Health Department
MEMORANDUM
Office of the Commissioner

TO: Halton Physicians, Medical Chiefs of Staff: Joseph Brant Memorial Hospital
Halton Healthcare Services
Oakville Site
Milton Site
William Osler Health Centre
Chairs of: Family Practice, Paediatrics, Internal Medicine, Emergency, Laboratory, Infection Control Practitioners
Post in Emergency Department and Physicians lounge

FROM: Robert M. Nosal, Medical Officer of Health

DATE: October 11, 2001

Re: **Bioterrorism**

There has been increased public concern regarding safety and potential bioterrorism incidents following events in the United States. Although the risk of bioterrorism in Ontario is considered to be low, steps are being taken regionally and provincially to ensure emergency preparedness.

Although correspondence from the Chief Medical Officer of Health to all physicians is planned, I am writing to you at this time to:

- emphasize the need for physicians to report any unusual clusters or manifestations of disease;
- provide information on various bioterrorism issues.

The attached material has been abstracted from documents produced by the New York City Department of Health and other Ontario Health Departments.

- Clinical Recognition and Management of Suspected Bioterrorism Cases
- Questions and Answers on Issues Associated with Bioterrorism
- Overview of the Five Agents Which May Be Used as Biological Weapons
- Bioterrorism References

If you have any questions, please call the Health Department at 905-825-6060 or 1-866-442-5866 ext. 7855.

Clinical Recognition and Management of Suspected Bioterrorism Cases

Healthcare providers should be alert to the illness patterns and diagnostic clues that might signal an unusual infectious disease outbreak due to the intentional release of a biological agent and should report these concerns immediately to Halton Region Health Department.

Unlike a chemical or nuclear release, the covert release of a biological agent will not have an immediate impact because of the delay between exposure and illness onset. Consequently, the first indication of a biological attack may only be recognized when ill patients present to physicians or other healthcare providers for clinical care.

The following are clinical symptoms and epidemiological clues that may be suggestive of a possible bioterrorism event:

- Any unusual increase or clustering in patients presenting with clinical symptoms that suggest an infectious disease outbreak (e.g., $\geq$ 2 patients presenting with an unexplained febrile illness associated with sepsis, pneumonia, adult respiratory distress, mediastinitis, or rash; or a botulism-like syndrome with flaccid muscle paralysis especially if occurring in otherwise healthy individuals).

- Any suspected or confirmed communicable disease case that is not endemic to Canada (e.g., anthrax, plague, tularemia, smallpox or botulism)

- Any unusual age distribution for common diseases (e.g., a cluster of sever chickenpox-like illness among adult patients who all report a previous history of varicella infection).

- Any unusual temporal and/or geographic clustering of illness (e.g., persons who attended the same public event or religious gathering).

- Any sudden increase in the following non-specific syndromes, especially if occurring in previously healthy individuals and if there is an obvious common site of exposure:
  - $\rightarrow$ Fever with respiratory, rash or gastrointestinal illness
  - $\rightarrow$ Encephalitis or meningitis
  - $\rightarrow$ Neuromuscular illness
  - $\rightarrow$ Bleeding disorders
  - $\rightarrow$ Simultaneous disease outbreaks in human and animal population

Most pathogens that could be used as a biological weapon would present initially as a non-specific influenza-like illness. Therefore, an unusual pattern should prompt physicians to alert the Health Department. These disease patterns might represent an early start to the influenza season, the introduction of a new pandemic strain of influenza, or an initial warning of a bioterrorism act.

Frequently Asked Questions Regarding Bioterrorism

Although the likelihood of a large-scale bioterrorist event is currently thought to be low, public concern and fears may remain heightened in the coming days. The following answers to frequently asked questions may assist you in dealing with patient concerns.

Should I have my own supply of antibiotics?

The Health Department strongly recommends that physicians not prescribe antibiotics for their patients to stockpile for future use: stockpiling of antibiotics could lead to inappropriate patient decisions to self-medicate, use of expired medications, and to the depletion of national supplies for medically indicated uses.

If an attack were detected, the Health Department would rapidly notify the medical community with detailed recommendations on diagnosis, treatment, and preventive measures for the specific biologic agent involved. The Centre for Emergency Preparedness holds the national stockpile System that contains Atropine, Diazepam, Ciprofloxacin, Tetracycline and Amoxicillin that could be used in response to a biological or chemical terrorist event. As well, the Ontario Government has also announced a plan to stockpile medicines for emergency use.

The use of prophylactic antibiotics should also be discouraged. Inappropriate use of antibiotics will lead to increased antibiotic resistance among microorganisms causing common bacterial infections (e.g., otitis media, pneumonia) and may result in serious adverse effects (e.g., *Clostridium difficile* colitis, allergic reactions, interactions with other medications).

Should I be vaccinated against Anthrax and Smallpox?

Anthrax and smallpox vaccines are not commercially available or recommended. There is currently no indication for the use of either vaccine. Both are in short supply and not available to the general public or the medical community. Anthrax vaccination currently requires 6 shots over an 18-month period with periodic boosters.

Smallpox vaccine is no longer a licensed product and was removed from the commercial market in 1983 as a result of the successful eradication of smallpox.

Should I purchase a Gas Mask?

Purchasing of gas masks for protection against biologic agents is also discouraged. Gas masks would only be protective if worn at the exact moment a bioterrorist attack occurred, and it is impractical to wear masks continuously as a protective measure against the possibility of a covert release of a biologic agent.

Moreover, masks need to be fitted properly. Improper use of gas masks can cause serious injury and death, especially among persons with underlying heart or lung disease.

Overview of the Five Agents Which May Be Used As Biological Weapons

Due to the events since September 11, 2001, health care providers are being asked to be extra vigilant for indications of illness related to biologic, chemical or other offensive weapons. The following provides a brief overview of the signs and symptoms of five agents that have the potential to be used as biologic weapons. These five agents are anthrax, small pox, plague, botulinum toxin, and tularemia.

Anthrax

Three forms of this zoonotic disease exist – cutaneous, gastrointestinal and inhalational. The inhalational form is of most concern in bioterrorist attacks since the *Bacillus anthracis* spores are most likely to be delivered by the aerosol route. The time from exposure to the development of clinical illness has been known to range from 2 to 43 days but may take as long as 60 days. This is the time period required for the spores to germinate and produce the toxin, which results in illness. Anthrax does not spread from person-to-person.

The clinical presentation has been described as a 2-stage illness. The first stage presents with a non-specific illness with fever, malaise and fatigue. A non-productive cough and vague chest discomfort may be present as can dyspnea, headache, vomiting, chills, weakness, abdominal pain, and chest pain. This stage of the illness lasts from hours to a few days. In some patients, a brief period of apparent recovery follows. Other patients progress directly to the second, fulminant stage of illness.

This second stage presents with the sudden onset of respiratory distress with dyspnea, diaphoresis, stridor, fever, cyanosis and shock. A chest X-ray most often shows a widened mediastinum due to massive lymphadenopathy that causes the stridor. This radiologic finding in a previously well patient with evidence of overwhelming flu-like illness is pathognomonic of advanced inhalational anthrax. Up to half of patients develop hemorrhagic meningitis with concomitant meningismus, delirium, and obtundation. Death usually follows in 24-36 hours. Inhalation anthrax has resulted in fatality rates of 86% or more in the past. Modern critical care medicine may result in somewhat lower mortality rates.

Small pox

Variola virus, the etiologic agent of small pox, was spread from person-to-person through direct deposit of infective droplets onto the nasal, oral, or pharyngeal mucosa membranes, or the alveoli of the lungs from close, face-to-face contact with an infectious person. Indirect spread (i.e., not requiring face-to-face contact with an infectious person) through fine-particle aerosols or articles containing the virus was less common. The incubation period for smallpox is 12 to 14 days (range: 7 to 17 days).

Symptoms began with a 2 to 3 day prodrome of high fever, malaise, and prostration with severe headache and backache. This pre-eruptive stage was followed by the appearance of a maculopapular rash (i.e., eruptive stage) that progresses to papules 1 to 2 days after the rash appeared; vesicles appeared on the fourth or fifth day; pustules appeared by the seventh day; and scab lesions appeared on the fourteenth day. The rash appeared first on the oral mucosa, face, and forearms, then spread to the trunk and legs. Lesions might erupt on the palms and soles as well. Smallpox skin lesions were deeply embedded in the dermis and felt like firm round objects embedded in the skin. As the skin lesions heal, the scabs separate and pitted scarring gradually developed.

Smallpox patients were most infectious during the first week of the rash when the oral mucosal lesions ulcerate and released substantial amounts of virus into the saliva. A patient was no longer infectious after all scabs had separated (i.e. 3-4 weeks after the onset of the rash).

During the smallpox era, overall mortality rates were approximately 30%. Other less common but more severe forms of smallpox included a) flat-type smallpox with a mortality rate >96% and characterized by severe toxemia and flat, velvety, confluent lesions that did not progress to the pustular stage; and b) hemorrhagic-type smallpox, characterized by severe prodromal symptoms, toxemia, and a hemorrhagic rash that was almost always fatal, with death occurring 5 to 6 days after rash onset.

The lesions of small pox can initially be confused with chickenpox except that unlike chickenpox, they are usually at the same stage of development on any given part of the body. Hemorrhagic cases were initially misdiagnosed as meningococcemia or severe acute leukemia. Malignant cases were often mistaken for hemorrhagic chickenpox or prompted surgery because of severe abdominal pain.

Plague

Plague normally appears in three forms in man: bubonic, septicemic, and pneumonic. It most commonly results from infected fleas bite, which lead to the swollen tender lymph node(s) of bubonic plague. Secondary septicemia is common, as greater than 80 percent of blood cultures are positive for the organism in patients with bubonic plague. However, only about a quarter of bubonic plague patients progress to clinical septicemia.

When used as an agent for bioterrorism, aerosolized *Yersinia pestis* will result in primary pneumonic plague, a form of the infection that is transmissible from person-to-person by the airborne droplet route. Surgical masks should be worn when primary pneumonic plague is suspected. The incubation period is 1 to 6 days.

The onset of pneumonic plague is acute and often fulminant. The first signs of illness include high fever, chills, headache, malaise, and myalgias, followed within 24 hours by a cough with bloody sputum. Although bloody sputum is characteristic, it can sometimes be watery or, less commonly, purulent. Gastrointestinal symptoms, including nausea, vomiting, diarrhea, and abdominal pain, may be present. Rarely, a cervical bubo might result from an inhalational exposure. The chest X-ray findings are variable, but most commonly reveal bilateral infiltrates, which may be patchy or consolidated. The pneumonia progresses rapidly, resulting in dyspnea, stridor, and cyanosis. The fatality rate when treatment is delayed more than 24 hours after symptom onset is extremely high.

Botulinum toxin

Botulinum toxin is the single most poisonous toxin known. It acts by blocking acetylcholine release into the neuromuscular junction and hence results in anticholinergic signs and symptoms. Two forms of botulism could be used for bioterrorist purposes – foodborne or inhalational. In foodborne disease, the *Clostridium botulinum* bacterium has produced the toxin in inadequately heated food. Inhalational botulism results from aerosolized botulinum toxin and is a man-made form of the disease that is not naturally occurring. Botulism is not communicable from person-to-person. The onset of symptoms depends on the quantity of toxin absorbed. It ranges from 2 hours to 8 days in foodborne botulism but is usually 12 to 72 hours. The incubation of inhalational botulism is uncertain because so few cases have occurred but is likely approximately 36 hours.

Botulism is an acute, afebrile symmetric, descending flaccid paralysis that always begins in the bulbar musculature. It is not possible to have botulism without having multiple cranial nerve palsies. Cranial nerve palsies are prominent early, with eye symptoms such as blurred vision due to mydriasis, diplopia, ptosis, and photophobia, in addition to other cranial nerve signs such as dysarthria, dysphonia, and dysphagia. Flaccid skeletal muscle paralysis follows, in a symmetrical, descending, and progressive manner. Collapse of the upper airway may occur due to weakness of the oropharyngeal musculature. As the descending motor weakness involves the diaphragm and accessory muscles of respiration, respiratory failure may occur abruptly. Progression from onset of symptoms to respiratory failure has occurred in as little as 24 hours in cases of severe foodborne botulism. The anticholinergic signs and symptoms include dry mouth, ileus, constipation, and urinary retention. Sensory symptoms usually do not occur. Botulinum toxins do not cross the blood/brain barrier so the patient is not confused or obtunded.

Tularemia:

Tularemia is a zoonotic disease cause by the bacteria *Francisella tularensis.* It is transmitted to humans by direct contact with or ingestion of infected animal tissues, through the bites of infected arthropods, by consumption of contaminated food or water, or from inhalation of aerosolized bacteria. It is not transmitted from person-to-person. The incubation period is 3-5 days with a range of 1 to 14 days.

There are a variety of clinical manifestations related to the route of introduction of the bacteria and the virulence of the agent. An aerosol release would have the greatest adverse impact as an offensive bioweapon. Inhalation of *F. tularensis* would result in typhoidal and pneumonic tularemia. These two forms often occur together.

Typhoidal tularemia has been used to describe illness in tularemia patients with systemic infections manifesting as fever and other constitutional signs without cutaneous or mucosal membrane lesions or regional lymphadenitis. The onset of tularemia is usually abrupt, with fever (38°C-40°C), headache, chills and rigors, generalized body aches (often prominent in the low back), coryza, and sore throat. A pulse-temperature dissociation has been noted in as many as 42% of patients. A dry or slightly productive cough and substernal pain or tightness frequently occur with or without objective signs of pneumonia, such as purulent sputum, dyspnea, tachypnea, pleuritic pain, or hemoptysis. Nausea, vomiting, and diarrhea sometimes occur. Sweats, fever and chills, progressive weakness, malaise, anorexia, and weight loss characterize the continuing illness. A case-fatality rate of 1-3% is seen in appropriately treated natural disease.

Tularemia pneumonia results from inhaling contaminated aerosols. It can also result from secondary spread via the blood and can accompany other forms of tularemia. An aerosol release of *F tularensis* would be expected to result in acute illness with signs and symptoms of one or more of pharyngitis, bronchiolitis, pleuropneumonitis, and hilar lymphadenitis, accompanied by various manifestations of systemic illness. Inhalational exposures, however, commonly result in an initial clinical picture of systemic illness without prominent signs of respiratory disease. The earliest pulmonary radiographic findings of inhalational tularemia may be peribronchial infiltrates, typically advancing to bronchopneumonia in 1 or more lobes, and often accompanied by pleural effusions and hilar lymphadenopathy. Signs may, however, be minimal or absent, and some patients will show only 1 or several small, discrete pulmonary infiltrates or scattered granuloma. Pulmonary infection can rapidly progress to severe pneumonia, respiratory failure, and death.

Other forms of tularemia include:

Ulceroglandular tularemia that is most often acquired through inoculation of the skin or mucous membranes with blood or tissue fluids of infected animals. It is characterized by fever, chills, headache, malaise, an ulcerated skin lesion, and painful regional lymphadenopathy. The skin lesion is usually located on the fingers or hand where contact occurs.

Glandular tularemia results in fever and tender lymphadenopathy but no skin ulcer.

Oculoglandular tularemia occurs after inoculation of the conjunctivae by contaminated hands, splattering of infected tissue fluids, or by aerosols.

Oropharyngeal tularemia refers to primary ulceroglandular disease confined to the throat. It is acquired through ingestion of the organism. It produces an acute exudative or membranous pharyngotonsillitis with cervical lymphadenopathy. It can also cause abdominal pain, diarrhea and vomiting.

Bioterrorism References

For more detailed clinical information on specific pathogens that might be used in a bioterrorist event, please consult the following references or Websites:

American College of Physicians: http://www.acponline.org/bioterr/

American Society of Microbiology: http://www.asmusa.org/pcsrc/bioprep.htm

Association for Infection Control Practitioners: http://www.apic.org/bioterror/

CDC Bioterrorism Preparedness and Response: http://www.bt.cdc.gov**.**

Infectious Disease Society of America: http://www.idsociety.org

Johns Hopkins Center for Civilian Biodefense: http://www.hopkins-biodefense.org

****** The Johns Hopkins Center for Civilian Biodefense has written consensus guidelines on the medical and public health management of the primary bioterrorist agents, including smallpox, anthrax, botulism, plague and tularemia. These guidelines were published in the Journal of the American Medical Association and archived copies are available at** http://jama.ama-assn.org**.**

US Army Medical Research Institute of Infectious Diseases:
http://www.usamriid.army.mil/education/bluebook.html