



BOTULISM

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 changes as comments are received, so please ensure that you have the latest version, which is available through the HPA website.

[http://www.hpa.org.uk/deliberate accidental releases/biological](http://www.hpa.org.uk/deliberate_accidental_releases/biological)

*For this version of the guidelines changes were made to the following sections of the previous version:
Frontpage, 1.1, 1.2, 2.1, 2.2, 3, 5, 6*

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 *Clostridium botulinum* or botulinum toxin.

1.1 Introduction

Botulinum neurotoxins are produced by the anaerobic spore forming bacterium *Clostridium botulinum* and, rarely, by *Clostridium baratii* and *Clostridium butyricum*. There are seven neurotoxins (A-G). Illness in humans is usually caused by types A or B or E, or rarely F. Types C, D and E cause illness in mammals, birds and fish. Type G has not been shown to be associated with disease.

All toxins block the release of acetylcholine at the neuromuscular junction, which results in flaccid paralysis.

There are three naturally occurring forms of illness:

- Food-borne botulism, caused by ingestion of pre-formed toxin
- Wound botulism, caused by growth of the bacterium and production of toxin in traumatic wounds
- Intestinal colonisation botulism, usually seen in infants, but also very rarely in adults, caused by growth of cells and production of toxin *in vivo*.

1.1.1 Deliberate release of botulinum toxin

A deliberate release may involve airborne dissemination of toxin, producing botulism through inhalation. Alternatively, it may involve contamination of food and water supplies either with toxin or with *C. botulinum* bacteria.

1.2 Epidemiology

1.2.1 Transmission

Food-borne botulism is caused by ingestion of preformed toxin. *C. botulinum* spores are found throughout the world in soil samples and marine sediments. A normal healthy adult can consume spores, for example, in raw vegetables and salad products with no ill effects. However, where food is contaminated before preservation and the spores germinate and grow in anaerobic conditions, toxin is produced which is highly poisonous when ingested. Most cases of food-borne botulism are associated with home preserved meats, fish and vegetables. The disease is rare in the UK, but more common in Southern and Eastern Europe where the practice of home preservation is more widespread. In 1989 the largest outbreak of food-borne botulism in the UK affected 27 people who had consumed hazelnut yoghurt. The illness was caused by type B toxin produced by bacteria growing in canned hazelnut conserve that had been inadequately heat-treated and was used to flavour the yoghurt. Between 1989 and 2005 there have been a further five unrelated incidents (6 cases) in the UK.

Wound botulism follows infection of wounds caused by penetrating injuries. *C. botulinum* spores, which are present in soil, then germinate and produce toxin *in vivo*. It has also been caused by injecting or sniffing drugs that are contaminated by spores. Wound botulism is now the most common form of botulism in the UK and Eire. There have been >100 clinically diagnosed cases of wound botulism between 2002 and 2007. All cases have been amongst illegal injecting drug users. Further information can be found at:

<http://www.hpa.org.uk/webw/HPAweb&Page&HPAwebAutoListName/Page/1191942152226>

Intestinal colonisation botulism occurs in infants of less than two years of age, and most are under 6 months of age. A small number of cases in older children and adults have been reported worldwide. Illness in infants and adults results from ingestion of *C. botulinum* spores followed by germination and colonisation of the gut and production of toxin. In the USA, infant botulism has been associated with the ingestion of honey, corn syrup and environmental sources of spores including dust or soil. There were eight cases of infant botulism detected in the UK between 1978 and 2007 – and whilst a route of infection was not detected for the majority of cases, in one case there was a possible exposure to spores in infant formula dried milk and in two others there was an association with spores in the environment.

Other routes of infection

Accidental botulism may follow mis-injection of pharmaceutical preparations of botulinum neurotoxin. Four cases occurred in December 2004 in Florida following cosmetic injection with botulinum toxin that was not approved for human use. There have been no reported cases in the UK.

Inhalation botulism does not occur naturally, but has been demonstrated in model systems and in real cases (three cases were reported in 1962 in veterinary technicians in Germany). Aerosolised toxin is a potential route for deliberate release.

Water-borne botulism may also be caused by ingestion of pre-formed toxin. This route will only pose a risk to humans in some deliberate release scenarios because the toxin is inactivated by normal treatment of mains water supplies. There have been no reported cases of illness in humans worldwide due to contaminated water supplies.

1.2.2 Incubation period

The duration before onset of symptoms depends on the time taken for ingested toxin to reach the target site. In food-borne botulism symptoms usually occur between 12 and 36 hours (median time is 24 hours) after consumption of contaminated food, but can occur as early as 6 – 8 hours or as late as 8 days, depending on the levels and serotype of toxin.

Following aerosol exposure onset of symptoms may be more rapid, although it will probably still take some hours. The onset was 3-4 days after exposure in three cases of accidental inhalation botulism.

1.2.3 Period of communicability

Person-to-person transmission does **not** occur. Toxin can be detected in the serum and faeces of cases, but normal infection control precautions will prevent ingestion.

1.3 Clinical features

Clinicians should be aware of the possibility of cases of botulism.

Any previously healthy patient with:

- **symmetrical descending flaccid paralysis with prominent bulbar palsies including diplopia, dysarthria, dysphonia and dysphagia**
- **afebrile**
- **no change in sensory awareness**

should immediately be reported to the Consultant in Communicable Disease Control at the local Health Protection Unit.

Gastrointestinal symptoms occur in food-borne and intestinal colonisation botulism. Nausea, vomiting and diarrhoea followed by constipation are typical features of food-borne botulism,

however ingestion of large amounts of toxin may lead directly to neurological symptoms, and the diagnosis should be considered in the absence of gastrointestinal symptoms. In intestinal botulism in infants, several days of profound constipation may precede neurological symptoms.

Neurological symptoms are the same irrespective of the route of entry of toxin, but may develop more quickly in the event of inhalation, depending on the dose. Symptoms are of a descending, symmetrical flaccid paralysis:

- Cranial nerve palsies produce diplopia, ptosis, facial weakness, dysphagia and dysarthria.
- This is followed by weakness in the neck and arms, after which respiratory muscles and muscles of the lower body are affected.
- In some cases, weakness in the neck and arms may be followed by respiratory paralysis or respiratory arrest and then by ptosis.
- In some cases, marked respiratory compromise or respiratory arrest may occur before typical oculobulbar weakness and weakness in limbs.
- There is no fever and no loss of sensory awareness.

Autonomic signs may be present, with dry mouth, fixed or dilated pupils, and cardiovascular, gastrointestinal and urinary autonomic dysfunction. Respiratory paralysis may be fatal.

Onset of gastrointestinal and neurological symptoms may be between 6 hours and 8 days. If onset is very rapid, there may be no symptoms before sudden respiratory paralysis occurs.

1.4 Mortality

Without treatment mortality can reach 100%, but this can be considerably reduced with supportive treatment and the use of antitoxin.

The lethal dose of *C. botulinum* toxin for an adult can be less than 1 microgram, depending on toxin type and route of administration. Exposure of rhesus monkeys to aerosols of botulinum toxin has shown that type F is about 60 times more toxic than type B and the order of toxicity is F>C>A>D>B.

1.5 Organism survival

C. botulinum is a spore-forming organism. Spores survive well in the environment, and may also survive heat and cooking. Spores do not produce toxin, but under anaerobic conditions may germinate, and toxin is then produced during growth of vegetative organisms. The toxin undergoes natural inactivation in surface and drinking water over several days and is destroyed by chlorine. The toxin is inactivated by boiling but may be present in ready-to-eat foods and survive mild heating.

1.6 Antimicrobial susceptibilities

- In cases of botulism which result from ingestion (in food or water) or inhalation of toxin, antibiotic therapy is **not** appropriate.
- In cases of wound infection, *C. botulinum* is susceptible to benzyl penicillin and metronidazole, which should be used together with surgical debridement.
- Intestinal colonisation botulism results from colonisation of the gut by vegetative cells. Risk factors are not completely understood, but changes in gut flora around the time of weaning may permit colonisation. Another factor may be decreased gut motility which results in increased anaerobicity in the gut. Antibiotic therapy is **not** appropriate, because there is a risk of further reducing the normal gut flora and therefore increasing susceptibility to colonisation, and because lysis of vegetative cells killed by antibiotics may result in release of toxin.

2 CLINICAL PROCEDURES

2.1 Diagnosis and collection of samples

2.1.1 Misdiagnosis and differential diagnoses

Misdiagnosis of botulism is not uncommon as botulism is often low on the list of differential diagnoses at presentation. The most frequent misdiagnoses and their distinguishing features are:

- Polyradiculoneuropathy (Guillain-Barre or Miller-Fisher syndrome): antecedent febrile illness, paresthesias, paralysis is often ascending, early loss of reflexes, increased protein in CSF (may not be seen early in illness), typical EMG (electromyography) findings.
- Myasthenia gravis: recurrent paralysis, sustained response to anti-cholinesterase therapy, supportive EMG findings.
- Stroke: often asymmetric paralysis, abnormal CNS imaging (MRI or CT).
- Intoxication (e.g. carbon monoxide, organophosphates, mushrooms): drug detected in body fluids.

Other misdiagnoses and their distinguishing features include:

- Tick paralysis: paresthesias, ascending paralysis, tick attached to skin.
- Poliomyelitis: antecedent febrile illness, asymmetric paralysis, CSF changes.
- CNS infections: changed mental status, changed CSF and EEG.
- Viral syndrome: no bulbar palsies and no flaccid paralysis.
- Psychiatric illness: EMG findings.
- Paralytic shellfish poisoning: onset of <1hr, paresthesia, food history

Several clinical tests are useful for distinguishing botulism from other diseases, but they may give misleading results:

- Deep tendon reflexes: may be present initially in botulism but decrease or disappear over the following days
- Tensilon tests: negative in botulism but can be transiently positive
- EMG: can be normal early in botulism

2.1.2 Confirmation of the clinical diagnosis

Confirmation is by the detection of botulinum toxin or the bacterium in the patients' faeces, stomach contents, or specimens from wounds, and the detection of toxin in serum samples. Routine laboratory tests are usually **not** helpful and **specimens should therefore be sent immediately to the reference laboratory** (see section 3.4). For food-borne botulism, toxin can be detected in the serum of >50% of cases if collected within 1 day of onset, but in <25% after 3 days. However the bacterium will be present in the faeces in >70% of cases within 2 days of onset and >40% after 10 days. For food-borne botulism, detection of toxin in left-over food may support the diagnosis.

2.1.3 Precautions for sampling

The samples outlined below should be taken to confirm the diagnosis. Standard Universal Precautions (gloves, gowns and hand washing) provide sufficient protection for healthcare workers attending patients and laboratory staff handling specimens. Procedures for transporting samples to the laboratory are outlined in section 3.5. The receiving laboratory should be telephoned to expect arrival. Chain of evidence documentation should also accompany all specimens; however in larger incidents this may only be required for the initial cases.

2.1.4 Samples

Samples taken from acutely ill patients to be sent to the National Reference Laboratory:

- **Serum.** At least 10ml of serum must be collected *before* antitoxin is administered. Do not send clotted blood.
- **Faeces.** At least 10g in a sterile container. A portion of the faecal sample (pea size) should be placed in cooked meat medium and sent together with the remaining sample to the Reference Laboratory. This assists detection and isolation of *C. botulinum*. Rectal washout may be required, since patients with food-borne botulism may have diarrhoea in the early stages, but this is followed by constipation.
- **Vomit, gastric washings or gut contents.** At least 10g in a sterile container.
- **Bronchiolar lavage** or similar in a sterile container.
- **Wound.** All available pus should be collected in a sterile container and transferred as soon as possible to an anaerobic transport medium. If pus is not available, a swab of the lesion should be taken and put immediately into a transport medium for anaerobic culture. If surgical debridement is performed, **biopsy tissues** should be placed immediately into a sterile container then transferred as soon as possible to an anaerobic transport medium.

Post-mortem specimens: Heart blood (10ml), if not haemolysed, should be separated into serum before dispatch to the reference laboratory. Specimens of faeces, stomach contents and from infected wounds may also be useful.

Food samples associated with suspect cases must be obtained as a matter of extreme urgency in order to prevent further cases. The local Consultant in Communicable Disease Control or the HPA CfI on call duty doctor (0208 200 6868/4400) should be contacted to arrange collection and transport to the reference laboratory by Environmental Health Departments or other agencies.

Water: If water is suspected as the source of illness, the HPA CfI on call duty doctor (0208 200 6868/4400) should be contacted to activate the Drinking Water Inspectorate emergency plans and arrange for testing of water samples.

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

In the event of deliberate release, those who have been exposed but have not developed any symptoms within the first few hours should be identified. Instructions should be given to the exposed cohort to seek immediate medical attention should symptoms develop later (see 2.1.2 for details of specimens to take to confirm diagnosis).

2.1.6 Transport of samples

Strict procedures should be followed for the transport of samples. All samples must be kept refrigerated after collection. Procedures for the transport of specimens, both from the clinical environment to the laboratory, and from local laboratories onto the reference laboratory are outlined in section 3.5. 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, Health and Safety Executive May 2005 at: <http://www.advisorybodies.doh.gov.uk/acdp/managingtherisks.pdf> Chain of evidence documentation should also accompany all specimens; however in larger incidents this would only be required for several of the initial cases.

2.2 Treatment

Specialist advice should be obtained from an Infectious Disease physician.

2.2.1 Adults (food-borne or aerosol)

Specific treatment is with antitoxin (see 2.2.4 for source). Antitoxin is held at different sites across the UK and must be accessed by contacting the duty doctor at HPA CfI (020 8200 6868 or 020 8200 4400; 24 hour service). Detailed instructions on administration are provided with each dose. Antimicrobial therapy is **not** appropriate.

The antitoxin must be given as early as possible after a clinical diagnosis has been made, and not delayed for the results of confirmatory laboratory tests. The risk of serum sickness or anaphylaxis is very low and a test dose or sensitivity testing is only necessary if there is a known history of allergy to sheep protein.

An effective treatment will prevent further progression of symptoms, but will not reverse established paralysis. Repeat doses are only necessary if the patient continues to deteriorate. The antitoxin dose may be repeated within 24 hours. A repeat dose given within 24-36 hours is most unlikely to cause a severe adverse reaction. Exceptionally a third dose (second repeat dose) may be given within 48 hours if the clinician felt that repeated doses were giving clinical benefit.

It is possible that there may be a late deterioration 2 or more days after an apparently successful treatment. If this occurs within 3 days of onset, further doses may be given, but the chances of an allergic reaction are higher and the patients should be closely observed for signs of anaphylaxis and serum sickness.

2.2.2 Wound botulism

The treatment for wound botulism differs in a number of ways from food-borne and intestinal colonisation:

- **surgical treatment is essential**
 - to eradicate the infected lesions
 - to stop toxin generation
- **antibiotics are indicated** - use penicillin and metronidazole according to standard dosing regimens
- **repeat doses of antitoxin** may be required with up to two repeat doses given within 48 hours

2.2.3 Intestinal colonisation (infant botulism)

Intestinal colonisation occurs very rarely in adults and treatment with antitoxin must be considered on a case by case basis.

In cases of infant botulism *C. botulinum* colonises the gut for some time. Human derived botulinum immunoglobulin (BabyBIG®) is now available for the specific treatment of infant botulism and was used for the first time in the UK at Great Ormond Street hospital in 2007. The treatment is only available from the Infant Botulism Treatment and Prevention Programme (IBTPP) <http://www.infantbotulism.org/>. Supportive treatment is important and although paralysis may persist for several weeks, full recovery may be expected as infants recover because they grow new nerve endings. Excellent advice is available on the infant botulism website given above or advice may be obtained from a paediatrician from a centre that has managed a case.

2.2.4 Antitoxin supplies

Antitoxin is held at sites around the UK - details are available from the duty doctor at HPA CfI (020 8200 6868 or 020 8200 4400; 24 hour service).

Antitoxin for infant botulism (BabyBIG®) is available from the IBTPP California USA (510)231-7600 for further details: <http://www.infantbotulism.org/>

In a major incident information on how to access stocks of botulinum antitoxin can be found on the DH website at:

<http://www.dh.gov.uk/en/Managingyourorganisation/Emergencyplanning/Deliberaterelease/DeliberatereleaseBotulism/index.htm>

2.3 Infection Control Procedures

2.3.1 Decontamination of exposed persons

Botulinum toxin naturally loses activity over a few days, and the toxin does not enter the body through intact skin. An incident specific risk assessment will be required.

The risk of infection from contaminated clothing is low. However, in the event of release of large amounts of toxin, clothing and other fomites may be sufficiently contaminated to pose a risk from hand-to-mouth ingestion. In such situations, decontamination may require:

- Removal of contaminated clothing and possessions – these should be stored in labelled double plastic bags until they can be washed with soap and water.
- 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 appropriate barrier protection – Universal Precautions - when handling contaminated clothing and other fomites.

2.3.2 Isolation of patients

Patient-to-patient transmission of botulism does not occur. Patient room selection should be consistent with availability, but single room placement is not necessary. Universal Precautions are sufficient for the nursing of patients.

2.3.3 Cleaning, disinfection & waste disposal

Standard hospital procedures apply. Contaminated environmental surfaces should be cleaned with hypochlorite solution (5,000ppm available chlorine).

2.3.4 Post-Mortem procedures

Autopsy examinations may be carried out with appropriate precautions and the use of standard post-mortem examination personal protective equipment (PPE).

Cremation is the preferred method for disposal of the deceased and **embalming** is discouraged.

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 people exposed to botulinum toxin

The use of antibiotics post-exposure is **not** indicated. Those who have been exposed should be monitored for symptoms and expert advice (see section 5) sought on treatment.

2.5 Environmental decontamination

Following a known release, re-aerosolisation of toxin is not thought to pose a serious risk, and the toxin naturally loses activity over a few days. The contaminated area will remain out of bounds for at least this period, and subsequently environmental decontamination is not necessary. In situations where surfaces have been grossly contaminated and cannot be avoided for these few days, they should be cleaned with a 5,000ppm solution of hypochlorite.

2.6 Protection of frontline workers

This includes all emergency staff involved in management at the scene of a release, and staff involved in the care of patients.

2.6.1 Protective clothing

The release of a botulinum toxin aerosol will create an **exposed zone** that presents a high risk of inhaling toxin. 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 should be worn.

Exposed persons will normally be moved from the exposed zone, through decontamination if necessary, and into a place of safety (see section 4.3.1) for medical assessment. Frontline workers involved in decontamination, and others who have had any contact with contaminated clothing and fomites need only observe standard Universal Precautions (gloves, gowns and hand washing) for adequate protection.

For healthcare workers involved in the management of hospitalised patients with all forms of botulism Universal Precautions provide sufficient protection. Mortuary staff should use similar barrier protection.

2.6.2 Antibiotic prophylaxis

No antibiotic prophylaxis or immunisations are necessary.

2.7 Other Considerations – patient, visitor and public information

Fact sheets have been prepared for distribution in the event of an incident.

<http://www.dh.gov.uk/assetRoot/04/01/88/32/04018832.pdf>

3 LABORATORY PROCEDURES

A key objective is to maximise the potential for laboratory confirmation of the clinical diagnosis. Blood should be separated and sent as serum. Samples should not be tested at the receiving laboratory but **must be sent immediately to the reference laboratory**.

3.1 Risk Assessment

C. botulinum is a Laboratory Containment Level 2 organism and normal laboratory precautions are sufficient to provide protection. Specimens can be handled on the open bench to prepare and package them for onward transportation to the reference laboratory.

3.2 Isolation and identification

Laboratory diagnosis is by detection and identification of neurotoxins from sera or other samples. Samples required for testing depend on the form of botulism suspected.

3.2.1 Confirmation

Confirmation is by detection of neurotoxin in patient body fluids, and/or the isolation of *C. botulinum* from a patient with a compatible illness.

3.3 Waste disposal

Waste should be disposed of according to local procedures for Laboratory Containment Level 2.

3.4 Reference Laboratory

All specimens should be sent directly to the reference laboratory. 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 Kathie Grant

HPA Centre for Infections
Foodborne Pathogens Reference Unit,
61 Colindale Avenue,
London NW9 5EQ

Tel: (+44) 020 8327 6505

E-mail: Kathie.grant@hpa.org.uk

For out of hours contact with the Reference Laboratory, telephone the CfI Duty Doctor (020 8200 6868, or 020 8200 4400).

3.5 Transportation of samples with suspicion of *C. botulinum*

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*. Advisory Committee on Dangerous Pathogens (ACDP), Health and Safety Executive (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>

A culture of *C. botulinum* is a Category A infectious substance capable of causing disease in humans or animals and is 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.

Clinical samples, such as serum, are generally classified as Category B and are assigned to UN3373 ("Biological Substance, 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 (e.g. 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 cultures that are suspected or known to contain *C. botulinum*. These apply within hospitals and laboratories as well as for specimens sent to the reference laboratory:

Every effort should be made to avoid external contamination of specimen containers during specimen collection.

- 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 or compartment 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).

3.5.1 Samples sent to the reference laboratory

- Secondary containers should be placed within a final outer tertiary packaging.
- This packaging **must** comply with UN-type approved packaging for the transport of infectious substances.
- The package should be certified to this standard and carry the appropriate UN certification numbers on the tertiary packaging along with the following information:
 - 1 BIOHAZARD – danger of infection symbol UN 6.2.
 - 2 Instructions not to open if found.

- 3 Telephone number of a responsible person e.g. Consultant Microbiologist, Laboratory Manager.
- The container should be transported without delay, directly to the reference laboratory, either by an approved courier for UN 2814 (infectious substances) or by post for UN 3373 (clinical samples).

3.5.2 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 a Containment Level 2 Laboratory".
- Specimens should be transported by hand by a responsible person using the above packaging.
- Vacuum-tube systems must **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.

4 PUBLIC HEALTH PROCEDURES

4.1 Surveillance and detection of deliberate releases of *C. botulinum*

Regardless of the circumstances, it must be remembered that a single case of botulism constitutes a public health emergency and requires immediate public health action.

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.

Naturally occurring botulism is very rare in the UK (see section 1.2.1); it is more common in the USA but even there the disease is not widespread.

Deliberate release should be considered in the event of:

- Outbreaks of two or more cases of acute flaccid paralysis, especially where there are common geographic factors between cases but no common dietary exposures may be suggestive of an aerosol attack.
- Multiple simultaneous outbreaks with no obvious common source.
- Cases of botulism with an unusual toxin type (ie, type C, D, F, or G, or type E toxin not acquired from an aquatic food).

Many animal species, including farm and domestic animals, are highly susceptible to botulinum toxin. Close coordination with veterinary colleagues is thus essential, as confirmed and suspected cases of botulism in animals may provide an early warning system. However, humans are not at risk of acquiring botulism from affected animals.

4.2 Case Definition

4.2.1 Suspected case

Clinicians should be alert to the possibility of cases of botulism. Any previously healthy patient with afebrile, descending, flaccid paralysis with an onset of hours to 8 days should be immediately reported to the CCDC at the local HPU.

In the event of a suspected deliberate release of botulism, a higher index of clinical suspicion should be maintained and the diagnosis considered if the symptoms outlined below present at medical services, especially if they arise in persons who have been within or in close proximity to the exposed zone. The level of suspicion of botulism depends on clinical symptoms and the circumstances, but if a case is suspected, microbiological specimens should be sent to the reference laboratory to eliminate or confirm the diagnosis, and empirical treatment should be considered in the interim.

The symptoms of botulism are due to muscle paralysis caused by the toxin:

- Symptoms in adults include:
 - Blurred or double vision, drooping eyelids, enlarged or sluggishly reactive pupils, slurred speech, difficulty swallowing and dry mouth, loss of head control, generalised hypotonia and weakness. Loss of the protective gag reflex may necessitate intubation and mechanical ventilation.
 - Deep tendon reflexes may be present initially but diminish or disappear in the ensuing days.
 - Diarrhoea, nausea and vomiting, followed by constipation, may occur in food-borne botulism.

- Infants with intestinal colonisation botulism appear lethargic, feed poorly, are constipated, and have a weak cry and poor muscle tone as well as symptoms in adults described above.
- In untreated persons, death results from airway obstruction (pharyngeal and upper airway muscle paralysis) and inadequate tidal volume (diaphragmatic and accessory respiratory muscle paralysis).
- Clinical tests that may help distinguish between other differential diagnoses include brain scan, CSF examination, nerve conduction tests (EMG), and a Tensilon test for myasthenia gravis (see section 2.1).

4.2.3 Confirmed case

A case that clinically fits the criteria for suspected botulism, and in addition the results of one or more pathological specimens fit one or more of the laboratory criteria for diagnosis (see below).

4.2.4 Laboratory criteria for diagnosis

Detection of botulinum toxin from serum or other body fluids and/or isolation of *C.botulinum* from a patient with a compatible illness is diagnostic.

4.3 Public Health Action

4.3.1 Procedure for handling exposed persons at the scene of an overt release

All individuals who were 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 (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 GP's and A&E departments after details of the incident have been made public. Procedures need to ensure that these individuals are identified for monitoring.

4.3.2 Follow-up of exposed persons

After an overt release, all exposed persons will be moved to a place of safety. It is possible that by the time this has occurred, the first casualties may be developing symptoms and will be transferred directly to hospital.

Follow-up monitoring arrangements will be made for those who remain free of symptoms for the first few hours after release. Instructions will be given to seek immediate medical attention should symptoms develop later. Antibiotic prophylaxis is not recommended.

4.3.3 Case finding

If cases of botulism arise and a covert release is suspected, health services should be contacted to raise awareness of the possibility of further cases, and determine whether any others might already have presented.

4.3.4 Preventing secondary spread

Person-to-person spread of botulism does not occur, and therefore there is no specific treatment or advice required for secondary contacts. There is no requirement for quarantine of infected patients.

4.4 Epidemiological investigation

In the event of **strongly suspected or confirmed** naturally occurring cases, the HPA CfI should be notified immediately.

A single case of botulism constitutes a public health emergency, and it is important to obtain a clear food history to enable identification and testing of high-risk foods. The usual response to a case normally also involves tracing others exposed to high risk foods and contacting local hospitals to determine whether there are other cases.

The principal use of epidemiological investigations in the event of a deliberate release is likely to be following the covert release of organisms or toxin into food or water supplies in order to identify and eliminate the source. Where cases arise in the absence of a known or obvious source such as a particular food item or a water quality zone, it is important to collect comprehensive details relating to diet and use of water supplies.

4.4.1 Epidemiological sampling

Where a food or water borne source of botulinum toxin is suspected, relevant samples are essential to aid identification of the source of infection.

5 LIST OF NATIONAL SPECIALISTS

Advice can be obtained from:

Dr Barbara Bannister
Infection Services
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Tel (switchboard): (+44) 020 7794 0500
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Liverpool L7 8XP
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Advice on Laboratory Diagnosis can be obtained from:

Dr Kathie Grant
HPA Centre for Infections
Foodborne Pathogens Reference Unit,
61 Colindale Avenue,
London NW9 5EQ
Tel: (+44) 020 8327 6505
E-mail: Kathie.grant@hpa.org.uk

Out-of-hours contact details are held at HPA Centre for Infections by the 24 hr on call duty doctor; Tel: (+44) 020 8200 6868 or 020 8200 4400

Public Health contact details are held at HPA Centre for Infections by the 24 hr on call duty doctor; Tel: (+44) 020 8200 6868 or 020 8200 4400

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