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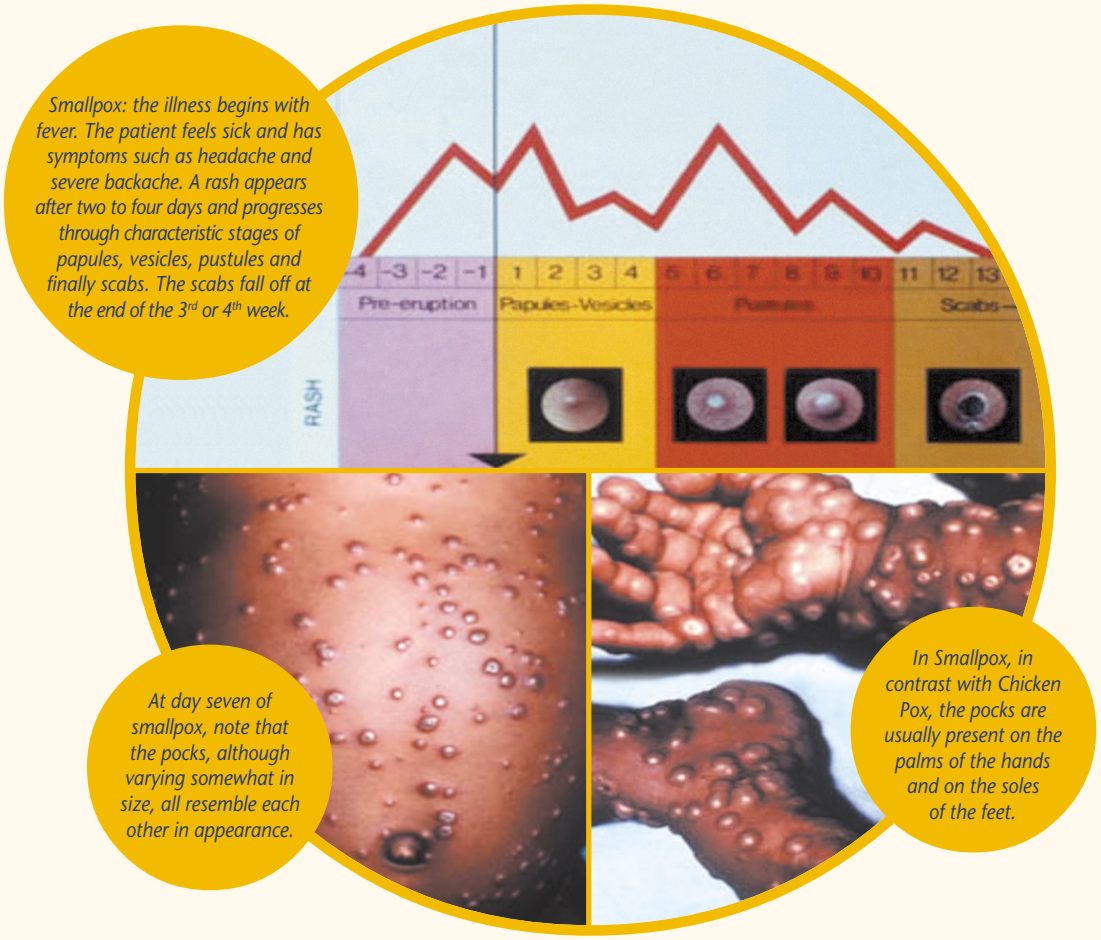
Bioterrorism:

Key Facts About Anthrax, Smallpox, Plague and Botulism



INSIDE ARTICLES ON BIOTERRORISM

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Bioterrorism: Key Facts About
Anthrax, Smallpox, Plague and Botulism

By Dr Richard Bellamy, Dr Nicholas I J Paton, Dr Timothy Barkham and Dr Yee Sin Leo

1. ANTHRAX

The recent deliberate use of anthrax in the USA has caused worldwide concern over the threat of bioterrorism. Many agents could be used as biological weapons but the four most feared are anthrax, smallpox, plague and botulism.

Anthrax causes infection by three different routes. Cutaneous disease causes a painless, black eschar with surrounding vesicles and oedema. Gastrointestinal anthrax causes haematemesis, dysentery and haemorrhagic ascites. Inhalational disease is the most severe form and has a case fatality rate of over 80% even with appropriate antibiotic therapy. Patients with inhalational anthrax initially suffer from non-specific flu-like symptoms such as fever, malaise, cough and chest discomfort. Typically there is then some brief improvement, followed by severe breathlessness, stridor, septic shock and death. The anthrax bacillus spreads rapidly to the mediastinal lymph nodes causing haemorrhagic lymphadenitis and haemorrhagic mediastinitis. The typical chest radiograph shows clear lung fields and a markedly widened mediastinum. In a previously healthy person this presentation is almost pathognomonic of anthrax.

Suspected anthrax cases should be discussed with the microbiology laboratory and an infectious diseases physician. Diagnosis is confirmed by culture of the bacteria from blood or affected tissues. Recommended treatment is initially with intravenous ciprofloxacin because of concerns that terrorists may possess antibiotic-resistant strains. Following confirmation of antibiotic susceptibilities, this should be changed to penicillin G or doxycycline. Person-to-person transmission does not occur so contacts of patients are not at risk and respiratory isolation is not required. Anthrax is identified in suspect material by rapid diagnostic tests and culture. Following confirmed exposure to anthrax spores, persons requiring antibiotics will be identified by public health officials and given oral ciprofloxacin. A sixty-day course of antibiotics is required for treatment or prophylaxis due to the risk of disease occurring following late germination of spores. Amoxicillin or doxycycline should replace ciprofloxacin once antibiotic susceptibilities are known. Nasal swabs are used for epidemiological purposes but are not reliable diagnostic tests in the absence of a confirmed anthrax exposure. They cannot be used to exclude anthrax and should not be performed on persons with a low probability of exposure. Anthrax vaccine is not currently available for health care workers or the general population.

2. SMALLPOX

Although smallpox has been eradicated, it is feared that it could be used by bioterrorists. A single case of smallpox would be an international emergency and immediate notification is required. Smallpox virus is highly infectious in aerosol form and has a case fatality rate of 30%. It is highly transmissible and could spread rapidly through susceptible populations. Prodromal symptoms are non-specific and include malaise, fever, rigors, vomiting, headache and backache. The skin rash progresses from macules to papules to vesicles to pustules and finally scabs. This rash is most likely to be confused with varicella. In smallpox the lesions are mostly on the face, arms and legs and there is relative sparing of the trunk. The lesions on one body site progress together and should therefore be at the same stage of development. In contrast, in varicella, lesions are more dense on the trunk than the peripheries, and macules, papules, vesicles and pustules may all occur together. A diagnosis of smallpox can be confirmed by electron microscopy, viral culture or PCR of vesicular fluid. However this requires a biosafety level four laboratory which would require samples to be sent abroad for analysis. Patients with smallpox are highly infectious and must be cared for in strict respiratory isolation until all of their scabs separate. There is no known effective treatment for smallpox. Those exposed to a smallpox aerosol or contacts of a case would require smallpox vaccine.

3. PLAGUE

Plague is a rodent zoonosis caused by the gram negative bacillus *Yersinia pestis*. Bubonic plague is caused by the bite of an infected rat flea. Patients who become septicaemic may develop secondary pneumonia and produce infectious respiratory droplets. Primary pneumonic plague can be caused by inhalation of these droplets and could also be caused if terrorists released an infectious aerosol. Between one and six days after inhalation, patients develop breathlessness and a productive cough. Abdominal symptoms are also common including nausea, vomiting, diarrhoea and abdominal pain. The patient rapidly develops high fevers, rigors, prostration and frequently meningism. Digital necrosis is a late complication and probably accounts for the name of "the Black Death" which plague acquired in the fourteenth century. The chest radiograph usually shows infiltrates or consolidation. The diagnosis of plague is established by culture of blood, sputum or lymph node aspirates. Plague is highly infectious and patients require respiratory isolation until they have received forty-eight hours of antibiotics and are improving. Streptomycin or gentamicin are the recommended antibiotics. Doxycycline and ciprofloxacin can be used for those who cannot be given aminoglycosides and these drugs are also used for prophylaxis of those exposed to a plague aerosol or who have been in face-to-face contact with a patient with pneumonic disease. Contacts should follow respiratory droplet precautions and wear a face mask for the first two days of treatment. There is no available effective vaccine.

4. BOTULISM

Botulism is caused by ingestion of the toxin produced by *Clostridium botulinum*, or by formation of the toxin by bacteria infecting a wound or the gastrointestinal tract. Botulinum toxin can also be inhaled and bioterrorists are most likely to try to produce an aerosol to utilise this route. This potent neurotoxin prevents acetylcholine release from the presynaptic

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nerve terminal producing neuromuscular and autonomic blockade. Initial symptoms and signs include blurred vision, diplopia, ptosis, dysarthria, dysphagia and ataxia. This is followed by a descending, symmetrical, progressive skeletal muscle paralysis. Autonomic effects include dry mouth, constipation and urinary retention. Patients may rapidly develop respiratory failure or aspiration pneumonia and adequacy of gag and cough reflexes, vital capacity, inspiratory force and oxygen saturations should be monitored. Respiratory support may be required for several months for patients with severe poisoning. Botulism is often mistaken for Guillain-Barre syndrome, myasthenia gravis, poliomyelitis, tick paralysis or psychiatric illness. Features suggesting botulism are the prominence of the cranial nerve palsies compared to the initial mild limb weakness, the symmetrical nature of the weakness, the absence of sensory involvement and the alert mental status. In food-borne botulism, toxin can be detected in stool, gastric aspirates, vomitus or suspected food but toxin is unlikely to be detectable in inhalational disease. Serum toxin analysis should be performed but it is unknown whether toxin will be detectable.

Any person with suspected botulism must receive antitoxin immediately as once the toxin binds to the receptor, the antitoxin is ineffective. There are seven types of botulinum toxin designated ABCDEFG. Only toxins ABEF have been proven to cause disease in humans although it is likely that all toxin types can do so. Standard antitoxin is only effective against types ABE and if a bioterrorist used a different toxin type the antitoxin would be ineffective. The US army has an experimental heptavalent antitoxin for use in this situation. Following confirmed exposure, prophylaxis with antitoxin is not currently recommended, but patients should be admitted to hospital for close observation and administration of antitoxin at the first onset of symptoms. Although there is a pentavalent toxoid (ABCDE) for pre-exposure prophylaxis against botulism, this is in scarce supply and cannot be given to the general population. It is not effective as post-exposure prophylaxis.

The risk of bioterrorism is probably now higher than ever before. Although many biological agents could be used, the four discussed above are the most important. It is essential for every doctor to know about these diseases, though we hope this knowledge will never be needed. ■

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