

Arboviral diseases in Southern Africa

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Abstract

Arthropod-borne viral diseases, better known as **arbovirus** diseases, are more common than we think and are often misdiagnosed or not diagnosed at all. More than 100 arboviruses causing human disease have been recognised worldwide. This presentation will provide a review of some of the arboviruses occurring in Southern Africa, and also some of the common diseases seen in travellers returning home from other African and overseas destinations. The clinical syndromes vary extensively, with signs and symptoms ranging from acute benign fevers of short duration to the very dramatic viral haemorrhagic fevers. The reservoirs and vectors of most viruses are well described, but even after years of extensive research there are still a few that remain elusive and pose great challenges for future study.

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INTRODUCTION

There are many arthropod-borne viruses (arboviruses) that produce clinical and subclinical infections in humans. Most of these viruses are maintained in zoonotic cycles and humans are usually an insignificant host in maintaining the cycle. The symptoms and signs can vary extensively (see Table I). Although there are more than 100 viruses classified as arboviruses that cause disease in humans, the most common belong to the family and genera listed in Table II. Some arbovirus infections may also present with haemorrhagic fever and these are called viral haemorrhagic fever (VHF) infections. It should be taken into account, however, that not all viruses causing haemorrhagic fever are classified as arboviruses.

Many arthropod vectors transmit viruses to humans:

- Mosquitoes- and midges
- Ticks
- Sand flies

Alpha and bunya viruses are usually mosquito borne. The flaviviruses are either mosquito or tick borne. Phleboviruses are generally trans-

Table I: The four major clinical syndromes seen with arboviral infections

| |
|---|
| Acute central nervous system illness |
| • Mild aseptic meningitis, encephalitis, coma, paralysis and even death |
| Acute benign fevers of short duration with or without skin involvement |
| Haemorrhagic fevers |
| Polyarthritis and rash |

Table II: The family and genera of the most common arboviruses

| Family | Genera | Name of virus |
|--------------|--|---|
| Togaviridae | <i>Alphavirus</i> | Chikungunya Sindbis |
| Bunyaviridae | <i>Bunyavirus</i> <i>Phlebovirus</i> <i>Nairovirus</i> | Oriboca Rift Valley fever Crimean-Congo haemorrhagic fever |
| Flaviviridae | <i>Flavivirus</i> | Yellow fever Dengue West Nile |

mitted by sand flies. The exception is Rift Valley fever (RVF), since it is transmitted by mosquitoes.

BUNYAVIRIDAE

Rift Valley fever

Cattle, sheep and goats serve as the natural host of the infection, and the *Culex* and *Aedes* mosquitoes act as vectors. Humans usually become infected by contact with infectious host products, such as the blood and meat of carcasses, and not by the bite of mosquitoes. Several clinical

syndromes have been recognized with RVF (see Table III).

Crimean-Congo haemorrhagic fever (CCHF)

CCHF is the most important VHF in South Africa.¹ The *Hyalomma* tick (bontpootbosluis) acts as vector (see Figure 1).² A number of cases are seen annually and many more suspected cases are investigated. These ticks occur throughout the country but are commonly found in drier regions such as the Northern

Table III: Clinical syndromes associated with RVF

| | |
|---|--|
| Rift Valley fever without complications. | <ul style="list-style-type: none"> Fever, headache, myalgia and arthralgia, nausea, vomiting and diarrhoea. Resolution is usually within a week. |
| Rift Valley fever with eye complications. | <ul style="list-style-type: none"> Fever, retinitis and even permanent blindness after retinal detachment. |
| Rift Valley fever with meningoencephalitis. | <ul style="list-style-type: none"> Neurological symptoms present five to 10 days after the fever. Disorientation, hallucinations and pareses may all occur. |
| Rift Valley fever with bleeding | <ul style="list-style-type: none"> Haematemesis, epistaxis, jaundice and skin bleeds may all be seen two to four days after the onset of the fever. This usually resolves, but may be fatal in rare cases. |

Cape. Various stages of ticks feed on small animals and birds, while adult ticks feed on large animals such as cattle and sheep. When the animals are slaughtered during the viraemic phase, the infection may be transmitted to humans. Certain occupations may pose an increased risk for this disease. A worker in the local commercial ostrich meat industry became ill after slaughtering ostriches on a farm.³ Subsequent outbreaks were also reported, with 17 cases of CCHF among workers in the same industry.⁴ There are frequent reports of viral isolation and/or disease from more than 30 countries in Africa, Asia, Europe and the Middle East.



Figure 1: The *Hyalomma* tick (bontpootbosluis). Photograph courtesy of the Department of Medical Virology, University of Pretoria.

Transmission occurs by:

- bite of an infected tick.
- crushing of an infected tick and subsequent exposure to the infective agent
- contact with infected products of animals or humans.

This infection may present with mal-

aise, weakness, sudden onset of fever, irritability, headache, severe pain in the limbs and anorexia. A fine petechial rash spreading from the chest and abdomen and areas of large purpuric bleeds may be seen (see Figure 2). In severe cases, bleeding from the gums, nose, lungs, uterus and intestine may occur. It is of utmost importance that medical personnel recognise this condition. Several cases of nosocomial spread have been reported. Nosocomially acquired infection is associated with increased mortality as was observed during the outbreak at Tygerberg Hospital in the Western Cape.³



Figure 2: Massive cutaneous ecchymosis on the arm of a CCHF patient, seven to ten days after clinical onset. Photograph courtesy of Prof. R Swanepoel.

The clinical diagnosis of a possible CCHF case can be made by taking the following criteria into account when accessing a patient.⁵

History of exposure to infection:

- Bitten by tick/s or crushed with bare hands
- OR
- Had direct contacts with fresh blood or other tissues of live stock or game animals
- OR
- Had direct contact with blood, se-

cretions or excretions of confirmed or suspected CCHF patients

OR
Resident in or visited a rural environment where contact with livestock or ticks was possible, but a specific incident constituting exposure cannot be identified.

Signs and symptoms:

- Sudden onset
- Fever
- Severe headache
- Myalgia
- Nausea and/or vomiting
- Bleeding tendency: petechial rash, ecchymoses, epistaxis, haematemesis, haematuria or melaena

Clinical pathology during first five days of illness:

- Leucopaenia or leukocytosis
- Thrombocytopenia
- Abnormal PI/PTT
- Raised transaminases

In addition to supportive measures, *in vitro* studies with the antiviral drug Ribavirin suggest it might be effective in treating CCHF.⁶

TOGAVIRIDAE

Chikungunya

Fever, headache and polyarthrits are characteristic features of this infection after an incubation period of three to eleven days. A maculopapular rash usually follows one to ten days after the onset of the arthritis. The rash resolves within seven to ten days, but the arthritis may persist for months. Minor haemorrhages have been reported in south-eastern Asia and India, but not in South Africa. The *Aedes aegypti* mosquito and possibly others transmit the virus.

Mpumalanga and Limpopo provinces are especially affected, with baboons and vervet monkeys being the natural hosts for the infection. The Indian Ocean islands of Reunion, Madagascar, Mayotte and Mauritius have seen a widespread outbreak, which was first reported in 2005. The authorities have reported imported cases in returning travellers to Europe.⁷

Sindbis

Fever, headache and arthralgia are features of this disease. A maculopopular rash appears on the body and limbs, but is not seen on the face. The rash has a typical "fried egg" appearance (see Figure 3). This infection can be seen in the wetter parts of the South African highveld, where the *Culex* mosquito breeds. Birds, especially water birds, serve as host for the infection. An increased frequency of this disease can be anticipated to coincide with increased rainfall periods, making the 2005/2006 season ideal for the breeding habits of the mosquitoes.



Figure 3: Sindbis skin rash with the "fried egg" appearance. Photograph courtesy of Dr L Blumberg.

FLAVIVIRIDAE

Yellow fever

Yellow fever is not an endemic disease in South Africa, but is seen in the tropical regions of South America and Africa. The endemic zone includes the area between 15° North

and 10° South latitude. Yellow fever exists in nature in two transmission cycles. The first is a jungle cycle that involves *Aedes* or *Haemagogus* mosquitoes, which feed on nonhuman primates, and the second is an urban cycle involving humans. The incubation period is three to six days. The clinical picture varies from very non-specific viral disease of short duration, characterised by the onset of headache, fever, chills, nausea and vomiting, to multiple organ dysfunction. Jaundice is moderate early in the disease and intensifies later. Cases may resolve at this stage or progress after a brief remission into a stage of haemorrhage and organ failure. A valid international certificate of immunisation against yellow fever is required by many countries for the entry of travellers coming from or going to a yellow fever zone. This certificate is valid for 10 years from 10 days after the date of vaccination.

Dengue fever

This virus is endemic in most countries in the tropics, including large parts of western Africa. Outbreaks have also been reported on the east coast from Ethiopia to Mozambique, as well as in the Comoros and Seychelles.⁸ The virus is transmitted by the bite of an *Aedes* mosquito. After an incubation period of two to seven days, an acute viral disease characterised by the sudden onset of fever, headache, arthralgia, retro-orbital pain, nausea, vomiting and rash is

observed. Cross-sensitisation of the four serotypes leads to a picture of Dengue haemorrhagic fever with subsequent infections (see Figure 4).

West Nile (WN)

This virus is widespread in Africa (including South Africa), North America, Europe, the Middle East and India. Birds are a source of mosquito infection. The infection is transmitted by the *Culex* mosquitoes in southern Africa. The virus causes a febrile illness, usually lasting a week or less. A rash is common, resembling a "fried egg".⁹ Meningoencephalitis has been recognised since 1999 in the USA and later in Canada as a prominent complication of this infection. About one in 150 people develop central nervous system disease.¹⁰

DIAGNOSIS

With all cases of suspected haemorrhagic fever, an extensive list of differential diagnoses must be considered. The most common are:

- Bacterial sepsis;
- Malaria and African trypanosomiasis;
- Rickettsial tick bite fever;
- Fulminating hepatitis due to other viral diseases (hepatitis viruses, herpes simplex virus, cytomegalovirus and Epstein-Barr virus); and
- Medical and chemical agents, e.g. anti-coagulants and heavy metal exposure.

Figure 4: Indistinct macular/scarlatini-form skin rash seen with Dengue. Photograph courtesy of Dr L Blumberg.



In South Africa, all diagnostic tests for arbovirus and VHF viruses are processed at the National Institute for Communicable Diseases (NICD) in Gauteng. The laboratory request should include clinical details, including the time since possible exposure to the vector/source. These are important for the interpretation of the results. The antibody-based assays may initially test negative or very low positive, as the immune system needs time to mount an immune response (antibodies) to the infection. However, the virus can be demonstrated earlier (during the first week of infection) in blood specimens by PCR and/or virus isolation.

Tests available at the NICD

The viruses listed in Table IV are screened for when VHF and/or arbovirus infections are suspected. Clotted and EDTA blood should be submitted to the laboratory.

A separate request for dengue and yellow fever should be included when the diagnosis is considered by the clinician. These tests should be added if the patient has recently travelled to an endemic area.

Table IV: Screening tests at the NICD

| VHF screen | Arbovirus screen |
|------------|------------------|
| RVF | RVF |
| Ebola | Sindbis |
| Marburg | Chikungunya |
| CCHF | West Nile |
| Lassa | |

MANAGEMENT

Patients should be treated with supportive measures, as specific antiviral agents do not exist. Mild disease can be managed with symptomatic treatment on an outpatient basis. Patients with more severe disease or suspected VHF should be admitted to hospital.

Infection control precautions

The infection control team of the relevant institution(s) should be notified immediately if a case of VHF is suspected. Appropriate personal protective equipment should be used, including surgical masks with

eye protection, plastic gowns and double gloves. The patient should be isolated and strict barrier nursing must be implemented. These patients should always be discussed with the pathologist **before** any samples are taken or submitted for testing. These would include samples destined for the local pathology laboratory. The NICD offers an on-call service to provide assistance for infectious disease outbreaks (tel. no. 011 386-6000).

SUMMARY

The early recognition and diagnosis of arbovirus diseases remain a challenge for all healthcare professionals. Bear in mind that this is not only a diagnosis made in the returning traveller from exotic tropical destinations. Many of these diseases are endemic to South Africa and do not always present in a spectacular manner. The astute clinician sometimes will have to evaluate non-specific signs and symptoms to come to the final diagnosis. Preventative measures, comprising vaccination and vector control, are the main weapons against these infections. Treatment remains mostly supportive, with special attention being paid to infection control in cases of suspected VHF.

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