November, 2015

Re: Anthrax Reporting and Case Investigation

Reporting of anthrax (Bacillus anthracis) is as follows:

**Laboratory:**
- All positive laboratory results for *B. anthracis* are reportable to the Public Health Surveillance Unit by secure fax (204-948-3044). A phone report must be made to a Medical Officer of Health at 204-788-8666 on the same day the result is obtained, in addition to the standard surveillance reporting by fax.

**Health Care Professional:**
- Probable and suspect cases (clinical) of anthrax are reportable to the Public Health Surveillance Unit using the Clinical Notification of Reportable Diseases form ([http://www.gov.mb.ca/health/publichealth/cdc/protocol/form13.pdf](http://www.gov.mb.ca/health/publichealth/cdc/protocol/form13.pdf)) ONLY if a positive lab result is not anticipated (e.g., poor or no specimen taken, person has recovered).
- Cooperation in Public Health investigations is appreciated.

**Regional Public Health or First Nations Inuit Health Branch (FNIHB):**
- Once the case has been referred to Regional Public Health or FNIHB, the Communicable Disease Control Investigation Form ([www.gov.mb.ca/health/publichealth/cdc/protocol/form2.pdf](http://www.gov.mb.ca/health/publichealth/cdc/protocol/form2.pdf)) should be completed and returned to the Public Health Surveillance Unit by secure fax (204-948-3044).

Sincerely,

“Original Signed By”

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1. Case Definition

1.1 Confirmed Case
Clinical illness^1^ with laboratory confirmation of at least one of:
- Isolation of *Bacillus anthracis* in a clinical specimen.
  OR
- Demonstration of *B. anthracis* in a clinical specimen by immunofluorescence (1).

1.2 Probable Case
Suspect case with detection of *B. anthracis* DNA in a clinical specimen (1).

1.3 Suspect Case
Clinical illness^1^ in a person who is epidemiologically linked to a confirmed or suspected animal case or contaminated animal product (1).

Note: It may not be possible to demonstrate *B. anthracis* in clinical specimens if the patient has been treated with antimicrobial agents (2).

2. Reporting and Other Requirements

2.1 Reporting of Anthrax in Humans

Health Care Professional:
- Same day reporting to Manitoba Health, Public Health Surveillance Unit is required when a health care professional becomes aware that a person meets or has recently met the probable or suspect case definition for anthrax (form available at: [http://www.gov.mb.ca/health/publichealth/cdc/protocol/form2.pdf](http://www.gov.mb.ca/health/publichealth/cdc/protocol/form2.pdf) or confirmed case definition for anthrax (form available at: [www.gov.mb.ca/health/publichealth/cdc/protocol/form13.pdf](http://www.gov.mb.ca/health/publichealth/cdc/protocol/form13.pdf)).

2.2 Reporting of Anthrax in Animals
- A person who is a veterinarian, an officer appointed under *The Wildlife Act* or *The Provincial Parks Act*, an inspector appointed or designated under *The Animal Diseases Act* or a wildlife biologist must report to Manitoba Health, Public Health Surveillance Unit as well as to the Canadian Food Inspection Agency (CFIA) ([www.inspection.gc.ca/animals/terrestrial-animals/offices/eng/1300462382369/1300462438912](http://www.inspection.gc.ca/animals/terrestrial-animals/offices/eng/1300462382369/1300462438912)) and the Chief Veterinary Officer of Manitoba ([http://www.gov.mb.ca/agriculture/foodsafety/chiefvo/cfs12s01.html](http://www.gov.mb.ca/agriculture/foodsafety/chiefvo/cfs12s01.html)) when they become aware that an animal in Manitoba has or may have anthrax.

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^1^ **Cutaneous:** Clinical illness is characterized by the appearance of small painless but often pruritic papules. As the papule enlarges, it becomes vesicular and, within two days ulcerates to form a distinctive black eschar, with surrounding edema.

**Inhalational:** Clinical illness is characterized by an upper-respiratory “flu-like” syndrome that, after a few days, takes a fulminant course manifested by dyspnea, cough, chills and a high-grade bacteremia.

**Gastrointestinal:** Clinical illness is characterized by abdominal pain, fever and signs of septicemia.

**Meningeal:** Acute onset of high fever possibly with convulsions and loss of consciousness, meningeal signs and symptoms (2).
3. **Clinical Presentation/Natural History**

In humans, infection is usually initiated when spores enter the host by one of three routes: the cutaneous route through a cut or abrasion in the skin, the gastrointestinal route by ingestion of contaminated meat and the inhalational route by breathing in airborne spores (3, 4). The non-cutaneous forms are associated with high mortality, at least partially because they are more difficult to diagnose early and the initiation of appropriate antibiotic treatment is often delayed (3).

**Cutaneous Anthrax:** Globally more than 95% of naturally occurring anthrax (i.e., not from bioterrorism) in humans presents as cutaneous infection (2, 5). Anthrax eschars are generally seen on exposed unprotected regions of the body, mostly on the face, neck, hands and wrists (2). The initial presentation is a small painless pruritic papule at the inoculation site (4-5). A ring of vesicles (that may exude fluid) develops around the papule (2). The lesion is usually 1-3 cm in diameter and remains round and regular (2). The original papule ulcerates to form the characteristic black eschar (2, 6), with surrounding edema, hyperemia and regional lymphadenopathy (6). Headache, malaise and low-grade fever may also occur (2, 5). Resolution of the eschar takes several weeks and is not hastened by antimicrobial treatment (2). Mortality among individuals with untreated cutaneous anthrax is approximately 20%, reduced to < 1% with appropriate antibiotic therapy (7).

**Inhalational Anthrax:** Inhalational anthrax is the most serious presentation (8, 9). Initial symptoms resemble a “flu-like” illness characterized by low-grade fever, headache, malaise, fatigue and myalgias (5). Additional signs and symptoms may include bloody sputum, shortness of breath, clinical features of sepsis, X-ray: large mediastinal nodes, and bloody pleural effusion. Inhalational anthrax may be confused with mycoplasma pneumonia, Legionnaire disease, psittacosis, tularemia, Q fever, viral pneumonia, histoplasmosis, coccidioidomycosis or malignancy (2). Blurred vision and photophobia occur in some cases (5). A relatively mild initial phase of nonspecific symptoms is followed by the sudden development of dyspnea, cyanosis and disorientation with coma progressing rapidly to death (2). Even a single case should raise the possibility of a deliberate spread of spores (bioterrorism) as naturally occurring inhalational disease is rare (5). Inhalational anthrax is almost 100% fatal if untreated (7).

**Ingestion Anthrax:** There are two clinical manifestations of anthrax that may result from ingestion of *B. anthracis* in contaminated food or drink — oropharyngeal anthrax and gastrointestinal anthrax (2). The spectrum of disease ranges from asymptomatic to severe, including sepsis, septic shock and death (2). Untreated cases are associated with a mortality rate of 25-75% (7).

a) **Oropharyngeal anthrax:** The lesion(s) is generally localized in the oral cavity, especially in the buccal mucosa, tongue, tonsils, or posterior pharynx wall (2). The main clinical features are sore throat, dysphagia and painful regional lymphadenopathy in the involved side of the neck (2). Oropharyngeal anthrax is identified less often than gastrointestinal disease (2, 8). Oropharyngeal anthrax can lead to toxemia and acute respiratory distress syndrome followed by shock, coma and death (2).

b) **Gastrointestinal anthrax:** The lesion may occur anywhere within the gastrointestinal tract but is usually in the ileum and cecum (2). Lesions are usually ulcerative, multiple, and superficial, with surrounding edema, and may bleed (2). Symptoms of gastrointestinal anthrax are usually nonspecific and include nausea, vomiting, anorexia, fainting spells, asthenia, mild diarrhea, fever and headache (2). With ulceration of the gastrointestinal mucosa, patients often vomit material that is blood-tinged or has a coffee-ground appearance (8). Intestinal lesions may cause hemorrhage, obstruction or perforation by themselves or in combination (2). The infection may become disseminated with sepsis and pulmonary or meningal involvement (2).

**Meningitis:** Meningitis due to infection with *B. anthracis* is associated with high mortality (10). Meningitis may follow any of the other three forms of anthrax (2) or may be the initial clinical presentation (6).
Emerging Presentations: In an anthrax outbreak in Scotland in 2009 attributed to use of contaminated heroin, the clinical presentation was mainly soft tissue sepsis, rather than the classic cutaneous presentation with black eschar (11). Anthrax infection and other spore-forming organisms causing disease should be considered in drug users, particularly heroin users who inject intramuscularly, intravenously or who take heroin by any other route (smoking, snorting) and present with cellulitis/soft tissue infection, especially if associated with significant local edema, with or without systemic illness (11). Clinical presentation is likely to vary depending on the route of drug use (i.e., whether the drug was smoked/inhaled, snorted, injected) and pathogens in addition to \textit{B. anthracis} may contribute to disease.

Complications: Systemic illness, including fever, shock and dissemination to other organs, can occur with any form of anthrax, and may include meningitis, which is usually fatal (12).

4. Etiology

Anthrax is caused by \textit{Bacillus anthracis}, an encapsulated spore-forming, non-motile, gram-positive, bacterial rod (12). There is little genetic diversity among isolates (5). Known virulence determinants of \textit{B. anthracis} include toxin production and the ability to avoid phagocytosis through the production of a protective capsule (2, 13).

5. Epidemiology

5.1 Reservoir

Herbivores (livestock and wildlife) dying of anthrax shed the vegetative bacilli into the environment which sporulate upon exposure to the air (2, 12). These spores resist adverse environmental conditions and disinfection (12). They can remain viable in soil for many years (4, 13) and may be distributed to other areas passively through the action of water, wind and other environmental factors (2). Processed skins/hides and bones from infected animals may harbour spores for years, allowing worldwide transmission (12). Because herbivorous livestock and wild animals are more susceptible to \textit{B. anthracis} than humans and, in general, soil sources do not present a direct threat to humans, the usual acquisition by human populations is through contaminated animal products (2).

5.2 Transmission

Humans acquire the natural disease directly or indirectly from infected animals or their products (e.g., carcasses, hides, bones, bone meal, horns etc.) (2, 5, 14-17). Person-to-person transmission is rare and only reported for cutaneous anthrax, where direct contact with skin lesions is required for infection (12). The disease is not spread by casual contact with cases or by coughing and sneezing (9, 18). Mechanical transmission by biting insects is believed in some countries to be an occasional mechanism by which anthrax is contracted by humans (2). Outbreaks of gastrointestinal illness have occurred after ingestion of anthrax contaminated meat (6, 19, and 20). Both inhalation and cutaneous anthrax have occurred in laboratory workers (6). Outbreaks of anthrax associated with contaminated heroin if the heroin was injected, smoked or snorted were reported in Scotland in 2009 and 2010 (21, 22).

5.3 Occurrence

General: WHO has estimated there are between 2,000 and 20,000 human cases of anthrax per year (5). The actual number of human anthrax cases worldwide is difficult to determine owing to poor reporting (5). Human case rates for anthrax are highest in Africa and central and southern Asia (2). Outbreaks following handling and consuming meat from infected cattle have occurred in Africa, Asia, Russia and the USA (12, 19).

\begin{footnote}
\textbf{b} The rate and extent of sporulation by vegetative cells shed from infected animals is affected in a complex manner by the environmental conditions into which they fall (2). Under certain laboratory conditions, sporulation was first apparent as early as 6 hours after the vegetative cells were exposed to air (2). In a field study, the earliest time at which spores were detected in the soil at a site in the Etosha National Park (Namibia) where a springbok had just died, was 8 hours (2).
\end{footnote}
The largest reported human outbreak of anthrax occurred in Zimbabwe from 1979-1985 with about 10,000 reported cases and 182 deaths (5). In most of Europe and North America, human cases are rare and animal cases sporadic and uncommon (5). In the USA in October 2001, anthrax spores were deliberately distributed through the postal system causing 22 infections and 5 deaths (12). In 2009-2010 in the United Kingdom and Germany, a total of 55 cases including 21 deaths were reported in injection drug users due to contaminated heroin (23).

Canada: Since 1931, 25 human anthrax cases have been reported in Canada, with most occurring in 1936 (24). The most recent cases were cutaneous anthrax; one in 2006 in Saskatchewan acquired through handling an infected animal carcass during an animal outbreak and another in 2001 in British Columbia where the source of infection was attributed to contaminated goat hides (24, 25).

Manitoba: No cases of human anthrax have been diagnosed in the last three decades.

5.4 Incubation Period
Cutaneous anthrax: usually two to six days but ranges from a few hours to three weeks (2). Ingestion or oral route anthrax: incubation period is usually three to seven days (2). Inhalational (pulmonary) anthrax: the median incubation period is four days (range 4-6 days) but may be as long as 10 or 11 days (2). Spore dormancy and slow clearance from lungs means the incubation period for inhalation anthrax may be prolonged, reported up to 42 days in humans (6). In individuals who developed anthrax after the use of contaminated heroin, symptoms occurred one to seven days after taking heroin (21).

5.5 Host Susceptibility
Circumstantial evidence indicates that humans are moderately resistant to anthrax (2). Human infectious doses have not been established (2). Severity of infection likely depends on route of infection, nutritional and other states of health on the part of the infected person and on the relative virulence of the infecting strain (2). Risk assessment following the 2001 anthrax letter events in the USA resulted in the conclusion that there is no safe level of contamination (2). The relative infectivity of vegetative cells as compared to spores, and the possible importance of this to oral infectious dose is not known (2).

5.6 Period of Communicability
Anthrax is not considered a contagious disease in humans (2, 26). Person-to-person transmission is very rare and has only been reported for cutaneous anthrax where it requires direct contact with skin lesions (12).

6. Laboratory Diagnosis
Laboratory confirmation is made by demonstration of *B. anthracis* in clinical specimens, preferably by culture. Cadham Provincial Laboratory (CPL) should be notified (204-945-6123) when isolation of anthrax is suspected and “Suspect Anthrax” should be clearly marked on the laboratory requisition.

The specimen should be taken before treatment is started. Submit a swab or pustular fluid from a skin lesion in standard transport medium. If the lesion is dry, moisten a swab in sterile water or non-bacteriostatic saline and insert swab beneath the edge of the eschar, rotate slowly for two to three seconds, and collect lesion material. Blood cultures should be sent to the local microbiology laboratory for processing. A sputum specimen should be collected for the rare instances of suspected pulmonary anthrax.

Where isolation of the *B. anthracis* organism is likely to be inhibited by prior antibiotic treatment, a Medical Officer of Health (MOH) may request PCR (polymerase chain reaction) for *B. anthracis* on clinical specimens, in consultation with CPL physicians.

7. Key Investigations for Public Health Response
- Close liaison with other Manitoba Government departments (e.g., Manitoba Agriculture, Food and Rural Initiatives, Workplace Safety and
Health, Office of Disaster Management, Emergency Measures Organization) and agencies (e.g., Canadian Food Inspection Agency, Public Health Agency of Canada – Emergency Preparedness, Canadian Armed Forces) as required/appropriate.

- Interview cases to determine source of infection including history of:
  - food consumption as appropriate;
  - exposure to ruminants that have died suddenly;
  - working with animals or animal hides;
  - making, owning or playing animal hide drums;
  - drug use (particularly heroin);
  - travel;
  - working in the postal/courier industry handling large volumes of packages/mail;
  - receiving letter or package containing white powder (27, 28).

- Identify other individuals (contacts) exposed to the presumed source of infection.

- Take measures to prevent further exposure to the source as appropriate.

8. Control

8.1 Management of Cases

Anthrax is an uncommon infection that may present with signs and symptoms suggesting a wide differential diagnosis and has a possibility for severe adverse outcomes if not managed appropriately early in the course of infection. Consultation with an expert in infectious diseases is recommended for the management of suspect, probable or confirmed cases.

Infection Control Measures:


- After an invasive procedure or autopsy, the instruments and area used should be cleaned and disinfected with a sporicidal agent.

Treatment:

**Cutaneous Anthrax:**

- Treatment with oral ciprofloxacin or doxycycline for 7-10 days is recommended for localized or uncomplicated cases of naturally acquired cutaneous anthrax (29). If susceptibility testing is supportive, oral therapy with penicillin V or amoxicillin may be used to complete the course of treatment (29). Topical therapy is not effective. For severe cases of naturally acquired cutaneous anthrax with signs of systemic involvement, extensive edema or lesions of the head and neck, intravenous (IV) therapy for 7-10 days using ciprofloxacin is preferred; IV penicillin G, if supported by susceptibility testing may be used to finish the 7-10 day course (29).

- Localized or uncomplicated cases of cutaneous anthrax associated with bioterrorism should continue oral therapy for 60 days to provide coverage for potential concomitant aerosol exposure (29). Bioterrorism-related cutaneous anthrax with signs of systemic involvement, extensive edema, or lesions of the head or neck should be treated as **Severe Systemic or Life-threatening Disease** addressed below.

- Antibiotic treatment does not prevent the formation of eschar. Excision of the lesion is contraindicated.

**Severe Systemic or Life-threatening Disease** (including inhalation anthrax and ingestion anthrax):

- Intravenous (IV) ciprofloxacin is recommended over doxycycline (unless ciprofloxacin is contraindicated) because of its bactericidal activity and higher central nervous system (CNS) penetration (29). In addition to ciprofloxacin or doxycycline, at least one or more agents with CNS penetration and in vitro activity against *B. anthracis* is recommended (e.g., ampicillin, penicillin, meropenem, rifampin, clindamycin or vancomycin) regardless...
of clinical suspicion of meningeal involvement (6, 29). Of the additional agents to consider for inclusion in the multidrug regimen, clindamycin or linezolid is strongly recommended because of the ability to inhibit protein synthesis which may reduce exotoxin production (29). Treatment should continue for a total of 60 days with adjustment to the regimen based on the clinical course of disease in the patient (29).

Treatment of Special Populations:
Consultation with an expert in infectious diseases is strongly recommended for treatment of children, pregnant women and other patients with special medical conditions.

- Treatment of anthrax during pregnancy should remain the same as for adults because of the severity of the disease; however, if doxycycline must be used prior to six months gestation, the course should be limited to 7-14 days (5).
- Recommendations for treatment of bioterrorism-related anthrax in pediatric patients should be consistent with adult antimicrobial agents, with ciprofloxacin favoured for severe disease (29).
- For patients with special medical conditions, drug selection and dosage should be adjusted for potential drug interactions and underlying diseases such as renal failure (29).

8.2 Management of Contacts
- Identify the source of infection of the case. Contacts are defined as other individuals exposed to the source of infection who were not wearing proper personal protective equipment. Exposures may include physical contact with a human or animal case or a contaminated product, ingestion of contaminated food or exposure to an airspace contaminated with aerosolized B. anthracis (26).
- Educate contacts about early signs and symptoms of infection and instruct to present immediately to a health care provider should any of these occur.

Risk Assessment Considerations to determine if an Exposure to Anthrax has occurred:
- Spores are formed within a few hours if an anthrax infected carcass is opened and B. anthracis is exposed to the air (30). If the carcass is not opened, the oxygen supply is insufficient for spore formation and the organisms are killed within a few days by the putrefactive process (30). Therefore, unopened, recently dead cattle are low risk. Vegetative forms of B. anthracis are no more resistant than most other bacteria and therefore much easier to destroy than the spores (30). The precise length of time after which no viable B. anthracis remain within a carcass is unpredictable but depends greatly on climatic conditions, particularly temperature (2). Spores will be confined to where blood has been shed through body orifices and will mostly be in the soil beneath these points (2).
- No anthrax cases occurred among family members of postal workers during the 2001 outbreaks, indicating that the risk of acquiring anthrax from the contaminated clothing of household members with inhalational or cutaneous anthrax is low (31). The risk would be higher if the clothes were heavily contaminated with a body fluid from an anthrax-infected carcass (e.g., blood) and this came into contact with an open sore on a person.
- Exposure to B. anthracis spores in soil is not considered a substantial risk for human inhalation anthrax because spores are bound to heavy soil particles (32).

Decontamination of Persons who have Handled Anthrax Infected Material:
- All persons who have accidentally handled anthrax infected material should immediately wash arms and hands and any other exposed areas thoroughly with liquid soap and water (30). These steps must be taken immediately after discovery of exposure, before the vegetative anthrax organisms have time to form spores (30). A brush or other suitable appliance should be used to ensure removal of all contaminating material from under and around fingernails (30).
This decontamination process is more effective when performed in repeated cycles of lathering and rinsing rather than spending the same amount of time in scrubbing with a single lather (30). After the arms and hands have been thoroughly rinsed free of soap, they may be immersed for about one minute in a solution of organic iodine, Dettol®, Lysol® or other comparable agent followed by a potable water rinse (30).

- A complete change of clothes should be made (30). Possibly contaminated clothing should be laundered separately in a washing machine using the hottest cycle possible (33). Hands should be washed after laundering clothes (33).

**Anthrax Post-Exposure Prophylaxis (PEP) After Exposure to Aerosolized Spores:**

- When the antimicrobial susceptibility of the implicated strain of *B. anthracis* is unknown, initial anthrax post-exposure prophylaxis (PEP) with oral ciprofloxacin or doxycycline is recommended for adults and children (6). Ciprofloxacin is recommended as the first-line antimicrobial agent of choice for PEP for asymptomatic pregnant or lactating women because of the severity of inhalation anthrax (32). If susceptibility of the organism to penicillin is confirmed, prophylactic therapy for children and pregnant and nursing women should be immediately changed to oral amoxicillin (6, 32), if not contraindicated.

- Levofloxacin is recommended as a second-line PEP antimicrobial agent (29, 32).

- Duration of antibiotic PEP is 60 days (29).

- Ensure that an infectious disease specialist is consulted for each case to ensure the latest appropriate prophylaxis is considered.

**Anthrax PEP for Other Potential Exposure Situations:**

- For persons who experience a naturally occurring gastrointestinal exposure such as those who eat meat from a carcass of an anthrax-infected animal, antimicrobial PEP for 7-14 days may be considered (32).

- When a naturally occurring cutaneous exposure occurs (i.e., not associated with bioterrorism), appropriate medical and public health personnel should be notified, and affected persons should be monitored for development of a spot, pimple, or boil-like lesion, especially in exposed areas (32).

- Anthrax post-exposure prophylaxis (PEP) is not indicated for health care workers using Routine Practices (26).

### 8.3 Management of Outbreaks

- Due to the severity and rarity of anthrax, a single confirmed case constitutes an outbreak (2).

- All cases and contacts should be managed as per this protocol.

### 8.4 Bioterrorist Threats or Suspected Bioterrorist Activity

- *B. anthracis* is one of the most likely agents to be used as a biological weapon, because the spores are highly stable, easily delivered by spray devices to highly populated areas, can infect via the respiratory route, and inhalation anthrax has a high mortality rate (6).

- For bioterrorist threats or suspected bioterrorist activity, the police should be contacted at 911 (24 hours) as well as the Office of Disaster Management Duty Officer at: 204-793-1632 (24 hours).

### 8.5 Preventive Measures

- The anthrax vaccine is currently not available for civilian use in Canada. Immunization of persons at high risk of coming into contact with anthrax (e.g., laboratory workers, veterinarians working in areas with high incidence of epizootic anthrax, workers who handle potentially infected raw materials, military personnel) should be considered (12). Vaccination for personnel in these high risk professions should be dealt with through their respective occupational health departments. Health Canada’s Special Access Program will assist in obtaining the necessary approvals to bring this vaccine into Canada.
• Antibiotic prophylaxis when known or suspected inhalation of substantial numbers of anthrax spores has occurred (i.e., exposure during deliberate or accidental release of spores) (2).
• Routine cross-notification between the veterinary and human health surveillance systems (2).
• Control of anthrax in animals:
  – Vaccination of livestock in endemic regions (2, 12);
  – Investigation of any sudden or unexpected death in livestock (2).
  – Suspected animal post-mortem procedures should follow appropriate contact and respiratory precautions to minimize the occupational risk encountered with this disease.
  – Appropriate on-farm decontamination of the site where the dead animal was found.
  – Appropriate on-farm management of an outbreak by the appropriate government agricultural department after a case of anthrax is diagnosed in a herd.
• Control of anthrax in industry:
  – Education about transmission to workers who handle materials potentially contaminated with anthrax spores (12).
  – Dust control, proper ventilation and protective apparel in work areas of industries working with materials potentially contaminated with anthrax spores (12).
  – Imported animals or animal products should be accompanied by international veterinary certificates that the animals involved were free from anthrax and were not on premises quarantined for anthrax at the time of harvest (12).
• Avoid street drug use (21).
• Education of heroin users on the infection risks of use and the early symptoms of anthrax (34).
• Refer to Canada Post guidelines available at:
  http://www.canadapost.ca/cpo/mc/assets/pdf/aboutus/suspiciousmailposter_en.pdf when suspicious mail/packages are received.

References


