FREQUENTLY ASKED QUESTIONS: CRIMEAN-CONGO HAEMORRHAGIC FEVER

Background

- **What is a viral haemorrhagic fever?**

A viral haemorrhagic fever is a disease which is caused by a virus and has a tendency to disturb blood clotting, so that patients may develop uncontrolled bleeding (haemorrhage). Many common infections and diseases can resemble viral haemorrhagic fever, but the term is reserved for a particular group of viral diseases associated with a high death rate. In Africa, these include Crimean-Congo haemorrhagic fever, Lassa fever, Marburg disease and Ebola fever. Apart from the fact that they cause similar disease, the viruses are not closely related to each other and are transmitted to humans in a variety of ways.

- **What is Crimean-Congo haemorrhagic fever?**

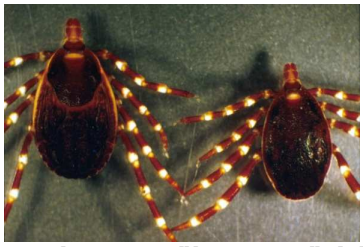
Crimean-Congo haemorrhagic fever is a tick-borne (i.e. transmitted by a ticks) viral disease of humans which occurs in Africa, Asia, the Middle East and Europe.

- **Why does it have the name 'Crimean-Congo haemorrhagic fever'?**

A disease given the name Crimean haemorrhagic fever was first recognised in Crimea in 1944-1945, although the virus which causes the disease was only identified in 1967. In 1956 a virus given the name Congo was isolated from a child with fever in the former Belgian Congo (now the Democratic Republic of Congo). In 1969 it was discovered that the two viruses were the same. Consequently, both the virus and the disease are called 'Crimean-Congo haemorrhagic fever'. The name is often abbreviated to 'CCHF' and in South Africa the disease is commonly called 'Congo fever'.

- **Where does the CCHF virus come from?**

The virus is transmitted mainly by *Hyalomma* ticks, which have distinctive brown and white bands on their legs; these are known in South Africa as bont-legged ticks (Afrikaans: bontpootbosluise). The virus can remain in the ticks for long periods, and even pass through the eggs to infect the next generation of ticks.



***Hyalomma* or "bontpoot" ticks often implicated in the transmission of CCHF virus**
(Picture may only be reproduced with permission)

There are three species of *Hyalomma* in South Africa, and although they are widely distributed, the ticks tend to be most numerous in the drier north-western parts of the country – the Karoo, western Free State, Northern Cape and North West Province.

Immature *Hyalomma* ticks (larvae and nymphs) feed on ground birds (such as guinea fowl) as well as small mammals up to the size of hares. Adult *Hyalommas*

feed on livestock (such as cattle, sheep and goats) as well as wild animals (such as antelope) and also ostriches.

Animals or ostriches bitten by infected ticks do not develop disease, but virus can circulate in their blood for up to a week, after which they become immune to further infection. Non-infected ticks become infected if they feed on animals during the short period when virus is circulating.

Modes of transmission

- Humans can become infected with CCHF virus in the following ways:
    - Being bitten by infected ticks
    - Squashing infected ticks (if fluid from the ticks enters into cuts/grazes on the skin, or splashes onto mucous membranes – including the eye, nose and mouth)
    - If blood/tissue from infected animals (during the short period that the animals have virus in circulation) comes into contact with cuts/grazes on the skin, or splashes onto mucous membranes – including the eye, nose and mouth.
    - If blood/tissue from infected humans comes into contact with cuts/grazes on the skin or splashes onto mucous membranes – including the eye, nose and mouth.
    - Needle-stick/sharps injuries in healthcare workers from infected patients.

People are not always aware of being bitten by ticks, and in patients with CCHF ticks have been found attached in concealed sites – such as on the scalp and between the toes.

- Risk factors for infection

Occupational groups such as herders, farmers, abattoir workers, veterinarians/animal health workers, hunters and persons informally slaughtering domestic/wild animals are at higher risk of infection. These persons often have exposure to ticks on the animals and in the animal environment, and also often have exposure to animal blood/tissues (for example during castration of calves, vaccination, notching/tagging of ears, slaughtering etc).

Within abattoirs, those who come into contact with fresh blood are at greatest risk. Once carcases have been bled out and hung to mature there is a sudden increase in acidity of the meat and the virus cannot be detected in the carcass. Ostriches appear to be the only birds in which there is similar circulation of virus in blood as occurs in mammals. Half-fed ticks which detach from the hides of recently slaughtered animals/ostriches may attach indiscriminately to hosts available in their environment, and thus infect abattoir workers. Although the proportion of mature animals/ostriches that will have virus in circulation may be extremely low, many thousands of animals are slaughtered each day at abattoirs.

Meat processed and matured according to standard abattoir practice does NOT constitute a danger to consumers.

Healthcare workers attending to humans with CCHF are also at risk of infection from needle-stick and splash exposures, and there have been several instances of secondary spread of infection from patients to healthcare workers in South Africa.

This can occur through contact of broken skin/mucous membranes with blood or blood-tinged body fluids and wastes of a CCHF patient, or via needle-stick/sharps injuries.

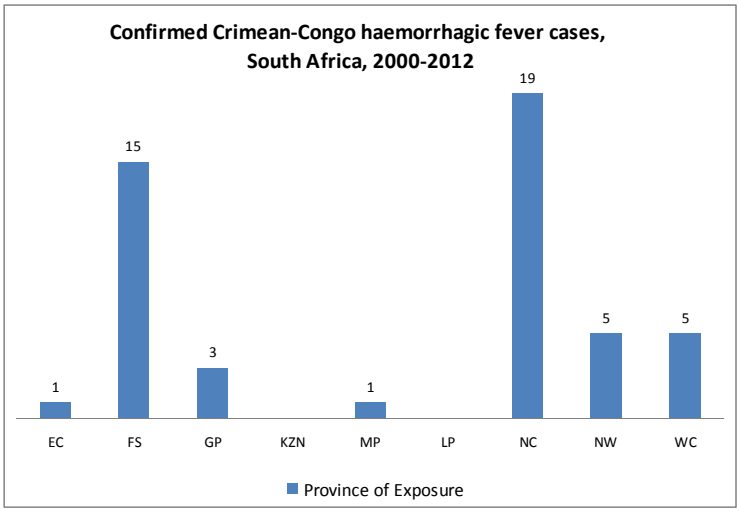
Persons living in the countryside, and town dwellers that visit the countryside for occupational or recreational purposes (including hunting and hiking), are also at risk from tick bites.

In some cases, no direct evidence can be obtained to indicate that a patient with CCHF had contact with animal blood or with ticks, and the only evidence to suggest possible exposure to infection is the fact that the patient lived in or visited an environment where such contact was possible.

Although spread of infection to family members as never been recorded in South Africa, it is possible. The only time that infection has been seen in groups of people is when they have been exposed together to a common source of infection, as in slaughtering of animals.

CCHF in South Africa

Human CCHF cases have been reported annually from South Africa since 1981, when it was first recognized in the country; between 0 and 20 cases of CCHF are diagnosed each year. Through nearly thirty years of passive surveillance, a total of 187 cases has been laboratory-confirmed. Although cases have been reported from all of the nine provinces, more than half of the cases originate from the semi-arid areas of Northern Cape Province (31.5% of cases) and Free State Province (23% of cases).



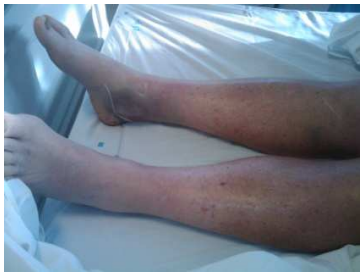
Fatality rate

According to various studies, the death rate from CCHF is reported to be 3-30%. However, the death rate can be much higher if patients do not receive prompt and proper medical attention.

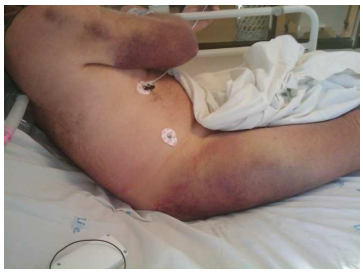
Course of infection and clinical features

- The typical course of CCHF disease has four distinct phases:

    1. Incubation period: this is usually short (3 – 7 days) but can range 1-9 days after exposure to the virus. The incubation period following exposure to infected blood/tissues is usually longer than that for tick-bite exposures (5-6 days, with a maximum of 13 days).
    2. Prehaemorrhagic period: sudden onset of non-specific symptoms including high fever (which usually persists for 4-5 days), headache, malaise, myalgia (particularly in the lower back and thighs). Conjunctivitis and hyperaemia (flushing) of the face, neck, and chest are commonly noted. Some patients may also experience nausea, abdominal pain, and diarrhoea. The prehaemorrhagic period lasts ±3 days (range 1-7 days).
    3. Haemorrhagic period: this is short (usually 2-3 days), develops rapidly, and usually begins between day 3 and 5 of the disease. Cutaneous haemorrhagic manifestations range from petechiae to large haematomas on the skin and mucous membranes; bleeding from venepuncture sites etc is common. Common bleeding sites include the nose (epistaxis), gastro-intestinal system (haematemesis, melaena and intra-abdominal), uterus (menometrorrhagia), urinary tract (haematuria) and respiratory tract (haemoptysis). Less common haemorrhagic manifestations include vaginal, gingival and intracerebral bleeding. Disseminated intravascular coagulation (DIC) and circulatory shock may ensue. Hepatomegaly and splenomegaly can occur in up to one-third of patients. Death is typically preceded by haemorrhagic diathesis, shock and multi-organ failure ±5-14 days after onset of illness.
    4. Convalescent period: in survivors, this begins ±10-20 days after onset of illness and a host of residual symptoms have been inconsistently reported, including labile pulse, tachycardia, loss of hair, polyneuritis, loss of hearing or memory, hepatorenal insufficiency. Patients who recover usually show sudden improvement from day 10 of illness onwards. Virus remains detectable in human blood for up to 2 weeks after the onset of illness, but once haematological and biochemical parameters have normalised, and the patient feel wells and is no longer bleeding, they can be discharged from hospital. Although there has been no indication that virus continues to be excreted in body fluids, patients should refrain from intimate contact with other people for 6 weeks after recovery from the disease as a precaution against spread of infection. Convalescent patients should not undertake heavy activities during this period. After recovery, patients are immune to further infection



Petechial rash on the legs of CCHF case (Picture may only be reproduced with permission).



Dispersed ecchymoses (bleeding under the skin) on the limbs and back of a CCHF case (Picture may only be reproduced with permission).

- Laboratory abnormalities:
    - Thrombocytopenia is a consistent feature of CCHF
    - Leucopoenia is common
    - Liver enzymes (AST, ALT and LDH) are usually elevated
    - Coagulation abnormalities may include: prolonged bleeding time (INR), prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT), elevated fibrin degradation products (FDP) and decreased fibrinogen.

Infection prevention and control precautions when caring for a patient with suspected/confirmed CCHF

Any patient with suspected/confirmed CCHF must be isolated in a private room.

Standard, Contact and Droplet infection control precautions must be instituted.

Restrict all non-essential staff from patient care area, and maintain a log of persons entering the patient's room.

Limit the number of visitors to only those necessary for the patient's well-being and care (such as a child's parent), and ensure that all visitors use personal protective equipment (PPE) and apply appropriate precautions as per the healthcare facility's protocol.

Ensure that non-clinical healthcare personnel (e.g. cleaners, porters) are also instructed with regards use of PPE and appropriate precautions.

In addition, take note of the following:

- Wear gloves (non-sterile examination gloves or surgical gloves) when entering the patient care area
- Facial protection to prevent splashes to nose, mouth and eyes is important. Wear a surgical mask + goggles/visor/eye glasses with side shields, OR a face shield
- Wear a disposable, impermeable gown to cover clothing and exposed skin. Wear a waterproof apron over any non-impermeable gown when undertaking any strenuous activity (e.g. carrying a patient).
- Wear closed, resistant shoes (e.g. boots)
- Although there is no evidence for airborne transmission of CCHF, as a precaution it is advised to wear N95 particulate respirators when performing procedures that generate aerosols (e.g. endotracheal intubation, bronchoscopy, suctioning, autopsy using oscillating saw)

- Percutaneous exposure (via needle-stick or sharps injuries) carries a particularly high risk for transmission. Safe use and disposal of needles and sharps must be emphasised. Limit the use of needles and other sharps as much as possible.

Further information regarding infection control recommendations for care of patients with suspected/confirmed viral haemorrhagic fevers can be accessed at:

- World Health Organization: http://www.who.int/csr/bioriskreduction/interim_recommendations_filovirus.pdf
- US Centers for Disease Control and Prevention: http://www.cdc.gov/HAI/pdfs/bbp/VHFinterimGuidance05_19_05.pdf

Treatment

Treatment consists essentially of supportive therapy, which comprises the following:

- Strict monitoring of fluid and electrolyte balance
- Replacement of blood, platelets and clotting factors
- Respiratory support and haemodialysis where indicated
- Prophylaxis of gastro-intestinal bleeding: oral/intravenous proton pump inhibitor therapy

The antiviral drug ribavirin may be of benefit in patients with CCHF and can be given orally/intravenously.

Action to be taken if a person is suspected of having CCHF

The disease may be suspected when a person suddenly becomes ill with headache, fever and chills, muscle pains etc less than 9 days after being exposed to a tick (being bitten by a tick or squashing a tick) or direct contact with blood/tissues of livestock, wild animals or human CCHF patients.

A doctor should be consulted immediately if CCHF is suspected. Healthcare workers must ensure that they apply strict infection prevention and control measures. On no account should patients suspected to be suffering from any haemorrhagic fever be referred to a hospital without first discussing with the relevant clinicians.

CCHF is a category A notifiable disease in South Africa, and the healthcare worker who makes the diagnosis must notify the Department of Health within 24 hours by telephone/fax and also complete a GW17/5 form.

Laboratory testing for CCHF

- **Specimen collection and transportation:** Contact the NICD Hotline (082-883-9920) to report the case. Submit 1-2 tubes of serum, clotted blood or whole blood. Liver biopsies may be submitted for post mortem case investigation. The sending laboratory is requested to clearly indicate the test requested. Submit a completed case history form with all specimens. Specimens should preferably be shipped on cold packs (or at 4 -8 °C). Standard good practice for the transportation of potentially infectious human specimens should be followed (for aerial transportation, IATA regulations; for transportation by road, National Road Traffic Act 93 of 96 and its subsequent amendments, Chapter VIII Transportation of

dangerous goods and substances by road, will apply). Transport specimens to the Centre for Emerging and Zoonotic Diseases, NICD-NHLS.

- **Tests:** Laboratory confirmation of CCHFV infection is carried out at the NICD-NHLS only. A full battery of specific tests is done for suspected CCHF cases to either exclude or confirm infection. This includes serological screening by indirect immunofluorescence assay (IFA) and/or enzyme-linked immunosorbent assay (ELISA) for anti-CCHF IgG and IgM antibodies. Reverse transcription polymerase chain reaction (RT-PCR) is used to detect viral genomic material or RNA in the clinical specimens. Virus isolation is also attempted to detect live virus from the patient's blood.

Precautions for persons who have potentially been exposed to infection

Local and provincial health officials are responsible for investigating the circumstances surrounding confirmed cases of CCHF, and instituting such control measures as may be necessary. Persons in the community at large, including family members, who have been in contact with confirmed CCHF patients, or who have been exposed to the same potential source of infection, are classified as being at zero, low, moderate or high risk according to defined criteria, and placed under appropriate observation as discussed below. Healthcare workers who have been exposed to patients are separately placed under observation of the infection prevention and control practitioners of the institution concerned.

Contacts considered to be at high risk would, for instance, include persons who have had accidental injury with a needle contaminated with the blood of a confirmed CCHF patient. Such persons would be placed under active observation which consists of reporting twice a day to a designated health official to be monitored for signs and symptoms of the disease and to have their temperature recorded for a period of 2 weeks after last contact with the patient (calculated to exceed the incubation period of CCHF by a wide margin of safety). Low risk contact of confirmed CCHF patients, who have not had closer than one metre face-to-face contact with the patient for instance, may be placed under passive observation, which could consist of reporting to the responsible health official daily by telephone rather than in person.

Note that persons under observation are not in quarantine and may continue with their normal activities, including attending to patients. They are only considered infectious once they become ill themselves. As soon as they develop signs and symptoms considered to be characteristic of CCHF disease, or a fever of $\geq 38.5^{0}$C, they are admitted to hospital as suspected cases.

Places such as abattoirs constitute a special case. Since exposure potentially occurs on a continuing basis (although the risk is actually low), there is seldom an indication for placing selected individuals under special observation. Instead, clinics attached to abattoirs should maintain a high degree of awareness of CCHF and other diseases that can be acquired from livestock at all times, and ensure that there is appropriate investigation of ill members of staff.

Family members and co-workers of patients who become infected on farms may be placed under observation depending on their degree of potential exposure to

infection, but since the ticks and virus are so widely distributed there is no logic in placing farms under quarantine.

Prevention of exposure to infection

There is no human vaccine at present.

Persons potentially exposed to tick bites can use certain pyrethroid acaricides (insecticides used against ticks) to treat clothing such as socks and trousers. Formulations which are generally available from shops that sell equipment for camping and outdoor activities, include aerosol sprays and sachets of concentrated acaricide used to prepare solutions into which clothing is dipped.

Abattoir workers, veterinary/animal health workers, farm workers and hunters etc should use appropriate impervious protective clothing and gloves when engaged in activities which carry a risk of exposure to animal blood.

Guidelines and Resources

- U.S. Centers for Disease Control and Prevention: CCHF
- U.K. Health Protection Agency: CCHF
- World Health Organization: CCHF

For more information:

- Medical / clinical related queries: NICD Hotline +27 82 883 9920 **(for use by healthcare professionals only)**
- Laboratory related queries:
    - Dr Jacqueline Weyer: (Tel) +27 11 386 6376, jacquelinew@nicd.ac.za
    - Mrs Patricia Leman: (Tel)+27 11 386 6339, patl@nicd.ac.za
- Results enquiries:
    - NICD Specimen Receiving Laboratory: +27 11 386 6404
    - Special Viral Pathogens Laboratory: +27 11 386 6339