

BIOLOGIC DISASTER

Tab G

I. Introduction

This Biologic Disaster policy is an addendum to the hospital's external disaster plan. Bioterrorism may occur as a covert event, in which persons are unknowingly exposed and an outbreak is suspected only upon recognition of unusual disease clusters or symptoms. Bioterrorism may also occur as announced events, in which persons are warned that an exposure has occurred.

II. Epidemiologic Features

Epidemiologic principles must be used to assess whether a patient's presentation is typical of an endemic disease or is an unusual event that should raise concern. Features that should alert healthcare providers to the possibility of a bioterrorism-related outbreak include:

- A rapidly increasing disease incidence (e.g., within hours or days) in a normally health population.
- An epidemic curve that rises and falls during a short period of time.
- An unusual increase in the number of people seeking care, especially with fever, respiratory, or gastrointestinal complaints.
- An endemic disease rapidly emerging at an uncharacteristic time or in an unusual pattern.
- Lower attack rates among people who had been indoors, especially in areas with filtered air or closed ventilation systems, compared with people who had been outdoors.
- Clusters of patients arriving from a single locale.
- Large numbers of rapidly fatal cases.
- Any patient presenting with a disease that is relatively uncommon and has bioterrorism potential (e.g., pulmonary anthrax, tularemia, or plague).

UMMC may be the initial site of recognition and response to a bioterrorism event. If a bioterrorism event occurs or is suspected management of the event will be the responsibility of the Medical Director, Chief of Staff, Hospital Epidemiologist, and Administrator on call. It will be their responsibility to notify the following of the suspicion of a bioterrorism event.

Internal Contacts

Vice Chancellor (601) 984-1010

Infection Control (601) 984-3942

Administrator on Call (601) 984-1000 Ask to page the AOC

External Contacts

State Epidemiologist (601) 576-7725 (day)
(601) 576-7400 (nights and weekends)

Infection Control Practices for Patient Management

III. Isolation Precautions

Agents of bioterrorism are generally not transmitted from person to person; re-aerosolization of these agents is unlikely. All patients in healthcare facilities, including symptomatic patients with suspected or confirmed bioterrorism-related illnesses should be managed utilizing Standard Precautions.

Standard Precautions are designed to reduce transmission from both recognized and unrecognized sources of infection in healthcare facilities, and are recommended for all patients receiving care, regardless of their diagnosis or presumed infection status. For certain diseases or syndromes (e.g., smallpox and pneumonic plague), additional precautions may be needed to reduce the likelihood for transmission. See Section II for specific diseases and requirements for additional isolation precautions.

IV. Standard Precautions prevent direct contact with all body fluids (including blood), secretions, excretions, non-intact skin (including rashes), and mucous membranes. Standard Precautions routinely practiced by healthcare providers include:

- **Hand washing**
Hands are washed after touching blood, body fluids, excretions, secretions, or items contaminated with such body fluids, whether or not gloves are worn. Hands are washed immediately after gloves are removed, between patient contacts, and as appropriate to avoid transfer of microorganisms to other patients and the environment. Either plain or antimicrobial-containing soaps may be used.
- **Gloves**
Clean, non-sterile gloves are worn when touching blood, body fluids, excretions, secretions, or items contaminated with such body fluids. Clean gloves are put on just before touching mucous membranes and non-intact skin. Gloves are changed between tasks and between procedures on the same patient if contact occurs with contaminated material. Hands are washed promptly after removing gloves and before leaving a patient care area.

- **Masks/Eye Protection or Face Shields**
A mask and eye protection (or face shield) are worn to protect mucous membranes of the eyes, nose, and mouth while performing procedures and patient care activities that may cause splashes of blood, body fluids, excretions, or secretions.
- **Gowns**
A gown is worn to protect skin and prevent soiling of clothing during procedures and patient-care activities that are likely to generate splashes or sprays of blood, body fluids, excretions, or secretions. Selection of gowns and gown materials should be suitable for the activity and amount of body fluid likely to be encountered. Soiled gowns are removed promptly and hands are washed to avoid transfer of microorganisms to other patients and environments.

V. Patient Placement

In small-scale events, routine facility placement and Infection Control Practice will be followed. If greater than five patients are admitted they will be cohorted to the end of Ward 6W. If additional patients must be admitted they will also be placed on Ward 6W with patients transferred to other wards or discharged. If Ward 6W exceeds capacity patients will be cohorted to successive wards.

The Incident Commander, with input from the Hospital Epidemiologist, Administrator on Call, and Director of Nursing, will designate additional resources as necessary to accommodate additional patients. Wards to be used will be determined according to the type of event.

VI. Patient Transport

Most infections associated with bioterrorism agents cannot be transmitted from patient-to-patient. Patient transport requirements for specific potential agents of bioterrorism are listed in Section II. In general, the transport and movement of patients with bioterrorism-related infections, as for patients with any epidemiologically important infections (e.g., pulmonary tuberculosis, chickenpox, measles), should be limited to movement that is essential to provide patient care, thus reducing the opportunities for transmission of microorganisms within healthcare facilities.

VII. Cleaning, disinfection, and sterilization of equipment and environment.

Cleaning and disinfection policies currently in place at UMMC are adequate in virtually all Bioterrorism sections and should be strictly

followed. Standard Precautions will be followed at all times. **See specific disease entities in Section II.**

VIII. Discharge Management

Ideally, patients with bioterrorism-related infections should not be discharged until they are deemed non-infectious. However, large numbers of individuals exposed may preclude hospitalization of all exposed individuals. In this event, family members should be supplied with a copy of the appropriate information sheet found in **Section III.**

IX. Management of those not acutely ill

In the event of a bioterrorism event, campus security will attempt to limit access of the Emergency Department to only those in acute need. The “worried well” i.e. those needing only some reassurance but manifesting no symptoms of an agent of bioterrorism will be referred to a clinic site at the University Hospital Pavilion. The Administrator on call will contact the Chairman of the Department of Medicine, Chairman of the Department of Emergency Medicine, Chief of Nursing Services and Chief of the Division of Infectious Diseases to arrange emergency staffing of this clinic. Ideally the clinic would be staffed by faculty of the Division of Infectious Diseases and Emergency Medicine Department and resident physicians from the same programs. Further sites could be opened at the Medical Mall or Student Union if the need arose.

*After coordination with the ED Faculty, mechanism for rapid evaluation/triage of less ill patients may be implemented.

1. **PURPOSE:** To describe procedures for management of an influx of infectious patients from a community or inpatient outbreak.
2. **POLICY:** The Vice Chancellor and/or Administrator on Call, or Hospital Epidemiologist, or designee will initiate immediate action where a cluster, endemic, epidemic, bioterrorism event, or other dangerous situation exists. This may include ordering cultures, isolation of a patient group, unit closing, halting services or other quarantine measures or initiating the Medical Center Emergency Plan. Further analysis, epidemiological investigation and action will occur as directed by the Hospital Epidemiologist or designee and/or the Emergency Operating Center. Refer to Attachment A for details specific to a pandemic influenza outbreak.
3. **DESCRIPTION:** An influx of infectious patients would involve an outbreak (epidemic) or increase of infections above the expected norm. The increase can occur with or without warning and may involve the facility, region, nation or across nations (pandemic). It may be naturally occurring or involve an act of bioterrorism. In most cases, it will occur gradually with some warning detected through surveillance systems which allows the Medical Center to plan and transition from daily operations to emergency treatment. There are two major elements of the Medical Center mission if an influx of infectious patients should occur: treatment of infectious patients and containment or prevention of transmission of infection.
4. **PROCEDURES:**

Notification of an Influx of Infectious Patients:

1. Unannounced – Clinics may be the first to recognize unusual disease occurrence and initiate a response. The situations and symptoms may alert you to the possibility of an event:
 - a. An unusual increase in patients, especially with fever, respiratory, or gastrointestinal complaints.
 - b. Clusters of patients arriving from a single locale.
 - c. A rapid increase in disease (e.g. within hours or days) in a normally healthy population.
 - d. A single patient with possible bioterrorism-related disease (e.g. anthrax, tularemia, or plague).
2. Announced – An outbreak may be detected through routine infection control surveillance or notification may be received through communication with public health agencies. Depending on the urgency of the infectious event, notices will be distributed by the hospital Chief Executive Officer via intranet, telephone and/or pager to

key medical center staff, including the Administrators, Hospital Epidemiologist, Infection Control Nurses, Safety Officer, Nurse Managers, and Police.

3. The first person to become aware of an actual or suspected influx of infectious patients should immediately notify their supervisor or during non-administrative hours, the Administrator on Call, who will notify the Hospital Epidemiologist and/or the Infection Control Nurses who will then notify the Medical Directors, Nurse Managers and the Chief of Staff.

Validation of Influx of Infectious Patients:

Upon notification of an event or impending event the Infection Control Department will verify the occurrence and nature of the infectious disease process, geographic locations, and transmission route. It may be necessary to initiate a response based on symptoms, rather than lab results. Upon verification of the event the Administrator on Call or designee at the recommendation of the Infection Control Department will activate the treatment and control measures below, in their entirety or any segment of the plan appropriate to the event.

Management:

1. Events limited in scope will be managed through Hospital Administration and the Infection Control Department with daily briefings to leadership. The Chief Executive Officer will identify and appoint key personnel to the team including the Hospital Epidemiologist, Infection Control Nurses, Microbiologists, and applicable Medical Directors and Nurse Managers.
2. Large-scale events will trigger activation of the Medical Center Emergency Plan. The Infection Control Department will be represented in the emergency Operating Center:

*Early decisions will be made in reference to establishing designated wards for management of these patients with appropriate isolation procedures.

3. The management team will:
 - a. Validate and determine the scope of influx event.
 - b. Direct implementation of emergency control actions.
 - c. Communicate with key personnel.
 - d. Establish communications with appropriate community, state and federal agencies.

- e. Maintain a chronological list of event activities.
- f. Ensure adequate assignment of medical and other personnel as required by the influx event.
- g. Disseminate any necessary information to key staff for distribution to all staff.
- h. Designate one or more wards as infectious disease wards.
- i. Establish appropriate staffing levels.
- j. Implement increased level/placement of hand washing/barriers material stations
- k. Establish/publish guidelines for accelerated discharge.
- l. Establish/publish guidelines for MedControl/ED/AMR management to allow refusals to transport for cases where medical indications/triage issues limit this resource.

General Control Measures:

1. Manage patients utilizing isolation precautions appropriate to the tentative diagnosis. Use standard precautions, including when appropriate to the disease, respiratory hygiene/cough etiquette on all patients.
 - A. Wear gloves if hand contact with respiratory secretions or potentially contaminated surfaces is expected.
 - B. Wear a gown if soiling of clothes with patient's respiratory secretions is expected.
 - C. Change gloves and gowns after each patient encounter and before touching any non-contaminated items or touching another patient, and perform hand hygiene.
 - D. Decontaminate hands before and after touching the patient, after touching the patient's environment or after touching the patient's respiratory secretions, whether or not gloves are worn.
 - E. When hands are visibly soiled or contaminated with respiratory secretions, wash hands with either a non-antimicrobial or an antimicrobial soap and water. Hand hygiene with plain soap or detergent for at least 15 seconds under running water is an effective method of removing soil and transient microorganisms. If sinks for hand hygiene are not readily available, alcohol-based agents can be used.
 - F. If hands are not visibly soiled and after glove removal, use an alcohol-based hand rub for

routinely decontaminating hands in clinical situations.

Alternatively, wash hands with an antimicrobial soap and water.

- Respiratory Hygiene/Cough Etiquette: For an organism that primarily is transmitted by respiratory secretions, efforts to decrease the spread of secretions and droplets may help limit transmission. A new program called Respiratory Hygiene/Cough Etiquette has been developed to do so. This program should be implemented at the first point of contact with a potentially infected person to prevent the transmission of all respiratory tract infections in healthcare settings, including influenza. A Respiratory Hygiene/Cough Etiquette program includes posting visual alerts instructing patients and persons who accompany them to inform healthcare personnel if they have symptoms of respiratory infection; providing tissues to patients and visitors to cover their mouth and nose when coughing and sneezing; providing dispensers of alcohol-based hand rubs; offering mask to persons who are coughing and encouraging coughing persons to sit at least 3 feet from others.

G. Appropriate use of masks for personnel or for patient should be reviewed under the individual disease in the attachment (i.e., Influenza Attachment A).

2. A triage area for patients and visitors may be set up outside the Emergency Department in the ambulance bay. It may be necessary to triage non-acute cases to an alternate location/clinic (Jackson Medical Mall) and accept only acute cases into the Emergency Department or hospital.
3. The Nurse Manager of each inpatient service will do inventory on existing bed capabilities in the hospital, arrange to discharge patients if necessary and report the number of available beds on an on-going basis.
4. Patients may be cohorted in a designated ward (i.e., 6W in the adult hospital, 2C in pediatric hospital) and follow appropriate isolation precautions if indicated. Limit new non-infected admission to the designated cohort area. Determination should be made at the recommendation of the Infection Control Department whether cohorting of staff (only designated personnel care for “outbreak” patients) is necessary. Movement of staff between wards should be restricted and minimize the number of staff having contact with infected patients to a single small group of healthcare providers if possible. As

applicable assign only vaccinated nursing personnel to work in the cohort when vaccination is possible.

5. The Administrator on Call or designee based on available beds, staff and service may halt elective admissions and procedures, cancel clinics, delay transfers, restrict patient movement/activities, limit visitors and activate any other control measures deemed necessary.
6. If additional isolated rooms are needed, the following units/locations are designated as alternative for admission of patients. These locations were chosen because of suction and oxygen availability, availability of negative-pressure if needed, and proximity to medical services:
 - Cohort cases on 6W in adult hospital, 2C in pediatric hospital
 - Create treatment rooms into patient rooms
 - If for some reason cohorting is not achievable, at least three feet spatial separations should be maintained between the infected patient and other patients and visitors.
 - Patients with known similar infectious diseases or in a confirmed outbreak with similar symptoms may be placed in a room together.
7. Movement and transport of patients with the outbreak infection should be limited as much as possible. In settings where patient transport is common, such as from the Emergency Department to radiology, the Infection Control Department should consider using alternate routes for persons with possible infection and those who have no symptoms of the outbreak infection.
8. Follow routine cleaning procedures. Instructions will be disseminated as needed if the cleaning schedule and waste removal schedule is changed.
9. Visitors with illness should be restricted. Post notices at entrances. If visiting is authorized, develop protocol outlining who can visit, when and limitations including options as only vaccinated visitors, not caring for anyone else, appropriate use of lounges, barrier use and hand hygiene.
10. Personnel with illness should be restricted. Similarly movement of staff between wards should be restricted and minimize the number of staff having contact with infected patients to a single small group of healthcare providers if possible. As applicable, assign only vaccinated nursing personnel to work in the cohort.
11. In the event of multiple ill staff, nursing education will provide education to non-trained and non-specialized workers to assist in patient areas.

a. Treatment:

- i. Current recommendations for treatment, post-exposure prophylaxis and immunization will be used. The Center for Disease Control and Prevention or Mississippi State Department of Health may be consulted, if necessary.
- ii. If mass prophylaxis or treatment with medications, antiviral or vaccinations becomes necessary, alternate sites for medication/vaccine administrations will be set up and information disseminated by Public Affairs.
- iii. Ideally, patients with infections will not be discharged until they are deemed noninfectious. However, in the event that large numbers of persons exposed may preclude admission of all infected patients, home care instructions should be provided (use of appropriate barrier precautions, hand washing, waste management, and cleaning and disinfection of the environment and patient-care items).
- iv. During a large-scale infection-related event, fear and panic can be expected from both patients and healthcare providers. Psychological responses may include anger, unrealistic concerns about infection, and fear of contagion. Minimize panic early by explaining risks, offering careful but rapid medical evaluation/treatment and information to all involved.
- v. Suspend routine environmental practices to support cleaning priority to high-risk areas. Disseminate instructions regarding methods of cleaning, priority areas, waste removal and use of barriers.
- vi. In the event that supplies become limited, instructions regarding conservation re-use, and cleaning will be issued based on recommendations from the ICT in conjunction with each of the services.
- vii. Establish priorities for laboratory studies in the event of overwhelming demand.

- viii. Continue surveillance for healthcare-acquired illness and secondary cases. Collect data related to the number of cases, disposition and clinical data to track the extent and severity of the outbreak. This will be led by the Infection Control Department.

(Reference: International Infection Control Council, *Strategies for Pandemics and Disasters Toolkit*, 2002; National Center for Infectious Diseases and National Immunization Program, *Detection and Control of Influenza Outbreaks*, 20)

Influenza or Infectious Agent with Respiratory Droplet Transmission G - 2 University of Mississippi Hospitals and Clinics Surge Plan for an Outbreak or Epidemic

1. Control of Influenza Outbreak or Epidemic

The primary control measure in a flu outbreak is the utilization of a vaccine that matches the outbreak strain. Other measures are to be utilized to limit the spread of the disease but utilization of vaccine is the primary control measure.

2. Surveillance/ Confirmation of Diagnosis

The Infection Control Department will establish flu syndromic surveillance in the Emergency Department and Outpatient areas and with hospital admissions during the flu season, (traditionally Oct – March). If an outbreak occurs, this surveillance will be utilized to track the percentage of flu-like illness that is seen at UMMC. Active surveillance for nosocomial influenza illness will include any patient with the onset of acute febrile respiratory illness or pneumonia (onset > 48 hours after admission). The former would include a new onset of fever > 100 degrees F, with or without myalgia, malaise, or headache, and with one or more of sore throat, cough, rhinorrhea, or nasal congestion. Respiratory specimens should be sent to the laboratory to determine whether influenza is the etiology. Syndromic surveillance utilized by the CDC will be followed.

If the etiologic agent of a respiratory illness outbreak has not yet been established, the Infection Control Department will obtain nasopharyngeal swabs on appropriate patients and work with the microbiology laboratory and the MSDH to confirm the presence of influenza and whether it is Type A or B.

3. Triage

In a known outbreak or epidemic hospital personnel should refer to infection control procedures listed below for influenza as soon as possible to protect

themselves and other non-infected patients. Also refer to infection control measures below for placement of patients on the floors and/or transport to and from tests or admission to the hospital.

This section is to serve as a guide for triage. The actual course of action taken at the time will be based upon the numbers of patients seen and the decision of the Incident Commander in consultation with the Infection Control Department.

The Triage Officer (or their designees) will establish a triage area for patients and visitors with flu-like illness. It may become necessary to triage non-acute cases to an alternate location/clinic (Jackson Medical Mall) and accept only acute cases into the Emergency Department or hospital.

A. Infection Control

Hand washing remains the primary infection control tool!!!

- a. **Flu Transmission:** Human influenza is transmitted from person to person primarily via virus-laden large droplets (particles $>5 \mu\text{m}$ in diameter) that are generated when infected persons cough or sneeze; these large droplets can then be directly deposited onto the mucosal surfaces of the upper respiratory tract of susceptible persons who are near (i.e., within 3 feet) the droplet source. Transmission also may occur through direct and indirect contact with infectious respiratory secretions.
- b. **Use of Masks:** A combination of infection control strategies is recommended to decrease transmission of influenza in health-care settings. These include placing influenza patients in private rooms when possible and having health-care personnel wear masks for close patient contact (i.e., within 3 feet) and gowns and gloves if contact with respiratory secretions is likely. The use of surgical, N-95, or procedure masks by infectious patients may help contain their respiratory secretions and limit exposure to others. Likewise, when a patient is not wearing a mask, as when in an isolation room, having health-care personnel mask for close contact with the patient may prevent nose and mouth contact with respiratory droplets. However, no studies have definitively shown that mask use by either infectious patients or health-care personnel prevents influenza transmission.

MASKS/Symptomatic or Infected Patients

During periods of increased respiratory infection activity in the community, masks should be offered as part of a respiratory hygiene/cough etiquette strategy to patients who are coughing or have other symptoms of a respiratory infection when they present for health-care services (see Respiratory Hygiene/Cough Etiquette in Healthcare Settings). Masks should be worn by these patients until it

is determined that the cause of symptoms is not an infectious agent that requires isolation precautions to prevent respiratory droplet transmission or the patient has been appropriately isolated, either by placement in a private room or by placement in a room with other patients with the same infection (cohorting). Once isolated, the patient does not need to wear a mask unless transport outside the room is necessary.

MASKS/Health-care Personnel

A surgical mask should be worn by health-care personnel who are in close contact (i.e., within 3 feet) with a patient who has symptoms of a respiratory infection, particularly if fever is present. These precautions should be maintained until the patient has been determined to be noninfectious or for the duration recommended for the specific infectious agent. (See the general information on the influx of infectious patients for recommendations on other control measures).

B. Prophylaxis

Vaccination – Vaccination with the pandemic strain vaccine should occur among those exposed but not ill as soon as it becomes available.

Chemoprophylaxis – 2004-05 Chemoprophylaxis and Treatment Guidelines

Patients/residents - Using antiviral drugs for treatment and prophylaxis of influenza is a key component of influenza outbreak control in institutions. When confirmed or suspected outbreaks of influenza occur in institutions that house persons at high risk, chemoprophylaxis should be started as early as possible to reduce the spread of the virus. When outbreaks occur in institutions, chemoprophylaxis should be administered to all residents, regardless of whether they received influenza vaccinations during the previous fall, and should continue for a minimum of 2 weeks. The dosage for each resident should be determined individually.

Staff - Chemoprophylaxis also can be offered to unvaccinated staff that provides care to persons at high risk. Prophylaxis should be considered for all employees, regardless of their vaccination status, if the outbreak is caused by a variant strain of influenza that is not well-matched by the vaccine.

6. Treatment - (See appendix A for complete dosing information)

In the United States, four antiviral medications (amantadine, rimantadine, oseltamivir, and zanamivir) are approved for treatment of influenza. When used for treatment within the first two days of illness, all four antiviral medications are similarly effective in reducing the duration of illness by one or two days. **People who are at high risk of serious complications** from influenza may benefit most from antiviral medications. Therefore, in general, people who fall into these high risk groups should be given **priority for use of**

influenza antiviral medications if there is any question of the supply available for the outbreak:

Treatment Priorities in an outbreak setting:

- Any person experiencing a potentially life-threatening influenza-related illness should be treated with antiviral medications.
- Any person at high risk for serious complications of influenza and who is within the first 2 days of illness onset should be treated with antiviral medications.

7. Cohorting - To limit the potential transmission of drug-resistant virus during outbreaks in institutions, whether in chronic or acute-care settings or other closed settings, measures should be taken to reduce contact as much as possible between persons taking antiviral drugs for treatment and other persons, including those taking chemoprophylaxis.

If at all possible, patients with flu-like illness should be placed on a ward of patients with similar symptoms who likely have the flu. Dedicated staff should be assigned to these wards. 6 West in the adult hospital and 2CHH in the pediatric hospital will serve as the primary locations if cohorting is deemed necessary.

8. Patient Transport – Movement and transportation of an influenza infected patient should be limited as much as possible. If patient must be transported, the patient should wear a surgical mask. If appropriate and feasible, dedicated routes and/or elevators for persons with flu-like symptoms and those who have no symptoms of influenza may be designated by the Infection Control Department.

9. Disinfection - Any EPA approved veridical solution is appropriate for cleaning. The influenza virus can live in the environment upwards to 6 hours. (See the general information).

(Dosing Guidelines – Check www.cdc.gov/flu for any updates)

Table 7

TABLE 7. Recommended daily dosage of influenza antiviral medications for treatment and prophylaxis

Antiviral agent	Age group (yrs)				
	1–6	7–9	10–12	13–64	≥65
Amantadine* Treatment, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Prophylaxis, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Rimantadine¶ Treatment,** influenza A	NA††	NA	NA	100 mg twice daily§ §§	100 mg/day
Prophylaxis, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	100 mg/day¶¶
Zanamivir*** ††† Treatment, influenza A and B	NA	10 mg twice daily	10 mg twice daily	10 mg twice daily	10 mg twice daily
Oseltamivir Treatment,§§§ influenza A and B	Dose varies by child's weight¶¶¶	Dose varies by child's weight¶¶¶	Dose varies by child's weight¶¶¶	75 mg twice daily	75 mg twice daily
Prophylaxis, influenza A and B	NA	NA	NA	75 mg/day	75 mg/day

NOTE: Amantadine manufacturers include Endo Pharmaceuticals (Symmetrel® — tablet and syrup); Geneva Pharms Tech and Rosemont (Amantadine HCL — capsule); USL Pharma (Amantadine HCL — capsule and tablet); and Alpharma, Copley Pharmaceutical, HiTech Pharma, Mikart, Morton Grove, Carolina Medical, and Pharmaceutical Associates (Amantadine HCL — syrup). Rimantadine is manufactured by Forest Laboratories (Flumadine® — tablet and syrup) and Corepharma, Impax Labs (Rimantadine HCL — tablet), and Amide Pharmaceuticals (Rimantadine ACL — tablet). Zanamivir is manufactured by GlaxoSmithKline (Relenza® — inhaled powder). Oseltamivir is manufactured by Hoffman-LaRoche, Inc. (Tamiflu® — tablet). This information is based on data published by the Food and Drug Administration (FDA), which is available at <http://www.fda.gov>.

* The drug package insert should be consulted for dosage recommendations for administering amantadine to persons with creatinine clearance ≤50 mL/min/1.73m².

† 5 mg/kg body weight of amantadine or rimantadine syrup = 1 tsp/22 lbs.

§ Children aged ≥10 years who weigh <40 kg should be administered amantadine or rimantadine at a dosage of 5 mg/kg body weight/day.

¶ A reduction in dosage to 100 mg/day of rimantadine is recommended for persons who have severe hepatic dysfunction or those with creatinine clearance ≤10 mL/min. Other persons with less severe hepatic or renal dysfunction taking 100 mg/day of rimantadine should be observed closely, and the dosage should be reduced or the drug discontinued, if necessary.

** Only approved by FDA for treatment among adults.

†† Not applicable.

§§ Rimantadine is approved by FDA for treatment among adults. However, certain specialists in the management of influenza consider rimantadine appropriate for treatment among children (see American Academy of Pediatrics, 2000 red book: report of the Committee on Infectious Diseases, 25th ed, Elk Grove Village, IL: American Academy of Pediatrics, 2000).

¶¶ Older nursing-home residents should be administered only 100 mg/day of rimantadine. A reduction in dosage to 100 mg/day should be considered for all persons aged ≥65 years, if they experience possible side effects when taking 200 mg/day.

*** Zanamivir is administered through inhalation by using a plastic device included in the medication package. Patients will benefit from instruction and demonstration of correct use of the device.

††† Zanamivir is not approved for prophylaxis.

§§§ A reduction in the dose of oseltamivir is recommended for persons with creatinine clearance <30 mL/min.

¶¶¶ The dose recommendation for children who weigh ≤15 kg is 30 mg twice a day. For children who weigh >15–23 kg, the dose is 45 mg twice a day. For children who weigh >23–40 kg, the dose is 60 mg twice a day. And, for children who weigh >40 kg, the dose is 75 mg twice a day.

Persons Aged ≥65 Years

Amantadine. The daily dosage of amantadine for persons aged ≥ 65 years should not exceed 100 mg for prophylaxis or treatment, because renal function declines with increasing age. For certain older persons, the dose should be further reduced.

Rimantadine. Among older persons, the incidence and severity of central nervous system (CNS) side effects are substantially lower among those taking rimantadine at a dosage of 100 mg/day than among those taking amantadine at dosages adjusted for estimated renal clearance (287). However, chronically ill older persons have had a higher incidence of CNS and gastrointestinal symptoms and serum concentrations 2--4 times higher than among healthy, younger persons when rimantadine has been administered at a dosage of 200 mg/day (235).

For prophylaxis among persons aged ≥ 65 years, the recommended dosage is 100 mg/day. For treatment of older persons in the community, a reduction in dosage to 100 mg/day should be considered if they experience side effects when taking a dosage of 200 mg/day. For treatment of older nursing home residents, the dosage of rimantadine should be reduced to 100 mg/day (286).

Zanamivir and Oseltamivir. No reduction in dosage is recommended on the basis of age alone.

Persons with Impaired Renal Function

Amantadine. A reduction in dosage is recommended for patients with creatinine clearance ≤ 50 mL/min/1.73m². Guidelines for amantadine dosage on the basis of creatinine clearance are located in the package insert. Because recommended dosages on the basis of creatinine clearance might provide only an approximation of the optimal dose for a given patient, such persons should be observed carefully for adverse reactions. If necessary, further reduction in the dose or discontinuation of the drug might be indicated because of side effects. Hemodialysis contributes minimally to amantadine clearance (288,289).

Rimantadine. A reduction in dosage to 100 mg/day is recommended for persons with creatinine clearance < 10 mL/min. Because of the potential for accumulation of rimantadine and its metabolites, patients with any degree of renal insufficiency, including older persons, should be monitored for adverse effects, and either the dosage should be reduced or the drug should be discontinued, if necessary. Hemodialysis contributes minimally to drug clearance (290).

Zanamivir. Limited data are available regarding the safety and efficacy of zanamivir for patients with impaired renal function. Among patients with renal failure who were administered a single intravenous dose of zanamivir, decreases in renal clearance, increases in half-life, and increased systemic exposure to zanamivir were observed (246,291). However, a limited number of healthy volunteers who were administered high doses of intravenous zanamivir tolerated systemic levels of zanamivir that were substantially higher than those resulting

from administration of zanamivir by oral inhalation at the recommended dose (292,293). On the basis of these considerations, the manufacturer recommends no dose adjustment for inhaled zanamivir for a 5-day course of treatment for patients with either mild to moderate or severe impairment in renal function (246).

Oseltamivir. Serum concentrations of oseltamivir carboxylate (GS4071), the active metabolite of oseltamivir, increase with declining renal function (247,294). For patients with creatinine clearance of 10--30 mL/min (247), a reduction of the treatment dosage of oseltamivir to 75 mg once daily and in the prophylaxis dosage to 75 mg every other day is recommended. No treatment or prophylaxis dosing recommendations are available for patients undergoing routine renal dialysis treatment.

Persons with Liver Disease

Amantadine. No increase in adverse reactions to amantadine has been observed among persons with liver disease. Rare instances of reversible elevation of liver enzymes among patients receiving amantadine have been reported, although a specific relation between the drug and such changes has not been established (295).

Rimantadine. A reduction in dosage to 100 mg/day is recommended for persons with severe hepatic dysfunction.

Zanamivir and Oseltamivir. Neither of these medications has been studied among persons with hepatic dysfunction.

Persons with Seizure Disorders

Amantadine. An increased incidence of seizures has been reported among patients with a history of seizure disorders who have received amantadine (296). Patients with seizure disorders should be observed closely for possible increased seizure activity when taking amantadine.

Rimantadine. Seizures (or seizure-like activity) have been reported among persons with a history of seizures who were not receiving anticonvulsant medication while taking rimantadine (297). The extent to which rimantadine might increase the incidence of seizures among persons with seizure disorders has not been adequately evaluated.

Zanamivir and Oseltamivir. Seizure events have been reported during postmarketing use of zanamivir and oseltamivir, although no epidemiologic studies have reported any increased risk for seizures with either zanamivir or oseltamivir use.

Route

Amantadine, rimantadine, and oseltamivir are administered orally. Amantadine and rimantadine are available in tablet or syrup form, and oseltamivir is available in capsule or oral suspension form (298,299). Zanamivir is available as a dry

powder that is self-administered via oral inhalation by using a plastic device included in the package with the medication. Patients will benefit from instruction and demonstration of correct use of this device (246).

Pharmacokinetics

Amantadine

Approximately 90% of amantadine is excreted unchanged in the urine by glomerular filtration and tubular secretion (258,300--303). Thus, renal clearance of amantadine is reduced substantially among persons with renal insufficiency, and dosages might need to be decreased (see Dosage) (Table 7).

Rimantadine

Approximately 75% of rimantadine is metabolized by the liver (251). The safety and pharmacokinetics of rimantadine among persons with liver disease have been evaluated only after single-dose administration (251,304). In a study of persons with chronic liver disease (the majority with stabilized cirrhosis), no alterations in liver function were observed after a single dose. However, for persons with severe liver dysfunction, the apparent clearance of rimantadine was 50% lower than that reported for persons without liver disease (286).

Rimantadine and its metabolites are excreted by the kidneys. The safety and pharmacokinetics of rimantadine among patients with renal insufficiency have been evaluated only after single-dose administration (251,290). Further studies are needed to determine multiple-dose pharmacokinetics and the most appropriate dosages for patients with renal insufficiency. In a single-dose study of patients with anuric renal failure, the apparent clearance of rimantadine was approximately 40% lower, and the elimination half-life was approximately 1.6-fold greater than that among healthy persons of the same age (290). Hemodialysis did not contribute to drug clearance. In studies of persons with less severe renal disease, drug clearance was also reduced, and plasma concentrations were higher than those among control patients without renal disease who were the same weight, age, and sex (286,305).

Zanamivir

In studies of healthy volunteers, approximately 7%--21% of the orally inhaled zanamivir dose reached the lungs, and 70%--87% was deposited in the oropharynx (246,306). Approximately 4%--17% of the total amount of orally inhaled zanamivir is systemically absorbed. Systemically absorbed zanamivir has a half-life of 2.5--5.1 hours and is excreted unchanged in the urine. Unabsorbed drug is excreted in the feces (246,293).

Oseltamivir

Approximately 80% of orally administered oseltamivir is absorbed systemically (294). Absorbed oseltamivir is metabolized to oseltamivir carboxylate, the active neuraminidase inhibitor, primarily by hepatic esterases. Oseltamivir carboxylate

has a half-life of 6--10 hours and is excreted in the urine by glomerular filtration and tubular secretion via the anionic pathway (247,307). Unmetabolized oseltamivir also is excreted in the urine by glomerular filtration and tubular secretion (308).

Side Effects and Adverse Reactions

When considering use of influenza antiviral medications (i.e., choice of antiviral drug, dosage, and duration of therapy), clinicians must consider the patient's age, weight, and renal function (Table 7); presence of other medical conditions; indications for use (i.e., prophylaxis or therapy); and the potential for interaction with other medications.

Amantadine and Rimantadine

Both amantadine and rimantadine can cause CNS and gastrointestinal side effects when administered to young, healthy adults at equivalent dosages of 200 mg/day. However, incidence of CNS side effects (e.g., nervousness, anxiety, insomnia, difficulty concentrating, and lightheadedness) is higher among persons taking amantadine than among those taking rimantadine (308). In a 6-week study of prophylaxis among healthy adults, approximately 6% of participants taking rimantadine at a dosage of 200 mg/day experienced one or more CNS symptoms, compared with approximately 13% of those taking the same dosage of amantadine and 4% of those taking placebo (308). A study of older persons also demonstrated fewer CNS side effects associated with rimantadine compared with amantadine (287). Gastrointestinal side effects (e.g., nausea and anorexia) occur among approximately 1%--3% of persons taking either drug, compared with 1% of persons receiving the placebo (308).

Side effects associated with amantadine and rimantadine are usually mild and cease soon after discontinuing the drug. Side effects can diminish or disappear after the first week, despite continued drug ingestion. However, serious side effects have been observed (e.g., marked behavioral changes, delirium, hallucinations, agitation, and seizures) (288,296). These more severe side effects have been associated with high plasma drug concentrations and have been observed most often among persons who have renal insufficiency, seizure disorders, or certain psychiatric disorders and among older persons who have been taking amantadine as prophylaxis at a dosage of 200 mg/day (258). Clinical observations and studies have indicated that lowering the dosage of amantadine among these persons reduces the incidence and severity of such side effects (Table 7). In acute overdose of amantadine, CNS, renal, respiratory, and cardiac toxicity, including arrhythmias, have been reported (288). Because rimantadine has been marketed for a shorter period than amantadine, its safety among certain patient populations (e.g., chronically ill and older persons) has been evaluated less frequently. Because amantadine has anticholinergic effects and might cause mydriasis, it should not be used among patients with untreated angle closure glaucoma (288).

Zanamivir

In a study of zanamivir treatment of influenza-like illness among persons with asthma or chronic obstructive pulmonary disease where study medication was administered after use of a B₂-agonist, 13% of patients receiving zanamivir and 14% of patients who received placebo (inhaled powdered lactose vehicle) experienced a >20% decline in forced expiratory volume in 1 second (FEV₁) after treatment (246,248). However, in a phase-I study of persons with mild or moderate asthma who did not have influenza-like illness, 1 of 13 patients experienced bronchospasm after administration of zanamivir (246). In addition, during postmarketing surveillance, cases of respiratory function deterioration after inhalation of zanamivir have been reported. Certain patients had underlying airways disease (e.g., asthma or chronic obstructive pulmonary disease). Because of the risk for serious adverse events and because the efficacy has not been demonstrated among this population, zanamivir is not recommended for treatment for patients with underlying airway disease (246). If physicians decide to prescribe zanamivir to patients with underlying chronic respiratory disease after carefully considering potential risks and benefits, the drug should be used with caution under conditions of appropriate monitoring and supportive care, including the availability of short-acting bronchodilators (277). Patients with asthma or chronic obstructive pulmonary disease who use zanamivir are advised to 1) have a fast-acting inhaled bronchodilator available when inhaling zanamivir and 2) stop using zanamivir and contact their physician if they experience difficulty breathing (246). No definitive evidence is available regarding the safety or efficacy of zanamivir for persons with underlying respiratory or cardiac disease or for persons with complications of acute influenza (277). Allergic reactions, including oropharyngeal or facial edema, have also been reported during postmarketing surveillance (246,253).

In clinical treatment studies of persons with uncomplicated influenza, the frequencies of adverse events were similar for persons receiving inhaled zanamivir and those receiving placebo (i.e., inhaled lactose vehicle alone) (236--241,253). The most common adverse events reported by both groups were diarrhea; nausea; sinusitis; nasal signs and symptoms; bronchitis; cough; headache; dizziness; and ear, nose, and throat infections. Each of these symptoms was reported by <5% of persons in the clinical treatment studies combined (246).

Oseltamivir

Nausea and vomiting were reported more frequently among adults receiving oseltamivir for treatment (nausea without vomiting, approximately 10%; vomiting, approximately 9%) than among persons receiving placebo (nausea without vomiting, approximately 6%; vomiting, approximately 3%) (242,243,247,309). Among children treated with oseltamivir, 14.3% had vomiting, compared with 8.5% of placebo recipients. Overall, 1% discontinued the drug secondary to this side effect (245), whereas a limited number of adults who were enrolled in clinical treatment trials of oseltamivir discontinued treatment because of these symptoms (247). Similar types and rates of adverse events were reported in studies of

oseltamivir prophylaxis (247). Nausea and vomiting might be less severe if oseltamivir is taken with food (247,309).

Use during Pregnancy

No clinical studies have been conducted regarding the safety or efficacy of amantadine, rimantadine, zanamivir, or oseltamivir for pregnant women; only two cases of amantadine use for severe influenza illness during the third trimester have been reported (134,135). However, both amantadine and rimantadine have been demonstrated in animal studies to be teratogenic and embryotoxic when administered at substantially high doses (286,288). Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, these four drugs should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus (see manufacturers' package inserts) (246, 247,286,288).

Drug Interactions

Careful observation is advised when amantadine is administered concurrently with drugs that affect CNS, including CNS stimulants. Concomitant administration of antihistamines or anticholinergic drugs can increase the incidence of adverse CNS reactions (235). No clinically substantial interactions between rimantadine and other drugs have been identified.

Clinical data are limited regarding drug interactions with zanamivir. However, no known drug interactions have been reported, and no clinically critical drug interactions have been predicted on the basis of in vitro data and data from studies using rats (246,310).

Limited clinical data are available regarding drug interactions with oseltamivir. Because oseltamivir and oseltamivir carboxylate are excreted in the urine by glomerular filtration and tubular secretion via the anionic pathway, a potential exists for interaction with other agents excreted by this pathway. For example, coadministration of oseltamivir and probenecid resulted in reduced clearance of oseltamivir carboxylate by approximately 50% and a corresponding approximate twofold increase in the plasma levels of oseltamivir carboxylate (247,307).

No published data are available concerning the safety or efficacy of using combinations of any of these four influenza antiviral drugs. For more detailed information concerning potential drug interactions for any of these influenza antiviral drugs, package inserts should be consulted.

Antiviral Drug-Resistant Strains of Influenza

Amantadine-resistant viruses are cross-resistant to rimantadine and vice versa (311). Drug-resistant viruses can appear in approximately one third of patients when either amantadine or rimantadine is used for therapy (257,312,313). During the course of amantadine or rimantadine therapy, resistant influenza strains can replace susceptible strains within 2--3 days of starting therapy (312,314). Resistant viruses have been isolated from persons who live at home or in an

institution where other residents are taking or have recently taken amantadine or rimantadine as therapy (315,316); however, the frequency with which resistant viruses are transmitted and their effect on efforts to control influenza are unknown. Amantadine- and rimantadine-resistant viruses are not more virulent or transmissible than susceptible viruses (317). The screening of epidemic strains of influenza A has rarely detected amantadine- and rimantadine-resistant viruses (312,318,319).

Persons who have **influenza A** infection and who are treated with either amantadine or rimantadine can shed susceptible viruses early in the course of treatment and later shed drug-resistant viruses, including after 5--7 days of therapy (257). Such persons can benefit from therapy even when resistant viruses emerge.

Resistance to zanamivir and oseltamivir can be induced in **influenza A and B** viruses in vitro (320--327), but induction of resistance requires multiple passages in cell culture. By contrast, resistance to amantadine and rimantadine in vitro can be induced with fewer passages in cell culture (328,329). Development of viral resistance to zanamivir and oseltamivir during treatment has been identified but does not appear to be frequent (247,330--333). In clinical treatment studies using oseltamivir, 1.3% of post treatment isolates from patients aged ≥ 13 years and 8.6% among patients aged 1--12 years had decreased susceptibility to oseltamivir (247). No isolates with reduced susceptibility to zanamivir have been reported from clinical trials; although the number of post treatment isolates tested is limited (334) and the risk for emergence of zanamivir-resistant isolates cannot be quantified (246). Only one clinical isolate with reduced susceptibility to zanamivir, obtained from an immunocompromised child on prolonged therapy, has been reported (331). Available diagnostic tests are not optimal for detecting clinical resistance to the neuraminidase inhibitor antiviral drugs, and additional tests are being developed (334,335). Postmarketing surveillance for neuraminidase inhibitor-resistant influenza viruses is being conducted (336).

Table 7

TABLE 7. Recommended daily dosage of influenza antiviral medications for treatment and prophylaxis

Antiviral agent	Age group (yrs)				
	1–6	7–9	10–12	13–64	≥65
Amantadine* Treatment, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Prophylaxis, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Rimantadine¶ Treatment,** influenza A	NA††	NA	NA	100 mg twice daily§ §§	100 mg/day
Prophylaxis, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	100 mg/day¶¶
Zanamivir*** ††† Treatment, influenza A and B	NA	10 mg twice daily	10 mg twice daily	10 mg twice daily	10 mg twice daily
Oseltamivir Treatment,§§§ influenza A and B	Dose varies by child's weight¶¶¶	Dose varies by child's weight¶¶¶	Dose varies by child's weight¶¶¶	75 mg twice daily	75 mg twice daily
Prophylaxis, influenza A and B	NA	NA	NA	75 mg/day	75 mg/day

NOTE: Amantadine manufacturers include Endo Pharmaceuticals (Symmetrel® — tablet and syrup); Geneva Pharms Tech and Rosemont (Amantadine HCL — capsule); USL Pharma (Amantadine HCL — capsule and tablet); and Alpharma, Copley Pharmaceutical, HiTech Pharma, Mikart, Morton Grove, Carolina Medical, and Pharmaceutical Associates (Amantadine HCL — syrup). Rimantadine is manufactured by Forest Laboratories (Flumadine® — tablet and syrup) and Corepharma, Impax Labs (Rimantadine HCL — tablet), and Amide Pharmaceuticals (Rimantadine ACL — tablet). Zanamivir is manufactured by GlaxoSmithKline (Relenza® — inhaled powder). Oseltamivir is manufactured by Hoffman-LaRoche, Inc. (Tamiflu® — tablet). This information is based on data published by the Food and Drug Administration (FDA), which is available at <http://www.fda.gov>.

* The drug package insert should be consulted for dosage recommendations for administering amantadine to persons with creatinine clearance ≤50 mL/min/1.73m².

† 5 mg/kg body weight of amantadine or rimantadine syrup = 1 tsp/22 lbs.

§ Children aged ≥10 years who weigh <40 kg should be administered amantadine or rimantadine at a dosage of 5 mg/kg body weight/day.

¶ A reduction in dosage to 100 mg/day of rimantadine is recommended for persons who have severe hepatic dysfunction or those with creatinine clearance ≤10 mL/min. Other persons with less severe hepatic or renal dysfunction taking 100 mg/day of rimantadine should be observed closely, and the dosage should be reduced or the drug discontinued, if necessary.

** Only approved by FDA for treatment among adults.

†† Not applicable.

§§ Rimantadine is approved by FDA for treatment among adults. However, certain specialists in the management of influenza consider rimantadine appropriate for treatment among children (see American Academy of Pediatrics, 2000 red book: report of the Committee on Infectious Diseases, 25th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2000).

¶¶ Older nursing-home residents should be administered only 100 mg/day of rimantadine. A reduction in dosage to 100 mg/day should be considered for all persons aged ≥65 years, if they experience possible side effects when taking 200 mg/day.

*** Zanamivir is administered through inhalation by using a plastic device included in the medication package. Patients will benefit from instruction and demonstration of correct use of the device.

††† Zanamivir is not approved for prophylaxis.

§§§ A reduction in the dose of oseltamivir is recommended for persons with creatinine clearance <30 mL/min.

¶¶¶ The dose recommendation for children who weigh ≤15 kg is 30 mg twice a day. For children who weigh >15–23 kg, the dose is 45 mg twice a day. For children who weigh >23–40 kg, the dose is 60 mg twice a day. And, for children who weigh >40 kg, the dose is 75 mg twice a day.

CDC GUIDELINES & RECOMMENDATIONS

Influenza Antiviral Medications: 2004-05 Interim Chemoprophylaxis and Treatment Guidelines

November 3, 2004 (Revised with updated information on antiviral use in children)

Influenza antiviral medications are an important adjunct to influenza vaccine in the prevention and treatment of influenza. In the setting of the current vaccine shortage, CDC has developed interim recommendations on the use of antiviral medications for the 2004-05 influenza season. These interim recommendations are provided, in conjunction with previously issued recommendations on use of vaccine, to reduce the impact of influenza on persons at high risk for developing severe complications secondary to infection. The recommendations are not intended to guide the use of these medications in other situations, such as outbreaks of avian influenza. These interim recommendations may be updated as more information on the supply of influenza vaccine and antiviral medications becomes available.

Background

Influenza antiviral medications have long been used to limit the spread and impact of institutional influenza outbreaks. They also are used for treatment and chemoprophylaxis of persons in other settings. In the United States, four antiviral medications (amantadine, rimantadine, oseltamivir, and zanamivir) are approved for treatment of influenza, though limited supplies of zanamivir are currently available. When used for treatment within the first two days of illness, all four antiviral medications are similarly effective in reducing the duration of illness by one or two days. Only three antiviral medications (amantadine, rimantadine, and oseltamivir) are approved for chemoprophylaxis of influenza. **More detailed information about each medication, including dosage and approved persons for use, may be found in [Antiviral Information for Health Care Professionals](#).**

2004-05 Antiviral Medications Usage Guidelines

CDC is issuing interim recommendations for the use of antiviral medications during the 2004-05 season. Local availability of these medications may vary from community to community, which could impact how these medications should be used.

1. CDC encourages the use of **amantadine or rimantadine for chemoprophylaxis and use of oseltamivir or zanamivir for treatment** as supplies allow, in part to minimize the development of adamantane resistance among circulating influenza viruses.

2. **People who are at high risk of serious complications** from influenza may benefit most from antiviral medications. Therefore, in general, people who fall into these high risk groups should be given **priority for use of influenza antiviral medications:**

Treatment

- Any person experiencing a potentially life-threatening influenza-related illness should be treated with antiviral medications.

Influenza Antiviral Medications: 2004-05 Interim Chemoprophylaxis and Treatment Guidelines

- Any person at high risk for serious complications of influenza and who is within the first 2 days of illness onset should be treated with antiviral medications. (Pregnant women should consult their primary provider regarding use of influenza antiviral medications.)

Chemoprophylaxis

- All persons who live or work in **institutions** caring for people at high risk of serious complications of influenza infection should be given antiviral medications in the event of an institutional outbreak.

This includes nursing homes, hospitals, and other facilities caring for persons with immunosuppressive conditions, such as HIV/AIDS. When vaccine is available, vaccinated staff requires chemoprophylaxis only for the 2-week period following vaccination. Vaccinated and

Unvaccinated residents should receive chemoprophylaxis for the duration of institutional outbreak activity. Rapid tests or other influenza tests should be used to confirm influenza as the cause of outbreaks as soon as possible. However, treatment and chemoprophylaxis should be initiated if influenza is strongly suspected and test results are not yet available. Other outbreak control efforts such as cohorting of infected persons, and the practice of respiratory hygiene and other measures also should be implemented. For further information on detection and control of influenza outbreaks in acute care facilities see Detection and Control of Influenza Outbreaks in Acute Care Facilities.

- All persons at high risk of serious influenza complications should be given antiviral medications if they are likely to be exposed to others infected with influenza. For example, when a high-risk person is part of a family or household in which someone else has been diagnosed with influenza, the exposed high-risk person should be given chemoprophylaxis for 7 days.

3. Antiviral medications can be **considered** in other situations when the available supply of such medications is locally adequate.

- **Chemoprophylaxis** of persons in communities where influenza viruses are circulating, which typically lasts for 6-8 weeks:
 - Persons at high risk of serious complications who are not able to get vaccinated.
 - Persons at high risk of serious complications who have been vaccinated but have not had time to mount an immune response to the vaccine. In adults, chemoprophylaxis should occur for a period of 2 weeks after vaccination. In children aged <9 years, chemoprophylaxis should occur for 6 weeks after the first dose, or 2 weeks after the second dose, depending on whether the child is scheduled to receive one or two doses of vaccine.
 - Persons with immunosuppressive conditions who are not expected to mount an adequate antibody response to influenza vaccine.
 - Health-care workers with direct patient care responsibilities that are not able to obtain vaccine.

Influenza Antiviral Medications: 2004-05 Interim Chemoprophylaxis and Treatment Guidelines (continued from previous page)

- **Treatment** of infected adults and children aged >1 year who do not have conditions placing them at high risk for serious complications secondary to influenza infection.

4. Where the supplies of both influenza vaccine and influenza antiviral medications may not be sufficient to meet demand, CDC does not recommend the use of influenza antiviral medications for chemoprophylaxis of non-high risk persons in the community.

Private Sector Sources of Influenza Antiviral Medications

Pharmaceutical distributors should be contacted directly for availability and procurement of antiviral medications.

Strategic National Stockpile

The United States has a limited supply of influenza antiviral medications stored in the Strategic National Stockpile for emergency situations. Efforts are underway by Health and Human Services to procure additional supplies of antiviral medications. Some of the supply will be held in reserve in the event of an influenza pandemic. However, some of the supply will be made available to States and Territories for use in **outbreak settings**, as might occur in a hospital or long term care facility.

Requesting Influenza Antiviral Medications from the SNS

Influenza antiviral medications in the SNS can be requested **only by State or Territory Health Departments**. Institutions (hospitals or long-term care facilities) experiencing an urgent need for such medications should convey their request to the State or Territory Health Department.

1. The State or Territory Health Department should call (770) 488-7100, the CDC 24/7 emergency number, to make a request for antiviral medications. A logistics plan is being drafted and will be available to all state and territorial health departments in the near future.

2. The State or Territory Health Department should indicate that there is an urgent priority use situation (as defined previously) that can be addressed by use of antiviral medications, and should indicate that all reasonable efforts have been made to procure influenza antiviral medications from private distributors.

Agent-Specific Recommendations

G-3

Anthrax

1. Description of Agent / Syndrome

a. Etiology

Anthrax is an acute infectious disease caused by *Bacillus anthracis*, a spore forming, gram-positive bacillus. Associated disease occurs most frequently in sheep, goats, and cattle, which acquire spores through ingestion of contaminated soil. Humans can become infected through skin contact, ingestion, or inhalation of *B. anthracis* spores from infected animals or animal products (as in “wool sorter’s disease” from exposure to goat hair). Person-to-person transmission of inhalational disease does not occur. Direct exposure to vesicle secretions of cutaneous anthrax lesions may result in secondary cutaneous infection.

b. Clinical features

Human anthrax infection can occur in three forms: pulmonary, cutaneous, or gastrointestinal, depending on the route of exposure. Of these forms, pulmonary anthrax is associated with bioterrorism exposure to aerosolized spores. Clinical features for each form of anthrax include:

Pulmonary

- Non-specific prodrome of **flu-like symptoms** follows inhalation of infectious spores.
- Possible brief interim improvement.
- Two to four days after initial symptoms, **abrupt onset of respiratory failure** and hemodynamic collapse, possibly accompanied by thoracic edema and a **widened mediastinum on chest radiograph** suggestive of mediastinal lymphadenopathy and hemorrhagic mediastinitis.
- Gram-positive bacilli on blood culture, usually after the first two or three days of illness.
- Treatable in early prodromal stage. Mortality remains extremely high despite antibiotic treatment if it is initiated after onset of respiratory symptoms.

Cutaneous

- Local skin involvement after direct contact with spores or bacilli.
- Commonly seen on the head, forearms or hands.
- Localized itching, followed by a papular lesion that turns vesicular, and within 2-6 days develops into a depressed black eschar.
- Usually non-fatal if treated with antibiotics.

Gastro-intestinal

- Abdominal pain, nausea, vomiting, and fever following ingestion of contaminated food, usually meat.
 - Bloody diarrhea, hematemesis.
 - Gram-positive bacilli on blood culture, usually after the first two or three days of illness.
 - Usually fatal after progression to toxemia and sepsis.
- c. Modes of transmission
- The spore form of *B. anthracis* is durable. As a bioterrorism agent, it could be delivered as an aerosol. The modes of transmission for anthrax include:
- Inhalation of spores.
 - Cutaneous contact with spores or spore-contaminated materials.
 - Ingestion of contaminated food.
- d. Incubation period
- The incubation period following exposure to *B. anthracis* ranges from 1 day to 8 weeks (average 5 days), depending on the exposure route and dose:
- 2-60 days following pulmonary exposure.
 - 1-7 days following cutaneous exposure.
 - 1-7 days following ingestion.
- e. Period of communicability
- Transmission of anthrax infections from person to person is unlikely. Airborne transmission does not occur, but direct contact with skin lesions may result in cutaneous infection.

2. Preventive Measures

a. Vaccine availability

- Inactivated, cell-free anthrax vaccine (Bioport Corporation 517/327-1500, formerly Michigan Biologic Products Institute*) – limited availability.

***Use of trade names and commercial sources is for identification only and does not constitute endorsement by CDC or the U.S. Department of Health and Human Services**

b. Immunization recommendations

- Routinely administered to military personnel. Routine vaccination of civilian populations not recommended.

3. Infection Control Practices for Patient Management

Symptomatic patients with suspected or confirmed infections with *B. anthracis* should be managed according to current guidelines specific to their disease state. Recommendations for chemotherapy are beyond the scope of this document. For up-to-date information and recommendations for therapy, contact the local and state health department and the Bioterrorism Emergency Number at the CDC Emergency Response Office, 770/488-7100.

a. Isolation precautions

Standard Precautions are used for the care of patients with infections associated with *B. anthracis*. Standard Precautions include the routine use of gloves for contact with nonintact skin, including rashes and skin lesions.

b. Patient placement

Private room placement for patients with anthrax is not necessary. Airborne transmission of anthrax does not occur. Skin lesions may be infectious, but requires direct skin contact only.

c. Patient transport

Standard Precautions should be used for transport and movement of patients with *B. anthracis* infections.

d. Cleaning, disinfection, and sterilization of equipment and environment

Principles of Standard Precautions should be generally applied for the management of patient-care equipment and for environmental control (see Section I for more detail).

e. Discharge management

No special discharge instructions are indicated. Home care providers should be taught to use Standard Precautions for all patient care (e.g., dressing changes).

f. Post-mortem care

Standard Precautions should be used for post-mortem care. Standard Precautions include wearing appropriate personal protective equipment, including masks and eye protection, when generation of aerosols or splatter of body fluids is anticipated.

4. Post Exposure Management

a. Decontamination of patients / environment

The risk for re-aerosolization of *B. anthracis* spores appears to be extremely low in settings where spores were released intentionally or were present at low or high levels. In situations where the threat of gross exposure to *B. anthracis* spores exists, cleansing of skin and potentially contaminated fomites (e.g. clothing or environmental surfaces) may be considered to reduce the risk for cutaneous and gastrointestinal forms of disease. The plan for decontaminating patients exposed to anthrax may include the following:

- Instructing patients to remove contaminated clothing and store in labeled, plastic bags.
- Handling clothing minimally to avoid agitation.
- Instructing patients to shower thoroughly with soap and water (and providing assistance if necessary).
- Instructing personnel regarding Standard Precautions and wearing appropriate barriers (e.g. gloves, gown, and respiratory protection) when handling contaminated clothing or other contaminated fomites.
- Decontaminating environmental surfaces using an EPA-registered, facility-approved sporicidal/germicidal agent or 0.5% hypochlorite solution (one part household bleach added to nine parts water).

b. Prophylaxis and post-exposure immunization

Recommendations for prophylaxis are subject to change. Up-to-date recommendations should be obtained in consultation with local and state health departments and CDC. Prophylaxis should be initiated upon confirmation of an anthrax exposure (Table 1).

Table 1. Recommended post-exposure prophylaxis for exposure to *Bacillus anthracis*

Antimicrobial agent	Adults	Children §
Oral Fluoroquinolones One of the following: Ciprofloxacin	500 mg twice daily	20-30 mg per kg of body mass daily, divided into two doses
Levofloxacin	500 mg once daily	Not recommended
Ofloxacin	400 mg twice daily	Not recommended
If fluoroquinolones are not available or are contraindicated Doxycycline	100 mg twice daily	5 mg per kg of body mass per day divided into two doses

§ Pediatric use of fluoroquinolones and tetracyclines is associated with adverse effects that must be weighed against the risk of developing a lethal disease. If *B. anthracis* exposure is confirmed, the organism must be tested for penicillin susceptibility. If susceptible, exposed children may be treated with oral amoxicillin 40mg per kg of body mass per day divided every 8 hours (not to exceed 500mg, three times daily).

Prophylaxis should continue until *B. anthracis* exposure has been excluded. If exposure is confirmed, prophylaxis should continue for 8 weeks. In addition to prophylaxis, post-exposure immunization with an inactivated, cell-free anthrax vaccine is also indicated following anthrax exposure. If available, post-exposure vaccination consists of three doses of vaccine at 0, 2 and 4 weeks after exposure. With vaccination, post-exposure antimicrobial prophylaxis can be reduced to 4 weeks.

c. Triage and management of large scale exposures / potential exposures

Advance planning should include identification of:

- Sources of prophylactic antibiotics and planning for acquisition on short notice.
- Locations, personnel needs and protocols for administering prophylactic post-exposure care to large numbers of potentially exposed individuals.
- Means for providing telephone follow-up information and other public communications services.

d. Intensive care unit managers will need to consider in advance:

- How limited numbers of ventilators will be distributed in the event of a large number of patients arriving with abrupt pulmonary decompensation.
- How additional ventilators can be obtained.
- In the event of severely limited ventilator availability, whether and when ventilator support will be discontinued for a terminally ill individual.

(See Section I for additional general details regarding planning for large-scale patient management.)

5. Laboratory Support and Confirmation

Diagnosis of anthrax is confirmed by aerobic culture performed in a BSL-2 laboratory.

a. Diagnostic samples

Diagnostic samples to obtain include:

- Blood cultures.
- Acute serum for frozen storage.
- Stool culture if gastrointestinal disease is suspected.

b. Laboratory selection

Handling of clinical specimens should be coordinated with local and state health departments, and undertaken in BSL -2 or -3 laboratories. The FBI will coordinate collection of evidence and delivery of forensic specimens to FBI or Department of Defense laboratories.

c. Transport requirements

Specimen packaging and transport must be coordinated with local and state health departments, and the FBI. A chain of custody document should accompany the specimen from the moment of collection. For specific instructions, contact the **Bioterrorism Emergency Number at the CDC Emergency Response Office, 770/488-7100**. Advance planning may include identification of appropriate packaging materials and transport media in collaboration with the clinical laboratory at individual facilities.

1. Description of Agent / Syndrome

a. Etiology

Clostridium botulinum is an anaerobic gram-positive bacillus that produces a potent neurotoxin, botulinum toxin. In humans, botulinum toxin inhibits the release of acetylcholine, resulting in characteristic flaccid paralysis. *C. botulinum* produces spores that are present in soil and marine sediment throughout the world. Foodborne botulism is the most common form of disease in adults. An inhalational form of botulism is also possible. Botulinum toxin exposure may occur in both forms as agents of bioterrorism.

b. Clinical features

Food-borne botulism is accompanied by gastrointestinal symptoms. Inhalational botulism and foodborne botulism are likely to share other symptoms including:

- Responsive patient with absence of fever.
- Symmetric cranial neuropathies (drooping eyelids, weakened jaw clench, difficulty swallowing or speaking).
- Blurred vision and diplopia due to extra-ocular muscle palsies.
- Symmetric descending weakness in a proximal to distal pattern (paralysis of arms first, followed by respiratory muscles, then legs).
- Respiratory dysfunction from respiratory muscle paralysis or upper airway obstruction due to weakened glottis.
- No sensory deficits.

c. Mode of transmission

Botulinum toxin is generally transmitted by ingestion of toxin-contaminated food. Aerosolization of botulinum toxin has been described and may be a mechanism for bioterrorism exposure.

d. Incubation period

- Neurologic symptoms of foodborne botulism begin 12 – 36 hours after ingestion.
- Neurologic symptoms of inhalational botulism begin 24- 72 hours after aerosol exposure.

e. Period of communicability

Botulism is not transmitted from person to person.

2. Preventive Measures

a. Vaccine availability

A pentavalent toxoid vaccine has been developed by the Department of Defense. This vaccine is available as an investigational new drug (contact USAMRIID, 301/619-2833). Completion of a recommended schedule (0, 2, 12 weeks) has been shown to induce protective antitoxin levels detectable at 1-year post vaccination.

b. Immunization recommendations

Routine immunization of the public, including healthcare workers, is not recommended.

3. Infection Control Practices for Patient Management

Symptomatic patients with suspected or confirmed botulism should be managed according to current guidelines. Recommendations for therapy are beyond the scope of this document. For up-to-date information and recommendations for therapy, contact CDC or state health department.

- a. Isolation precautions
Standard Precautions are used for the care of patients with botulism.
- b. Patient placement
Patient-to-patient transmission of botulism does not occur. Patient room selection and care should be consistent with facility policy.
- c. Patient transport
Standard Precautions should be used for transport and movement of patients with botulism.
- d. Cleaning, disinfection, and sterilization of equipment and environment
Principles of Standard Precautions should be generally applied to the management of patient-care equipment and environmental control (see Section I for more detail).
- e. Discharge management
No special discharge instructions are indicated.
- f. Post-mortem care
Standard Precautions should be used for post-mortem care.

4. Post Exposure Management

Suspicion of even single cases of botulism should immediately raise concerns of an outbreak potentially associated with shared contaminated food. In collaboration with CDC and local /state health departments, attempts should be made to locate the contaminated food source and identify other persons who may have been exposed. Any individuals suspected to have been exposed to botulinum toxin should be carefully monitored for evidence of respiratory compromise.

- a. Decontamination of patients / environment
Contamination with botulinum toxin does not place persons at risk for dermal exposure or risk associated with re-aerosolization. Therefore, decontamination of patients is not required.
- b. Prophylaxis and post-exposure immunization
Trivalent botulinum antitoxin is available by contacting state health departments or by contacting CDC (404/639-2206 during office hours, 404/639-2888 after hours). This horse serum product has a <9% percent rate of hypersensitivity reactions. Skin testing should be performed according to the package insert prior to administration.
- c. Triage and management of large scale exposures / potential exposures
Patients affected by botulinum toxin are at risk for respiratory dysfunction that may necessitate mechanical ventilation. Ventilatory support is required, on

average, for 2 to 3 months before neuromuscular recovery allows unassisted breathing. Large-scale exposures to botulinum toxin may overwhelm an institution's available resources for mechanical ventilation. Sources of auxiliary support and means to transport patients to auxiliary sites if necessary should be planned in advance with coordination among neighboring facilities. (See Section I for additional general details regarding planning for large-scale patient management.)

5. Laboratory Support and Confirmation

a. Obtaining diagnostic samples

Routine laboratory tests are of limited value in the diagnosis of botulism. Detection of toxin is possible from serum, stool samples, or gastric secretions. For advice regarding the appropriate diagnostic specimens to obtain, contact state health authorities or CDC (Foodborne and Diarrheal Diseases Branch, 404/639-2888).

b. Laboratory selection

Handling of clinical specimens should be coordinated with local and state health departments. The FBI will coordinate collection of evidence and delivery of forensic specimens to FBI or Department of Defense laboratories.

c. Transport requirements

Specimen packaging and transport must be coordinated with local and state health departments, and the FBI. A chain of custody document should accompany the specimen from the moment of collection. For specific instructions, contact the **Bioterrorism Emergency Number at the CDC Emergency Response Office, 770/488-7100**. Advance planning may include identification of appropriate packaging materials and transport media in collaboration with the clinical laboratory at individual facilities.

6. Patient, Visitor, and Public Information

Fact sheets for distribution should be prepared, including explanation that people exposed to botulinum toxin are not contagious. A clear description of symptoms including blurred vision, drooping eyelids, and shortness of breath should be provided with instructions to report for evaluation and care if such symptoms develop.

1. Description of Agent / Syndrome**a. Etiology**

Plague is an acute bacterial disease caused by the gram-negative bacillus *Yersinia pestis*, which is usually transmitted by infected fleas, resulting in lymphatic and blood infections (bubonic and septicemia plague). A bioterrorism-related outbreak may be expected to be airborne, causing a pulmonary variant, pneumonic plague.^{3,10}

b. Clinical features

Clinical features of pneumonic plague include:

- Fever, cough, chest pain.
- Hemoptysis.
- Muco-purulent or watery sputum with gram-negative rods on gram stain.
- Radiographic evidence of bronchopneumonia.

c. Modes of transmission

- Plague is normally transmitted from an infected rodent to man by infected fleas.
- Bioterrorism-related outbreaks are likely to be transmitted through dispersion of an aerosol.
- Person-to-person transmission of pneumonic plague is possible via large aerosol droplets. Incubation period
- The incubation period for plague is normally 2 – 8 days if due to fleaborne transmission. The incubation period may be shorter for pulmonary exposure (1-3 days).

d. Period of communicability

Patients with pneumonic plague may have coughs productive of infectious particle droplets. Droplet precautions, including the use of a mask for patient care, should be implemented until the patient has completed 72 hours of antimicrobial therapy.

2. Preventive Measures**a. Vaccine availability**

Formalin-killed vaccine exists for bubonic plague, but has not been proven to be effective for pneumonic plague. It is not currently available in the United States.

b. Immunization recommendations

Routine vaccination requires multiple doses given over several weeks and is not recommended for the general population. Post-exposure immunization has no utility.

3. Infection Control Practices for Patient Management

Symptomatic patients with suspected or confirmed plague should be managed according to current guidelines. Recommendations for specific therapy are beyond the scope of this document. For up-to-date information and recommendations for therapy, contact CDC or state health department.

- a. Isolation precautions
For pneumonic plague, Droplet Precautions should be used in addition to Standard Precautions.
- Droplet Precautions are used for patients known or suspected to be infected with microorganisms transmitted by large particle droplets, generally larger than 5 μ in size, that can be generated by the infected patient during coughing, sneezing, talking, or during respiratory-care procedures.
 - Droplet Precautions require healthcare providers and others to wear a surgical-type mask when within 3 feet of the infected patient. Based on local policy, some healthcare facilities require a mask be worn to enter the room of a patient on Droplet Precautions.
 - Droplet Precautions should be maintained until patient has completed 72 hours of antimicrobial therapy.
- b. Patient placement
Patients suspected or confirmed to have pneumonic plague require Droplet Precautions. Patient placement recommendations for Droplet Precautions include:
- Placing infected patient in a private room.
 - Cohort in symptomatic patients with similar symptoms and the same presumptive diagnosis (i.e. pneumonic plague) when private rooms are not available.
 - Maintaining spatial separation of at least 3 feet between infected patients and others when cohorting is not achievable.
 - Avoiding placement of patient requiring Droplet Precautions in the same room with an immunocompromised patient.
 - Special air handling is not necessary and doors may remain open.
- c. Patient transport
- Limit the movement and transport of patients on Droplet Precautions to essential medical purposes only.
 - Minimize dispersal of droplets by placing a surgical-type mask on the patient when transport is necessary.
- d. Cleaning, disinfection, and sterilization of equipment and environment
Principles of Standard Precautions should be generally applied to the management of patient-care equipment and for environmental control (see Section I for more detail).
- e. Discharge management
Generally, patients with pneumonic plague would not be discharged from a healthcare facility until no longer infectious (completion of 72 hours of antimicrobial therapy) and would require no special discharge instructions. In the event of a large bioterrorism exposure with patients receiving care in their homes, home care providers should be taught to use Standard and Droplet Precautions for all patient care.
- f. Post-mortem care
Standard Precautions and Droplet Precautions should be used for post-mortem care.

4. Post Exposure Management

a. Decontamination of patients / environment

The risk for re-aerosolization of *Y. pestis* from the contaminated clothing of exposed persons is low. In situations where there may have been gross exposure to *Y. pestis*, decontamination of skin and potentially contaminated fomites (e.g. clothing or environmental surfaces) may be considered to reduce the risk for cutaneous or bubonic forms of the disease. The plan for decontaminating patients may include:

- Instructing patients to remove contaminated clothing and storing in labeled, plastic bags.
- Handling clothing minimally to avoid agitation.
- Instructing to patients to shower thoroughly with soap and water (and providing assistance if necessary).
- Instructing personnel regarding Standard Precautions and wearing appropriate barriers (e.g. gloves, gown, face shield) when handling contaminated clothing or other contaminated fomites.
- Performing environmental surface decontamination using an EPA-registered, facility-approved sporicidal/germicidal agent or 0.5% hypochlorite solution (one part household bleach added to nine parts water).

b. Prophylaxis

Recommendations for prophylaxis are subject to change. Up-to-date recommendations should be obtained in consultation with local and state health departments and CDC. Post-exposure prophylaxis should be initiated following confirmed or suspected bioterrorism *Y. pestis* exposure, and for post-exposure management of healthcare workers and others who had unprotected face-to-face contact with symptomatic patients (Table 2).

Table 2. Recommended post-exposure prophylaxis for exposure to *Yersinia pestis*.

Antimicrobial agent	Adults	Children §
First choice Doxycycline	100 mg twice daily	5 mg per kg of body mass per day divided into two doses
2nd choice Ciprofloxacin	500 mg twice daily	20-30 mg per kg of body mass daily, divided into two doses

§ Pediatric use of tetracyclines and flouoroquinolones is associated with adverse effects that must be weighed against the risk of developing a lethal disease.

- Prophylaxis should continue for 7 days after last known or suspected *Y. pestis* exposure, or until exposure has been excluded.
 - Facilities should ensure that policies are in place to identify and manage health care workers exposed to infectious patients. In general, maintenance of accurate occupational health records will facilitate identification, contact, assessment, and delivery of post-exposure care to potentially exposed healthcare workers.
- c. Triage and management of large scale exposures / potential exposures
- Advance planning should include identification of sources for appropriate masks to facilitate adherence to Droplet Precautions for potentially large numbers of patients and staff. Instruction and reiteration of requirements for Droplet Precautions (as opposed to Airborne Precautions) will be necessary to promote compliance and minimize fear and panic related to an aerosol exposure.
- Advance planning should also include identification of:
- Sources of bulk prophylactic antibiotics and planning for acquisition on short notice.
 - Locations, personnel needs and protocols for administering prophylactic post-exposure care to large numbers of potentially exposed individuals.
 - Means for providing telephone follow-up information and other public communications services. See Section I for additional general details regarding planning for large-scale patient management.

5. Laboratory Support and Confirmation

Laboratory confirmation of plague is by standard microbiologic culture, but slow growth and misidentification in automated systems are likely to delay

diagnosis. For decisions regarding obtaining and processing diagnostic specimens, contact state laboratory authorities or CDC.

a. Diagnostic samples

Diagnostic samples to obtain include:

- Serum for capsular antigen testing.
- Blood cultures.
- Sputum or tracheal aspirates for Gram's, Wayson's, and fluorescent antibody staining.
- Sputum or tracheal aspirates for culture.

b. Laboratory selection

Handling of clinical specimens should be coordinated with local and state health departments, and undertaken in Bio-Safety Level (BSL) -2 or -3 laboratories. The FBI will coordinate collection of evidence and delivery of forensic specimens to FBI or Department of Defense laboratories.

c. Transport requirements:

Specimen packaging and transport must be coordinated with local and state health departments, and the FBI. A chain of custody document should accompany the specimen from the moment of collection. For specific instructions, contact the **Bioterrorism Emergency Number at the CDC Emergency Response Office, 770/488-7100**. Advance planning may include identification of appropriate packaging materials and transport media in collaboration with the clinical laboratory at individual facilities.

1. Description of Agent / Syndrome

a. Etiology

Smallpox is an acute viral illness caused by the variola virus. Smallpox is a bioterrorism threat due to its potential to cause severe morbidity in a nonimmune population and because it can be transmitted via the airborne route. A single case is considered a public health emergency.

b. Clinical features

Acute clinical symptoms of smallpox resemble other acute viral illnesses, such as influenza. Skin lesions appear, quickly progressing from macules to papules to vesicles. Other clinical symptoms to aid in identification of smallpox include:

- 2-4 day, non-specific prodrome of **fever, myalgias.**
- **rash most prominent on face and extremities** (including palms and soles) in contrast to the truncal distribution of varicella.
- **rash scabs over in 1-2 weeks.**
- In contrast to the rash of varicella, which arises in “crops,” **variola rash has a synchronous onset.**

c. Mode of transmission

Smallpox is transmitted via both large and small respiratory droplets. Patient-to-patient transmission is likely from airborne and droplet exposure, and by contact with skin lesions or secretions. Patients are considered more infectious if coughing or if they have a hemorrhagic form of smallpox.

d. Incubation period

The incubation period for smallpox is 7-17 days; the average is 12 days.

e. Period of communicability

Unlike varicella, which is contagious before the rash is apparent, patients with smallpox become infectious at the onset of the rash and remain infectious until their scabs separate (approximately 3 weeks).

2. Preventive Measures

a. Vaccine availability

A live-virus intradermal vaccination is available for the prevention of smallpox.

b. Immunization recommendations

Since the last naturally acquired case of smallpox in the world occurred more than 20 years ago, routine public vaccination has not been recommended.

Vaccination against smallpox does not reliably confer lifelong immunity. Even previously vaccinated persons should be considered susceptible to smallpox.

3. Infection Control Practices for Patient Management

Symptomatic patients with suspected or confirmed smallpox should be managed according to current guidelines. Recommendations for specific therapy are beyond the scope of this document. For up-to-date information

and recommendations for therapy, contact the CDC or state health department.

a. Isolation precautions

For patients with suspected or confirmed smallpox, both Airborne and Contact Precautions should be used in addition to Standard Precautions.

- Airborne Precautions are used for patients known or suspected to be infected with microorganisms transmitted by airborne droplet nuclei (small particle residue, 5 μ or smaller in size) of evaporated droplets containing microorganisms that can remain suspended in air and can be widely dispersed by air currents.
- Airborne Precautions require healthcare providers and others to wear respiratory protection when entering the patient room. (Appropriate respiratory protection is based on facility selection policy; must meet the minimal NIOSH standard for particulate respirators, N95).
- Contact Precautions are used for patients known or suspected to be infected or colonized with epidemiologically important organisms that can be transmitted by direct contact with the patient or indirect contact with potentially contaminated surfaces in the patient's care area.
- Contact precautions require healthcare providers and others to:
 - Wear clean gloves upon entry into patient room.
 - Wear gown for all patient contact and for all contact with the patient's environment. Based on local policy, some healthcare facilities require a gown be worn to enter the room of a patient on Contact Precautions. Gown must be removed before leaving the patient's room.
 - Wash hands using an antimicrobial agent.

b. Patient placement

Patients suspected or confirmed with smallpox require placement in rooms that meet the ventilation and engineering requirements for Airborne Precautions, which include:

- Monitored negative air pressure in relation to the corridor and surrounding areas.
- 6 – 12 air exchanges per hour.
- Appropriate discharge of air to the outdoors, or monitored high efficiency filtration of air prior to circulation to other areas in the healthcare facility.
- A door that must remain closed.
- **Healthcare facilities without patient rooms appropriate for the isolation and care required for Airborne Precautions should have a plan for transfer of suspected or confirmed smallpox patients to neighboring facilities with appropriate isolation rooms.**
- Patient placement in a private room is preferred. However, in the event of a large outbreak, patients who have active infections with the same disease (i.e., smallpox) may be cohorted in rooms that meet appropriate ventilation and airflow requirements for Airborne Precautions.

c. Patient transport

- Limit the movement and transport of patients with suspected or confirmed smallpox to essential medical purposes only.

- When transport is necessary, minimize the dispersal of respiratory droplets by placing a mask on the patient, if possible
- d. Cleaning, disinfection, and sterilization of equipment and environment
A component of Contact Precautions is careful management of potentially contaminated equipment and environmental surfaces.
 - When possible, noncritical patient care equipment should be dedicated to a single patient (or cohort of patients with the same illness).
 - If use of common items is unavoidable, all potentially contaminated, reusable equipment should not be used for the care of another patient until it has been appropriately cleaned and reprocessed. Policies should be in place and monitored for compliance.
- e. Discharge management
In general, patients with smallpox will not be discharged from a healthcare facility until determined they are no longer infectious. Therefore, no special discharge instructions are required.
- f. Post-mortem care
Airborne and Contact Precautions should be used for post-mortem care.

4. Post Exposure Management

- a. Decontamination of patients / environment
 - Patient decontamination after exposure to smallpox is not indicated.
 - Items potentially contaminated by infectious lesions should be handled using Contact Precautions.
- b. Prophylaxis and post-exposure immunization
Recommendations for prophylaxis are subject to change. Up-to-date recommendations should be obtained in consultation with local and state health departments and CDC.
 - Post-exposure immunization with smallpox vaccine (vaccinia virus) is available and effective. Vaccination alone is recommended if given within 3 days of exposure. Passive immunization is also available in the form of vaccinia immune-globulin (VIG) (0.6ml/kg IM). If greater than 3 days has elapsed since exposure, both vaccination and VIG are recommended. VIG is maintained at USAMRIID, 301/619-2833.
 - Vaccination is generally contraindicated in pregnant women, and persons with immunosuppression, HIV-infection, and eczema, who are at risk for disseminated vaccinia disease. However, the risk of smallpox vaccination should be weighed against the likelihood for developing smallpox following a known exposure. VIG should be given concomitantly with vaccination in these patients.
 - Following prophylactic care, exposed individuals should be instructed to monitor themselves for development of flu-like symptoms or rash during the incubation period (i.e., for 7 to 17 days after exposure) and immediately report to designated care sites selected to minimize the risk of exposure to others.

- Facilities should ensure that policies are in place to identify and manage health care workers exposed to infectious patients. In general, maintenance of accurate occupational health records will facilitate identification, contact, assessment, and delivery of post-exposure care to potentially exposed healthcare workers.
- c. Triage and management of large scale exposures / potential exposures
Advance planning must involve IC professionals in cooperation with building engineering staff, to identify sites within the facility that can provide necessary parameters for Airborne Precautions. See Section I for additional general details regarding planning for large-scale patient management.

5. Laboratory Support and Confirmation

- a. Diagnostic samples to obtain
For decisions regarding obtaining and processing diagnostic specimens, contact state laboratory authorities or CDC.
- b. Laboratory selection
Handling of clinical specimens must be coordinated with state health departments, CDC, and USAMRIID. Testing can be performed only in BSL - 4 laboratories.¹¹ The FBI will coordinate collection of evidence and delivery of forensic specimens to FBI or Department of Defense laboratories.
- c. Transport requirements
Specimen packaging and transport must be coordinated with local and state health departments, and the FBI. A chain of custody document should accompany the specimen from the moment of collection. For specific instructions, contact the **Bioterrorism Emergency Number at the CDC Emergency Response Office, 770/488-7100**. Advance planning may include identification of appropriate packaging materials and transport media in collaboration with the clinical laboratory at individual facilities.