expatriates from Europe and Canada.

many other duties to be performed, and consequently the post-mortem was incomplete . . .'' (Thomas, 1910). The patient died from peritonitis, which was believed to be due to the lesions caused by the worm. The small intestine, and particularly the last 35 cm of the ileum before the ileo-caecal valve, the caecum, and the first part of the ascending colon, were studded with small raised dark-brown tumours, typically 6–9 mm in diameter but sometimes elongated and flatter and up to 23 mm in length. Searching with the naked eye, 187 cysts were found. Each cyst contained one worm, never more. The juvenile worms in the cysts were 16–22 mm long. Neither mature adults nor eggs were found during the pathological examination of the material of this patient performed by Railliet and Henry (1909). The intestinal lumen did not contain any *Oesophagostomum* worms, only some hookworms. The wall of the ileum was very thin and transparent; that of the colon thickened and fibrotic with many adhesions. Nodules in the sub-mucosa bulged into the intestinal lumen and several were about to cause intestinal occlusion. It is intriguing to note that in addition to the '*ordinary cysts*' 'minute larvae of a nematode were found in various parts of the bowel wall'. Such small larval stages have not been observed again by any of the later investigators! The juvenile adults were identified as *O. stephanostomum*; the identity of the larvae, however, could not be determined (Railliet and Henry, 1909).

Similar cases, with massive involvement of the entire colon, have been described in Sudan (Jacques and Lynch, 1964), in former Southern Rhodesia (Gordon et al., 1969), in Ethiopia (Leoutsakos et al., 1977) and in Ghana (Barrowclough and Crome, 1979; Haaf and Van Soest, 1964). In some cases the oesophagostomes were shown to be *O. stephanostomum*, but in most they were identified as *O. bifurcum*.

In other patients, the clinical picture is somewhat different and the pathology more localised. Those described by, for example, Joe (1949), Elmes and McAdam (1953), Baylet and Paillet (1959), and some of the cases described by Haaf and van Soest (1964) and Anthony and McAdam (1972), were characterised first of all by their presentation as abdominal masses and finding of abscesses of ceacum and colon. In most of these patients more lesions were found outside the mass. Sometimes lesions outside the intestinal wall were described, with or without simultaneous colonic lesions (Ross et al., 1989).

3.2.2. Early findings of adult *Oesophagostomum* worms

Apart from the description of clinical cases with tissue-dwelling juvenile worms, lumen-dwelling adult worms have been found in three instances, all in the early 1900s, and all in patients treated with ancient drugs for ancylostomiasis. Leiper's description, referred to in the introduction to this paper, was based on the accidental finding of adult specimens of

O. apiostomum while searching for hookworms in a stool sample from a Nigerian patient (Leiper, 1911). Shortly after, in a report on helminth infections among prisoners in the same area of Northern Nigeria, Johnson (1913) examined stool samples from all 200 prisoners in Zungeru prison. Among them 42% appeared to excrete hookworm eggs. Upon treatment of all prisoners with thymol or eucalyptus, *Oesophagostomum* worms were found in eight but the numbers of worms were small. In seven of the eight cases, hookworms were expelled as well. No symptoms could be attributed to the *Oesophagostomum* infections. Finally, in a helminthological survey in man and a variety of animals in Guinea, Henry and Joyeux (1920) made mention of a similar finding of some *Oesophagostomum* worms after treatment of two hookworm patients (Brumpt, 1936).

3.2.3. Oesophagostomiasis, a common infection of man around Dapaong

During nearly 4 years as a surgeon in Dapaong's regional hospital, Dr Sénamé Baeta undertook 203 surgical interventions (excluding hernias). In 51 cases (25%), the presence of a '*Tumeur de Dapaong*' was the reason for the intervention. 'Dapaong Tumour' was the description used for the presence of a hard, painful or painless abdominal mass. In this series, there was a very strong preponderance of children: 59% were less than 10 years of age, with a further 24% aged between 10 and 19 years; 53% were males and 47% females. Although half of the cases came from Dapaong and its immediate surroundings, 88% were described as coming from rural households (Baeta, unpublished report) (Gigase et al., 1987). In their discussion Gigase et al. conclude that ''both the Dapaong and the Bawku experiences (Barrowclough and Crome, 1979; Haaf and Van Soest, 1964) seem to indicate a high frequency of human oesophagostomiasis in this sub-Sahelian area''. Reliable diagnostic methods to study the relation of pathology with infection outside the operation theatre were not available during the time of this study.

Three principal presentations were recognised by Baeta (Gigase et al., 1987) and later summarised by Gigase (2008).

Patients with:

- a painful abdominal mass (39%);
- a disfiguring, non-painful abdominal mass (35%), adherent to the abdominal wall and discharging through the skin, in two cases; and
- acute intestinal obstruction (26%).

In 42 out of 51 cases (82%) the tumour was visible or palpable.

Stool examination using a simple direct smear method was performed in 38 cases; in 10, hookworm eggs were found.

Prof. Paul Gigase, former pathologist at the Institute of Tropical Medicine in Antwerp, repeatedly wrote how impressed he was by the severity and the unique and characteristic features of the lesions, after histopathological examination of many thousands of specimens of African origin, which till then were unknown to him (Gigase, personal communication). ''At surgical intervention, the colon is found to be more or less completely studded with abcedated nodules, 2–3 cm in diameter, mostly on its whole length (57%) or on its right half (31%). In one case the nodules were found only on the peritoneal serosa and omentum, not on the bowel itself. Associated localisations were furthermore common: on the small bowel, omentum, mesentery, liver, bladder, abdominal wall'' (Bogers et al., 2001; Gigase et al., 1987). Most nodules were in the colon wall; on two occasions lesions were found in the wall of the small intestine. The lesions are spherical abscesses filled with yellowish-greenish, non-smelly necrotic or caseous-like material containing many neutrophils and eosinophils. ''The inflammatory reaction reaches far out from the contents of the nodule and induces the extensive adhesions around the bowel''. The abscesses are nearly always located between the serosa and the muscular layer. The nodules contained never more than a single juvenile adult worm (M/F ratio 1:2); sometimes they were empty. Males were 8.0–8.9 mm and females 10.0–11.4 mm long. Three patients, with intestinal occlusion due to massive *Oesophagostomum* tumours, died in hospital.

3.2.4. Two distinct clinical presentations

The observations of Storey et al. (2000) and Storey (2001) are quite similar to those of Gigase and earlier reports but, because of the additional tools at his disposal (stool culture experience and ultrasound), prospective clinical studies could be added and a more elaborate analysis was possible. The descriptions that follow are based on the observations made during a weekly *Oesophagostomum* clinic held at the Baptist Medical Centre in Nalerigu, Northern Region, Ghana.

During a 34-month period (1996–1998) 156 patients were seen at the weekly clinic, an incidence comparable to that of tuberculosis, typhoid fever and infectious hepatitis at the same hospital. Incision and drainage were undertaken in 34 patients, with laparotomy in a further 16. Towards the end of Storey's study, surgery was rarely considered necessary: confirmation of the clinical diagnosis through ultrasound and treatment with albendazole had become the preferred approach. 82% of the oesophagostomiasis patients during the 3-year study were less than 15 years old; 58% were males. These data correspond closely with the earlier observations of Gigase et al. (1987).

Two distinct clinical pictures were defined: 'Multinodular Disease' and 'Dapaong Tumour'. In multinodular oesophagostomiasis the colon

wall is studded with hundreds of pea-sized nodules and grossly thickened and oedematous. The most common presenting symptoms were of general abdominal pain, persistent diarrhoea and weight loss. The intense, short-lived, colicky pain of temporary, self-resolving intestinal obstruction was described by half of the patients in this category. The colon was palpable in half the cases, and *Oesophagostomum* L_3 larvae were cultured from the faeces in 65% of cases. In all patients examined juvenile adult worms were found in at least some of the nodules.

The most common presentation of Dapaong Tumour was a painful, well-demarcated, smooth, spherical peri-umbilical mass, adherent to the abdominal wall. Storey's description of a 'wooden' mass corresponds rather well with the description of a 'tortoise in your belly', given by Moba villagers around Dapaong. Short-lived colicky pain and vomiting were described by 24% of the patients. Stool cultures were positive for *Oesophagostomum* in 26% of the patients. Most (88%) Dapaong Tumour patients had a single mass but multiple discrete masses or conglomerations of tumours were also found. Indeed, the differentiation between Multinodular Disease and Dapaong Tumour is not always clear. At surgery the Dapaong Tumours appeared to be between 2 and 8 cm, but sometimes up to 11 cm in diameter; with the cavity containing thick creamy yellow-green pus. Juvenile adult worms were recovered in 16 of 43 (37%) of the cases.

Characteristic presentations of the Dapaong Tumour and of the findings during surgery and subsequent pathological examination are depicted in Figs. 3.1 and 3.2.

3.2.5. Local transmission?

The observations of Haaf and van Soest (1964) originating from Bawku Presbytarian Hospital in the extreme north eastern corner of Ghana together with Baeta's description of surgical cases from nearby Dapaong, in the North Western tip of Togo, 20 years later, as quoted by Gigase et al. (1987), were strongly suggestive of local transmission. The parasite involved, *O. bifurcum*, was known to be a frequent parasite of primates that are no longer common in the catchment area of either hospital and infection from such a reservoir would seem unlikely, especially as most of the surgical cases were young children.

In September 1986, two of us (A.M.P., S.B.) and Prof. Paul Gigase, from the Department of Pathology of the Institute of Tropical Medicine in Antwerp, visited the '*Centre Hospitalier Regional*' in Dapaong, Togo and the Presbytarian Hospital in Bawku, Ghana. In Bawku, the hospital staff were unaware of a problem of intestinal nodules and the previous reports from the same hospital had been forgotten. In Dapaong, on the other hand, Dr Baeta and his visitors were received with keen interest. One patient

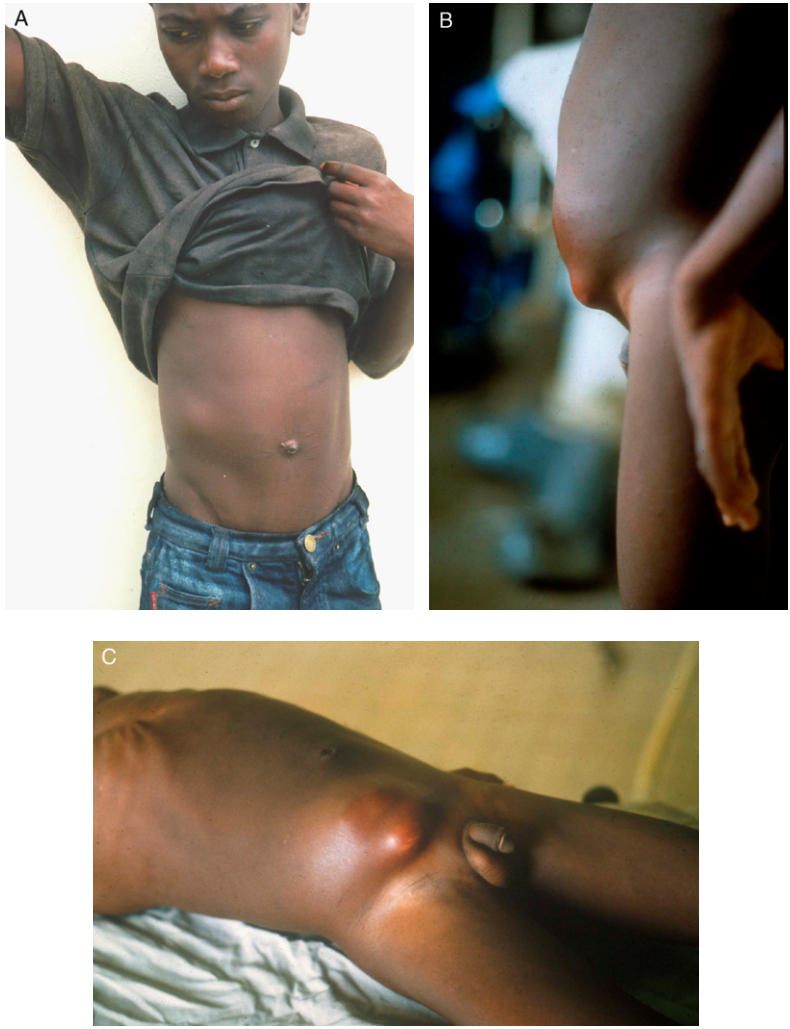


FIGURE 3.1 The presentation of characteristic Dapaong Tumours. Characteristic Dapaong Tumours, mainly seen in children, vary from invisible, hardly palpable to disfiguringly and hard abdominal masses. Photos: Polderman and Spannbrucker: authors of this review. Krepel.

with a characteristic '*Tumeur de Dapaong*' was in hospital (Figure 3.1C) and it was confirmed that similar cases were regularly seen although no further surgery had been performed after Dr Baeta's departure.

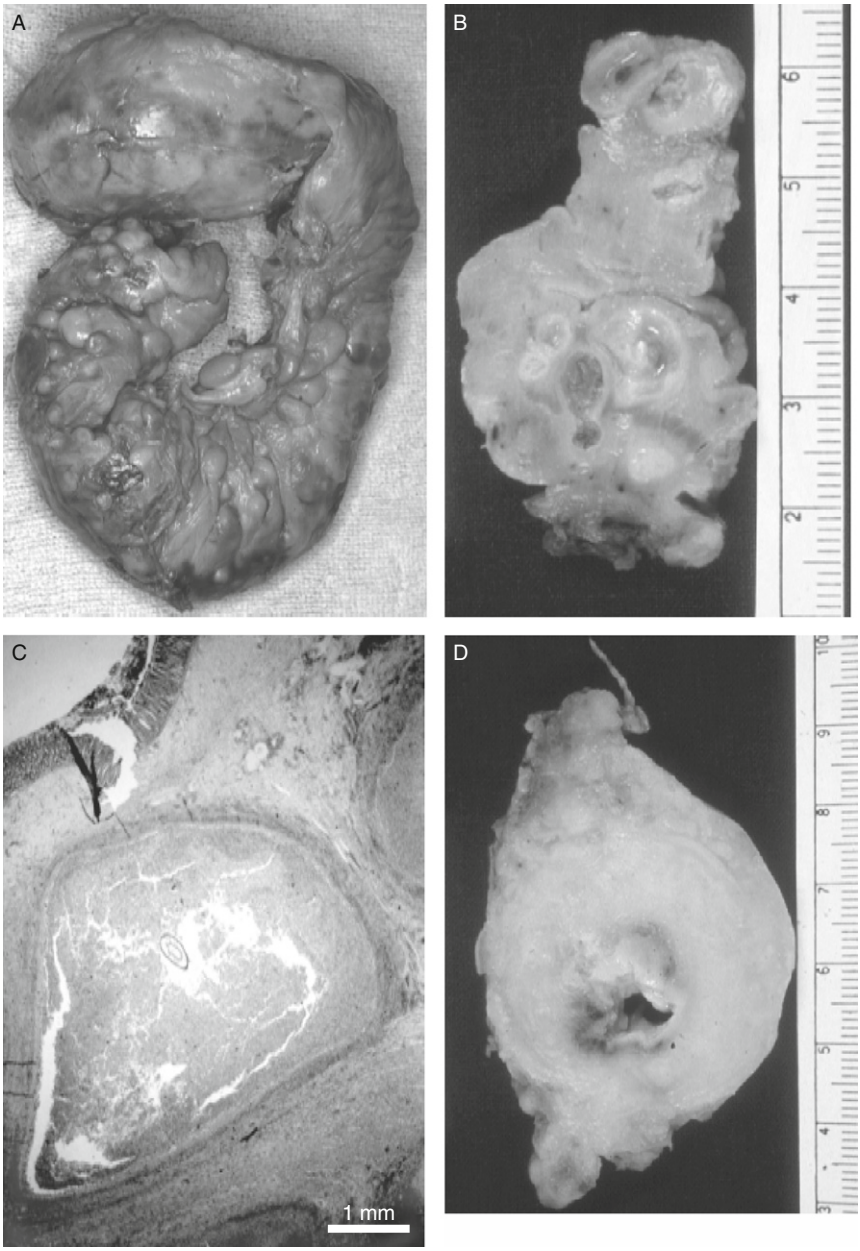


FIGURE 3.2 Presentation of severe *Oesophagostomum* infection in laparotomy and pathological examination. (A) Colon studded with nodules containing a juvenile adult worm. (B) Cross-section of part of congested and fibrotic colon wall of a patient with multinodular disease. Juvenile worms are visible in the nodules. (C) H&E-stained section showing a nodule in the colon's sub-mucosa. The nodule is filled with degenerated eosinophils and neutrophils and shows a cross-section of a juvenile specimen of *O. bifurcum*. (D) An *Oesophagostomum*-based bowel obstruction is one of the possible complications. Photos: Prof. van Marck.

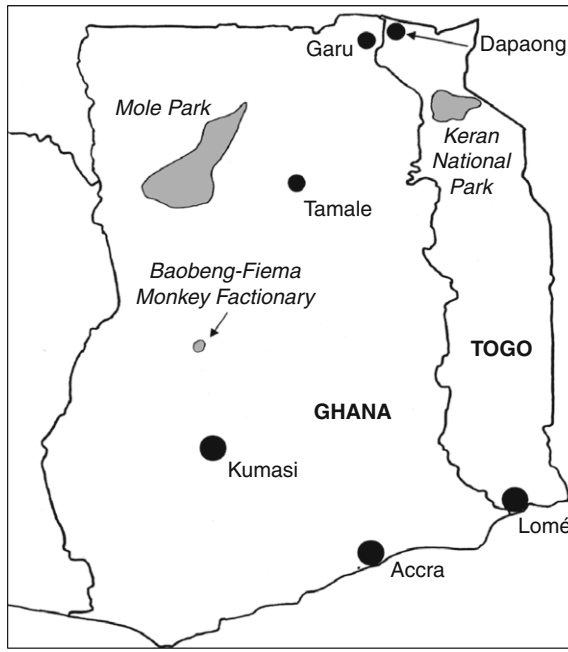


FIGURE 3.3 Sketch map of Ghana and northern Togo.

3.2.6. Local knowledge of the parasite

During discussions with the hospital staff and nurses in the hospital and in a number of health centres outside Dapaong, it became clear that:

- Abdominal masses, palpable and often visible, are well known in Dapaong and the surrounding area. For many years they had been referred to as '*Tumeur de Dapaong*', because it was recognised to be a syndrome characteristic of the area, not seen elsewhere in the country.
- Older nurses reported that they had been aware of the syndrome for many years. One of them told us that in the late 1940s or early 1950s the newly arrived French military doctors were asked for their advice. ''We were told, however, to stick to nursing and to leave medical problems to the doctor and his textbooks''.
- Furthermore, in the countryside, the villagers appeared to be acquainted with the Dapaong Tumour and in different local languages; the disease was referred to in quite descriptive ways. The Moba people around Dapaong referred to the abdominal mass as '*Koulkoul*' implying something like 'having a turtle in your belly'; in Gourma a somewhat less specific description is used: '*Tougnale*', meaning, 'abscess in the

abdomen'. (The local people convincingly differentiated the Dapaong Tumours from the common umbilical hernias. It later appeared that on the other side of the border, in Ghana, the local knowledge of the tumours was much less developed).

Stool examination of affected patients mentioned above did not reveal anything special apart from a low number of 'hookworm eggs' in some cases. Fresh stool samples were collected from 50 hospitalised patients for laboratory culture and subsequently three fresh monkey droppings were collected in the Kéran Game Reserve between Dapaong and Sansanné-Mango, while returning to Lomé, That evening, both the patient and the monkey samples were sent to the Department of Parasitology in Leiden and placed in culture the following morning. Five days later, two of the patient cultures and two of the three monkey cultures appeared to show the same, beautifully structured L_3 larvae, which were clearly different from the commonly cultured hookworm and *Strongyloides stercoralis* larvae (Fig. 3.4).

3.2.7. The parasite involved

Oesophagostomum species involved in human infections have been referred to as *O. brumpti*, *O. apiostomum*, *O. bifurcum*, *O. stephanostomum* and possibly as *O. aculeatum*. The first three are now considered identical and referred to as *O. bifurcum*. They are the most commonly found species in man. *Oesophagostomum aculeatum* is believed to be the species prevalent in East Asia but, although commonly found in monkeys, it is not clear whether the cases from Indonesia, Malaysia and Brunei were due to *O. aculeatum* or to the morphologically very similar *O. bifurcum* (Joe, 1949; Karim and Yang, 1992; Ross et al., 1989; Siang and Joe, 1953). *Oesophagostomum stephanostomum* commonly found in gorillas in Africa has been described in one of the cases from Senegal (Chabaud and Larivière, 1958), in a child and an adult male from Côte d'Ivoire (Baylet and Paillet, 1959; Curan, 1975) and most convincingly in the Wolferston Thomas case in Brazil (Thomas, 1910). The other human cases originating in various countries in Africa, and the infections endemic in northern Ghana and Togo, are all caused by *O. bifurcum*.

The morphological features of the eggs, the various larval stages and the adult worms of *O. bifurcum* isolated from humans have been described in detail by Blotkamp et al. (1993). The most relevant characteristics of the diagnostically important L_3 larvae and the adult worms are depicted in Figs. 3.4 and 3.5. The juvenile tissue-dwelling worms share most characteristics of the adults apart from the sexual apparatus that is not fully developed, and their size, being a little smaller than full grown adults. The features differentiating specimens of *O. bifurcum* from those of other

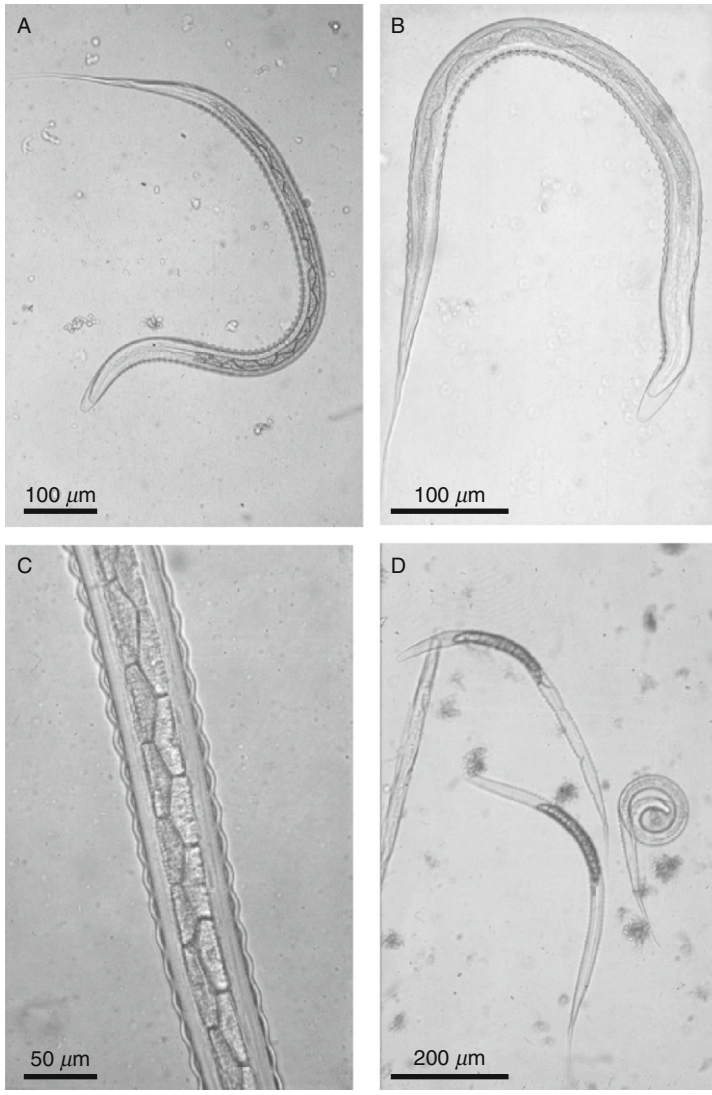


FIGURE 3.4 L_3 larvae of *O. bifurcum* from a culture of a human stool sample. (A) L_3 larva, approximately 820 μm in length. Note the characteristic features: some 30 prominent intestinal cells and transverse striation of the sheath and a finely tapered tail of sheath. (B) The number of intestinal cells is variable and may be 20 or less. (C) Detail of the regularly shaped intestinal cells. (D) During desiccation the larva shrinks within the sheath to about one-third of its original length. After adding water the larva will quickly expand to its original size; it will actively move and will be infective again. Photos: J. Blotkamp (Department of Parasitology, Leiden). (A) and (C) have been published previously: Blotkamp et al. (1993). (D) Previously published in Polderman and Blotkamp (1995) (reproduced with permission).

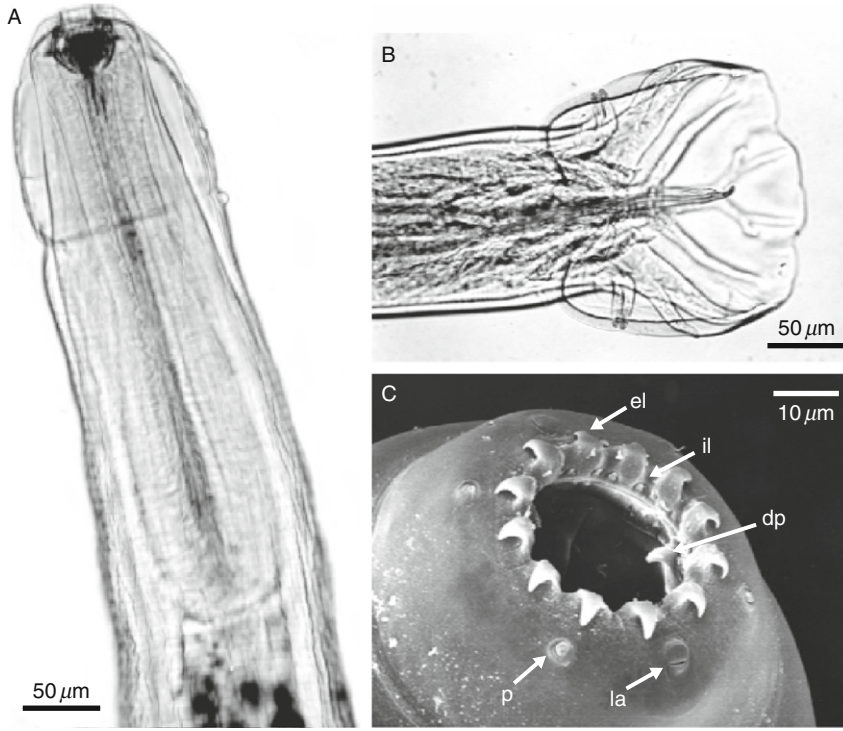


FIGURE 3.5 Morphological features of *O. bifurcum*. (A) Anterior end of an adult *O. bifurcum*. Note the ventral groove. (B) Bursa copulatrix of a male. (C) Scanning electron micrograph of the anterior end of an adult *O. bifurcum*. The number of leaves (el) of the external leaf crown varies somewhat but is mostly 12; the smaller internal leaves (il) (24 in this case) are also clearly visible (dp: one of the three denticular projections; la: one of the two lateral amphids; p: one of the four papillae). For further details, see Blotkamp et al. (1993). (A) and (C) have been published previously: Blotkamp et al. (1993) (reproduced with permission).

species occasionally found in humans, that is the shape and number of leaves of the mouth beaker, can already be reliably recognised in the juvenile stage.

An extraordinary aspect of the L_3 larvae of *O. bifurcum* is the capacity to survive adverse conditions. Twenty percent of larvae survived 6 months of complete desiccation and one quarter of larvae frozen at -15 °C for more than 4 days regained activity when brought back to room temperature (Pit et al., 2000). L_3 larvae of *Necator americanus* subjected to identical conditions lacked this capacity. *O. bifurcum* L_3 larvae desiccated for a week have been shown not only to be able to move

around actively after rehydration but also to remain infective (Eberhard et al., 2001; Pit et al., 2000). The function of the larva's capacity to survive drought and low temperatures can only be guessed.

3.2.8. Concluding remarks

Although rare in the world literature and considered an accidental zoonotic infection, human *Oesophagostomum* infection appears to be a common and serious infection in northern Ghana and Togo. It is always the juvenile adult worm that is the cause of nodular pathology. No explanation can be given as to why infection resulted in multinodular disease in some patients and in a solitary mass in others. Differences in the infective dose and in the host response or a combination of both are possible explanations.

The parasite involved in the endemic area of northern Ghana and Togo is *Oesophagostomum bifurcum*. The L_3 larval stages, the immature, tissue-dwelling juvenile worms as well as the lumen-dwelling adults can be reliably recognised and differentiated from the other species occasionally infecting man.

On the basis of the findings and as a follow-up of an earlier overview, concerning human infections in northern Togo and Ghana (Polderman and Blotkamp, 1995), more extensive research on various aspects of the life history of human oesophagostomiasis was begun. In the following pages the major findings of that research are summarised and discussed. The findings are compared with available information on *Oesophagostomum* infections in other hosts. Discussion is restricted to observations from that particular endemic area simply because no information is available from elsewhere.

3.3. DIAGNOSIS

Much of the uncertainty and confusion around human *Oesophagostomum* infections has resulted from the difficulty of recognising infection with egg-laying adult worms because *Oesophagostomum* and hookworm eggs look alike. In the Togo–Ghana endemic area it was not possible to undertake comparative morphometric observations of *Oesophagostomum* eggs in human stools since virtually all had mixed infections with hookworms. The dimensions of eggs in those mixed infections fell within the dimensions of hookworm eggs and there was no evidence of a biphasic frequency distribution expected when two species are present (Blotkamp et al., 1993). Therefore, simple microscopic stool examination (Kato thick smear or any alternative procedure) cannot be used to discriminate between hookworm and *Oesophagostomum* infection. To demonstrate the presence of mature, egg-laying oesophagostomes alternative methods have to be used.

3.3.1. Stool culture

The diagnostic approach that all field studies have relied on are adaptations of the classical coproculture as used by Loos, Fülleborn and Brumpt in the first decade of the twentieth century. Stool samples (1–3 g) were mixed with charcoal or vermiculite and cultured for 5–7 days in a Petri dish (Krepel et al., 1992; Polderman, 2005). The method is simple and cheap and can be used both for diagnostic purposes in individual patients and for community surveillance.

BOX 3.1 The stool culture procedure (after Polderman et al, 1991)

- ~ 3 g of stool is mixed with equal amount of vermiculite
- Round PVC-disc (Ø ~25 mm; thick ~4 mm) is placed in plastic Petri dish
- Filter paper (diameter ~2 cm less than Petri dish) is placed on PVC-disc
- ~ 1/3 of stool–vermiculate mix is placed on the filter paper; two more cultures are done simultaneously
- Water is added: the stool–vermiculite mixture shall not be immersed
- The mix is cultured for (5–) 7 days at tropical room temperature (between 25 °C and 37 °C)
- During the week of culture, regular inspection is needed to keep the culture moist, to remove maggots (if present) and to gently stir the mixture to minimise fungal growth
- At day 7 (or slightly earlier) the culture fluid is poured into a 25 ml conical tube; the Petri dish is rinsed and the rinsing water is added to the conical tube
- After 2 h of sedimentation (no centrifugation!) 100 µl of the sediment is carefully pipetted from the bottom of the tube and placed on a microscope slide
- Larvae are immobilised and stained with a small drop of iodine
- The slide is examined under a microscope at low power, with or without cover slip

The eggs hatch rapidly. After 1 day, only L1 larvae are found in a stool sample with a mixed *Oesophagostomum*–hookworm infection, but the two infections cannot yet be reliably differentiated. The following day, most L_1s

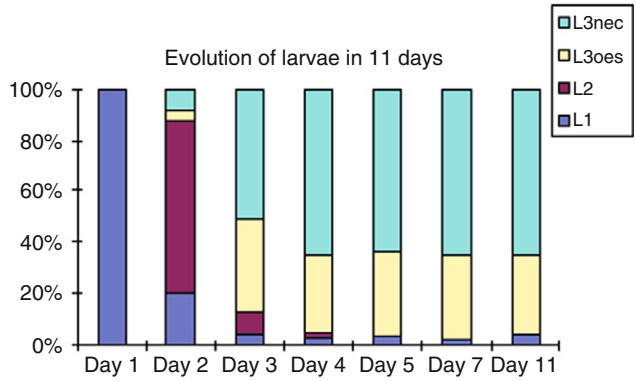


FIGURE 3.6 The growth of *Oesophagostomum* and hookworm larvae in stool culture. In the great majority of *Oesophagostomum* infections the human host has a hookworm infection as well. Eggs, L_1 and L_2 larvae cannot be differentiated. By day 3 most eggs have developed into L_3 larvae. It takes some more days before the L_3's have migrated from the faeces–vermiculite mixture into the culture water. Sensitive culture reading can be done from day 5 onwards (Pit, personal communication: unpublished data).

have developed to L_2 larvae while a few L_3 larvae can already be found. By day 3 the great majority of L_2s have developed into L_3s (see Fig. 3.6, Polderman, Pit and Blotkamp, unpublished data). To harvest large numbers of identifiable larvae it is better to wait longer before reading the culture. Maximum numbers of L_3 larvae were found after 11 days of culture but after 7 days of culture already 92% of the maximum could be found (Pit, 2000).

Although stool culture has been used for the detection and quantification of strongylid larvae for many years in veterinary practice, its use as a semi-quantitative tool in human parasitology had not been evaluated. Data presented by Krepel et al. (1995b) and subsequently by Pit et al. (1999a) showed that the procedure is not only sensitive and generally reproducible; the results can also be used for semi-quantitative analysis. With a single culture, 84% of infections in a heavily infected community could be detected, and even in a lightly infected subgroup (less than 10 larvae per culture) the sensitivity of a single culture was around 66%. The within-specimen variation of larval counts did not differ significantly from the day-to-day variation (Pit et al., 1999a).

At a population level, a log-normal frequency distribution of larval counts is approached for both *Oesophagostomum* and hookworm larvae (but not for mixed infection). The frequency distributions are similar to those seen for a variety of helminth egg counts (e.g. hookworm, *Ascaris lumbricoides* and schistosomes) (Krepel et al., 1995b). The correlation between the number of

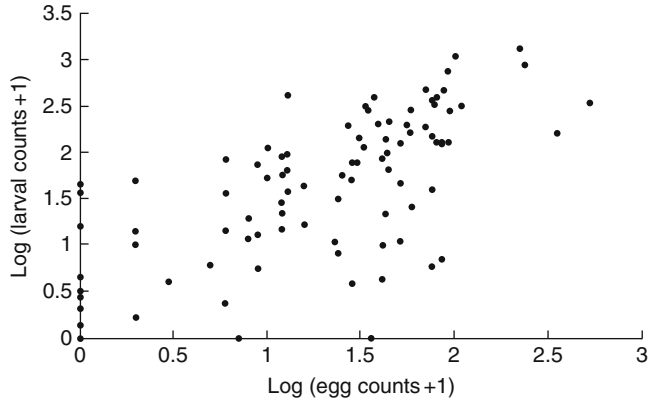


FIGURE 3.7 Correlation of egg counts and larval counts. Larval counts in stool cultures from 102 subjects infected with *O. bifurcum* and/or hookworm correlate closely with egg counts in 25 mg Kato thick smears (Spearman rank correlation: $r = 0.74$; $p < 0.001$) (larval counts expressed as the numbers of larvae harvested from 1-g cultures). Source: Krepel et al. (1995b) (reproduced with permission).

eggs (*O. bifurcum* + hookworm) found in a Kato thick smear, and the total number of larvae found in a stool culture (*O. bifurcum* + hookworm) is highly significant, as illustrated in Fig. 3.7. It has been concluded that larval counts may be used as a proxy for the number of egg excreting adult (female) worms, and that stool culture is about eightfold more sensitive compared to the Kato thick smear (Krepel et al., 1995b).

Krepel and Polderman (1992) attempted to estimate the relationship between the number of eggs recovered in a Kato thick smear, the number of larvae cultured from the same stool sample and the number of male and female worms that were expelled after treatment with pyrantel pamoate. Up to 300 worms were obtained from a single patient, and in the 12 patients studied, the proportion of female worms varied from 43% to 64% (mean 55.7%). There were 1.87 L_3 larvae cultured for every adult female worm, and 1.0 larvae for any adult worm (male or female). Although numbers were small, the results were similar for the three adults and nine children in this study. The daily egg output per female worm was estimated to be 5055 eggs (based on a stool production of 150 g per person per day).

Pit (2000) further demonstrated that larval hatching in coproculture was very variable but that an estimated 22% of eggs developed into L_3 larvae and that slightly less than half of the larvae present in a culture are detected in routine microscopic examinations of the coproculture sediment. These data correspond very well with recoveries described by Krepel and Polderman (1992).

BOX 3.2 Quantitative interpretation of the larval culture procedure. (based on: Krepel and Polderman, 1992; Pit, 2000)

Taking all sorts of inaccuracies into account, and accepting fairly wide confidence margins, we can stick to the following rules of thumb:

- One larva found in a 1-g stool culture corresponds to about 8 eggs per gram of stool;
- One female worm produces about 5000 eggs per day;
- Two L_3 larvae in a culture represent two adult worms: one male and one female;
- A minimally light infection (one pair of worms) can just about be detected: it will result in one larva per culture.

Even though stool culture can be considered an adequate diagnostic procedure, there remain a number of problems:

- For unknown reasons, some cultures do not grow. This is also seen when culturing stools to diagnose *Strongyloides* infection.
- Over the course of 5–7 days, maggots and fungi tend to develop and destroy the cultures. Careful daily checks and cleaning rounds are necessary!
- Diagnosis takes time and fresh stools are needed.
- *Oesophagostomum* larvae are often found together with larger numbers of other larvae (hookworms, *Strongyloides*) and are easily missed when their numbers are small.

3.3.2. Serology

It is, therefore, understandable that alternative diagnostic procedures have been sought. First, serological tests were tried to determine whether they would be helpful (Pit, 2000; Polderman et al., 1993). As with other nematode infections, the host response had to be assessed in a (sub)-class-specific manner as both sensitivity and specificity of the IgG-responses were too low. A specific IgG_4-ELISA and an IgE-ELISA showed better results but the only real benefit of these tests compared to stool culture is that fresh material is not required. A considerable problem is that antigen preparation requires properly prepared adult worms that are not readily available.

3.3.3. Polymerase chain reaction (PCR)

Extending logically from a range of studies (Romstad et al., 1997a,b; Verweij et al., 2001, 2007) which critically assessed the suitability of the second internal transcribed spacer (ITS-2) of nuclear ribosomal DNA as a

genetic marker for the specific diagnosis of *O. bifurcum* infection and its differentiation from hookworm infection, a real-time PCR (rt-PCR) was developed (Verweij et al., 2007) for the simultaneous, semi-quantitative and specific detection of DNA from *O. bifurcum*, *A. duodenale* and *N. americanus* in alcohol-preserved faecal samples. An analysis of samples from villages endemic for *Oesophagostomum* in northern Ghana showed that 71 of 83 larval cultures containing *O. bifurcum* were also test-positive using the rt-PCR assay; in addition, 32 of 256 culture-negative samples gave positive PCR results. The specificity and sensitivity of the rt-PCR in relation to stool culture were similar to the performance of the assay for the diagnosis of *N. americanus* infection. Moreover, there was a significant correlation between the numbers of larvae cultured and the cycle threshold (Ct) values in the assay. Although this rt-PCR approach cannot be performed in the field, it is a significant advance for laboratory-based diagnosis. Currently, the rt-PCR is being used for epidemiological studies and to monitor the success of anthelminthic treatment in regions endemic for oesophagostomiasis and hookworm disease (van Lieshout et al., in preparation).

3.3.4. Clinical examination and ultrasonography

Symptoms of clinical oesophagostomiasis are related to the development of nodular lesions in the anterior abdominal wall and can be characterised as either a '*Tumour de Dapaong*' or multinodular disease of the colon wall. Whereas lesions within the abdominal wall can be detected easily by clinical examination, that is by inspection and palpation, lesions in the colon wall are missed by clinical investigation in most of the cases and can only be recognised by laparotomy.

Symptoms of oesophagostomiasis affecting the intestine are uncharacteristic and range from fever and mild abdominal pain to an acute abdomen. Anthony and McAdam (1972), for example, complained: ''The clinical presentation is variable and misdiagnosis is frequent even when special experience can be called upon. The condition may imitate carcinoma, appendicitis, or appendicular abscess, diverticular disease, ileocaecal tuberculosis, Crohn's Disease, amoebiasis, and schistosomiasis. . .'' Even the investigation of stool samples is not very helpful. Experience has shown that symptomatic patients will often have continuously negative stool cultures while, on the other hand, the majority of patients with positive stool cultures do not seem to suffer from any form of *Oesophagostomum* pathology (Storey et al., 2000, 2001d). On the initiative of Dr Ekkehard Doehring, abdominal ultrasound was introduced as a tool to visualise the nodular colonic lesions that were until then only recognised by the naked eye (Gigase and Baeta's 'disfiguringly massive Dapaong Tumours'), by palpation, and most convincingly in the operating theatre. In these investigations a portable ultrasound machine, equipped

with a 3.5–4.5-MHz convex array transducer and powered by a generator, was used to systematically scan the abdomen of each individual in the supine position. Some representative pictures are given in Figure 3.8.

In a number of carefully designed studies it was demonstrated that

- Dapaong Tumours, diagnosed on the basis of clinical presentation and palpation, could be recognised by ultrasound (Storey et al., 2001c);
- lesions in the intestinal wall, recognised as *Oesophagostomum* nodules by ultrasound, could later be confirmed as such during laparotomy (Storey et al., 2001b);
- recognition by ultrasound of lesions was shown to be reproducible and intra- and inter-observer variation was shown to be minimal (Storey et al., 2002);
- ultrasonography was superior to clinical investigation in detecting lesions in the colon wall (Storey et al., 2001c);
- ultrasonography was shown to be sensitive and practicable not only to diagnose clinical oesophagostomiasis but also to monitor the presence of sub-clinical lesions in population surveys (Storey et al., 2001c);
- similar lesions could not be demonstrated in subjects outside the endemic area, thus showing the high specificity of ultrasound for the detection of oesophagostomiasis (Storey et al., 2001c).

While the presence of gas in the lumen of intestine hinders ultrasonic investigation of the gastrointestinal tract considerably, one has to take into account that not all lesions can be detected by ultrasound. Since alternative imaging techniques like computer tomography (CT) or magnetic resonance tomography (MRT) were not available, the sensitivity could only roughly be estimated. From other studies investigating the efficacy of ultrasonography in detecting intestinal pathology a comparable sensitivity of 75–85% can be deduced.

In conclusion, the studies demonstrate that *O. bifurcum* infection can accurately be diagnosed by ultrasound investigation, particularly with regard to the uncharacteristic symptoms and the variable clinical presentation of oesophagostomiasis. The high specificity and sensitivity of ultrasound in detecting the histotropic stage of infection indicates that ultrasonography can directly provide early information about the progression of lesions following *O. bifurcum* infection and aids management and monitoring of the impact of morbidity control.

3.4. EPIDEMIOLOGY

Making use of stool cultures as a reliable and semi-quantitative diagnostic method, extensive epidemiological studies have been performed in the area in northern Ghana and Togo where the clinical case series were described (Gigase et al., 1987; Haaf and Van Soest, 1964).

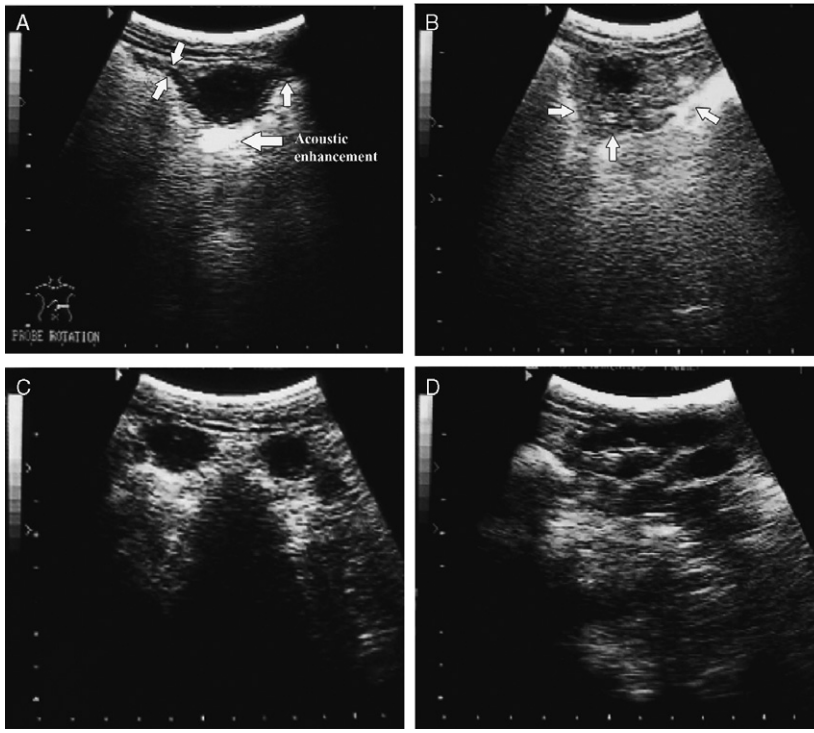


FIGURE 3.8 Ultrasound representation of *Oesophagostomum bifurcum*-induced nodular lesions. *O. bifurcum*-induced lesions appear in the abdominal ultrasound investigation as anechogenic lesions with a characteristic round-to-oval shape and posterior wall acoustic enhancement. These lesions typically present either as solitary or as complex lesions (83% and 16%, respectively, in Northern Ghana [Ziem, 2006, thesis, Chapter 4]). (A) A cross-sectional view of a characteristic solitary lesion with posterior wall acoustic enhancement (arrows) detected in the transverse colon near the splenic flexure. Mostly, the hyper-echogenic thickening of the colon wall adjacent to lesions is ultrasonically visible as illustrated in (B). Lesions in a complex appear in two different patterns as shown in (C) and (D). (C) A cross-sectional view of the ascending colon showing two adjacent lesions with a characteristic hyper-echogenic mucosa reaction. (D) A second type of complex formation: an anechogenic mass consisting of several lesions aggregated in 'grape-like' clusters with visible scattered reflexes. Sometimes the entire length of the colon is studded with several aggregates of lesions, associated with decreased diameter of the bowel lumen. In those cases the colon wall shows an enlarged echo-low band, an indication of mucosa distension. Ultrasonographically, lesions differed with regard to their bordering rim; in some cases the edges are sharply discernible without neighbouring tissue reaction as shown in (A), but in most cases, the adjacent neighbouring colon wall showed a diffuse hyper-echogenic texture (arrows in (B)) an image which has been described as '*thyroid in the abdomen*' indicating oedema and inflammation of the colon wall. Pictures Dr Spannbrucker not published previously.

3.4.1. Prevalence and geographical distribution

Under the title 'Oesophagostomiasis, a common infection of man in Northern Togo and Ghana' the first of a series of papers was published in which it was shown that *O. bifurcum* was indeed a very common infection in that area. Of 3242 villagers examined in what could be described as the principal catchment area of the Dapaong and Bawku hospitals, 562 (17.3%) were positive for *O. bifurcum* on stool culture. In these first surveys, young boys were more commonly infected than young girls (11.6% vs. 8.5%). However, above 10 years of age, females were significantly more commonly infected than males (28.5% vs. 17.0%) (Polderman et al., 1991).

On the basis of these findings, which might be seen as alarming and which were at least surprising, systematic area-wide surveys were carried out, both in the Région de Savannes of Northern Togo, and in the Northern and Upper East Regions in Ghana (Pit et al., 1999b; Yelifari et al., 2005). In both surveys similar sampling and diagnostic procedures were used and there was a regular communication between both research groups.

BOX 3.3 Details of the sampling and culturing procedures in northern Ghana and Togo

The surface of northern Togo and Ghana was divided in squares of 342 km^2. Within each square, four villages (with more than 200 but less than 1000 inhabitants) were randomly selected, and from each village 20 randomly selected households were included in the study. From each household two adults (one male, one female, between 20 and 60 years of age) and two children (one boy, one girl, between 5 and 19 years of age) were selected to participate in the study. When these selection criteria could not be met neighbours were included.

All participants were asked for a stool sample, which was collected the following morning. The stool samples were transferred to laboratories in Dapaong, Bolgatanga and Tamale and placed in culture the same day. The cultures were based on 2-g samples and read 7 days later.

The survey included almost 4000 cultures read in Togo and just over 20,000 in Ghana.

(for further details: Pit et al., 1999b; Yelifari et al., 2005)

The surveys led to a number of important conclusions, and raised many questions as well:

- The distribution of *Oesophagostomum* infections in man is limited to a comparatively small area, being 300 km from East to West, and 100 km from North to South (see Figs. 3.3 and 3.9).

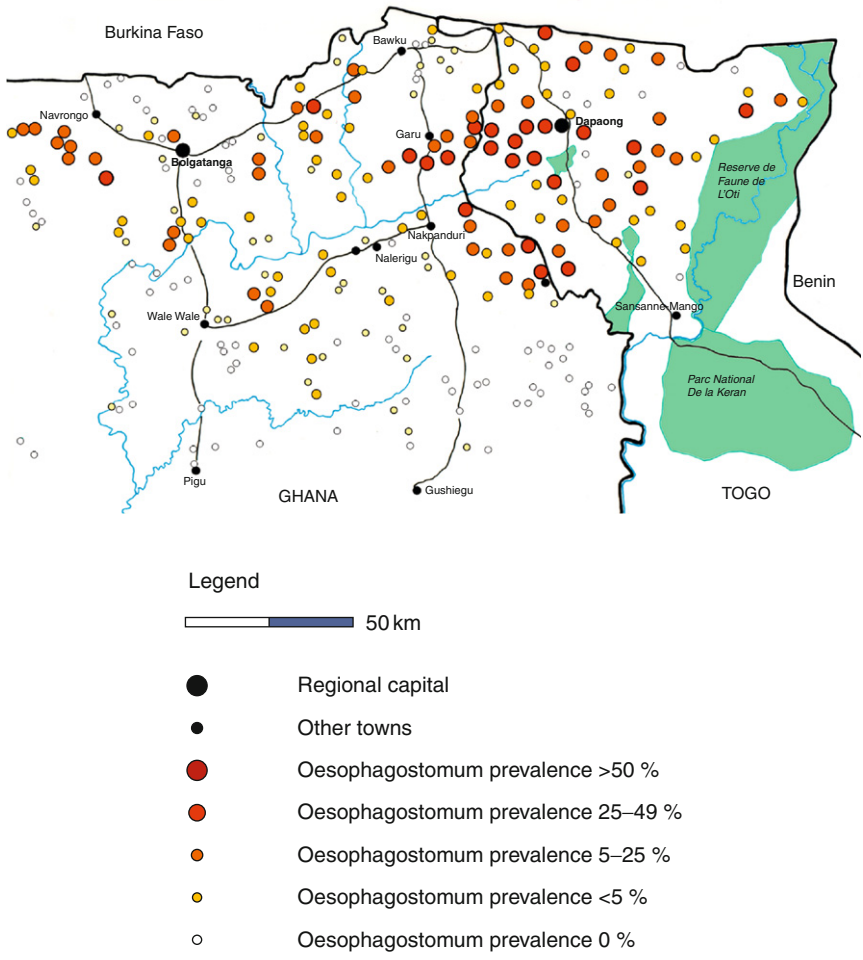


FIGURE 3.9 Geographical distribution of *Oesophagostomum bifurcum* in North Ghana and Togo. The village-specific prevalences are based on stool cultures from 23,909 stool specimens collected from inhabitants of 216 geographically representative villages in Ghana and 65 in Togo. Communities with more than 1000 and less than 200 inhabitants were not incorporated in the survey. The map is based on data from the studies of Pit et al. (1999b) and Yelifari et al. (2005). Details on sampling procedures and further findings are given in those publications.

- Overall, *Oesophagostomum* prevalences in the Togo and Ghana studies were 30% and 12%, respectively, meaning that at least a quarter of a million subjects within the survey area were infected. No *Oesophagostomum* infection was found in 87 of the 280 (31%) villages examined,

while prevalences of 40% and above were found in 39 of the 193 infected villages (20%). The core of the endemic area straddles the Ghana–Togo border.

- Within this endemic area, the prevalence varied greatly from one community to another. Even over short distances great differences in village-specific prevalence occurred.

The infection rates, the focality of infection within the area and the very limited area of endemicity called for a more in depth study in the heart of the endemic zone. Such study, just west of the Ghana–Togo border, was carried out by Ziem over the period 2001–2004 (Ziem et al., 2006b).

In the 35 'villages' included in the survey, *Oesophagostomum* prevalence ranged from 8% to 94%, the average being 45%. These 'villages' consist of groups of compounds, loosely scattered over an area of some 100 km^2. The villages (Fig. 3.10) are not clearly separated from each other and are inhabited

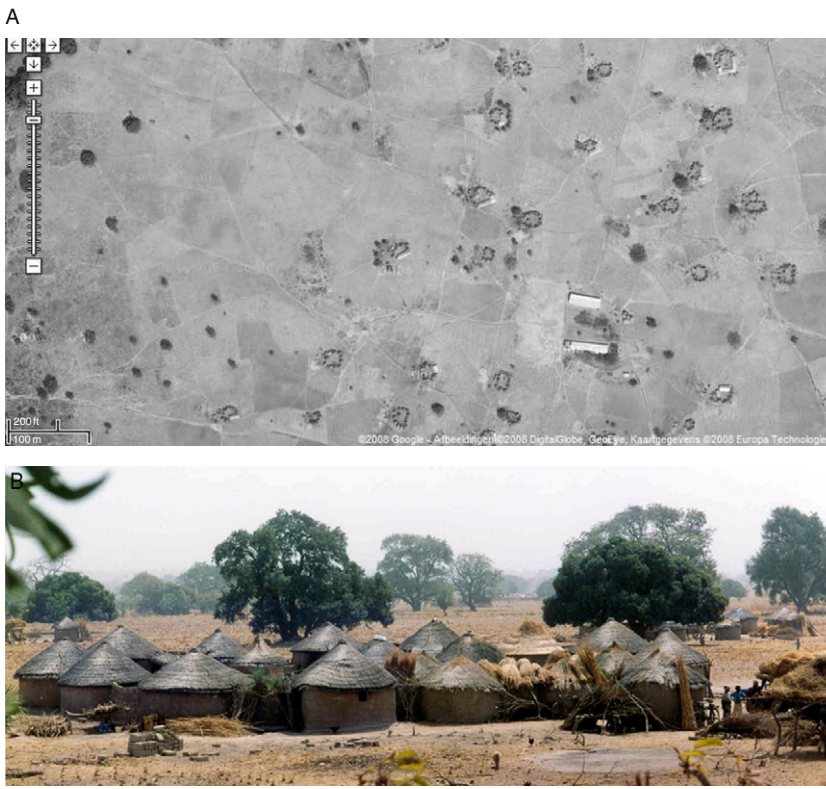


FIGURE 3.10 Characteristic Bimoba village in the heart of the *Oesophagostomum*-endemic area. (A) The farmers' compounds are widely scattered over the area (from Google maps). (B) An extended family compound (from A. M. Polderman).

by either Bimoba or Kusasi (the two main tribal groups in the area) or by both in mixed villages. Attempts to correlate infection rates with tribal characteristics, with occupation, with animals sharing the villagers' houses or with (rather subjective) indicators for wealth, all failed to yield any relationship. The only association of any significance was that between village and altitude: the lower the altitude, the higher the prevalence of infection. At the compound level, however, the association ceases to be recognisable. Differences in humidity and microclimate might possibly be of importance.

3.4.2. Who is (heavily) infected?

A consistent picture emerged from analysis of the age and gender associations of *Oesophagostomum* infection (Krepel et al., 1992; Pit et al., 1999b; Polderman et al., 1991; Yelifari et al., 2005; Ziem et al., 2006b). For comparative reasons, similar associations were looked for in hookworm infections, in the same populations.

1. In highly infected communities, a plateau of infection is reached by the age of 10. This is also true for hookworm, in the same populations.
2. Even very young children may be infected, the youngest being less than 1 year of age (Fig. 3.11). This is also true for hookworm.
3. In young children, boys are more often infected than girls, while from the age of 10 years females are consistently more infected than males. For hookworm the picture is clearly different (Fig. 3.12).

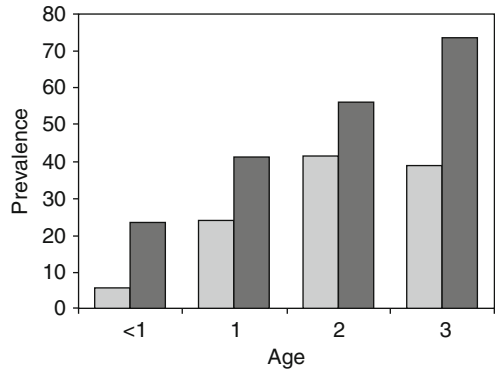


FIGURE 3.11 The prevalence of *O. bifurcum* and hookworm infection in very young children. Lightly shaded: *O. bifurcum*; darkly shaded: hookworm. The figure shows a rapid increase of infection rates at a very young age, for both hookworm and *Oesophagostomum*. (Figure newly composed on the basis of data presented in Ziem et al., 2006a).

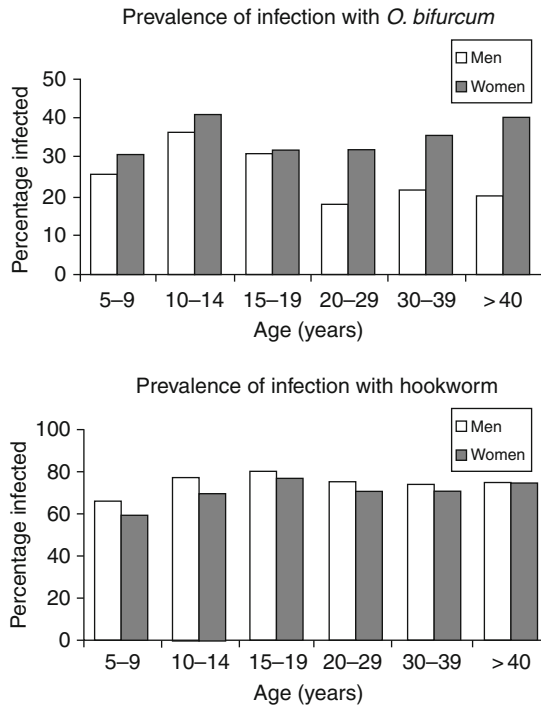
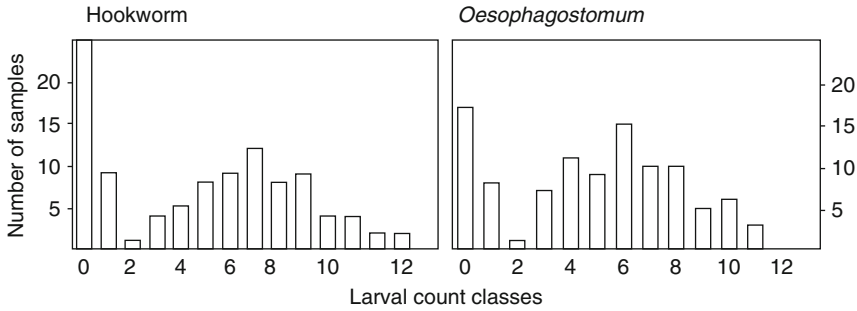


FIGURE 3.12 Gender- and age-specific prevalences of *O. bifurcum* and hookworm in northern Togo. Data from Pit et al. (1999b). The study population consists of a random sample of 3659 subjects from 65 villages representative villages in North Togo. Note significant difference between infection rates of *Oesophagostomum* in adult females and males. Figure published earlier: Pit et al. (1999b) (reproduced with permission).

4. Repeatedly, representatives of the Bimoba tribe appear to be the most heavily infected (Storey et al., 2000; Yelifari et al., 2005). Is this because the Bimobas happen to live in places where transmission is taking place most effectively or does the Bimoba way of life make them more susceptible to infection? Although the Bimoba and the Kusasi normally live in separate villages, representatives of both groups were equally infected in the few villages that were shared by both tribes (Ziem, 2006).
5. There is no support for the idea that differences in behaviour and way of life are a determining factor for a high prevalence of infection for particular tribal groups.
6. Infections are aggregated and over-dispersed as seen in other helminth infections: The most heavily infected 20% of the population is responsible for 80% of the larval production (Krepel et al., 1995b). The same is true for hookworm. This is a consequence of the near-log-normal frequency distribution of larval counts (Fig. 3.13).



Legend: The larval count classes represent the following larval counts on the X-axis.

Class	*Larval count*	Class	*Larval count*	class	*Larval count*	Class	*Larval count*
0	*0*						
1	*1*	5	*10–17*	9	*100–171*	13	*> 1000*
2	*2–3*	6	*18–31*	10	*178–316*		
3	*4–5*	7	*32–56*	11	*317–561*		
4	*6–9*	8	*57–99*	12	*562–999*		

FIGURE 3.13 Frequency distributions of L3 larvae in stool samples for hookworm (left) and *Oesophagostomum* (right). The figure is based on analysis of the larval counts of cultures from 102 subjects in Lotogou and Dassoute in Northern Togo. The logarithms of the larval counts are the basis for equal class widths on the *X*-axis: 0 stands for no larvae cultured, 1 for 10^{0}–$10^{1/4}$, 2 for $10^{1/4}$–$10^{1/2}$, etc. 11 for $10^{21/2}$–$10^{23/4}$ [or 317–561]).

7. In all of the villages studied, there is a close association between *Oesophagostomum* and hookworm infection. This is true in terms of prevalence (Krepel and Polderman, 1992). The association remains when corrected for age and gender. At the quantitative level, there is also a close association: subjects passing many *Oesophagostomum* eggs pass many hookworm eggs as well (Fig. 3.14) (Ziem et al., 2006b): ''Cross tabulation of hookworm infection with that of *O. bifurcum* gave a significant association (Odds Ratio (OR) = 11.4; 95%; Confidence Interval (CI) 6.5–19.8, $p < 0.001$). The relative risk was 5.2, that is the risk for being infected with *O. bifurcum* was more than 5 times higher when infected with hookworm''.

The various investigators looking at these data were all confronted with similar problems of interpretation. Ziem's detailed small-scale

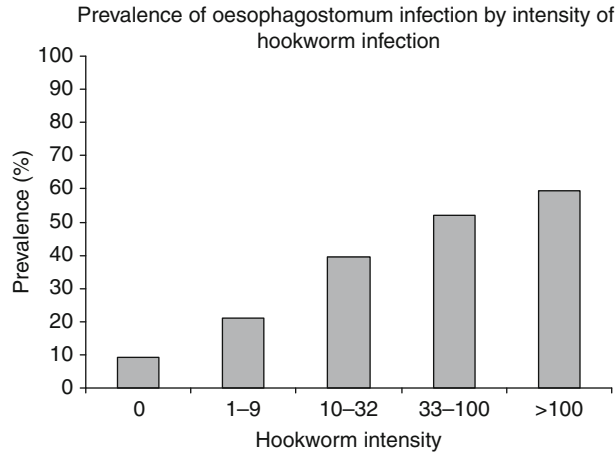


FIGURE 3.14 Prevalence of *Oesophagostomum* infection by intensity of hookworm infection. The figure is based on the results of duplicate stool cultures from 1011 subjects (all ages) in North Ghana. Data based on Ziem et al. (2006b).

studies did not provide the answers he was hoping for. Instead, the questions became more sharply focused.

- Why such a limited area of (frequently very intense) transmission?
- Why such a high degree of clustering within the endemic area?
- Why are women more likely to be infected than men?
- Why such a strong correlation with the percutaneously transmitted hookworm-infections?

These important questions will be addressed later.

3.4.3. Seasonality of transmission (see Section 3.8.3)

The endemic area of northern Ghana and Togo has a very clear-cut rainy season, lasting roughly from June to early September; between October and April precipitation is usually minimal. Seasonal transmission of both *Oesophagostomum* and concomitant hookworm infection is therefore to be expected. Pit (2000) carried out a longitudinal study in which the prevalence and intensity of infection, in terms of numbers of larvae cultured, were followed for 19 consecutive months in a group of 50 persons in the highly affected rural area in Northern Togo, along the Ghana border. The 50 participants successfully submitted their stool samples in not less than 14 of the 19 surveys. It was shown that, apart from 2 outlying months, the prevalence was fairly stable at around 50%. Fluctuations in the intensity of infection were more pronounced for hookworm infections. The results of these observations are depicted in Fig. 3.15. The picture is essentially similar for hookworm infections. It should be noted that even in

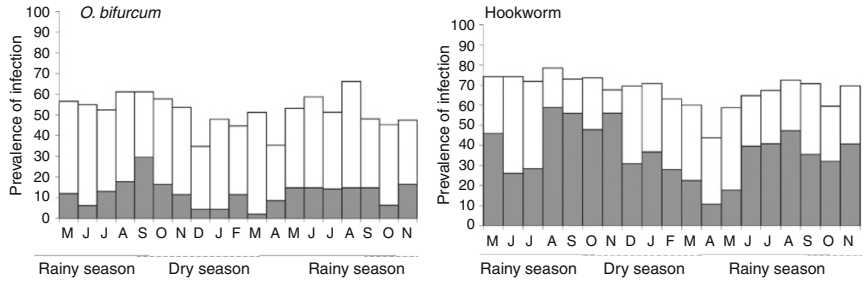


FIGURE 3.15 The fluctuations in prevalence and intensity of infection for *O. bifurcum* and hookworm. The data are based on repeated examination of 50 inhabitants of the villages of Lotogou and Tampialime close to the Ghanaian border in north Togo. All subjects participated in at least 15 of the 19 stool culture surveys. All received treatment at the end of the study. Shaded: more than $10^{1½}$ L_3 larvae per 3-g coproculture (i.e. 32 and more). Figure published earlier: Pit (2000).

hookworm infections, the wormload in the population varies considerably. For hookworm the fraction of heavily infected subjects varies from less than 20% to 60%. These fluctuations do not seem to be random variations but seasonal fluctuations. Transmission seems to be unstable. Both for hookworm and for *Oesophagostomum* the peak prevalence was lower in the second year of observation than in the first year.

Another consequence of these observations on fluctuations in prevalence and intensity is that the *Oesophagostomum* life span is likely to be fairly short, probably in the same order of magnitude as that of *N. americanus*.

3.4.4. Concluding remarks

The data show that the prevalence of *Oesophagostomum* infection is sometimes high but can vary considerably both in place and over a period of time. The limits of the area of endemicity, the differences in the presence and intensity of infection in households and between ages and genders are not, as yet, well explained. The high prevalence in the very young and the early peak in both *Oesophagostomum* and hookworm suggest that transmission may be intense, at least during certain periods of the year.

3.5. CLINICAL EPIDEMIOLOGY

There is very little literature on the clinical epidemiology of oesophagostomiasis. Only Paul Gigase and Sénamé Baeta and their colleagues, in Togo (Gigase et al., 1987) and, more extensively, Phil Storey and collaborators in Ghana (Storey, 2001) have examined a sufficient number of patients to consider their data from a clinical epidemiological perspective. The

most important features of Baeta's and Gigase's clinical observations have been discussed already. Combining the use of ultrasound to visualise pathology and stool cultures to assess the presence of adult, egg-excreting worms enabled Storey and co-workers (Storey, 2001; Storey et al., 2000, 2001a,c,d) to get a better understanding of the relation between infection and pathology. The principal findings are discussed in the next section.

3.5.1. Ultrasound

Ultrasound analysis carried out at a population level in high (Sanakpesir) and low (Kumpac) infected Ghanaian communities close to the Togo border showed that about three times more *Oesophagostomum* nodules are found by ultrasound than by palpation. In more than half of the people in a highly endemic community, *Oesophagostomum* lesions can be found, while no *Oesophagostomum* lesions were found in a control village (Kplin) near Tamale, outside the area of *Oesophagostomum* endemicity (Fig. 3.16) (Storey et al., 2001c).

In the lightly infected village of Kumpac 70% of the nodules were found in the caecum and ascending colon; few were seen more distally.

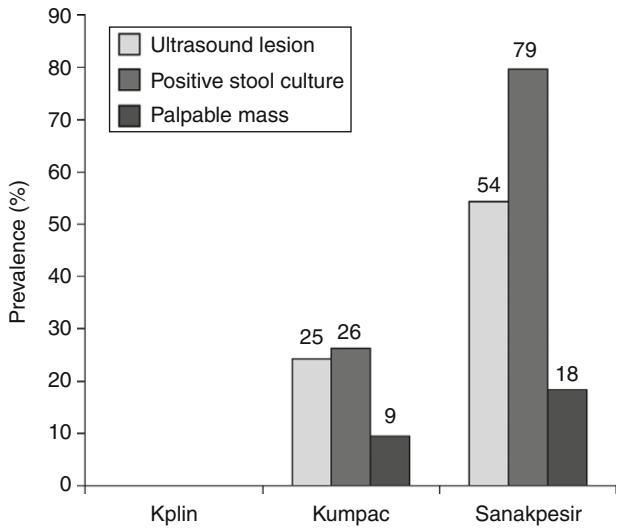


FIGURE 3.16 The sensitivity of three different diagnostic approaches: stool culture, palpation for abdominal masses and ultrasonography. The prevalence of infection was assessed in three villages in North Ghana: a non-endemic village (Kplin, $n = 100$), a lightly infested village (Kumpac, $n = 233$) and a heavily infested one (Sanakpesir, $n = 131$). Palpation recognises only a very small proportion of the infections; stool culture is most sensitive. Ultrasound-based findings reflect parasitological findings: no ultrasound positivity in non-infected villages, and ultrasound positivity is highest in the most intensely infected villages. Figure published earlier: Storey et al. (2001c) (reproduced with permission).

In the heavily infected village of Sanakpesir the lesions were more dispersed along the colon. In the heavily infected village more than five lesions were seen in 20% of the people examined, while in the lightly infected village only 4% had five or more lesions. In both Kumpac and Sanakpesir, *Oesophagostomum* nodules were seen in approximately 60% of infected subjects (i.e. culture and/or ultrasound positive). Ultrasound-visible pathology does not develop (or cannot be recognised) in all infected subjects. Conversely, stool culture remains negative in many cases with ultrasound-visible pathology, particularly in the lightly infected village (Table 3.3). Analysing more than 900 subjects in an area-wide survey with quantitative stool culture and ultrasonography, it was demonstrated that, at the population level, a significant association exists between the intensity of infection and morbidity parameters (Ziem et al., 2005) (Table 3.4).

TABLE 3.3 Ultrasound and stool-culture positivity in a lightly and a heavily infested village in Ghana

	Moderately infected village Kumpac		Heavily infected village Sanakpesir	
	Ultrasound-positive	Ultrasound-negative	Ultrasound-positive	Ultrasound-negative
Stool-culture positive	22	39	61	43
Stool-culture negative	35	137	10	17

Data based on observations of Storey et al. (2000).

TABLE 3.4 Severity of nodular pathology in relation to the intensity of infection, in terms of the numbers of L_3 larvae cultured

Larval counts	*N*	No pathology *n* = 614	Uni-nodular pathology *n* = 144	Multinodular pathology *n* = 170
0	524	402	71	51
1–9	199	121	36	42
10–32	104	52	18	34
33–100	64	30	14	20
>100	37	9	6	22
Total	928	614	145	169

Table derived from data in Ziem et al. (2005).

In a subsequent study, subjects in another moderately infected village (Mangol), 299 inhabitants (all aged over 5 years) were followed by stool culture, palpation and ultrasound examination (Storey et al., 2001d). Each was examined four times: shortly after the rains (November), in the middle of the dry season (February), during the early rainy season (June) and again after the rains (October). At the population level it was shown that ultrasound positivity fell from 28% in November to 17% in February and 11% in June. After the rains, in October, it had returned to just over 30%. At the individual level, it was shown that between November and June, 73 out of 84 originally ultrasound-positive subjects became negative. Likewise, 76 out of the 270 ultrasound-negative subjects in June became ultrasound-positive 4 months later, in October. Among those changing from ultrasound negative to positive in October, the incidence is more than twice as great in those under 20 years of age as compared to those aged 20 years and above. Among those remaining ultrasound-positive through the entire 12 months, the number of nodules reduced quickly: from 234 in November, to 127 in February, 51 in June and 21 in October. Clearly, during the course of a season most ultrasound-visible nodules disappear and the half life of a nodule was shown to be between 3 and 4 months. The half-life of colonic nodules was reduced to 1–2 months if treated with albendazole (10 mg/kg for 5 days) (Storey et al., 2001a) (Fig. 3.17). Follow-up of nodules during the course of a dry season showed that the geometric mean size of the nodules increased significantly (from 17 to 24 mm) in untreated subjects but remained the same in treated subjects.

3.5.2. Concluding remarks

It was found that pathologic lesions can be visualised by ultrasound in 43% of lightly infected subjects ($\leq$30 larvae) and in 61% of heavily infected subjects ($>$30 larvae) (Table 3.4). Palpation alone misses at least two-thirds of these cases. Although ultrasound-positivity is not necessarily the result of parasitologically proven infection, or vice versa, both indicators of infection are correlated. Infection does not necessarily lead to pathological lesions and the presence of pathological lesions does not guarantee the presence of intestinal-dwelling adult worms. It would seem that only some of the larvae that entered a person's body are able to successfully complete the histotropic phase; many others fail to develop into adult worms. The latter are the cause of pathology. Indeed, *O. bifurcum* does not seem to be smoothly adapted to its human host.

Follow up of individual patients also showed that the life span of the nodules is short and can be further reduced by treatment with albendazole. Storey's observation of finding only immobilised dead worms in a patient where laparotomy was performed a week after albendazole treatment confirms the effect of the drug on the histotropic stages (Storey, 2001).

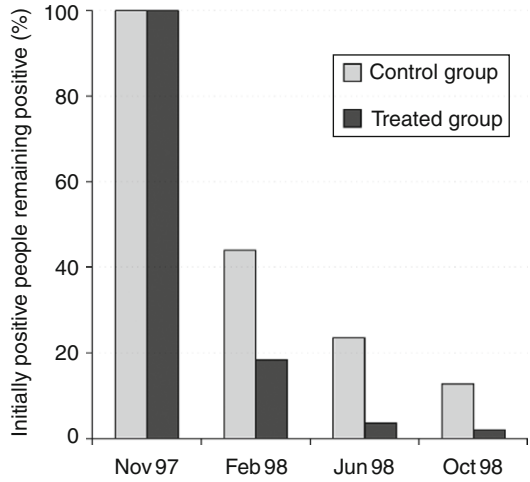


FIGURE 3.17 The evolution of ultrasound-positivity in schoolchildren with and without treatment. The data are based on Storey's longitudinal study of 99 schoolchildren in Ghana's Bunkpurugu area, at the Togo border. The children in the control group ($n = 55$) were not treated, those in the treatment ($n = 54$) group were treated with albendazole for 5 days, 400 mg/day). N.B. In the February and June 1998 surveys (dry season!) no new nodules were found. In October 2008 ultrasound-positivity rose again to 48% and 39% in the Control and Treatment group, respectively. The numbers of original nodules, however, continued to decrease, as shown in the figure. The study dates back to 1997 when the safety of treatment of asymptomatic carriers of *Oesophagostomum* infection was still disputed. The data have been presented by Storey et al. (2001a); the figure has earlier been published in the discussion of Storey's PhD thesis (2001c).

3.6. ZOONOTIC CHARACTERISTICS

The investigators who originally described cases of human *Oesophagostomum* infection in northern Togo and Ghana found the number of monkeys present in the area too small, and the intensity of possible monkey–man contacts too low, to consider these non-human hosts as a functional reservoir of infection for humans (Gigase et al., 1987; Haaf and Van Soest, 1964). In truth, very little was known of the infection status of the monkeys. For a proper understanding of human infection it was considered relevant to study infection of monkeys in and beyond the area endemic for human oesophagostomiasis.

3.6.1. *Oesophagostomum* in monkeys in Ghana

Initially, de Gruijter et al. (2004) reported on examination of five patas monkeys (*Cercopithecus patas*), captured by local hunters some 30 km from Bawku, in the centre of the area of human oesophagostomiasis. Four of

them were shown to be infected. Subsequently, careful quantitative and longitudinal observations on large numbers of animals have been carried out further to the south in Mole National Park and Baobeng-Fiema Monkey Sanctionary (Fig. 3.3) (Van Lieshout et al., 2005). In Mole large groups of Olive baboons (*Papio anubis*) were seen roaming around the village where the staff and other workers in the Park lived. In Baobeng Fiema, some 400 Mona monkeys (*Cercopithecus mona*) and 200 Black and White Colobus (*Colobus vellerosus*) are traditionally worshipped and protected by the villagers. The baboons and Mona monkeys were seen sharing their habitat with humans; they steal their food, use their wells and foul their houses. Monkey–man contact is intense (Fig. 3.18). The Colobus monkeys, on the other hand, live and stay in the trees.

The infection rates determined by stool culture were 92% for the baboons in Mole park ($n = 173$), 75% for the Mona monkeys in Baobeng-Fiema ($n = 51$) and 0% in the Colobus ($n = 55$). In more than half of the *Oesophagostomum*-positive cultures the intensity of infection was very high, with more than 100 larvae counted per culture (Van Lieshout et al., 2005).

During the same period of observation for the baboons and Mona Monkeys, 100 villagers in Baobeng-Fiema and 487 (Kleppe, Brienen and Polderman, unpublished internal report, 2004) in the workers' village in Mole National Park were investigated by stool culture. All were negative for *Oesophagostomum*.

The epidemiological evidence strongly suggests the strains or species of *Oesophagostomum* in the baboons and Mona monkeys in Mole and Baobang-Fiema are unable to infect man. The monkeys are numerous, the man–monkey contact is intense and practically all monkeys are infected, and much more heavily so than was normally seen in humans. Yet, the monkey and baboon infections do not serve as a reservoir for *Oesophagostomum* transmission to man.

3.6.2. Morphological differences between *Oesophagostomum* of monkeys and humans

Is there other evidence to support the view that the parasite commonly found in humans around Dapaong and Bawku differs from that so abundantly present in monkeys and baboons outside the area endemic for human infection? Morphological studies were conducted by de Gruijter et al. (2006). ANOVA and scatter plot principal component analysis of morphometric characteristics of adult male and female worms collected from humans (Garu District, northern Ghana), Mona monkeys (Baobeng-Fiema), a Green monkey (*Cercopithecus sabeus*) (Mole) and Olive baboons (Mole) showed that there are significant morphological differences.

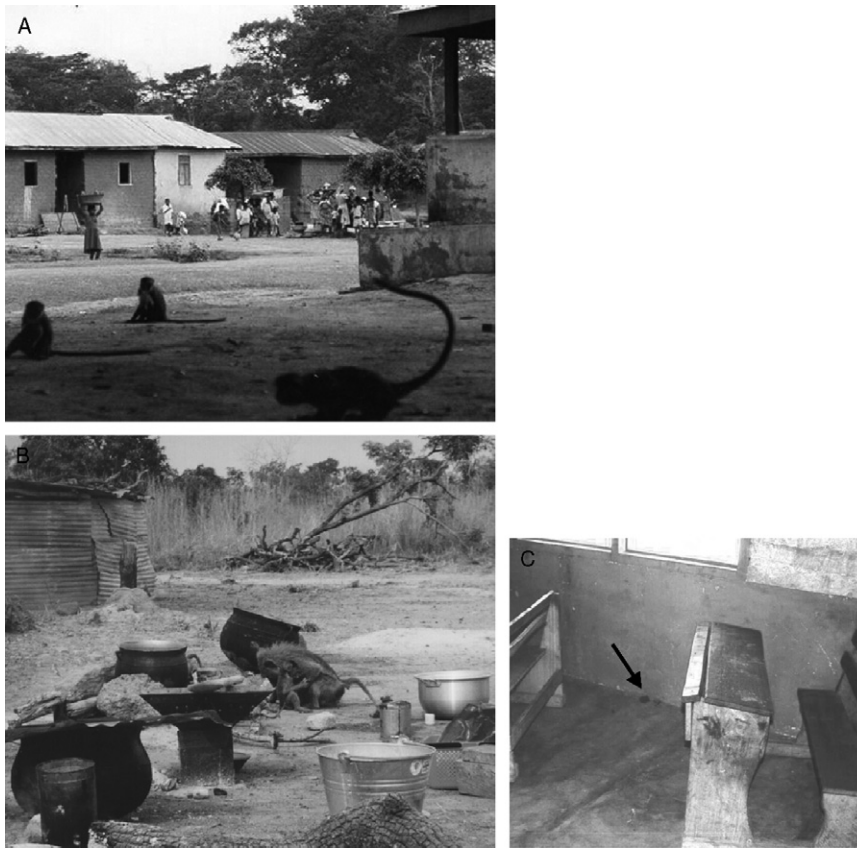


FIGURE 3.18 The contacts between baboons and Mona monkeys and man is intense in Mole Game reserve and Baobeng Fiema monkey sanctionary. In Baobeng Fiema a population of about 500 Mona monkeys is worshipped by the human population. Man and monkeys live closely together (A). In Mole Park, Ghana's biggest game reserve, specialising in walking safaris, baboons regularly enter the human dwellings (B). Upon inspection of the local school, fresh baboon droppings were found on the classroom floor (C). Photos: Department of Parasitology, Leiden.

Whether such differences are genetically or ecologically determined cannot be decided on the basis of morphological studies.

3.6.3. Molecular differences between *Oesophagostomum* of monkeys and humans

Genetic relationships were studied in using two fingerprinting methods, random amplification of polymorphic DNA (RAPD) and amplified fragment length polymorphism (AFLP). RAPD analysis revealed a high

degree of polymorphism (320 polymorphic bands) among individuals of *O. bifurcum* ($n = 41$) from different species of primate from different regions in Ghana (de Gruijter et al., 2004). Cluster analysis of the profile data (comprising 326 RAPD bands) showed that *O. bifurcum* formed three distinct groups, namely those from humans, those from Patas and Mona monkeys, and those from the Olive baboon (Fig. 3.19). This revealed population genetic sub-structuring within *O. bifurcum* essentially according to host species. The fact that *O. bifurcum* from humans and from Patas monkeys (from the Bolgatanga-Bawku region) formed different clusters (i.e. I and II, respectively) suggested that there was no association between *O. bifurcum* genotype and the geographical origin of the host

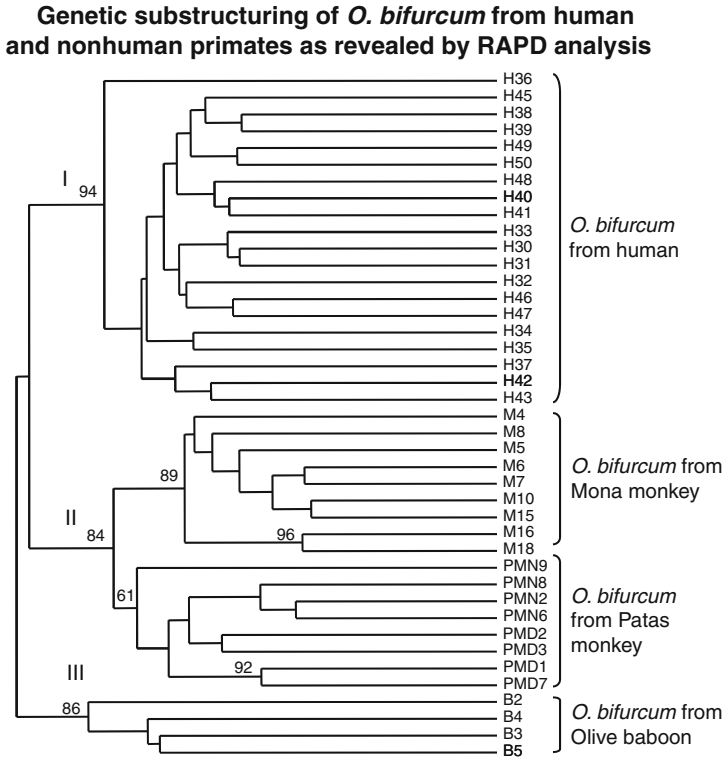


FIGURE 3.19 Dendogram based on cluster analysis of RAPD data for 41 individuals of *O. bifurcum* from humans, Mona monkeys, Patas monkeys and Olive baboon from Ghana. The figure illustrates the host-specificity of the various *O. bifurcum* isolates. Similarity coefficients were calculated according to Nei and Li (1979). The branch lengths represent genetic distances between the individuals and the numbers on branches are bootstrap values (using 200 re-samplings). Further details given in De Gruijter et al. (2004) and Gasser et al. (2009). Figure published earlier: De Gruijter et al. (2004) (reproduced with permission).

species based on the RAPD data set. This was also indicated for *O. bifurcum* from the Patas monkeys and from the Olive baboon (from the Tamale region), which were divided into clusters II and III, respectively. Extending from the RAPD analyses (de Gruijter et al., 2004), AFLP was used as a comparative tool (de Gruijter et al., 2005*a*). Analysis of 63 *O. bifurcum* adults from human, Patas monkey, Mona monkey and Olive baboon hosts from Ghana revealed four genetically distinct groups, namely *O. bifurcum* from the Patas monkey, from the Mona monkey, from humans and from the Olive baboon. These results were very similar to those achieved using the RAPD analysis. Therefore, in contrast to earlier investigations employing nuclear and mitochondrial loci, DNA fingerprinting data revealed genetically distinct, host species-affiliated variants of *O. bifurcum* in Ghana (De Gruijter et al., 2002; Gasser et al., 1999). Larger numbers of samples from disparate geographical regions needed to be studied to confirm the present fingerprinting data. The use of molecular methods for elucidating primate–pathogen relationships has been reviewed recently (Gasser et al., 2009).

3.6.4. Experimental infections in monkeys

The idea that the human parasite indeed differs from the one that normally parasitizes monkeys is also supported by limited experimental data (Eberhard et al., 2001). Out of 17 macaque monkeys inoculated with larvae of the 'human strain' of *O. bifurcum*, 13 seroconverted between day 19 and 62. Seven sacrificed between day 19 and 22 all harboured small L_4 larvae, 2.1–3.5 mm long. Four of the 10 animals followed for 88–420 days shed eggs, beginning on day 88–134 and only one animal shed low numbers of eggs consistently over 400 days (and had 14 worms recovered at necropsy at day 400). Upon autopsy that animal harboured four juvenile adult worms, 7.0–9.5 mm long. Although many different monkey species have been shown to be excellent hosts for *O. bifurcum*, experimental infections of macaques with the human strain of parasite from Dapaong resulted in very few infections; the pre-patent periods were unexpectedly long and the egg excretion very low, mostly of very short duration. This observation must be interpreted with some care because it cannot be excluded that infection may have established more easily in monkeys from the endemic area than in macaques of South East Asian origin.

3.6.5. Concluding remarks

The observations on infections in monkeys and man suggest that, around the centres of Dapaong and Bawku, *O. bifurcum* developed into a parasite of humans that differs in many respects from the parasite normally found

in monkeys. Accepting that this adaptation took place, and in addition, that transmission in human populations managed to be intense and effective (see Section 3.5, 'epidemiology'), it is puzzling why the endemic area has not expanded beyond the limited area around the provincial capitals of Dapaong and Bawku. Is there a human factor that is responsible for the limitation of distribution (e.g. tribes, behaviour or food), or are there geographical or climatic factors that prevent effective transmission beyond the current endemic area? No evidence has been found so far to believe that tribal factors play a role (as discussed in section 3.4.4. of this chapter). Geographical factors, such as differences in temperature, humidity and soil characteristics, can also not easily be considered as factors limiting the geographical expansion of *O. bifurcum* distribution since the primate strains survive very well over a large and geographically heterogeneous area. Indeed, the human parasite possesses characteristics, unknown so far, that prevent its dissemination over wider areas, and is different from the parasite normally seen in non-human primates.

3.7. TREATMENT AND CONTROL

When discussing treatment and control of *Oesophagostomum* infections, the impact of intervention should be measured both in terms of infection and of the disease and pathology. Before we were able to assess infection with the adult worm, we still had to rely on clinical examination and history taking. It was already clear that, even without specific treatment, many patients improved in the course of time (Gigase et al., 1987; Dr Vince Waite, Nalerigu Baptist Medical Center, personal communication). Following the introduction of stool culture to evaluate the level of intestinal infection, and of ultrasound to establish the degree of colonic wall involvement, it became possible to monitor the effect of therapeutic intervention more accurately.

3.7.1. Impact of treatment on infection

Only one preliminary comparative study has been done to assess the impact of different anthelminthics on the adult worms (Krepel et al., 1993). It was shown that the cure rates (stool culture becoming negative) were best after treatment with albendazole (400 mg once or twice) or pyrantel pamoate (at a double dose, i.e. 10 mg/kg, for 2 days). Cure rates of less than 60% were found using levamisole (5 mg/kg) and thiabendazole (50 mg/kg) (Krepel et al., 1993). Similar low cure rates were noted with mebendazole (200 mg) or ivermectin (150 μg/kg) (Krepel, personal communication). In further studies, the excellent effects of albendazole, using a single 400 mg dose (young children and pregnant

women excluded) were later confirmed by Ziem et al. (2004). The cure rate for *Oesophagostomum*, measured 3–4 weeks after treatment, was as high as 98%. For hookworm it was considerably lower: 51%, if based on the interpretation of stool cultures, and 79% when based on Kato thick smears.

3.7.2. Impact of treatment on pathology

The impact of treatment on the resolution of nodular pathology is slower and more difficult to assess because nodules can resolve without specific treatment and because new infections resulting in new nodules may develop during follow-up of more than a few months. Storey et al. (2001a) followed the disappearance of ultrasound-visible *Oesophagostomum* nodules over the course of a year. In 55 children who were not treated, the half-life of colonic nodules was 3–4 months; in children treated with albendazole ($n = 54$) (albendazole, 10 mg/kg for 5 days), the half-life was reduced to 1–2 months. The direct impact of albendazole treatment on the tissue-dwelling juvenile worms was vividly illustrated by Storey: during laparotomy of a patient who received albendazole treatment shortly before the operation, the colonic nodules were shown to contain only dead and degenerating juvenile worms (Storey, 2001).

3.7.3. Re-infection after treatment

The results of studies on the impact of treatment showed that the cure rate with albendazole (defined as the interruption of egg excretion recognised by stool cultures becoming negative) is very high and that the resolution of nodular pathology is significantly and measurably enhanced. Treatment with albendazole was therefore considered to be a potentially useful tool both for infection and for morbidity control (Storey, 2001).

Extensive longitudinal studies on the impact of treatment and the process of re-infection were performed by Pit et al. (2000). The result of Pit's observations in 1995 and 1996 are summarised in Fig. 3.20.

The data contained in this figure lead to a number of important conclusions.

Following treatment in May 1995 ($n = 61$), there was a rapid re-infection: both the prevalence of infection and the number of heavy infections (>32 larvae per culture) had almost returned to pre-treatment levels in October, 5 months after treatment. This was true both for *Oesophagostomum* (Fig. 3.20A) and for hookworm (Fig. 3.20D). Concurrent rises in intensity of infection during and shortly after the rains were also seen in those not treated (Fig. 3.16). Treatment after the rains of 1995 or in the middle of the dry season (Fig. 3.20B, E and C, F, respectively) did not result in rapid re-infection. The observation supports the notion that

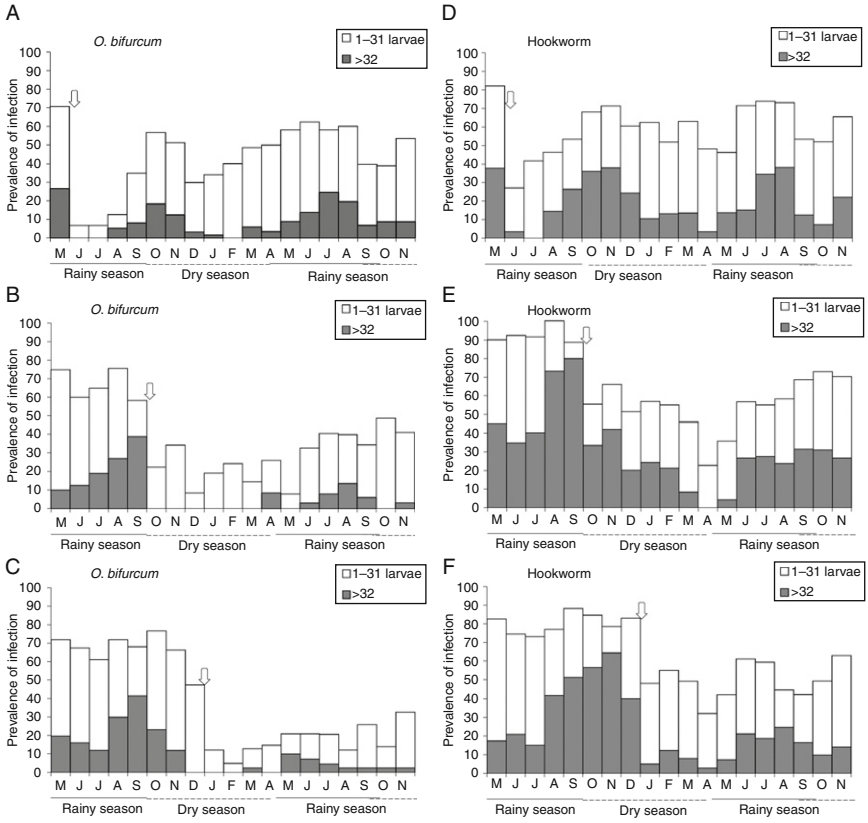


FIGURE 3.20 Re-infection of *O. bifurcum* and hookworm after albendazole treatment at different times. For each of the three groups,treated at different times of the year (just before therains [A and B], just after the rains [C and D], and in the middle of the dry season [E and F]) the data are based on repeated examination of 40–61 inhabitants of the villages of Lotogou and Tampialime close to the Ghanaian border in north Togo. All subjects participated in at least 15 of the 19 stool culture surveys. See also Fig. 3.15. For further details, see text, Section 3.7.3. Arrows indicate the time of intervention. Shaded: more than $10^{1½}$ L_3 larvae per 3-g coproculture (i.e. 32 and more). At the end of the study all were treated with albendazole. Published earlier: Pit (2000).

transmission is seasonal, and takes place during and shortly after the rains. In that sense, transmission of *Oesophagostomum* follows that of hookworm. A similar pattern of season-dependent patterns of re-infection was described by Krepel (1994) and Krepel et al. (1995a). The figure also suggests that transmission was less intense during the 1996 rains than in 1995. That tendency was apparent for hookworm but more obvious with *Oesophagostomum*. In fact, important season-to-season variation in

transmission should be expected in this climatic zone. Even during the rainy season, rain is intermittent and a couple of dry days are certainly sufficient to kill all developing L_1 and L_2 larvae.

3.7.4. Control

At the regional meeting on Human Oesophagostomiasis in Tamale, 1998, the Ghana Ministry of Health, the Regional Directors of Health of the Northern Provinces in Ghana and the University of Development Sciences (UDS) in Tamale expressed the need to attempt control of the disease because of its burden on public health in the northern regions (Polderman et al., 1999). Juventus Ziem, a student at UDS, has reported on the results of those efforts in a number of publications (Ziem, 2006; Ziem et al., 2006a,c,d).

As shown by Pit (2000), and referred to above (under epidemiology), re-infection after treatment was sometimes rapid and sometimes much slower, depending on the timing of treatment and apparently faster in 1 year than in another. Pit's observations gave an impression of the intensity of transmission, and not of the possibilities of treatment-based control. No attempt was made to achieve high coverage: only some 147 persons volunteering to participate in the study, out of a total of about 4000 inhabitants were treated, and not even at the same time. The considerable reservoir of infected hosts (prevalence, based on a single stool culture, of *Oesophagostomum* and hookworm 68% and 82%, respectively) was left largely untouched. The rapid re-infection described by Pit suggested that repeated treatments would be necessary to reduce the worm load and that the benefits of treatment should be evaluated in terms of impact on morbidity rather than on infection.

Ziem et al. (2006a,c,d) aiming at operational control, made a great effort to minimise the size of the reservoir of untreated hosts. When applying mass treatment, a fairly large and well demarcated population was covered in some 20 villages (approximately 13,000 people). In that way it was hoped to minimise the contaminating effect of influx of villagers from untreated neighbouring villages. The impact of treatment was compared with that in five control villages where no mass treatment was given. The results, being quite different from what was expected, will be discussed in the final section of this review, under the heading 'The fragility of the host–parasite system'.

3.7.5. Concluding remarks

Treatment appeared very effective at killing the lumen-dwelling adult worms and also in killing the histotropic juvenile worms. Local experience in Nalerigu Hospital was such that laparotomy routinely performed

both in Dapaong and in Nalerigu, was abandoned as the preferred type of intervention. Albendazole treatment is given upon clinical suspicion or US-based diagnosis of both multinodular and mono-nodular oesophagostomiasis. Albendazole was so effective that its use in mass treatment appeared altogether appropriate.

3.8. DISCUSSION

3.8.1. The life cycle

3.8.1.1. The nature of the pathologic histotropic stage

Observations and considerations on the life cycle of oesophagostomes in both humans and non-human primates have largely been based on clinical and pathological observations in sick individuals and post-mortem examinations. Apart from those performed by Mark Eberhard, no experimental infections have been carried out, and until the 1980s no systematic epidemiological studies of *O. bifurcum* had been undertaken. The interpretation of findings in individual cases was therefore based on what was known of 'nodular worm disease' in ruminants and pigs. Careful analysis of the nodules causing nodular worm disease in these animals and the colonic lesions in monkeys and humans shows, however, that the nature of these nodules differs substantially.

In *O. columbianum*, *O venulosum*, *O. radiatum*, *O. dentatum* and *O. quadrispinulatum*, the nodules contain L_4 larvae. In man, apes and monkeys, on the other hand, the nodules of *O. bifurcum*, *O. stephanostomum* and probably of *O. aculeatum*, characteristically found in affected individuals, are inhabited by juvenile adult worms, by 'L_5's. Even in *O. dentatum* infections in pigs and *O. columbianum* in sheep, where arrested larval development was noted and where living larvae were found several months after infection, no fourth moult took place during the histotropic phase; L_4s did not develop into L_5s. Clearly, the nodule-harbouring L_4s, found in ruminant and pig intestinal walls, return to the intestinal lumen for further development. There is little reason to believe that the much larger juvenile worms found in the nodules in humans, apes and monkeys retain the same capacity after their fourth moult and after having grown into (juvenile) adult worms in the nodule.

Unfortunately, though understandably, very few *Oesophagostomum* infections have been carefully followed in primates. The few experimental infections in 17 macaques conducted by Eberhard et al. (2001), however, showed that L_4 containing nodules were found in the early stage of infection (at week 3 PI) while later (4–14 months PI) L_4 nodules were no longer found and only L_5 nodules and/or lumen-dwelling adult worms could be demonstrated. In human surgical cases, nodules

have never been shown to harbour L_4 larvae. It suggests that the juvenile worms found in the nodules are unable to reach the intestinal lumen. It is most likely that the histotropic L_4 phase in human infections is short, as in other hosts, and that the juvenile worms found in the nodules are specimens that failed to return to the intestinal lumen. Only Thomas (1911) has described the presence of small larval stages in the intestinal wall of his patient; these, however, were not surrounded by a nodule and the identity of the larvae was not established (Thomas, 1910).

In the clinical cases examined by Storey et al. (2000) only 31% were positive on stool culture. This could mean that the juvenile worms caught in the nodules had yet to return to the intestinal lumen or that, in clinical infections, most or all larval stages failed to complete development successfully. In this context it is interesting to note that Storey (2001d), in his longitudinal follow up of patients, observed that only one-sixth of the people becoming stool positive at the start of the rains had, had ultrasound visible nodules in the previous months. Furthermore, the proportion that became culture positive was even lower in the Dapaong Tumour cases (26%), than in cases of multimodal disease (65%) (Storey, 2001; Storey et al., 2000). The lack of correlation between ultrasound and culture-positivity suggests that the proportion of larvae able to develop successfully to egg-producing adult worms varies from one individual host to the other.

When considering human infections at the population level, as done by Ziem et al. (2005), there is no longer a complete absence of correlation between nodule positivity and culture positivity. The observation merely reflects that in patients harbouring many lumen-dwelling adult *Oesophagostomum* worms, it is more likely that more tissue-dwelling juvenile worms will be found as well. This observation is not in conflict with Storey's observation mentioned in the previous paragraph.

All the pieces of information gathered so far would seem to imply that man is not a very suitable host for *O. bifurcum*! It can further be concluded that the life cycle of *O. bifurcum* (and probably of *O. aculeatum* and *O. stephanostomum* as well) is likely to be similar to that of the other oesophagostomes, but that the adult worm-containing nodules are a dead end in the life cycle, not capable of further development in humans. Thus far, the small L_4-containing nodules have been missed in autopsy. The life cycle should therefore be adapted, and summarised as drawn in Fig. 3.21.

Since the pathogenic stage of the parasite in human oesophagostomiasis is different from that in 'nodular worm disease' in pigs and ruminants, it is proposed not to use this colloquial description for *Oesophagostomum* disease in man any longer.

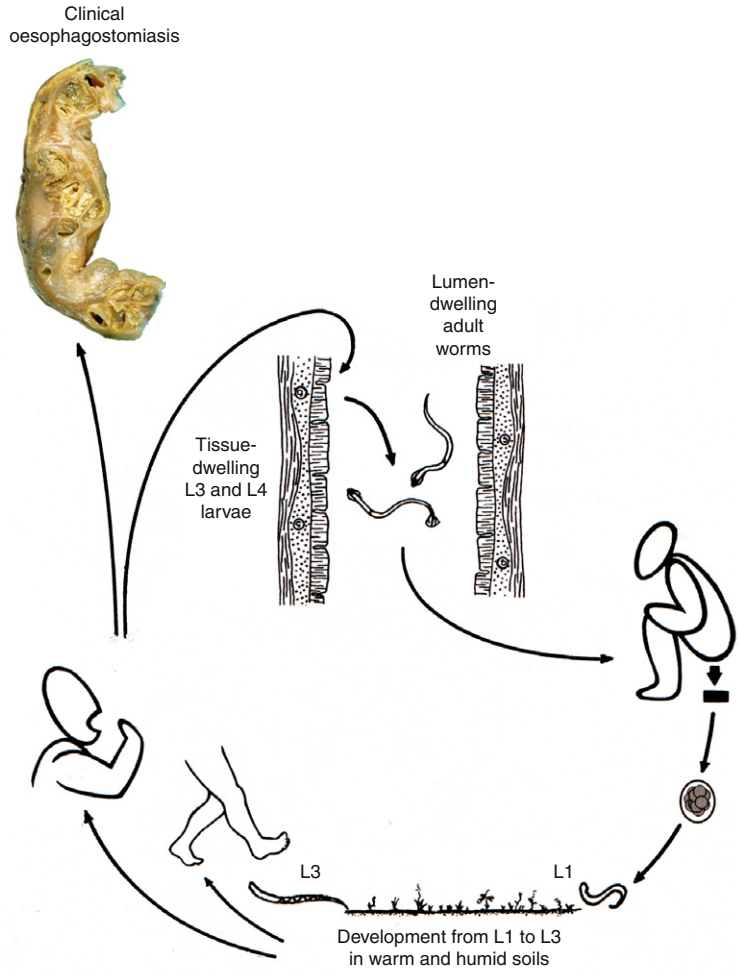


FIGURE 3.21 The suggested life cycle of *O. bifurcum* of man.

3.8.1.2. The route of infection

It is not easy to visualise why transmission is taking place so effectively. Latrines are not used and very rare anyway, and defecation is done 'free range' in the fields around the compounds. On the other hand human stools are greedily eaten by the large numbers of pigs and it is uncommon to come across fresh stool specimens. Pigs could function as a transport host to bring *Oesophagostomum* eggs back to the compounds, as

demonstrated by Steenhard et al. (2000), who demonstrated that 3.5% of the ingested eggs of *Oesophagostomum* and hookworm passed the pigs' intestinal tract within 24 h without loosing the capacity to hatch. Indeed, even the first step in transmission, from freshly excreted egg to entry into a new human host, remains little understood.

Oesophagostomum infections in animals have been shown to normally take place via the oral route. This is the case for *O. venulosum* and *O. columbianum* in sheep and goats, for *O. radiatum* in cattle and for *O. dentatum* and *O. quadrispinulatum* in pigs. Although, earlier, no experimental infections in monkeys and apes had been carried out it was logically assumed that *O. bifurcum* and *O. stephanostomum* infect their simian hosts in the same way. This route of infection has indeed been confirmed in the experimental infections performed by Eberhard et al. (2001). It has always been assumed that human infections would also take place in this way (Beaver et al., 1984). Such assumptions were supported by the observations that the L_3 larvae were able to survive exposure to gastric juices and bile. After 24 h of gastric acid incubation, all *O. bifurcum* L_3s were alive whereas none of the simultaneously exposed L_3 larvae of *N. americanus* survived (Pit et al., 2000). It was further observed in a small scale and preliminary experiment that active L_3 larvae placed on the skin of the forearm of a human volunteer did not show any activity suggestive of skin penetration (Krepel et al., 1992).

On the other hand, it was demonstrated many years ago that *O. radiatum* L_3 larvae are able to infect cattle percutaneously as well as orally (Mayew, 1939). Similarly, Gerber (1975) concluded that *O. dentatum* is able to infect pigs after skin penetration of L_3 larvae. More recently, Nosal et al. (1998) showed that small numbers of L_3 larvae applied experimentally to pigs' ears were able to grow into adult worms. These observations show that the L_3 larvae of several *Oesophagostomum* species are at least capable of infecting their host both orally and percutaneously. It is reasonable to assume that this, potentially, holds true for *O. bifurcum*. The question is not really how infection can take place but how it does take place under the prevailing conditions and the characteristics of oral and skin contact. In baboons and other monkeys it is easy to visualise how oral infection takes place. This, however, is not the case for humans in the endemic areas of Ghana and Togo. Uncooked fruits or vegetables are not part of the diet, and certainly not for very young children. Moreover, most families get their drinking water from protected wells (May, personal communication) and repeated examination of water samples obtained from the sources of drinking water never contained *Oesophagostomum* larvae (Polderman, unpublished data).

Data on the epidemiology of *Oesophagostomum* and hookworm infection and on behaviour of the human host did not give many clues to the actual route of infection. One set of data, however, strongly supports the notion of a significant role of percutaneous infection. In descriptive studies on the epidemiology of *O. bifurcum* in Togo and Ghana, time and again the authors were struck by the close association between infection with *Oesophagostomum* and hookworm (Krepel et al., 1992; Pit et al., 1999b; Yelifari et al., 2005; Ziem et al., 2006b). The hookworm infections in the area are principally caused by *N. americanus* and only in some communities have a few cases of concurrent *A. duodenale* been found (De Gruijter et al., 2005b). Analysing the association of *Oesophagostomum* and hookworm infection at the individual level, Ziem et al. (2006b) for instance, observed an odds ratio of 11.4 ($p < 0.001$): hookworm-infected individuals had a five times higher risk of being infected with *O. bifurcum*, as compared to the hookworm-negative subjects. At the population level, too, analysing the *Oesophagostomum* and hookworm prevalence in 133 villages in the endemic area of northern Ghana, a similar association was seen (Yelifari et al., 2005). Prevalence of *O. bifurcum* was significantly higher in villages with high hookworm prevalence than in those with lower hookworm prevalence.

Krepel et al. (1992) indicated that ''the most obvious explanation for this association is a similarity in transmission'' (Krepel et al., 1992). That was rejected on the simple assumption of the need for oral infection. On the basis of observations, we believe, however, that it is not appropriate to simply discard this explanation. Experimental infections in animals, observations on behavioural patterns of man and most importantly on the recurrently observed strong association with infection with *N. americanus* suggest that transmission of *O. bifurcum* might be percutaneous, like that of the local hookworms, rather than oral. This does not mean that oral transmission cannot, or does not play a role as well. Without experimental data, solid conclusions cannot be drawn on how transmission does take place in reality.

In fact a similar debate on how transmission takes place is seen for hookworms. Even though it was recognised that *A. duodenale* can be transmitted both percutaneously and via the oral route, authors remain undecided which route is the principal one in practice. In Manson's *Tropical Diseases* (Cook and Zumla, 2009), both percutaneous and oral infection are noted to occur. However, according to Muller (2002), oral infection with infective L_3 larvae is thought to be more important than skin penetration. Epidemiological data like those of Udonsi showing clearly different profiles of age-specific infection with *N. americanus* and *A. duodenale* seem to justify the latter hypothesis but definite proof is not easily obtained and the main route may be different in different settings (Udonsi, 1984).

3.8.2. The fragility of the host–parasite relationship

3.8.2.1. Zoonotic infections and the species' delicate adaptation to different hosts

Epidemiological, molecular and morphological observations on *O. bifurcum* of humans and various monkeys made it clear that different strains of *O. bifurcum* had developed. The fingerprinting analysis of de Gruijter et al. (2004, 2005a) showed that the genome of worms derived from different hosts varies with the host species and differs in humans from that of monkeys in northern Ghana and Togo. The genetic variation within one monkey species in geographically different regions was significantly less. Indeed, endemic oesophagostomiasis of humans, in Northern Togo and Ghana, is caused by a recognisably different strain of *O. bifurcum*. It may be assumed that genetic characteristics of worms isolated from individual 'zoonotic cases' of human infection retain the characteristics of the non-human simian parasite, but there is no proof for such assumptions as yet.

3.8.2.2. The parasite's limited distribution

One of the most remarkable features of *Oesophagostomum* infection in man is that the geographic distribution of human infections is so limited while within that endemic region prevalences are—or rather, were—extremely high and transmission must have been very intense. A most revealing observation was made by the late Djemila Pit (Pit, 2000). Between 1988 and 1998, 90 Moba migrants moved from their highly *Oesophagostomum*-endemic homelands close to Dapaong and settled near Sokodé, some 250 km south of Dapaong. They established a new and rather remotely situated village, Kedjibi, shaped in Moba style, with the characteristic compound structure as described on page 123. Upon stool culture, 58% of the new settlers appeared to be hookworm positive but *Oesophagostomum* larvae were found in only three. The average *Oesophagostomum*-prevalence in their villages of origin was over 40%. The three *Oesophagostomum*-positive persons had settled in Kedjibi for less than 3 years, previously. Apparently, local transmission did not take place, even though daily life was organised in a very similar manner to that in the villages from where the settlers originated, even though temperature, humidity and yearly precipitation were not very different and obviously suitable for hookworm transmission.

Within the endemic area in Northern Ghana and Togo the infection rates also varied considerably from one village to another. Plausible explanations for such variation were not found. Only proximity to streams and very small differences in altitude (unpublished data) would seem to suggest that small differences in humidity might play a role.

As shown in Fig. 3.15, transmission intensity can vary considerably from 1 year to another. The yearly precipitation is abundant (varying from 850 to 1150 mm in Garu [Ghana Meteorological Services, 1994–1998]), but even during the rainy season, rainy days are often interrupted by dry episodes during which eggs, L_1 and L_2 larvae, which are not resistant to desiccation, are likely to succumb. The number of rainy days followed by at least two more rainy days can be calculated to vary from 17 to 34 per annum (between 1994 and 1998, in Garu) and are therefore much more variable than the annual precipitation. Little is known of the impact of these factors on the microclimate. The uncertainties and variations in appropriate (micro-) climatic conditions are likely to be at least as detrimental to hookworm as to *Oesophagostomum*. L_1 and L_2 larvae of both species are vulnerable to desiccation but *Oesophagostomum* L_3s are capable of resisting periods of drought while those of hookworm are not.

However the village-to-village and year-to-year fluctuations may be ultimately explained, we cannot avoid concluding that factors governing transmission are finely tuned and minor variations in largely unknown environmental factors are readily detrimental to transmission. The parasite does not seem to be very successful in spreading in the human host and the environment!

3.8.2.3. Pathology and response to treatment

The parasite is not only vulnerable in man's external environment; it does not seem to be able to survive well inside the human host either. A great number of tissue-dwelling L_4s appear incapable of completing their life cycle successfully. Baeta, Storey and Ziem and co-workers all demonstrated that juvenile adult worms, probably unable to develop further, can be found in human host tissues while in the majority of clinical cases presenting at hospital, no lumen-dwelling adult worms appeared to be present (Storey et al., 2000).

When treated with albendazole, the parasite appears more vulnerable to treatment than most of the common nematode parasites of man. A cure rate of over 95%, based on the use of highly sensitive stool cultures, is very high indeed and much higher than that in hookworm infections where only 51% of the infected subjects were culture-negative 2 weeks after treatment (Ziem et al., 2004).

3.8.2.4. 'Give a push and see what happens'

O. columbianum has been described as 'an example of a parasite in its wrong host' (Dash, 1982). The position of *O. bifurcum* in humans would seem to be similar. It has been concluded that '*O. bifurcum*' in humans is a

parasite of man, not requiring another animal host for transmission. At the same time, a diversity of arguments has been brought forward to indicate that the host–parasite relationship is fragile in different ways. *O. bifurcum* failed to expand over a wider geographical area, it was not very successful in reliably completing its life cycle and was causing a lot of morbidity, as compared to other *Oesophagostomum* species and could readily be killed by treatment of the host. Probably there is no better way to assess whether or not the relationship between the parasite and its host is indeed fragile and easily disturbed than by 'giving a push and seeing what happens' (Bradley, 1972). Such an epidemiological experiment was done by Ziem (2006). His findings and the consequences are summarised in the final section on control.

3.8.2.5. Control

The results of control efforts are summarised in Fig. 3.22, based on Ziem et al. (2006a,c,d). For a full understanding, some details of Ziem's experiment must be given (see Box 3.4).

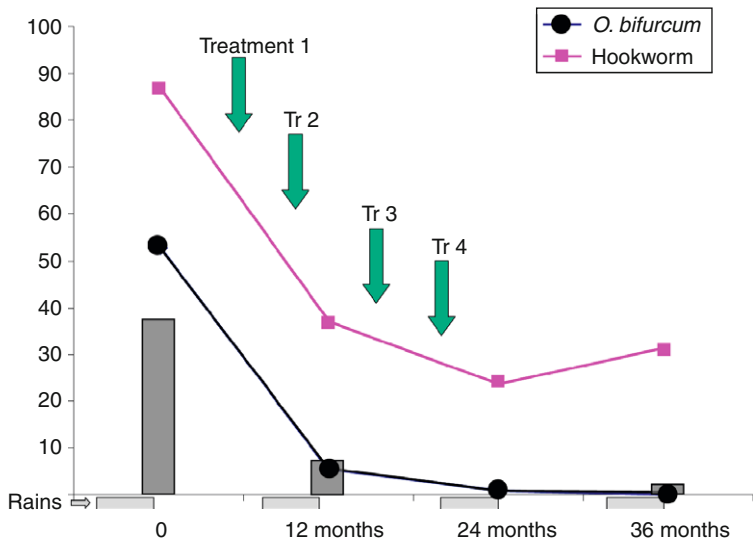


FIGURE 3.22 The impact of albendazole-based mass treatment in Ziem's study in North Ghana. Following four rounds of mass treatment both infections, as measured by stool culture, morbidity and as reflected by ultrasound-visible pathology, were resolved. Further details are given in Box 3.4. The figure is based on data presented by Ziem et al. (2005) and Ziem et al. (2006c,d).

BOX 3.4 Ziem's (2006) research approach

Ziem's efforts to control human oesophagostomiasis consisted of two phases: first a well controlled phase in which the evolution of infection rates of *Oesophagostomum* and hookworm in the intervention and control villages was assessed after two rounds of albendazole mass treatment in 1 year. Thereafter, albendazole mass treatment was continued in the intervention villages, and expanded to both the control villages and to the entire *Oesophagostomum*-endemic region of Northern Ghana (and Togo) through the Lymphatic Filariasis Elimination Programme.

In the two treatments of the first year, during the 'small-scale' research phase of control, albendazole coverage was very high: 78.8% and 76.3%, respectively, of the total population living in the intervention villages. After 1 year, the prevalence of *Oesophagostomum* positivity in stool culture fell from 53.0% to 5.4% (numbers of persons examined 1011 and 535, respectively) in the intervention villages and rose from 18.5% to 37.0% (number of people examined 303 and 173, respectively) in the control villages (Ziem et al., 2006c).

In Ziem's study the impact of treatment was assessed not only at the population- but also at the individual level. These individualised data are very revealing. They show that (1) the prevalence in migrants who came from outside the intervention villages was high and (2) even among those who received two albendazole treatments the prevalence of *Oesophagostomum* infection was still as high as 4.2%, even though the efficacy of one tablet of albendazole had been shown to be as high as 98%, in the same population. It was concluded that transmission continued and it was postulated that such continued transmission was due to the reservoir of infection brought in by the immigrants. A similar picture was seen for hookworm. After expanding the albendazole intervention to the whole of the *Oesophagostomum*-endemic area, re-infections with *O. bifurcum* no longer occurred and the prevalence of infection continued to fall. This was not the case for hookworm.

There are some possible explanations for the difference. In general terms: hookworm transmission is well established and likely to be more stable. More specifically: the cure rate of albendazole was very much lower and the reservoir of infection was not eliminated after treatment, and, even after expansion of the control area, immigration of new infection sources from outside the intervention area continued.

In 2008, 4 years after Ziem's final survey, another stool culture and ultrasound survey was done in the area. In the meantime, the albendazole–ivermectin-based Lymphatic Filariasis Elimination Programme had

continued. It became apparent that *Oesophagostomum* infection had disappeared altogether, and ultrasound analysis showed no more than a couple of old scars. At the same time hookworm prevalence had fallen significantly (unpublished results; report in preparation by van Lieshout, Ziem, Spannbrucker and Polderman).

The efforts to control human oesophagostomiasis and hookworm infections through mass treatment resulted—for the time being—in a complete disappearance of *Oesophagostomum* infections and a marked reduction of both the prevalence and the intensity of hookworm infections. As concluded by Ziem in the general discussion of his thesis, a number of factors are likely to have contributed to the success of mass treatment in eliminating human oesophagostomiasis: most notably the high cure rate of albendazole, the extension of treatment over the entire endemic area, and the vulnerability of the parasite, ill-adapted to its human host, and the hostile environment (Ziem, 2006). This last factor is likely to have influenced the changes in prevalence and intensity of hookworm infections as well.

3.8.3. Finally...

Returning to the concept of the epidemiological experiment, it can be concluded that disturbing the natural process of transmission in northern Ghana has resulted in a complete disappearance of *Oesophagostomum bifurcum*. Although it cannot be excluded that pockets of infection may remain in isolated corners of the endemic area, such foci are unlikely to be the core of a new epidemic. A reservoir of high level background infection was shown to be necessary to support continued *Oesophagostomum* transmission.

Looking, in Bradley's words, at what happened after disturbing the balanced host–parasite relation, it becomes clear that the *O. bifurcum* strain of man, in Northern Ghana (and Togo) was unable to cope with the disturbance. This observation, together with those on the finely tuned adaptation of the strain to the human host, on the inability of the parasite to increase its distribution, and on the unexpectedly severe pathology, as compared to that of related species, is the final argument to conclude that indeed the host–parasite relationship between *O. bifurcum* and its human host is of great fragility. It could be concluded that the originally zoonotic parasite adapted to man, achieved the level of more or less stable and seemingly successful transmission but was, in the end, incapable of surviving the adverse conditions. The adverse conditions imposed on the parasite consisted, first of all, of large scale and intense mass treatment. Additional environmental factors may have played a role as well but their extent remains uncertain.

For the time being, this is the end of the *Oesophagostomum* saga: which involved the recognition of the local importance of a new helminth parasite of man, highly prevalent, causing a considerable amount of pathology and well recognised by the local people; a period subsequently characterised by studies on a variety of epidemiological, molecular and clinical aspects; and finally the realisation of effective control and possible eradication through mass treatment, all in a period of just over 20 years.

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