



A N T H R A X

GUIDELINES FOR ACTION IN THE EVENT OF A DELIBERATE RELEASE

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Note: Comments are welcome from healthcare, laboratory and public health professionals, and should be sent to DRcomments@hpa.org.uk. These guidelines may be subject to change as comments are received, so please ensure that you have the latest version available through the HPA website: [http://www.hpa.org.uk/deliberate accidental releases/biological](http://www.hpa.org.uk/deliberate_accidental_releases/biological)

<i>For this version of the guidelines changes were made to the following sections of the previous version:</i>			
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1 BACKGROUND

These guidelines are intended for healthcare, laboratory and public health professionals to guide clinical and public health action in the event of a deliberate release of anthrax.

1.1 Introduction

Anthrax is an acute infection caused by the Gram-positive, spore-forming bacterium *Bacillus anthracis*. Anthrax naturally infects many species of grazing mammals such as sheep, cattle and goats, which are infected through ingestion of soil contaminated by *B.anthraxis* spores. There are different forms of human disease depending on how infection is acquired: cutaneous, inhalation, ingestion and injection. In over 95% of naturally occurring cases the infection is cutaneous, acquired by inoculation of spores into small abrasions on the skin, usually during handling of untreated animal hides.

1.1.1 Deliberate release of anthrax

The deliberate release of anthrax would be by release of large quantities of spores in an aerosol. This threat is considered serious because:

- the organism is relatively easy to cultivate from environmental sources
- the inhalation form of disease has a high mortality rate

Despite this, the creation of an infective anthrax aerosol is not easy – particles need to be between 1 and 5µm in size and sufficient energy is required to disperse them.

A deliberate release of anthrax spores occurred in 2001 in the USA. Letters containing the spores were sent through the postal system and resulted in 22 human cases: 11 cutaneous disease and 11 inhalation anthrax. Five of the patients with inhalation anthrax died: case-fatality rate of 45%.

1.2 Epidemiology

Anthrax is a zoonosis to which most mammals, especially grazing herbivores, are susceptible. Human infections usually result from contact with infected animals or animal products. Direct exposure to secretions from cutaneous anthrax lesions may result in secondary cutaneous infection, but there have been **no known cases of person-to-person transmission of inhalation disease**.

1.2.1 Transmission

The spores of *B. anthracis* are extremely durable. Modes of transmission include:

- cutaneous contact with spores, spore contaminated materials or infected skin lesions - infection usually requires an existing break in the skin to initiate infection, though in many cases this may be so small as to be unnoticed
- inhalation of spores
- ingestion of contaminated meat

1.2.2 Infectious dose

The ID₅₀ for inhalation anthrax (infectious dose required to cause disease in 50% of those exposed by inhalation) is generally regarded to be around 10,000 spores; however it may be considerably lower if the infectious particles have been modified or if the person is particularly vulnerable (e.g. elderly). The infective dose for cutaneous or gastrointestinal anthrax is not known.

1.2.3 Incubation period

The incubation period varies and is dependent on dose and exposure route. The following incubation periods are generally accepted, although inhalation anthrax in particular may have a much longer incubation period of 43 days or more.

- 1-7 days following cutaneous exposure
- 1-6 days following inhalation exposure
- 1-7 days following ingestion
- 1-2 days or longer following injection

Modelling suggests that the incubation period for inhalational anthrax is dose-dependent and that a relatively long incubation period would be expected if the level of exposure was low (as in the Sverdlovsk incident). During the 2001 US deliberate release the last (eleventh) case of inhalation anthrax had an onset of symptoms 56 days after the first letters containing anthrax were mailed and at least 3 weeks after the onset of illness of the tenth case of inhalation anthrax. However, the actual incubation period could not be determined (Barakat *et al.* 2002).

1.2.4 Period of communicability

- Transmission of anthrax infection from person-to-person is highly unlikely.
- Contact with skin lesions can occasionally result in subsequent cutaneous infection.
- Airborne transmission from person-to-person does **not** occur.

1.3 Clinical features

Human anthrax can occur in four forms: inhalation/pulmonary, cutaneous, gastrointestinal, or injection anthrax depending on the route of exposure and details of these are given below. It can be expected that any malicious or deliberate release of anthrax spores will involve aerosol exposure.

Clinicians should be aware of the possibility of cases of inhalation anthrax, and any previously healthy patient with the following clinical presentations should be immediately reported to the Consultant in Communicable Disease Control at the local Health Protection Unit and to the 24 hour duty doctor at HPA Colindale (020 8200 6868).

- **Rapid onset of severe, unexplained febrile illness or febrile death.**
- **Rapid onset of severe sepsis not due to a predisposing illness, or respiratory failure with a widened mediastinum.**
- **Severe sepsis with Gram-positive rods or *Bacillus species* identified in the blood or cerebrospinal fluid and assessed not to be a contaminant.**

Clinical pictures illustrating the different forms of anthrax infection are available at:
<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/AnthraxDR/Images/>

1.3.1 Inhalation/pulmonary

- Following inhalation of spores, there is a non-specific prodrome of flu-like illness (fever, headache, myalgia and non-productive cough). Symptoms more often associated with inhalation anthrax than other flu-like illness include: nausea, vomiting, pallor or cyanosis, sweating, altered mental status and raised red blood cell count.
- Two to four days after initial symptoms, there is **abrupt onset of respiratory failure** and on chest X-ray a **widened mediastinum** is often present, suggestive of mediastinal lymphadenopathy and haemorrhagic mediastinitis. The most accurate predictor of inhalation anthrax cases is mediastinal widening or pleural effusions. Note that a widened mediastinum may also be apparent in cases of TB due mediastinal lymphadenopathy.

- Gram-positive bacilli seen in blood cultures (if taken before antibiotic treatment), usually after 2-3 days of onset of illness.
- Treatment may be successful in the prodromal stage, but by the time respiratory or bacteraemic symptoms develop, treatment may not arrest the disease before a fatal outcome.
- Algorithm for clinical evaluation and management of inhalation anthrax is available at: <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/AnthraxDR/Guidance/>

1.3.2 Cutaneous

- Local skin involvement after direct contact
- Commonly seen on hands, forearms, head and neck
- Three days after exposure a raised, itchy, inflamed pimple appears followed by a papule that turns vesicular. Extensive oedema accompanies the lesion – the swelling tends to be much greater than would normally be expected for the size of the lesion and this is usually **PAINLESS**. Then 2-6 days later the classical black eschar develops.
- Responds to oral antibiotics
- Rarely may progress to bacteraemia or meningitis without treatment
- Algorithm for clinical evaluation and management of cutaneous anthrax is available at: <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/AnthraxDR/Guidance/>

1.3.3 Gastrointestinal

- Rare – there are two forms abdominal and oropharyngeal (this is even less common)
- Characterised by severe abdominal pain, loss of appetite, malaise, fever, nausea and vomiting with watery or bloody diarrhoea
- Bacteraemia may develop 2-3 days after onset
- Usually fatal if it progresses to bacteraemia

1.3.4 Injection Anthrax

A novel form of anthrax has recently been recognised. Since December 2009, drug users in Scotland, England and Germany have been found to have acquired anthrax through using heroin contaminated with anthrax spores (Ramsay *et al* 2010). Users have frequently but not exclusively been injectors (Booth *et al* 2010). For the latest information in England and links to information in Scotland, see:

<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Anthrax/AnthraxOutbreakInformation/>

This type of anthrax had only reported once before, in Norway in 2000. Cases in the UK have presented in a variety of ways:

- Severe soft tissue infection, including necrotizing fasciitis and cellulitis/ abscess, particularly if associated with oedema which is often marked. Compartment syndrome has also been noted.
- Signs of severe sepsis, with or without evidence of soft tissue infection.
- Meningitis (especially haemorrhagic meningitis) including clinical and/or CT evidence suggestive of subarachnoid haemorrhage or intracranial bleed.
- Gastrointestinal symptoms - abdominal pain, nausea, vomiting, diarrhoea, GI haemorrhage.
- Algorithm for clinical evaluation and management of drug users with possible anthrax is available at: <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Anthrax/AnthraxOutbreakInformation/AnthraxInformationForHealthcareProfessionals/>

1.4 Mortality

Systemic infection resulting from inhalation of the organism has a mortality rate approaching 100%, with death usually occurring within a few days after the onset of symptoms. Cutaneous anthrax, the most common form, is usually curable with antibiotics (less than 1% fatality). The mortality rate among people with infection resulting from ingestion is variable, but may also approach 100%. There has been a 33% case fatality rate amongst the 52 cases of injection anthrax reported in the UK between December 2009 and December 2010.

1.5 Organism survival

Anthrax spores have no detectable metabolism, and are resistant to drying, heat, UV light, gamma irradiation and many disinfectants. In some types of soil, anthrax spores can remain dormant for decades.

1.6 Antimicrobial susceptibilities

Most naturally occurring anthrax strains are sensitive to penicillin, which historically has been the preferred therapy for the treatment of anthrax. However, the deliberate release of anthrax spores in the US in 2001 and the subsequent experience of treating patients with inhalation and cutaneous anthrax have led to the CDC issuing revised guidance on treatment and prophylaxis – CDC documents on anthrax treatment are available from their website at <http://www.bt.cdc.gov/agent/anthrax/treatment/index.asp>

Ciprofloxacin or doxycycline should be considered an essential part of the first-line therapy for inhalation anthrax. Due to concerns about constitutive and inducible β -lactamases in *B. anthracis*, penicillin and ampicillin should not be used alone for the treatment of inhalation anthrax (See Table 1, Section 2.2).

2 CLINICAL PROCEDURES

2.1 Diagnosis and collection of samples

Despite its reputation, anthrax is not contagious, and humans are not highly susceptible to the disease. While theoretically it only takes one spore to initiate a cutaneous infection, *B. anthracis* is not invasive and usually requires a portal of entry through the skin, although in many cases this may be so small as to be unnoticed. Standard Universal Precautions (gloves, gowns, masks and hand washing) should be adopted to take the samples.

2.1.1 Precautions for sampling

The samples outlined below should be taken to confirm the diagnosis. These must be taken using Universal Precautions and with the utmost care to avoid inoculation injuries. The procedures for transporting samples to the laboratory are outlined in section 3.6. The receiving laboratory should be telephoned to expect arrival. Chain of evidence documentation should also accompany all specimens; however in larger incidents this would only be required for several of the initial cases.

2.1.2 Samples to be taken from acutely ill patients

- Blood for culture (taken before antibiotic treatment).
- Nasal swabs (laboratory diagnosis is easier if these are sent dry since this prevents growth of other organisms and facilitates detection of anthrax spores).
- Respiratory samples including lung aspirates, pleural fluids, or sputum samples and swabs from cutaneous lesions.

2.1.3 Post-mortem specimens

Samples may be taken from dead humans to assist diagnosis, including:

- Blood from a vein (the blood is non-clotting at death in anthrax).
- Respiratory tract samples.
- Swabs of haemorrhagic exudate from orifices.
- Swabs or sample of other body fluids if appropriate.

However, full post-mortem examinations are strongly discouraged if anthrax is suspected (see 2.3.4). If a post-mortem is carried out, swabs or samples of lung, spleen or lymph node tissue should be sent (transport medium is not necessary, but it will not damage specimens).

2.1.4 Samples to be taken from the environment

Samples should be taken from any material (soil, dust, clothing, swabbing etc.) in the environmental area thought to have been exposed to anthrax spores, or soiled by exudates from humans (or animals). Further advice on environmental sampling methods will be provided if a release is suspected.

2.1.5 Samples to be taken from others who have or may have been exposed

Depending on the scale of a release, it may be possible to obtain nasal swabs from people present within and around the exposed area at the time of release. This is to inform epidemiological investigations and guide confirmation of the release and designation of an exposed zone. **If a release is suspected, antibiotic prophylaxis should not be delayed for the result of nasal swabs.**

2.1.6 Transport of samples

Strict procedures should be followed for the transport of samples of suspected anthrax, both from the clinical environment to the laboratory, and from local laboratories onto the reference laboratory. These are outlined in section 3.6. *B. anthracis* cultures fall into category A for the purposes of transport. All samples should be transported as per UN 602 as described in "Appendix 1.2 Transport of infectious substances" in "Biological agents: Managing the risks in

laboratories and healthcare premises." Advisory Committee on Dangerous Pathogens (ACDP), Health and Safety Executive (HSE) May 2005 accessed at: <http://www.advisorybodies.doh.gov.uk/acdp/managingtherisks.pdf>

2.2 Treatment

Ciprofloxacin is not licensed for use in children or pregnant women, but may be indicated in life-threatening illness. Although doxycycline is not recommended in childhood or pregnancy its use would be considered in a serious infection such as anthrax. There have been no formal studies of the use of ciprofloxacin during pregnancy, but it is unlikely to be associated with a high risk of abnormalities of foetal development. There is some evidence that the use of fluoroquinolones in children (including by breast feeding mothers) may be associated with tendinopathy and arthropathy.

Where the diagnosis is suspected but not confirmed, it may be necessary to start empirical treatment to cover the possibility of anthrax. Early treatment reduces fatality therefore ciprofloxacin should commence as soon as anthrax is suspected. Because the initial symptoms are difficult to distinguish from other flu-like disease (see 1.3.1) a suggested strategy is to treat with a short three day course of ciprofloxacin until blood culture results are available. However, in these circumstances, it will also be necessary to treat concurrently for other causes of acute respiratory illness.

2.2.1 Inhalation and ingestion anthrax

Initially intravenous (IV) antibiotics should be administered. The recommended treatment for inhalation and ingestion anthrax is shown in Table 1. Once the patient's condition improves and the susceptibility of the organism is available, therapy can be switched to a single oral antibiotic (ciprofloxacin or doxycycline) – for further information consult the British National Formulary (also at <http://www.bnf.org>).

It should be noted that benzylpenicillin or amoxicillin should NOT be used alone in initial treatment of anthrax and that cephalosporins are ineffective for the treatment of anthrax.

The combination of rifampin and clindamycin demonstrated a synergistic effect *in vitro* against two strains of *B. anthracis* - Sterne and STi, both of which lack the pathogenicity plasmid (Athamna *et al* 2005). A number of other antibiotic combinations were either indifferent or antagonistic.

Sejvar *et al* (2005) suggest that for anthrax meningitis initial treatment should include an intravenous fluoroquinolone and not doxycycline, because doxycycline has poor central nervous system (CNS) penetration. In addition to an IV fluoroquinolone, one or two other agents that have good CNS penetration and activity against *B. anthracis* should be added (ie, penicillin, ampicillin, meropenem, vancomycin, rifampin). Case reports suggest that adding corticosteroids may be of benefit in the management of cerebral oedema/inflammation.

The early initiation of multi-drug antibiotic therapy is associated with decreased mortality in cases of inhalation anthrax (Holty *et al* 2006). It is suggested that the addition of vaccination to a short course of antibiotics would enhance protection afforded by antibiotics alone (Vietri *et al*. 2006).

Table 1: Recommended treatment for inhalation and ingestion anthrax

	Initial Therapy	Duration
Adults (including pregnant women)	<p>Ciprofloxacin 400mg IV every 12hr (<u>or</u> when appropriate 500mg oral twice daily)</p> <p>OR</p> <p>Doxycycline 100mg oral twice daily (when appropriate)</p> <p>PLUS</p> <p>One or two additional antibiotics (agents with <i>in vitro</i> activity include rifampicin, vancomycin, gentamicin, chloramphenicol, penicillin, amoxicillin, imipenem, meropenem and clindamycin)</p>	60 days
Children	<p>Ciprofloxacin 10mg/kg IV every 12hr, not to exceed adult dose of 1500mg per day (change to oral therapy, 15mg/kg PO not to exceed 1500mg per day, when appropriate)</p> <p>OR</p> <p>Doxycycline 100mg oral twice daily (NB: only for children > 8yrs and >45kg)</p> <p>PLUS</p> <p>One or two additional antibiotics (agents with <i>in vitro</i> activity include rifampicin, vancomycin, gentamicin, chloramphenicol, penicillin, amoxicillin, imipenem, meropenem and clindamycin)</p>	60 days

2.2.2 Cutaneous anthrax

Ciprofloxacin or doxycycline should be considered first-line therapy. Treatment should be initiated with oral ciprofloxacin 500mg or doxycycline 100mg twice daily for 7 days. This can be changed to oral amoxicillin if the organism is found to be susceptible or if the patient cannot take a fluoroquinolone or tetracycline class drug. Adults are recommended to take 500mg amoxicillin 3 times a day. For children, 80mg/kg amoxicillin divided into 3 doses given 8 hourly is an option for completion of therapy after clinical improvement. The oral amoxicillin dose is based on the need to achieve appropriate minimum inhibitory concentration levels.

Cutaneous anthrax with signs of systemic involvement, extensive oedema, or lesions on the head or neck requires intravenous therapy and a multi-drug approach is recommended.

Treatment may need to be continued for up to 60 days if there is suspicion of deliberate release in order to provide cover for inhalation anthrax, which may have been acquired concurrently.

2.3 Infection control practice

2.3.1 Decontamination of exposed persons

In the event of a known exposure to anthrax spores, the risk for re-aerosolisation is uncertain and is likely to depend on a number of variables, including the quantity of spores on the surface; the type of surface and host factors. However, even low numbers of spores could potentially lead to infection in any person having contact. An incident specific risk assessment will be required.

In situations where the threat of exposure to *B. anthracis* spores exists, cleansing of skin and potentially contaminated fomites such as clothing, personal possessions or environmental surfaces should take place. Decontamination of persons exposed to anthrax includes:

- Removal of contaminated clothing and possessions – it should be stored in labelled double plastic bags until exposure to anthrax has been ruled out
- If anthrax is confirmed, all contaminated material must be incinerated or autoclaved.
- Minimal handling of clothing and fomites to avoid agitation
- Instructing exposed persons to shower thoroughly with soap and water- appropriate facilities will be provided at the scene as necessary
- Instructing attending personnel to wear full PPE when handling contaminated clothing and other fomites

2.3.2 Isolation of patients

- Standard Universal Precautions should be used for the care of patients infected with *B.anthraxis* – gloves, gowns, masks and hand washing
- Single room placement for anthrax patients is **not** necessary
- Airborne transmission does **not** occur
- Skin lesions may be infectious, but this requires direct skin contact
- Standard Universal Precautions should be maintained when patients are moved

2.3.3 Cleaning, disinfection & waste disposal

Contaminated environmental surfaces should be cleaned with hypochlorite solution (10,000ppm available chlorine).

2.3.4 Post-mortem procedures

Autopsy - The risk of acquiring anthrax following contact with the body of a person who has died from the disease is negligible, because person-to-person transmission is not documented for inhalational disease and there is no evidence of autopsy transmission.

Autopsy examinations are strongly discouraged if anthrax infection is suspected, as the body fluids in a patient who has died of anthrax are likely to have large numbers of the causative bacteria present and opening the body increases the risk that sporulation of the anthrax bacilli will occur. If an autopsy is necessary expert advice must be sought from the HPA. The Pathologist must be informed of the known or suspected diagnosis. Standard precautions for post-mortem examinations on patients infected with Containment Level 3 organisms are appropriate. Instruments should be autoclaved.

Similarly, body preparation should be carried out with normal control of infection procedures. Standard precautions for the disposal of bodies infected with Containment Level 3 pathogens should be observed, and the undertaker should be informed. **Cremation** is the preferred method for disposal of the deceased. **Embalming** of bodies should not be undertaken because the body fluids are likely to contain large numbers of the causative bacteria and therefore the process of embalming exposes the embalmer to an unacceptable risk.

Pacemaker removal is permitted. Pacemaker should be treated with hypochlorite solution (10,000 ppm available chlorine), bagged and disposed of appropriately (not by incineration).

2.4 Prophylactic treatment for persons exposed to anthrax spores

In the event of a known exposure to anthrax spores, antibiotic prophylaxis should be initiated as soon as possible– as described in Table 2. Prophylaxis should continue until *B.anthraxis* exposure has been excluded. For adults, children and pregnant women, ciprofloxacin is the drug of choice. Pharmacokinetic studies have shown that ciprofloxacin achieves far higher concentrations in lung macrophages than penicillins, and is therefore a more effective prophylactic antibiotic. Ciprofloxacin has the added advantage that it is also an effective prophylactic treatment for other potential agents that may be used in deliberate release scenarios such as plague and tularemia.

The risk of adverse effects from prophylaxis must be weighed against the risk of developing a serious disease.

After initial treatment with ciprofloxacin, doxycycline may be substituted to complete the 60 day prophylaxis. The duration of initial course of antibiotic treatment is 5 days. Only the initial course of antibiotics for prophylaxis is held in pods as part of the antibiotic stockpile. Arrangements for the supply of the remainder of the prophylactic course are being developed and individuals should be advised to report to their own GP. See DH Patient Group Directions for the initial and further supply of ciprofloxacin and the further supply of doxycycline in the event of exposure to a suspect biological agent http://www.dh.gov.uk/en/Policyandguidance/Emergencyplanning/DH_4069610

In a major incident, for information on how to access stocks of antibiotics for initial treatment or prophylaxis see:
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_112635

Table 2: Recommended prophylaxis after exposure to *B. anthracis*

	Antimicrobial agent	Duration
Adults (including pregnant women)	Initial (5 day) therapy Ciprofloxacin 500mg orally every 12 hr Further (55 day) therapy Ciprofloxacin 500mg orally every 12 hr OR Doxycycline 100mg orally every 12 hr Alternative therapy if strain is susceptible Amoxicillin 500mg orally three times daily	60 days
Children	Initial (5 day) therapy Ciprofloxacin 15mg/kg orally (maximum 500mg) every 12 hr (not to exceed 1g per day) Further (55 day) therapy Ciprofloxacin 15mg/kg orally (maximum 500mg) every 12 hr (not to exceed 1g per day) Ciprofloxacin dose depends on age and weight, as a guide: newborn – 6 months 100mg/day 1 year – <3 years 200mg/day 3 years – <5 years 300mg/day 5 years – <7 years 400mg/day 7 years – <12 years 500mg/day 12 years+(adult dose)1000mg/day OR Doxycycline 100mg every 12hr (NB: only for children > 8yrs and >45kg: Alternative therapy if strain is susceptible Amoxicillin , 80mg/kg per day, in three doses (not to exceed 500mg/dose)	60 days

If *B. anthracis* exposure is confirmed, the organism must be tested for penicillin susceptibility. If susceptible, exposed persons may be treated with oral amoxicillin as an alternative to ciprofloxacin or doxycycline. The prophylaxis should continue for 60 days (recommended because of prolonged latency period that can elapse before germination of inhaled spores). During this period, no special precautions are required for exposed persons, but they should receive an anthrax information sheet and be instructed to seek medical attention immediately in the event of any suspicious symptoms.

2.4.1 Immunisation

In certain circumstances, in addition to antimicrobial prophylaxis, post-exposure immunisation may also be indicated. This consists of three doses of vaccine at 0, 3 and 6 weeks after exposure (with added doses at 6 months and 1 year if there is continued exposure). With vaccination, post-exposure antibiotic prophylaxis can be reduced to **4 weeks**. Prompt post-exposure prophylaxis with antibiotics and vaccine appears to be highly effective (Doolan *et al.* 2006).

Note that anthrax vaccination is currently only available for people with an occupational risk of exposure. This includes people who work with animal hides or products and laboratory staff who handle the organism routinely. Prophylactic anthrax vaccination is not required for other members of the public. In the event of a deliberate release, individuals will be considered for vaccination on a case-by-case basis, according to their risk of exposure.

2.4.2 Contacts of cases

There is no need to provide antibiotic prophylaxis or immunisation to contacts of patients unless there is concern that they were also exposed to the initial release.

2.5 Environmental decontamination

The greatest risk to human health following a release of anthrax spores occurs during the period in which anthrax spores remain airborne, called primary aerosolisation.

The duration and scale of the infectious risk depends on the duration for which spores remain airborne and the distance they travel before they fall to the ground. This depends on meteorological conditions and aerobiological properties of the dispersed aerosol. The aerosol is likely to be fully dispersed within hours to one day at most, well before the first symptomatic cases would be seen.

In the event of a known release, an **exposed zone** will be defined according to the time and place of release in order to identify all persons exposed to primary aerosolisation. This is explained in section 4. The area surrounding the site of release will remain designated as an exposed zone until sufficient time has elapsed and there is no further risk of infection.

Expert advice will be provided to determine the time after release for which spores are likely to remain airborne. Once they have settled, although they remain infectious for long periods, the risk to human health is much lower. Decontamination of small areas may be achieved with hypochlorite solution (10,000ppm available chlorine).

2.6 Protection of frontline workers

This includes all emergency staff involved in management at the scene of a release, as well as those involved in treating patients with anthrax.

2.6.1 Protective clothing

The overt release of anthrax spores will create an **exposed zone**, the area affected by primary aerosolisation will depend on the time and place of release. This exposed zone presents a high risk of infection. Any personnel entering this zone should wear a biologically-resistant suit with outer gloves and boots (for example a CR1, PRPS or gas-tight suit), and a correctly fitting high-efficacy particulate respirator of FFP3 standard **AT ALL TIMES**.

Healthcare workers will not normally be asked to enter this zone, but may be called into it to treat casualties, for example if an explosive device has accompanied the release of biological agent. In this case the appropriate protective clothing and equipment should be worn.

Exposed persons will normally be moved from the exposed zone, through decontamination, and into a place of safety (see section 4.3.1) for medical assessment and administration of prophylactic treatment. Frontline workers involved in decontamination, and others who have who have any contact with contaminated clothing and fomites should wear the appropriate protective clothing and equipment. Emergency staff who attend exposed persons after decontamination has been completed do not need to take any special precautions.

For healthcare workers involved in the management of hospitalised patients with all forms of anthrax, standard Universal Precautions (gloves, gowns, masks and hand washing) provide sufficient protection, and mortuary staff should use similar barrier protection. More sophisticated countermeasures for airborne protection such as high-efficacy air filter masks are **not** required.

2.6.2 Antibiotic prophylaxis and immunisation

Frontline workers entering the **exposed zone** should be offered antibiotic prophylaxis as in Table 2, and in addition, should be offered a course of vaccination at 0, 3 and 6 weeks following exposure (with added doses at 6 months and 1 year if there is continued exposure) subject to availability.

Prophylactic treatment may also be considered for frontline workers involved in other activities including:

- Decontamination of exposed persons.
- Handling exposed persons.
- Management of patients or disposal of bodies infected with anthrax.

Decisions about who should receive prophylaxis should be taken on an individual basis according to duration and degree of potential exposure, and taking into account the availability and side effects of prophylactic treatments.

2.7 Other Considerations – patient, visitor and public information

Information sheets have been prepared by Department of Health for distribution in the event of an incident. <http://www.dh.gov.uk/assetRoot/04/01/89/33/04018933.pdf>

3 LABORATORY PROCEDURES

3.1. Risk assessment

B. anthracis is a Hazard Group 3 pathogen, and should thus be covered by existing risk assessments for handling such organisms in diagnostic microbiological laboratories. Note that blood samples from anthrax patients for clinical chemistry and haematology pose no special risk and can be handled according to normal procedures.

3.1.1 Receipt of samples

Samples should have been labelled as 'High risk' by the submitting staff, and should be handled according to local protocols for such samples. All laboratory procedures should be performed, by experienced scientists, in a containment level 3 facility using a Class 1 protective safety cabinet. Chain-of-evidence documentation should accompany specimens. In larger incidents, this would only be required for several of the initial cases.

3.2 Isolation and identification

Two smears should be made on microscope slides and fixed by immersion in absolute ethanol for 1 minute. Slide 1 should be stained with Giemsa or Gram's stain, and the typical capsulated short chains of "box-car" bacilli looked for under oil immersion. Their presence is highly suggestive of anthrax. If numerous bacilli in short chains are visible, dispatch the second slide to a reference laboratory for confirmation. The specimens should also be cultured on to blood agar for incubation at 37°C in air/CO₂. Antimicrobial susceptibility tests must be set up as soon as possible.

3.2.1 Culture

B. anthracis is a non-motile, Gram-positive, aerobic bacillus 1.2 to 10µm in length, capable of forming central and terminal spores. Cultures should be inoculated onto an agar slope in a bijoux bottle and incubated overnight. After incubation, the typical white, non-haemolytic colonies, with bees-eye appearance (that is, oval, slightly granular but not dry, about 2-5mm diameter) and characteristically tacky on teasing with a loop, will be apparent in large numbers.

These can be subcultured to a slope, in a Class 1 protective cabinet within a containment level 3 facility, which can then be sent to the reference laboratory for confirmation.

Information on the laboratory investigation of possible anthrax in drug users is available at:

<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Anthrax/AnthraxOutbreakInformation/AnthraxInformationForHealthcareProfessionals/>

Laboratory pictures of anthrax are available via the HPA website at:

<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/AnthraxDR/Images/>

3.2.2 Antibiotic susceptibility

Organisms should be tested for sensitivity to antibiotics including ciprofloxacin, penicillin, doxycycline and gentamicin.

3.3 Confirmation

Clinical microbiology laboratories should take care not to regard all isolates of *Bacillus* species as contaminants, especially if isolated from sterile sites (blood, cerebrospinal fluid) and/or multiple cultures are positive from the same patient.

All sterile site *Bacillus* isolates should be further evaluated, and if non-motile or non-haemolytic (particularly if they form short chains), and/or if the clinical syndrome is suggestive of anthrax, the isolates should be immediately referred to the reference laboratory.

3.4 Waste disposal

In the laboratory, hypochlorite (10,000ppm) disinfection is necessary for decontaminating surfaces that may have been exposed to *B. anthracis* spores. All other waste containers should be autoclaved.

3.5 Reference laboratory

All positive isolates and cultures should be sent to the reference laboratory for confirmation. In addition, samples may be sent there directly if local laboratories lack the facilities for dealing with them. All samples and cultures must be packaged appropriately, taking care to observe the procedures outlined in section 3.6. The sender's name and address should be clearly marked. The reference laboratory should be telephoned prior to sending to expect the sample. **Samples should be forwarded urgently to:**

Dr Tim Brooks
Special Pathogens Reference Unit
HPA Centre for Emergency Preparedness and Response
Porton Down
Salisbury SP4 0JG
Tel: (+44) 01980 612100 (24hours)

Further information on SPRU and referral of specimens and samples:

<http://www.hpa.org.uk/ProductsServices/InfectiousDiseases/SpecialPathogensReferenceUnit/>

3.6 Transportation of samples with suspicion of *B. anthracis*

Strict procedures apply for transport of samples to the laboratory. Biological agents, or materials that contain or may contain them, are allocated to UN Division 6.2 – infectious substances.

Infectious substances are divided into Category A or Category B. Full details are given in Appendix 1.2 Transport of infectious substances in *Biological agents: Managing the risks in laboratories and healthcare premises*. ACDP HSE May 2005, available at

<http://www.advisorybodies.doh.gov.uk/acdp/managingtherisks.pdf> and in the Department of Health's guidance, available at <http://www.dh.gov.uk/assetRoot/04/11/48/13/04114813.pdf>

Cultures of *B. anthracis* are Category A infectious substances capable of causing disease in humans or animals and are therefore assigned to UN2814 and must be packaged in accordance with UN Packaging Instructions PI620 (road/rail) /PI602 (air). P620 and P602 are identical specifications but given different codes in ADR and ICAO regulations respectively (for a full description of PI see <http://www.unece.org/>). Category A transfers should be individually requested through an approved courier. The service will be a next day, tracked door-to-door delivery, which must be signed for at collection and receipt.

For current arrangements for transportation on samples see:

http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1202487028723

Clinical samples are generally classified as Category B and are assigned to UN3373 (Biological Substances, Category B) and should be packaged in accordance with UN PI650. Clinical samples may be posted.

Packaging must meet with UN performance requirements i.e. UN-type approved packaging for Division 6.2 substances. The packaging should consist of an inner package (watertight receptacle, watertight secondary packaging, an absorbent material in sufficient quantity to absorb the entire contents placed between the receptacle and the secondary packaging) and a rigid outer package of adequate strength for capacity, mass and intended use. Packages should be marked with the proper shipping name i.e. "Infectious substance affecting humans", the appropriate UN number (i.e. UN 2814), and the appropriate warning label (i.e. the danger sign for infectious substances). The following procedures should be adopted for the transport of all specimens, and also all cultures for confirmation. These apply within hospitals and laboratories as well as for specimens sent to the reference laboratory:

- The primary container (bijoux or similar) should be screwed tight, labelled and placed in an intact plastic bag.
- A "High Risk" label should be affixed to both specimen and request form. The latter should include any other relevant information and include adequate clinical details to indicate level of suspicion.
- Under no circumstances should the request form be placed in the same bag as the specimen.
- The bag should be sealed, using tape or heat sealer. Pins, staples and metal clips should not be used. A separate bag should be used for each specimen.
- Each specimen must then be placed in a leak-proof secondary container with sufficient absorbent material to absorb all the contents should leakage occur.
- Each specimen must be packaged individually - i.e. three specimens, three separate packages.
- The secondary container should be externally disinfected – e.g. by wiping with hypochlorite (1,000ppm).

3.6.1 Samples sent to the reference laboratory

- Secondary containers should be placed within a final outer tertiary packaging.
- This packaging **must** comply with the UN-type approved packaging for the transport of infectious substances by air, road or rail.
- The package should be certified to this standard and carry the appropriate UN certification numbers on the tertiary packaging along with the following information:
- BIOHAZARD – danger of infection symbol Class UN 6.2.
- Instructions not to open if found.
- Telephone number of a responsible person - e.g. Consultant Microbiologist or Laboratory Manager.
- The container should be transported either by an approved courier for cultures (UN 2814) or by post for clinical samples (UN 3373), without delay, directly to the reference laboratory.

3.6.2 Samples sent within hospitals and laboratories

- Samples should be transported according to local arrangements for High Risk specimens. Precautions should include:
- Secondary containers should be placed in a good quality box, which is well taped up and clearly labelled "Pathological Specimen – Open only in Laboratory".
- Specimens should be transported by hand by a responsible person using the above packaging. Vacuum-tube systems should **not** be used for transportation of specimens within hospitals or laboratories.
- Extra care should be taken to ensure that laboratory records are kept to a high standard.

3.7 Protection of laboratory staff

All laboratory procedures must be performed in a Containment Level 3 facility using a Class 1 biological safety cabinet. Under these circumstances there is no indication for antibiotic prophylaxis for laboratory staff unless there is an inoculation injury or a spillage releasing aerosols containing spores. Anthrax vaccine is only indicated for laboratory staff routinely working with the organism.

Any member of laboratory staff, working with specimens or cultures of anthrax, who develops a febrile/ respiratory illness, should seek urgent medical attention.

4 PUBLIC HEALTH PROCEDURES

4.1 Surveillance and detection of deliberate releases of anthrax

A deliberate release may be overt with an announcement and/or confirmation by environmental sampling. However, it is also possible that a deliberate release may be covert and will not be identified until the first cases of disease arise.

Anthrax is a rare disease. In the last 20 years there has been less than one case per year in the UK. These are mainly cutaneous and are due to handling hides imported from countries with endemic disease (and thus often associated with the leather industry).

Deliberate release should be considered in the event of:

- Single **confirmed** case of inhalation anthrax.
- Single **confirmed** case of cutaneous anthrax arising in individuals who do not routinely have contact with animals or animal hides.
- Two or more **suspected** cases of anthrax that are linked in time and place, especially geographical related groups of illness following a wind direction pattern (analogous to legionnaire's disease).

Close co-ordination with veterinary colleagues is essential: grazing animals (cows, sheep, and goats) are far more susceptible to disease and have a shorter incubation period than humans. Confirmed and suspected cases of anthrax in animals may provide an early warning system. Infected animals could also act as an ongoing source of potential human infection. Incident managers should ensure that appropriate veterinary advice is taken. An incident specific risk assessment will be required.

4.2 Case Definition

4.2.1 Suspected cases

Any previously healthy patient with the following clinical presentations should be immediately reported to the Consultant in Communicable Disease Control at the local Health Protection Unit and to the duty doctor at HPA Colindale (020 8200 6868 - 24 hour service).

- **Rapid onset of severe, unexplained febrile illness or febrile death.**
- **Rapid onset of severe sepsis not due to a predisposing illness, or respiratory failure with a widened mediastinum.**
- **Severe sepsis with Gram-positive rods or *Bacillus species* identified in the blood or cerebrospinal fluid and assessed not to be a contaminant.**

If anthrax is suspected, microbiological specimens should be sent to the reference laboratory, and consideration should be given to initiating empirical treatment pending results. Obviously the level of suspicion of anthrax depends on local circumstances at the time – in the event of a known or suspected deliberate release the threshold for making a diagnosis of anthrax should be lower.

As discussed in section 3.3, clinical microbiology laboratories should also be alert to the possibility of anthrax. All sterile site *Bacillus* isolates should be carefully evaluated, and if suspicious, and/or if the clinical syndrome is suggestive of anthrax, they should be immediately referred to the reference laboratory.

4.2.2 Confirmed case

A case that clinically fits the criteria for suspected anthrax, and in addition, definitive positive results are obtained on one or more pathological specimens by the reference laboratory.

4.2.3 Definitive diagnosis in the reference laboratory

The definitive test for *B. anthracis* is polymerase chain reaction (PCR). This test can be applied to cultures sent from local laboratories, in which case results will be available in three hours from receipt of specimen. It can also be applied to isolates and other clinical samples, but this will normally require overnight culture at the reference laboratory, so the result will take 24 hours.

4.3 Public Health Action

4.3.1 Procedure for handling exposed persons

Depending on the site and method of release, anthrax spores may be dispersed over a wide area. Expert advice will be provided to define an exposed zone in time and space. All individuals who have been present in the exposed zone need to be identified. In the event of an overt release, some of them will still be at the scene when emergency services respond to the incident. This group will be decontaminated and then referred to health workers at a nearby place of safety for assessment and prophylaxis (this will be a clinical area just outside the exposed zone and within the cordon that will be established at the scene of the incident). Others will have left the scene before emergency services arrive and will be identified later when they approach GPs and A&E departments after details of the incident have been made public. Procedures need to ensure that these individuals are appropriately decontaminated, receive prophylaxis, and have their details collected for follow-up.

4.3.2 Post-exposure prophylaxis

There are two groups of individuals for which prophylaxis is indicated:

- I **Individuals who have been present in the exposed zone** should be offered post-exposure prophylaxis as outlined in Table 2.
- II **Front-line workers** may require prophylaxis as described in section 2.6.2.

If suspected or confirmed cases of anthrax arise among persons who have been outside but in close proximity to the exposed zone in time or space, the defined parameters of the exposed zone should be reviewed with a view to extending post-exposure prophylaxis.

Prophylaxis for other groups may be considered in the event of an incident. However, it is not advisable to give antibiotics to people who do not have a clear history of having been present at the time and site of release. It is inappropriate to provide antibiotics to large numbers of people who may be concerned, but have not been exposed.

4.3.3 Follow-up of exposed persons

After an overt release, a basic set of personal details needs to be collected from all persons present in the exposed zone.

4.3.4 Case finding

If cases of anthrax arise and a covert release is suspected, health services should be contacted to determine whether other possible cases have presented.

4.3.5 Preventing secondary spread

As previously mentioned, person-to-person spread of anthrax is negligible, and therefore there is no specific treatment or advice required for secondary contacts. There is no requirement for

quarantine of infected patients. However those contaminated with anthrax spores will need to be decontaminated as described in section 2.3.1.

There is no need to provide antibiotic prophylaxis or immunisation to contacts of patients unless there is concern that they were also exposed to the initial release.

4.4 Epidemiological investigation

If a case is strongly suspected or confirmed, the HPA Colindale should be notified immediately (020 8200 6868, 24 hours). If cases arise due to a covert release, or following an overt release but in people who have not been present in the exposed zone, it is important to collect some epidemiological details in addition to a basic set of personal details. This is in order to define or redefine the exposed zone and aid identification of others at risk of infection. Details should be as thorough as possible, whilst recognising that in the event of a large release with multiple exposed persons or cases, it may not be possible to collect comprehensive information from everyone.

The aim of epidemiological investigations may be:

- Following a covert release, to assist definition and ongoing review of the temporal and spatial parameters of the exposed zone so that post exposure prophylaxis can be distributed appropriately.
- Following an overt release, to guide review of the exposed zone if cases arise in persons who were not present within it.

4.4.1 Epidemiological sampling

Microbiological samples will be taken from the environment by the police. These will be tested in designated laboratories. Depending on the scale of the release, it may be possible to take nasal swabs from people present in the exposed zone. These may provide further information to help guide ongoing administration of post exposure prophylaxis. However, if people are known to have been in the exposed zone, antibiotic prophylaxis should be given immediately (see section 2.4) and not withheld until the results from nose swabs are known.

5. LIST OF NATIONAL EXPERTS

Advice on any aspect of anthrax including diagnosis, management and public health aspects can be obtained from:

Clinical advice

Dr Robert C Spencer
Health Protection Agency South West
Level 8
Bristol Royal Infirmary
Marlborough Street
Bristol BS2 8HW
Tel: (+44) 0117 342 3242
e-mail: bob.spencer@hpa.org.uk

Diagnostic Laboratory and Environmental

Dr Tim Brooks
HPA Centre for Emergency Preparedness and Response
Special Pathogens Reference Unit
Porton Down
Salisbury SP4 0JG
Tel: (+44) 01980 612774 (direct)
(+44) 01980 612100 (24hours)
e-mail: tim.brooks@hpa.org.uk

Public Health

Dr Dilys Morgan
HPA Colindale
Gastrointestinal, Emerging and Zoonotic Infections
61 Colindale Avenue
London, NW9 5HT
Tel: (+44) 0208327 7474
e-mail: dilys.morgan@hpa.org.uk

Out of Hours Contact details are held at HPA Colindale by the 24 hour on call duty doctor; **Tel: (+44) 020 8200 6868**

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