

HEALTHCARE WORKERS HANDBOOK

ON

BIOTERRORISM

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Developed by:
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PREFIX AND DISCLAIMER

The recommendations herein are based on current Centers for Disease Control and Prevention (CDC) guidelines and other expert recommendations as referenced.

This material is intended for use by healthcare professionals. While the greatest care has been taken in the development of the document, the National Institute for Communicable Diseases, of the National Health Laboratory service, does not accept responsibility for any errors or omissions. All healthcare professionals should exercise their own professional judgement in confirming and interpreting the findings presented in the guidelines.

1. INTRODUCTION

Bioterrorism is the use of biological agents against civilians or non-combatants with the intention of causing widespread panic and social disruption. Concern about the use of microbes as weapons for terror has increased significantly since the 2001 attacks in the United States (US) when *Bacillus anthracis* spores were disseminated via the US postal system using letters. South Africa had a spate of “white powder” threats in 2002, and although no anthrax was cultured, investigations were very costly and the incidents incited public panic.

The release of biological weapons can be covert or overt. In the case of an overt release, the usual responders are the police / military, fire department and emergency personnel. In a covert release the responders will be healthcare workers as the recognition of an attack is often delayed. Public health and medical communities need to be prepared to recognize and respond to a threat or real attack with biological weapons.

2. HEALTHCARE WORKER AND HOSPITAL PREPAREDNESS

How do you recognize a possible bioterrorism–related outbreak?

Features that should alert healthcare workers to the possibility of a bioterrorism-related outbreak include:

- A rapidly increasing disease incidence (e.g., within hours or days) in a normally healthy population.
- An epidemic curve that rises and falls during a short period of time.
- An unusual increase in the number of people seeking care, especially with fever, respiratory, or gastrointestinal complaints.
- An endemic disease rapidly emerging at an uncharacteristic time or in an unusual pattern.
- Lower attack rates among people who had been indoors, especially in areas with filtered air or closed ventilation systems, compared with people who had been outdoors.
- Clusters of patients arriving from a single locale.
- Large numbers of rapidly fatal cases.
- Any patient presenting with a disease that is relatively uncommon and has bioterrorism potential (e.g., pulmonary anthrax, tularemia, or plague).

Who should you alert when a patient is suspected of having a bioterrorism-related illness?

Should a bioterrorism event be suspected, a network of communication must be activated to involve the Infection Control team in the facility, facility management, Provincial and National Departments of Health, the South African Police Service (SAPS) and Military Health Services (MHS), and the National Institute for Communicable Diseases (NICD). All facilities are encouraged to compile a list of relevant contact numbers that can be easily accessed in case of a bioterror incident.

3. PUBLIC HEALTH SYSTEM PREPAREDNESS

Identification of a bioterrorism release requires the determination of the source so that all who have been exposed can be attended to. An epidemiological investigation should take place to identify time, place and persons exposed. Depending on the suspected bioterrorism pathogen, human specimens may need to be processed at specialized laboratories at the NICD (Special Bacterial Pathogens Unit or the Special (Viral) Pathogens Unit). A bioterrorist attack will require a collaborative response from the Department of Health together with the SAPS, MHS and other stakeholders.

If the disease is contagious, the patient will need to be isolated and close contacts identified. Treatment and chemoprophylaxis for category A pathogens are described in a later section.

4. LABORATORY PREPAREDNESS

The NICD has specialised units which have the facilities to safely provide laboratory confirmation of a bioterror pathogen. The first responder to a suspected bioterror incident should be the SAPS and they will contact the Chemical and Biological Unit (CBU) of the MHS. Suspected substances or articles will be secured, packed and transported to a military-contracted laboratory. Suspected bioterror-related human specimens should be sent to the relevant unit at the NICD. Table 1 lists appropriate specimens to submit, and tests offered for Category A bioterror pathogens (Appendix) at the NICD. Please note: The units **must** be notified that specimens are being sent and specimens should be labelled and addressed as follows:

For specimens from cases with suspected anthrax, plague, botulism and tularaemia:

Special Bacterial Pathogens Reference Unit, NICD-NHLS
 1 Modderfontein Road (R25)
 Sandringham, Johannesburg, 2192

For specimens from cases with suspected smallpox or viral haemorrhagic fever:

Special Pathogens Unit, NICD-NHLS
 1 Modderfontein Road (R25)
 Sandringham, Johannesburg, 2192

Table1: Appropriate specimens to submit and tests offered at the NICD for category A bioterror pathogens

Pathogen & comments	Tests to request	Sample Source and Type	Sample Collection / Special Instructions
Anthrax: Disease in humans <i>Bacillus anthracis</i>	Anthrax - ELISA	Clotted human blood or serum	Safety precautions when handling samples
	Anthrax culture and confirmation	Skin lesion swab, gastric washing, sputum, nasal swab, and post-mortem samples.	
	Anthrax PCR	Cultures	
Anthrax: White powder incidents Testing of suspicious substances/articles	Anthrax	Suspicious substances and/or articles	Chemical and Biological Unit (CBU) of the Military Health Service to ensure safe transport to testing laboratory.
Anthrax: White powder incidents	The collection of human (clinical) specimens is generally <u>not indicated</u> following exposure to a suspected white powder incident. Laboratory investigations of humans specimens is only recommended in the case of suspected anthrax disease.		
Plague: <i>Yersinia pestis</i> Dead rodents or fleas may also be submitted.	Plague - ELISA	Clotted human blood or serum	Safety precautions when handling samples
	Plague - culture and confirmation	Bubo aspirate, sputum, blood cultures, post-mortem samples, rodents and fleas	
	Plague - DFA		
	Plague - ELISA	Rodent clotted blood or serum	

Pathogen & comments	Tests to request	Sample Source and Type	Sample Collection / Special Instructions
Botulism: <i>Clostridium botulinum</i>	Botulism testing	Serum, stool and vomitus and/or gastric contents. Implicated food item.	Transport refrigerated, do NOT freeze.
Tularaemia: <i>Francisella tularensis</i>	Liaise with Special Bacterial Pathogens Unit laboratory		
Smallpox virus (<i>Variola</i>)	PCR	Cutaneous lesion scabs OR vesicular fluid	Observe appropriate infection prevention and control protocols when collecting and handling specimens.
Viral haemorrhagic fevers	Serology: Fluorescent antibody test, IgG and IgM	Clotted blood or serum (liver biopsies optional)	Tubes in sealed in plastic bags and secondary containers with absorbent material. Label clearly as biohazardous, transport at 4°C
	ELISA, IgG and IgM		
	PCR		
	Virus isolation		

5. PATHOGENS OF GREATEST CONCERN: Category A bioterror pathogens

According to the CDC classification of bioterror agents (Appendix 1), pathogens in category A with priority level 1 constitute the greatest threat for mass morbidity and mortality.

5.1 Anthrax

Anthrax is an acute infectious disease caused by the spore-forming bacterium *Bacillus anthracis*. Anthrax most commonly occurs in wild and domestic animals (e.g. cattle, sheep, goats, antelopes, and other herbivores), but it can also occur in humans. It can present in three forms: cutaneous, gastrointestinal and inhalational anthrax. The most common form of endemic anthrax is cutaneous.

Transmission: Anthrax is not known to spread from person-to-person. *B. anthracis* spores can live in the soil for many years, and humans can become infected with anthrax by handling products from infected animals or by inhaling anthrax spores from contaminated animal products. Anthrax can also be spread by eating undercooked meat from infected animals. When anthrax spores are used as bioterror agents the most likely scenario is an aerosol release, resulting in inhalational anthrax (which is more frequently fatal than other forms of anthrax).

Symptoms of inhalational anthrax: These symptoms can occur between 2 to 10 days of infection:

- Fever, which may be accompanied by chills or night sweats.
- Flu-like symptoms.
- Cough (usually non-productive), chest discomfort, shortness of breath, fatigue, muscle aches.
- Sore throat, followed by difficulty swallowing, enlarged lymph nodes, headache, nausea, loss of appetite, abdominal discomfort/pain, vomiting, or diarrhoea.

Diagnosis: On chest X-ray, a patient with inhalational anthrax will have a widened mediastinum ± a pleural effusion or pneumonic changes. Laboratory parameters to look for are decreased levels of sodium, calcium and albumin; elevated liver enzymes (AST and ALT) and a high haematocrit. Blood cultures are often positive. Other specimens which may be helpful (positive microscopy/culture) include sputum if present, and pleural fluid. There is no screening test for anthrax; the only way exposure can be determined is through a public health investigation.

Treatment:

- **Suspected systemic anthrax (i.e. bloodstream, gastrointestinal or inhalation anthrax):** Treatment of anthrax is with 3-drug intravenous antibiotic therapy which includes ciprofloxacin and one or two other agents such as ampicillin, clindamycin, vancomycin, penicillin, chloramphenicol, imipenem, rifampicin and clarithromycin.
- **Suspected cutaneous anthrax:** Oral amoxicillin or ciprofloxacin.
- Antimicrobial resistance is a theoretical concern for genuine bioterrorism incidents. Healthcare workers should liaise closely with the NICD to inform treatment choice.

Management of 'white powder incidents' or other suspected anthrax bioterrorism exposures:

The first responder is the SA Police Service (SAPS), in its capacity as primary manager of all suspicious package investigations; substances or articles suspected of being of biological hazard will be secured, then passed to the Chemical and Biological Unit (CBU) of the Military Health Services, who are responsible, after rendering items safe to transport, for delivering the material to the NICD and/or another contracted agency and/or the Onderstepoort Veterinary Research Institute (OVRI) for identification of any anthrax spores or bacilli.

Human contacts should be subjected to a simple algorithm (Figure 1). The collection human specimens is generally not indicated following exposure to a suspected white powder incident, but only recommended in the case of suspected anthrax disease. Specimens from humans can be sent directly to NICD or submitted to any NHLS lab (or other private lab) for forwarding to NICD. The NICD must be notified in advance of sending specimens by contacting one of the telephone numbers below, and then specimens should be labelled and addressed as follows:

Human samples for anthrax investigation (URGENT)**Dr Jenny Rossouw****Special Bacterial Pathogens Reference Unit****NICD-NHLS****1 Modderfontein Rd (R25)****Sandringham 2192****Johannesburg****Tel: 011-555-0331/0306 (office hours only)****NICD Hotline 082-883-9920 (all hours, for use by healthcare professionals only)**

Preventive Measures: There is no human anthrax vaccine available in South Africa. Antibiotics used in post-exposure prophylaxis (PEP) are very effective in preventing anthrax disease from occurring after an exposure to inhaled spores. Table 2 shows the recommendations for PEP following exposure to anthrax spores.

If patients are suspected of being exposed to anthrax, should they be isolated?

Anthrax is not known to spread from person-to-person. Therefore, there is no need to isolate individuals suspected of being exposed to anthrax or to treat contacts of persons ill with anthrax, such as household contacts, friends, or coworkers, unless they also were also exposed to the same source of infection.

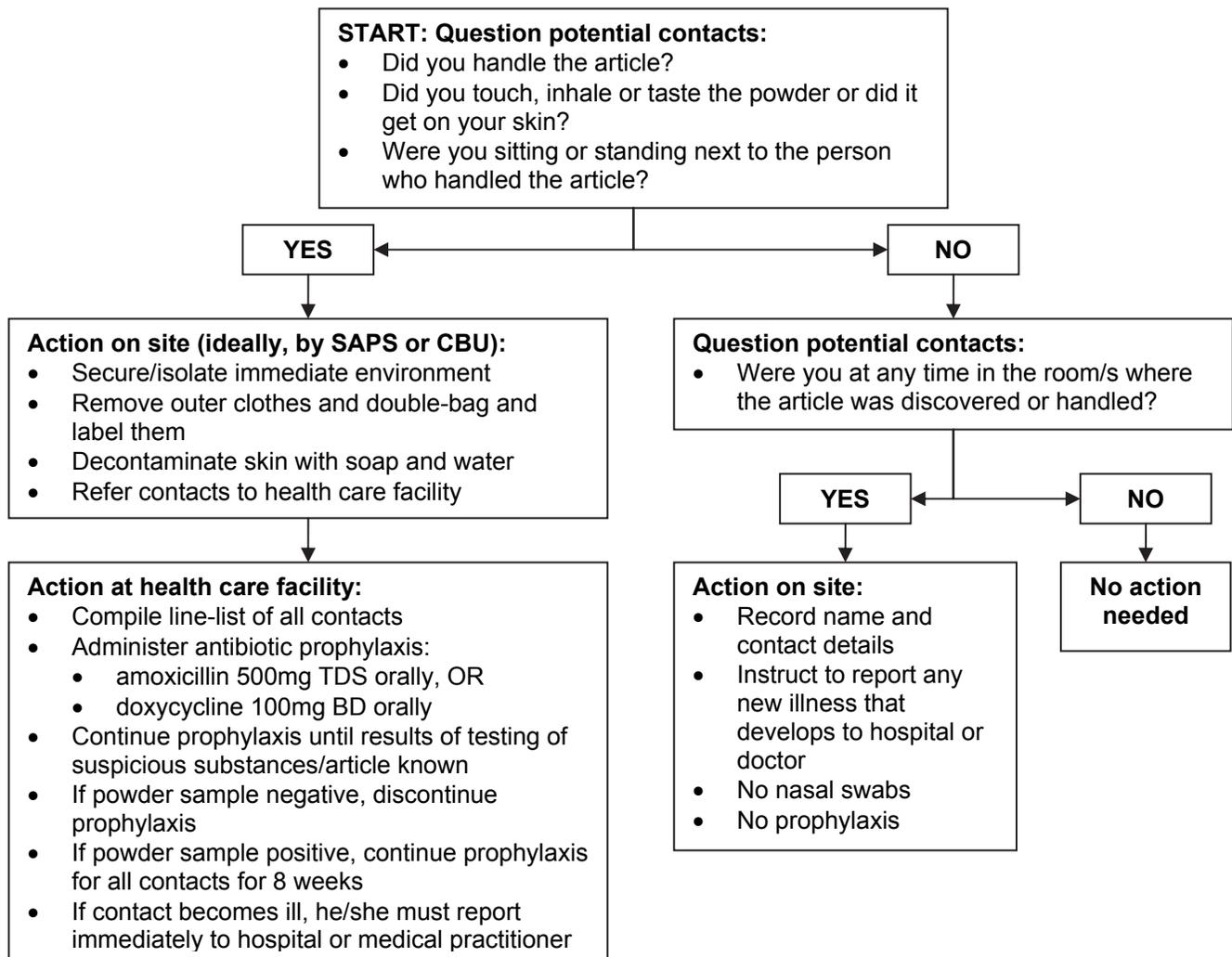


Figure 1: Algorithm for management of ‘white powder incidents’ or other suspected anthrax bioterrorism exposures

Table 2: CDC recommendations for post-exposure prophylaxis after exposure to *Bacillus anthracis* spores

Patient	Recommended initial antibiotic	Duration
Adults (including pregnant or breastfeeding women)	<ul style="list-style-type: none"> • Ciprofloxacin 500mg orally twice daily or, • Levofloxacin 500mg orally twice daily or, • Doxycycline 100mg orally twice daily • (Amoxicillin 500mg orally three times daily may be substituted if anthrax isolate has been found to be a penicillin-sensitive strain). 	60 days
Children	<ul style="list-style-type: none"> • Ciprofloxacin 10 -15mg/kg not to exceed 500mg orally twice daily or, • Levofloxacin 16mg/kg not to exceed 250mg orally twice daily or, • Doxycycline: <ul style="list-style-type: none"> ○ >8 years and >45kg: 100mg orally twice daily ○ >8 years and <45kg: 2.2mg/kg orally twice daily ○ <8years: 2.2mg/kg not to exceed 100mg orally twice daily • If anthrax isolate is penicillin-sensitive amoxicillin may be substituted. <ul style="list-style-type: none"> ○ <20 kg: 80mg/kg orally in three divided doses ○ >20kg:500mg orally three times a day 	60 days

5.2 Botulism

Botulism is an intoxication caused by extremely potent toxins preformed in improperly prepared or stored foods. The toxins are produced by the bacterium *Clostridium botulinum*. A bioterrorist attack with the toxin can cause intoxication via ingestion or aerosolization.

Transmission: Person-to-person transmission of botulism does not occur. Botulism is mainly foodborne intoxication but it can also be transmitted through wound infections or intestinal infection in infants. The botulinum toxin has been found in a variety of foods, including low-acid preserved vegetables, such as green beans, spinach, mushrooms, and beets; fish, including canned tuna, fermented, smoked and salted fish; and meat products, such as ham, chicken and sausage. The toxin can be weaponised for use as an aerosol or to contaminate food/water sources.

Clinical features in deliberate attack: The symptoms of a victim of a bioterrorist attack are no different to those of a natural outbreak of botulism. A deliberate attack should be suspected when large numbers of people present with acute flaccid paralysis and prominent bulbar palsies. Epidemiological investigations might reveal a common source of exposure that is not typically associated with botulism. The symptoms usually appear within 12 to 36 hours (range 4 hours to 8 days) after exposure. In the case of inhalational botulism (following inhalation of the toxin in an aerosol), the incubation period may be longer.

Clinical features include marked fatigue, weakness, and vertigo, usually followed by blurred vision, dry mouth, and difficulty in swallowing and speaking (bulbar palsy). Vomiting, diarrhoea, constipation and abdominal swelling may occur. The disease can progress to weakness in the neck and arms, after which the respiratory muscles and muscles of the lower body are affected (flaccid paralysis). The paralysis may make breathing difficult. There is no fever and no loss of consciousness.

Diagnosis: Diagnosis is through demonstration of the botulinum toxin in serum, gastric secretions, and stool or food samples, or culture of the organism. Laboratory evaluation includes:

- Mouse toxicity assays
- Anaerobic cultures from the specimens
- Enzyme-linked immunosorbent assay may be used to detect toxin in food
- Polymerase chain reaction (PCR), although cellular components of samples may limit sensitivity

If botulinum toxin is used in a bioterrorist attack, the diagnosis would depend on the route of exposure.

Treatment: Incidence of botulism is low, but the mortality rate is high if treatment is not immediate and appropriate. The disease can be fatal in 5 to 10% of cases, but can be up to 60% if left untreated. At present, there is no antitoxin available in South Africa. Severe botulism cases require supportive treatment, especially mechanical ventilation, which may be required for weeks or months. Antibiotics are not required (except in the case of wound botulism).

Prevention: Prevention of botulism is based on safe food preparation (particularly preservation) practices and hygiene. Botulism may be prevented by inactivation of the bacterial spores in heat-sterilized, canned products or by inhibiting growth in all other products. Refrigeration temperatures combined with salt content and/or acidic conditions will prevent the growth or formation of toxin.

If exposure to the toxin via an aerosol is suspected, in order to prevent additional exposure to the patient and health care providers, the clothing of the patient must be removed and stored in plastic bags until it can be washed with soap and water. The patient must shower thoroughly. Food and water samples associated with suspect cases

must be obtained immediately, stored in proper sealed containers, and sent to the relevant laboratory at the NICD. There is no vaccine licensed for use in South Africa.

5.3 Plague

Plague is caused by the microbial agent *Yersinia pestis*, which is found in rodents and their fleas. It has caused three large pandemics between the 6th and the 20th century leading to over 200 million deaths. The zoonotic foci still exists on all continents except Australia, and the disease continues to cause sporadic illness, mainly in Africa.

Characteristics of a deliberate attack: The release of *Yersinia pestis* as a biological weapon is likely to be covert because aerosolized *Y. pestis* is odourless and colourless. Detection will coincide with or be later than the first clinical case which will occur 1 to 7 days after exposure. The clinical spectrum of disease has preponderance towards pneumonic rather than bubonic plague. Bubonic plague is not transmitted from person-to-person and is the endemic form of plague. Clinical features include fever, productive cough which is watery, bloody and has Gram-negative bacilli on microscopy; haemoptysis, chest pain and evidence of bronchopneumonia (without a widened mediastinum) on a chest X-ray.

Transmission: Transmission can take place if someone inhales *Y. pestis*, which could happen in an aerosol release during a bioterrorism attack. Pneumonic plague is also transmitted by breathing in *Y. pestis* suspended in respiratory droplets from a person (or animal) with pneumonic plague. Respiratory droplets are spread most readily by coughing or sneezing. Becoming infected in this way usually requires direct and close (within ±2 metres) contact with the ill person or animal.

Diagnosis: Gram, Wayson's and antibody fluorescent stain, and culture of respiratory specimens in the case of pneumonic plague can yield a preliminary diagnosis. Blood samples and aspirates from lymph nodes may also contain the organism. Other tests which maybe used to confirm a diagnosis are available at reference laboratories and these include fluorescent antibody tests, PCR and antigen-capture ELISA.

Treatment: Antibiotic treatment should be commenced immediately when a case is suspected. Post-exposure prophylaxis should be given to asymptomatic people with known exposure to an aerosol of *Y. pestis* or who have come into close contact with an infected person. Table 3 shows treatment recommendations. There is no vaccine licensed for use in South Africa.

Table 3: Recommendations for the treatment of adult patients with pneumonic plague†

Setting	Preferred treatment		Alternative treatment	
	Drug	Dose	Drug	Dose
Contained casualty setting	Streptomycin	1g IM twice daily	Doxycycline	200mg orally twice daily
	Gentamicin	5 mg/kg IM or IV once daily or 2 mg/kg loading dose followed by 1.7mg/kg IM or IV 3 times daily	Ciprofloxacin	400mg IV twice daily
			Chloramphenicol	25mg/kg IV 4 times daily
Mass casualty setting or post-exposure prophylaxis	Doxycycline	100 mg orally twice daily	Chloramphenicol	25mg/kg orally 4 times daily
	Ciprofloxacin	400mg orally twice daily		

†Adapted from Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a biological weapon: Medical and public health management. Working Group on Civilian Biodefense. JAMA. 2000;283:2281-2290.

5.4 Smallpox

Smallpox is an acute viral illness caused by the variola virus. It has been eradicated worldwide through a successful vaccination program; the last naturally occurring case of smallpox was in 1977 in Somalia. Routine vaccination against smallpox is no longer necessary. Smallpox is a bioterrorism threat due to its potential to cause severe morbidity in a nonimmune population, and because it can be transmitted via the airborne route, as well as by contact with skin lesions or secretions of infected persons. A single case is considered a public health emergency.

Clinical features: The incubation period for smallpox is 7-17 days; the average is 12 days. Acute clinical symptoms of smallpox resemble other acute viral illnesses, i.e. a flu-like illness. Skin lesions appear, quickly progressing from macules to papules to vesicles. Other clinical symptoms to aid in identification of smallpox include:

- 2-4 day, non-specific prodrome of fever and myalgia.
- Rash: most prominent on face and extremities (including palms and soles) in contrast to the truncal distribution of varicella.
- Rash scabs over in 1-2 weeks.
- In contrast to the rash of varicella, which arises in “crops,” variola rash has a synchronous onset.

Transmission: Direct and prolonged face-to-face contact is required to spread smallpox from one person to another. Smallpox can also be spread through direct contact with infected bodily fluids or contaminated objects such as bedding or clothing. Rarely, smallpox has been spread by virus carried in the air in enclosed settings such as buildings, buses, and trains. It can be weaponised for airborne transmission.

Diagnosis: The CDC has developed tools to assist clinicians in the diagnosis of smallpox. The tools can be found on <http://www.bt.cdc.gov/agent/smallpox/diagnosis>. The diagnosis of smallpox is clinical, and through nucleic acid testing in the laboratory. Appropriate specimens include samples from the skin lesions, blood, tonsillar swabs and lesion punch biopsies.

Treatment and preventive measures: There is no proven treatment for smallpox. Patients with smallpox may be given supportive care including intravenous fluids, pain relief and antibiotics if secondary bacterial infections develop. All suspected cases of smallpox should be reported immediately so that the appropriate response is activated. Suspected smallpox cases MUST be isolated and appropriate infection prevention and control measures instituted. There is no smallpox vaccine currently licensed for use in South Africa.

5.5 Tularaemia

F. tularensis subspecies *tularensis* (type A) is one of the most infectious pathogens known in human medicine. The infective dose in humans is extremely low: 10 bacteria when injected subcutaneously and 25 when given as an aerosol. It has the potential to cause significant mortality and morbidity which makes this organism an attractive bioterrorist weapon. Tularaemia has been reported in many countries of the northern hemisphere, but to date has not been described in the southern hemisphere.

Clinical features in deliberate attack: Aerosolization is the most likely method of dispersion of *F. tularensis* in a deliberate attack. The incubation period is 3 to 5 days. Initial symptoms include fever between 38°C and 40°C, malaise, headache, rigors, coryza and sore throat. After inhalation, the two presentations of tularaemia that are likely to be seen are either typhoidal or pneumonic disease:

1. Typhoidal tularaemia: Historically, the typhoidal form was defined as tularaemia devoid of skin or mucous membrane lesion and/or a remarkable lymph node enlargement. Only when no route of infection can be established, as might be the case in a deliberate attack, may the term still be acceptable.
2. Pneumonic tularaemia: chills, high fever, dyspnoea, dry or productive cough, pharyngitis, chest pain, headache, profuse sweating, drowsiness, general weakness and hilar lymphadenopathy.

Transmission: *F. tularensis* is transmitted to humans by (i) arthropod bites, (ii) direct contact with infected animals, infectious animal tissues or fluids, (iii) ingestion of contaminated water or food, or (iv) inhalation of infective aerosols. There is no documented human-to-human transmission.

Diagnosis: The diagnosis of tularaemia requires a high index of suspicion and most often the diagnosis is made on clinical grounds. Tularaemia may be mistaken for a range of other diseases. Among these are a wide variety of conditions presenting with fever and lymph node enlargement. Serological tests are preferred to cultures for routine diagnosis of endemic tularaemia; however antibodies are not measurable before 2 weeks. Highly sensitive PCR and real-time PCR assays have been developed for use in human specimens, including blood. Appropriate specimens may include: blood cultures, swabs from skin, conjunctiva and pharyngeal lesions; respiratory secretions from bronchoalveolar lavage washings, endotracheal aspirates, and expectorated sputum; lymph node aspirates and tissue biopsy specimens.

Treatment: Recommendations for therapy following an intentional attack are summarized in Table 4 below. The treatment strategy varies depending on the numbers of people infected. In mass casualty situations, a minimum of 14 days treatment is required. People who are immunosuppressed should receive a minimum of 10 days treatment with either gentamicin 5 mg/kg/day IV or IM, or they should receive streptomycin 1g 12 hourly IM.

Table 4: Treatment and post-exposure prophylaxis guidelines for tularaemia†

	Antibiotic	Adults	Children	Pregnancy
Serious disease	Streptomycin	1g IM 12hrly for 10days	1g IM 12hrly for 10days	1g IM 12hrly for 10days
	Gentamicin	5mg/kg/day IV or IM for 10 days	5mg/kg/day IV or IM for 10 days	5mg/kg/day IV or IM for 10 days
Less serious disease	Streptomycin or gentamicin	As above	As above	As above
	Ciprofloxacin	400mg IV twice daily for 10 days	15mg/kg IV twice daily for 10 days do not exceed 1g per day	400mg IV twice daily for 10 days
	Chloramphenicol	15mg/kg qid for 14 -21days	15mg/kg qid for 14 -21days	15mg/kg qid for 14 -21days
Post-exposure prophylaxis	Ciprofloxacin	500mg orally twice daily for 14 days	15m/kg orally twice daily for 14 days	500mg orally twice daily for 14 days
	Doxycycline	100mg twice daily for 14 days	100mg twice daily for 14 days if weight ≥45kg; 2.2 mg/kg twice daily orally if weight <45kg	100mg twice daily for 14 days

†Adapted from Dennis DT, Inglesby TV, Henderson DA et al. Tularemia as a biological weapon: medical and public health management. *JAMA*, 2001; 285:2763-2773.

Preventive Measures: Post-exposure prophylaxis is recommended for individuals who have been exposed to the organism. In the hospital setting, isolation is not required as there is no person-to-person transmission. Laboratory and autopsy personnel are at risk from infection by aerosolisation of infected tissues during laboratory/autopsy procedures and should be notified of suspected tularaemia cases in order to ensure appropriate safety measures are observed.

5.6 Haemorrhagic Fevers

Viral hemorrhagic fevers (VHFs) refer to a group of illnesses that are caused by several distinct families of viruses (Table 5). With the exception of dengue haemorrhagic fever, VHF viruses can be transmitted via aerosol infection and are therefore potential bioterror agents.

Table 5: Viral Haemorrhagic Fevers

Family/Genus	Disease (Virus)
Arenaviridae	Lassa fever Bolivian HF Argentine HF Other South American HF
Bunyaviridae <ul style="list-style-type: none"> ▪ Phlebovirus ▪ Nairovirus ▪ Hantavirus 	Rift Valley fever Crimean-Congo HF HF with renal syndrome, HFRS (Hantaan and others) Hantavirus pulmonary syndrome, HPS (Sin Nombre, Andes and others)
Filoviridae	Marburg HF Ebola HF
Flaviviridae	Yellow fever Dengue Tick-borne virus HF

Clinical features in deliberate attack: Specific signs and symptoms vary by the type of VHF, but initial signs and symptoms often include marked fever, fatigue, dizziness, muscle aches, loss of strength, and exhaustion. Patients with severe cases of VHF often show signs of bleeding under the skin, in internal organs, or from body orifices like the mouth, eyes, or ears. However, although they may bleed from many sites around the body, patients rarely die because of blood loss. Severely ill patient cases may also show shock, nervous system malfunction, coma, delirium, and seizures. Some types of VHF are associated with renal (kidney) failure.

Laboratory diagnosis: During the acute phase diagnosis is by PCR, ELISA or viral isolation. IgM antibodies are detected as the patient improves. Hantaviruses have antibodies present in serum at the time of onset of disease which can be detected in an IgM capture-ELISA. Tests for special pathogens are done at the NICD Special (Viral) Pathogens Unit.

Treatment: Patients receive supportive therapy but there is no other treatment or established cure for VHFs. Ribavirin has been effective in treating some individuals with CCHF, Lassa fever or HFRS. Maintenance of balance of body fluids and management of bleeding diatheses are the general principles of therapy. Treatment with convalescent-phase plasma has been used with success in some patients with Argentine HF.

Preventive measures: VHF viruses are highly infectious in aerosol spread in the laboratory. Certain VHFs are easily transmitted nosocomially and from person-to-person due to contact with infected body fluids. Infection prevention and control measures therefore depend on the type of VHF suspected.

In the event of a possible VHF bioterror incident, all relevant authorities must be notified immediately and specialist advice sought regarding infection prevention and control measures and referral of patients to dedicated facilities that are prepared for managing patients with VHFs.

Comprehensive documents detailing the necessary precautions and infection control practice can be accessed as follows:

- Reference guide for healthcare workers: WHO Infection Control for viral haemorrhagic fevers in the African health care setting: http://www.who.int/csr/resources/publications/ebola/WHO_EMCSR_98_2_EN/en/
- Reference guide for laboratory staff: Q-Pulse, document number GPL 0890 (Infection Control Services Laboratory, Johannesburg) and GPL 0947 (Virology Laboratory, Groote Schuur Hospital).

6. REFERENCES

1. Borio L, Hynes NA, Henderson DA. Biodefense. In: Mandell GL, Bennett JE, Dolin R. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 7th ed. Philadelphia: Churchill Livingstone Elsevier; 2009. pp. 3951-3998.
2. Frean J. Lecture: Bioterrorism. OutNet Workshop held at NICD, April 2010.

APPENDIX 1: CDC BIOTERRORISM AGENTS AND DISEASE CATEGORIES

Category Priority	A 1	B 2	C 3
Characteristics	<ul style="list-style-type: none"> • Easily disseminated or spread person-to-person • Highly lethal • Serious public health effects • May cause great panic and social disruption 	<ul style="list-style-type: none"> • Moderately easy to disseminate • Moderate morbidity • Less lethal than category A agents • Requires fewer special public health preparations 	<ul style="list-style-type: none"> • Includes emerging infectious diseases • Potential for wide dissemination in the future could result in high morbidity, lethality, and major public health effects
Disease (agent)	<ul style="list-style-type: none"> • Anthrax (<i>Bacillus anthracis</i>) • Botulism (<i>Clostridium botulinum</i> toxin) • Plague (<i>Yersinia pestis</i>) • Smallpox (<i>Variola</i>) • Tularemia (<i>Francisella tularensis</i>) • Haemorrhagic fever viruses 	<ul style="list-style-type: none"> • Brucellosis (<i>Brucella</i> species) • Epsilon toxin of <i>Clostridium perfringens</i> • Food safety threats (e.g. <i>Salmonella</i>) • Glanders (<i>Burkholderia mallei</i>) • Psittacosis (<i>Chlamydia psittaci</i>) • Q fever (<i>Coxiella burnetii</i>) • Ricin toxin from <i>Ricinus communis</i> (castor beans) • Staphylococcal enterotoxin B • Typhus fever (<i>Rickettsia prowazekii</i>) • Viral encephalitis (e.g. Venezuelan equine encephalitis) • Water safety threats (e.g., <i>Vibrio cholerae</i>) 	<ul style="list-style-type: none"> • Emerging infectious disease threats such as Nipah virus and Hantavirus