Viral Hemorrhagic fevers (VHF), Onchocerciasis and Leprosy

General Objective

To familiarize participants with the epidemiological and clinical characteristics of viral hemorrhagic fevers (VHF), Onchocerciasis and Leprosy

Specific Objectives

At the end of the session, participants will be familiar with:

- The biology and epidemiology of Viral hemorrhagic fevers (VHF), Onchocerciasis and Leprosy
- The management of VHF, Onchocerciasis and Leprosy
- Appropriate interventions during outbreaks of VHF

Content

- Biology, epidemiology and management of Viral hemorrhagic fevers (VHF)
- Biology, epidemiology and management of Onchocerciasis and Leprosy
- Surveillance and outbreak control
Introduction

Viral Hemorrhagic fevers (VHF) are caused by a number of different viruses some of which are associated with arthropods (ARBO) and rodents but may also infect humans. They mostly cause mild disease but they are capable of causing severe disease with high fatality and some of them can lead to devastating epidemics in certain areas of the world. Each VHF has its own distinct clinical profile but all of them share a common clinical profile of fever and a bleeding tendency with an often devastating result such as severe hemorrhage and shock. These diseases can cause a serious public health threat as they can have a high epidemic potential, high fatality rate up to 50-80% in the case of Ebola and extreme difficulties in treatment and prevention measures. By consequence they warrant strict safety procedures in health facilities, labs and the community. Effective vaccines exist only in the case of yellow fever and Rift Valley fever indicated only for high risk individuals. Antiviral treatment is not available except in the case of Lassa fever (ribavirin) and thus, treatment is symptomatic. Management of fluid and electrolyte balance from the onset is the most significant measure.

Onchocerciasis is a parasitic disease caused by the filarial worm *Onchocerca volvulus*. It is transmitted through the bites of infected blackflies of *Simulium* species, which carry immature larval forms of the parasite from human to human. In the human body, the larvae form nodules in the subcutaneous tissue, where they mature to adult worms. After mating, the female adult worm can release up to 1000 microfilariae a day. These move through the body, and when they die they cause a variety of conditions, including blindness, skin rashes, lesions, intense itching and skin depigmentation. In a number of countries, onchocerciasis has been controlled through spraying of blackfly breeding sites with insecticide. In addition, a drug is available that kills the microfilariae, alleviating symptoms and reducing transmission. An international control effort aims to bring annual treatment with this drug to all populations at risk by the year 2010. When that is achieved, onchocerciasis may cease to be a public health problem.

Leprosy is caused by a slow-growing bacillus, *Mycobacterium leprae*. It is transmitted via droplets from the nose and mouth of untreated patients with severe disease, but is not highly infectious. If left untreated, the disease can cause nerve damage, leading to muscle weakness and atrophy, and permanent disabilities. Leprosy can be easily treated with a 6–12-month course of multidrug therapy. The treatment is highly effective, and has few side-effects and low relapse rates; there is no known drug resistance.

Methodology

- PPT Presentations
- Lecture/discussion format
- Case study presentation (Marburg/Ebola)
Yellow fever

Yellow fever is a viral disease that has caused large epidemics in Africa and the Americas. It can be recognized from historic texts stretching back 400 years. Infection causes a wide spectrum of disease, from mild symptoms to severe illness and death. The "yellow" in the name is explained by the jaundice that affects some patients. Although an effective vaccine has been available for 60 years, the number of people infected over the last two decades has increased and yellow fever is now a serious public health issue again.

CAUSE

The disease is caused by the yellow fever virus, which belongs to the flavivirus group. In Africa there are two distinct genetic types (called topotypes) associated with East and West Africa. South America has two different types, but since 1974 only one has been identified as the cause of disease outbreaks.

SYMPTOMS

The virus remains silent in the body during an incubation period of three to six days. There are then two disease phases. While some infections have no symptoms whatsoever, the first, "acute", phase is normally characterized by fever, muscle pain (with prominent backache), headache, shivers, loss of appetite, nausea and/or vomiting. Often, the high fever is paradoxically associated with a slow pulse. After three to four days most patients improve and their symptoms disappear.

However, 15% enter a "toxic phase" within 24 hours. Fever reappears and several body systems are affected. The patient rapidly develops jaundice and complains of abdominal pain with vomiting. Bleeding can occur from the mouth, nose, eyes and/or stomach. Once this happens, blood appears in the vomit and faeces. Kidney function deteriorates; this can range from abnormal protein levels in the urine (albuminuria) to complete kidney failure with no urine production (anuria). Half of the patients in the "toxic phase" die within 10-14 days. The remainder recover without significant organ damage.

Yellow fever is difficult to recognize, especially during the early stages. It can easily be confused with malaria, typhoid, rickettsial diseases, haemorrhagic viral fevers (e.g. Lassa), arboviral infections (e.g. dengue), leptospirosis, viral hepatitis and poisoning (e.g. carbon tetrachloride). A laboratory analysis is required to confirm a suspect case. Blood tests (serology assays) can detect yellow fever antibodies that are produced in response to the infection. Several other techniques are used to identify the virus itself in blood specimens or liver tissue collected after death. These tests require highly trained laboratory staff using specialized equipment and materials.

---

1 All information on disease from WHO Health Topics site, http://www.who.int/
REGIONS AFFECTED

The virus is constantly present with low levels of infection (i.e. endemic) in some tropical areas of Africa and the Americas. This viral presence can amplify into regular epidemics. Until the start of this century, yellow fever outbreaks also occurred in Europe, the Caribbean islands and Central and North America. Even though the virus is not felt to be present in these areas now, they must still be considered at risk for yellow fever epidemics.

Thirty-three countries, with a combined population of 508 million, are at risk in Africa. These lie within a band from 15°N to 10°S of the equator. In the Americas, yellow fever is endemic in nine South American countries and in several Caribbean islands. Bolivia, Brazil, Colombia, Ecuador and Peru are considered at greatest risk.

There are 200,000 estimated cases of yellow fever (with 30,000 deaths) per year. However, due to underreporting, only a small percentage of these cases are identified. Small numbers of imported cases also occur in countries free of yellow fever. Although yellow fever has never been reported from Asia, this region is at risk because the appropriate primates and mosquitoes are present.

TRANSMISSION

Humans and monkeys are the principal animals to be infected. The virus is carried from one animal to another (horizontal transmission) by a biting mosquito (the vector). The mosquito can also pass the virus via infected eggs to its offspring (vertical transmission). The eggs produced are resistant to drying and lie dormant through dry conditions, hatching when the rainy season begins. Therefore, the mosquito is the true reservoir of the virus, ensuring transmission from one year to the next.

Several different species of the *Aedes* and *Haemogogus* (S. America only) mosquitoes transmit the yellow fever virus. These mosquitoes are either domestic (i.e. they breed around houses), wild (they breed in the jungle) or semi-domestic types (they display a mixture of habits). Any region populated with these mosquitoes can potentially harbour the disease. Control programmes successfully eradicated mosquito habitats in the past, especially in South America. However, these programmes have lapsed over the last 30 years and mosquito populations have increased. This favours epidemics of yellow fever.

INFECTION OF HUMANS

There are three types of transmission cycle for yellow fever: sylvatic, intermediate and urban. All three cycles exist in Africa, but in South America, only sylvatic and urban yellow fever occur.
• **Sylvatic (or jungle) yellow fever**: In tropical rainforests, yellow fever occurs in monkeys that are infected by wild mosquitoes. The infected monkeys can then pass the virus onto other mosquitoes that feed on them. These infected wild mosquitoes bite humans entering the forest resulting in sporadic cases of yellow fever. The majority of cases are young men working in the forest (logging, etc). On occasion, the virus spreads beyond the affected individual.

• **Intermediate yellow fever**: In humid or semi-humid savannahs of Africa, small-scale epidemics occur. These behave differently from urban epidemics; many separate villages in an area suffer cases simultaneously, but fewer people die from infection. Semi-domestic mosquitoes infect both monkey and human hosts. This area is often called the "zone of emergence", where increased contact between man and infected mosquito leads to disease. This is the most common type of outbreak seen in recent decades in Africa. It can shift to a more severe urban-type epidemic if the infection is carried into a suitable environment (with the presence of domestic mosquitoes and unvaccinated humans).

• **Urban yellow fever**: Large epidemics can occur when migrants introduce the virus into areas with high human population density. Domestic mosquitoes (of one species, Aedes aegypti) carry the virus from person to person; no monkeys are involved in transmission. These outbreaks tend to spread outwards from one source to cover a wide area.

**TREATMENT**

There is no specific treatment for yellow fever. Dehydration and fever can be corrected with oral rehydration salts and paracetamol. Any superimposed bacterial infection should be treated with an appropriate antibiotic. Intensive supportive care may improve the outcome for seriously ill patients, but is rarely available in poorer, developing countries.

**PREVENTION**

Vaccination is the single most important measure for preventing yellow fever. In populations where vaccination coverage is low, vigilant surveillance is critical for prompt recognition and rapid control of outbreaks. Mosquito control measures can be used to prevent virus transmission until vaccination has taken effect.

**VACCINATION**

Yellow fever vaccine is safe and highly effective. The protective effect (immunity) occurs within one week in 95% of people vaccinated. A single dose of vaccine provides protection for 10 years and probably for life. Over 300 million doses have been given and serious side effects are extremely rare. However, recently a few serious adverse outcomes, including deaths, have been reported in Brazil, Australia and the United States. Scientists are
investigating the cause of these adverse events, and monitoring to ensure detection of any similar incidents.

The risk to life from yellow fever is far greater than the risk from the vaccine, so those who may be exposed to yellow fever should be protected by immunization. If there is no risk of exposure, for example, if a person will not be visiting an endemic area, there is no necessity to receive the vaccine. Since most of the other known side effects have occurred in children less than six months old, vaccine is not administered to this age group. The vaccine should only be given to pregnant women during vaccination campaigns in the midst of an epidemic.

Vaccination can be part of a routine preventive immunization programme or can be done in mass "catch-up" campaigns to increase vaccination coverage in areas where it is low. The World Health Organization (WHO) strongly recommends routine childhood vaccination. The vaccine can be administered at age nine months, at the same time as the measles vaccine. Eighteen African nations have agreed to incorporate yellow fever vaccine into their routine national vaccination programmes. This is more cost effective and prevents more cases (and deaths) than when emergency vaccination campaigns are performed to control an epidemic.

Past experience shows the success of this strategy. Between 1939 and 1952 yellow fever cases almost vanished from French West Africa after intensive vaccination campaigns. Similarly, Gambia instituted mass routine vaccination after its 1979/1980 epidemic and later incorporated yellow fever vaccine into its childhood immunization programme. Gambia reported 85% vaccine coverage in 2000. No cases have been reported since 1980, yet the virus remains present in the environment.

To prevent an epidemic in a country, at least 80% of the population must have immunity to yellow fever. This can only be achieved through the effective incorporation of yellow fever into childhood immunization programmes and the implementation of mass catch-up campaigns. The latter is the only way to ensure that coverage of all susceptible age groups is achieved and will prevent outbreaks from spreading. Very few countries in Africa have achieved this level to date.

Vaccination is highly recommended for travellers to high-risk areas. A vaccination certificate is required for entry to many countries, particularly for travellers arriving in Asia from Africa or South America. Fatal cases in unvaccinated tourists have been reported.

SURVEILLANCE

Because vaccination coverage in many areas is not optimal, prompt detection of yellow fever cases and rapid response (emergency vaccination campaigns) are essential for controlling disease outbreaks. Improvement in yellow fever surveillance is needed as evidenced by the gross underreporting of cases (estimates as to the true number of cases vary widely and have put the
underreporting factor between three- and 250-fold). A surveillance system must be sensitive enough to detect and appropriately investigate suspect cases. This is facilitated by a standardized definition of possible yellow fever cases, that is "acute fever followed by jaundice within two weeks of onset of symptoms, or with bleeding symptoms or with death within three weeks of onset". Suspect cases are reported to health authorities on a standardized case investigation form.

Ready access to laboratory testing is essential for confirming cases of yellow fever, as many other diseases have similar symptoms. WHO has recently recommended that every at-risk country have at least one national laboratory where basic yellow fever blood tests can be performed. Training programmes are being conducted and test materials are provided by WHO.

Given the likelihood that other cases have occurred (but have not been detected), one confirmed case of yellow fever is considered to be an outbreak. An investigation team should subsequently explore and define the outbreak. This produces data for analysis, which guides the epidemic control committee in preparing the appropriate outbreak response (e.g. emergency vaccination programmes, mosquito control activities). This committee should also plan for the long term by implementing or strengthening routine childhood yellow fever vaccination.

MOSQUITO CONTROL

In general, eliminating potential mosquito breeding sites is an important and effective means for controlling mosquito-transmitted diseases. For prevention and control of yellow fever, priority is placed on vaccination programmes. For example, mosquito control programmes against wild mosquitoes in forested areas are not practical or cost-effective for preventing sylvatic infections. Spraying to kill adult mosquitoes during epidemics may have value by interrupting virus transmission. This "buys time" for immunity to develop after an emergency vaccination campaign.

IN SUMMARY

Over the last 20 years the number of yellow fever epidemics has risen and more countries are reporting cases. Mosquito numbers and habitats are increasing. In both Africa and the Americas, there is a large susceptible, unvaccinated population. Changes in the world's environment, such as deforestation and urbanization, have increased contact with the mosquito/virus. Widespread international travel could play a role in spreading the disease. The priorities are vaccination of exposed populations, improved surveillance and epidemic preparedness.
Dengue and dengue haemorrhagic fever

KEY FACTS

- Dengue is a mosquito-borne infection that causes a severe flu-like illness, and sometimes a potentially lethal complication called dengue haemorrhagic fever.
- Global incidence of dengue has grown dramatically in recent decades.
- About two fifths of the world's population are now at risk.
- Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas.
- Dengue haemorrhagic fever is a leading cause of serious illness and death among children in some Asian countries.
- There is no specific treatment for dengue, but appropriate medical care frequently saves the lives of patients with the more serious dengue haemorrhagic fever.
- The only way to prevent dengue virus transmission is to combat the disease-carrying mosquitoes.

Dengue is a mosquito-borne infection that in recent decades has become a major international public health concern. Dengue is found in tropical and sub-tropical regions around the world, predominantly in urban and semi-urban areas.

Dengue haemorrhagic fever (DHF), a potentially lethal complication, was first recognized in the 1950s during dengue epidemics in the Philippines and Thailand. Today DHF affects most Asian countries and has become a leading cause of hospitalization and death among children in the region.

There are four distinct, but closely related, viruses that cause dengue. Recovery from infection by one provides lifelong immunity against that virus but confers only partial and transient protection against subsequent infection by the other three viruses. There is good evidence that sequential infection increases the risk of developing DHF.

Global burden of dengue

The incidence of dengue has grown dramatically around the world in recent decades. Some 2.5 billion people – two fifths of the world's population – are now at risk from dengue. WHO currently estimates there may be 50 million dengue infections worldwide every year.

In 2007 alone, there were more than 890 000 reported cases of dengue in the Americas, of which 26 000 cases were DHF.

The disease is now endemic in more than 100 countries in Africa, the Americas, the Eastern Mediterranean, South-east Asia and the Western
TM6 Viral hemorrhagic fevers (VHF), Oncocerciasis and Leprosy

Pacific. South-east Asia and the Western Pacific are the most seriously affected. Before 1970 only nine countries had experienced DHF epidemics, a number that had increased more than four-fold by 1995.

Not only is the number of cases increasing as the disease is spreading to new areas, but explosive outbreaks are occurring. In 2007, Venezuela reported over 80,000 cases, including more than 6,000 cases of DHF.

Some other statistics:

- During epidemics of dengue, infection rates among those who have not been previously exposed to the virus are often 40% to 50%, but can reach 80% to 90%.
- An estimated 500,000 people with DHF require hospitalization each year, a very large proportion of whom are children. About 2.5% of those affected die.
- Without proper treatment, DHF fatality rates can exceed 20%. Wider access to medical care from health providers with knowledge about DHF - physicians and nurses who recognize its symptoms and know how to treat its effects - can reduce death rates to less than 1%.

The spread of dengue is attributed to expanding geographic distribution of the four dengue viruses and their mosquito vectors, the most important of which is the predominantly urban species *Aedes aegypti*. A rapid rise in urban mosquito populations is bringing ever greater numbers of people into contact with this vector, especially in areas that are favourable for mosquito breeding, e.g. where household water storage is common and where solid waste disposal services are inadequate.

DengueNet: WHO surveillance

Transmission

Dengue viruses are transmitted to humans through the bites of infective female *Aedes* mosquitoes. Mosquitoes generally acquire the virus while feeding on the blood of an infected person. After virus incubation for eight to 10 days, an infected mosquito is capable, during probing and blood feeding, of transmitting the virus for the rest of its life. Infected female mosquitoes may also transmit the virus to their offspring by transovarial (via the eggs) transmission, but the role of this in sustaining transmission of the virus to humans has not yet been defined.

Infected humans are the main carriers and multipliers of the virus, serving as a source of the virus for uninfected mosquitoes. The virus circulates in the blood of infected humans for two to seven days, at approximately the same time that they have a fever; *Aedes* mosquitoes may acquire the virus when
they feed on an individual during this period. Some studies have shown that
monkeys in some parts of the world play a similar role in transmission.

**Characteristics**

Dengue fever is a severe, flu-like illness that affects infants, young children
and adults, but seldom causes death.

The clinical features of dengue fever vary according to the age of the patient.
Infants and young children may have a fever with rash. Older children and
adults may have either a mild fever or the classical incapacitating disease with
abrupt onset and high fever, severe headache, pain behind the eyes, muscle
and joint pains, and rash.

Dengue haemorrhagic fever (DHF) is a potentially deadly complication that is
characterized by high fever, often with enlargement of the liver, and in severe
cases circulatory failure. The illness often begins with a sudden rise in
temperature accompanied by facial flush and other flu-like symptoms. The
fever usually continues for two to seven days and can be as high as 41°C,
possibly with convulsions and other complications.

In moderate DHF cases, all signs and symptoms abate after the fever
subsides. In severe cases, the patient's condition may suddenly deteriorate
after a few days of fever; the temperature drops, followed by signs of
circulatory failure, and the patient may rapidly go into a critical state of shock
and die within 12 to 24 hours, or quickly recover following appropriate medical
treatment (see below).

**Treatment**

There is no specific treatment for dengue fever.

For DHF, medical care by physicians and nurses experienced with the effects
and progression of the complicating haemorrhagic fever can frequently save
lives - decreasing mortality rates from more than 20% to less than 1%.
Maintenance of the patient's circulating fluid volume is the central feature of
DHF care.

**Immunization**

There is no vaccine to protect against dengue. Although progress is
underway, developing a vaccine against the disease - in either its mild or
severe form - is challenging.

- With four closely related viruses that can cause the disease, the
  vaccine must immunize against all four types to be effective.
- There is limited understanding of how the disease typically behaves
  and how the virus interacts with the immune system.
- There is a lack of laboratory animal models available to test immune
  responses to potential vaccines.
Despite these challenges, two vaccine candidates have advanced to evaluation in human subjects in countries with endemic disease, and several potential vaccines are in earlier stages of development. WHO provides technical advice and guidance to countries and private partners to support vaccine research and evaluation.

**Prevention and control**

At present, the only method of controlling or preventing dengue virus transmission is to combat the vector mosquitoes.

In Asia and the Americas, *Aedes aegypti* breeds primarily in man-made containers like earthenware jars, metal drums and concrete cisterns used for domestic water storage, as well as discarded plastic food containers, used automobile tyres and other items that collect rainwater. In Africa the mosquito also breeds extensively in natural habitats such as tree holes, and leaves that gather to form "cups" and catch water.

In recent years, *Aedes albopictus*, a secondary dengue vector in Asia, has become established in the United States, several Latin American and Caribbean countries, parts of Europe and Africa. The rapid geographic spread of this species is largely attributed to the international trade in used tyres, a breeding habitat.

Vector control is implemented using environmental management and chemical methods. Proper solid waste disposal and improved water storage practices, including covering containers to prevent access by egg-laying female mosquitoes are among methods that are encouraged through community-based programmes.

During outbreaks, emergency vector control measures can also include broad application of insecticides as space sprays using portable or truck-mounted machines or even aircraft. However, the mosquito-killing effect is transient, variable in its effectiveness because the aerosol droplets may not penetrate indoors to microhabitats where adult mosquitoes are sequestered, and the procedure is costly and operationally difficult. Regular monitoring of the vectors' susceptibility to widely used insecticides is necessary to ensure the appropriate choice of chemicals. Active monitoring and surveillance of the natural mosquito population should accompany control efforts to determine programme effectiveness.

**Lassa fever**
Lassa viral haemorrhagic fever is an acute illness of 1-4 weeks duration that occurs in West Africa. Though first described in the 1950s, the virus causing the disease was not identified until 1969. The virus is a single-stranded RNA virus belonging to the virus family Arenaviridae. Lassa fever is known to be endemic in Guinea (Conakry), Liberia, Sierra Leone and parts of Nigeria, but probably exists in other West African countries as well.

SIGNS AND SYMPTOMS

About 80% of human infections are asymptomatic; the remaining cases have severe multi-system disease, where the virus affects several organs in the body, such as the liver, spleen and kidneys. The incubation period of Lassa fever ranges from 6-21 days. The onset of the disease is usually gradual, starting with fever, general weakness, and malaise. After a few days, headache, sore throat, muscle pain, chest pain, nausea, vomiting, diarrhoea, cough, and abdominal may follow. Severe cases may progress to show facial swelling, fluid in the lung cavity, bleeding from mouth, nose, vagina or gastrointestinal tract, and low blood pressure. Protein may be noted in the urine. Shock, seizures, tremor, disorientation, and coma may be seen in the late stages. Deafness occurs in 25% of patients of whom half recover some function after 1-3 months. Transient hair loss and gait disturbance may occur during recovery.

MORBIDITY AND MORTALITY

Some studies indicate that 300 000 to 500 000 cases of Lassa fever and 5000 deaths occur yearly across West Africa. The overall case-fatality rate is 1%, up to 15% among hospitalized patients. Death usually occurs within 14 days of onset in fatal cases. The disease is especially severe late in pregnancy, with maternal death and/or fetal loss occurring in greater than 80% of cases during the third trimester.

ANIMAL RESERVOIR

Lassa fever is a zoonotic disease, meaning that humans become infected from contact with infected animals. The animal reservoir, or host, of Lassa virus is a rodent of the genus Mastomys, commonly known as the “multimammate rat.” Mastomys infected with Lassa virus do not become ill, but they can shed the virus in their excreta (urine and faeces).

PEOPLE AT RISK

Lassa fever occurs in all age groups and in both men and women. Persons at greatest risk are those living in rural areas where Mastomys are usually found, especially in areas of poor sanitation or crowded living conditions. Health care workers are at risk if proper barrier nursing and infection control practices are not maintained.

TRANSMISSION
Humans usually become infected with Lassa virus from exposure to excreta of infected Mastomys. Both direct exposure, (touching the excreta) and Lassa virus may also be spread between humans through direct contact with the blood, urine, faeces, or other bodily secretions of a person with Lassa fever. There is no epidemiological evidence supporting airborne spread between humans. Person-to-person transmission occurs in both community and health care settings, where the virus may be spread by contaminated medical equipment, such as re-used needles. Sexual transmission of Lassa virus has been reported.

DIAGNOSIS

Because the symptoms of Lassa fever are so varied and non-specific, clinical diagnosis is often difficult, especially early in the course of the disease. Lassa fever is difficult to distinguish from many other diseases which cause fever, including malaria, shigellosis, typhoid fever, yellow fever and other viral haemorrhagic fevers.

Definitive diagnosis requires testing that is available only in highly specialized laboratories. Laboratory specimens may be hazardous and must be handled with extreme care. Lassa fever is diagnosed by detection of Lassa antigen, anti-Lassa antibodies, or virus isolation techniques.

TREATMENT AND PROPHYLAXIS

The antiviral drug ribavirin is effective treatment for Lassa fever if given early on in the course of clinical illness. There is no evidence to support the role of ribavirin as post-exposure prophylactic treatment for Lassa fever.

PREVENTION

Prevention of Lassa fever in the community centers on promoting good “community hygiene” to discourage rodents from entering homes. Effective measures include storing grain and other foodstuffs in rodent-proof containers, disposing of garbage far from the home, maintaining clean households and keeping cats. Because Mastomys are so abundant in endemic areas, it is not possible to completely eliminate them from the environment.

INFECTION CONTROL

Family members and health care workers should always be careful to avoid contact with blood and body fluids while caring for sick persons. Routine barrier nursing precautions probably protect against transmission of Lassa virus in most circumstances. However, for added safety, patients suspected to have Lassa fever should be cared for under specific “isolation precautions,” which include the wearing of protective clothing such as masks, gloves, gowns, and face shields, and the systematic sterilization of contaminated equipment (see also detailed guidelines in “Infection Control for Viral Hemorrhagic Fevers in the African Health Care Setting”)\(^1\)
ONGOING INITIATIVES

Civil unrest in many of the countries where Lassa fever is endemic has impeded effective control. However, recent peace initiatives have opened new opportunities to combat the problem. The Ministries of Health of Guinea, Liberia and Sierra Leone, WHO, the Office of United States Foreign Disaster Assistance, the United Nations, and other partners have worked together to establish the Mano River Union Lassa Fever Network. The programme supports these three countries in developing national prevention strategies and enhancing laboratory diagnostics for Lassa fever and other dangerous diseases. Training in laboratory diagnosis, clinical management, and environmental control is also included. In addition, a new ward dedicated to the care of patients with Lassa fever is under construction in Sierra Leone, sponsored by the European Union.

INTERNATIONAL PUBLIC HEALTH IMPLICATIONS

On rare occasions, travellers from areas where Lassa fever is endemic export the disease to other countries. Although malaria, typhoid fever, and many other tropical infections are much more common, the diagnosis of Lassa fever should be considered in febrile patients returning from West Africa, especially if they have had exposures in rural areas or hospitals in countries where Lassa fever is known to be endemic. Health care workers seeing a patient suspected to have Lassa fever should immediately contact local and national experts for advice and to arrange for laboratory testing.
Crimean-Congo haemorrhagic fever

Crimean-Congo haemorrhagic fever (CCHF) is a viral haemorrhagic fever of the *Nairovirus* group. Although primarily a zoonosis, sporadic cases and outbreaks of CCHF affecting humans do occur. The disease is endemic in many countries in Africa, Europe and Asia, and during 2001, cases or outbreaks have been recorded in Kosovo, Albania, Iran, Pakistan, and South Africa.

The disease was first described in the Crimea in 1944 and given the name Crimean haemorrhagic fever. In 1969 it was recognized that the pathogen causing Crimean haemorrhagic fever was the same as that responsible for an illness identified in 1956 in the Congo, and linkage of the 2 place names resulted in the current name for the disease and the virus. CCHF is a severe disease in humans, with a high mortality rate. Fortunately, human illness occurs infrequently, although animal infection may be more common.

The geographical distribution of the virus, like that of its tick vector, is widespread. Evidence of CCHF virus has been found in Africa, Asia, the Middle East and Eastern Europe. Healthcare workers in endemic areas should be aware of the illness and the correct infection control procedures to protect themselves and their patients from the risk of nosocomial (hospital-acquired) infection.

CCHF VIRUS

The virus which causes CCHF is a *Nairovirus*, a group of related viruses forming one of the five genera in the *Bunyaviridae* family of viruses. All of the 32 members of the *Nairovirus* genus are transmitted by argasid or ixodid ticks, but only three have been implicated as causes of human disease: the Dugbe and Nairobi sheep viruses, and CCHF, which is the most important human pathogen amongst them.

CCHF RESERVOIRS AND VECTORS

- The CCHF virus may infect a wide range of domestic and wild animals. Many birds are resistant to infection, but ostriches are susceptible and may show a high prevalence of infection in endemic areas. Animals become infected with CCHF from the bite of infected ticks.
- A number of tick genera are capable of becoming infected with CCHF virus, but the most efficient and common vectors for CCHF appear to be members of the *Hyalomma* genus. Trans-ovarial (transmission of the virus from infected female ticks to offspring via eggs) and venereal transmission have been demonstrated amongst some vector species, indicating one mechanism which may contribute to maintaining the circulation of the virus in nature.
- However, the most important source for acquisition of the virus by ticks is believed to be infected small vertebrates on which immature *Hyalomma* ticks feed. Once infected, the tick remains infected through
its developmental stages, and the mature tick may transmit the infection to large vertebrates, such as livestock. Domestic ruminant animals, such as cattle, sheep and goats, are viraemic (virus circulating in the bloodstream) for around one week after becoming infected.

- Humans who become infected with CCHF acquire the virus from direct contact with blood or other infected tissues from livestock during this time, or they may become infected from a tick bite. The majority of cases have occurred in those involved with the livestock industry, such as agricultural workers, slaughterhouse workers and veterinarians.

CLINICAL FEATURES

- The length of the incubation period for the illness appears to depend on the mode of acquisition of the virus. Following infection via tick bite, the incubation period is usually one to three days, with a maximum of nine days. The incubation period following contact with infected blood or tissues is usually five to six days, with a documented maximum of 13 days.
- Onset of symptoms is sudden, with fever, myalgia (aching muscles), dizziness, neck pain and stiffness, backache, headache, sore eyes and photophobia (sensitivity to light). There may be nausea, vomiting and sore throat early on, which may be accompanied by diarrhoea and generalised abdominal pain. Over the next few days, the patient may experience sharp mood swings, and may become confused and aggressive. After two to four days, the agitation may be replaced by sleepiness, depression and lassitude, and the abdominal pain may localize to the right upper quadrant, with detectable hepatomegaly (liver enlargement).
- Other clinical signs which emerge include tachycardia (fast heart rate), lymphadenopathy (enlarged lymph nodes), and a petechial rash (a rash caused by bleeding into the skin), both on internal mucosal surfaces, such as in the mouth and throat, and on the skin. The petechiae may give way to ecchymoses (like a petechial rash, but covering larger areas) and other haemorrhagic phenomena such as melaena (bleeding from the upper bowel, passed as altered blood in the faeces), haematuria (blood in the urine), epistaxis (nosebleeds) and bleeding from the gums. There is usually evidence of hepatitis. The severely ill may develop hepatorenal (i.e., liver and kidney) and pulmonary failure after the fifth day of illness.
- The mortality rate from CCHF is approximately 30%, with death occurring in the second week of illness. In those patients who recover, improvement generally begins on the ninth or tenth day after the onset of illness.

DIAGNOSIS

- Diagnosis of suspected CCHF is performed in specially-equipped, high biosafety level laboratories. IgG and IgM antibodies may be detected in serum by enzyme-linked immunoassay (the "ELISA" or "EIA" methods) from about day six of illness. IgM remains detectable for up to four
months, and IgG levels decline but remain detectable for up to five years.

- Patients with fatal disease do not usually develop a measurable antibody response and in these individuals, as well as in patients in the first few days of illness, diagnosis is achieved by virus detection in blood or tissue samples. There are several methods for doing this. The virus may be isolated from blood or tissue specimens in the first five days of illness, and grown in cell culture. Viral antigens may sometimes be shown in tissue samples using immunofluorescence or EIA.

- More recently, the polymerase chain reaction (PCR), a molecular method for detecting the viral genome, has been successfully applied in diagnosis.

**TREATMENT**

- General supportive therapy is the mainstay of patient management in CCHF. Intensive monitoring to guide volume and blood component replacement is required.

- The antiviral drug ribavirin has been used in treatment of established CCHF infection with apparent benefit. Both oral and intravenous formulations seem to be effective.

- The value of immune plasma from recovered patients for therapeutic purposes has not been demonstrated, although it has been employed on several occasions.

**PREVENTION AND CONTROL**

- Although an inactivated, mouse brain-derived vaccine against CCHF has been developed and used on a small scale in Eastern Europe, there is no safe and effective vaccine widely available for human use. The tick vectors are numerous and widespread and tick control with acaricides (chemicals intended to kill ticks) is only a realistic option for well-managed livestock production facilities.

- Persons living in endemic areas should use personal protective measures that include avoidance of areas where tick vectors are abundant and when they are active (Spring to Fall); regular examination of clothing and skin for ticks, and their removal; and use of repellents.

- Persons who work with livestock or other animals in the endemic areas can take practical measures to protect themselves. These include the use of repellents on the skin (e.g. DEET) and clothing (e.g. permethrin) and wearing gloves or other protective clothing to prevent skin contact with infected tissue or blood.

- When patients with CCHF are admitted to hospital, there is a risk of nosocomial spread of infection. In the past, serious outbreaks have occurred in this way and it is imperative that adequate infection control measures be observed to prevent this disastrous outcome.

- Patients with suspected or confirmed CCHF should be isolated and cared for using barrier nursing techniques. Specimens of blood or tissues taken for diagnostic purposes should be collected and handled
TM6 Viral hemorrhagic fevers (VHF), Oncocerciasis and Leprosy

using universal precautions. Sharps (needles and other penetrating surgical instruments) and body wastes should be safely disposed of using appropriate decontamination procedures.

- Healthcare workers are at risk of acquiring infection from sharps injuries during surgical procedures and, in the past, infection has been transmitted to surgeons operating on patients to determine the cause of the abdominal symptoms in the early stages of (at that moment undiagnosed) infection. Healthcare workers who have had contact with tissue or blood from patients with suspected or confirmed CCHF should be followed up with daily temperature and symptom monitoring for at least 14 days after the putative exposure.
Marburg haemorrhagic fever

Marburg haemorrhagic fever is a severe and highly fatal disease caused by a virus from the same family as the one that causes Ebola haemorrhagic fever. Viewed under electron microscopy, the viruses show particles shaped like elongated filaments, sometimes coiled into strange shapes, that give the Filoviridae family its name. These viruses are among the most virulent pathogens known to infect humans.

Though caused by different viruses, the two diseases are clinically similar. Both diseases are rare, but have a capacity to cause dramatic outbreaks with high fatality. Historically, outbreaks have tended to reach the attention of health authorities only after transmission has been amplified by inadequate infection control in health care settings.

Neither disease has a vaccine or specific treatment. Ecological studies are in progress to identify the natural reservoir of both Marburg and Ebola. There is evidence that bats are involved, but much work remains to be done to definitively describe the natural transmission cycle. Monkeys are susceptible to infection but are not considered plausible reservoir hosts as virtually all infected animals die too rapidly to sustain survival of the virus. Infection of humans occurs sporadically.

Natural history and clinical features


Geographical occurrence. A large, 2-centre outbreak in Marburg, Germany, and Belgrade, former Yugoslavia, in 1967 led to the initial recognition of the disease. The outbreak was associated laboratory work using African green monkeys (Cercopithecus aethiops) imported from Uganda. Subsequently, outbreaks and sporadic cases have been reported in Angola, Democratic Republic of the Congo, Kenya, South Africa (in a person with a recent travel history to Zimbabwe) and Uganda.

Transmission. Transmission of the virus from person to person requires close contact with a patient. Transmission does not occur during the incubation period. Infection results from contact with blood or other body fluids (faeces, vomitus, urine, saliva, and respiratory secretions) with high virus concentration, especially when these fluids contain blood. Transmission via infected semen can occur; virus has been detected in semen up to seven weeks after clinical recovery.

Patients become increasingly infectious as their illness progresses, and are most infectious during the phase of severe illness. Close contact with a severely ill patient, during care at home or in hospital, and certain burial practices are common routes of infection. Transmission via contaminated injection equipment or through needle-stick injuries is associated with more severe disease, rapid deterioration, and possibly higher fatality.
Incubation period. 3 to 9 days.

Susceptibility. All age groups are susceptible to infection, but most cases have occurred in adults. Prior to the present outbreak in Angola, paediatric cases were considered extremely rare. In the largest outbreak previously recorded, which occurred in the Democratic Republic of the Congo from late 1998 to 2000, only 12 (8%) of the cases were under the age of 5 years.

Clinical features. Illness caused by Marburg virus begins abruptly, with severe headache and severe malaise. Muscle aches and pains are a common feature.

A high fever usually appears on the first day of illness, followed by progressive and rapid debilitation. A severe watery diarrhoea, abdominal pain and cramping, nausea, and vomiting begin about the third day. Diarrhoea can persist for a week. The appearance of patients at this phase has been described as showing “ghost-like” drawn features, deep-set eyes, expressionless faces, and extreme lethargy. In the 1967 European outbreak, a non-itchy rash was a feature noted in most patients between days 2 and 7 after symptom onset.

Many patients develop severe haemorrhagic manifestations between days 5 and 7, and fatal cases usually have some form of bleeding, often from multiple sites. Findings of fresh blood in vomitus and faeces are often accompanied by bleeding from the nose, gums, and vagina. Spontaneous bleeding at venipuncture sites can be particularly troublesome. During the severe phase of illness, patients have sustained high fevers. Involvement of the central nervous system can result in confusion, irritability, and aggression. Orchitis has been reported occasionally in the late phase of disease (day 15).

In fatal cases, death occurs most often between 8 and 9 days after symptom onset, usually preceded by severe blood loss and shock.

Natural reservoir of the virus. Unknown.

History of recorded outbreaks

1967: Germany and Yugoslavia. Marburg haemorrhagic fever was initially detected following simultaneous outbreaks in Marburg and Frankfurt, Germany and Belgrade, former Yugoslavia. The initial cases occurred in laboratory workers handling African green monkeys imported from Uganda. The outbreaks involved 25 primary infections, with 7 deaths, and 6 secondary cases, with no deaths. The primary infections were in laboratory staff exposed to Marburg virus while working with monkeys or their tissues. The secondary cases involved two doctors, a nurse, a post-mortem attendant, and the wife of a veterinarian. All secondary cases had direct contact, usually involving blood, with a primary case. Both doctors became infected through accidental skin pricks when drawing blood from patients.
1975: South Africa, possibly via Zimbabwe. In mid-February 1975, an Australian, aged 20 years, was admitted to a hospital in Johannesburg, South Africa. During early February, he and a companion had travelled extensively through Zimbabwe, often camping outdoors. He died of Marburg haemorrhagic fever four days after hospital admission. His travelling companion became infected, as did a nurse who attended both patients. Both secondary cases recovered.


1987: Kenya. In August 1987, a 15-year-old Dane, was admitted to a hospital in Kenya, suffering from Marburg haemorrhagic fever. His illness proved fatal. Nine days prior to symptom onset, he had visited Kitum Cave in Mount Elgon National Park. No further cases were detected.

1998–2000: Democratic Republic of the Congo. The outbreak in DRC marked the first large outbreak of this disease under natural conditions. The outbreak, which occurred from late 1998 to 2000, involved 154 cases, of which 128 were fatal, representing a case fatality of 83%. The majority of cases occurred in young male workers at a gold mine in Durba, in the northeastern part of the country, which proved to be the epicentre of the outbreak. Cases were subsequently detected in the neighbouring village of Watsa. Family members involved in the close care of patients accounted for some cases, but secondary transmission appeared to be rare. Subsequent virological investigation indicated that virus of several different strains was introduced to human populations, from some yet unknown environmental source, on more than seven separate occasions.

2004–2005: Angola. In what was to become the largest outbreak of MHF in history, this outbreak is believed to have begun in Uige Province in October 2004. By the time the last laboratory-confirmed case was identified in July 2005, the Ministry of Health had reported a total of 374 cases, including 329 deaths (CFR 88%) countrywide. Of these, 368 cases, including 323 deaths, were reported in Uige Province. All cases detected in other provinces have been linked directly to the outbreak in Uige.

2008. In July 2008, a Dutch tourist developed Marburg four days after returning to the Netherlands from a three-week holiday in Uganda. To-date, the source of the exposure has not been confirmed, although it is known that the woman visited caves in western Uganda where bats were present.
Ebola haemorrhagic fever

The Ebola virus belongs to the Filoviridae family (filovirus) and is comprised of five distinct species: Zaïre, Sudan, Côte d'Ivoire, Bundibugyo and Reston.

Zaïre, Sudan and Bundibugyo species have been associated with large Ebola hemorrhagic fever (EHF) outbreaks in Africa with high case fatality ratio (25–90%) while Côte d'Ivoire and Reston have not. Reston species can infect humans but no serious illness or death in humans have been reported to date.

Human infection with the Ebola Reston subtype, found in the Western Pacific, has only caused asymptomatic illness, meaning that those who contract the disease do not experience clinical illness. The natural reservoir of the Ebola virus seems to reside in the rain forests of the African continent and in areas of the Western Pacific.

TRANSMISSION

- The Ebola virus is transmitted by direct contact with the blood, secretions, organs or other body fluids of infected persons.
- Burial ceremonies where mourners have direct contact with the body of the deceased person can play a significant role in the transmission of Ebola.
- The infection of human cases with Ebola virus through the handling of infected chimpanzees, gorillas, and forest antelopes -- both dead and alive -- has been documented in Côte d'Ivoire, the Republic of Congo and Gabon. The transmission of the Ebola Reston strain through the handling of cynomolgus monkeys has also been reported.
- Health care workers have frequently been infected while treating Ebola patients, through close contact without correct infection control precautions and adequate barrier nursing procedures.

Incubation period: two to 21 days.

SYMPTOMS

Ebola is characterized by the sudden onset of fever, intense weakness, muscle pain, headache and sore throat. This is often followed by vomiting, diarrhoea, rash, impaired kidney and liver function, and in some cases, both internal and external bleeding. Laboratory findings show low counts of white blood cells and platelets as well as elevated liver enzymes.

DIAGNOSIS

Specialized laboratory tests on blood specimens detect specific antigens and/or genes of the virus. Antibodies to the virus can be detected, and the virus can be isolated in cell culture. Tests on samples present an extreme biohazard risk and are only conducted under maximum biological containment conditions. New developments in diagnostic techniques include non-invasive
methods of diagnosis (testing saliva and urine samples) and testing inactivated samples to provide rapid laboratory diagnosis to support case management during outbreak control activities.

THERAPY AND VACCINE

- Severe cases require intensive supportive care, as patients are frequently dehydrated and in need of intravenous fluids or oral rehydration with solutions containing electrolytes.
- No specific treatment or vaccine is yet available for Ebola haemorrhagic fever. Several potential vaccines are being tested but it could be several years before any is available. A new drug therapy has shown some promise in laboratory studies and is currently being evaluated. But this too will take several years.
- Experimental studies using hyper-immune sera on animals have shown no protection against the disease.

CONTAINMENT

- Suspected cases should be isolated from other patients and strict barrier nursing techniques implemented.
- Tracing and following up people who may have been exposed to Ebola through close contact with patients are essential.
- All hospital staff should be briefed on the nature of the disease and its transmission routes. Particular emphasis should be placed on ensuring that invasive procedures such as the placing of intravenous lines and the handling of blood, secretions, catheters and suction devices are carried out under strict barrier nursing conditions. Hospital staff should have individual gowns, gloves, masks and goggles. Non-disposable protective equipment must not be reused unless they have been properly disinfected.
- Infection may also spread through contact with the soiled clothing or bed linens from a patient with Ebola. Disinfection is therefore required before handling these items.
- Communities affected by Ebola should make efforts to ensure that the population is well informed, both about the nature of the disease itself and about necessary outbreak containment measures, including burial of the deceased. People who have died from Ebola should be promptly and safely buried.

CONTACTS

- As the primary mode of person-to-person transmission is contact with contaminated blood, secretions or body fluids, people who have had close physical contact with patients should be kept under strict surveillance. Their body temperature should be checked twice a day, with immediate hospitalization and strict isolation in case of the onset of fever.
Hospital staff who come into close contact with patients or contaminated materials without barrier nursing attire must be considered as contacts and followed up accordingly.

HISTORY

The Ebola virus was first identified in a western equatorial province of Sudan and in a nearby region of Zaïre (now the Democratic Republic of the Congo) in 1976 after significant epidemics in Yambuku in northern Democratic Republic of the Congo, and Nzara in southern Sudan.

- Between June and November 1976, the Ebola virus infected 284 people in Sudan, causing 151 deaths. In the Democratic Republic of the Congo, there were 318 cases and 280 deaths in September and October. An isolated case occurred in the Democratic Republic of the Congo in 1977, and there was another outbreak in Sudan in 1979 (33 cases, including 22 deaths).
- In 1989, Reston, an Ebola virus subtype, was isolated in quarantined laboratory cynomolgus monkeys (Macaca fascicularis) in Reston, Virginia, USA. From 1989 to 1996, several outbreaks caused by the Ebola Reston subtype occurred in monkeys imported from the Philippines to the USA (Reston in Virginia, Alice in Texas and Pennsylvania) and to Italy. Investigations traced the source of all Ebola Reston outbreaks to one export facility near Manila in the Philippines, but the mode of contamination of this facility was not determined. Several monkeys died, and at least four people were infected, although none of them suffered clinical illness.
- One human case of Ebola haemorrhagic fever of the Cote d'Ivoire subtype and several cases in chimpanzees were confirmed in Côte d'Ivoire in November 1994.
- A large epidemic occurred in Kikwit, the Democratic Republic of the Congo in 1995 with 315 cases, 250 of whom died.
- In Gabon, Ebola haemorrhagic fever was first documented in 1994 (19 cases including 9 deaths). Successive outbreaks occurred in February (37 cases including 21 deaths) and July of 1996 (60 cases including 45 deaths).
- In October 2000, Ebola was reported in Gulu district in northern Uganda. Between September 2000 and January 2001, the Sudan subtype of the Ebola virus infected 425 cases, including 224 deaths, making this the largest epidemic so far documented of Ebola. This was the first reported emergence of the Sudan Ebola virus since 1979.
- From October 2001 to December 2003, several Ebola outbreaks of the Zaïre subtype were reported in Gabon and the Republic of the Congo with a total of 302 cases and 254 deaths.

About 1850 cases with over 1200 deaths have been documented since the Ebola virus was discovered.
NATURAL RESERVOIR

- The natural reservoir of the Ebola virus is unknown despite extensive studies, but it seems to reside in the rain forests on the African continent and in the Western Pacific.
- Although non-human primates have been a source of infection for humans, they are not thought to be the reservoir. They, like humans, are believed to be infected directly from the natural reservoir or through a chain of transmission from the natural reservoir.
- On the African continent, Ebola infections of human cases have been linked to direct contact with gorillas, chimpanzees, monkeys, forest antelope and porcupines found dead in the rainforest. So far, the Ebola virus has been detected in the wild in carcasses of chimpanzees (in Côte-d'Ivoire and the Republic of the Congo), gorillas (Gabon and the Republic of the Congo) and duikers (the Republic of the Congo).
- Different hypotheses have been developed to explain the origin of Ebola outbreaks. Laboratory observation has shown that bats experimentally infected with Ebola do not die, and this has raised speculation that these mammals may play a role in maintaining the virus in the tropical forest.
- Extensive ecological studies are under way in the Republic of the Congo and Gabon to identify the Ebola's natural reservoir.
Case studies - Ebola outbreaks

1. Ebola of outbreak in the Democratic Republic of the Congo


17 February 2009 -- The Ministry of Health of the Democratic Republic of the Congo (DRC) has on 16 February 2009 declared the end of the Ebola epidemic in the Mweka and Luebo health zones in the Province of Kasai Occidental. The last person to be infected by the virus died on 1 January 2009. This is more than double the maximum incubation period (42 days) for Ebola.

As of today, the health authorities have reported a total of 32 cases, including 15 deaths from Ebola. These 32 cases include confirmed, probable and suspect cases. During this outbreak, the Ebola virus was confirmed by laboratory tests at the Institut National de Recherches Biologiques (INRB) in Kinshasa, the Centre International de Recherches Médicales de Franceville (CIRMF) in Gabon, and the National Institute for Communicable Diseases (NICD), South Africa.

The WHO Country Office, Regional Office and Headquarters supported the MoH in Kinshasa and in the field at the location of the outbreak. The international response to the outbreak also involved UNICEF, the United Nations Organization Mission in the Democratic Republic of the Congo (MONUC), and the World Food Programme (WFP), as well as support from Caritas (Belgium), and the Congolese (DRC) Red Cross, together with partners in the Global Outbreak Alert and Response Network (GOARN), including the National Microbiology Laboratory (NML) of the Public Health Agency of Canada (PHAC), CIRMF, and NICD, and Médecins Sans Frontières (Belgium).


An outbreak of an unusual severe febrile illness characterized by gastroenteritis, headache, conjunctivitis and occasional hemorrhagic signs, with significant mortality, was reported to the Ministry of Health in Kampala on 8 October 2000, by both the medical superintendent of St Mary’s hospital in Lacor and the acting district director of health services, Gulu district, Uganda. A preliminary assessment of the situation by the Ministry of Health revealed additional evidence of disease in the community as well as in Gulu hospital, the regional referral hospital for the north-eastern region.

On 10 October, an isolation ward was put in place in Lacor hospital. The clinical suspicion of haemorrhagic fever was confirmed on 15 October, when the National Institute of Virology, Johannesburg (South Africa)
identified Ebola virus infection among specimens from a cluster of cases including student nurses at St Mary’s hospital. The laboratory testing included a combination of virus antigen detection and antibody ELISA tests, and reverse transcriptase polymerase chain reaction (RT-PCR). The virus associated with this outbreak is Ebola- Sudan and differed at the nucleotide sequence level from earlier Ebola-Sudan isolates by 3.3% and 4.2% in the polymerase (362 nucleotides) and nucleocapsid (146 nucleotides) protein encoding genes, respectively. The Ministry of Health requested WHO to coordinate the international response of health organizations worldwide. This article describes the control activities in the 3 affected districts, and preliminary clinical and epidemiological findings of the Ministry of Health in conjunction with the international epidemic response team.

**Epidemic response**

Control activities were organized around surveillance and epidemiology, clinical case management, social mobilization, and coordination and logistic support. An active surveillance system for Ebola haemorrhagic fever (EHF) was initiated to determine the extent and magnitude of the outbreak, identify foci of disease activity, and detect cases early. The system was designed to be very sensitive and detect all persons whose illness might be EHF. Ill persons were encouraged to be assessed at a hospital and, if indicated, to be hospitalized to diminish further community transmission. Targeted prevention activities included: following up contacts for 21 days (maximum incubation period), establishment of trained burial teams for all potential and confirmed EHF deaths, community education, cessation of traditional healing practices and burials and of large public gatherings, and updating hospital infection control measures. Initial laboratory testing was performed at a field laboratory established at St Mary’s hospital, by the Centers for Disease Control and Prevention (CDC), Atlanta, United States, and supplemented by additional testing at CDC and the National Institute of Virology (South Africa).

**Surveillance**

A reinforced active surveillance system was established during the third week of October, with 3 case notification categories: alert, suspect, probable. The .alert. category was restricted to community use for notification to mobile teams, peripheral health units, private clinics and pharmacies, of individuals with sudden onset of high fever, sudden death, or any haemorrhagic signs. The .suspect. case definition was used by the mobile teams and peripheral health units to categorize potential cases and to determine if any patient required transport to an isolation ward. This category included all persons with fever and contact with a potential case of EHF, all persons with unexplained bleeding of any kind, all persons with fever and 3 or more specified symptoms (i.e. headache, vomiting, anorexia, diarrhoea, weakness or severe fatigue, abdominal pain, body aches or joint pains, difficulty in swallowing, difficulty in breathing and hiccoughs), and all unexplained deaths. The probable. case definition was identical to the suspect
definition but with the requirement that it was described by a physician. Where possible, verbal autopsies were conducted on unexplained community deaths to obtain additional clinical and epidemiological information. If laboratory samples were obtained at an appropriate time during the illness, these notification categories were reclassified into laboratory-confirmed cases and not a case. Laboratory-confirmed cases were either positive for Ebola virus antigen or Ebola IgG antibody; not a case had no Ebolaspecific detectable antibody or antigen. Individuals identified with isolated IgG antibodies without symptoms were not included as cases.

An independent rapid reporting system which was initially established to estimate the magnitude of the outbreak at the national level was also continued. New admissions at hospital isolation wards, in addition to incident deaths identified in those wards and the community, were reported every morning as clinical EHF cases. This system formed the basis of daily press briefings and resource allocation and mobilization.

**Case description**

Among 62 patients with laboratory-confirmed EHF admitted to Gulu hospital between 5 October and 27 November 2000, the most commonly reported signs and symptoms on admission included diarrhoea (66%), asthenia (64%), anorexia (61%), headache (63%), nausea and vomiting (60%), abdominal pain (55%) and chest pain (48%). Patients presented for care a mean of 4.2 days after the onset of symptoms. Bleeding was seen in only about 20% of patients and primarily involved the gastrointestinal tract. A preliminary analysis of these laboratory-confirmed cases compared with 92 laboratory-negative patients showed the following signs and symptoms to be significantly (p<0.05) more common among Ebola cases than in patients presenting with other illnesses: asthenia, anorexia, sore throat, right upper quadrant abdominal tenderness, conjunctival injection or haemorrhage, fine papular rash, and gingival bleeding.

The cumulative case-fatality rate in this hospitalized group was 58%, but was higher (80%) in children aged < 15 years. Spontaneous abortions were noted among pregnant women infected with Ebola virus. Fatal cases usually exhibited a rapid progression of shock, increasing coagulopathy, and loss of consciousness.

**Epidemiology**

As of 23 January 2001, a total of 425 presumptive² cases of Ebola haemorrhagic fever were recorded from 3 districts in Uganda: 393 (93%) from Gulu, 27 (6%) from Masindi, and 5 (1%) from Mbarara with a combined area of 31 000 km² and an estimated current population of 1.8 million (based on the 1991 census and movement of displaced persons) (Map 1). The earliest reported presumptive case had disease onset on 30 August 2000, and the last case on 9 January 2001 (Fig. 1). There were 269 (63%) women and 156 (37%) men with 224 deaths (case-fatality rate = 53%). The mean age was 27 years ± 16 years; the youngest was aged 3 days and the oldest 72 years; 20% of presumptive cases were aged < 13 years. There were 29 infected health care workers.
The mean time from symptom onset until death was 8 ± 5 days. Laboratory confirmation was established for 218 (51%) of the presumptive cases. As of 23 January 2001, a total of 428 clinical EHF cases were reported to and by the Ministry of Health. However, the number of reported deaths was 173. Although the discrepancy in deaths was expected because of the addition of retrospective unexplained deaths in the reinforced active surveillance system and updating of the final outcome of admissions, the concordance in the two systems of estimating the magnitude of the outbreak in the community was remarkable. The smaller total number can be explained by subsequent laboratory testing of admissions that excluded Ebola infection.

Although the outbreak was reported following a cluster of cases including health care workers, it was retrospectively recognized among sporadic cases in the hospital and community.

The 3 most important defined means of amplification were: attendance at funerals of presumptive EHF cases where ritual contact with the deceased was the norm; patients with multiple familial care providers; or nosocomial transmission from other patients or staff members. Fourteen (64%) of 22 health care workers in Gulu district were infected after establishing the isolation wards which required subsequent reinforcement of infection control measures. Two distant focal outbreaks were initiated by movement of infected contacts of EHF cases from Gulu to Mbarara and Masindi districts. National notification and surveillance efforts led to the quick identification of these foci and their effective containment.

**Editorial note**

Ebola haemorrhagic fever is a viral haemorrhagic fever associated with infection with any 3 of the 4 members of the genus Ebola virus in the family Filoviridae. The purported zoonotic reservoir for the viruses remains unknown. However, outbreaks of EHF are most often associated with the introduction of the virus into the community via a single infected human followed by dissemination by human-to-human transmission, often within medical facilities. This is the largest reported EHF outbreak, and only the third known Ebola-Sudan virus-associated outbreak. The first occurred in 1976 in southern Sudan in the towns of Nzara and Manidi, and was concurrent with an Ebola-Zaire outbreak in Zaire. The second Ebola-Sudan outbreak occurred in 1979 in the same locations. As in this outbreak, both the 1976 and 1979 outbreaks had a case fatality of approximately 50%. Also similar to previous Ebola outbreaks, the current outbreak seems to have been initiated by the introduction of the virus into Gulu municipality followed by transmission in the community and in medical care facilities.

However, the early cases of this outbreak remain obscure, which has limited the ability to track back to the initial case to allow any further investigation of the possible reservoir of the virus.

Transmission in the community was eliminated by recognition of the outbreak and initiation of case finding and hospitalization of identified cases in medical care facilities where barrier nursing was implemented. Education of the community about the dangers of close contact with symptomatic and deceased EHF cases and awareness of the disease among medical staff were all employed to diminish further transmission. Despite the inauguration
of barrier nursing practices in special isolation wards, transmission to medical care providers occurred during this outbreak.

However, the use of isolation facilities to diminish community transmission of the virus and reduce the overall burden of EHF in the community remains the single most effective means of controlling outbreaks of EHF. National efforts limited the scope of this outbreak during the course of the outbreak approximately 5,600 contacts were under surveillance for 21-day periods in Gulu district by over 150 trained volunteers. Efforts have been initiated to better understand this outbreak, identify specific risk factors for disease acquisition in the community and hospital, determine antibody prevalence in selected groups, and examine virological and clinical parameters of infection to refine future prevention activities. Efforts are also under way to increase the frequency of reporting of additional diseases of epidemic potential such as EHF into the national integrated disease surveillance system.

The international outbreak response team, working with the Ministry of Health of Uganda under the leadership of WHO, was made up of partners in the Global Alert and Response Network. The international team included: International Committee of the Red Cross, International Federation of Red Cross and Red Crescent Societies, International Rescue Committee, Médecins sans frontières (Holland and Belgium); and teams from the following countries: Belgium (Institute for Tropical Medicine, Antwerp); Canada (Health Canada); France (Epicentre, Paris); Germany (Tropical Medicine Institute, Hamburg); Italy (Istituto superiore di sanità, Italian Cooperation); Japan (Nagoya City University Medical School, National Institute of Infectious Diseases, Ministry of Health, Labour and Welfare, Institute of Medical Science, Tokyo); South Africa (National Institute of Virology, Johannesburg); Uganda (Red Cross); United Kingdom (National Health Service and Public Health Laboratory Services); United States (Centers for Disease Control and Prevention, Atlanta). The Global Outbreak Alert and Response Network is a technical partnership of national and international institutions and networks that mobilize and pool resources to detect, verify and respond effectively and efficiently to outbreaks of potential international importance.
Map 1 Sites of outbreak of Ebola haemorrhagic fever, Uganda, Aug 2000-Jan 2001
Leprosy

CAUSE

- Leprosy is a chronic disease caused by a bacillus, Mycobacterium leprae;
- M. leprae multiplies very slowly and the incubation period of the disease is about five years. Symptoms can take as long as 20 years to appear;
- Leprosy is not highly infectious. It is transmitted via droplets, from the nose and mouth, during close and frequent contacts with untreated cases.

SYMPTOMS

- Leprosy mainly affects the skin and nerves;
- If untreated, there can be progressive and permanent damage to the skin, nerves, limbs and eyes.

HISTORY

- Leprosy was recognized in the ancient civilizations of China, Egypt and India;
- The first known written mention of leprosy is dated 600 BC;
- Throughout history, the afflicted have often been ostracized by their communities and families.

TREATMENT TODAY

- Leprosy is a curable disease and treatment provided in the early stages averts disability;
- With minimal training, leprosy can be easily diagnosed on clinical signs alone;
- A World Health Organization (WHO) Study Group recommended multidrug therapy (MDT) in 1981. MDT consists of three drugs: dapsone, rifampicin and clofazimine. This drug combination kills the pathogen and cures the patient;
- MDT is safe, effective and easily administered under field conditions. MDT is available in convenient monthly calendar blister packs to all patients;
- Since 1995, WHO provides free MDT for all patients in the world, initially through the drug fund provided by the Nippon Foundation and since 2000, through the MDT donation provided by Novartis and the Novartis Foundation for Sustainable Development.

HIGH EFFECTIVENESS OF MULTIDRUG THERAPY

- PB patients treated with MDT are cured within six months;
- MB patients treated with MDT are cured within 12 months;
Patients are no longer infectious to others after the first dose of MDT. In other words, transmission of leprosy is interrupted; there are virtually no relapses, i.e. recurrences of the disease after treatment is completed; no resistance of the bacillus to MDT has been detected; WHO estimates that early detection and treatment with MDT has prevented about four million people from being disabled. This suggests great cost-effectiveness of MDT as a health intervention, considering the economic and social loss averted.

HISTORY OF TREATMENT

- The first breakthrough occurred in the 1940s with the development of the drug dapsone, which arrested the disease. But the duration of the treatment of leprosy was many years, even a lifetime, making it difficult for patients to follow; in the 1960s, M. leprae started to develop resistance to dapsone, the world’s only known anti-leprosy drug at that time; rifampicin and clofazimine, the other two components of MDT, were discovered in the early 1960s.

THE ELIMINATION OF LEPROSY AS A PUBLIC HEALTH PROBLEM

- In 1991 World Health Assembly passed a resolution to eliminate leprosy as a public health problem by the year 2000. Elimination of leprosy as a public health problem is defined as a prevalence rate of less than one case per 10 000 persons; the target was achieved on time.
- The widespread use of MDT has reduced the disease burden dramatically; over the past 20 years, more than 14 million leprosy patients have been cured about 4 million since 2000.
- The prevalence rate of the disease has dropped by 90% – from 21.1 per 10 000 inhabitants to less than 1 per 10,000 inhabitants in 2000.
- A dramatic decrease in the global disease burden: from 5.2 million in 1985 to 805 000 in 1995 to 753 000 at the end of 1999 to 286 000 cases at the end of 2004.
- Leprosy has been eliminated from 113 countries out of 122 countries where leprosy was considered as a public health problem in 1985. An additional 13 countries achieved the elimination target since 2000.
- A 20% annual decrease in new cases detected globally since 2001.
- Absence of resistance to drugs used in MDT.
- Efforts currently focus on eliminating leprosy at a national level in the remaining endemic countries and at a sub-national level from the others.

FIGURES ON THE CURRENT LEPROSY SITUATION
• Approximately 410 000 new cases of leprosy were detected during 2004 compared to a peak of 804 000 in 1998. At the beginning of 2005, 290 000 cases were undergoing treatment;
• In 9 countries in Africa, Asia and Latin America leprosy is still considered a public health problem; These countries account for about 75% of the global disease burden.
• According to the latest available information, intensive efforts are still needed to reach the leprosy elimination target in five countries: Brazil, India, Madagascar, Mozambique, and Nepal.

ACTIONS AND RESOURCES REQUIRED

• Political commitment needs to be sustained in countries where leprosy remains a public health problem;
• In order to reach all patients, treatment of leprosy needs to be fully integrated into general health services. This is a key to successful elimination of the disease;
• Partners in leprosy elimination need to continue to ensure that human and financial resources are made available for the elimination of leprosy;
• The age-old stigma associated with the disease remains an obstacle to self-reporting and early treatment. The image of leprosy has to be changed at the global, national and local levels. A new environment, in which patients will not hesitate to come forward for diagnosis and treatment at any health facility, must be created.

THE STRATEGY FOR LEPROSY ELIMINATION

The following actions are part of the ongoing leprosy elimination campaign:

• Ensuring accessible and uninterrupted MDT services available to all patients through flexible and patient-friendly drug delivery systems;
• Ensuring the sustainability of MDT services by integrating leprosy services into the general health services and building the ability of general health workers to treat leprosy;
• Encouraging self-reporting and early treatment by promoting community awareness and changing the image of leprosy;
• Monitoring the performance of MDT services, the quality of patients’ care and the progress being made towards elimination through national disease surveillance systems.
Onchocerciasis (river blindness)

Definition

Onchocerciasis is an insect-borne disease caused by a parasite Onchocerca volvulus and transmitted by blackflies of the species Simulium damnosum. Onchocerciasis is often called “river blindness” because the blackfly which transmits the disease abounds in fertile riverside areas, that frequently remain uninhabited for fear of infection. O. volvulus is almost exclusively a parasite of man. Adult worms live in nodules in a human body where the female worms produce high numbers of first-stage larvae known as microfilariae. They migrate from the nodules to the sub-epidermal layer of the skin where they can be ingested by blackflies. They further develop in the body of the insect from which more people can be infected. Eye lesions in humans are caused by microfilariae. They can be found in all internal tissues of the eye -- except the lens -- where they cause eye inflammation, bleeding, and other complications that ultimately lead to blindness.

Magnitude

Onchocerciasis is a major cause of blindness in many African countries. As a public health problem, the disease is most closely associated with West and Central Africa, but it is also prevalent in Yemen and six countries in Latin America. Onchocerciasis has in the past greatly reduced the economic productivity in infected areas and left vast tracts of arable land abandoned. It is estimated that there are about half a million blind people due to river blindness.

Prevention and treatment

Much progress has been made in fighting the disease in several countries through control of the blackfly, however, the disease can now also be treated with an annual dose of the drug ivermectine, Mectizan®, which also relieves the severe skin itching caused by the disease.
References

2. E. Giamarellou et al. Infections and Antimicrobial Therapy. 3rd Volume. Litsas 2005
3. Up-to-date, 16.3