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PREPARING FOR BIOTERRORIST THREATS IN CORRECTIONS

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A tabloid worker dies in Florida. Two postal workers die in Washington, D.C. A homebound retiree dies in Connecticut. An envelope packed with a white substance raises alarm when it is opened for routine screening at a US correctional facility. The common link? Spores from *Bacillus anthracis*. Fortunately, the white powder at the correctional facility did not contain anthrax spores, and moreover, correctional officials recognized the potential anthrax threat, deposited the envelope in a secure receptacle, quarantined the area and alerted the authorities. Proper training and access to appropriate protocols for handling suspect substances (Table 1) allowed the correctional officers to maintain calm while experts were consulted.

Bioterrorism is an offshoot of biological warfare. Biological warfare is the use of bacterial or viral agents as weapons. Waging biological warfare is a violation of the Geneva Convention of 1925, which was reaffirmed by the UN General Assembly in 1966. Despite these affirmations, bioterrorism has recently occurred.

Medical events related to exposure to anthrax have been reviewed in detail in several publications.^{1,2} Lane, La Montagne and Fauci, and others have reviewed the etiologic agents of biological terrorism.^{3,4} A wealth of bioterrorism resources are also now available in medical journals^{5,6,7,8} and on the web (see Resources). Because knowledge is the best defense against terror, this article will review some biological agents of terror, appropriate medical responses, and available means of treatment or prevention.

The seven characteristics of a bioterrorism agent are listed in Table 2. Of the seven, four (virulence, infectivity, stability and transmissibility) can be affected by modifying the genetic sequence of the bioterrorism pathogen. Research on these four characteristics is the primary thrust of most modern biological warfare research laboratories, and antibiotic resistance will be a significant concern during future bioterrorist events. On the other hand, mutations introduced in the anthrax used in the most recent outbreak may eventually yield up its identity.⁶

TABLE 1: What to do if you suspect Anthrax in the mail

- G** Do not handle the mail piece or package suspected of contamination.
- G** Make sure that damaged or suspicious packages are isolated and the immediate area cordoned off.
- G** Ensure that all persons who have touched the mail piece wash their hands with soap and water.
- G** Notify your local law enforcement authorities.
- G** List all persons who have touched the letter and/or envelope. Include contact information and have this information available for the authorities.
- G** Place all items worn when in contact with the suspected mail piece in plastic bags and have them available for law enforcement agents.
- G** As soon as practical, shower with soap and water.
- G** Notify the Center for Disease Control Emergency Response at 770-488-7100 for answers to any questions.

Adapted from the USPS website:
http://www.usps.com/news/2001/press/pr01_1010tips.htm

Lethal agents are also very effective bioterrorism tools because of the "panic effect" on susceptible populations (recent events certainly confirm this observation).⁷ Potentially lethal agents that have been placed in category A (high threat) include smallpox (*Variola*), bubonic plague (*Yersinia pestis*), tularemia (*Francisella tularensis*) and anthrax (*Bacillus anthracis*). (Table 3) These will be reviewed here.

ANTHRAX

Pathogen and Immunopathogenesis

Bacillus anthracis is a gram-positive spore-forming bacteria. The bacterium only sporulates under adverse conditions (lower oxygen availability or declining pH); thus production of

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anthrax spores requires familiarity with these conditions. Anthrax disease is initiated by introduction of endospores by inhalation or via cutaneous contact (usually with skin that is otherwise compromised). At the site of entry, macrophages endocytose the anthrax spores and transport them to regional (in cutaneous anthrax) and thoracic (in inhalation anthrax) lymph nodes. Within the first few hours of infection, anthrax bacilli escape from the phagocytic vesicles of macrophages and replicate within the cytoplasm of these cells. The next phase of infection involves release of the mature bacilli from infected macrophages, four to six hours after the initial phagocytosis.¹¹ Proteins secreted by the mature bacilli combine to form the two anthrax toxins: lethal toxin (LT) and edema toxin (ET).¹² These toxins attack and destroy macrophages, causing them to spill their contents and damage surrounding tissues.

Anthrax: Clinical course

Of 10 recent cases described in JAMA, all but one was known to have handled mail contaminated with spores; the time of exposure to onset of symptoms (when known) was four to six days.² Symptoms at presentation included fatigue or malaise, fever or chills with sweats, dyspnea, minimal or nonproductive cough, and nausea or vomiting. The white blood count was elevated but not markedly so, at 9.8 X 10³/mm³ (range 7.5 to 13.3). Increased neutrophils and band forms were present. Six of the 10 patients were hypoxic, and all 10 chest X-rays were abnormal. On the X-rays, pulmonary infiltrates, pleural effusions, or mediastinal widening were noted, and involvement of the mediastinal nodes was confirmed with chest CTs. It is notable that inhalation of anthrax spores was previously believed to be lethal even at low doses. In the most recent reports, there was a 60% survival rate after exposure, which improved with prompt treatment, and chemoprophylaxis may have decreased the number of individuals who became overtly ill. Given a high enough index of suspicion and early aggressive treatment with effective antibiotics, recovery has now been shown to be possible. Thus, the threat of anthrax is much diminished in a vigilant clinical environment.

Anthrax: Treatment and Vaccine

Since anthrax is only contagious by spores, isolation and quarantine of infected individuals is not thought to be necessary. Prompt antibiotic treatment with potent anti-gram positive agents such as ciprofloxacin, clindamycin, amoxicillin, clarithromycin, imipenem, vancomycin, rifampin, or even

TABLE 2: Seven criteria determine the potency of a biological weapon

| |
|---|
| <ol style="list-style-type: none"> 1. Virulence- the damage inflicted by the weapon must be severe, though not necessarily fatal; 2. Infectivity- the size of the dose required to initiate an infection (best if low dose for economy of distribution) including the method of dosing; 3. Stability- the organism must survive and remain infectious until it reaches the host; 4. The extent of natural immunity (the target population must have low immunity for the agent to be effective); 5. The availability of vaccines and other protective measures to the user, but not to the target; 6. The availability and ease of therapy (the organism should not be readily treatable by common anti-infective agents); 7. Transmissability, which is person to person spread of the disease (in warfare transmissability needs to be low to hit the target population and not start a worldwide pandemic. In terrorism, that approach may not be necessary.) |
|---|

TABLE 3: Potential bioterrorist agents categorized by level of threat to public health

| CATEGORY A | CATEGORY B | CATEGORY C |
|---|--|--------------------------------|
| <i>Bacillus anthracis</i> (anthrax) | <i>Coxiella burnetti</i> (Q fever) | Nipah virus |
| <i>Clostridium botulinum</i> toxin (botulism) | <i>Brucella</i> species (brucellosis) | Hantaviruses |
| <i>Yersinia pestis</i> (plague) | <i>Burkholderia mallei</i> (glanders) | Tickborne encephalitis viruses |
| <i>Variola major</i> (smallpox) | Ricin toxin from <i>Ricinus Communis</i> | Yellow fever |
| <i>Francisella tularensis</i> (tularemia) | Toxin of <i>Clostridium perfringens</i> | Multidrug-resistant TB |
| Viral hemorrhagic fevers | <i>Staphylococcus enterotoxin B</i> | |

Adapted from Lane and Fauci³

chloramphenicol is recommended (see Table 4). All of these agents have been shown to be active in vitro against the Ames strain of anthrax associated with recent exposures. Penicillin (in combination with another agent), chloramphenicol, vancomycin or rifampin should be considered when CNS involvement is suspected. Because of concern about possible antibiotic resistance of *B. anthracis* used in a bioterrorist attack, doxycycline or ciprofloxacin was chosen initially for antibiotic chemoprophylaxis until the susceptibilities were known. Recommendations switched to penicillin VK or amoxicillin once antibiotic susceptibilities were known. The required duration of prophylaxis is unknown, but is believed to be at least 90 days post exposure, based on available information on the persistence of vegetative spores.¹³

The BioPort Company makes the existing anthrax vaccine from a cell-free filtrate of *B. anthracis* cultures. The strain used to prepare the vaccine is V770-NP1-R, a toxigenic, nonencapsulated strain.¹⁴ Vaccination using the inactivated cell-free filtrate vaccine requires six injections. As many as 30% of recipients experience local reactions, and life-threatening anaphylaxis has been associated with the existing vaccine.^{15,16,17} Currently, the vaccine is neither recommended nor required, except for military personnel. Vaccine may be available

to individuals who wish to be immunized, but not to children and pregnant women. Development of a new anthrax immunization strategy has become a national priority.

PLAGUE

Plague: Pathogen

The very threat of exposure to *Yersinia pestis*, the causative agent of plague, strikes fear in the heart of any individual who is familiar with world history: Between one third to one-half the population (approximately 50 million people) died from *Y. pestis* during the years of Black Death in Europe. During the epidemic of plague in London during the late 1600's, physicians abandoned the hospitals to the care of orderlies and fled, aware that exposure to diseased individuals could lead to transmission of the disease and death.¹⁸ While antibiotics such as tetracycline and streptomycin can now prevent plague after exposure and treat all forms of the disease, Black Death remains a bioterrorist threat¹⁹ that is compounded by the existence of antibiotic resistant strains²⁰ and widespread availability of the pathogen due to recurrent epidemics.²¹ Airborne dissemination of drug-resistant plague by terrorists would have a devastating impact on civilians, hospital staff, and military personnel.

Yersinia pestis, the etiologic agent of plague, is a gram-negative obligate aerobic

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LETTER FROM THE EDITOR

Being Prepared

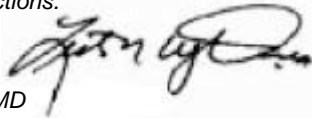
Y-2-K awakened us to our potential vulnerability through MIS. We worked long and hard to prepare. January 1, 2000 came and went and "the world as we know it" did not end. But we were ready and we learned some things. One was reinforcement of our emergency operations procedures, or red books.

September 11 awakened us to the reality of terrorist-caused mass casualty incidents IN THE U.S.A.! We knew they happened in the Middle East; we knew they happened in Northern Ireland; we knew they happened in Britain; we knew they happened in Sri Lanka; but this was in the U.S. of A. We were NOT well prepared. We've had to scramble since then and we continue to react.

And then along came anthrax. That awakened us to the reality of bioterrorism IN THE U.S.A.! We thought nobody would dare; but somebody did. And it is much easier and less expensive to grow bacteria cultures or virus than it is to build a nuclear bomb or many other potential weapons of terrorism.

Although it seems unlikely that terrorists would directly target corrections, as part of larger communities we are at risk and would be affected by bioterrorism or other types of mass casualty incidents. We must be sure our emergency operations procedures include plans to deal with bioterrorism and that we have established lines of communications with both public safety and public health agencies. As you read about specific potential bioterrorism agents, think also about your response system and your communication links, especially with public health. The agent used could be something nobody has discussed but our systems must be ready to rapidly exchange information and respond. Safety and lives of our staff and our inmates may depend upon it.

After reading this issue, providers should be familiar with the presentations of and treatments for the bioterrorism pathogens discussed. Furthermore, since we hope that smallpox will not be common in corrections we have included an algorithm for the management of VZV, a pox more common in corrections. In addition, providers should have a sense of the various viral infections associated with HIV infection including their manifestations and ways to treat and prevent these infections.



Lester N. Wright, MD

Published monthly and distributed by fax, HEPP News provides up-to-the-moment information on HIV and hepatitis treatment, efficient approaches to administering treatment in the correctional environment, national and international news related to HIV and hepatitis in prisons and jails, and changes in correctional care that impact HIV and hepatitis treatment.

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belonging to Enterobacteriaceae. The bacterium has several chromosomal and plasmid-associated factors that are linked with virulence and survival in mammalian hosts (such as rats) as well as the flea vector. Plague is endemic in certain areas of the world, causing epidemics when local conditions contribute to rodent infestation of human living quarters. More than 18,000 cases of plague were reported to WHO between 1980 and 1994.²² One recent outbreak (Madagascar, 1996) was also marked by the discovery of two strains of multi-drug resistant *Y. pestis*, raising concern about the efficacy of antibiotics against plague in the future.²¹

Plague: Clinical course

Infection follows transmission by flea bite, by direct contact with infectious body fluids or by inhalation of airborne aerosolized bacteria. Infection causes an illness that is characterized by severe fever, myalgia, malaise, shaking chills, prostration, and gastrointestinal symptoms. The three forms of plague are bubonic, pneumonic, and septicemic.

Bubonic plague is the most common form of the disease, or 80 to 90% of the cases reported to the CDC in the United States. The incubation period of bubonic plague is two to six days. The most striking physical manifestations of bubonic plague are enlarged, necrotic lymph nodes (buboes) of the groin or armpit closest to the site of infection. Buboes are caused by *Y. pestis* infected macrophages migrating to the local lymph nodes. Septicemic plague occurs when *Y. pestis* invades and multiplies in the blood stream. The case-fatality rate of septicemic plague is 50% (most of these cases received treatment). Pneumonic plague is the most dangerous and fatal form of the disease, and the form most likely to occur when used as a terrorist weapon. The incubation period is one to three days, and patients who do not receive adequate treatment within 18 hours after the onset of respiratory symptoms are unlikely to survive.

An aerosolized plague weapon could cause fever, cough, chest pain, and hemoptysis with signs consistent with severe pneumonia one to six hours after exposure. Rapid evolution of disease would occur in the two to four days after symptom onset and would lead to septic shock with high mortality without early treatment. If 50 kg of *Y. pestis* were released as an aerosol over a city of five million, pneumonic plague would occur in as many as 150,000 persons, and 36,000 could die.²³

Plague: Treatment and Vaccine

Early treatment and prophylaxis with tetracy-

TABLE 4. Treatment of Infections from Pathogens Likely to be used in Bioterrorism

| Pathogen | Preferred Treatment | Alternative Treatment | Comments |
|------------------------------------|--|--|---|
| Inhalation ^I Anthrax | Initial (intravenous): Ciprofloxacin 400 mg every 12h OR Doxycycline 100 mg every 12 h AND one or two additional antimicrobials | Immunocompromised individuals: same as non-immunocompromised adults** | IV initially. Switch to oral antimicrobial therapy when appropriate: Ciprofloxacin 500 mg po BID OR Doxycycline 100 mg po BID Continue for 60 days (IV and po combined) |
| Cutaneous ^I Anthrax | (oral): Ciprofloxacin 500 mg po BID OR Doxycycline 100 mg po BID | Immunocompromised individuals: same as non-immunocompromised adults** | 60 Days |
| Plague ^{II} | contained casualty setting: Streptomycin 1 g IM twice daily | contained casualty setting: Doxycycline, 100 mg IV twice daily or 200 mg IV once daily Ciprofloxacin, 400 mg IV twice daily Chloramphenicol, 25 mg/kg IV 4 times daily** | For mass casualty and postexposure prophylaxis, see www.bt.cdc.gov/Agent/Plague/Consensus.pdf |
| Tularemia ^{III} | Streptomycin 15-20 mg/kg/day IM in divided doses x 7-14 days | Gentamicin 2-5 mg/kg/day in divided doses x 7-14 days | Clinical relapse occurs more frequently when tetracycline or chloramphenicol are used (loading dose 30 mg/kg orally, then 30 mg/kg/day orally in divided doses x 14 D) |
| Small Pox ^{IV} | There is no proven treatment for smallpox. Patients with smallpox can benefit from supportive therapy (intravenous fluids, medicine to control fever or pain, etc.) and antibiotics for any secondary bacterial infections that occur. | | In people exposed to smallpox, the vaccine can lessen the severity of, or even prevent illness if given within 4 days after exposure. |

I. MMWR 50 (42): 917-919.

II. These guidelines are from a consensus paper. There have not been large published trials of treating plague in humans. <http://www.bt.cdc.gov/Agent/Plague/Consensus.pdf>

III. Mandell GL, Douglas RG, Bennett JE eds. *Principles and Practice of Infectious Diseases*. Churchill Livingston Inc; New York: 1985.

IV. http://www.bt.cdc.gov/DocumentsApp/FactsAbout/facts_about.pdf

*For more guidelines, visit the CDC at <http://www.bt.cdc.gov/DocumentsApp/Anthrax/10312001/han51.asp> and <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5043a6.htm>

** For guidelines on pregnant women and children, see MMWR 50 (42): 917-919.

cline (doxycycline) or fluoroquinolones (Ciprofloxacin, ofloxacin) is effective. Streptomycin or gentamicin is also effective.¹⁹ Killed bacteria have been used in plague vaccine since 1896. The only whole cell (killed) vaccine produced in the U. S. was discontinued by its manufacturers in 1999. Plans for future production or licensing are unclear. The vaccine was prepared from formalin-inactivated *Y. pestis* organisms. Reactions to the vaccine were reported, tended to increase in number and severity as the number of doses increased, and, on occasion, were fatal.²⁴ However, the vaccine appears to be effective. Only eight cases of plague were diagnosed among U.S. personnel in Vietnam who received

plague vaccine (one case per 106 person years of exposure). In contrast, there were thousands of cases of plague among citizens in Vietnam during the same period (333 cases per 106 person years of exposure, 1961-1971). It is not clear whether the vaccine protects against pneumonic plague, as there were at least two reported cases of pneumonic plague in successfully vaccinated military personnel.²⁵

TULAREMIA

Tularemia: Pathogen

Tularemia is a disease caused by the facultative intracellular bacterium, *Francisella tularensis*. Infection is usually associated with exposure to rabbits, and tick bites

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appear to be the main means of transmission to humans. The peak incidence was in 1939, when about 2,300 cases were reported. An outbreak of tularemia recently occurred on Martha's Vineyard.²⁶

Tularemia: Clinical Course

After cutaneous exposure, Tularemia can present as slow to heal ulcer at the site of contact, along with swelling of the regional lymph nodes. Oral ingestion can cause pharyngitis, abdominal pain, diarrhea and vomiting. Inhalation of infectious material may be followed by pneumonic involvement or a primary septicemic syndrome. The pneumonic/septicemic syndrome is associated with a 30%-60% case-fatality rate if untreated, and it is very similar to the presentation of anthrax.

Tularemia: Treatment and Vaccine

Prompt treatment with streptomycin, gentamicin, doxycycline, or ciprofloxacin is recommended. Prophylactic use of doxycycline or ciprofloxacin may be useful in the early postexposure period.²⁷ Immediately after a bioterrorist event, 14 days of oral doxycycline or ciprofloxacin should be administered to exposed persons, as only 10 organisms are required to produce disease. If the attack is only recognized after several persons have become ill, persons who may have been exposed should not take prophylaxis, instead, they should be instructed to begin a "fever watch" (notifying their physician if a fever develops and seeking prompt treatment). Any unexplained fever or flu-like illness that occurs within 14 days of exposure would indicate that treatment should begin.

The existing Tularemia vaccine is a live organism derived by attenuation (LVS). The molecular basis of attenuation of the LVS strain and the degree of attenuation is unclear. Protective immunity is incomplete.²⁸ Furthermore, quality control type problems with "scale up" of the existing vaccine may impede the use of the LVS as a preventive vaccine in the context of large-scale vaccination campaigns.

SMALLPOX

Smallpox: Pathogen

Smallpox is the most feared and potentially devastating of all commonly discussed bioterrorist agents because of the potential for dissemination from person to person after a terrorist event, and the lack of antiviral agents for treatment. Smallpox spreads from person to person via respiratory secretions, direct contact with lesions, and by contaminated clothing and linens (infected blankets were once used by British troops to disseminate smallpox among American Indians). Smallpox is fatal in approximately a third of previously unvaccinated persons.

Smallpox can be manufactured in large quantities, can be stored for long periods of time, and is infectious as when distributed as an aerosol. Furthermore, because the WHO campaign in the 1970's eradicated circulating virus, vaccination was discontinued and therefore, a large percentage of the current population has no immunity to the virus. The stockpile of smallpox vaccine currently available is controlled by the CDC and is decades old. It is thought not to be nearly enough to contain a US outbreak.²⁹

The incubation period for smallpox (variola) has been estimated to be from nine to 13 days. Onset is marked by the occurrence of the first lesions - as these are usually flattened, brown, macules and not vesicles, so the prodromal stage may be missed by inexperienced medical personnel. The infected individual is contagious once these macules have occurred. Fever develops late in the prodrome (2nd or 3rd days). The overtly symptomatic stage, which coincides with the onset of a vesicular rash predominantly on the extremities and face and less prominent on the trunk (that progresses, over weeks, to eschars), typically occurs 48 to 72 hours after the onset of fever, and lasts up to 21 days. The infected individual is contagious during the entire symptomatic period, however, the prodromal phase (when the patient is not yet confined to bed by severe illness) is the period when dissemination is expected to occur. Quarantine is an extremely effective measure.

Smallpox: Treatment and Vaccine

One antiviral agent, Cidofovir, has recently proven useful in the treatment of cowpox infections in mice. Whether or not it can be used to treat smallpox in a bioterrorist event is not clear (and is not approved).³⁰

Smallpox (variola) immunity is achieved by vaccination with a live, related virus (vaccinia, or cowpox), using methods first described by Jenner in the late 1700's. If mass vaccination were necessary now, it would be difficult to screen out individuals at risk for adverse vaccination effects. Severe, occasionally fatal, cases of cowpox have occurred in eczematous and immunosuppressed individuals, although cowpox has not yet been reported in anyone infected with the human immunodeficiency virus.³¹ Furthermore, because the smallpox vaccine is live, the infection can be passed from person to person. Although this is not a complication for healthy people, it has the potential to cause problems for immunocompromised (i.e. HIV-positive) people, if they were to come into contact with vaccinated individuals. The impact of vaccination of large populations, especially in cities where HIV infection is common, is difficult to assess.

Another problem with the smallpox vaccine is the medium used to propagate the virus.

Smallpox vaccine was made by Wyeth Laboratories from a strain originally isolated by the New York City Board of Health. Live vaccine strain vaccinia (cowpox) was originally harvested from the lesions on vaccinia-infected cows. Wyeth discontinued making the vaccine available for public use in 1983, however, they recently received several billion dollars from the department of defense to re-develop the facilities, infrastructure, and expertise to produce the smallpox vaccine, using cell culture techniques. Continued use of cows or other live animals for vaccine production may pose many complications including contamination with bacteria, viruses, or prions, and animal proteins causing adverse reactions in humans. Regardless of the type of vaccine that is made, in the U.S. alone at least 40 million doses of small pox vaccine are needed in order to stop an outbreak following a bioterrorist event.²⁹

CONCLUSION

The four most important lessons learned in the context of recent bioterrorist events are that: 1) Delay in intervention can be costly, leading to an increase in the number of cases that occur and mortality associated with those cases; 2) Post-attack intervention should combine rapid treatment of individuals who have the disease, quarantine (if smallpox), antibiotic prophylaxis (if indicated) and vaccination (if available); 3) Proper planning includes training of medical, public health and public safety personnel to recognize the infectious agent or event and respond appropriately; and 4) Stockpiles of vaccines and antibiotics should be developed by the authorities. Public health authorities and policymakers need to make detailed response plans available (on the web and in other public locations). And, as we learned from our own experience in corrections, a large part of the preparation for bioterrorist events involves educating medical personnel and staff so that they are familiar with bioterrorism agents and aware of the appropriate procedures and protocols to follow.

*Consultant & Speaker's Bureau: Abbott, Agouron Pharmaceuticals, Merck, Roche, Boehringer-Ingelheim/Roxane Laboratories.

**Nothing to disclose

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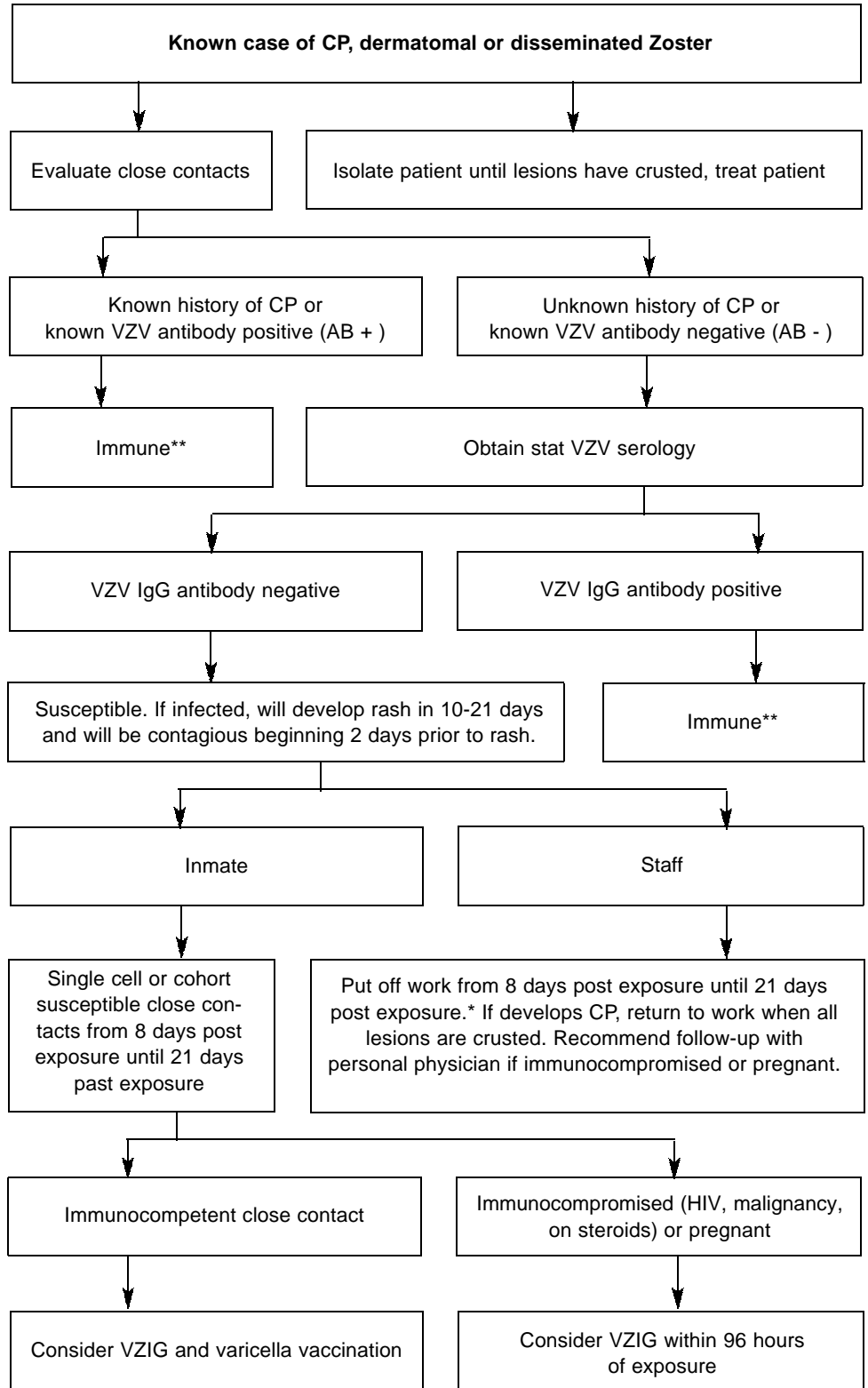
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HEPPIGRAM: A More Common Pox

Management of Varicella Zoster Exposure in a Congregate Living Environment (Chicken Pox (CP) or Shingles)



Developed by Joseph Bick, M.D., Editor, HEPP News. ^Nothing to disclose

VZV=Varicella Zoster Virus

VZIG=Varicella Zoster Immune Globulin

*Alternatively, assign to work in area where no contact with immunocompromised or pregnant individuals.

**And has been observed in both HIV-positive and HIV-negative patients. These cases are rare and tend to be mild.

Management of HIV-Related Viral Diseases

| Common Name | Scientific Name | Virus Family | Manifestation | Treatment | Prevention |
|---|--|-----------------------|---|--|--|
| Flu | Influenza | Orthomyxo- viridae | Bronchopneumonia, interstitial infiltrates | (not yet standard) Amantadine/ramanta- dine or neuramidase inhibitors | Preferred: Flu vac- cine 0.5 mL IM yearly (Oct/Nov) |
| Chicken Pox | Varicella Zoster (primary) | Herpesviridae | Vesicles on erythema- tous base | Acyclovir 800 mg PO 5x/D x 7-10 D (acy- clovir resistant: Foscarnet 40 mg/kg IV q8h) ** | If necessary after exposure*: VZIG 5 vials (6.25 mL) IM within 48-96 h of exposure (AIII) |
| Shingles | Varicella Zoster (dermatomal zoster) | Herpesviridae | Vesicles on erythema- tous base, usually uni- lateral, dermatomal | Acyclovir 10 mg/kg IV q8h x 7 D or 800 mg PO 5x/D x 7-10 D* (acyclovir resistant: Foscarnet 40 mg/kg IV q8h)** | If necessary after exposure*: VZIG 5 vials (6.25 mL) IM within 48-96 h of exposure (AIII) |
| CMV | Cytomegalovirus | Herpesviridae | Ophthalmitis, Pneumonia, Hepatitis, Gastroenteritis | Ganciclovir 5mg/kg IV bid x 14-21 days or foscarnet 60 mg/kg IV q8h x 14-21 D | Oral ganciclovir 1g PO tid (CI) |
| "Mono" and Oral Hairy Leukoplakia | Epstein Barr Virus | Herpesviridae | White plaques with vertical folds; patches/ confluent on tongue, usually lateral surface ± dorsum | Acyclovir 800 mg PO 5x/day x 2-3 weeks, then 1.2-2g/day; Tretinoin (Retin A) 0.025% to 0.05% solu- tion applied 2-3x/day | No prevention; Present in approxi- mately 20% of asymptomatic HIV- positive patients, common as the dis- ease progresses |
| Kaposi's Sarcoma | KSHV or Human Herpes Virus-8 (HHV8) | Herpesviridae | One or more red or violaceous macules, papules or nodules (usually in cooler loca- tions of the body) | IF local: topical liquid nitrogen; intralesional vinblastine (0.01 mg - 0.02 mg/ lesion) q 2 wks x3; radiation (low does, eg 400 rads/ week x 6 weeks); laser† | ART often improves KS lesions in the absence of specific therapy |
| G Cold sores | G Herpes Simplex Virus 1 (HSV1) | Herpesviridae | Cluster of vesicles on erythematous base | Acyclovir 200 mg PO 5x/D or 400 mg 3x/D; p to 800 mg PO 5x/D or IV acyclovir 5 to 10 mg/kg q8h x 5 to 7 D; famciclovir 125 mg PO bid; valacyclovir 0.5 to 1 g PO bid; or foscar- net 40 mg/kg IV q8 h or 60 mg q12h | Acyclovir 400 mg PO bid or famciclovir 125-250 mg PO bid or valacyclovir 500 mg PO bid or 1 g/D |
| G Genital Herpes | G Herpes Simplex Virus 2 (HSV2) | | | | |

†IF Systemic KS: Liposomal daunorubicin (DaunoXome) 40-60 mg/m² IV q 2 weeks or liposomal doxorubicin (Doxil) x 10-20 mg/m²; Taxol 100-135 mg/m² q 2-3 weeks; adriamycin, bleomycin, and either vincristine or vinblastine (ABV); vincristine/vinblastine; bleomycin/vinca alkaloids; alpha interferon (18-36 million IU/D) IM or SC x 10-12 weeks then 18 M.U./D-36 M.U. 3X/ week = million units

*Indications for VZIG = exposure to varicella zoster in: a non-immune immunocompromised individual, an immunocompromised person whose varicella status is unknown; and a non-immune pregnant woman

** Famciclovir or valacyclovir are frequently preferred for oral therapy of shingles due to easier adherence, better efficacy, or improved drug levels.

Strength of Recommendation Ratings: A: Should always be offered; B: Should generally be offered; C: Optional; D: Should generally NOT be offered; E: Should NEVER be offered

Quality of Evidence: I: Evidence from at least one properly randomized, controlled trial; II: Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than once center), or from multiple time-series studies. Or dramatic results from uncontrolled experiments; III: Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

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SAVE THE DATES

2002 National STD Prevention Conference

March 4-7, 2002

San Diego, California

Fee: after Feb. 8: \$165

Visit: <http://www.stdconference.org/>

Call: Glenda Vaughn,

404.639.8260

Email: ghv1@cdc.gov

Management of HIV/AIDS in the Correctional Setting: A Live Satellite Videoconference Series

"Dermatological Manifestations of HIV Infection"

March 12, 2002

12:30-3:30 p.m. EST

Call: 518-262-4674

Email: ybarraj@mail.amc.edu

Visit: www.amc.edu/patient/HIV/hivconf.htm

CME credit Available

American Correctional Health Services Association Annual Conference

March 14-17, 2002

Portland, Oregon

"Corrections in the Continuum of Care"

Fee: members \$245;

nonmembers \$295

Email: achsa@mindspring.com

Call: 636.561.8857

Fax: 636.625.6356

Visit: <http://www.corrections.com/achsa/>

14th National HIV/AIDS Update Conference (NAUC)

March 19-22, 2002

San Francisco, California

Sponsored by amfAr

Fee: Dec 15-March 1: \$325;

After March 1: \$375

(special rates available)

Visit: <http://www.amfar.org/cgi-bin/iowa/nauc/index.html>

CME credit available

International Conference on Emerging Infectious Diseases (ICEID)

March 24-27, 2002

Atlanta, Georgia

Fee: before March 4: \$300;

on-site: \$350

Visit: <http://www.cdc.gov/iceid/>

Call: Charles Schable,

404.639.4581

Email: cas1@cdc.gov

INSIDE NEWS

HIV

Half of HIV-positive Patients Harbor Drug-Resistant Virus

Washington Post, 12/19/01

A report at the annual American Society of Microbiologists (ASM) meeting revealed that approximately half of HIV-positive patients are infected with virus resistant to at least one anti-retroviral drug. The study surveyed patients in cities and rural areas across the US, in small clinics and large hospitals in 1999. The study found 37% of patients with no detectable virus, while of the remaining 63% of patients with detectable virus, 78% had drug-resistant virus. Overall, 49% of HIV-positive patients are infected with drug-resistant virus. A similar study presented at ICAAC linked the lowest CD4+ cell count in the patient's history to the likelihood of developing drug resistance. Ninety percent of patients whose lowest CD4+ cell count was <50 had developed drug resistance compared with 80% of patients whose lowest CD4+ count was between 50 and 200, 50% of patients whose CD4+ count never dropped below 500. Experts interpret this as support for starting treatment early.

STI Looks Promising for Some Patients

A new review of information on Structured Treatment Interruption (STI) has revealed that HAART treatment that incorporates STI may be beneficial for patients who are newly infected with HIV. Studies of small patient cohorts have found that newly infected patients who are put on a HAART regimen that includes STI are able to maintain long-term control of viral replication. The optimal length of the on-drug/off-drug cycle has not yet been determined and it is not known if STI could provide any benefit to chronically-infected HIV patients with significant immune system damage (Lori, JAMA 2001; 286:2981-2987). To help answer some of these questions, the National Institute of Allergy and Infectious Diseases (NIAID) is organizing a larger study on the outcomes of patients placed on a Structured Treatment Interruption (STI) regimen. Half of the participants will be put on continuous HAART

therapy while the other half will be put on a HAART regimen including STI. Possible STI benefits include fewer side effects from drug toxicity for the patient and a cost reduction for Medicaid and insurance companies (Rocky Mountain News, 1/10/02; Denver Post, 1/10/02). For more on STI, see HEPP News, Oct. 2001.

HIV-Positive Californians Guaranteed Access to HIV Specialists

BW HealthWire, 1/6/02

California currently has a law that requires managed care companies to provide HIV-positive patients with HIV medical specialists. Beginning July 1, 2002, those who wish to be recognized as HIV specialists must be certified by the American Academy of HIV Medicine (AAHIVM), or meet the specific accreditation criteria. For information on free accreditation, visit www.aahivm.org or call 866-241-9601.

HEPATITIS

Demand Exceeds Supply: PEG-Intron

Wall Street Journal, 1/16/02

Schering-Plough announced that demand for the new HCV drug PEG-Intron (pegylated interferon) (see Newsflashes, HEPP News October 2001) currently exceeds supply. To address this, Schering has developed a procedure for all patients who wish to begin drug treatment. Most new patients may wait 10-12 weeks before beginning their PEG-Intron treatment. However, all 60,000 patients who are already being treated with the medication should not experience any problems with the supply. There is supply set-aside for "urgent" requests for PEG-Intron, which will be reviewed by a medical committee. For more information, call 908.298.2202.

Hepatitis C Protease Inhibitor

New York Times, 1/7/02

Like HIV, Hepatitis C Virus (HCV) needs its protease enzyme for replication. Eli Lilly and Co. and Vertex Pharmaceuticals have been working on a new anti-HCV drug, a protease inhibitor that blocks the function of the protease enzyme. This new drug can be taken orally and is expected to enter human trials in 2003.

RESOURCES & WEBSITES

CDC Public Health Emergency Preparedness and Response

information on various biopathogens is available from the CDC at:

www.bt.cdc.gov/

www.cdc.gov/mmwr/indexbt.html

www.cdc.gov/mmwr/PDF/wk/mm5041.pdf

www.cdc.gov/mmwr/PDF/wk/mm5042.pdf

www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp

www.bt.cdc.gov/Agent/Anthrax/Anthrax.asp

www.bt.cdc.gov/Agent/Tularemia/Tularemia.asp

www.bt.cdc.gov/Agent/Botulism/Botulism.asp

www.cdc.gov/mmwr/preview/mmwrhtml/mm5041a2.htm

Educational Video on Bioterrorism in the Mail

available for people who sort, process and deliver mail. Order from the Public Health Foundation

(PHF): call 877.252.1200; fax 301.843.0159; or visit <http://bookstore.pfh.org>

Anthrax Information

<http://www.anthrax.osd.mil/>

HIV TREATMENT RESOURCES

NEW Adult and Adolescent HIV Treatment guidelines

<http://www.hivatis.org/guidelines/adult/>

Feb04_02/AdultGdl.pdf

NEW HHS Guidelines for the use of Antiretrovirals in Pregnant Women

<http://www.hivatis.org/guidelines/perinatal/>

Feb4_02/Perin.pdf

SELF-ASSESSMENT TEST FOR CONTINUING MEDICAL EDUCATION CREDIT

Brown Medical School designates this educational activity for 1 hour in category 1 credit toward the AMA Physician's Recognition Award. To be eligible for CME credit, answer the questions below by circling the letter next to the correct answer to each of the questions. A minimum of 70% of the questions must be answered correctly. This activity is eligible for CME credit through August 31, 2002. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. Which of the following is the correct treatment for dermatomal zoster (shingles)?
 - a) Acyclovir 10 mg/kg IV q8h x 7 D or 800 mg PO 5x/D x 7-10 D
 - b) Oral ganciclovir 1g PO tid
 - c) Ganciclovir 5mg/kg IV bid x 14-21 days
 - d) Acyclovir 800 mg PO 5x/day x 2-3 weeks, then 1.2-2g/day; Tretinoin (Retin A) 0.025% to 0.05% solution applied 2-3x/day
 - e) Ganciclovir 10 mg/kg IV q 8h x 7D or 800 mg PO 5x/D x 7-10 D

2. How many days prior to developing a VZV rash is the infected individual considered contagious?
 - a) 24 hours
 - b) 2 days
 - c) 8 days
 - d) 10 days
 - e) 21 days

3. True or False: If a letter is suspected to be contaminated with anthrax, all persons who have handled the letter and/or envelope should wash their hands with soap and water.
 - a) True
 - b) False

4. What is the preferred treatment for a case of inhalation anthrax (initial regimen)?
 - a) oral ciproflaxin 500 mg po BID
 - b) ciproflaxin 400 mg every 12 h IV
 - c) streptomycin 15020 mg/kg/day IM in divided doses
 - d) doxycycline 100 mg every 12 h IV and one or two additional antimicrobials
 - e) b or d

5. Which antibiotics were recommended in the most recent anthrax cases?
 - a) Doxycycline + ciproflaxin
 - b) penicillin VK + amoxicillin
 - c) piperacillin + gentamicin
 - d) a and b
 - e) a, b, and c

6. Which of the following antimicrobials is effective against plague?
 - a) streptomycin
 - b) doxycycline
 - c) gentamicin
 - d) ciproflaxin or ofloxacin
 - e) all of the above

HEPP NEWS EVALUATION

5 Excellent 4 Very Good 3 Fair 2 Poor 1 Very Poor

1. Please evaluate the following sections with respect to:

| | educational value | clarity |
|----------------|-------------------|-----------|
| Main Article | 5 4 3 2 1 | 5 4 3 2 1 |
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