Summary

- Main clinical features: fever, haemorrhagic disease and neurological symptoms (FD, HS, NS), hepatitis
- Acute disease mainly of African domesticated ruminants, sometimes humans
- Transmission via mosquitoes and direct contact with infected animals
- Intermittent but severe epidemics

Virus

The virus which causes Rift Valley Fever (RVF) is a Phlebovirus and belongs to the Bunyaviridae family. There are several subtypes with each apparently having their own pathogenic capability. Zinga virus is currently regarded as a variant of the RVF virus. It is possibly identical.

Transmission

Between the epidemics it has never been possible to demonstrate a sylvatic vertebrate reservoir, but RVFV has been isolated from over 30 species of mosquitoes in six genera. The virus is passed from generation to generation of mosquito via the transovarial route. Mechanical transmission by arthropods is also documented.

The disease is primarily a zoonosis which affects sheep, goats, cattle and buffalo. Rodents are highly susceptible, although subclinical infections do occur. Birds, reptiles and amphibians are refractory. An epidemic in animals is called an epizootic. In animals the virus causes a severe infection with high mortality, mainly in newborn lambs. Adult pregnant animals often abort. A subclinical infection may occur in dogs, cats and camels (can abort). Horses and pigs are resistant.

The disease was first described in detail by Daubney, in Kenya in 1931 (epidemic in sheep on a farm near Lake Naivasha, one of the lakes in the Rift Valley). Until 1977 it was assumed that the illness only occurred in sub-Saharan Africa and Madagascar, but in 1977-78 there was a great epidemic in Egypt so that the area of distribution was found to be more extensive. Other important epidemics occurred in 1950-51 in South Africa (sheep: an

estimated 100,000 dead and 500,000 abortions), in the river basin of the Senegal river in Senegal and southern Mauritania (1987) and in Kenya-Somalia (1997-1998). In 2000 numerous cases were reported from Saudi Arabia and the neighbouring Yemen. More than 200 people died. It was the first time the virus was detected outside Africa.

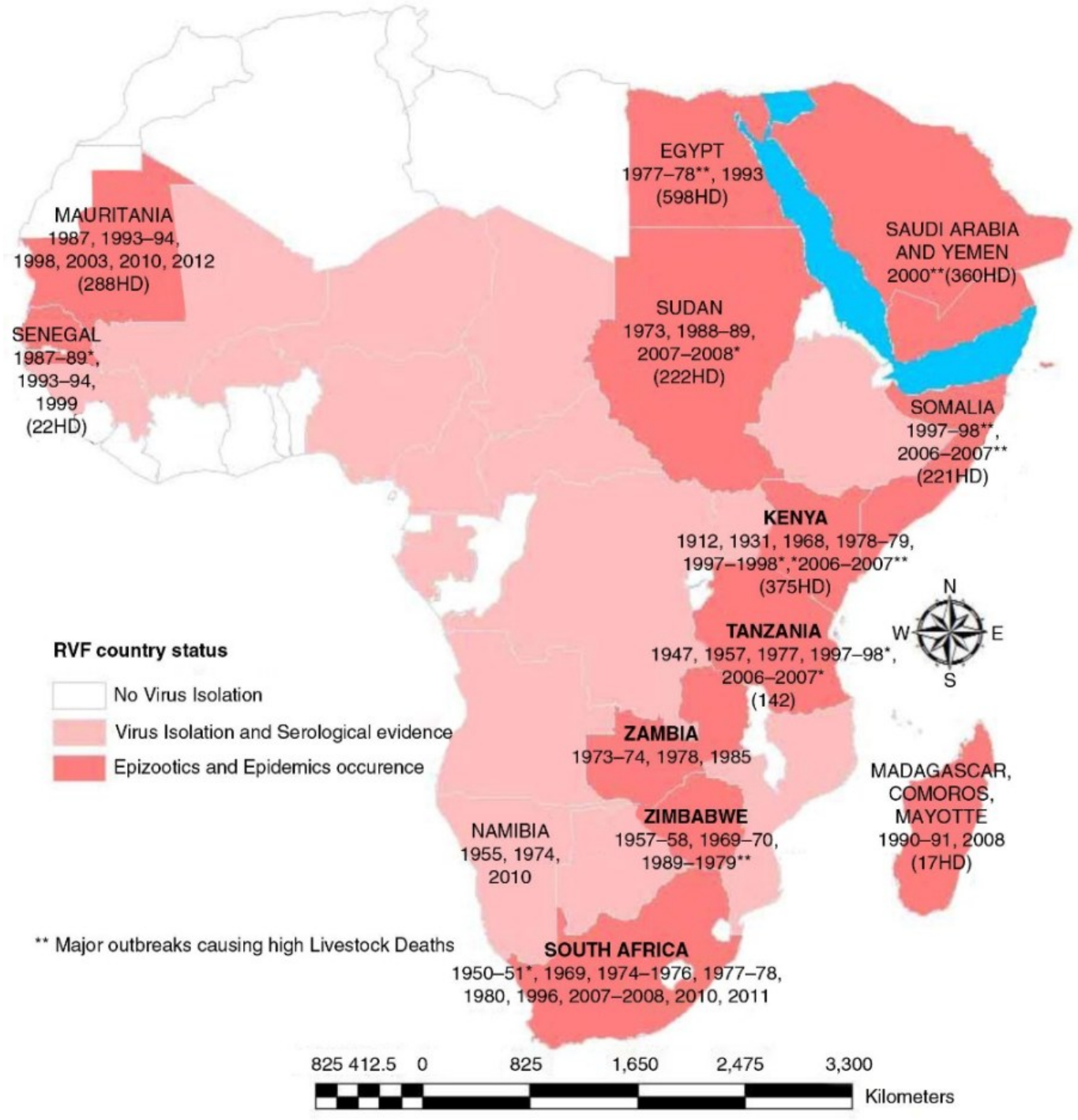

Figure: Rift Valley Fever epidemics (Nanyingi et al, Infect Ecol Epidemiol)

Rift Valley Fever occurs in intermittent epidemics with intervals of 10 to 15 years, mainly after periods of exceptionally heavy rainfall. It has been proposed that factors such as

rainfall, ocean temperature and climate change all play roles in determining the likelihood of an epidemic.

Transmission of Rift Valley Fever to man can occur either via direct contact with the blood of a viraemic animal (e.g. in slaughterhouses, farmers, butchers, ranchers, veterinary surgeons, herdsmen, etc.), possibly via the milk of an infected animal or via a bite from an infected insect. There are numerous types of mosquitoes which can transmit the virus. Aedes sp. are usually the most important but Anopheles, Culex, Eratmopodites, Mansonia, Mansonoides and Coquillettidiae mosquitoes also play a role. The virus can be transmitted transovarially in Aedes mcintoshi (= Aedes lineatopennis sl.) and can survive for a long time (years) in a mosquito egg. In heavy rainfall, floods etc. numerous infected mosquito eggs will simultaneously hatch due to the rising water level and moistening of the eggs.

Rift Valley Fever virus can also be transmitted by mechanical vectors such as stomoxyds, phlebotomes, simulids and Culicoides sp. Infected insects can be carried over large distances by the prevailing winds such as the north and south trade winds. Transporting infected cattle to a non-epidemic area is an important factor in the epidemiology.

Clinical aspects

The incubation period of Rift Valley fever is 3 to 7 days. Clinically the disease can provoke a non-specific flu-like syndrome, sometimes with biphasic fever. Fever develops together with muscle and joint pain, anorexia, diarrhoea, vomiting, headache and sometimes photophobia and retro-orbital pain. Sometimes there is petechial rash. The acute phase of the disease lasts 4-7 days. Complications occur in fewer than 5% of cases. In case of a haemorrhagic form, diffuse intravascular coagulation, bleeding (epistaxis, melena, haematemesis, seeping of blood at infusion and needle prick sites) and jaundice predominate such that the disease resembles yellow fever. Pneumonitis, shock, hepatic failure and renal failure with proteinuria and shock can occur. Sometimes bilateral vision disturbances occur about a week after the start of the fever. These are the result of vasculitis of the retina with arteriolar thrombosis, retinitis, retinal ischaemia, bleeding and detachment of the retina. The macular and peri-macular areas are affected preferentially. The lesions can result in permanent blindness or slowly improve over the course of the following weeks. Neurological complications also occur (< 1%): meningeal signs, dizziness, confusion, hallucinations, hypersalivation, grinding of

teeth, chorea, convulsions and other signs of encephalitis. Coma, with or without decerebration, can occur in the terminal stage. In the complicated forms mortality is high.

Diagnosis

The disease may be suspected if large numbers of young lambs and goats die, with or without epidemic abortion among the animals and when at the same time multiple human cases with fever and haemorrhagic or neurological symptoms occur in an endemic area. In animals there is congestion in the liver, with small haemorrhagic areas and necrotic foci. The bile may be dark, almost black, and may contain blood. Tissue biopsies of animals can be used for anatomopathology, immunoperoxidase techniques for detecting the virus and of course virus isolation. Confirmation of the diagnosis in man is based on serology (IgM antibodies, including in the cerebrospinal fluid) and on virus isolation. Definitive identification is based on neutralisation tests with reference sera. Initially there is leukocytosis, then leukopenia and thrombocytopenia. Schistocytes may be found. With neurological symptoms lymphocytes predominate in the cerebrospinal fluid.

Treatment

There is no specific treatment. Symptomatic therapy is essential and occasionally requires intensive level care. There are insufficient data about the use of ribavirin and/or of convalescent plasma. Ribavirin inhibits virus replication in cell culture. Ribavirin is a ribonucleoside analogue that induces lethal mutagenesis of RNA viral genomes. The possible therapeutic place of interferon is not clear yet. Hepatotoxic medication as well as aspirin and NSAIDs should be avoided during the acute disease.

Prevention

Vaccination

A live attenuated strain (also known as the Smithburn strain) has shown to be potent in inducing protection from viral infection, and it is used as a vaccine for livestock. However, its ability to induce abortions and exhibit pathogenicity in European cattle has limited its use to areas threatened by an imminent outbreak. Studies on new vaccines are ongoing. These

candidate vaccines can be classified into four groups: live attenuated, inactivated, viral-recombinant, and DNA vaccines. There is still no commercial vaccine available for humans.

Vector control

The transport of animals should be limited. In epidemics the transporting of cattle should be prohibited, or the animals must be quarantined. Contact with sick or dead animals must be avoided. Cattle can be vaccinated. If the epidemic has already started it is usually too late to employ with vaccination as a control strategy. Thus in sheep-farming areas it is advised that the animals be vaccinated regularly either with the live Smithburn vaccine (single dose, life-long protection), or vaccination with the formol-inactivated vaccine (boosters needed).

Because of the variety of vectors, it is difficult to control insects breeding sites. Sometimes in epidemics insecticides are used on a large scale. For personal protection covering clothing (long sleeves, long trousers), insect repellents (best with DEET) and impregnated mosquito nets are adequate in normal situations. Barrier-nursing is indicated in the care of patients.