EBOLA – haemorrhagic fever (EHF), commonly known simply as Ebola – is a highly infectious viral disease, and one of the deadliest diseases to have emerged in recent decades. The first identified human case occurred in Africa in 1976, near the Ebola River in the Democratic Republic of Congo (formerly Zaïre), and sporadic, localized outbreaks of the disease have since flared up in a number of countries in sub-Saharan Africa. Ebola is characterized by massive internal and external bleeding, and death from surgical shock and respiratory arrest occurs in some 50 to 90 per cent of all cases. The risk for anyone in contact with the Ebola virus is so great that the disease is classified as a 'Biosafety Level-4' pathogen, which requires the strictest safety precautions for laboratory investigation. There is as yet no approved vaccine or known cure for Ebola, and many mysteries about its origins remain unsolved.

In late August 1976 a schoolteacher called Mabalo Lokela living in Yambuku, a remote town in northern Zaïre (now the Democratic Republic of Congo), developed a fever. At the local mission hospital they thought he might be suffering from malaria, but an injection of chloroquine failed to control his feverish symptoms. A week later he returned to the hospital, critically ill. He had begun to experience uncontrollable vomiting, acute diarrhoea and a blinding headache. He was also severely dehydrated, and had trouble breathing. Frighteningly, he then started bleeding from his nose, gums and eyes, and there was blood in his stools. There was no doctor in the hospital, but the Sisters who ran the mission did all they could to care for him. They had no idea what was wrong. Mabalo Lokela died on 8 September 1976.

Funerals, families, friends and health workers

Lokela's body was cleansed and prepared in the traditional way for his funeral. Not long afterwards, many members of his family and friends who had attended the ceremony succumbed to the same symptoms, and several of the staff at the mission hospital became desperately ill. Panic broke out: it seemed as if people were literally bleeding to death. The mission hospital at Yambuku was eventually closed on 30 September, and the whole area sealed off by the Zaïrian army. A microbiologist and epidemiologist were sent from the National University of Zaïre to investigate the epidemic at Yambuku. The disease ultimately spread to more than 50 villages in the vicinity of Yambuku, as well as to Kinshasa, the capital of Zaïre, resulting in a total of 318 cases and 280 deaths – a mortality rate of nearly 90 per cent.

Wearing protective clothing, officials bury a victim of the Ebola virus. Such extreme care is a necessity – Ebola can spread during the preparation of infected corpses.

timeline

1976 *Between June and November, the Ebola-Sudan virus infects 284 people in Sudan, causing 151 deaths. In the first outbreak to receive attention in the Democratic Republic of the Congo (then Zaire), there are 318 cases and 280 deaths from Ebola-Zaïre virus during September and October.*

In the high-security laboratory at Porton Down, England, one investigator narrowly escapes death after accidentally infecting himself with the virus via a contaminated needle.

1979 *Sudan experiences a second outbreak, with 34 cases and 22 deaths.*

1989 *Ebola-Reston virus is introduced into quarantine facilities by cynomolgus monkeys (Macaca fascicularis) imported from the Philippines to Reston, Virginia, USA. Four people develop antibodies to Ebola-Reston but do not fall ill.*

1989–90 *High mortality from Ebola-Reston virus among cynomolgus monkeys in a primate facility in the Philippines responsible for exporting animals to the USA.*

1990–6 *Ebola-Reston virus again introduced into quarantine facilities in Reston, Virginia, and Alice, Texas, USA, by monkeys imported from the Philippines. The disease also appears among laboratory monkeys in Siena, Italy, in 1992.*

Many of the infected monkeys die.

1994 *Several cases of Ebola in chimps discovered in the Tai Forest in Côte d'Ivoire, West Africa. A scientist performing an autopsy on an infected chimpanzee becomes sick. She is treated and recovers.*

1994 *Ebola is first documented in Gabon in gold-mining camps deep in the forest. It is initially thought to be yellow fever but subsequently identified as Ebola, with 52 cases and 31 deaths.*

1995 *Epidemic in Kikwit, Democratic Republic of the Congo, traced to a person who worked in the forest adjoining the city. The epidemic spreads through families and hospitals, with 315 cases and 250 deaths.*

1996 *A chimpanzee found dead in the forest in Gabon is eaten by people hunting for food: 19 of those involved become ill, with other cases in family members. In total, 21 people die.*

A medical professional travels from Gabon to Johannesburg, South Africa, after having treated patients infected with Ebola. He is hospitalized and recovers. A nurse taking care of him contracts Ebola and dies.

1996–present *Several further outbreaks of Ebola in Gabon, Uganda, the Democratic Republic of the Congo, the Republic of Congo and Sudan. Since 1976 there have been some 1800 cases and 1200 deaths.*

2004 *Two cases – one fatal – of Ebola among laboratory workers, one in the Russian Federation and the other in the USA.*

MONKEY ALARMS

In 1967 clinicians at a hospital for infectious diseases in Marburg, Germany, were shocked and mystified to see several severely ill patients whose fever was accompanied by agonizing pain and bleeding from multiple sites on the skin and the mucous membranes. It turned out that all the affected patients had worked for the same pharmaceutical company, and had acquired the virus from infected African green monkeys. The monkeys, half of which had been dead on arrival from Uganda, were used in the preparation of cell cultures for vaccines. Seven of the infected lab workers died. Further cases occurred in Belgrade, Serbia (then part of Yugoslavia) and Frankfurt, Germany. A 'new' deadly disease had arrived – Marburg virus or green monkey disease.

Shipments of the crab-eating macaque imported into the USA and Italy from the Philippines were found to be carrying the deadly Ebola virus.

In 1989 alarm bells rang again – this time in the USA. A shipment of 100 cynomolgus monkeys, also known as crab-eating macaques (*Macaca fascicularis*), was sent from Manila in the Philippines to a quarantine laboratory in Reston, Virginia, for research. The monkeys started dying. Officials of the US Army Medical Research Institute were called in and found that the monkeys were dying from a form of Ebola virus – which was labelled Ebola-Reston. While it was highly lethal to monkeys, no humans were infected, though four of the animal handlers developed specific antibodies to this form of Ebola. The remaining monkeys were destroyed and the lab decontaminated. But this wasn't the only scare. Several more times in the course of the next few years, both in the USA and in Italy, monkeys shipped from the same export facility in the Philippines were found to be infected and dying of Ebola-Reston.

While no locally acquired human cases of Ebola have been found outside Africa, the presence of the virus in monkeys in Asia is an extremely worrying aspect of this deadly and mysterious disease. Where else in the world is Ebola circulating in the wild, waiting to jump species?

Some two months earlier, an ominously similar disease had broken out in Nzara and Maridi in the south of Sudan, a country bordering Zaïre in the northeast. This outbreak had led to the deaths of 151 people out of 284 cases (a 53 per cent mortality rate). The local hospital soon turned into a morgue, and many of the patients, as well as relatives and hospital staff, succumbed to the disease.

As later in Zaïre, people were petrified – it is said that some of the fearful victims in the last stages of the dreadful disease threw off their clothes and staggered out naked into the streets, while the surviving medical staff panicked and simply ran off to escape.

Identifying the cause

The Sudan outbreak did not initially receive international attention. But when news of the terrible mortalities in Zaïre reached the World Health Organization (WHO) headquarters in Geneva, Switzerland, and at the same time reports of the Sudan outbreak arrived, alarm bells rang. Blood samples were sent to a number of laboratories in Europe and the USA. A major international investigation was launched into the causes of the outbreaks, to see whether there was a link, and whether further epidemics could be prevented.

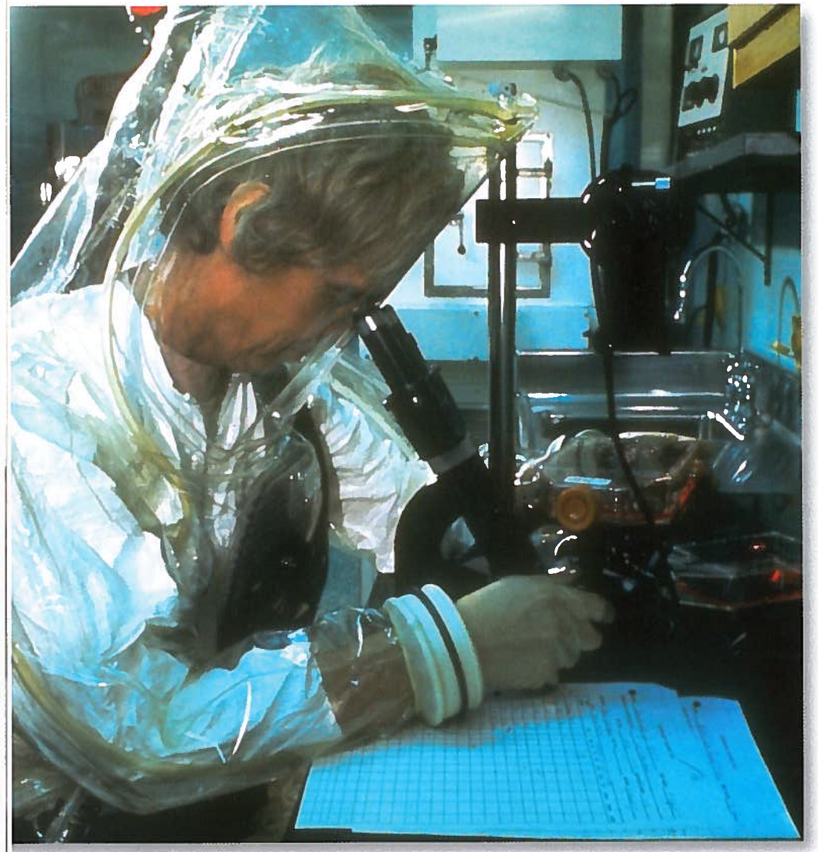
In their maximum-security laboratories, peering down their electron microscopes at the blood of a patient from Yambuku, scientists were both shocked and puzzled. The disease initially appeared to be similar to another scary 'new' haemorrhagic fever – Marburg disease or green monkey virus. This had first been identified a decade earlier and named after the German town of Marburg, where a shipment of African green monkeys had infected laboratory staff at a pharmaceutical research company (see Monkey Alarms, left). Common features included the high mortality and the severe haemorrhagic fever (the word 'haemorrhage' comes from the Greek words *haima*, 'blood', and *rhēgnumai*, 'to break forth'). Both diseases seemed to be caused by viruses that looked like threads or spindly filaments. There were, however, serological differences between the two, and in early November 1976 the 'new' highly pathogenic virus was named 'Ebola' after a small river in the vicinity of Yambuku.

Ebola shocks the world

For Western medicine, the 1950s and 1960s had been decades of tremendous optimism. Books on the history of disease were published with titles that incorporated such promising phrases as 'the rise and fall of … ', 'the conquest of … ' and 'the eradication of … '. Epidemic infectious diseases seemed to be becoming a thing of the past. The eradication of smallpox in 1979 was an especially key moment in medical history (see page 136).

> 'Weak, emaciated men and women lay about the mud-and-stick chamber, staring out of ghost eyes at the white men. The virus was so toxic that it caused their hair, fingernails and skin to fall off. Those who healed grew new skin.'
>
> A DESCRIPTION OF THE 1976 OUTBREAK IN SUDAN, FROM LAURIE GARRETT, *THE COMING PLAGUE: NEWLY EMERGING DISEASES IN A WORLD OUT OF BALANCE* (1994)

But from the 1950s through to the end of the 20th century, previously unknown and deadly diseases, including a number of haemorrhagic fevers, had begun to surface in various parts of the world. The real significance of these diseases was not fully recognized in the West until their impact began to be felt in Europe and the USA. Marburg fever (first identified in Germany in 1967), Lassa fever (recognized in Lassa, Nigeria, in 1969, when it struck down an American nurse), Lyme disease (first observed in the town of Old Lyme, Connecticut, USA, in 1975), Legionnaires' disease (which caused the deaths of 29 members of the American Legion attending a conference in Philadelphia in 1976), Ebola in 1976, and HIV/AIDS in the 1980s (see pages 192–201) – all these shattered the general mood of complacency. By the 1990s books had begun to



A scientist wearing protective clothing carries out tests for the Ebola virus in Atlanta, USA. Ebola is classified as 'Biosafety Level-4', meaning it is regarded as an extremely dangerous agent which poses a high individual risk of life-threatening disease. There is also a risk that such diseases might be harnessed as bioterrorist weapons.

appear with such titles as *The New Killer Germs, Quest for the Killers and The Coming Plague*, reminding readers that poxes, pestilences and plagues were by no means vanquished. As the English chemist and physiologist John Mayow (1640–79) had observed in the 17th century:
'As a rule disease can scarcely keep pace with the itch to scribble about it.'

Ebola was perhaps the grisliest of the new plagues, provoking, as one scientist has put it, *'convulsive shudders'* in the public imagination. Ebola made it not only into the news, but also into gruesome novels and movies, and images of scientists in protective spacesuits arriving in African villages and carrying lethal viruses back to high-security labs, not to mention graphic depictions of ghastly symptoms and agonizing deaths, scared many people witless. While reports of internal organs dissolving into mush and victims squirting blood from every orifice are exaggerated, there is no doubt that when Ebola hit the headlines in the late 1970s (a few years before HIV/AIDS), it was seen as the most frightening and lethal of the newly emerging diseases.

THE VIRUS HUNTERS

As scientists in high-security laboratories – such as those in Atlanta, Georgia, and Porton Down in England – wrestled to identify and understand the Ebola virus, others in remote parts of Sudan and Zaïre were tracking down the epidemiology of the disease and doing all they could to arrest its spread. These 'disease cowboys', as the medical detectives in Africa were called, faced almost insuperable difficulties as they tried to contain the nightmare of Ebola.

Joe McCormick and Susan Fisher-Hoch, in their 1996 book *The Virus Hunters: Dispatches from the Front Line*, narrate just how tragic it was to witness the impact of this deadly virus in parts of Africa where there were limited health facilities and few safety precautions, and where the population was consumed by grief and terror. Jonathan Mann (1947–98), in his preface to Laurie Garrett's book

The Coming Plague, described the 'disease cowboys' – comprising both international and local teams of scientists and health workers – as:

> *'Heroes of a special kind: bonding science, curiosity and humanitarian concern combined with a practical attitude … who [went] into the field armed only with … will, intelligence, and confidence that a way forward would be found.'*

Their stories could have been written a hundred years ago by their predecessors in tropical medicine – men and women who had grappled to understand and control diseases such as malaria, yellow fever and sleeping sickness.

Many significant discoveries about Ebola were made during these first outbreaks. It appears that the Sudan and Zaïre epidemics of Ebola were coincidental and probably unrelated. Both, however, spread rapidly through personal contact, especially within hospitals and clinics, via infected bodily fluids, blood, tissues and organs. Funeral customs – handling and cleansing the corpses – were also instrumental in spreading the infection. A particularly rapid transmission of the virus occurred through the practice of using and re-using unsterilized syringes in medical centres. In Yambuku, following Mabalo Lokela's illness and death, it is thought that about 300 to 600 people a day were injected at the mission hospital with the same five hypodermic needles. Some patients came for a minor complaint, only to leave with the deadly virus now in their bloodstream.

Since its first reported case in 1976, there have been around 1800 cases and 1200 deaths from Ebola, with fatality rates in each of the outbreaks varying from around 50 to 90 per cent. No locally acquired human cases have occurred outside Africa. Ebola has been placed, along with Marburg, in a new family of viruses, the Filoviridae or filoviruses (after the Latin word *filo*, 'thread').

Four sub-types of the Ebola virus have been identified: Ebola-Zaïre, Ebola-Sudan, Ebola-Côte d'Ivoire and Ebola-Reston. The first three have been found to cause haemorrhagic fever in both humans and animals. The last form was identified in a shipment of cynomolgus monkeys dispatched from the Philippines to laboratories in Reston, Virginia, USA, in 1989. Many of the monkeys died, generating a major global scare. However, Ebola-Reston is the only form that has not so far caused clinical illness in humans (see Monkey Alarms, page 186). The Ebola-Zaïre strain is the most lethal form, with death rates as high as 90 per cent, while the Ebola-Sudan

BUSHMEAT AND THE GREAT APES

In some African countries political instability, a rising population and deplorable economic conditions have forced many people to become dependent on 'bushmeat' (the meat of wild animals), either by selling it or by consuming it themselves. Hunters usually either use wire snares to trap the animals, or simply shoot them.

While conservationists are concerned about over-hunting and the threat to wildlife, epidemiologists are worried about the risk of infected wild animals spreading diseases like Ebola to the human population, as well as the risk of Ebola for populations of great apes. Researchers in the region straddling the border between Gabon and the Republic of the Congo believe that some 5000 gorillas have been wiped out by Ebola, with suggestions that the disease is now passing from gorilla to gorilla through direct contact.

PREVENTING FUTURE OUTBREAKS

Since the 1980s health agencies have recognized the serious threat presented by 'new' diseases, as well as by re-emerging 'old' diseases such as malaria and tuberculosis. Quests to find either a vaccine or cure for diseases such as Ebola are of immediate priority, and one or two promising candidates are on the horizon.

In the meantime, various measures can be put in place to contain outbreaks. Immediate diagnosis is paramount, followed by strict isolation and the use of barrier nursing techniques – not only involving protective clothing and disposable gowns, masks, goggles, and gloves but also the sterilization of all contaminated medical equipment and soiled bedding and clothing. Patients have the best chance of survival if their fluid and electrolyte balance is maintained, and, in the case of the critically ill, if blood and plasma are given to those who are haemorrhaging. Also vital to prevent the spread of Ebola is the rapid and safe disposal of corpses and liquid and solid wastes. Warning local hunters about the dangers of contracting Ebola from forest animals is another part of the jigsaw. However, in many poor and remote parts of Africa, it is difficult to implement such measures.

A worker uses spraying equipment to disinfect a hospital bed used by an Ebola virus victim at Kikwit General Hospital, Zaïre (now Democractic Republic of the Congo), during the Ebola epidemic of 1995. This Ebola outbreak killed 250 people in the city of Kikwit over a period of just a few months.

For the affected nations of Africa – including the Democratic Republic of Congo, Sudan, the Republic of Congo, Uganda and Gabon – Ebola is yet one more merciless microbe that has been tragically unleashed on a continent that already suffers the heaviest burden of old and new diseases on Earth. The incidence and impact of Ebola in Africa is currently not on anything like the same scale as that of malaria or HIV/AIDS. But Ebola – one of the most virulent diseases known to humankind – still has the ability to destroy lives and shatter families and communities, and the power to spread terror across the rest of the world.

strain kills about half of all known cases. The reasons for this varying mortality rate, and why some people survive the disease, are not fully understood.

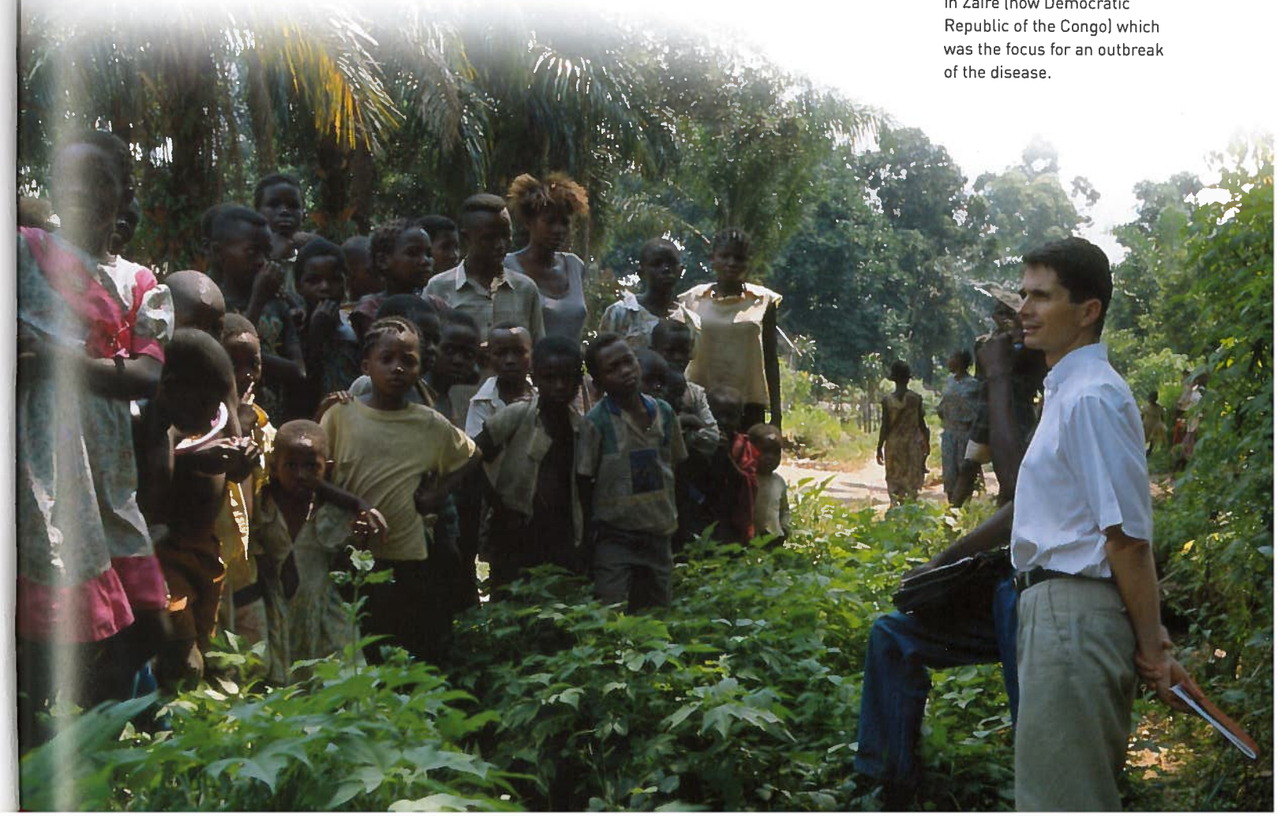
Where did Ebola come from?

There are many other outstanding puzzles about the Ebola virus, especially regarding its origins. Where did it come from, and why did it apparently suddenly infect humans? During the first outbreaks, numerous species of animal were collected and tested by the virus hunters in an attempt to track down a non-human reservoir. Bedbugs, mosquitoes, pigs, cows, bats, monkeys, squirrels and other rodents showed no signs of the Ebola virus, in either Zaïre or Sudan. It has subsequently been shown, however, that a number of non-human primates – including monkeys, chimpanzees and gorillas – seem to be susceptible to the

virus, along with forest antelopes and porcupines. These animals also appear to be able to transmit the disease to people. Mabalo Lokela had eaten antelope meat shortly before he showed his first symptoms, and he and another patient had also handled fresh monkey meat. In 1994 a scientist contracted the disease in the Tai Forest of Côte d'Ivoire while performing an autopsy on the carcass of an infected wild chimpanzee. In 1996, in the Mayibout area of Gabon in West Africa, a chimpanzee was found dead in the forest and eaten by hunters, 19 of whom became ill. Some of their relatives also came down with Ebola.

The high mortality among monkeys infected with the Ebola-Reston virus in the USA suggests that these non-human primates, may, like humans, be 'new' to the virus. The disease probably originated not with monkeys, chimps or antelopes, but with some as yet unidentified host.

One of the first cases in the 1976 Sudan outbreak was a man who worked in a local cotton factory. The factory was also home to a number of bats and, although none were found to be harbouring the Ebola virus at the time, bats have remained a possible, but not proven, suspect of other outbreaks. Laboratory observation has shown that fruit- and insect-eating bats experimentally infected with Ebola do not become ill or die, and this has raised speculation that these mammals may play a role in maintaining the virus in the tropical rainforest. Until scientists can track down its natural host or reservoir, understanding and breaking the transmission cycle of Ebola will be fraught with difficulties. Indeed, even if the true reservoir is ever discovered, there is still the intractable question of how to deal with Ebola.



May, 1995. A World Health Organization official supervises the distribution of information about Ebola to residents of Kikwit – the city in Zaïre (now Democratic Republic of the Congo) which was the focus for an outbreak of the disease.