Anthrax - the deadly weapon of biological warfare

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After the devastating attack on the World Trade Centre in U.S.threat of biological warfare is looming large in our minds. The Government is on a high state of alert, and in the 21st century, discussion on biological and chemical terrorism is no longer restric ted to scientific fiction books. As per the W.H. O. expert committee estimate, there would be 2.5 lakhs causalities if 50 kg of anthrax spore was released from an aircraft over an urban population of one million.

Before an effective vaccine became available in late 1930's, Anthrax was one of the foremost causes of heavy losses in cattle, sheep and goats throughout the world. Anthrax is a peracute disease characterised by septicaemia and sudden death accom panied by exudation of tarry blood from the natural orifices of the carcase. *Bacillus anthracis* is the specific cause of the disease. They are aerobic, spore forming, capsulated gram positive rods. Polychrome methylene blue stain gives a characteristic differentiation between capsule and body of the organism. The capsule material is stained pale pink and bacillary body takes blue colour. This reaction of the dye is known as "Mc Fadyean" reaction.

The bacteria is very resistant in its spore form which are formed in presence of sufficient oxygen and can resist heat for long periods (dry heat at 140°C for 1-3 hrs and moist heat at 100°C for 5-10 mts). Spores never occur in tissues, sporulation occurs only when the bacteria are shed eg. from nose, mouth and anus of the affected animal and when grown on artificial media. A new variant of anthrax toxin which is totally resistant to antibiotics has been developed in Russia, a sinister production in the field of biological warfare. The spores of anthrax can survive for many years. There is evidence that *B. antracis* can multiply in the soil under favourable conditions of temperature, pH and nutrients, and thus be responsible for serious outbreaks in both domestic and wild animals especially in tropical and subtropical countries. The usual cycle of infection consists of

- uptake of spores by the animal during feeding or drinking
- entry of spore through a lesion at some point along the gastrointestinal tract and carriage to the regional lymph node and beyond
- multiplication in the lymph nodes and spleen.
- endothelial breakdown of vessels and sudden release of bacilli and toxin leading to death.
- shedding of vegetative bacilli by the dying or dead animal
- sporulation on exposure to oxygen in the air
- infection of a further animal by the spores.

If anthrax is suspected, the carcase should not be opened, contamination of the environment with spilled body fluids and subsequent spore formation are thus avoided. If anthrax was not suspected and the carcase opened, dark unclotted blood and strikingly enlarged haemorrhagic spleen should alert the investigator. The infected carcasses should be immediately burned or burried. Burrial should be at least 2 m deep with an ample supply of quicklime added. Strong solutions of formalin or sodium hydroxide (5-10%) are the most effective disinfectants.

Anthrax in man

Anthrax in primarily a disease of herbivores. Humans are incidental hosts and are fairly resistant to the disease. Human anthrax can be classified into

(a) non-industrial occurring in butchers, farmers,

pathologists and veterinarians as a result of close contact with the infected animal.

(b) industrial - occurring in those employed in the processing of wool, hair, bones or other animal products.

The non-industrial type of anthrax usually manifest itself as cutaneous anthrax. Insect transmitted anthrax also takes the cutaneous form. Intestinal anthrax resulting from the consumption of infected meat also belongs to the non-industrial category. Industrial form of anthrax has higher chance of taking the pulmonary manifestation as a result of inhalation of spores.

Transmission

Infection usually occurs through the skin when comes directly or indirectly in contact with the infected tissues, blood, contaminated materials such as hair, wool, hides etc. Biting flies may also transmit the disease. Inhalation of spores is also a mode of infection leading to fulminating pneumonia. Intestinal anthrax is due to the ingestion of infected materials like meat.

Anthrax takes one of three forms. The cutaneous form is acquired through a lesion in the skin, the intestinal form through a lesion on the mucosa of the gastro intestinal tract and the pulmonary form by inhalation. Cutaneous anthrax accounts for 95-99 per cent of human cases. All the three forms are potentially fatal but the cutaneous type is often self-limiting. The characteristic eschar or carbuncle is surrounded by an oedematous zone which may extend some distance from the lesion. The main dangers are meningitis or cellulitis and when the lesion is on the face or neck obstruction of air ways by compression from the cutaneous swelling. The intestinal and pulmonary forms are regarded as more fatal than cutaneous anthrax.

Cutaneous Anthrax

Cutaneous anthrax takes the form of a localised pimple which develops rapidly in 2-3 days into a dry, black adherent scab surrounded by a circle of purplish vesciles. This is the typical anthrax sore (Malignant pustale, carbuncle; eschar) which is neither malignant nor pustalar. It is usually 2-3 cm in diameter but may be as large as 6-7 cm and is surrounded by extensive oedema. The anthrax sores may be acquired by scratching an itchy part with infected fingers. Pus is present in the lesion only if the lesion is secondarily infected by pyogenic organisms.

Intestinal Anthrax

In intestinal anthrax lesions develop on the mucosa of intestine after the ingestion of spores in meat. The characteristic eschar occurs on the wall of the terminal ileum or caecum. The oropharynx, stomach, duodenum and upper ileum are occasionally affected. Symptoms range from mild gastro intestinal disturbances to nausea, vomiting, anorexia, fever, abdominal pain and bloody diarrhoea. The incubation period as in cutaneous form is 2-5 days. If an early diagnosis is made the disease can be cured. In fatal cases shock, collapse and death occurs within a few hours.

Pulmonary Anthrax

This form develops by inhalation of spores. Incubation period is 2-5 days. Symptoms are fever, malaise, myalgia, and cough. Moist rales are heard on aucultation of the chest. After the mild initial phase these will be sudden onset of acute illness characterised by acute dyspnoea and subsequent cyanosis. Moist cripitant rales and signs of pleural effusion result from the internal oedema. Terminally the pulse become accelerated and feeble and is followed by comma and death.

Anthrax meningitis

In majority of cases anthrax meningitis is secondary to cutaneous anthrax. Anthrax meningitis can't be differentiated from other forms of meningitis unless evidence of one of the other forms of disease is also present.

Diagnosis

Smears of fluid from the early anthrax papule may be stained with polychrome methylene blue and examined microscopically for the presence of pink staining capsule (Mc Fadyean reaction); the material from the same site may be cultured. On agar surface colonies are opaque, greyish white, with an irregular border from which long strands of cells are seen in parallel arrangement resembling a "Medusa head".

Antigenicity

B. anthracis has a complex antigenic structure. The capsule and production of exotoxin are of prime importance for virulence. The capsule is D. glutamic acid polypeptide of single antigenic specificity. The capsule protects the organism from phagocytosis. The exotoxin produces extensive oedema and death. Exotoxin has three components - oedema factor, protective antigen and lethal factor. These factors are proteins or protein carbohydrate complexes.

Prevention and treatment

Pasteur made an attempt to produce an immunizing agent during the last century. He observed attenuation of bacteria when incubated at 42°C. In 1934

sterne developed attenuated live spore vaccine from an avirulent uncapsulated strain of *B. anthracis* (34 F_2). Spores of this strain suspended in 0.5% saponin in 50% glycerol saline remain the active ingredient of livestock vaccine in most countries of the world today. Analogous live spore human vaccine are used in Russia and China.

The US. vaccine for anthrax in humans consists of an alhydrogel-adsorbed culture filtrate of a non capuslating, nonproleolytic derivative (V 770-NPI-R) of *B. anthracis* strain V 770 and the U.K. vaccine consists of an alum precipitated culture filtrate of the sterne strain (34 F_2). At present boosters are administered to humans 6 months after the initial series of three doses and annually thereafter.

Treatment

Anthrax is lethal if not detected shortly after exposure to the bacterial spores. Antibiotics are effective in halting it, if administered soon after exposure. *B. anthracis* is susceptible to a wide range of antibiotics and in many parts of the world ciprofloxacins, penicillins, aminoglycosides, tetracyclines etc. are used for the treatment of the disease. Antibiotics are not active against spore forms of *B. anthracis*. Within the body spores germinate to form vegetative bacteria. Hence when substantial exposure to aerosolized spores is suspected it may be considered prudent to administer an antibiotic prophylactically for several weeks in parellel with vaccine so that the exposed person is protected while the vaccine induced immunity develops.

Conclusion

On of the reasons why the world is so terror stricken by the spate of anthrax-laced letters is the lack of a foolproof vaccine against anthrax. But the researchers from the Ohio State University, U.S.A. have reported that a new DNA based vaccine developed by their team could be effective against anthrax. The team has successfully demonstrated that mice innoculated with DNA fragments from anthrax bacteria show immunity against the disease. The latest study published in the journal of *Infection and Immunity* suggested that DNA based vaccines might be effective. In India human anthrax vaccine is not available.

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