Chapter 25
Epidemic Disease in African History I: Micro and Macro Parasites, Zoonoses, Introduction, Viral and Protozoal Diseases

25.1 Introduction

In the past Africans were often referred to as prone to psychosomatic illness but new techniques are enabling identification of a whole host of previously unsuspected diseases ranging from debilitating to fatal. Most actual and potential human pathogens are endemic to tropical zones and Darlington (1969) considered disease had obstructed every racial and cultural development in Africa, the greater part of man's diseases arising there where man had his origins but climatically indifferent, as they are due to viruses and bacteria which are directly infectious and contagious. Probably all are the object of genetic adaptations favouring resistance arising in populations that have long been exposed to them. But those diseases carried by, or directly due, to tropical animal parasites, have not resulted in the same, if any, genetic resistance in man. As Anderson and May (1991) pointed out, to be successful parasites need not necessarily evolve to be harmless, it depends upon the relation between virulence and transmissibility and the cost to the host of evolving resistance. It is these tropical diseases, chiefly due to protozoa and helminth metazoans, which began to cripple the development of African societies just at the moment when populations reached the numbers and densities necessary for civilization. These chronic diseases may have suppressed or retarded development in Africa so that more of "wild Eden" has survived into present times, but it is the epidemic diseases the author suggests have had a recurrent effect upon the ecology of Africa, preventing populations from becoming too dense rather than limiting their development. Buffon, early to realise the importance of epidemic disease, in his *Histoire Naturelle* of 1748 considered it had a role in changing people, "[mankind] has undergone various changes by the influences of climate, food, mode of living, epidemic diseases, and the mixture of dissimilar individuals". But not only do diseases suppress populations both by debilitating them and by removing numbers, together with famine they lower fertility, particularly noticeable in lowered female birth-rates. However there are indications that extreme malnutrition in times of drought among West African pastoralists made them less susceptible to malaria

C.A. Spinage, *African Ecology - Benchmarks and Historical Perspectives*, Springer Geography, DOI 10.1007/978-3-642-22872-8_25,

(Murray and Murray 1977). A disease can cause immune suppression thus paving the way for another, however the control of diseases and parasitic infections means that any sporadic outbreaks have a potentially greater effect because of lack of developed immune response which repeated exposure provides, and lack of cross-immunity. Thus Gabonese schoolchildren with schistosomiasis have fewer allergic reactions to dust mites, and Ethiopian and Gambian adults have less asthma when infected with nematodes (Wilson and Maizells 2004). Short (1749) considered a severe fatal epidemic was generally succeeded by an uncommon healthiness, the epidemic removing most of the declining worn-out constitutions. Modern studies have shown nutritional state of the individual is crucial in determining death or survival from disease, but Dawson (1979) argued famine and smallpox so often go together because of human behaviour, the social reactions to famine such as migration to centres in search of food, and smallpox epidemics are not caused by malnutrition.

The protozoal disease Leishmania occurs in two main forms, a skin disease and an internal frequently fatal disease known as kala azar caused in East Africa by *Leishmania donovani*. Parasites causing the skin disease have been isolated in Kenya from *Tatera robusta*, *A. niloticus*, *M. natalensis*, *Taterillus emini* and *Aethomys kaiseri*. The vectors are sandflies of the genera *Phlebotomus* and *Sergentomyia*. Kala azar is important in the Sudan where it is spreading into many areas in which it was unknown previously (Gratz 1997), *A. niloticus* and *Acomys cahirinus* having been found positive for *L. donovani* in Upper Nile province. In 1991 some 18.2% of persons examined had been exposed to the infection and it was believed the disease had already killed thousands and was spreading. In western Upper Nile province at least 30,000 people were believed to have died and it had largely depopulated an area of some 50 km in diameter, but this epidemic situation could be related to great ecological changes in the area caused by civil war, a result of politics (Ashford and Thomson 1991).

As in the consideration of other diseases and, for example, locust plagues, the historical references presented here are designed to show how prevalent and widespread these devastating epidemics were. There are many chronic diseases and parasitic infections which served to depress the human populations but which would have led to a balance between human and animal occupation of living space, as opposed to the chaos introduced by epidemics. Hieronymus wrote of plague at the beginning of the fifth century that the human race had been "all but destroyed" and the earth was returning to a state of deserts and forests, an early description illustrating the importance of diseases, whether human or animal, in the dynamics of ecosystems. Most new pathogens are not sufficiently transmissible to cause large epidemics, this requires they spread extensively through the human population without involvement of the original host, and implies that the basic reproductive rate, R_0, is greater than one, i.e. that a single primary case will generate, on average, more than one secondary cases. To achieve this, firstly R_0 can increase as a result of ecological changes, e.g. increase of host population density for directly transmissible diseases, or of vector for vector-borne diseases. Secondly the pathogen can evolve to become better adapted to the human host but may then do worse in the reservoir host leading to specialization in the human population and ultimately

speciation (Woolhouse and Antia 2007). Accidental infections are more likely when reservoir host and novel host are phylogenetically related, thus humans are more readily infected with parasites from other primates than they are from rodents, and more easily from rodents than fish. But more than 80 diseases are naturally transferred from vertebrate animals to man, the majority in Africa. Of these at least 30 are from dogs, 24 from rodents and 22 from sheep and cattle. Others remain unknown, thus Gamitto reported in 1832 (Gamitto 1960) in the land of Kazembe in northern Zambia the people said the black and white colobus monkey *C. guereza* could not be captured because its bite was fatal. An indication it was carrying a lethal virus. Squirrels in Uganda harbour a lethal virus earning them the reputation among Africans of being poisonous. Discovered in 2004, Simian Foaming Virus SFV is a benign virus found in at least three different species of primate and also in bush-meat hunters, which could conceivably mutate into a pathogenic form.

Employing an holistic approach to ecology it is pertinent to consider the role of man in the environment, and just as enzootic disease outbreaks are important in the context of animal populations, so too are human epidemic diseases of importance in their cybernetic effects in relation to habitat occupation. The destruction of natural hosts also may make humans more sought after by blood-sucking invertebrates, increasing the threat of arthropod-borne diseases and reducing chances of cross-immunity. The prevalence of diseases may be altered also by changes in the structure of ecological communities, thus vegetation can exert important effects upon both vectors and hosts. An unusual abundance of annual fruits may lead to an increased concentration of those species which feed upon them, or an increase in population, leading to facilitation of disease transmission. As Polunin (1967) discussed, primitive populations exerted only minor disturbance on the environment, even shifting cultivation at low levels has minor influence. More massive permanent crop husbandry leads to a decrease in the number of floral species and an increase in the population densities of those of the favoured monocultures, several hundred forest tree species may be replaced with a mono-dominant thicket. The same has been observed in rodents, removal of forest reducing a diverse array of species to one or two dominants.

The encouragement of selected species intentionally or unintentionally can lead to changes in human disease patterns, for example encouraging rodents as harbourers of plague or redistributing mosquito populations. The most significant African disease, human trypanosomiasis, has been considered already, but other infections have played major roles in limiting human populations and influencing the constriction and expansion of animal habitats. Trypanosomiasis not only affects human populations directly by causing death, but also indirectly by lowering the birth rate of women. When the rate of infection is more than 3% populations decrease, when below that level they increase. It was suggested (Ledentu 1931) that people with blood group ‘O’ have extra sensitivity to trypanosomiasis, just as with cholera this blood group is more predisposed towards severe effects, but the blood group is significantly less common in parts of Africa perhaps indicating an evolutionary weeding-out by these diseases (although only 42% of American whites have it (Trowell 1960)). Ceccaldi et al. (1946) gave an average value of

41% in West Africa ranging to 51% in South Africa, with most races between these values but Mourant (1954) claimed Negroes tended to have a high 'O' frequency. Thus a little below half of Africans have blood group 'O', only Congo Pygmies having a significantly low proportion of about 30%, which might well indicate an evolutionary weeding-out. People whose ethnic origin is closer to the equator are at greater risk of suffering from high blood pressure, suggesting selection in relation to ecological factors for hypertension related genes (Young et al. 2005).

Extensive fossil occurrence of numerous carbonized oil palm kernels in charcoal deposits and their relatively abrupt disappearance about 1600 B.P. from Nigeria, south-east Cameroun, south-west CAR, and northern DR Congo, has suggested to some a widespread human population crash followed by forest regeneration. In Gabon's middle Ogooué valley, evidence of a population of ironworkers from 2500 to 1500 B.P. vanishes from 1400 to 800 B.P., suggesting disappearance of the human population although there is evidence of its continuation in the coastal provinces and Nyanga and Upper Ogooué. Oslisly (2001) is one of the few to suggest a widespread epidemic causing the human population to crash, referring to bubonic plague devastating populations in many parts of Gabon in the early twentieth century. Oslisly found sites that seemed almost intact, with artefacts lying on the surface of the ground as if suddenly abandoned. But due to its ecology bubonic plague is unlikely to have been the cause if epidemic disease was the reason, as is indicated by the wide spread of the phenomenon. Of other possibilities, malaria, trypanosomiasis, influenza, and a deadly arbovirus, trypanosomiasis seems most probable and is known to depopulate areas. The period was relatively humid and it is possible the prevalence of trypanosomiasis increased related to long term cycles driven by climatic changes, man being forced either into closer contact with the tsetse fly vector or the fly increasing favoured by increased humidity. Malaria is known to be an ancient disease and the quasi-immunity that Africans possess today would probably have already been well established. Influenza is a contact disease and populations could probably have avoided it. Most vector-borne viruses have a wide host range and very narrow range of vectors, although numbers were relatively low, man at this time would have been in much more intimate contact with animals harbouring arboviruses, but the vector range being more restricted epidemics caused by such viruses have not been found to extend as widely as trypanosomiasis. Populations reappeared in the middle Ogooué valley from A.D. 1200 after an absence of 600 years. The hiatus with the absence of regular burning by man would have allowed forest to advance rapidly into the savannah and by the 1990s the area was delimited by forests which supported a high mammalian biomass (White 1994).

Although primitive human communities may have been too small to support constantly present endemic pathogens, they were regularly infected by zoonoses through contact with infected animals. Almost 60% of human pathogens are zoonotic and thus constrained by the animal host's spatial range. Hartwig and Patterson (1978) conjectured early hunter/gatherer man had millenniums to achieve biological harmony with pathogenic parasites or parasitic diseases, although it can take as little as 150 years for a zoonotic disease to become established as a human

pathogen (Crawford 2007). It had been argued long before. Wells (1818), first to recognize the principle of natural selection in Darwin's (1866) words, stated in 1813, "Of the accidental varieties of man, which would occur among the first few and scattered inhabitants of the middle regions of Africa, some one would be better fitted than the others to bear the diseases of the country. This race would consequently multiply, while the others would decrease, not only from their inability to sustain the attacks of the disease, but from their incapacity of contending with their more vigorous neighbours".

But it works both ways. Diseases at the same time had millennia to continually adapt to resistance. Further, Patterson and Hartwig postulated that natural barriers such as oceans and deserts, combined with slow communication, prevented most epidemics from reaching sub-Saharan Africa (that is, European epidemics), but concede that endemic diseases and natural disasters such as droughts and locust plagues affected population growth. Lambrecht (1967) argued the important selective factors which may have existed in early times should be sought among parasitic diseases or zoonoses transmitted by an insect vector, because populations were too sparse for infectious diseases transmitted by direct contact to have much effect. However, the equatorial African environment appears always to have been benign for the development of diseases within the history of man, providing plentiful opportunities for disease organisms that would have little chance in temperate zones due to lowered temperatures, and initially hunter/gatherer populations were probably smaller outside of Africa than within and thus less likely to experience epidemics. Viruses and bacteria are ubiquitous in the environment and extremely abundant in the aquatic environment, but protozoan infections are relatively rare in temperate climates. In the tropics the reverse is true but most human groups in the past lived in an environment saturated with infection, as Beale wrote in 1863, "Disease germs are liable to be suspended in the air we breathe, or they may be disseminated through the water we drink, or hidden in the food we eat". Epidemics could well have arisen frequently among hunter/gatherers in Africa from their close association with a variety of animal species upon which they depended for food, and from which they may have contracted diseases as adventitious hosts especially by handling and consuming animals which had died of disease, but thinly-scattered populations are unable to maintain diseases. But they would have been boosted when man began a herding existence in Europe and Asia, becoming prone to adopting diseases from his neo-domesticated animals, firstly sheep and goats, and later cattle.

Moodie (1967) postulated that diseases are much more prevalent now than ever before in earth's history, arguing there are no descriptions of pathological conditions in fossil animals prior to the Carboniferous. Instances then increased, falling suddenly at the end of the Cretaceous with extinction of the dinosaurs, only to rise again into modern times and, "according to present evidences" disease is relatively recent from the geological standpoint, afflicting the earth's inhabitants for the last quarter of the earth's history only. But bacteria would have been among the first forms of life, exploiting protozoa and metazoa as the latter classes of organisms

evolved, whereas it is argued viruses represent degenerate descendants of larger pathogenic micro-organisms.

Burnet (1945) gives the evolutionary sequence as free-living saprophytic micro-organism (bacterium, protozoon, or fungus) → facultative parasite → obligatory parasite with subsequent degeneration to virus. As forms of life diversified, so would diseases. That does not mean to say that such diversification might not have outstripped the diseases, especially after the Cretaceous, and now the diseases are catching up. Brier (2004) postulates smallpox and cholera (as well as influenza and measles), diseases which live a short time in the host and cause high mortality but confer immunity upon survivors, must have arisen late in history, for in the small isolated populations of early man everyone would soon be dead or immune if infection was contracted. Such diseases require a large population with high rates of birth and infant survival. Bartlett (1957) calculated measles can persist only in populations of at least 250,000 individuals. Thus Anderson and May (1991) argue that directly transmitted infections such as smallpox and cholera have high threshold densities for epidemics to take place and so could not have been present in the pre-agricultural era.

Gill (1928) propounded his "quantum theory" to explain the cause of epidemics, all epidemics he suggested depending upon four factors: a reservoir, a parasite, an immunity, and transmission. Epidemics resulted from quantitative changes in these factors upsetting the equilibrium between infection and immunity. These four factors can be found in *Trypanosoma* sp. which sometimes form disease complexes in which there is an agent, a vector, a host, and a reservoir of infection. These have significant ecological implications, not only in their direct relationships with particular vegetation types and ecological situations, but also in the indirect effects produced upon human and animal distributions, and consequently upon vegetation, but such complexes often have weak links.

But the complexity does not end there. A multiplicity of hosts introduces conflicting selective pressures on the pathogen to which a compromise solution must be found. Multi-host pathogens are likely to exhibit dynamics in time and space different to host specific pathogens, and different host species may vary in their response to infection, possess varying contact patterns based on social behaviour and different spatial distributions across the landscape. Whereas these factors could play a role in human disease transmission they are more common among animal species.

The very variety of animal and plant species in the tropics will have been key also to development of a wide range of disease organisms which drive species' diversity. Although it has conventionally been argued there is an evolutionary pressure on parasites to become less virulent and develop a benign relationship with a host, virulence is associated often with transmission, and theoretical analysis indicates evolution of pathogens is highly dependent on the coupling between transmissibility and virulence (Scott and Duncan 2001). If it is hard for them to transfer from one host to another then they may become more benign. An example is the virulent AIDS-causing virus found in East Africa which occurs at much lower levels in West Africa, where it is largely replaced by a closely related but less

virulent virus. But an inability to maintain a parasite means also that pathogenic parasites maintain their virulence, striking a population anew each time. Anthrax is an ubiquitous genetically stable bacterial pathogen with minimal mutation over hundreds of years of which death of the host ensures its maintenance. In the case of host population regulation by macroparasites, the death of a few heavily infected hosts means the death of a large number of parasites. This tends to reduce the impact of the parasite on host abundance (Anderson 1991).

We may suppose ancestors of *Homo sapiens* were infected by many viruses and man has inherited many of them today. McNeill (1977) points out the sort of infections now prevailing among monkeys and apes may resemble the parasitic populations with which remote ancestors of man co-existed. He considers the great variety of human parasites which exists in Africa suggests Africa was the nascent centre for humankind and the warm tropics provided a benign environment allowing parasites to evolve. Non-human primates are host to a formidable array of parasites and infections, such as 15–20 species of malaria *plasmodium*. Apes can be infected with human strains of *plasmodium* and humans can likewise be infected with some of the kinds found among non-human primates. Some 25 species of *plasmodium*-carrying anopheles mosquitoes show specialization restricting them to either the treetops, middle stratum, or ground level, of tropical rain forests, all of which levels can be exploited by non-human primates, and which suggests a very long evolutionary association between primate, mosquito, and *plasmodium*. Sub-Saharan Africa appears to have been a principal, and perhaps the only, centre for the development of this type of parasitism, and malaria may be a disease of earliest humans in Africa. Bruce-Chwatt (1966) suggested, originating in tropical Africa malaria spread from there up the Nile valley to the Mediterranean, and independently to Mesopotamia, the Indian peninsula and China, the last three areas being the main centres from which it invaded a large part of the globe; but its presence in the New World was difficult to explain. Many small organisms which cannot withstand low temperatures or low humidity thrive in tropical rain forests and the warmth and moisture allow single-celled parasites to survive often for long periods outside of a host, while some can exist indefinitely in a free-living state. Thus scant populations of potential hosts can still experience widespread infection and infestation, because even if contact between host and parasite is rare, the parasite can wait. Paul the Deacon wrote *c*790 that the north "in proportion that it is removed from the heat of the sun . . ." was much more healthful for men and fitted for the propagation of nations, just as the nearer a southern region was to the sun, the more it abounded in diseases (Foulke 1907). The number of arboviruses endemic to a certain geographical region increases towards the equator, subtropical and tropical regions harbouring by far the greater number.

Although the bacterial infection diphtheria *Corynebacterium diptheriae* is regarded as extremely rare in Africa it may have been what the ancient Greeks called the "Egyptian disease", perhaps introduced to them from North Africa by Hannibal's soldiers. Ramon and Erber (1935) found significant amounts of diphtheria antitoxin in the blood of 53% of sampled baboons from Congo Republic (presumably *Papio anubis* as the species *cynocephalus* and *hamadryas* which they

claimed to have examined do not occur there), the level of which appeared to increase with age, and the bacillus has been isolated from their throats also; but it was not found in the chimpanzees and macaques examined. Many different species of mammal have their own species of *Corynbacterium* in the throat. The natural immunity shown is a consequence of unapparent infections.

Attempts to link disease epidemics to increased contact and mobility brought about by colonialism (e.g. Brown 1978) ignore large-scale climatic fluctuations, variations in humidity playing an important role in the checking or expansion of many diseases. It is conventional wisdom that diseases introduced into previously unchallenged populations cause high mortality, but because a disease causes high mortality that is not to say it is new to a population. With a life expectancy of 20–25 years estimated for Nyamwezi males in the nineteenth century (Southon 1880), if this represented a wider pattern on average the majority of immunes in a population would have disappeared within about 30 years, and we see that many epidemic disease outbreaks occur at intervals in excess of this period. Park (1799) considered few of the Mandingoes of West Africa survived to 55 or 60, and most were grey-haired and wrinkled at 40. Ovington (1696) however considered people of Cabinda on the west coast lived to 70 or 80 and were a very healthy people. But at Benin, in the vicinity of the Bonny and New Calabar rivers, Owen (1833) noted in 1827 that during the unhealthy months from September to June many of the natives were destroyed annually by either dysentery or the jungle fever (malaria). At the beginning of the twentieth century the average length of life of an African was less than 30 years. By the 1990s this had risen to more than 50. In epidemics generally it is considered there is a higher mortality among Africans exposed to smallpox, influenza, pneumonia, plague, and certain spirochaete infections; but this may reflect nutritional status. We know however that recurrent outbreaks of cholera and smallpox could cause just as high mortality among Europeans before the outbreaks were counteracted by medicine. Thus whereas the principle is not denied, the case can be overstated.

Where it is reported that children were affected first by an epidemic this implies the population had experienced the same infection not more than about 10 years before, and where only old people have survived an epidemic this implies a previous visitation at a much earlier date. In epidemics some persons almost always survive, thus in reports of plague in East Africa between 1902 and 1913 survival ranged from nil to 67.7%, averaging 18% (Milne 1915). Epidemics can exert their effects upon a population for many years afterwards, as in north-west England where an unidentified plague killing 40% of a population in the sixteenth century was shown to affect population structure initiating oscillations in the annual numbers of births and deaths for 150 years (Scott and Duncan 2001). It has been suggested that long-term demographic trends in western societies may have been caused not by fluctuations in food supplies, but by independent biological changes in the virulence of disease and the fluctuations of great epidemics. In Africa this may have been even more true, with the added effect of influencing the dynamics of the wild animal populations which the human populations hunted for food or deprived of living space. The effects of depopulation in Uganda by sleeping

sickness have already been described. Lubogo (1986) refers to Busoga by 1919 having a very sparse population "the country was mostly inhabited by wild animals". Johnston (1908) wrote that in the Congo basin across the Lualaba between the Tanzanian coast and the upper Lomami River there had been much depopulation due to sleeping sickness, smallpox, military mutinies, and old Arab raids. He considered smallpox must have been a significant factor in keeping down the population of Africa since an introduction which he attributed to the Abyssinians or Arabs about A.D. 500.

Anderson (1991) pointed out that if a population increased at 4%/annum, with an average duration of infection of 2 weeks and a 50% mortality rate with lifelong immunity for survivors, smallpox could not regulate a human population; but population increase would have been much less than 4% in historical times. Whereas Hartwig (1979) was critical of the evidence for population decline in earlier times he conceded to the opinion the population of East Africa suffered a serious decline from about 1895 to 1920 due to disease and famine, offsetting any gains the abolition of slavery and intertribal warfare may have conferred. Prior to this it is assumed the overall population of East Africa was fairly stable, occasional drought, famine, or wars, exerting localized effects only, although on balance there was a slow increase in population size as agriculturalists extended into previously uncultivated areas. But the localized effects could be sufficient to create a dynamic interchange in the ecology of areas, with "wild nature" gaining the upper hand at one point following disease or famine, and losing it the next.

In the years A.D. 400, 407, 417, and 419, "pestilence" desolated Africa (as well as Asia and Europe), while in 480 Africa and Asia were allegedly "nearly depopulated" by epidemic disease. There was widespread "pestilence" in Africa, including Egypt and the Middle East, Asia, and China, in 1346 (Bascombe 1851). Africa in these contexts meaning North Africa and perhaps Nubia (Botero (1588) referred to Morocco "at this day" as the seat of the King of Africa). Cholera, plague, smallpox, and influenza, have shown similar geographical coverage in more recent history.

Except where given a specific name Arab chroniclers refer to epidemic diseases as *wabā*', the term for bubonic plague, but it was probably used in a general sense for any disease causing high mortality.[1] However moist humid conditions would be favourable to outbreaks of bubonic plague following increases in rat populations, but the insanitary conditions caused by large numbers of deaths could equally lead to cholera. It is often difficult in early accounts to identify whether a disease is cholera or plague and in Upper Egypt during plague outbreaks in the early twentieth century, typhus and relapsing fever were active at the same time. Hirsch (1883) noted that during famine, for example, a mixture of various diseases breaks out, such as diarrhoea, dysentery, scurvy, typhus, and frequently malaria and typhoid; all of which have been often grouped together by chroniclers and historians as a single disease. But in 1089, a great year of pestilence, in north-east France we can identify it as cholera because many men were tortured by contraction of the muscles "twisting this way and that", characteristic of cholera cramps.

Why reported symptoms sometimes differ from modern descriptions may have been due to people carrying latent infections of many diseases, e.g. smallpox. Thus in a weakened state, as from cholera, these latent infections rapidly developed. Such an effect occurred with rinderpest in cattle, where weakening of the immune system by the infection caused latent infection of dermatophilosis to erupt causing pustules (see Spinage 2003). Kâti (Houdas and Delafosse 1964) referred to an epidemic termed *gafé*, a West African Songhai word for "dry season", killing many people in Mali in 1535 possibly lasting until 1548. This might have been cholera, plague, or meningitis; but smallpox which is not mentioned is more associated with famine. In the Niger Bend several epidemics were reported from the sixteenth century onward which may have been smallpox and sometimes plague, but in 1704 famine was followed by an epidemic termed *baana faasa* which translates as "nervous sickness".

Curtin (1968) argued that Africans died from greater susceptibility to diseases when moved from their adapted environment to elsewhere in Africa. The same can happen with animals, an example on a larger scale where the susceptibility is related to genera, is that of the herpes virus in African and Asian elephants, benign in the former and fatal in the latter.

Prior to flooding of Lake Kariba on the Zambesi River, 6,000 people were moved to Lusitu where a violent epidemic erupted in 1959 in the second rainy season after occupation, killing 51 young women and children variously attributed to poisoning or witchcraft (Howarth 1961), but the origin was not determined although it seemed to be an unknown poison. With the influx of this large number of people a population threshold level for a malignant arbovirus may have been reached. Women and children are the ones who traditionally draw water and are the most likely to come into contact with mosquito vectors, although this was apparently at pumps but mosquitoes would be attracted to the damp earth and puddles of spillage. That young women and children only succumbed suggests prior exposure to a milder strain which had produced an immunity in older persons. The epidemic ceased with abandonment of the new villages.

It was observed in the 1870s in the Luanda hinterland that Africans often suffered grave consequences from malaria when they moved from one area to another, but this may have been the result of labour to which they were unaccustomed lowering resistance to an already present infection. Bérenger-Féraud (1874) believed the insusceptibility of Africans to yellow fever was dependent upon their remaining in the regions of their birth, implying a species-specific immunity. But much of the increased mortality may be attributable to either poor nourishment and conditions, in the case of slaves awaiting transportation, or to being required to work excessively, allowing latent infections to take the upper hand. Furthermore, a debilitated host is advantageous for parasite transmission as the immune system is weakened. When the slave trade stopped the formerly enslaved populations began to increase which may have been related to less forced labour. The main traditional response to a short life expectancy which disease entailed was a high birth rate. Adoption of modern medicine has resulted in the prolongation of life expectancy

without a fall in birth rate, thus creating overpopulation and the threat of sudden large-scale mortality.

At Kulubarti in northern Sudan typically childhood bone lesions in skulls from two cemeteries dating A.D. 500–1500+ are suggestive of malnutrition and parasitism. Porotic hyperostosis or *cribra orbitalia* found in 45% of skulls peaks in frequency at ages four to six, remaining greater than 70% up to age 13 and then averaging 30% from age 17 onward. Thus whatever caused the bone changes greatly reduced survival to maturity. Only once teenage years were passed were those affected no longer at a relative disadvantage. These were however township populations and not rural, but it indicates how urban populations were limited. Where there was water to provide for concentrated crop production, then there were diseases also, such as malaria and schistosomiasis.

In order to illustrate their ubiquity, in this and the following chapters known histories of some major epidemic diseases affecting Africa are outlined, as well as reference to their history outside of Africa where this occurs. But perhaps it is appropriate to be reminded here of one sixteenth century writer's caution, "The reliance that can be placed upon historical recording is in inverse ratio to the time that has elapsed since the events took place".

25.2 Influenza

Humans are infected by three related influenza viruses, termed A, B, and C, from the family Orthomyxoviridae. Influenza C viruses are relatively harmless, while B are not normally life-threatening, but A, of which aquatic birds are the natural reservoir, cause serious epidemics. Particular serotypes of influenza A infect many other mammals, particularly pigs and horses. Hippocrates appeared to describe influenza epidemics in 412 B.C. and later Livy mentioned an apparent epidemic in Syracuse, Sicily, in 212 B.C. which attacked the Roman army and the Carthaginian defenders. The infection known in Europe from mediaeval times, an English prelate travelling to Italy observed in December 1173, "In those days the whole world was infected by a nebulous corruption of the air, causing catarrh of the stomach and a general cough, to the detriment of all and the death of many" (de Diceto 1652). In 1557–1558 and 1678–1682 pandemics overran all Europe. Several others followed and that of 1775 witnessed by Gregory was considered to have broken out somewhere on the north and west coast of Africa, spreading from there north into Europe and eastward to Egypt, Arabia, the Middle East, Asia Minor, India, and the whole of China, returning westward north through Russia and all over Europe again in 1782 (Christison 1885–1886). But the association with Africa was probably simply inferred because the pandemic moved from south to north, thus Creighton (1891–1894) wrote, "Throughout the rest of the eighteenth century there were numerous and varied experiences of influenza ... coming up from the south as if from Africa, or from the east as if from Central Asia ...". In an outbreak in 1837 black sailors arriving at Liverpool from the West African coast contracted it upon

arrival in port, and they would no doubt have carried infection back with them. In 1863 a French frigate encountered no cases of influenza at Gorée but 4 days out an epidemic erupted on board, although another vessel leaving Gorée 2 days earlier was unaffected.

In Ethiopia following famine caused by locusts in 1747 and 1748, which caused great mortality through starvation, the survivors were then assailed by an epidemic of influenza. According to the chronicler not one was not affected and many died suddenly without being ill even for 1 day (Guidi 1912). There had been a previous outbreak apparently of a type of influenza in 1685. Often underrated because the symptoms of most strains are not life-threatening, the Spanish influenza pandemic reportedly killed 40,000 people in Addis Ababa alone, but was greater in the countryside where tens of thousands died or were debilitated, the infection persisting in the north-east for over a year, while untended cattle severely damaged crops.

It killed 1,072 people in Sierra Leone in 5 weeks beginning in mid-August 1918 when a ship with infected sailors docked in the port. It then spread to Gambia, Senegal, and other West African countries. In Ashanti it killed a known 9,000 people, estimated at 2% of the population; and at least 12,500 people, an estimated 3.2% of the population, throughout Nigeria. Moir (1891) reported an epidemic at the mission station at Blantyre in Malawi in 1890 but no deaths. An epidemic occurred in the Congo basin and Togo in 1892 but was not reported in Cameroun (Plehn 1897).

In 1919–1920 the pandemic is estimated to have killed 50,000–80,000 people in Tanzania (Anon. 1920). After a lull a fresh wave swept the country in 1921 missing only Lake Victoria and the Usambara, Uluguru, and Ulanga highlands. Rungwe District escaped the first pandemic only to experience mortalities of up to 28% in the new wave.

Influenza is remarkable for its unavailing persistence for more than 2,000 years, still mutating into new and virulent forms. Creighton (1891–1894) considered "in the theory of influenza, the first requisite is an explanation of its phenomenal uprisings and wave-like propagation at longer or shorter intervals, during a period of many centuries". Where there is very high mortality of the host, the disease has a low basic reproductive ratio, that is, the number of secondary cases produced by an infectious individual in a totally susceptible population, and cannot spread. A low host mortality allows the pathogen to spread further and has little effect on population size. By contrast it is the intermediate state which has the most effect and could lead to population extinctions (Keeling and Rohani 2008).

25.3 The "New" Diseases

"Emerging diseases" are defined as those of which the geographical range, host range, or prevalence of the disease, have been increasing. These are twice as likely to be of zoonotic origin as other diseases and to have the broadest host ranges.

On a scale of one to ten most emerging diseases are attributed to changes in land use or agricultural practices and least to climate change (Woolhouse and Gowtage-Sequeria 2005). "New" diseases, usually related to viruses, are probably existing diseases only recently identified, or becoming more common due to changes in contact.[2] In Angola's Kasanje district a disastrous epidemic in 1690 of "swelling" *inchação* which the population of the capital fled into the forest to escape, has never been identified (Miller 1982); but sleeping sickness was sometimes referred to as "swelling disease" due to enlarged cervical glands. Rarely is there disease with both successful invasion and persistence within a new host species, by far the majority of pathogens which invade a new host species exhibit little or no onward transmission. Viral change seems more important in adaptation to take advantage of ecological niches that open up through shifts in the environment and through travel and transport of reservoirs and vectors, rather than from mutation (Peters 2008).

O'nyong nyong, first identified in Uganda in 1959, believed to result from transfer of an arbovirus from monkeys to humans by *Anopheles gambiæ* and *A. funestus* mosquitoes, was probably not new. It spread rapidly and widely but its effects were mild and recovery was quick providing immunity. Failing to establish itself as an endemic human infection it suddenly disappeared, to remain restricted to the treetops where it was believed to be enzootic (Fiennes 1967). Towards the end of 1960 it was diagnosed in several parts of Tanzania, although there were regional variations in the symptoms, and spread rapidly across Lake Province affecting nearly everybody. A similar condition was reported from Liuli at Lake Malawi but thought to be a similar virus that had spread from Mozambique or Malawi, while another infection in the Uluguru Mountains named *bunduga* was thought to have been present in the area for much longer than was consistent with the appearance of O'nyong nyong (Clyde 1962).

RNA viruses, examples of which include HIV, Ebola, and Marburg, have very high nucleotide substitution rates and thus the potential to evolve very rapidly. This implies they may be especially able to adapt to new host species and greatly increase the likelihood of successfully invading human populations. Pathogens that are already capable of infecting a broad taxonomic range of non-human hosts are the most likely to turn up in humans.

Outbreaks of "new" viruses have not been confined to Africa. Nipah, a Paramyxovirus distantly allied to measles, recently erupted in Malaysia; and Hendra, also a Paramyxovirus, in Australia. Both have fruit bats *Pteropus* spp. as their natural reservoir hosts. The former occurred with fatal effect on humans via pigs, the second primarily infected horses but caused some human deaths also. The conclusion drawn from these emerging infections is that their causes are ecological rather than evolutionary, changes in habitats and human population densities causing spillovers from natural cycles between wild hosts. Illustrative of the effects of man-made habitat changes, in Kibale NP Uganda, red-tailed monkeys *Cercopithecus ascanius* in logged forest, logging having removed about half of the trees including primate food trees in the late 1960s, were found to have both a higher intensity of infection and more macroparasite species/individual (*Entamoeba coli*, *E. histolytica*, *Iodameoba buetschlii*, *Trichuris* spp., *Oesophagostomum spp.,*

Sytrongyloides fulleborni, *Streptopharagus* spp., *Chilomastix mesnili*, *Giardia lamblia*, and *Dicrocoeliid* sp.) than those in unlogged forest. But the effect was not shared by red colobus *Piliocolobus badius* and black-and-white colobus *C. guereza* living in the same area and sharing most of the parasite fauna, these species showing no differences (Gillespie et al. 2005). The red-tail is frugivorous and the colobus monkeys folivorous and it was suggested the guenon had a larger feeding range in the logged forest thus encountering patches with high densities of infective parasite stages more frequently than in unlogged forest, but it may have been suffering dietary stress also making it more susceptible to infection. While the red-tail monkey was declining in numbers in logged forest the red colobus was recovering its numbers and black-and-white colobus increasing. The red-tail had a density in undisturbed forest more than eight times that in logged forest, the density of red colobus was almost 1.7 times greater, while that of black-and-white colobus was 4.6 times greater in logged forest. It is easy to see how this kind of man-induced changes could lead to changes in disease ecology, affecting not only the animals themselves but also transmission of "new" diseases to man.

The popularly regarded "new" diseases such as Ebola virus and HIV emerging in Africa are probably ancient diseases erupting as a consequence of increased human contact, or they have not been identified previously as a cause of death. Ebola is regarded as having separated into subtypes thousands of years ago, while Lassa strains, a lethal viral disease causing haemorrhagic fever identified in eastern Nigeria in 1969 carried by rodents, particularly the widely distributed multimammate rat *M. natalensis* (*huberti*), show clear phylogenetic divergence across West Africa, indicative of age.

The culex mosquito-transmitted West Nile arbovirus, a flavivirus allied to yellow fever, has been identified in monkeys in Uganda and in 18 large mammals in CAR ranging from grey duiker to elephant (Thal 1972). It is transmitted from the rodent *Acomys cahirinus* also. Isolated from a woman in West Nile region first in 1937, subsequent serological surveys found antibodies in indigenous populations in DR Congo, Sudan, Uganda, and Kenya. In Uganda's West Nile and Madi districts almost 31% of people (n = 121) tested positive for exposure to the virus. It was found that 43% (n = 221) of birds sampled in Uganda had been exposed to it, and introduced or re-introduced by migratory birds its range extends from Portugal, France, across Europe to Austria, including countries bordering the Mediterranean, Egypt, Israel, and Cyprus, to the former USSR. It is found in Asia also, was identified in New York in 1999 and again in 2000, where it became established as a bird virus and killed horses, countless birds, and several people. Regarded as a parasite of birds believed carried to New York from Israel by an infected air passenger, it spread throughout America in the space of 4 years, infection of humans, equines, and dogs, believed to represent an end-point in transmission. In addition to isolations from mosquitoes the virus has been found in ixodid ticks in which it is capable of replicating, *A. variegatum* and *Rhipicephalus mushamae* in Africa, and from both ixodid and argasid ticks in the former USSR. On islands in the Caspian Sea it was found in *Ornithodoros capensis* in herring-gull nesting sites

where mosquitoes are completely absent, with transmission between argasid ticks and birds.

Had West Nile fever occurred in America or elsewhere a century or more ago it would not have been identified because the techniques for doing so were not available. In 1973 more than 28 "new" disease-causing microbes were identified (Olshansky et al. 1997). Zinssner (1935) noted that "new" disease need not be conceived as the acquisition *de novo* of forms of parasitism that have not previously existed. While the process was probably continuing it was too gradual to be traceable from an established disease to its ultimate origin. There were two chief sources of new diseases within historical periods: the modifications of parasites already existing in man by gradual adaptive changes in their mutual relations, and invasion of man by parasites well established in the animal kingdom by new contacts with animals and insects to which man was not previously exposed. Zinssner considered many diseases existed in nature already which man had not hitherto acquired only because of lack of opportunity, quoting the chlamydian bird disease psittacosis as an example, found in parrots and other psittacine birds, particularly from South America and Australia, highly infectious to man but unlikely to infect him unless infected birds are kept as pets. But rather than new contacts, probably increased frequency of contacts enables the parasite to hit on a host that does not resist it, or only partially. Such a disease is probably Ebola, which began an epidemic in DR Congo and Sudan in 1979.

25.4 Rickettsias

Many rickettsias are ixodid tick borne diseases, "tick fever" occurring both in the Old, including Australia, and New Worlds; but epidemic typhus is transmitted to man by the body louse *Pediculus humanis corporis*, formerly thought to be the sole cycle of maintenance but epidemic typhus can be transmitted by ticks also and occurs in all countries. Human mortality can reach 60% in epidemic typhus, and in central Africa and Zimbabwe exposure may be as high as 45%, while in Sierra Leone and Ivory Coast 7% of the population in some areas has been found to have been exposed to it. The major endemic focus is in the highlands of Ethiopia where an annual epidemic coincides with the influence of the cool rainy season on human behaviour. Infection has been found also in flying squirrels (Weatherall et al. 1987), but Thal's results (1972) show that it is clearly much more widely spread in the animal kingdom. It can recur in humans years after an original attack.

Murine or endemic typhus, found in both black and brown rats, and mice, is transmitted to man by the rat flea *Xenopsylla cheopis* and can cause some 2% mortality. It is probably present throughout most of coastal Africa and inland where the rats are present together with *X. cheopis*. Antibodies may be found in up to 20% of a human population.

Fatal cases are unusual in Q (=query) fever, which occurs worldwide. It is transmitted by ticks and found in small mammals, cattle, sheep, and goats, but

the principal means of transmission to man is by inhalation of dried infective material. Rickettsias are passed transovarially in ticks so larval ticks provide an infective stage. In East Africa and southern Ethiopia *Amblyomma hebræum*, *R. appendiculatus*, *B. decoloratus*, and the dog tick *H. leachi*, are known vectors of *Rickettsia conorii*, which has been isolated from the laminate-toothed rat *Otomys angoniensis* and striped grass mouse *Lemniscomys striatus* (Heisch et al. 1957), *Otomys irroratus*, and black rat in South Africa, and a large number of rodent species in Kenya including black rat, *A. niloticus*, *M. natalensis*, *Aethomys kaiseri*, *Lophuromys flavopunctatus*, and *L. striatus* (Gratz 1997).

In Rwanda a rickettsia has been found transmitted by *O. moubata*. In March 1893, Hinde (1897) had an epidemic of fatal "influenza" in camp in Kasongo, southern DR Congo, considered similar to tick fever. The sick people attributed their illness to the bite of the soft tick *kimputu* (*O. moubata*), and although Hinde lost some men from the disease he believed the tick was harmless and the people had died from superstition. This opinion was shared by many other Europeans in the region who considered the people were simply malingering when they attributed illness to the tick. Torday (1913) recorded in 1900 in Kasongo the Africans "pretended that if they were bitten by a certain bug of this name [*kimputu*] they fell ill, and that the only thing left for them to do was to die. Now this was attributed largely to auto-suggestion, and by pointing out how ridiculous it was to suppose that this one little parasite could kill such big men, it was hoped that people would fight instead of "giving in". Monsieur Malfeyt ... tried to use his influence for this purpose, but with little good result ...". Torday himself was bitten and seriously ill for several months. Krapf (1849) did not have such prejudices, on his way to Usambara in 1848 simply reporting that two of his bearers were seized with fever "in consequence of having been bitten by a pasi [tick] in the lower country". In Uganda, where the tick was known as *bibo*, Christy in 1902 found the disease dreaded by the Africans, particularly in Toro, although it was not fatal and the majority was immune. He later found the tick fairly common in Uganda, Rwanda, and at Wadelai on the Nile. Some specimens he found at Fort Portal had been carried in bags of salt from Lake Katwe, a district where the tick was abundant (Christy 1903).

25.4.1 Tropical Typhus

Erupting in Burkina Faso in 1946, Congolese Red Fever, Congo Red River fever, or Tropical typhus, seemed to create symptoms similar to epidemic typhus. Described first in 1927 among Europeans in the Congo Republic (Lefrou 1927) and studied in CAR from 1938 to 1940, it occurred each year in CAR in the savannah belt in the dry season between November and April, always some 15 days after the grass had been fired. Known in Banda as *bakandjia* it developed in bursts, striking large numbers of people quickly and strongly, infecting everyone and passing from one to another with an annual mortality across the country of 2,000–3,000.[3] It was

characterized by massive pulmonary congestion and sometimes spitting of blood, differing in one or more symptoms from all other known fevers, the closest appearing to be Malaysian scrub typhus. It affected only those people hunting rats and mice capturing them in burrows which were exposed after fire had cleared the ground, not occurring in forest areas. The periodic epidemic "Bougbous sickness", named after the tribe in which it occurred in the Lower Kotto area of eastern CAR, was considered to be the same disease. In 1940 grass burning was delayed 2 months and outbreak of the disease was delayed for the same period. It occurred only where hunting rodents took place and did not affect fishermen. Among the Bougbous only women hunted rats and for every ten persons affected, seven to eight were women. Mortality was high (Le Gac 1946). The same disease was found in Burkina Faso among the Mossi in 1941, after burning when the hunting and trapping of rats was taking place. Le Gac (1946a) concluded it was endemic, carried by rodents and transmitted to man by the rat flea *X. cheopis*, discounting lice, ticks, and other invertebrates, as not fitting the pattern of outbreaks. However Gaud (1949) considered the dog tick *R. s. sanguineus* the natural vector. Most favoured species of rats were the "red rat" *A. niloticus* (=*Mus rufinus*), *Pelomys fallax* (=*M. golunda campanae*), multimammate rat (= *M. rattus*), striped grass mouse *L. striatus* (= *M. musculus*), and the very common giant rat. People termed the outbreak period the "month of doctors", and the disease "hunting sickness", making the connection between burning and hunting, and man and an animal reservoir.

Baoulé legend had it that in the rainy season the spirits of the bush sent their cattle to pasture in the savannahs, and to punish men for burning the savannahs each year and thus disturbing their cattle they poisoned the rats. Those rats which were captured transmitted to the hunters *ko-houlé* or "spitting blood". Among certain tribes the "red rat" was held most responsible and its consumption forbidden, but this may have been simply because its reddish colour was equated with the colour of blood.

In December 1941, two missionaries who had accompanied natives on a rat hunt after grass burning were hospitalized in Ouagadougou. Cases among Europeans also occurred at Ouagadougou and at Pô always about 15 days after the grass was fired. It was considered to run a shorter and more benign course in children.

Le Gac considered the fever reported by Gordon and Davey (1936) among several people hospitalized in Freetown, Sierra Leone, to be the same disease, but this was not a haemorrhagic fever. Gordon and Davey likened it to reports from West Africa and DR Congo of epidemics of unknown origin termed "pseudo-dengue" or "red congo fever", but considered the symptoms of all of these diseases were not only similar to each other but also to cases described from Ghana and Nigeria which resembled tropical typhus found in Zimbabwe. But Jadin (1944) considered the diseases described by numerous doctors in West Africa since 1921 were not similar. Existing the length of the Zaïre and Ubangi rivers "red congo fever" was a type of eruptive rodent typhus caused by *Rickettsia prowazeki var. mooseri*, transmitted principally by the flea *X. cheopis*, but possibly by the louse *Pediculus vestimenti* also. It was suggested (Fuller 1974) this might have been Lassa fever, but Manson-Bahr (1963) upheld Jadin's conclusion that it was an

eruptive form of Q fever. It is now classed as a rickettsial fever caused by *C. burneti* which produces pneumonia-like symptoms. In 1950, 34.8% of the herding Bororo population sampled (n = 89) in CAR had been exposed to *C. burneti*, reaching 62.5% (n = 8) in herdsmen, contact with cattle and meat representing a serious risk of infection. A later study showed an average of 69% of persons had been exposed. Further studies showed the significance of domestic animals as a source of infection.

The disease reported in 1921 in CAR by Clapier, which he termed similar to dengue, differed from Congolese Red Fever in that it was only a debilitating eruptive fever which did not cause mortality and its occurrence in children gave adult immunity. He saw only a dozen cases in Bangui which occurred throughout the year in both wet and dry seasons, and far from occurring there only, Dr. Benjamin had noted it since a long time at Ndélé in the north of the country where he termed it "dengue". Kerneis had identified it at Brazzaville where it was termed *likoutombo*. At the same time it was reported in Nigeria by Davies and Johnson, considered to resemble dengue fever. A similar infection had been reported from the Sudan, and there had been cases at Libenge, DR Congo, and in 1914 at Dongou on the Oubangui River, the fever being widespread in central Africa in isolated localities. Perhaps this was chikungunya. Red Congo fever has been identified as murine typhus.

25.5 Spirochætes

Spirochætes, formerly regarded as protozoa, are now regarded as bacteria. The spirochæte *Borrelia duttoni* of "relapsing fever" was seen first in the blood of a Ugandan in 1903, and Dutton and Todd (1905) demonstrated transmission by *O. moubata* in Manyema, describing transovarial transmission in the tick also. At the same time Koch (1906) in Tanzania also demonstrated transovarial transmission and the development cycle of the spirochætes in the tick. No animal reservoir has been identified.

A deadly epidemic swept across equatorial Africa from upper Guinea in 1921 thought to have been introduced by soldiers from Morocco and Algeria, spreading down the Niger invading Dori in 1922 causing 80,000–100,000 deaths. In 1924 it killed at least 20,000 people in upper Senegal and Burkina Faso spreading in 1925 to the Lake Chad region, and in 1927 to western Darfur where 10,000 people died of a population of 40,000. This is thought to have been louse-born typhus spread only by the louse, rather than tick-borne relapsing fever, although spirochætes have been found in rodents in western Africa and southern DR Congo.

It was noted in 1928 that Africans in Malawi in tick-infested areas seemed to possess a tolerance to infection and possible immunity exhibiting only slight symptoms despite heavy spirochæte infection, although visitors to the area reacted strongly to low infections. Residents were aware of this immunity which was lost if they left the area for any length of time, so some took ticks with them when

travelling allowing the ticks to feed periodically in order to maintain immunity (Scott 1939).

First identified in America in 1975 and South Africa in 1989, cases now having been reported from both east and west Africa, is the spirochæte disease *Borrelia burgdorferi*, or Lyme disease, which affects both people and animals, especially domestic animals. The vector is an ixodid tick. It has spread widely recently in Asia and Europe, including Britain where deer appear to be the reservoir, but rodents are known to be an important reservoir elsewhere although in Africa the reservoir has yet to be identified. On Madeira both black and brown rats are reservoirs.

25.6 Viral Diseases

25.6.1 Family Retroviridae

25.6.1.1 HIV and AIDS

In the 1990s it was estimated 500,000 people would be dying of AIDs each year in Africa by the end of the twentieth century, but at the end of 2005 it was estimated 2 million died that year and 24.5 million were infected. AIDS was found first in groups of people living on outer Japanese islands and later clustered in populations there, the Caribbean, Surinam, and Italy. Yet the original source of the AIDS pandemic has been traced back to the central African chimpanzee *Pan troglodytes troglodytes* in Cameroun, hunters becoming exposed during killing and butchering infected beasts. Climate change, deforestation, and the widespread trade in and consumption of, bush meat, provide increasing facilitation for the transfer to man of such diseases previously locked into a forest cycle. As Scott and Duncan (2001) expressed it, the virus had probably been living harmlessly in chimpanzees for centuries, but more likely millennia, transferring to humans throughout history. It is known to have jumped from apes to humans on at least seven separate occasions but the socio-economic changes in Africa provided the particular circumstances leading to the spread of HIV and AIDS, providing one of the rare cases of an accidental infection establishing itself in the human population and which is still in the initial epidemic phase in many parts of the world.

Among theories to explain its spread out of Africa one is that it was carried by African slaves, another by Portuguese sailors in the sixteenth century (Fleming 1984, Garrett 1984). By the 1980s infection was widespread in Africa, in Kenya 80% of the nomadic Turkana in the north-east were found infected.

The two closely-related viruses HIV-1 and HIV-2, members of the Family Retroviridae, cause AIDS, Acquired Immune Deficiency Syndrome, which is the destruction of the body's immune system. Neither actually causes death itself but leaves the body open to other life-threatening infections and illustrates just how all-pervading the latter are without an immune system to block them. In Africa most

AIDS-related deaths are caused by the bacterium *Salmonella typhimurium*, but HIV-positive people are also more likely to develop TB when newly infected or re-infected with *M. tuberculosis* with which about one third of people in Sub-Saharan Africa are latently infected.

Now found in India and other countries in the world, HIV-2 was isolated only in 1985 in West Africa where it is common but takes much longer to develop, with an incubation period of 8–10 years compared to HIV-1s two years or so, and has not spread so widely nor so rapidly. However in baboons the disease acts swiftly, producing symptoms of secondary infections in 18 months. Similar viruses termed Simian Immunodeficiency Viruses, or SIV, have now been isolated from at least 26 species of African primates, particularly prevalent among green monkeys *Cercopithecus* sp. (half of all tested) and so common it probably does little harm, but many of the monkeys are hunted and consumed by man. In some areas more than 50% of monkeys may be infected. In chimpanzee a strain close to HIV-1 has been found. So far SIVs have not been found in Asian monkeys, which are susceptible to them, suggesting simian viruses most likely originated in Africa. SIVs are the closest relatives to HIV-2 and infect sooty mangabeys *Cercocebus atys* across their range in West Africa, representing the natural reservoir of these viruses and the source of infection for humans in West Africa. HIV-2 strains fall into eight distinct groups labelled A to H, and the closest sooty mangabey SIV relatives of groups A and B have been found in Ivory Coast, suggesting cross-species transmission giving rise to the human viruses occurred in the easternmost part of the sooty mangabey's range (Santiago et al. 2005).

The closest relatives of HIV-1 are found in chimpanzee but in two of the four subspecies only, *P. t. troglodytes* from west central Africa comprising southern Cameroun, Gabon, and neighbouring areas; and the eastern chimpanzee *P. t. schweinfurthii* from central Africa north of the Zaïre river in DR Congo and adjacent countries north and east. The western *P. t. verus* from west Africa, and Nigerian *P. t. vellerosus* from Nigeria and northern Cameroun, do not appear infected. Strains of chimpanzee SIV from the central and eastern races form two distinct subspecies-specific clades, and HIV-1 strains lie within the clade from central chimpanzees indicating the origin of HIV-1 was in west central Africa. Sampling across this region has shown the prevalence of SIV infection in some chimpanzee groups to be as high as 30%. Strains from the south-east corner and south central Cameroun point to these regions as the locations of chimpanzee to human transmissions. Strains of HIV-1 group O have been found now in gorillas, most likely infected from chimpanzees, but it is not clear if group O-like viruses were transmitted independently from chimpanzees to humans, or whether gorillas were the source of the human viruses (Van Heuverswyn et al. 2006). The basal rate of evolution of HIV-1 is more than one million times faster than that of its host. The last common ancestor of group M has been placed at about 1930, indicating chimpanzee to human transmission must have occurred before then. Group M sequences had been diversifying for about 75 years, rapidly evolving and recombining (Sharp et al. 2007). The greatest diversity of group M strains has been found in Kinshasha, suggesting that is where the epidemic multiplied first.

Evolutionarily HIV viruses 1 and 2 groups are far apart from the two main groups of simian viruses, one of which comes from the African green, vervet, or savannah, monkeys, *C. aethiops pygerythrus*; the other from the related Syke's monkey of East Africa (now gentle monkey *C. nictitans mitis*); and a mandrill baboon *Mandrillus sphinx*, which is an extreme west African species. The SIV isolated from chimpanzee is some distance from the two major types of HIV-1 and if it invaded chimpanzees from humans it must have done so a relatively long time ago. A large proportion of monkeys in the wild is infected but the monkeys show no apparent ill effects, although perhaps we have insufficient knowledge of their natural demography to conclude this. Although not recorded until 1959 in DR Congo, HIV-1 virus may have been infecting small numbers of humans in Africa long before this, its symptoms possibly confused with those of sleeping sickness, until social upheavals on a grand scale disturbed its equilibrium. It has been found in stored blood samples of Africans from the 1950s but did not spread significantly between humans until the 1970s. Examination of stored blood collected in 1973 from schoolchildren in Uganda's West Nile region showed that 66% had been infected nearly a decade before AIDS was discovered, but that found in 1959 in a man in England, who may have picked it up in Morocco, cannot now be confirmed definitely (Wills 1996). In 2004 it was reported people in Cameroun were showing up with symptoms of HIV but testing negative for both virus and its primate equivalent SIV. This suggests new strains of an HIV-like virus are circulating in wild animals and infecting people who eat them. However, examination of one group which would be expected to be the most exposed to such infection, the Pygmies inhabiting the rain forest of Cameroun, Congo Republic, and CAR, proved negative for HIV in the 1970s, and again in the 1980s.

Examination of HIV-1 indicated it was mutating at an overall rate of 1%/year, which if constant since its emergence suggested a common HIV ancestor existed perhaps around 1962. After mutating in a single direction for 10 years at the beginning of the 1970s it had suddenly spread out, producing six distinct lineages or clades. Of these, type A was found in people in central Africa and India, presumably carried to the latter country by Indians from Africa. Type B was the only clade found in North America, but occurred also in Europe, Brazil, southern Thailand, and several parts of Africa. The most lethal clade, D, was found exclusively in the Lake Victoria region of Rwanda, Uganda, and Tanzania. Other studies supported the suggestion of a sudden change in central Africa around 1975 (Garrett 1984). But explosion into a global pandemic in 2 years from an obscure virus that infected less than 1%, for example, of rural Yambuku and N'zara populations in DR Congo in 1976, and perhaps less than 0.1% of isolated populations of Europe or North America, was due solely to human behaviour.

It was predicted in 1991 that HIV would reverse the size of population growth rates in Africa over timescales of a few to many decades, being likely to outstrip the explosive population growth, and some countries might actually experience negative growth (Anderson et al. 1991). But by 2010 this was still far from being the case.

25.6.2 Family Herpesviridae

25.6.2.1 Herpes Viruses

In 1965 a researcher died apparently of B-virus of monkeys contracted from the bite of a vervet monkey *C. aethiops* in Uganda, a virus closely allied to the *Herpesvirus simplex* of the common cold sore in man. The last common ancestor of apes and Old World monkeys is thought to have lived around 25 Mya and under the host-virus-co-speciation hypothesis (Sharp et al. 2007) was infected with the last common ancestor of the closely related herpes viruses infecting humans and Old World monkeys today. Which is why humans are now infected by numerous different types of herpes viruses. Monkeypox is an African zoonotic disease harboured by flying tree squirrels which can spread rarely to humans and is known to have been contracted from eating infected red colobus monkeys. It has spread recently in the United States.

25.7 Arboviruses

Investigations into yellow fever in Uganda in the 1940s revealed a number of other arboviruses, isolated either from mosquitoes or bait monkeys: Semliki Forest, Bunyamwera, Mengo, Ntaya, Uganda S, and Zika. RVF was isolated on a number of occasions also. Each virus, other than RVF, was a distinct entity, only Mengo identical with those of the encephalomyocarditis (damaging brain and heart muscle) group. At Kumba in Cameroun a virus identical with Semliki Forest virus was isolated. More than 150 have now been isolated in countries from Russia to Brazil, most of them infectious to man and the majority transmitted by mosquitoes. Many monkeys are primary hosts but other mammals and many birds carry them also.

An 18 year observation of 350 Pygmies south of Bokoka, Lower Lobaye, in CAR, revealed antibodies to the following (as per cent): Sindbis (4.7); chikungunya (9.4); Semliki Forest (13.3); Bunyamwera (10.7); West Nile (3.4); Uganda S (7.0); Zika (0.8) and yellow fever (10.9) (Sureau in Desowitz 1978). Whether in man or animals a high presence of antibodies may indicate simply that infection has occurred early in life and recovery has taken place, or that a population has recently been exposed to a highly virulent disease and only the survivors are encountered.

In northern Sudan several arboviruses have been associated with outbreaks of human disease, namely RVF, yellow fever, West Nile, chikungunya, Sindbis, dengue 1 and 2, Sandfly Fever Sicilian, and Sandfly Fever Naples. Antibodies indicating prior exposure in people increase with age for yellow fever and West Nile suggesting infrequent epidemics and not continuous exposure (Watts et al. 1994). Several arboviruses are endemic in the Sudan, but although outbreaks of febrile illness coincide with high populations of phlebotomine sandflies there is no

evidence they are the vectors. Arbovirus infections, especially outbreaks of Sandfly Fever Naples, had not been demonstrated previously in northern Sudan.

25.7.1 Family Togaviridae

25.7.1.1 Chikungunya

Chikungunya, a non-fatal infection causing joint pains, was isolated first in 1953 from patients and mosquitoes in an epidemic on the Makonde Plateau, Tanzania, believed introduced recently to this treeless plateau from the surrounding forested region by *Ae. aegypti* mosquitoes. Pantropical in occurrence it has been found since to occur widely in Africa as well as India and Southeast Asia. Whereas it is not known to be pathogenic in Africa, in Asia it may cause haemorrhagic fever. Transmission is by *Ae. africanus* and *Ae. aegypti*. Weatherall et al. (1987) state no vertebrate host other than humans has been discovered, although evidence has been found that monkeys might be a maintenance host in Africa and Debbie (1970) listed it for several animals in Kenya and elephant in Tanzania (Table 23.3), but it was not isolated from elephant in CAR. Infection was found in a golden sparrow *Passer luteus* near Lake Chad (and see other examples in Chap. 23), but the forest host in Tanzania and the reason for the outbreak remain unknown. It was found also in bed bugs in the houses of infected persons.

The virus has been isolated also from the mosquitoes *Ae. cordillieri*, *Ae. furcifer*, *Ae. luteocephalus*, *Ae. otok*, *Ae. taylori*, and *Mansonia africana*, but *Anopheles albimanus* is the only known anopheline mosquito to transmit it. In 1956 it was found in South Africa and in 2006 on Réunion Island. Human infections occur primarily in the rainy seasons when mosquitoes are most numerous, surveys have shown that from 20% to 90% of a population may be immune indicating exposure to the virus. Carey (1971) considered the disease originally described as dengue in East Africa, which was linked to India, Java, and the West Indies, by trade and slaving, was in fact chikungunya.

25.7.1.2 O'nyong Nyong

O'nyong nyong, which in 1959 caused a major epidemic beginning in Acholi, Uganda, spreading to Kenya, Tanzania, and Malawi, affected an estimated two million people in Uganda and ten million in total. It resembles closely chikungunya but is transmitted by the anopheline mosquitoes *Anopheles funestus* and *An. gambiae*. Having disappeared apparently for 20 years it resurfaced in western Kenya in 1979 where young children were found to have been exposed to it. Primate and other vertebrate hosts are as yet unknown. In north-east DR Congo adjacent to Arua in Uganda it is believed to have been confused with measles, and some workers consider it impossible to distinguish from chikungunya.

25.7.2 Family Flaviviridae

25.7.2.1 Dengue

Dengue is a rarely fatal arbovirus of the genus Flavivirus but considered as one of the most important emerging pathogens (Sharp et al. 2007), one of thirteen viruses that can cause haemorrhagic fever in humans. Closely related to yellow fever and West Nile viruses, it is the most widespread in the world, occurring in almost every country between the Tropics although its extent in Africa is unknown; West Nile, chikungunya, Sindbis, Sandfly fever, and RVF, often being indistinguishable clinically. The vector in Africa is *Ae. aegypti*.

Aubrey (1729), who resided for many years in Guinea, described in his book *The Sea Surgeon or the Guinea Man's Vade Mecum*, what Creighton (1891–1894) considers was quite clearly long after described in the West Indies as dengue, Aubrey giving a series of case histories from the ship *Peterborough* in 1717, stating it affected both Negroes and white men, spreading by contagion, but believed its cause was the poisonous nature of the miasmata. It was reported next in 1779 at Batavia and in Cairo, which Carey (1971) suggests was chikungunya. Christie (1881) suggested there had been three epidemics in the eastern hemisphere before his time, in 1779–1784, known on the east African coast in 1780 which he considered by no means certain to refer to dengue basing his observation on its reported presence in Cairo at the time; followed by an outbreak in 1823–1829 first appearing in 1823 on Zanzibar or somewhere on the east African coast under the name *dinga* or *dyenga*, spreading to India and apparently carried with slaves to Havana, where an extensive outbreak in 1827–1828 in New Orleans was referred to as "dengue, danga or dandy fever" (Dumaresq 1828). The third epidemic appeared in Zanzibar in July 1870. Hadramut Arabs in Zanzibar said the disease was familiar in their own country while old residents said there had been an epidemic 48–49 years before. Christie received no reports of it inland, the disease diffusing along the lines of intercourse reaching the Red Sea and Aden in early 1871 when it had almost died out in Zanzibar, to finally become extinct in Cairo in 1880. Bombay was infected directly from Zanzibar, the disease spreading over the Indian subcontinent. It was termed *dinga* or *dyenga* again but also *dengue*. Christie noted the name given to it in Kiswahili in the 1823 epidemic was *kidinga pepo*, which he translated into "a disease characterized by a sudden cramp-like seizure, caused by an evil spirit". He could find no evidence of the disease having been introduced into Zanzibar from without, it had appeared at the height of the south-west monsoon and for at least 3 months before dhow communication from the north had been impossible, leading him to the reluctant conclusion it had arisen spontaneously. Only infrequent epidemics were reported until the middle of the twentieth century, but within the past 50–60 years it has spread throughout the tropics. An epidemic at Durban in 1927 had 40,000 cases, some with haemorrhagic complications.

Its origin appears to have been in non-human primates in South-east Asia. Transition to infection of humans involved a switch both of vector and of

geographic niche, as *Ae. aegypti* is peri-domestic, found primarily around human settlements, while sylvatic forms are transmitted among monkeys by forest canopy mosquitoes. Sylvatic strains of one of the four known serotypes, DENV-2, have been found in Africa in red monkey *Cercopithecus* (=*Erythrocebus*) *patas* confirming the existence of a sylvatic form already presumed in Burkina Faso and Ivory Coast. It is also transmitted transovarially by the mosquito although the role of this in maintaining the virus in the wild is not known. All four serotypes infect humans across Africa and the Americas. Preliminary findings suggest human strains originated only 100–300 years ago, and characterization of further sylvatic strains may find others more closely related to the human viruses reducing the upper limit of this time depth. Divergence among the four serotypes would have occurred much earlier. Janssens and Vandergroen (1992) consider the African tropics provide a vast endemic foyer with transmission exclusively by mosquitoes.

25.7.3 Family Arenaviridae

25.7.3.1 Lassa Fever

Lassa fever, caused by a virus of the Family Arenaviridae a group confined mainly to rodents in both Old and New Worlds, is known only from Africa where it is widespread in west and central regions. It seems to be a chronic infection of two races of multimammate rat, *M.* (*natalensis*) *coucha* and *M. erythroleucus*. Adult *Mastomys* exposed to the virus develop immunizing infection after brief viraemia, and it is not thought to affect the rodent host significantly, although some internal pathologic abnormalities have been observed at autopsy. Evidence of exposure is found in neonates suggesting maternal transmission of infection and it may be that chronic infection is lifelong. Litter size is not affected. Most human infections appear to be acquired from *Mastomys* invading huts. Infection is associated with high rodent infestation in homes and is relatively focal in villages, even extending to an individual hut. It is among the most numerous of rodents in villages in the enzootic area and usually absent only when the black rat has migrated from coastal sites and displaced it. First identified in Jos, Nigeria, outbreaks of the virus have occurred in Sierra Leone, Liberia, Burkina Faso, CAR, Ivory Coast, Gambia, Ghana, Guinea, Mali, and Senegal; and four strains have been identified, Nigeria, Mozambique, Zimbabwe, and CAR.

In CAR *Praomys* spp.[4] appeared to be the main carriers with 18% (n = 153) of a sample being positive and *Mastomys* negative (n = 65), but sample sizes were small. *Praomys* infections ranged from 9.1% to 31.7% of samples taken from 30 to 125 km north of Bangui, populations being highest in the forest-savannah ecotone. The CAR virus varies somewhat from other Old World arenaviruses.

Population irruptions of *Mastomys* might influence outbreaks of Lassa fever contracted by people inhaling dust contaminated with the urine of infected rats, or direct contact with rat excreta. In the northern savannah areas of Sierra Leone

studies found that up to 40% of adults in some places carried antibodies. This contrasts with CAR where only 0.4% of a sample (n = 1,898) were found to have been exposed. Here *Praomys*, particularly *P. tulbergi* and *P. jacksoni*, and *Mastomys*, are in close contact with humans at the forest edge and in cultivated fields. *Mastomys* is more commonly found in houses but together with *Praomys* often captured for food. In the endemic areas of west Africa *Mastomys* is predominant and disturbance of the secondary forest is greater. Gonzalez et al. (1983) considered the geographical distribution of Lassa in *Mastomys* is discontinuous because that recovered from *Praomys* appears to occupy the niche occupied to the north-west and south-east by *Mastomys*-borne related viruses. The low prevalence in humans in CAR may be an artefact of sampling or it may be due to the weakness of the virus, a relatively low effective human-rodent contact, or the rodent host being a poor disseminator. It is not known whether the virus causes chronic infection in *Praomys*.

In 1977 the Mopeia strain was isolated from the multimammate rat in Mozambique and Zimbabwe, given the name of Mozambique virus, in Zimbabwe isolated from both *M. natalensis* and *Aethomys chrysophilus*, but it is not known to be pathogenic to man. It has been found in rodents in Kruger NP also. Eventually one or the other strain was found in *Mastomys* spp. from Mozambique to Zimbabwe, and north to Senegal and Mali, indicating the disease was enzootic over a wide area. It was found to be common in certain areas of West Africa, about 10% of cases of high fever among villagers in Sierra Leone was caused by Lassa and most of the time people recovered from it.

In a study in Guinea (Demby et al. 2001) *Mastomys* spp. comprised more than 90% of 1,616 small mammals collected (n = 956), predominating in all areas except the coastal urban areas where *M. musculus* was dominant (n = 538), but this species was not found east of Kindia which may indicate the limit of inland penetration to date, the species having been introduced by ship to coastal areas. Lassa virus was isolated from *Mastomys* only, although evidence of exposure to infection was found also in *M. musculus* and black rat. The highest *Mastomys* infection was found in the savannah followed by forest but was present in all areas, although rarely present in urban areas possibly due to displacement of *Mastomys* by other species, particularly black rat. In houses a mean of 1.7 *Mastomys* was found to be positive (range 1–6). Other species collected were black rat (64), *Mus minutoides* (13), *Praomys* spp. (17), *Uranomys ruddi* (4), *Dasymus incomtus* (3), *Hylomyscus alleni* (1), *Malacomys edwardsi* (1), *Tatera kempi* (4), and shrews *Crocidura* spp. (15). Of 96 *Mastomys* 11% had antibodies, and of 46 specimens 95% had antigens, to Lassa virus. Infection per region ranged from 0% to 9% of captures, the highest being in the savannah forest in localized foci. The reasons for this patchy distribution of *Mastomys* infection with Lassa both within and between villages remains unknown. *Mastomys* occurred in 68% (n = 444) of houses examined and in 91% was the sole rodent species. *M. musculus* occurred in 67% (n = 137), while black rat was the sole species in 28% (n = 39), co-existing with *Mastomys* in 21% (n = 8). The black rat had a consistently low presence (4%) in each region: coastal, savannah/forest transition, and forest, but was absent from the savannah.

Overall in West Africa the human population experienced 100,000–300,000 infections/year. The ubiquitous nature of *Mastomys* across the region implies that Lassa fever could have epidemic potential over a vast area if the virus is introduced into local, previously uninfected, *Mastomys* populations (Demby et al. 2001).

25.7.4 Family Bunyaviridae

Bunyamwera virus is widespread in sub-Saharan Africa but known to cause mild fever in man only. This serogroup contains RVF, Saint-Floris, Gordil, Arumowot, and Germiston viruses. Germiston virus has been isolated from humans in South Africa and Mozambique only, and from *C. rubinotus* mosquitoes in South Africa, but also from rodents in Uganda.

Another serogroup, Bwamba, is named after the Bwamba virus isolated from humans at Bwamba in 1937. More than 75% of tested adults in Nigeria had antibodies to this virus, and more than 95% in Tanzania and Uganda. It has been found also in Senegal, Cameroun, CAR, and South Africa. It causes fever but no fatalities have been recorded. It is the tenth most frequent arbovirus infecting humans in Africa, and the most common in CAR where it is isolated most often during the dry season. The principal vector is unknown but it has been isolated from *Anopheles* mosquitoes in Senegal, Nigeria, Ivory Coast, CAR, and Uganda; from *Aedes* in Senegal and Nigeria, and *Mansonia uniformis* in Nigeria. No isolations have been made from wild animals. Antibodies may be confused with a very closely related virus, Pongola, isolated many times from divers mosquito species in CAR, Uganda, Kenya, Zimbabwe, and South Africa; but not known to infect man.

Crimean-Congo haemorrhagic fever CCHF is a pathogenic Nairovirus disease found in many parts of Africa, the Middle East, and parts of Russia and China, transmitted primarily by *Hyalomma*, *Amblyomma*, and *Boophilus* ticks, small mammals and birds hosting the larval tick stages and large mammals the adult stages. Mortality is about 15–30%. Outbreaks have occurred in South Africa where it is seasonal. It is apparently traced back to the twelfth century in Tadzhikistan described in 1110 in the *Thesaurus of the Shah of Khwarazm* (Hoogstraal 1979). Potentially fatal it causes clearly defined disease in humans alone, and epizootic episodes in the wild are indicated solely when outbreaks occur in humans. Only four distinct outbreaks are recorded, all in the Palaearctic Region, plus one suspected in Pakistan. The virus has been reported from much of the south-eastern zone of the Palaearctic Region, the neighbouring western zones of the Oriental Region, and neighbouring northern zones of the Ethiopian Region south to slightly beyond the equator; a remarkably extensive distribution range for an arthropod-borne virus, occurring in numerous ecological environments in three different Faunal Regions, enzootic from Senegal and Nigeria east to Egypt, Ethiopia, DR Congo, Uganda, Kenya, and Tanzania. The evidence from Senegal, Nigeria, CAR, and Ethiopia, suggests foci in semi-desert or savannah regions with long dry seasons; whereas in DR Congo, Uganda, Kenya, and Tanzania, the virus appears

associated with higher rainfall regions where people live in close contact with domestic animals. Although the chief common faunal denominator responsible for its enzootic distribution appears to be the *Hyalomma* tick which commonly infests domestic and wild vertebrates in all the zones, it is also remarkable for the variety of reservoir-vector species linked with it.

Known for centuries in southern Uzbekistan it was diagnosed first in the Crimea in 1942 before becoming epidemic there in 1944. Wartime devastation of the countryside resulted in a population explosion of hares and the vector tick *H. m. marginatum*. Heavy rains and sleet in late 1944 to early 1945 caused a great reduction in the hare and tick populations in 1945 and in human morbidity, the virus becoming enzootic in the Crimea thereafter, with only occasional human cases to 1969 despite high *H. m. marginatum* populations in some areas (Hoogstraal 1979). Based on strains from Nigeria it was later (1969) found identical with Congo virus isolated from a sick child in Kisangani, DR Congo, in 1956. Apart from this child and the doctor who treated him, no other cases were reported subsequently from DR Congo. It was first identified in southern Africa in 1981, since which time sporadic cases and deaths have occurred regularly and severe disease elsewhere in Africa, possibly because of greater awareness of the symptoms, but infection of humans occurs with disproportionately low frequency in relation to the extensive circulation of the virus in livestock and wild animals.

In 1959 to 1961 there was a number of deaths in Kenya's Rift Valley from symptoms similar to those seen in cattle in marginal forest areas in the same region, but the cause was not verified although suspected to be CCHF. A haemorrhagic disease was reported also among Turkana in 1972. A general paucity of information on the distribution and frequency of CCHF virus south of the equator compared to that in the Palaearctic region is believed by Hoogstraal (1979) due probably to a lack of studies and failure to recognize the disease.

25.7.5 Family Hantaviridae

Hanta viruses, which cause haemorrhagic fever with kidney failure, are widespread in the world and appear to be spreading further or are being recognized in countries where they were previously unknown. In Africa infection is widespread in humans and rodents and has been reported from Benin, Burkina Faso, Cameroun, CAR, Chad, Equatorial Guinea, Gabon, Mauritania, Nigeria, Senegal, Uganda, and Zanzibar; but little is known of their prevalence or importance, although up to 20% mortality has been reported from them in China. The first human case was reported from Bangui, CAR, in 1987, and humans have been found to have been exposed to the virus as far apart as from Bico Island in Equatorial Guinea to Pemba Island off the east coast.

25.7.6 Family Filoviridae

25.7.6.1 Marburg Virus

In December 1998 a protracted epidemic of Marburg haemorrhagic fever virus, a virus of the family Filoviridae, allied to Ebola, broke out in an isolated area of north-east DR Congo causing upwards of 83% mortality among gold miners who had been working in bat infested caves. Cases of haemorrhagic fever among workers at the mine had been known since 1987. Monkeys died too quickly to be hosts to the virus and it was believed to be carried by bats, as is Ebola, but it was imported to Germany by vervet monkeys *C. aethiops* from Uganda destined for the pet trade, killing seven people in 1967. Of 99 monkeys, 49 had died from the disease en route.

From stored blood samples, monkeys captured near Entebbe in 1961 were shown to have been infected, numbers increasing each year to 1967 when a third of some monkey groups carried the virus. All actively infected monkeys were either vervets or red-tailed monkeys. Sampled gorillas, chimpanzees, baboons, and talapoins, were shown to have been exposed to the virus and carried antibodies in their blood, but extensive searching failed to reveal a carrier or vector. In 1975 an Australian tourist at Hwange in Zimbabwe was bitten on the leg by an unknown creature and fatally infected with the virus, transferring it to two others whose lives were saved. It thus clearly extends beyond the rainforest region. Subsequent studies of bats from the cave where the gold miners worked demonstrated 9.7% ($n = 20$) of a species of insectivorous bat *Rhinolophus eloquens*, and 20.5% ($n = 230$) of the very common and ubiquitous species of fruit bat *Rousettus aegyptiacus*, showed positive reactions to presence of the virus. Nothing was detected in six other bat species (five insectivorous and one frugivorous) as well as seven rodent species, three shrews, and a large number of invertebrates; but all of the mammals were sampled at much lower levels than the species found to be positive.

Sporadic cases and short chains of human to human transmission suggest infection has been repeatedly introduced into the human population. This was substantiated by the fact that at least nine genetically distinct strains were circulating during the outbreak. Genetic sequences of the antibodies suggested the virus evolves slowly and bats in the mine area must have been in contact with it for a long time. The diversity of the sequences suggests also restricted circulation of the virus in bat colonies, as would occur if the colonies were discrete and cross-breeding with others was limited. Alternatively the bats could be simply intermediate hosts of the virus. Whether insectivorous bats, fruit bats, or both, are likely to be the primary source of infection, and whether a particular species is involved with secondary transmission of infection to other species, remains unclear. The ultimate source of infection may be external, such as bat parasites, or seasonally active insects in the bats' diet (Swanepoel et al. 2007). So far it has failed to evolve into a spreading human disease. The virus has been shown to remain infective in *Aedes* mosquitoes for 3 weeks after experimental inoculation.

The ecological centre of both Marburg and Ebola viruses appears to be central and south central Africa, particularly the Mount Elgon area of western Kenya and eastern Uganda. The original Marburg infected group of monkeys originated from the Lake Kyoga region of Uganda and surveys identified neutralizing antibody in at least three monkeys from there. A boy who contracted infection in 1987 had spent some time in Kitum Cave on Mount Elgon which houses a large population of bats, but surveys failed to find evidence of infection in bats or other wild animals in the area.

25.7.6.2 Ebola Virus

Ebola virus, a haemorrhagic fever filovirid virus with high genetic stability, was identified first in 1976 at Yambuku near Ebola in DR Congo. Its wild reservoir remains unknown but evidence strongly implicates fruit bats, and isolates from them show genetic variation which suggests all strains in bats have descended from a common ancestor in bats since 1976 (Biek et al. 2006). Whether this is due to a genetic bottle neck or there is another as yet unidentified reservoir is not known, but there is no evidence to date of an epizootic wave with associated spillovers occurring in other regions from where the virus has been isolated. The death of chimpanzees in Taï NP suggests a single event with no local or regional epizootic causing further deaths in susceptible primate or duiker species.

Descent from a common bat ancestor in the past 30 years to 2006 suggests destruction of the bats' habitat, i.e. forest, causing compression and intermixing of colonies and disruption of isolation of the infection in a particular carrier.

Strains of the virus were found in macaque monkeys in the Philippines in 1989. The most lethal strains, causing up to 88% mortality, occur in Gabon, Congo Republic, and DR Congo, belonging to the Zaïre subtype, one of four known subtypes which diverged thousands of years ago and which do not spread rapidly from one region to another of the forest block. The subtypes are *Ebola Sudan*, *E. Zaïre*, *E. Ivory Coast*, and *E. Reston*. *E. Reston* originates in Asia and has never been known to cause human disease. Mortality rates are about 80% of patients with *E. Zaïre* and 50% with *E. Sudan*, incubation taking about a week. Outbreaks occur abruptly, the first three known were between 1976 and 1979 in DR Congo, after which none were reported again until late 1994, then occurring eight times, in Gabon, Congo Republic, Ivory Coast, and Uganda, among people who had handled gorilla, chimpanzee, and duiker carcasses, populations of which animals declined markedly apparently in an epizootic outbreak. Among an escalation of outbreaks due to *E. Zaïre* a new subtype *E. Ivory Coast* was identified. The first case identified in this outbreak was from a dead chimpanzee in Ivory Coast Taï NP. Recovered carcasses were infected by a variety of strains suggesting outbreaks result from multiple introductions from the unknown reservoir. Examination of human patients revealed eight viral strains indicating the five human outbreaks involved distinct animal sources and viral strains.

Over an 8 month period in Gabon at least 64 animal carcases comprising gorillas, chimpanzees, and duikers, were encountered in one outbreak area of 3,000 km^2, with a peak in November–December, all carcases being not more than 1 month old. Most were of gorillas. It is considered that these and the disappearance of signs indicated the deaths of hundreds of animals (Leroy et al. 2004). Resurgence of *E. Sudan* was seen also in 2000–2004 in Sudan and Uganda. In Gabon eight groups of gorillas totalling 143 animals in all, monitored for 10 years in one area, disappeared within 3 months between October 2002 and January 2003. Duiker disappeared also and involvement of this forest floor species poses an interesting question as to how they contract the infection and apparently not other bovids. The most likely possibility is from feeding upon the ape carcases which remain infective for 3–4 days only.

Deaths in wild animals tend to precede human infections. In Gabon's Lossi sanctuary gorillas and chimpanzees died of *E. Zaïre* in early December 2002 and the first human cases appeared at the end of the month. Between 2001 and 2003 in Gabon and Congo Republic 50 gorillas, 14 chimpanzees, and 14 duikers, were found dead in human outbreak areas, while in the Lossi Sanctuary gorilla and duiker populations were estimated to have declined by 50%, and chimpanzee populations by 88%, between 2002 and 2003. In the case of apes this suggests massive simultaneous infection from some animal reservoir connected to the environmental conditions, the transitional period between the dry season and the rains. If this is the forest fruiting period then contamination of the fruit by chronically infected fruit bats which show no seasonal surge in infection, might be the cause. On the other hand, in epizootics bats might cause contamination of leaves through urine or faeces which are ingested by the apes (and those falling to the ground could be consumed by duikers as could fruits). Hendra and Nipah viruses carried by fruit bats *Pteropus* spp. in Australia and Southeast Asia respectively can be transmitted directly to humans apparently by consumption of fruit contaminated with infective bat saliva. Comparison of genetic analysis of the human DR Congo 1976/1995 outbreaks with Booué in Gabon in 1996 showed minor divergence only despite the 20 year interval and 3,000 km separation, indicating that multiple independent introductions from the reservoir to the apes which infected the humans had occurred. It is considered that virus transmission between different groups of apes is unlikely because infectivity is short-lived and physical contact between different groups is rare. Thus different strains may be widespread throughout the forest with simultaneous infection of apes occurring from an unknown source and under particular environmental conditions. Outbreaks have always been reported at the beginning of the dry seasons (Leroy et al. 2004). In 2001–2002 in Gabon and Congo Republic gorilla carcases were the source of chains of human infection in four outbreaks, chimpanzee carcases in two, and duiker carcases in three (Pourrut et al. 2005). There is no evidence of direct infection of humans from a reservoir species but the possibility exists that this could happen through contact with bats, a possible source of infection. Transmission by mosquitoes is possible. All outbreaks originate in forest regions near the equator characterized by dense vegetation and a tropical climate.

In a survey of 720 animals based on twenty primate species in Cameroun, Gabon, and Congo Republic, 12.9% of chimpanzees were found to have been exposed to the Ebola virus, some positive samples preceding the first human outbreaks. This suggests they are in regular contact with the virus and some survive it, thus the virus has probably been present for a very long time. Five drills *Mandrillus leucophaeus*, one mandrill *M. sphinx*, one baboon *Papio papio*, and one *Cercopithecus* spp. showed prior exposure also. The ground dwelling apes could have been infected in the same manner as duikers probably are.

A total of 30,161 arthropods (mosquitoes, fleas, lice, bedbugs, ticks, and blood-sucking flies), 165 reptiles and amphibians, 533 birds, and 7,018 vertebrates was examined between 1976 and 1999 connected with outbreaks at Yambuku, Zara, Cameroun-DR Congo, Kikwit, Täi, and CAR. This revealed a red colobus monkey *C. badius* had been exposed to the virus in Täi. In CAR in 1998, 24 bats, 163 rodents, and 56 insectivores were examined; revealing exposure to the virus of *Mus setulosus*, *Praomys* spp., and a shrew *Sylvisorex ollula*, but did not provide conclusions as to the reservoir status of these species due to a lack of specific serologic responses, lack of nucleotide specificities in the amplified viral sequences, failure of virus isolation, and non-reproducible nature of the results (Pourrut et al. 2005). Examination of 1,030 small invertebrates during human and great ape outbreaks in Gabon and Congo Republic in 2001–2005 provided evidence of asymptomatic infection in three species of fruit bat, suggesting these may act as the reservoir, or one of the reservoirs (Leroy et al. 2005). Although the virus itself was not isolated immunoglobulin IgG specific for the virus was detected in hammer-headed fruit bat *Hypsignathus monstrosus* (4 in 17); epauletted bat *Epomops franqueti* (8 in 117), and little collared fruit bat *Myonycteris torquata* (4 in 58).

Mortality among great apes from Ebola infection can increase in the dry season when fruit is scarce leading to contact as they compete with the bats for food. Immune function in bats changes at this time also as a result of food scarcity or of pregnancy, which would favour viral replication. This could cause increased infection among great apes and account for the episodic nature of the virus outbreaks. However in Odzala NP of Congo Republic, it was suspected gorillas were infecting one another, the death rate being consistent with an epizootic model in which group-living gorillas catch the disease from other group members and pass it on also to solitary males. Mortality outbreaks lasted also for 10 months every year, longer than the dry season during which gorillas encounter fruit bats.

Man is presumably infected by an increasing consumption of bush meat which includes fruit bats. It has broken out in Congo Republic, DR Congo, Gabon, Sudan, Ivory Coast, and Uganda, and is normally a disease of the tropical forest and the communities within, the exception being the Uganda outbreak at Gulu, where the habitat is dry bushed savannah. In the rain forest upper Ogooué region of Gabon it was found people were routinely exposed, 6% of those examined carrying antibodies to the virus. Of more than 4,000 blood samples taken in central Africa, 24% revealed prior infection with the disease (Oldstone 1998). The outbreaks have been due to poor hospital practice and contact with the cadavers, an infected person would normally die in relative isolation in the forest without spreading the disease.

Before the outbreak in Yambuku, it occurred at Nzara 640 km distant in southern Sudan also in 1976 and. In this case the victims were working in a cotton factory and the strain was not as deadly, with a 53% mortality rate compared to 88% for the DR Congo strain. It occurred at Nzara again in 1979 and suspicion centred on bats in the cotton factory, but a source was never isolated. RNA maps of the DR Congo and Sudan viruses showed strains at each locale were different, either coincidence or some more subtle factor had caused the two outbreaks to occur simultaneously. It was considered isolation of the two centres made it impossible for transference to have taken place by being carried from one to the other by human agency.

In 1994, 12 members of a troop of chimpanzees died of the disease in Taï Forest, the deaths corresponding with a time when the chimpanzees were hunting and eating western red colobus monkeys *P. badius*, those eating the most meat being the most likely to die. But they had been observed feeding also in a wild fig tree for 2 weeks prior to the fatalities, suggesting they may have contracted it from bats feeding on the fruit also. Or it may have been transmitted to the red colobus monkeys by consumption of infected bats which would have become easier to catch if they were affected by the disease, and this might have been the cause of an apparent tendency on the part of the chimpanzees to hunt colobus at this time of the year, September–October. The chimpanzee mortality of 37% was similar to an increase in 1992 when it reached 27% (Formenty et al. 1999), suggesting an earlier outbreak.

In 1995 the disease surfaced again among humans in DR Congo, 16 years after its former outbreak. Again deaths were due to the hospital practices and contact with cadavers. In Gabon in 1996 a group of people found a dead chimpanzee and ate it, 19 of the people involved contracting the disease and infecting a further 18 family members, in all 57% of those infected dying. This was followed by another outbreak in which a hunter living in a forest camp became infected and spread the disease, 75% totalling 45 of 60 people infected dying. A dead chimpanzee found in the forest was infected with the virus and chimpanzees may have been involved in the hunter's death. In 1980 it was found 15% of Pygmies in the Cameroun rainforest had antibodies to Ebola showing they had been infected with it. Antibodies were found in a flying tree squirrel also.

A theory was proposed the virus might be a plant virus because outbreaks in the chimpanzee population in Taï Forest coincided with the flowering of a particular species of plant. It is more likely infective bats are attracted to the flowers or to insects visiting the flowers, or an insect visiting the flowers might be the carrier. Which species visited the flowering plants was not studied. Fruit bats migrate long distances to find flowering and fruiting trees feeding exclusively on forest flowers and fruits, and destruction of these food sources will alter the bats' foraging habits. But the theory proposed stems from the hypothesis that many insect-borne diseases may originally have been plant parasites or commensals which, thousands of millions of years ago, transferred to insects such as aphids feeding on plant juices. Viroids, the smallest known agents of infectious disease, are known to occur only in higher plants with the exception of man, in which they cause hepatitis D, but may be present in many animals causing as yet unrecognized diseases.

Whereas as late as 50 years ago a family living on its own in the West African forest might have contracted say, HIV, or Ebola, the chances were the family by reason of its isolation would die without transmitting the viruses to others and the living site would soon become overgrown in the forest. Increasing human density and the increasing proximity of people to one another resulting in repeated contacts has changed this balance between isolation and spread of the virus when invading an adventitious host.

25.8 Bunyavirus-Like Viruses

Similar to the Bunyaviridae but having structural and genetical differences are members of a group known as the bunyavirus-like phlebotomus fever serogroup, which morphologically and morphogenetically are similar to Bunyamwera virus. The Saint-Floris and Gordil viruses from adjacent areas in the north of CAR, have been isolated from rodents. Arumowot virus has been isolated from mosquitoes and rodents in Senegal, Nigeria, and Sudan; Gabek forest virus from rodents and a monkey in Sudan. Arumowot, Gordil, Saint-Floris, and Gabek forest virus, are all regarded as phleboviruses, members of the *Phlebovirus* genus of the *Bunyaviridae*. Unlike RVF they do not affect sheep (Swanepoel et al. 1986).

There is a number of relatively benign bunyaviruses or bunyavirus-like viruses also of which little is known, such as Ilesha and Tataguine, mosquito-borne viruses found in CAR and western Africa; and Bangui virus an unclassified bunyavirus from CAR of which nothing is known except that it causes a fever. The vector is unknown. Tataguine is in the Congo red fever group and causes mild fever but is apparently not related antigenically to other bunyaviruses. It was isolated from mixed *Culex* and *Anopoheles* mosquitoes in Senegal in 1966. Antibodies have been found in 57% of people sampled in Senegal, 26–61% of Nigerians, and has been found also in man in Cameroun, CAR, and Ethiopia, but not in wild animals. It is isolated from mosquitoes only in the dry season. All of these viruses have the potential to erupt into epidemics and to evolve into more lethal forms if the natural milieu is disturbed.

25.9 Protozoa

25.9.1 Malaria

Recurrent disease outbreaks of significant proportions of which we have the most information were cholera, smallpox, bubonic plague, and yellow fever. Malaria,[5] caused by species of the protozoan *Plasmodium* first described by Laveran in North Africa in 1880,[6] a genus thought to have descended from a dinosaur parasite and

now infecting birds and reptiles and all other major groups of terrestrial vertebrates, although the most widespread and accounting for high mortality is persistent, and so does not usually exhibit epidemic upsurges and declines, but a mixed epidemic of *P. falciparum* and *P. vivax* at higher altitudes in Ethiopia in 1963–1964 caused over 10,000 deaths and an estimated 100,000 acute cases. Its presence limits population distribution and Bernsten (1979) suggested it may have been more important than tsetse fly in restricting areas of occupation by the pastoralist Maasai of East Africa, as lacking the sickle-cell gene which gives some protection, but the distribution of which corresponds almost exactly to the area of tropical rain forest, they suffer high mortality from it. Hinde and Hinde (1901) reported Maasai considered mosquito bites fatal. Merker (1904) observed also they attributed malaria to the bite of a mosquito. Koch (1898) referred to Africans in the Usambara mountains calling malaria *mbu* and if asked where they caught the infection replied that there were insects in the lowland called *mbu*, i.e. mosquitoes, which had stung them and that is how they acquired it. The sickle-cell gene in East Africa reaches the exceptionally high frequency of 45% among the pygmoid Bwamba in western Uganda, who resemble genetically the Nilotic tribes of Kenya more than true Pygmies (Allison et al. 1952).

Varro in 36 B.C. provided an early illustration of malaria limiting areas of occupation when he advised Romans to build their farm houses at the base of a well-wooded mountain where there were wide pastures, and avoid swampy ground, "Note also if there be any swampy ground ... certain minute animals, invisible to the eye, breed there, and, borne by the air, reach the inside of the body by way of the mouth and nose, and cause diseases which are difficult to get rid of" (Storr-Best 1912).[7] Varro did not connect these "minute animals" with mosquitoes as vectors although his "diseases" apparently referred to malaria, for he continued, "What shall I do to escape malaria, if I am left an estate of such a kind? ... You must sell it for as many pence as you can get, or if you can't sell it you must quit it". Columella, *c*A.D. 55, referred specifically to mosquitoes, "nor indeed must there be a marsh near the buildings ... for the former ... breeds animals armed with mischievous stings, which fly upon us in exceeding thick swarms ... whereby hidden diseases are often contracted" (Anon. 1745).

When Cullen wrote in the *Encyclopædia Britannica* in 1771 that endemic tertian fever was "proper to certain places, as a low situation and full of marshes, producing a great number of gnats", he probably had Varro in mind. As perhaps did the originator of a Freetown, Sierra Leone, ordinance of 1812, which enjoined inhabitants to prevent the formation of stagnant pools in front of their plots "which generate disease and mosquitoes over the town".

De la Courbe, who visited Senegal in 1685, referred in some detail to the numerous mosquitoes which sought out humid places and thus in the dry season were in the woods but during the rains were spread everywhere, forming one of the greatest disadvantages of the country "and which is one of the principal causes of diseases", although he did not make a positive link with malaria. He referred to a forest at Gerege (Gerengue near present Georgetown, Gambia?) as "full of mosquitoes", especially the mangroves (Cultru 1913).

Alpinus (1735) in 1581–1584 had written that pestilential fevers, both epidemic and fatal, occurred in Alexandria after the Nile floods receded, but made no connection with mosquitoes although noting mosquitoes were so abundant that without linen cloths in the tents (mosquito nets?) one could not sleep. Funerary inscriptions in the Nile Valley dating from about the fourth to the tenth centuries A.D. indicate a unimodal seasonal distribution in mortality peaking in the first half of the year homogenous across the Nile Valley from Nubia to Memphis (Scheidel 2001), which would imply endemic seasonal infection such as malaria. Although the records refer mainly to adults as child deaths are more likely to have gone unrecorded, a regular seasonal occurrence of malaria may be suggested by an inscription which reads, "The hot south and west winds in summer bring 'the pestilence of the year' which kills people".

Crawford had published a paper in 1807 on the "Mosquital Origin of Malarial Disease" in the *Baltimore Observer* (King 1883); and Nott (1848) also in America suggested the "mosquito of the lowlands" as a probable cause of malarial fever in place of marsh vapours, but the connection seems to have been largely forgotten until towards the end of the nineteenth century. Moore (1862), treating of diseases in India, considered stagnant water absorbed malaria and malarious fevers were produced, among other causes, by using contaminated water. Livingstone (Livingstone and Livingstone 1865) noted "myriads of mosquitoes showed, as they probably always do, the presence of malaria", but did not realize the significance of his observation.

King (1883) produced arguments in favour of the mosquito-malaria theory but admitted the data did not prove it. Laveran suggested it much later in 1891 and Manson in 1894, but it was left to Ross (1898) to demonstrate it finally in 1895. It seems unlikely that Emin Pasha when travelling in the southern Sudan always used a mosquito net as a precaution against malaria as Bignami (1896) asserted, in view of the fact that Emin wrote in 1898, "Last night we suffered much from mosquitoes . . ." (Schweitzer 1898). In his *Guide to Health in Africa* Parke (1893), who as medical officer had accompanied Stanley's expedition to rescue Emin, recommended covering the face and other exposed parts at night with mosquito netting because mosquitoes were sometimes the agents for introducing through their blood-sucking punctures *Bitharzia* sic (=*Schistosoma*) *haematobia*, which is a water-borne infection.

Malaria is transmitted by anopheline mosquitoes, 25 species of *Plasmodium* parasitizing primates, four of which infect humans: *P. vivax*, *P. falciparum*, *P. malariae*, *P. ovale*. *P. vivax* is thought to be the oldest passed to man by primates, 95% of Africans are completely refractory to it, lacking a specific antigen,[8] resulting in it possibly having died out in Africa, replaced by *P. falciparum* and *P. malariae* becoming widespread. *P. falciparum* can be maintained only in an environment where the mean temperature is about 21°C, but *P. vivax* requires a temperature only above 15.5°C. Unlike the other three, *P. falciparum* does not set up chronic infections which can last a lifetime but causes severe and often fatal disease. Not easily transmitted between humans it is dependent almost entirely on *An. gambiae* for transmission, evidence pointing to a West African origin most closely related to

a chimpanzee parasite *P. reichenowi*, from which it is estimated to have diverged 4–10 Mya.[9]

A rare species, *P. cephalophi*, was recovered from grey duiker in Malawi by Bruce in 1912 and not found again until 1964 (Keymer 1966). Another, *P. brucei*, was found also in grey duiker by Bruce. But *Plasmodium* is rare in ungulates although one species, *P. limnotragi*, has been recovered from sitatunga in Akagera NP. The vector of these ungulate Plasmodia is unknown, but *Anopheles rufipes* has been suggested as a vector of the duiker parasite in Zimbabwe.

A malaria-like blood parasite *Hepatocystis hippopotami* has been recovered from hippopotamus in Zimbabwe.

25.10 Rodents and Disease

Elton (1925) stated the possibility of rodents acting as reservoirs for human diseases other than plague should not be ignored, and periodic fluctuations in rodent numbers could cause outbreaks of human disease. Rodents are known now to be the most important disease carriers affecting man in Africa, especially *Mastomys* spp., and host to at least three types of haemorrhagic fever virus, Congo, Lassa, and Hanta; four types of other arbovirus, West Nile, Quaranfil, Bunyavirus, Saboya virus; four rickettsial species, *Rickettsia conorii*, *R. typhi*, *R. africae*, *Coxiella burnetti*; seven bacterial diseases, *Brucella suis*, *Spirillum minus*, *Borrelia* spp., *B. burgdorferi*, *Leptospira icterohaemorrhagie*, *Y. pestis*, *Salmonella* spp.; and four types of protozoal disease, *Leishmania donovani*, *L. tropica*, *L. major*, *Toxoplasma gondii*. Congo virus is transmitted from rat to man by ticks of the genera *Hyalomma*, *Rhipicephalus*, and *Boophilus*. Ticks are the vector of several other diseases, Lassa and Hanta viruses are transmitted directly, but Hanta virus can be transmitted from the rat *A. niloticus* by Culex mosquitoes also.

The role of rodents in the ætiology of diseases in Africa remains largely unknown.

25.11 Notes

1. Lack of clarification concerns interpretation of the Arabic words *tāʻūn*, meaning plague as ascribed to the Black Death, and *wabā*' meaning an epidemic disease such as smallpox.
2. Between 1975 and 2005 there were 48 newly recognized pathogen species worldwide of which 30 were viruses (Woolhouse and Antia 2007).
3. Working in the savannah belts of CAR from 1971 to 1977 and Burkina Faso from 1977 to 1979, the author heard no mention of this fever.
4. Delany (1975) re-classified *Mastomys* as *Praomys* but this seems not generally accepted.

5. In 1978 dysenteric infections caused more than seven times more deaths in Africa than did malaria, and respiratory infections 4.5 times more.
6. It was probably first described unknowingly by Delafield in 1871 in his *Handbook of Post-mortem Examinations and Morbid Anatomy*, or even by Meckel in 1847, but Laveran realised its significance.
7. As the minute animal was invisible to the naked eye and there were no microscopes in those days, Varro was just guessing, but it was a very prescient guess.
8. The "Duffy antigen", the antigen alleles Fy^a and Fy^b which appear to act as receptors for penetration of the red cell by the merozoites, without them penetration cannot occur.
9. Crawford (2007) briefly summarizes the controversies over the date derived from the genetic code of when *P. falciparum* may have emerged first in humans. Consideration has to be given not to the parasite alone but to evolution of transmission by the mosquito also.