Santa Clara County PUBLIC HEALTH

Santa Clara County Public Health Department

2011 ZEBRA PACKET

Clinicians Guide to Biological, Chemical and Radiological Exposure

CONTENTS

Welcome to the Zebra Packet

The Zebra Packet was prepared by the Santa Clara County Public Health Department in San Jose, California in 2000 as a hard copy reference for clinicians on biological exposures. The Santa Clara County Public Health Department has now updated the Zebra Packet to make it available online and to provide quick and comprehensive access to clinical information when treating biological, chemical and radiation exposure.

The Zebra Packet website is intended to be a one-stop hub in finding biological, chemical radiological information as well as providing information to clinicians on how to report potential exposures to the Santa Clara County Public Health Department.

All of the source information found within in the Zebra Packet is from the Centers for Disease Control (CDC) and the Agency for Toxic Substances and Disease Registry (ATSDR) websites. The Zebra Packet.com is not a proprietary website, but a tool developed by the Santa Clara County Public Health Department to aid clinicians in Santa Clara County.

The Zebra Packet summarizes current Medical Management Guidelines (MMGs) published by the CDC and ATSDR. Links are provided back to the CDC/ATSDR websites for further information.

The updated Zebra Packet can be viewed at this website (www.ZebraPacket.com) from a computer or from a Smartphone. You can also download a complete PDF version from the Santa Clara County Public Health Department website.

Letter from the Health Officer

Date: July 2011

To: Hospital Emergency Room Directors
Emergency Room Physicians
Urgent Care, Clinic and Primary Care Physicians
Laboratory Directors
Emergency Medical Services Personnel

From: Martin Fenstersheib, MD, MPH, Health Officer and
Sara Cody, MD, Communicable Disease Control Officer

Re: Recognizing Terrorism Agents

It is crucial that emergency room physicians and other clinicians have a clear understanding of how to recognize a patient presenting with possible exposure to a biological or chemical agent or radiation. Although this situation has not presented in Santa Clara County, there are truly dire consequences of not recognizing a potential incident and reporting it to the Public Health Department.

In October 2000, we published the first *Zebra Packet: Bioterrorism Information for Clinicians*. In the decade since the Zebra Packet was first designed, much has changed. Clinical protocols have been refined and disease reporting instructions have evolved. Most importantly, quick access now means immediate viewing on a smart phone or downloading a document from a website. We also recognize the need to add medical management guidelines for exposure to chemical agents and radiation.

This updated ZebraPacket carefully summarizes the Medical Management Guidelines (MMGs) published by the Center for Disease Control and Agency for Toxic Substances and Disease Registry (CDC/ATSDR). Links are provided back to the CDC/ATSDR websites for further information.

The ZebraPacket can be viewed at the ZebraPacket website (www.zebrapacket.com) from a computer or from a Smartphone. You can also download a complete .pdf version from the Santa Clara County Public Health Department website http://www.sccgov.org/sites/sccphd/en-us/Pages/default.aspx.

We all remember the medical school adage, “When you hear hoof beats, think horses, not zebras”. But today, the public health and medical community continues to be challenged by the threat of terrorism incidents. It remains vital to increase awareness of clinical syndromes and medical management of each potential terrorism agent.

Disease Reporting Guidelines

FOR CLINICIANS IN SANTA CLARA COUNTY, CALIFORNIA ONLY:

- **Follow Mandatory Disease Reporting Guidelines** :

Disease Prevention & Control

Public Health Department

Santa Clara Valley Health & Hospital System

MANDATORY DISEASE REPORTING GUIDELINES

Physicians and health care providers are mandated by Title 17, California Code Regulations (CCR), § 2500 to report the following conditions. Suspected, lab-confirmed, and/or clinical diagnoses are reportable within specific intervals. Failure to report is a citable offense under the Medical Board of California's Citation and Fine Program.

PHONE IMMEDIATELY (408) 885-4214 after 5 PM (408) 998-3438

- Anthrax
- Avian Influenza (human)
- Botulism
- Brucellosis
- Cholera
- Dengue
- Diphtheria
- Escherichia Coli:
  - shiga toxin producing (STEC) including E. coli O157:H7
- Hantavirus Infections
- Hemolytic Uremic Syndrome
- Meningococcal infections
- Plague, human or animal
- Rabies, human or animal
- Seafood poisoning
  - Ciguatera
  - Domoic Acid
  - Scombroid
  - Paralytic Shellfish
- Severe Acute Respiratory Syndrome (SARS)
- Shiga toxin (detected in feces)
- Smallpox (Variola)
- Tularemia
- Viral Hemorrhagic Fevers
- Yellow Fever

OCCURRENCE OF ANY UNUSUAL DISEASE
OUTBREAKS OF ANY DISEASES INCLUDING THOSE NOT LISTED

THANK YOU FOR YOUR VIGILANCE AND PROMPT RESPONSE

7/10

WITHIN ONE WORKING DAY PHONE (408) 885-4214 FAX (408) 885-3709

- Amebiasis
- Babesiosis
- Campylobacteriosis
- Chickenpox (hospitalizations and deaths only)
- Colorado Tick Fever
- Cryptosporidiosis
- Encephalitis (bacterial, fungal, parasitic, viral)
- Foodborne Diseases
- Haemophilus Influenzae (invasive)
- Hepatitis A
- Listeriosis
- Malaria
- Measles (rubeola)
- Meningitis (bacterial, fungal, parasitic, viral)
- Pertussis (whooping cough)
- Poliovirus infection
- Psittacosis
- Q Fever
- Relapsing Fever
- Salmonellosis
- Severe Staphylococcus aureus
- Shigellosis
- Streptococcal Infection: outbreaks and individual cases in food and dairy workers only
- Syphilis
- Trichinosis
- Tuberculosis
- Typhoid Fever (cases and carriers)
- Vibrio Infection
- Water-Associated Diseases (swimmer's itch or Hot Tub Rash)
- West Nile Virus Infection
- Yersiniosis

Food or waterborne associated diseases

WITHIN ONE WEEK PHONE, FAX OR MAIL

- AIDS
- Anaplasmosis/Ehrlichiosis
- Chancroid
- Chlamydial Infections, including Lymphogranulom Venereum (LGV)
- Coccidioidomycosis
- Creutzfeldt-Jakob (CJD) and other Transmissible Spongiform Encephalopathies (TSE)
- Cystericercosis or Taeniasis
- Giardiasis
- Gonococcal infections
- Hepatitis B, C, D
- Hepatitis, other viral
- HIV Infection
- Influenza deaths (less than 18 yrs)
- Kawasaki's syndrome
- Legionellosis
- Leprosy (Hansen Disease)
- Leptospirosis
- Lyme Disease
- Mumps
- PID
- Rheumatic Fever, acute
- Rocky Mountain Spotted Fever
- Rubella (German Measles)
- Rubella Syndrome, congenital
- Tetanus
- Toxic Shock Syndrome
- Typhus Fever

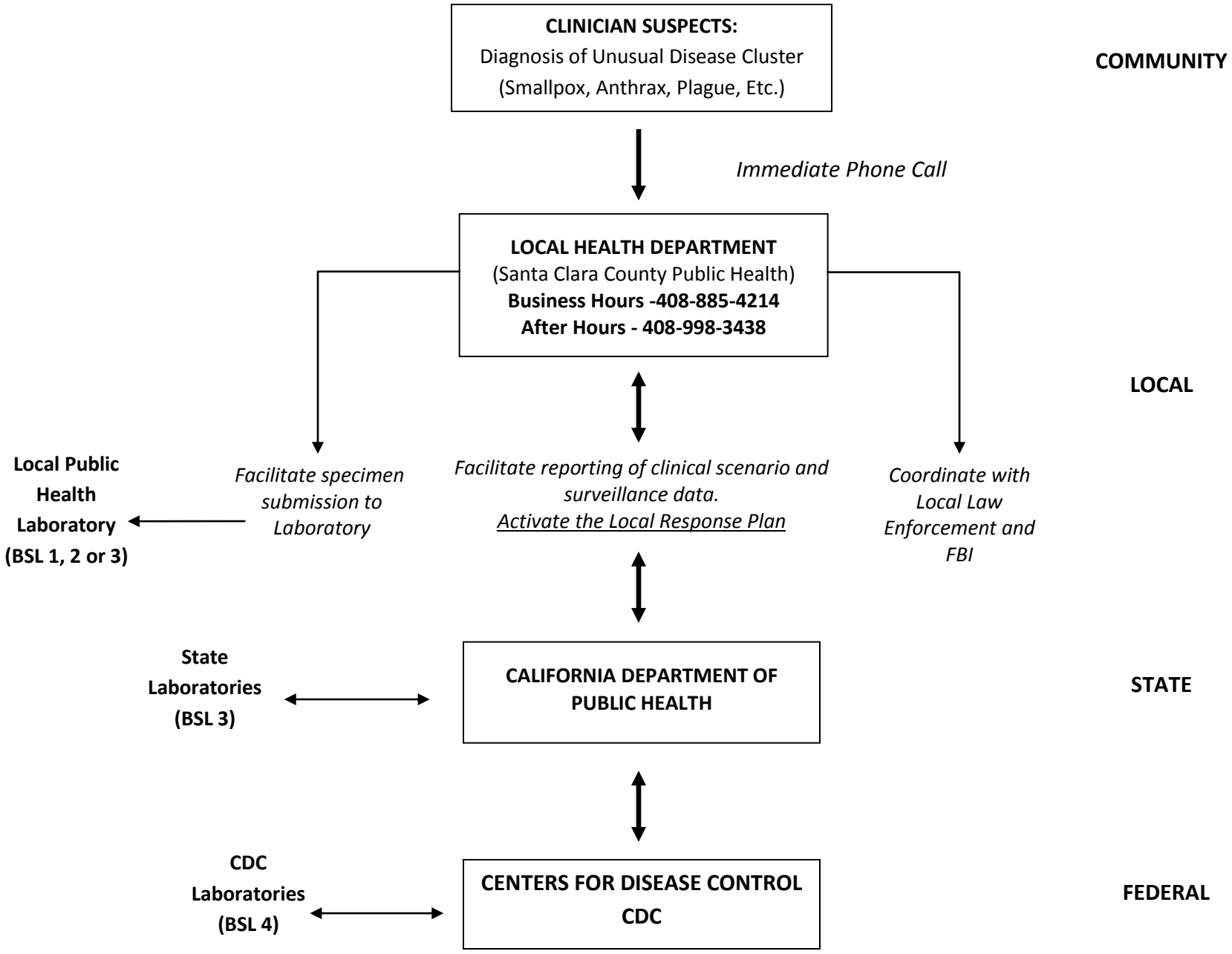
Santa Clara County Public Health Department
Monday – Friday
8 AM to 5 PM
Phone (408) 885-4214
Fax (408) 885-3709

Disease Reporting Guidelines

FOR CLINICIANS IN SANTA CLARA COUNTY, CALIFORNIA ONLY:

- **Disease Reporting Flow Chart:**

REPORTING SUSPECTED BIOTERRORISM RELATED ILLNESS



June 2011, Santa Clara County Public Health Department

Disease Reporting Guidelines

FOR CLINICIANS IN SANTA CLARA COUNTY, CALIFORNIA ONLY:

- **Link to the Santa Clara County Public Health Website "How to Report"** http://www.sccgov.org/sites/sccphd/en-us/HealthProviders/DiseaseReporting/Pages/HowReport.aspx

- **Telephone reporting in Santa Clara County, California**.

During business hours:

Report suspect cases of human or animal anthrax to: Santa Clara County Public Health Department, Disease Prevention and Control at **408-885-4214.**

After business hours

Call County of Santa Clara Communications at **408-998-3438 and ask to speak with the Public Health Officer on call.**

Detecting Bioterrorism: The Clinicians Role

Health care providers are “first responders” in a public health emergency or bioterrorism attack. **Early detection by astute clinicians and rapid reporting to the local health department will be critical** in minimizing the impact of a public health emergency. Bioterrorism attacks are likely to present as acute outbreaks of an unusual syndrome, or outbreak of illnesses in the “wrong” season, or geographic area.

Contact the Public Health Department if you see patient(s) with any of the following clinical syndromes:

1. Acute severe pneumonia or respiratory distress
2. Encephalopathy
3. Acute onset neuromuscular symptoms
4. Otherwise unexplained rash with fever
5. Fever with mucous membrane bleeding
6. Unexplained acute icteric syndromes
7. Massive diarrhea with dehydration and collapse

In the setting of any of the following:

1. Atypical host characteristics:
    - Young (< 50 years)
    - Immunologically intact
    - No underlying illness
    - No recent international travel or other exposure to potential source of infection

2. Serious, unexpected, acute illness:
    - Abrupt onset
    - Prostration
    - Cardiovascular collapse
    - Respiratory distress
    - Obtundation/change in mental status
    - Disseminated intravascular coagulation

3. Multiple similarly presenting cases, especially if:
    - Geographically associated, or
    - Closely clustered in time
4. Increases in common syndromes occurring out of season
    - Influenza-like-illness in the summer

BIOTERRORISM: ANTHRAX

EPIDEMIOLOGY

- Anthrax can be transmitted by inhalation, ingestion, or inoculation (inhalation is the most likely during a bioterrorist attack).
- The spore form of anthrax is highly resistant to physical and chemical agents; spores can persist in the environment for years .
- **Anthrax is not transmitted from person to person.**

CLINICAL

- Incubation period is 1-5 days (range up to 43 days).
- Inhalation anthrax presents as acute hemorrhagic mediastinitis.
- Biphasic illness, with initial phase characterized by nonspecific flu-like illness followed by acute phase characterized by acute respiratory distress and toxemia (sepsis).
- Chest x-ray findings: Mediastinal widening in a previously healthy patient in the absence of trauma is pathognomonic for anthrax.
- Mortality rate for inhalation anthrax approaches 90%, with treatment. Shock and death within 24-36 hours.

LABORATORY DIAGNOSIS

- Laboratory specimens should be handled in a Biosafety Level 2 facility.
- Gram stain shows gram positive bacilli, occurring singly or in short chains, often with squared off ends (safety pin appearance). In advanced disease, a gram stain of unspun blood may be positive.
- Distinguishing characteristics on culture include: non-hemolytic, non-motile, capsulated bacteria that are susceptible to gamma phage lysis.
- ELISA and PCR tests are available at national reference laboratories.

PATIENT ISOLATION

- Standard barrier isolation precautions. Patients do not require isolation rooms.
- **Anthrax is not transmitted person to person.**

TREATMENT

- Prompt initiation of antibiotic therapy is essential.
- Antibiotic susceptibility testing is KEY to guiding treatment.
- Ciprofloxicin (400 mg IV q 12 hr) is the antibiotic of choice for penicillin-resistant anthrax or for empiric therapy while awaiting susceptibility results.
- All patients should be treated with anthrax vaccine if available; antibiotic treatment should be continued until 3 doses of vaccine have been administered (day 0, 14 and 28). If vaccine is unavailable, antibiotic treatment should be continued for 60 days.

PROPHYLAXIS

- If vaccine is available, all exposed persons (as determined by local and state health depts) should be vaccinated with 3 doses of anthrax vaccine (days 0, 14 and 28).

- Start antibiotic prophylaxis immediately after exposure with ciprofloxicin (500 mg po q 12 hrs) or doxycycline (100 mg po q 12 hrs). (If strain is penicillin-susceptible, therapy can be modified to penicillin or amoxicillin).
- Antibiotic prophylaxis should be continued until 3 doses of vaccine have been administered; if vaccine is unavailable, antibiotics should be continued for 60 days.

Medical Management Guidelines for Bioterrorism Agents

MEDICAL MANAGEMENT GUIDELINES FOR ANTHRAX

For more information go to: http://emergency.cdc.gov/agent/anthrax/anthrax-hcp-factsheet.asp

BACKGROUND INFORMATION

Anthrax is a disease caused by Bacillus anthracis which can infect most warm-blooded animals, including man. Transmission to humans usually occurs through contact with infected animals or contaminated animal products. Humans become infected by inoculation, inhalation, or ingestion of the bacterium. In humans, naturally-occurring anthrax primarily involves the skin or rarely, the lungs or the gastrointestinal tract. **The bacillus produces a resistant spore which could be dispersed as a small particle aerosol. In the event of a biologic terrorist attack, aerosolization is the most likely mode of transmission, and inhalational anthrax would be the predominant form of disease affecting persons exposed to the aerosol**.

The spore form of B. anthracis is highly resistant to physical and chemical agents. The organism has been shown to persist for years in factories contaminated during the processing of infected animal products. Soil, animal feed, and to a lesser extent, ground water are the major reservoirs for anthrax.

Although human anthrax is infrequent and sporadic in the United States and most other industrialized countries, human cases (primarily cutaneous) continue to be reported from Africa, Asia, Europe, and the Americas. Although anthrax-contaminated soil exists in many foci throughout the United States, the number of cases reported annually has declined throughout the last five decades; five human cases (all cutaneous anthrax) were reported between 1981-1996. **A suspected case of anthrax in a patient without a clear exposure history (e.g., a traveler returning from an area with known animal cases or a person with exposure to imported animal hides) may be the first clue of a bioterrorist attack. Therefore, even a single, suspect case should prompt immediate notification of the Santa Clara County Public Health Department, Disease Prevention and Control (Business hours: 408-885-4214; After hours: 408299-2501).**

ROUTE OF EXPOSURE/TRANSMISSION AND USE AS A BIOTERRORISM AGENT

During an act of bioterrorism, release of an aerosol will be the most likely route of transmission. Given this, most exposed individuals will present with symptoms of inhalation anthrax with only a few, if any, presenting with the cutaneous form of the disease. Gastrointestinal anthrax would be much less likely.

- Anthrax has been weaponized by many countries during the last 50 years, including the United States (during the 1950's) and Iraq during the Gulf War.
- Anthrax is easy to cultivate and spores are readily produced.
- Anthrax spores are highly resistant to heat and disinfection.
- If aerosolized spores are inhaled, a severe hemorrhagic mediastinitis can occur with mortality rates approaching 90% even with appropriate treatment.
- Currently, anthrax vaccine is in limited supply in the United States and not available to the general public.

CLINICAL MANIFESTATIONS

Inhalation Anthrax presents as acute hemorrhagic mediastinitis after inhalation of airborne particles contaminated with B. anthracis spores. Inhalation anthrax does **not** present as an acute pneumonia.

- **Incubation period** - illness usually occurs within 1-5 days of exposure (may be as long as 43 days)

Inhalation Anthrax Symptoms

- Typically biphasic illness
- **Initial Phase** is characterized by flu-like symptoms:
  - Mild, nonspecific respiratory illness
  - Malaise, fatigue, myalgia
  - Low-grade fever
  - Nonproductive cough
  - Mild chest discomfort (occasionally)
  - Rhonchi may be heard, exam otherwise normal
- **Acute Phase** develops after 2-5 days, it may be briefly preceded by 1-2 days of improvement. Characteristic findings include:
  - Acute severe respiratory distress
  - Dyspnea, cyanosis, stridor and profuse diaphoresis
  - Subcutaneous edema of chest and neck
  - Markedly elevated temperature, pulse, respiratory rate
  - Moist crepitant rales
  - X-ray **mediastinal widening in an otherwise healthy persons is a Pathognomonic sign**; pleural effusion may be present, evidence of pneumonia is often lacking .
  - Shock develops rapidly, sometimes accompanied by evidence of hemorrhagic meningitis, and patients usually die within 24 hours of onset of the acute phase. In prior outbreaks, mortality rates approached 90% despite appropriate antibiotic therapy.
- The differential diagnosis of acute mediastinitis includes: esophageal perforation; trauma; contiguous spread from a head, neck or thoracic infection; and postsurgical infections after cardiothoracic procedures.
- **Anthrax should be strongly considered in any previously healthy patient with acute mediastinitis.**
- **The diagnosis of inhalation anthrax requires a very high index of suspicion, most often based on epidemiologic evidence of a potential exposure. In the initial stages after a bioterrorist attack, a recognized source of exposure would likely be absent --clinical suspicion is of utmost importance.**

Cutaneous Anthrax: presents as a "malignant pustule or malignant carbuncle" resulting from introduction of the anthrax bacillus beneath the skin by inoculation or contamination of a pre-existent break in the skin.

- **Incubation period** - ranges from 1-7 days but is commonly 2-5 days.

Cutaneous Anthrax Symptoms

- **Symptoms** - an evolving skin lesion, usually located on the exposed parts of the body (face, neck, arms), with a varying degree of associated edema. The skin lesion typically progresses as follows:
- Small, painless, pruritic papule **>>>** small ring of vesicles that coalesce into a single large vesicle **>>>** vesicle ruptures to form depressed ulcer **>>>** 1-3 cm eschar develops in center (7-10 days from onset of lesion) **>>>** eschar falls off (after 1-2 weeks) leaving a permanent scar.
- Systemic symptoms including fever, headache, myalgias, and regional lymphangitis/lymphadenopathy have been described. Lesions on the face and neck may be associated with significant edema and impingement of the trachea from neck swelling can occur. "Malignant edema" describes a syndrome with marked edema, induration and multiple bullae at the site of inoculation associated with generalized toxemia. Septicemia is rare. Untreated cutaneous anthrax has a case fatality rate up to 20%, but fatalities are rare (< 1%) with effective antibiotic treatment.

Gastrointestinal Anthrax: occurs after the ingestion of contaminated food, particularly raw or undercooked meat

from infected animals.

- **Incubation period** - ranges from 2-7 days

Gastrointestinal Anthrax Symptoms

Two clinical presentations, intestinal and oropharyngeal, have been described. The symptoms of intestinal anthrax are initially nonspecific and include nausea, vomiting, anorexia and fever. As the disease progresses, abdominal pain, hematemesis and bloody diarrhea develop, occasionally accompanied by ascites. The patient may present with the findings of an acute surgical abdomen. Oropharyngeal anthrax is associated with cervical edema and necrosis. A lesion, resembling a cutaneous anthrax lesion, may be seen in the oral cavity on the posterior wall, the hard palate or the tonsils. Patients typically complain of fever, dysphagia and lymphadenopathy. Toxemia, shock and cyanosis characterize the terminal stages of both forms of the disease. The case fatality rate for gastrointestinal anthrax ranges from 25 to 60%.

Meningitis: Meningitis occurs in less than 5% of cases, and may be a complication of any form of anthrax (inhalational, gastrointestinal or cutaneous). Rarely does it occur without a primary focus. It is usually hemorrhagic.

- **Incubation period** - concurrent with or one to several days after the onset of cutaneous, inhalation or gastrointestinal anthrax.

Symptoms - abrupt onset of meningeal symptoms including nausea, vomiting, myalgia, chills and dizziness. Laboratory findings are notable for a hemorrhagic meningitis. Encephalomyelitis and cortical hemorrhages have been reported; death occurs in 1-6 days.

LABORATORY DIAGNOSIS

Laboratory work with clinical specimens must be done under Biosafety Level 2 conditions. Culture is the definitive test for anthrax. Bacillus anthracis can be isolated from blood, pleural fluid, CSF, ascitic fluid, vesicular fluid or lesion exudate. Sputum cultures are rarely positive. When culturing a lesion, collect either vesicular fluid or exudate from the ulcer. If there is no visible exudate, lift the edge of the eschar with a pair of forceps and collect the fluid near the edge.

Blood cultures may be positive for bacterial growth in 12-48 hours using standard technology; however, the ability of most clinical microbiology laboratories to definitively identify B. anthracis may be limited.

MICROSCOPY

Gram stain

- Gram stain should be performed on vesicular fluid or exudate from ulcerative lesions for suspected cutaneous anthrax, pleural fluid for suspected inhalation anthrax, and CSF for suspected meningeal anthrax. In advanced disease, a gram stain of unspun blood may be positive. The Gram stain shows gram positive bacilli, usually occurring singly or in short chains, often with squared-off ends (safety-pin appearance).

Direct Fluorescent Antibody (DFA) Test

- Rapid diagnostic staining technique. This test has been used to examine exudate from cutaneous lesions, CSF and tissue. Not generally helpful for inhalation anthrax because respiratory/pleural fluid specimens are usually negative in the early stages of disease when rapid diagnosis is most critical. This test is currently available only at national reference laboratories.

Rapid diagnostic tests

- An ELISA assay for protective antigen detection and PCR for detection of nucleic acid can provide a preliminary diagnosis of anthrax within several hours. Currently, these tests are only available at reference laboratories.

EVALUATION OF A BLOOD CULTURE THAT IS SUSPICIOUS FOR ANTHRAX:

The following steps are needed to presumptively identify anthrax in the microbiology laboratory:

- Overnight incubation on a blood or nutrient agar isolation plate.
- Gram stain shows large gram positive rods with square or concave ends.

- Blood agar colonies are non-hemolytic, rough, gray-white, tenacious colonies with comma- shaped protrusions.
- Subculture to blood agar plates to test for lysis with gamma phage and penicillin susceptibility. (NOTE: Although naturally-occurring anthrax is penicillin-sensitive, in the event of a bioterrorist event, an anthrax strain resistant to penicillin may have been released).
- Test for lack of growth on phenylethyl alcohol blood agar, lack of gelatin hydrolysis, and lack of salicin fermentation.
- The bacterial capsule can be demonstrated on nutrient agar containing 0.7% sodium bicarbonate incubated overnight in a candle jar. Examine for capsule with methylene blue or India ink.
- To distinguish Bacillus anthracis from other Bacillus species: Distinguishing features include that Bacillus anthracis is non-hemolytic, non-motile, capsulated and susceptible to gamma phage lysis.

SUMMARY

- Bacillus anthracis is a gram positive bacillus that is white or gray in color, nonhemolytic or weakly so, nonmotile, gamma phage and usually penicillin susceptible, and able to produce the characteristic capsule.

SEROLOGY - not helpful for rapidly establishing the diagnosis during the acute illness.

AUTOPSY FINDINGS - identifying thoracic hemorrhagic necrotizing lymphadenitis and hemorrhagic necrotizing mediastinitis in a previously healthy patient is essentially pathognomonic for inhalation anthrax. Hemorrhagic meningitis would also be a distinct clue to the diagnosis of anthrax.

**NOTE: In the event of a bioterrorist event, the anthrax strain may be penicillin resistant. There are currently no NCCLS standards for susceptibility testing for B. anthracis. Microbiology laboratories must alert the Santa Clara County Public Health Laboratory (408-885-4272, after hours 408-299-2501) as soon as B. anthracis is identified so that susceptibility testing at a national reference laboratory can be arranged. The results of susceptibility testing are crucial in guiding both therapy and prophylaxis for potentially infected persons.

HANDLING LABORATORY SPECIMENS

Biosafety Level 2 practices, containment equipment and facilities are recommended for procedures on clinical materials suspected as being positive for anthrax. Laboratory staff handling specimens from persons who might have anthrax must wear surgical gloves, protective gowns and shoe covers. Laboratory tests should be performed in Biological Safety Level 2 cabinets and blood cultures should be maintained in a closed system. Every effort should be made to avoid splashing or creating an aerosol, and protective eye wear and masks should be worn if work cannot be done in a Biological Safety Level 2 cabinet.

A full-face mask respirator with a HEPA (high efficiency particulate air) filter is an acceptable alternative to masks and protective eye wear, but use of this equipment is not mandatory.

Accidental spills of potentially contaminated material should be decontaminated immediately by covering liberally with a disinfectant solution (5% hypochlorite or 10% formalin), left to soak for 30 minutes, and wiped up with absorbent material soaked in disinfectant. All biohazardous waste should be decontaminated by autoclaving. Contaminated equipment or instruments may be decontaminated with a hypochlorite solution, hydrogen peroxide, iodine, peracetic acid, 1% glutaraldehyde solution, formaldehyde, ethylene oxide, copper irradiation or other O.S.H.A. approved solutions, or by autoclaving or boiling for 10 minutes.

TREATMENT

The key to successful treatment is prompt administration of an antimicrobial at the first suspicion of anthrax. During a biologic emergency, before susceptibility

is determined (which may take several days), assume penicillin and tetracycline resistance and treat with ciprofloxacin at 400 mg IV every 12 hours. Penicillin is the antibiotic of choice for treating infections with penicillin-sensitive anthrax.

TREATMENT FOR NON-PREGNANT ADULTS

Inhalation Anthrax (this regimen is also recommended for gastrointestinal and meningeal anthrax.

- For penicillin resistant anthrax, administer ciprofloxacin at 400 mg IV every 8 to 12 hours (Alternative quinolone options include: ofloxacin 400 mg IV every 12 hours or levofloxacin 500 mg IV every 24 hours). If the isolate is tetracycline susceptible, doxycycline 200 mg initially, followed by 100mg IV every 12 hours is equally efficacious.
- For penicillin susceptible anthrax, administer Penicillin G IV 80,000 units/kg body weight in the first hour followed by a maintenance dose of 320,000 units/kg body weight/day. The average adult dose is 4 million units every 4 hours; can also be administered as 2 million units every 2 hours. (Amoxicillin 500 mg IV every 8 hours is an alternative regimen, with a dosing schedule that may be easier to administer in the event of a large-scale outbreak.)
- Supportive therapy is often required (e.g., volume expanders, vasopressor agents and oxygen). A tracheotomy may be needed if cervical edema compromises the airways.

Cutaneous Anthrax

Mild disease

- Penicillin susceptible anthrax - Potassium penicillin V orally at 30 mg/kg body weight/day in four equal portions every 6 hours, or amoxicillin 500 mg orally every 8 hours. Penicillin resistant anthrax - ciprofloxacin 500 mg orally every 12 hours or (if tetracycline susceptible) doxycycline 100 mg orally every 12 hours.

Extensive lesions

- Penicillin susceptible anthrax - Penicillin G IV 2-4 million units every 4-6 hours or amoxicillin 500 mg IV every 8 hours. Penicillin resistant anthrax - Ciprofloxacin 400 mg IV every 12 hours or (if tetracycline susceptible) doxycycline 100 mg IV every 12 hours. When the edema and systemic symptoms have improved, treatment may be completed with the above oral regimens. In the absence of an aerosol exposure, therapy should be continued for 7-10 days. The skin lesions will continue to evolve despite the use of effective antibiotics but severe edema and systemic symptoms will be prevented. Glucosteroids for the first 3-4 days of treatment may reduce morbidity and mortality in severe cutaneous anthrax (malignant edema), particularly in the setting of laryngeal edema.

ALTERNATIVE THERAPIES****

- In the event of severe penicillin allergy, documented resistance of Bacillus anthracis to penicillin, inability to administer the frequent IV dosing required for penicillin, or the exhaustion of penicillin supplies; Ciprofloxacin (400 mg IV every 12 hours), Ofloxacin (400 mg IV or orally every 8 to 12 hours), Levofloxacin (500 mg IV or orally every 24 hours) or Doxycycline (100 mg IV every 12 hours) (if proven susceptible) are the preferred alternatives.
- In addition, the following drugs have been shown to have in vitro activity against anthrax and could potentially be used as alternative agents in the event of an emergency, if the preferred antimicrobials listed above are unavailable or in short supply:

Erythromycin	aminoglycosides	vancomycin
imipenem	cephalothin/cefazolin	chloramphenicol
clindamycin	tetracycline	extended-spectrum penicillins

********In vitro testing suggests that B. anthracis is generally resistant to sulfamethoxazole, trimethoprim, cefuroxime, cefotaxime, ceftriaxone, ceftazadime, and aztreonam. Therefore, these antibiotics should not be used for treatment or prophylaxis of anthrax infection.

TREATMENT IN PEDIATRIC PATIENTS AND PREGNANT WOMEN

- For penicillin-resistant anthrax, although ciprofloxacin is not generally given to children less than 16 years of age due to concerns about the development of arthropathy, the high mortality rate from anthrax infection weighs heavily in favor of using ciprofloxacin in this clinical situation. Ciprofloxacin should be given at 2030 mg/kg/day orally or IV in 2 divided doses, not to exceed 1 gram/day.
- For penicillin-susceptible anthrax, Penicillin G is the drug of choice. The recommended intravenous dose for children with severe cutaneous anthrax, inhalation anthrax, or gastrointestinal anthrax is 250,000 units/kg body weight/day administered every 4 hours. Amoxicillin 500 mg IV every 8 hours for children > 20 kg and 40 mg/kg/day IV in divided doses every 8 hours for children < 20 kg, is an alternative antibiotic. Oral formulations can be used for milder disease or when IV therapy is not available.
- If ciprofloxacin supplies are exhausted and the patient is penicillin allergic or the anthrax strain is not susceptible to penicillin, doxycycline would be the preferred alternative agent (5 mg/kg/day IV or orally divided every 12 hours). Although doxycycline is not routinely administered to children < 8 years of age because of the risk of discoloration of teeth, the high mortality rate from systemic anthrax makes use of this agent the greater priority.
- Penicillin G is the drug of choice for pregnant women, if the isolate is penicillin-susceptible. The dosing schedule is as outlined for adults above. Ciprofloxacin, although not routinely prescribed during pregnancy, is the preferred alternative drug for penicillin-resistant strains, as tetracyclines can result in rare but serious liver toxicity during pregnancy. If doxycycline is used because of exhaustion of quinolone supplies or severe allergy to either penicillin or ciprofloxacin, liver function tests should be performed.

VACCINATION AND DURATION OF THERAPY

- All patients treated for inhalational anthrax should also receive anthrax vaccine due to the risk that delayed germination of mediastinal spores can result in disease recurrence. Three doses of vaccine (Days 0, 14 and 28) should be administered.
- In the absence of available anthrax vaccine, antibiotic treatment for inhalation anthrax should be continued for 60 days. (Patients should be switched to oral medications, as soon as possible.) If anthrax vaccine is available for post-exposure vaccination, antibiotic therapy can be discontinued after three doses of vaccine (Days 0, 14, and 28) have been administered.

ISOLATION OF PATIENTS

Inhalation, cutaneous and gastrointestinal anthrax have never been transmitted directly from human-to-human. All staff should observe **Standard Precautions** when caring for patients with suspected or confirmed anthrax. In addition, the following is advised:

- For cutaneous anthrax, cover the lesion with a sterile dressing. Contact Wound and skin precautions should be observed for patients with skin lesions.
- Gloves should be worn for touching potentially infective material; gowns should be worn only if soiling is likely. Masks are not necessary, since patients with inhalation anthrax do not produce small particle aerosols containing sufficient spore counts (8,000 to 10,000 spores) to cause secondary infections.
- **HANDS MUST BE WASHED AFTER TOUCHING THE PATIENT OR POTENTIALLY CONTAMINATED ARTICLES AND BEFORE TAKING CARE OF ANOTHER PATIENT.**
- Patients do not require isolation rooms.
- Articles contaminated with infective material including bandages should be discarded and bagged and labeled before being sent for decontamination and reprocessing.

DISPOSAL OF INFECTIOUS WASTE

- Use of tracking forms, containment, storage, packaging, treatment and disposal methods should be based upon the same rules as all other regulated medical wastes.

AUTOPSY AND HANDLING OF CORPSES

- All postmortem procedures should be performed using Universal Precautions.
- All persons performing or assisting in postmortem procedures must wear mandated P.P.E. (personal protective equipment) as delineated by O.S.H.A. guidelines.
- Instruments should be autoclaved or sterilized with a 10% bleach solution or other solutions approved by O.S.H.A. Surfaces contaminated during postmortem procedures should be decontaminated with an appropriate chemical germicide such as iodine, 10% hypochlorite or 5% phenol (carbolic acid).

MANAGEMENT OF EXPOSED PERSONS

- In the event of a bioterrorist release of Bacillus anthracis spores, it may be difficult to define who has been exposed. Once the site of the attack is determined, all persons at the site of the release or downwind of the release (assuming an aerosol dispersal) would be considered potentially exposed.
- Since inhalation anthrax does not spread from person to person, household and other contacts (such as healthcare workers caring for cases) of exposed persons are not considered exposed and do not require prophylaxis (unless they too were exposed to the aerosolized anthrax spores at the time of the attack).

• **Inhalational exposures:** Initiation of antibiotic therapy quickly after exposure has been shown to markedly reduce the mortality of inhalation anthrax in animal studies. The best available prophylactic regimen is the combination of antibiotic therapy and vaccination. Antibiotic susceptibility information on clinical isolates should guide prophylactic antibiotic choices. While awaiting antibiotic susceptibility test results, or if susceptibility results confirm **penicillin resistance**, begin therapy immediately with oral ciprofloxacin (500 mg po bid), levofloxacin (500 mg po per day), ofloxacin (400 mg po per bid), or doxycycline (100 mg po bid). If the isolate is **penicillin susceptible**, potassium penicillin V (30 mg/kg/day in 4 divided doses) or amoxicillin (500 mg po every 8 hours) are the preferred preventive treatment.

- **Recommendations for prophylactic treatment of children**, while awaiting antibiotic susceptibility results or if susceptibility results confirm **penicillin resistance**, include: ciprofloxacin (20-30 mg per kg of body mass per day divided every 12 hours) or doxycycline (5 mg per kg of body mass per day divided every 12 hours). If the isolate is **penicillin-susceptible**, all children should be treated with a penicillin antibiotic (for children weighing at least 20 kg, amoxicillin 500 mg po every 8 hours; for children < 20 kg, amoxicillin 40 mg per kg per day in divided doses every 8 hours).
- **Duration of antibiotic prophylaxis:** Therapy should be continued for at least 4 weeks, or until **three** doses of anthrax vaccine have been administered (Days 0, 14 and 28). **If vaccine is unavailable**, antibiotic prophylaxis should be continued for at least 60 days, and withdrawn under medical supervision.
- **Exposures through cuts, abrasions or injections:** Immediately wash the infected part, and apply a disinfectant solution such as hypochlorite solution. Promptly begin therapy as outlined under the treatment section for "Cutaneous anthrax-mild disease"; continue therapy for 7-10 days. Anthrax vaccine is not indicated.
- **Ingestional exposures:** Treat as for exposure by cuts or abrasions.
- **All persons exposed to anthrax should be instructed to watch for signs/symptoms of flu-like illness for at least 7 days.** Should such symptoms occur, patients must be immediately evaluated by a physician for the possible institution of intravenous antibiotic therapy.

VACCINATION

- An alum-absorbed, cell-free killed vaccine for anthrax has been developed and used primarily by the military and laboratory workers/veterinarians. The vaccine efficacy against cutaneous anthrax has been documented for humans; evidence for protection against inhalation and gastrointestinal anthrax is limited to animal studies.
- For prophylaxis, the vaccine is given parenterally (0.5mL subcutaneously) in three doses 2 weeks apart (Days 0, 14 and 28). Currently, there are limited vaccine supplies in the United States, and distribution is restricted to the military or persons at high-risk due to occupational exposures. (NOTE: Data from animal studies suggest that two doses of anthrax vaccine given two weeks apart may be sufficient, and in the setting of limited vaccine supplies may be a practical alternative).
- Adverse reactions to anthrax vaccine are not common. About 6% of patients may develop a local reaction and 2-3% experience mild systemic symptoms. (NOTE: The FDA has only licensed the vaccine for use in healthy adults aged 18-65 years; the safety and efficacy of the vaccine for children and pregnant women has not been studied).
- For current information about the availability of human anthrax vaccine, call the Santa Clara County Public Health Department, Disease Prevention and Control at 408-885-4214.

Fact Sheet: Anthrax Information for Health Care Providers

Cause	*Bacillus anthracis* • Encapsulated, aerobic, gram-positive, spore-forming, rod-shaped (bacillus) bacterium
Systems Affected	• Skin or cutaneous (most common) • Respiratory tract or inhalation (rare) • Gastrointestinal (GI) tract (rare) • Oropharyngeal form (least common)
Transmission	• Skin: direct skin contact with spores; in nature, contact with infected animals or animal products (usually related to occupational exposure) • Respiratory tract: inhalation of aerosolized spores • GI: consumption of undercooked or raw meat products or dairy products from infected animals • NO person-to-person transmission of inhalation or GI anthrax
Reporting	• Report suspected or confirmed anthrax cases immediately to your local or state department of health.

Cutaneous Anthrax

Incubation Period	• Usually an immediate response up to 1 day
Typical Signs/Symptoms	• Local skin involvement after direct contact with spores or bacilli • Localized itching followed by 1) papular lesion that turns vesicular and 2) subsequent development of black eschar within 7–10 days of initial lesion
Treatment **(See "Cutaneous Anthrax Treatment Protocol" for specific therapy*)**	• Obtain specimens for culture BEFORE initiating antimicrobial therapy. • Do NOT use extended-spectrum cephalosporins or trimethoprim/sulfamethoxazole because anthrax may be resistant to these drugs.
Precautions	• Standard contact precautions. Avoid direct contact with wound or wound drainage.

* http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5042a1.htm

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Inhalation Anthrax

Incubation Period	• Usually <1 week; may be prolonged for weeks (up to 2 months)	
Typical Signs/Symptoms **(often biphasic, but symptoms may progress rapidly)**	**Initial phase** • Non-specific symptoms such as low-grade fever, nonproductive cough, malaise, fatigue, myalgias, profound sweats, chest discomfort (upper respiratory tract symptoms are rare) • Maybe rhonchi on exam, otherwise normal • Chest X-ray: o mediastinal widening o pleural effusion (often) o infiltrates (rare)	**Subsequent phase** • 1–5 days after onset of initial symptoms • May be preceded by 1–3 days of improvement • Abrupt onset of high fever and severe respiratory distress (dyspnea, stridor, cyanosis) • Shock, death within 24–36 hours
Laboratory	• Coordinate all aspects of testing, packaging, and transporting with public health laboratory/Laboratory Response Network (LRN). • Obtain specimens appropriate to system affected: o blood (essential) o pleural fluid o cerebral spinal fluid (CSF) o skin lesion	**Clues to diagnosis** • Gram-positive bacilli on unspun peripheral blood smear or CSF • Aerobic blood culture growth of large, gram-positive bacilli provides preliminary identification of *Bacillus* species.
Treatment **(See "Inhalational Anthrax Treatment Protocol"* for specific therapy)**	• Obtain specimens for culture BEFORE initiating antimicrobial therapy. • Initiate antimicrobial therapy immediately upon suspicion. • Do NOT use extended-spectrum cephalosporins or trimethoprim/sulfamethoxazole because anthrax may be resistant to these drugs. • Supportive care including controlling pleural effusions	
Precautions	• Standard contact precautions	

* http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5042a1.htm

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Gastrointestinal Anthrax

Incubation Period	• Usually 1–7 days	
Typical Signs/Symptoms	**Initial phase** • Nausea, anorexia, vomiting, and fever progressing to severe abdominal pain, hematemesis, and diarrhea that is almost always bloody • Acute abdomen picture with rebound tenderness may develop. • Mesenteric adenopathy on computed tomography (CT) scan likely. Mediastinal widening on chest X-ray has been reported.	**Subsequent phase** • 2–4 days after onset of symptoms, ascites develops as abdominal pain decreases. • Shock, death within 2–5 days of onset
Laboratory	• Coordinate all aspects of testing, packaging, and transporting with public health laboratory/LRN. • Obtain specimens appropriate to system affected: o blood (essential) o ascitic fluid	**Clues to diagnosis** • Gram-positive bacilli on unspun peripheral blood smear or ascitic fluid • Pharyngeal swab for pharyngeal form • Aerobic blood culture growth of large, gram-positive bacilli provides preliminary identification of *Bacillus* species.
Treatment **(See "Inhalational Anthrax Treatment Protocol"* for specific therapy)**	• Obtain specimens for culture BEFORE initiating antimicrobial therapy. • Early (during initial phase) antimicrobial therapy is critical. • Do **NOT** use extended-spectrum cephalosporins or trimethoprim/sulfamethoxazole because anthrax may be resistant to these drugs.	
Precautions	• Standard precautions	

* http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5042a1.htm

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Oropharyngeal Anthrax

Incubation Period	• Usually 1–7 days	
Typical Signs/Symptoms	**Initial phase** • Fever and marked unilateral or bilateral neck swelling caused by regional lymphadenopathy • Severe throat pain and dysphagia • Ulcers at the base of the tongue, initially edematous and hyperemic	**Subsequent phase** • Ulcers may progress to necrosis • Swelling can be severe enough to compromise the airway
Laboratory	• Coordinate all aspects of testing, packaging, and transporting with public health laboratory/LRN. • Obtain specimens appropriate to system affected: o blood (essential) o throat	**Clues to diagnosis** • Aerobic blood culture growth of large, gram-positive bacilli provides preliminary identification of *Bacillus* species.
Treatment **(See "Inhalational Anthrax Treatment Protocol"* for specific therapy)**	• Obtain specimens for culture BEFORE initiating antimicrobial therapy. • Do **NOT** use extended-spectrum cephalosporins or trimethoprim/sulfamethoxazole because anthrax may be resistant to these drugs. • Supportive care including controlling ascites	
Precautions	• Standard contact precautions	

* http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5042a1.htm

FACT SHEET

Anthrax: What You Need To Know

What Is Anthrax?

Anthrax is a serious disease caused by ***Bacillus anthracis***, a bacterium that forms spores. A bacterium is a very small organism made up of one cell. Many bacteria can cause disease. A spore is a cell that is dormant (asleep) but may come to life with the right conditions.

There are three types of anthrax:

- **skin (cutaneous)**
- **lungs (inhalation)**
- **digestive (gastrointestinal)**

How Do You Get It?

Anthrax is not known to spread from one person to another.

Anthrax from animals. Humans can become infected with anthrax by handling products from infected animals or by breathing in anthrax spores from infected animal products (like wool, for example). People also can become infected with gastrointestinal anthrax by eating undercooked meat from infected animals.

Anthrax as a weapon. Anthrax also can be used as a weapon. This happened in the United States in 2001. Anthrax was deliberately spread through the postal system by sending letters with powder containing anthrax. This caused 22 cases of anthrax infection.

How Dangerous Is Anthrax?

The Centers for Disease Control and Prevention classifies agents with recognized bioterrorism potential into three priority areas (A, B and C). Anthrax is classified as a Category A agent. Category A agents are those that:

- pose the greatest possible threat for a bad effect on public health
- may spread across a large area or need public awareness
- need a great deal of planning to protect the public's health

In most cases, early treatment with antibiotics can cure cutaneous anthrax. Even if untreated, 80 percent of people who become infected with cutaneous anthrax do not die. Gastrointestinal anthrax is more serious because between one-fourth and more than half of cases lead to death. Inhalation anthrax is much more severe. In 2001, about half of the cases of inhalation anthrax ended in death.

What Are the Symptoms?

The symptoms (warning signs) of anthrax are different depending on the type of the disease:

- Cutaneous: The first symptom is a small sore that develops into a blister. The blister then develops into a skin ulcer with a black area in the center. The sore, blister and ulcer do not hurt.
- Gastrointestinal: The first symptoms are nausea, loss of appetite, bloody diarrhea, and fever, followed by bad stomach pain.

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- Inhalation: The first symptoms of inhalation anthrax are like cold or flu symptoms and can include a sore throat, mild fever and muscle aches. Later symptoms include cough, chest discomfort, shortness of breath, tiredness and muscle aches. (Caution: Do not assume that just because a person has cold or flu symptoms that they have inhalation anthrax.)

How Soon Do Infected People Get Sick?

Symptoms can appear within 7 days of coming in contact with the bacterium for all three types of anthrax. For inhalation anthrax, symptoms can appear within a week or can take up to 42 days to appear.

How Is Anthrax Treated?

Antibiotics are used to treat all three types of anthrax. Early identification and treatment are important.

Prevention after exposure. Treatment is different for a person who is exposed to anthrax, but is not yet sick. Health-care providers will use antibiotics (such as ciprofloxacin, levofloxacin, doxycycline, or penicillin) combined with the anthrax vaccine to prevent anthrax infection.

Treatment after infection. Treatment is usually a 60-day course of antibiotics. Success depends on the type of anthrax and how soon treatment begins.

Can Anthrax Be Prevented?

Vaccination. There is a vaccine to prevent anthrax, but it is not yet available for the general public. Anyone who may be exposed to anthrax, including certain members of the U.S. armed forces, laboratory workers, and workers who may enter or re-enter contaminated areas, may get the vaccine. Also, in the event of an attack using anthrax as a weapon, people exposed would get the vaccine.

What Should I Do if I Think I Have Anthrax?

If you are showing symptoms of anthrax infection, call your health-care provider right away.

What Should I Do if I Think I Have Been Exposed to Anthrax?

Contact local law enforcement immediately if you think that you may have been exposed to anthrax. This includes being exposed to a suspicious package or envelope that contains powder.

What Is CDC Doing To Prepare For a Possible Anthrax Attack?

CDC is working with state and local health authorities to prepare for an anthrax attack. Activities include:

- Developing plans and procedures to respond to an attack using anthrax.
- Training and equipping emergency response teams to help state and local governments control infection, gather samples, and perform tests. Educating health-care providers, media, and the general public about what to do in the event of an attack.
- Working closely with health departments, veterinarians, and laboratories to watch for suspected cases of anthrax. Developing a national electronic database to track potential cases of anthrax.
- Ensuring that there are enough safe laboratories for quickly testing of suspected anthrax cases.
- Working with hospitals, laboratories, emergency response teams, and health-care providers to make sure they have the supplies they need in case of an attack.

For more information, visit www.bt.cdc.gov/agent/anthrax,
or call CDC at 800-CDC-INFO (English and Spanish) or 888-232-6348 (TTY).

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BIOTERROISM: BOTULISM

EPIDEMIOLOGY

- Botulism neurotoxins (A-F) could be transmitted by aerosol or contamination of food and water supplies.
- **Botulism is not transmitted from person to person.**

CLINICAL

- Incubation period is 12-36 hours (can be several days).
- Early symptoms include blurred vision, diplopia, and dry mouth.
- Later symptoms include dysarthria, dysphagia, dysphonia, ptosis and the development of a symmetrical, descending progressive paralysis and respiratory failure.
- Patients are usually alert and afebrile.

LABORATORY DIAGNOSIS

- Diagnosis is primarily based on a compatible clinical presentation.
- Spinal protein is normal and characteristic findings are seen on EMG (facilitation of the compound muscle action potential on repetitive nerve stimulation).
- Toxin can be detected in serum (collect 30 cc in red top) and stool (foodborne botulism) by mouse neutralization bioassay performed at California Microbial Diseases Laboratory.

PATIENT ISOLATION

- Standard precautions. Patients do not require isolation rooms.

TREATMENT

- Supportive care is the mainstay of therapy; prolonged ventilatory support is often required in severe cases.
- Botulism anti-toxin (for A, B and E toxins) is in limited supply and is available only from the Division of Communicable Disease Control, California Dept of Health Services.

PROPHYLAXIS

- Currently, there is no available post-exposure prophylaxis.

Medical Management Guidelines for Bioterrorism Agents

MEDICAL MANAGEMENT GUIDELINES FOR BOTULISM

For more information go to: http://emergency.cdc.gov/agent/botulism/clinicians/index.asp

BACKGROUND INFORMATION

- Botulism is a neuroparalytic disease caused by a neurotoxin produced by the anaerobic spore-forming bacterium, Clostridium botulinum. Two additional bacteria, Clostridium barati and Clostridium butyricum, can also occasionally produce botulinum toxin. Botulinum toxins are designated A through G based on antigenic differences. Human botulism is caused by toxin types A, B, E and rarely, F; botulism associated with toxin type A is most severe. In the eastern United States, botulism is primarily caused by the botulinum toxin type B. Botulism is classically acquired by the ingestion of preformed neurotoxin, although botulism can also be caused by localized infection with C. botulinum (wound botulism) or C. botulinum colonization of the intestine with in vivo toxin production (infant botulism).
- Botulinum neurotoxins irreversibly bind to presynaptic receptors of peripheral nerves and subsequently inhibit release of acetylcholine. Both the neuromuscular junctions and cholinergic autonomic synapses are affected, resulting in skeletal muscle and bulbar paralysis. Recovery can take weeks to months, requiring the regeneration of presynaptic axons and formation of new synapses.
- Botulism in the United States is now most commonly recognized as wound botulism, which develops as a complication of injecting drug use. Botulism can also present in small clusters or single cases related to home-canned foods or vegetables of low acidity (e.g., beans, peppers, carrots and corns). Recent examples of foodborne botulism due to non-preserved foods include foil-wrapped baked potatoes and sauteed onions. Foodborne botulism is always transmitted by foods that are not heated thoroughly before eating. In 1999, there were 26 cases of foodborne botulism and 41 cases of wound botulism reported in the U.S. Thirty eight of the 41 wound botulism cases were reported in California.
- Airborne transmission of botulinum neurotoxin does not usually occur naturally, although three persons were infected by aerosolized toxin while disposing of rabbits and guinea pigs whose fur had been coated with previously aerosolized botulinum toxin during a laboratory accident in Germany in 1962. If used in a bioterrorist attack, aerosolization of preformed toxin would likely occur causing disease by the inhalation route. The clinical manifestations of disease would be identical to foodborne botulism, except for the absence of prodromal gastrointestinal symptoms. Deliberate contamination of food or water supplies is also possible.
- Botulism is not transmitted by human-to-human contact.

ROUTE OF EXPOSURE/TRANSMISSION/USE AS A BIOTERRORISM AGENT

An outbreak of botulism with the following characteristics should raise suspicion of a bioterrorist attack:

- An unusual toxin type for California.
- Multiple, simultaneous cases with no common food exposure, no wounds, and no history of injecting drug use.
- Absence of gastrointestinal prodromal symptoms would suggest an aerosolized route of exposure in patients with a clinical presentation compatible with botulism.

MEDICAL MANAGEMENT GUIDELINES FOR BOTULISM

Use as a bioterrorism agent:

- Botulinum toxin is one of the most potent compounds known; it is 100,000 times more toxic than sarin.
- Could be released as an aerosol or used to contaminate water or food supplies.
- Iraq deployed 12,000 liters of botulinum toxin in over 100 munitions during the Gulf War in 1991.
- The Aum Shinrikyo cult released botulinum toxin during a failed bioterrorist attack in Japan.
- A massive outbreak of botulism would easily overwhelm both the existing supply of botulinum antitoxin and intensive care support (ventilator) capacity at acute care hospitals.

CLINICAL MANIFESTATIONS

- During an act of bioterrorism, release of an aerosol will be the most likely route of transmission. The clinical presentation would be similar for both the inhalational and foodborne routes of transmission, with the exception that inhalational botulism would not have prominent gastrointestinal prodromal symptoms.
- Incubation period -typically 12-36 hours, can be several days (dose-dependent). Inhalational botulism may have an incubation period up to 3 days.

Symptoms

Patients may exhibit some or all of the following signs or symptoms. These findings may appear in any order, the following represents the classical temporal relationship:

- Early Symptoms (Cranial nerve abnormalities precede peripheral muscle weakness):
  - Blurred vision
  - Diplopia (double vision)
  - Dry mouth
- Later Symptoms (more severe disease):
  - Dysphonia (hoarse voice)
  - Dysarthria (difficulty articulating words)
  - Dysphagia (difficulty swallowing)
  - Ptosis
  - Symmetrical, descending, progressive muscular weakness with fatiguability with repetitive muscle activity
  - Respiratory failure
- The patient may have dilated or fixed pupils. Patients are typically alert and responsive and sensory deficits (other than blurred vision) do not occur.
- Deep tendon reflexes may be symmetrically depressed or remain normal.
- Fever does not occur unless there is a complicating infection.
- The differential diagnosis of botulism includes myasthenia gravis and Lambert-Eaton myasthenic syndrome (lack autonomic features), tick paralysis (tick should be attached), acute inflammatory polyneuropathy (Guillain-Barre syndrome {GBS} usually begins with sensory complaints, rarely begins with cranial nerve abnormalities, and the progression of motor weakness may be ascending as opposed to the descending progression seen with botulism {except for the Miller-Fisher variant}; in addition, the CSF protein is usually elevated in GBS, although it may take 1 – 2 weeks to see an increase), polio (febrile illness with asymmetric weakness), magnesium intoxication and brain stem infarction.

MEDICAL MANAGEMENT GUIDELINES FOR BOTULISM

- The diagnosis of botulism requires a very high index of suspicion, and is most often based on epidemiologic evidence of a potential exposure. In the event of a bioterrorist attack, a recognized source of exposure may be absent. Clinical suspicion is of utmost importance**.**

LABORATORY DIAGNOSIS

- Laboratory diagnosis is made by mouse neutralization assay, which is performed only at the California Microbial Diseases Laboratory. If botulism is suspected, please call the Santa Clara County Public Health Department, Disease Prevention and Control at 408885-4214 to arrange for submission of specimens for testing. After hours call County Communications at 408-299-2501.
- The diagnosis of botulism requires a compatible clinical syndrome. The detection of botulinum neurotoxin in the patient's serum and/or stool (in the case of food-borne botulism) serves to confirm the diagnosis. The detection of toxin will be dependent on the total dose absorbed and the time from onset of symptoms to testing. The specimens will be evaluated by mouse neutralization bioassay, currently the gold standard assay. This assay can detect as little as 0.03 ng of botulinum toxin.

Processing of Specimens

- Obtain serum (draw 30 cc in a tube with no anticoagulant, refrigerate until well-clotted, centrifuge and separate the serum into a sterile tube for transport), stool (at least 25 gm), and gastric aspirate if available. Immediately call the Public Health Department Disease Prevention and Control at 408-885-4214 (408-299-2501 after hours) to arrange for testing.
- Serum specimens must be taken before antitoxin treatment to demonstrate the presence of botulinum toxin.
- In California, anti-toxin and laboratory testing for toxin are available only from the state Department of Health Services. The Santa Clara County Public Health Department Laboratory and Disease Prevention and Control Program facilitate routing of laboratory specimens and evaluation of need for anti-toxin.
- All specimens should be refrigerated, and not frozen, and examined as quickly as possible after collection. Freezing will hamper recovery of Clostridium botulinum, but will not prevent detection of toxin.

Communication of Results

- Toxin test results may take up to 4 days to complete after specimens are received. Results will be given by the Santa Clara County Public Health Laboratory and Disease Prevention and Control Program. The lack of detection of toxin in serum of patients with clinically compatible illness does not necessarily rule out the diagnosis of botulism, particularly in the event of inhaled botulism neurotoxin.

Bacterial Cultures, Antibody Tests, And Routine Laboratory Tests

- Blood, stool, sputum and urine cultures are not helpful in confirming a diagnosis of inhalational botulism.
- Patients do not generally develop an antibody response due to the subimmunogenic amount of toxin necessary to produce disease.
- Routine laboratory tests, including chemistries and hematologic profiles are generally within normal limits unless a secondary process (e.g., nosocomial infection) has occurred.
- Cerebrospinal fluid tests are generally normal in botulism (CSF protein may be elevated after 1 – 2

weeks with Guillain Barre Syndrome).

Electrophysiologic Studies

- Should be performed on clinically-involved muscles
- Tensilon test -normal (differentiates botulism from myasthenia gravis)
- Nerve conduction velocity - normal Repetitive nerve stimulation at 50 Hz -facilitation of the compound muscle action potential (rates 20-50 per second)(EMG shows an incremental response to repetitive stimulation)
- These studies may support the diagnosis of botulism but a normal
- electromyelogram does not rule out disease.

HANDLING LABORATORY SPECIMENS

- Biosafety Level 2 practices, containment equipment and facilities are recommended for all activities with materials known or potentially containing toxin. Laboratory staff handling specimens from persons who might have botulism must wear surgical gloves, protective gowns, and shoe covers if performing procedures with high splash potential or risk of aerosolization. Laboratory tests should be performed in Biological Safety Level 2 cabinets and blood cultures should be maintained in a closed system. Every effort should be made to avoid splashing or creating an aerosol, and protective eye wear and masks should be worn if work cannot be done in a Biological Safety Level 2 cabinet.
- Accidental spills of potentially contaminated material should be decontaminated immediately by covering liberally with a disinfectant solution (a strong alkaline solution {e.g, 0.1M sodium hydroxide} for botulinum toxin or a 1:10 bleach solution for the Clostridium organism) for at least 15 minutes to ensure effective inactivation. If the material is suspected to contain both toxin and organisms, the spill must be sequentially treated with bleach and sodium hydroxide.
- All biohazardous waste should be decontaminated by autoclaving. Contaminated equipment or instruments may be decontaminated with a hypochlorite solution, hydrogen peroxide, peracetic acid, 1% glutaraldehyde solution, formaldehyde, ethylene oxide, copper irradiation, or other O.S.H.A. approved solutions, or by autoclaving or boiling for 10 minutes.

TREATMENT

- Supportive care combined with the rapid administration of botulinal antitoxin are the keys to successful management of botulism.
- With improvements in intensive care support and early administration of antitoxin, mortality rates for botulism have been approximately 6% in recent years.
- Respiratory failure due to paralysis of respiratory muscles is the most serious complication as well as the most common cause of death.

Botulinum Antitoxin

- In uncontrolled studies, use of antitoxin has been associated with lower mortality rates and, if administered early after onset of symptoms, a shorter course of illness. A licensed trivalent antitoxin is available. Contrary to the package insert directions, current recommendations are to administer ONE 10 ml vial of antitoxin per patient, intravenously in a normal saline solution over 20 minutes. Antitoxin need not be repeated since the circulating antibodies have a half-life of 5 to 8 days. Contact Santa Clara County Public Health Department Disease Prevention and Control

MEDICAL MANAGEMENT GUIDELINES FOR BOTULISM

(408) 885-4214(after hours 408-299-2501) and they will assist in obtaining antitoxin from the state.

- The antitoxin is of equine origin and requires skin testing for hypersensitivity before administration of the antitoxin. About 9-21 % of patients will develop either acute or delayed-type sensitivity reactions. Serum sickness reactions appear to be dose-related and may be less likely with the newer dosing recommendations.
- Skin testing is performed by injecting 0.1 ml of a 1:10 dilution (in sterile physiologic saline) of antitoxin intradermally in the patient's forearm with a 26 or 27 gauge needle. The injection site should be monitored and the patient observed for allergic reactions for 20 minutes.
- The skin test is positive if any of the following occur:
    - Hyperemic areola (> 0.5 cm) at the site of the injection
    - Fever or chills
    - Hypotension (greater than 20 mm Hg drop in blood pressure)
    - Skin rash or generalized itching
    - Respiratory difficulty
    - Nausea or vomiting

Supportive Therapy

- Improvements in intensive care have significantly decreased mortality rates for botulism. Monitoring of the vital capacity is crucial and intubation is usually indicated when the vital capacity falls below 12ml/kg, without waiting for a rise in PCO2 or fall in oxygen saturation. Ventilatory support may be required for weeks to months.

Therapy In Pediatric Patients And Pregnant Women

- Therapy is identical to the recommendations outlined above.

Aminoglycoside antibiotics

- Aminoglycoside antibiotics are contraindicated for treatment of secondary infections since they can exacerbate the neuromuscular blockade.

ISOLATION OF PATIENTS

- Botulism has not been transmitted from human-to-human. All staff should observe Standard Precautions when caring for patients with suspected or confirmed botulism. Patients do not require isolation rooms.

DISPOSAL OF INFECTIOUS WASTE

- Use of tracking forms, containment, storage, packaging, treatment and disposal methods should be based upon the same rules as all other regulated medical wastes.

AUTOPSY AND HANDLING OF CORPSES

- All postmortem procedures are to be performed using Universal Precautions. In addition, due to concerns about aerosolization of the virus, personnel should use particulate respirators as recommended under Strict Isolation precautions.
- All persons performing or assisting in postmortem procedures must wear mandated P.P.E. (personal protective equipment) as delineated by O.S.H.A. guidelines.
- Instruments should be autoclaved or sterilized with a 10% bleach solution or other solutions approved

MEDICAL MANAGEMENT GUIDELINES FOR BOTULISM
by O.S.H.A. Surfaces contaminated during postmortem procedures should be decontaminated with an appropriate chemical germicide such as 10% hypochlorite or 5% phenol (carbolic acid).
MANAGEMENT OF EXPOSED PERSONS • An exposed person is defined as a person who has been directly exposed to botulinum neurotoxin. In the case of a bioterrorist event, the exposure will most likely occur by inhalation of toxin. • There is currently no available post-exposure prophylaxis for asymptomatic exposed persons. Such persons should be educated regarding the signs and symptoms of clinical botulism and instructed to seek medical care immediately if symptoms occur.
CDC Botulism Fact Sheet for Providers: http://emergency/cdc/gov/agent/botulism/hcpfacts.asp

FACT SHEET

Facts about Botulism

Botulism is a muscle-paralyzing disease caused by a toxin made by a bacterium called *Clostridium botulinum*.

There are three main kinds of botulism:

- Foodborne botulism occurs when a person ingests pre-formed toxin that leads to illness within a few hours to days. Foodborne botulism is a public health emergency because the contaminated food may still be available to other persons besides the patient.
- Infant botulism occurs in a small number of susceptible infants each year who harbor *C. botulinum* in their intestinal tract.
- Wound botulism occurs when wounds are infected with *C. botulinum* that secretes the toxin.

With foodborne botulism, symptoms begin within 6 hours to 2 weeks (most commonly between 12 and 36 hours) after eating toxin-containing food. Symptoms of botulism include double vision, blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, muscle weakness that always descends through the body: first shoulders are affected, then upper arms, lower arms, thighs, calves, etc. Paralysis of breathing muscles can cause a person to stop breathing and die, unless assistance with breathing (mechanical ventilation) is provided.

Botulism is not spread from one person to another. Foodborne botulism can occur in all age groups. A supply of antitoxin against botulism is maintained by CDC. The antitoxin is effective in reducing the severity of symptoms if administered early in the course of the disease. Most patients eventually recover after weeks to months of supportive care.

For more information, visit www.bt.cdc.gov or call the CDC public response hotline at (888) 246-2675 (English), (888) 246-2857 (Español), or (866) 874-2646 (TTY)

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BOTERRORISM: PLAGUE

EPIDEMIOLOGY

- Highly infectious after aerosolization.
- Person-to-person and animal-to-human transmission can occur with pneumonic plague via respiratory droplet.

CLINICAL

- Incubation period is 1-3 days (ranges up to 7 days).
- Aerosolization would most likely result in pneumonic plague.
- Pneumonic plague presents with acute onset of high fevers, chills, headache, malaise and a productive cough, that is initially watery before becoming bloody.

LABORATORY DIAGNOSIS

- Bacterial cultures (blood, sputum, or lymph node aspirate specimens) should be handled in a Biosafety Level 2 facility.
- Wright, Giemsa, or Wayson stain shows gram negative coccobacilli with bipolar "safety-pin" appearance.
- Organism grows slowly (48 hrs for observable growth) on standard blood and MacConkey agar.
- Immunoflourescent staining for capsule (F1 antigen) is diagnostic.

PATIENT ISOLATION

- Strict respiratory isolation with droplet precautions (gown, gloves, and eye protection) until the patient has received at least 48 hours of antibiotic therapy and shows clinical improvement .

TREATMENT

- Streptomycin (1 g IM bid) or gentamicin (5 mg/kg IM or IV qd) are the preferred antibiotics.
- Tetracyclines or flouroquinolones are alternative choices.
- Co-trimoxazole is recommended for pregnant women and children between the ages of 2 months and 8 years.
- Chloramphenicol should be used for plague meningitis.

PROPHYLAXIS

- Antibiotic prophylaxis is recommended for all persons exposed to the aerosol or persons in close physical contact with a confirmed case.
- Tetracyclines or flouroquinolones are recommended for 7 days from last exposure to a case.

Medical Management Guidelines for Bioterrorism Agents

MEDICAL MANAGEMENT GUIDELINES FOR PLAGUE

For more information go to: http://www.cdc.gov/ncidod/dvbid/plague/index.htm

BACKGROUND INFORMATION

Plague is transmitted by a gram-negative bacillus, Yersinia pestis, of the family Enterobacteriaceae. Plague is a zoonosis and can be transmitted by flea vectors from rodents to humans, and by respiratory droplets from animals to humans and humans to humans. Plague has three clinical forms: bubonic, primary septicemic and pneumonic

disease.

Naturally-occurring plague is a disease primarily affecting rodents. Transmission between rodents is via infected fleas. Transmission to humans can occur by respiratory droplets from rodents, from other infected animals/materials to humans or from human to human.

In the United States, transmission to humans has been primarily from the bites of fleas from infected rodents. Less frequently, infection is caused by direct contact with body fluids or tissues while handling an infected animal.

Currently in the United States, infected cats are the only source of primary pneumonic plague for humans, since persons who develop secondary plague pneumonia usually receive appropriate isolation and treatment before secondary transmission can occur.

Human plague has been reported most often from the four western states of New Mexico, Arizona, Colorado and California. In the United States, 341 cases of human plague were reported during 1970-1995; the overwhelming majority of cases were bubonic plague.

Since primary pneumonic plague can be transmitted from person to person, patients with compatible clinical symptoms should be placed in respiratory isolation.

USE AS A BIOTERRORISM AGENT

Primary pneumonic plague would be the most likely presentation in the event of a biological attack:

- Plague could be released as an aerosol during a bioterrorist attack.
- Plague has been weaponized by the United States, former Soviet Union and Japan. Japan purportedly released plague over China during World War II.
- Plague has the potential for secondary transmission is highest with pneumonic plague.
- Aerosolized plague would cause pneumonic disease, with high mortality rates if untreated.

CLINICAL MANIFESTATIONS

- During an act of bioterrorism, release of an aerosol will be the most likely method of dispersal, so that most patients will present with primary pneumonic plague.

MEDICAL MANAGEMENT GUIDELINES FOR PLAGUE

Primary Pneumonic Plague

- Incubation period – typically 1-3 days (ranges up to 7 days)
- Symptoms - Patients exhibit acute & often fulminant onset of high fever, malaise, headache, myalgias and cough with production of sputum that is initially watery, before becoming bloody. Pneumonia rapidly progresses to dyspnea, stridor and cyanosis. Patients may develop respiratory failure, shock & ecchymoses.

Primary Septicemic Plague

- Incubation period - 1-7 days
- Symptoms - Clinically resembles septicemia caused by other gram negative bacteria. Patients are febrile and often have chills, headache, malaise and gastrointestinal disturbances. May progress rapidly to septic shock, consumptive coagulopathy, meningitis and coma. Patients may develop secondary plague pneumonia.

Bubonic Plague

- Incubation period - 2-7 days
- Symptoms - Patients develop fever, headache, chills and swollen, extremely painful lymph nodes (buboes). Nausea, vomiting and diarrhea are common. Swollen nodes typically involve the nodes that drain the site of initial infection. Patients generally do not have overlying skin lesions. Patients may develop secondary septicemic plague or secondary plague pneumonia.

LABORATORY DIAGNOSIS

Laboratory work must be done in Biosafety Level 2 facilities. If plague is suspected, please call the Santa Clara County Public Health Laboratory at 408-8854272 to arrange for submission of specimens for testing and/or confirmation at the state Microbial Diseases Laboratory. After hours, please call County Communications at 408-299-2501**.**

The diagnosis of plague may be suspected based on characteristic findings on microscopic staining of appropriate body fluids and confirmed by immunofluorescent staining for the capsule or bacterial culture. Serology is generally used retrospectively to confirm suspect cases.

Staining of Specimens

- Appropriate clinical specimens include: blood, bubo aspirates, sputum, CSF (if signs/symptoms of meningitis) and skin scrapings (if a lesion is present).
- Gram stain: polymorphonuclear leukocytes and bipolar staining, "safetypin" ovoid, gram-negative cocco-bacilli identified in bubo aspirate, sputum or CSF are highly suggestive of plague.
- Wayson stain: Yersinia pestis appears as light blue bacilli with dark blue polar bodies on a contrasting pink ground.
- Immunofluorescent staining of capsule (F1): A positive finding is diagnostic. Must use fresh specimens to

avoid false negatives. This test is available only at reference laboratories.

Bacterial Cultures

- Blood, bubo aspirates, sputum, CSF and skin scrapings can be cultured.
- Materials should be inoculated into blood and MacConkey agar plates and infusion broth. It generally takes 2 days to identify visible colonies. Rapid biochemical identification systems may not be reliable for identification due to slower growth rate of Y. pestis.

Serologic Testing

- Several serologic tests are available including a passive hemagglutination test (CDC). A fourfold or greater rise is diagnostic, a single titre of > 1:16 in someone without prior immunization against plague is suggestive. Serology is not useful for rapid diagnosis.

HANDLING LABORATORY SPECIMENS

- Laboratory staff handling specimens from persons who are suspected of having plague should follow Biosafety Level 2 precautions. Staff must wear surgical gloves, protective gowns and shoe covers. Laboratory tests should be performed in Biological Safety Level 2 cabinets, and blood cultures should be maintained in a closed system. Every effort should be made to avoid splashing or creating an aerosol, and protective eye wear and masks should be worn if work cannot be done in a Biological Safety Level 2 cabinet.
- Laboratories working with a large amount of organism or doing studies on antibiotic resistant strains should use Biological Safety Level 3 cabinets. A full-face mask respirator with a HEPA (high efficiency particulate air) filter is an acceptable but cumbersome alternative to masks and protective eye wear.
- Accidental spills of potentially contaminated material should be decontaminated immediately by covering liberally with a disinfectant solution (0.1% sodium hypochlorite or sodium hydroxide (0.1N)). All biohazardous waste should be decontaminated by autoclaving. Contaminated equipment or instruments may be decontaminated with a hypochlorite solution, hydrogen peroxide, peracetic acid, 1% glutaraldehyde solution, formaldehyde, ethylene oxide, copper irradiation, or other O.S.H.A. approved solutions, or by autoclaving or boiling for 10 minutes.

TREATMENT

- Supportive care combined with the rapid administration of parenteral antibiotics are the keys to successful management of plague. Plague pneumonia is almost always fatal if antibiotics are not begun within 24 hours of onset of symptoms.

Recommended Antibiotics

- Antibiotic choice may need to be altered as susceptibility information becomes available.
- The drug of choice for primary pneumonic plague is **streptomycin** [30 mg /kg/day administered by intramuscular injection every 12 hours (15 mg/kg) for 10 days]. However, since streptomycin may be in short supply, **Gentamicin** [1.7 mg/kg every 8 hours intravenously or intramuscularly for 10 days] and **doxycycline** [200mg intravenous loading dose, followed by 100mg IV every 12 hours for 10-14 days] are

alternative agents.

- **Chloramphenicol** should be used for plague meningitis due to its better CNS penetration [loading dose of 25 mg/kg intravenously followed by 50-75 mg/kg/day divided into four equal doses; continue for 10 days after clinical improvement].

Alternative Antibiotics

- **Ciprofloxacin** [400 mg intravenously every 12 hours], **Levofloxacin** [500 mg intravenously every 24 hours], and **Ofloxacin** [400 mg orally every 12 hours] are acceptable alternative agents. The efficacy of quinolones in humans has not been formally evaluated.
- **Bactrim** [1 double-strength tablet orally every 12 hours or its intravenous
- equivalent] may also be efficacious based on animal and in vitro studies.
- Much less effective drugs (**do not use** unless all other alternatives are unavailable) include: rifampin, aztreonam, ampicillin, ceftazadime, cefotetan and cefazolin.

Supportive therapy

Supportive care is essential, including intravenous fluids and hemodynamic monitoring.

TREATMENT FOR PEDIATRIC PATIENTS

- First-line agents: streptomycin [15 mg/kg intramuscularly every 12 hours] or gentamicin [1.7 mg/kg intramuscularly or intravenously every 8 hours].
- Alternatively: If > or = 8 years of -Doxycycline [100 mg intravenously or orally every 12 hours] if <45kg.
- If < 8 years of age -Co-trimoxazole [4 mg/kg orally or intravenously every 12 hours].
- Newborns up to age 2 months, ciprofloxacin 10-20 mg/kg intravenously or orally twice daily, do not exceed 1 gram/day.

TREATMENT FOR PREGNANT WOMEN

- Avoid streptomycin in pregnancy due to its association with irreversible deafness in children exposed in utero. Gentamicin can be used (1.7 mg/kg every 8 hours).
- Bactrim DS [1 tablet twice daily or its I.V. equivalent] is the preferred therapy for pregnant women, except at term, when a fluoroquinolone (Ciprofloxacin 500 orally or intravenously every 12 hours) is preferred.
- If worsening illness, add a tetracycline agent as the benefits outweigh the risks. (NOTE: Liver function tests should be monitored due to potential hepatotoxicity with tetracycline use during pregnancy).

ISOLATION OF PATIENTS

- Pneumonic plague can be spread from person-to-person by droplet transmission (coughing, sneezing). All staff should observe **Standard Precautions** when caring for patients with suspected or confirmed plague.
- Patients with **pneumonic plague** should be placed on **strict respiratory isolation with Droplet Precautions until 48 hours of appropriate antibiotics** have been administered AND the patient is showing clinical improvement.
- Droplet precautions require that the patient be placed in a private room and that persons entering the

patient room wear a surgical mask, especially when within three feet of the patient.

- Negative pressure rooms are not indicated. Transmission can occur from plague skin lesions (such as draining buboes or abscesses) to contacts; wound and skin precautions should be followed if skin lesions are present.

DISPOSAL OF INFECTIOUS WASTE

- Use of tracking forms, containment, storage, packaging, treatment and disposal methods should be based upon the same rules as all other regulated medical wastes.

AUTOPSY AND HANDLING OF CORPSES

- All postmortem procedures should be performed using Universal Precautions.
- All persons performing or assisting in postmortem procedures must wear mandated P.P.E. (personal protective equipment) as delineated by O.S.H.A. guidelines.
- Instruments should be autoclaved or sterilized with a 10% bleach solution or other solutions approved by O.S.H.A. Surfaces contaminated during postmortem procedures should be decontaminated with an appropriate chemical germicide such as iodine, 10% hypochlorite or 5% phenol (carbolic acid).

MANAGEMENT OF EXPOSED PERSONS

- An exposed person is defined as a person who has been exposed to aerosolized Yersinia pestis or has been in close physical contact with a confirmed case-patient (contact at less than 2 meters during a period when the case was symptomatic and before the case had received 48 hours of antibiotic therapy).
- Household contacts and healthcare worker contacts should be considered exposed and should receive prophylaxis.

ANTIBIOTICS

- All antibiotic therapy should continue for 7 days from last exposure to the case. Decisions on antibiotic therapy should be based on susceptibility results.

Non-pregnant Adult Post-Exposure Prophylaxis

- Tetracycline 500 mg every 6 hours, orally
- Doxycycline 100 mg every 12 hours, orally
- Ciprofloxacin 500 mg every 12 hours, orally Ofloxacin 400 mg every 12 hours, orally
- Levofloxacin 500 mg every 24 hours, orally

Alternative Therapy

- Trimethoprim/sulfamethoxazole 40 mg/kg/day in 2 equal doses at 12 hour intervals, orally.

Pediatric Post-Exposure Prophylaxis

- Co-trimoxazole is the preferred antibiotic, or when benefits outweigh the risks, consider use of doxycycline or fluoroquinolones.

MEDICAL MANAGEMENT GUIDELINES FOR PLAGUE

- If > or = 8 years of age: Doxycycline:
    - If > or = 45 kg - 100 mg orally every 12 hours
    - If < 45 kg - 2.2 mg/kg orally every 12 hours
- If < 8 years of age: Co-trimoxazole
    - 4 mg/kg orally every 12 hours
- Chloramphenicol 25 mg/kg orally every 12 hours

- **Newborns** up to age 2
    - Ciprofloxacin 10-20 mg/kg orally twice daily, months: do not exceed 1 gram/day.
- **Pregnant Women Post-Exposure Proph**ylaxis
    - Co-trimoxazole [1 DS tablet orally twice daily], is the preferred antibiotic, except at term, when the risk of kernicteris is greatest -use fluoroquinolones [ciprofloxacin 500 mg orally twice daily].

CDC Plague Diagnosis for Healthcare Providers: http://www.cdc.gov/ncidod/dvbid/plague/diagnosis.htm

FACT SHEET

Facts about Pneumonic Plague

Plague is an infectious disease that affects animals and humans. It is caused by the bacterium Yersinia pestis. This bacterium is found in rodents and their fleas and occurs in many areas of the world, including the United States.

Y. pestis is easily destroyed by sunlight and drying. Even so, when released into air, the bacterium will survive for up to one hour, although this could vary depending on conditions.
Pneumonic plague is one of several forms of plague. Depending on circumstances, these forms may occur separately or in combination:

- **Pneumonic plague** occurs when *Y. pestis* infects the lungs. This type of plague can spread from person to person through the air. Transmission can take place if someone breathes in aerosolized bacteria, which could happen in a bioterrorist attack. Pneumonic plague is also spread by breathing in *Y. pestis* suspended in respiratory droplets from a person (or animal) with pneumonic plague. Becoming infected in this way usually requires direct and close contact with the ill person or animal. Pneumonic plague may also occur if a person with bubonic or septicemic plague is untreated and the bacteria spread to the lungs.

- **Bubonic plague** is the most common form of plague. This occurs when an infected flea bites a person or when materials contaminated with Y. pestis enter through a break in a person's skin. Patients develop swollen, tender lymph glands (called buboes) and fever, headache, chills, and weakness. Bubonic plague does not spread from person to person.

- **Septicemic plague** occurs when plague bacteria multiply in the blood. It can be a complication of pneumonic or bubonic plague or it can occur by itself. When it occurs alone, it is caused in the same ways as bubonic plague; however, buboes do not develop. Patients have fever, chills, prostration, abdominal pain, shock, and bleeding into skin and other organs. Septicemic plague does not spread from person to person.

Symptoms and Treatment
With pneumonic plague, the first signs of illness are fever, headache, weakness, and rapidly developing pneumonia with shortness of breath, chest pain, cough, and sometimes bloody or watery sputum. The pneumonia progresses for 2 to 4 days and may cause respiratory failure and shock. Without early treatment, patients may die.

Early treatment of pneumonic plague is essential. To reduce the chance of death, antibiotics must be given within 24 hours of first symptoms. Streptomycin, gentamicin, the tetracyclines, and chloramphenicol are all effective against pneumonic plague.

Antibiotic treatment for 7 days will protect people who have had direct, close contact with infected patients. Wearing a close-fitting surgical mask also protects against infection.
A plague vaccine is not currently available for use in the United States.

For more information, visit www.bt.cdc.gov or call the CDC public response hotline at (888) 246-2675 (English), (888) 246-2857 (Español), or (866) 874-2646 (TTY)

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BIOTERRORISM: Q FEVER

EPIDEMIOLOGY

- Coxiella burnettii is highly infectious by the aerosol route.
- Q Fever is **rarely** transmitted from person to person.

CLINICAL

- Incubation period is 10-40 days.
- Acute infection may be asymptomatic or a self-limited febrile illness.
- Chest x-ray evidence of pneumonia is present in up to 50% of cases.
- Mortality rate is less than 2%.

LABORATORY DIAGNOSIS

- Requires serologic confirmation (IFA or ELISA)
- Isolation of organism is not recommended due to significant hazards from handling bacterial cultures in the laboratory

PATIENT ISOLATION

- Universal precautions. Patients do **not** require isolation rooms.

TREATMENT

- Illness usually resolves **without** treatment.
- Tetracyclines are the antibiotics of choice for more severe illnesses.

PROPHYLAXIS

- Tetracycline antibiotics are very effective if administered **8 to 12 days AFTER exposure.**
- Starting prophylaxis immediately after exposure can delay symptom onset but does not prevent illness.

Medical Management Guidelines for Bioterrorism Agents

MEDICAL MANAGEMENT GUIDELINES FOR Q FEVER

For more information go to: http://emergency.cdc.gov/agent/qfever/clinicians/index.asp
And http://www.cdc.gov/qfever/symptoms/index.html

BACKGROUND INFORMATION

- Q fever is a zoonotic disease caused by Coxiella burnetii, a rickettsia-like organism. C. burnetii is unable to replicate outside host cells, but there is a spore-like form of the organism that is extremely resistant to heat, dessication and many standard antiseptic compounds.
- The organism can persist in the environment for long periods under harsh conditions. Despite the inherent resilience of C. burnetii and its ease in transmissibility, generally by inhaled aerosols, the acute clinical disease of Q fever is usually benign, although temporarily incapacitating.
- Coxiella burnetii is extremely infectious. Humans have been infected most commonly by contact with domestic livestock, particularly goats, cattle and sheep but household pets, notably cats, have also been associated with infection. The risk is highest when humans are exposed to these animals at parturition, presumably via aerosolization of the organism from the uterus during birthing. Coxiella organisms can persist in the local environment, and produce infection, for weeks or months after contamination.

ROUTE OF EXPOSURE/TRANSMISSION/USE AS A BIOTERRORISM AGENT

- Q fever has VERY RARELY been transmitted from person-to-person (specifically, transmission has occurred to attendants during autopsies and from an infected patient to the attending obstetrician during delivery).
- Persons exposed to an aerosol of Coxiella burnetii do not present a risk for secondary transmission to others or for reaerosolization of the organism.

Use as a Bioterrorism Agent

- The spore-like form of the organism is resistant to heat and dessication, and can persist in the environment for long periods of time.
- Highly infectious when aerosolized and inhaled; a single organism may cause clinical illness
- Aerosolized Coxiella burnetii can result in an incapacitating respiratory illness; however, severe illness and fatalities are rare.

CLINICAL MANIFESTATIONS

- **During an act of bioterrorism, release of an aerosol will be the most likely route of transmission.**

Acute Q Fever

- **Incubation period** - 10 - 40 days, duration of the incubation period is inversely correlated with the size of the inoculum.
- **Symptoms** - Acute disease is **not** clinically distinct, and illness resembles viral respiratory infections or atypical pneumonias. Can be divided into 3 main categories:
    - Asymptomatic infection (seroconversion) - occurs in up to 50% of exposed persons
    - Self-limited febrile flu-like illness without pneumonia lasting 2 to 14 days
    - Pneumonia.
- Hepatitis, meningo-encephalitis, myocarditis, and pericarditis may be present acutely but are relatively uncommon.
- Symptomatic patients exhibit any combination of the following (in order of decreasing frequency of

appearance):

SYMPTOM	RELATIVE FREQUENCY
Fever (present in all symptomatic patients)	80-100%
Chills, rigors	75-100%
Severe headache, retro orbital pain (may be useful clue to diagnosis)	50-100%
Fatigue, anorexia, weight loss	50-85%
Cough	50-60 %
Myalgia	45-84%
Pleuritic chest pain	40-50%
Nausea, vomiting	15-20%
Diarrhea	5-20%
Neck stiffness	5-7%

- Pneumonia -Chest x-ray evidence of pneumonia may be present in up to 50% of patients. There are three possible presentations: (a) atypical pneumonia (dry nonproductive cough) (b) rapidly progressive pneumonia (often mimicking Legionnaire's disease), or (c) pneumonia with fever but no pulmonary symptoms [most common clinical scenario for acute Q fever]. Radiographic findings: Variable; may have pleural-based opacities, multiple rounded opacities, about 35% have pleural effusion, hilar adenopathy is uncommon.
- **Duration -** 2 days - 2 weeks.
- **Mortality -**Low, estimated to be about 2% (usually in patients with co-morbid conditions).

CHRONIC Q FEVER

- Chronic infection due to Q fever is uncommon, occurring in less than 1% of acute infections. Endocarditis is the usual manifestation of Q fever but a wide array of syndromes have been described including: infection of vascular grafts, osteomyelitis, infectious arthritis, chronic hepatitis, pseudotumor of the lung, chronic pulmonary fibrosis, infection during pregnancy with miscarriage and prolonged fever.
- Incubation period - varies, can be months to several years

Symptoms

- Variable depending on specific clinical syndrome.
- Most often diagnosed in patients with either a cardiovascular abnormality (valvulopathy, prosthesis or aneurysm) or an underlying immunocompromised state (i.e., HIV infection or cancer).

LABORATORY DIAGNOSIS

- The diagnosis of Q Fever requires a high index of suspicion since the disease often presents with nonspecific symptoms which can be difficult to distinguish from viral illnesses or atypical pneumonia.
- The diagnosis is generally confirmed serologically; most laboratories are not equipped to isolate Coxiella burnetii and isolation of the organism is not recommended due to the significant hazards from handling bacterial cultures in the laboratory.

Serology

- Several assays are available; antibody detection by indirect fluorescent antibody (IFA) or ELISA are used most commonly and appear to be the most sensitive.

MEDICAL MANAGEMENT GUIDELINES FOR Q FEVER

- Significant IgM antibody does not appear until 2-3 weeks into illness and may persist for years. Acute and convalescent (2-3 months after onset of illness) antibody titres show a four-fold rise. In acute Q fever, antibodies to phase II antigens are higher than those to phase I antigens, in chronic Q fever the reverse occurs. Antibodies of the IgM type are usually observed for the first 6-12 months after infection, with IgG persisting afterward.

HANDLING LABORATORY SPECIMENS

- Laboratory staff handling specimens from persons who might have Q fever must wear surgical gloves, protective gowns, and shoe covers.
- Laboratory tests, such as serological examinations and staining of tissue impression smears, can be performed in Biological Safety Level 2 cabinets; although not recommended, blood cultures should be maintained in a closed system.
- Every effort should be made to avoid splashing or creating an aerosol. Biosafety Level 3 practices and facilities should be used for inoculation, incubation and harvesting of cell cultures and the manipulation of infected tissues.
- Accidental spills of potentially contaminated material should be decontaminated immediately by covering liberally with a disinfectant solution (0.05% hypochlorite, 5% peroxide, or 1:100 solution of Lysol).
- All biohazardous waste should be decontaminated by autoclaving.
- Contaminated equipment or instruments may be decontaminated with a hypochlorite solution, hydrogen peroxide, peracetic acid, 1% glutaraldehyde solution, formaldehyde, ethylene oxide, copper irradiation, or other O.S.H.A. approved solutions, or by autoclaving or boiling for 10 minutes.

TREATMENT ACUTE Q FEVER

- Pneumonia usually resolves without treatment in 15 days; therefore, in the event of a bioterrorist attack, therapy may only be required for persons with more severe illness.
- Several antibiotics have been evaluated as therapeutic agents for acute Q fever.
- Tetracyclines have been shown to shorten the duration of illness and are considered the **drug of choice**, particularly for severe infection:
    - **Adult dosages:**
        - **Doxycycline** 100 mg every 12 hours po or IV for 15-21 days or **tetracycline** 500 mg po every 6 hours for 15-21 days. (**NOTE:** For milder illnesses, 5-7 days of therapy may be sufficient)

Alternatives:

- Quinolones, chloramphenicol, trimethroprim-sulfamethoxazole are also probably effective.
- Studies of erythromycin (500 mg -1 gram every 6 hours p.o. or IV) have shown conflicting results, and erythromycin is probably not preferred for cases of severe pneumonia. Azithromycin appears to be another option but little clinical information is available. Beta-lactam antibiotics are generally ineffective.

Pediatric dosages:

- For more severe illnesses, when benefits outweigh the risks, consider use of doxycycline (or co-trimoxazole or chloramphenicol).
    - If > or = 8 years of age: Doxycycline:
    - If > 45 kg - 100 mg IV or po every 12 hours If < 45 kg - 2.2 mg/kg IV or po every 12 hours
    - If < 8 years of age: Co-trimoxazole 4 mg/kg IV or orally every 12 hours
- Chloramphenicol 25 mg/kg orally every 12 hours

MEDICAL MANAGEMENT GUIDELINES FOR Q FEVER

Newborns up to age 2

- Ciprofloxacin 10-20 mg/kg orally twice daily, **months:** do not exceed 1 gram/day.

Pregnant Women Post-Exposure Prophylaxis

- Co-trimoxazole [1 DS tablet orally twice daily], is the preferred antibiotic, except at term, when the risk of kernicteris is greatest --use fluoroquinolones [ciprofloxacin 500 mg orally twice daily].

TREATMENT CHRONIC Q FEVER

- Endocarditis requires combination therapy, usually with doxycycline plus rifampin or possibly a quinolone plus rifampin. The duration of therapy is for years and a valve replacement is often necessary.

ISOLATION OF PATIENTS

- Q fever is not transmissible from person-to-person. Standard precautions should be followed for all patients. Respiratory isolation rooms are not required.

DISPOSAL OF INFECTIOUS WASTE

- Use of tracking forms, containment, storage, packaging, treatment and disposal methods should be based upon the same rules as all other regulated medical wastes.

AUTOPSY AND HANDLING OF CORPSES

- All postmortem procedures are to be performed using Respiratory Precautions.
- Efforts should be made to avoid aerosolization.
- All persons performing or assisting in postmortem procedures must wear mandated P.P.E. (personal protective equipment) as delineated by O.S.H.A. guidelines.
- Instruments should be autoclaved or sterilized with a 10% bleach solution or other solutions approved by O.S.H.A. Surfaces contaminated during postmortem procedures should be decontaminated with an appropriate chemical germicide such as 10% hypochlorite or 5% phenol (carbolic acid).

CDC Q Fever Information for Clinicians: http://www.cdc.gov/qfever/symptoms/index.html

BIOTERRORISM: SMALLPOX

EPIDEMIOLOGY

- Highly infectious after aerosolization.
- Person-to-person transmission can occur via droplet nuclei or aerosols expelled from the oropharynx and by direct contact.
- Contaminated clothing or bed linens can also spread the virus.
- About 30% of susceptible contacts will become infected.
- Incubation period is 12-14 days (ranges 7-17 days)

CLINICAL

- Incubation period is 12-14 days (ranges 7-17 days)
- Characteristic rash appears 2-3 days after nonspecific, flu-like prodrome (fever and headache)
- Maculopapular rash begins on mucosa of mouth and pharynx, face, hands, forearms and spreads to legs and centrally to trunk; lesions are more predominant on the face and extremities than on the trunk.
- Lesions progress synchronously on any given part of the body from macules to papules to vesicles to pustules to crusty scabs

LABORATORY DIAGNOSIS

- Mask and gloves should be worn by person obtaining specimen, preferably a person who has been recently vaccinated
- Vesicular fluid is obtained by opening lesions with the blunt edge of a scalpel, harvesting fluid with a cotton swab; scabs can be removed by forceps. Swabs and scabs should be placed in a vacutainer, sealed with tape, and placed in a second, durable, watertight container
- Laboratory specimens must be handled in a Biosafety Level 4 facility (e.g. CDC) and will be evaluated with electron microscopy and cell culture

PATIENT ISOLATION

- Strict isolation in negative pressure room (high efficiency particulate air filtration ideal) from onset of rash until all scabs separate
- Laundry and waste should be autoclaved before being laundered or incinerated

TREATMENT

- Supportive care is the mainstay of therapy
- In-vitro antiviral activity against poxviruses has been shown with adefovir, cidofovir, dipivoxil, and ribavirin. (Animal studies suggest that cidofovir may be most effective).

PROPHYLAXIS

- Smallpox vaccine would be required for all persons exposed at the time of the bioterrorist attack or anyone with close personal contact with a smallpox case
- Vaccine is most effective if given before of within 3 days of exposure
- Ideally, all exposed persons should be placed in strict quarantine for 17 days after last contact with a smallpox case

Medical Management Guidelines for Bioterrorism Agents

MEDICAL MANAGEMENT GUIDELINES FOR SMALLPOX

For more information go to: http://emergency.cdc.gov/agent/smallpox/diagnosis/casedefinition.asp

BACKGROUND INFORMATION

Smallpox is caused by an *Orthopoxvirus*, variola, a large enveloped DNA virus. The last occurrence of endemic smallpox was in Somalia in 1977 and the last human cases were laboratory-acquired infections in 1978. Smallpox was declared eradicated in 1980 by the World Health Organization.

Variola is infectious only for humans; there is no animal reservoir. Other key epidemiologic points include:

- The virus is highly stable and retains infectivity for long periods outside the host. Historically, smallpox was more common in the winter and spring; with aerosol infectivity decreasing with higher temperatures and humidity.
- Approximately 30% of susceptible contacts became infected during the era of endemic smallpox.
- Smallpox is transmitted by respiratory secretions, most efficiently during the early stages of the rash illness; it is generally believed that close person-to-person proximity is required for reliable transmission to occur. Patients are considered infectious from the time of development of the eruptive exanthem (usually 2-3 days after fever begins) until all scabs separate. In addition, virus can readily be recovered from scabs throughout convalescence.
- Fomites and inanimate objects are considered potential vehicles of transmission. However, since laundry from infected patients may contain viable virus, bedding and clothing of smallpox patients should be autoclaved.
- **Patients with confirmed or suspected smallpox should be placed on strict isolation until no longer considered infectious.**
- **Strict quarantine with respiratory isolation for 17 days is recommended for all persons in direct contact with a case.** In the setting of a large outbreak due to bioterrorism, this may not be possible - in which case, quarantine of exposed persons in their home with a daily fever watch may be an alternative public health measure.

ROUTE OF EXPOSURE/TRANSMISSION

During an act of bioterrorism, release of an aerosol will be the most likely route of transmission.

- Variola major *Incubation period* - typically 12-14 days, can be 7-17 days.
- Acute onset of malaise, fever, rigors, vomiting, headache and backache.

CLINICAL MANIFESTATIONS

Symptoms

- **Prodrome**: backache. 15% develop delirium. 10% of light skinned patients have an erythematous rash.
- **Exanthem:** Appears as soon as 2-3 days after prodrome, just as fever peaks.
- Discrete maculopapular rash on face, hands, forearms, and mucous membranes of mouth and pharynx. Involvement of palms and soles is common.
- Rash spreads to legs and then centrally to trunk during Week 2.
- Lesions quickly progress from macules to papules to vesicles to pustular vesicles (umbilicated) to crusty scabs.
- Scabs form 8-14 days after onset, leaving depressions and depigmented scars primarily on the face

which has more sebaceous glands.

CLINICAL CLUES TO DISTINGUISH SMALLPOX FROM CHICKEN POX:

- Smallpox has many more lesions on face and extremities than trunk (Centrifugal spread).
- Smallpox lesions are synchronous in their stage of development.
- Smallpox lesions are more common on palms and soles.
- Smallpox lesions are more deeply imbedded in the dermis compared with the superficial lesions of chickenpox.

VARIATIONS IN VARIOLOA MAJOR

Major Flat-type/"malignant" smallpox: Occurs in 2-5% of smallpox cases due to lack of adequate cell-mediate immune response. Notable for severe systemic toxicity and slow evolution of flat, soft, focal skin lesions. These papules coalesce and never become pustular. Skin develops a fine-grained reddish color, resembling crepe rubber. The mortality among unvaccinated persons is 95%.

Hemorrhagic-type smallpox: Occurs in < 3% of smallpox cases. Notable for extensive petechia, mucosal hemorrhage and intense toxemia (high fevers, headache, backache and abdominal pain). Seen more commonly in pregnant women. Patients usually die before development of typical pox lesions. Differential diagnosis includes: meningococcemia and acute leukemia.

VARIOLA MINOR (ALASTRIM)

- **Incubation period - 7-17 days**
- **Symptoms -** Clinically resembles variola major but with milder systemic toxicity and sometimes more diminutive pox lesions. Lesions on the face are typically more sparse and evolve more rapidly than those on the arms and legs. Mortality in the unvaccinated is usually less than 1%.

CLINICAL COMPLICATIONS OF SMALLPOX

Pulmonary edema:	Common in hemorrhagic and flat-type smallpox.
Orchitis:	Noted in 0.1% of patients.
Encephalitis:	Developed in 1 in 500 patients with variola major.
Keratitis/corneal ulcers:	Progresses to blindness in about 1% of cases.
Disease during pregnancy:	Precipitated high perinatal mortality.

MONKEYPOX

Naturally-occurring relative of variola, monkeypox virus, is a rare zoonosis that occurs in the rain forest areas of Africa and is felt to be rodent borne. The disease it causes, monkeypox, is clinically indistinguishable from smallpox, except for notable swelling of cervical and inguinal lymph nodes.

LABORATORY DIAGNOSIS

If smallpox is suspected, please call the Santa Clara County Public Health Department at 408-885-4214 to arrange for submission of specimens to CDC for testing. After hours, please call County Communications at

MEDICAL MANAGEMENT GUIDELINES FOR SMALLPOX

408-299-2501.

- The diagnosis of smallpox requires astute clinical evaluation. The clinical diagnosis may be confused with chickenpox, erythema multiforme with bullae or allergic contact dermatitis.
- The diagnosis of smallpox is an international emergency and confirmation of the diagnosis by laboratory techniques requires coordination between the medical and laboratory community and local, state, federal and international agencies. If you clinically suspect even a single case of smallpox, notify the Santa Clara County Public Health Department IMMEDIATELY at 408-885-4214 (AFTER HOURS CALL 408-299-2501).
- In the event of a bioterrorist release of smallpox, confirmation by a reference laboratory will be necessary for the earliest (index) cases. After a smallpox outbreak is confirmed, diagnosis of subsequent cases will need to be based on a compatible clinical presentation.
- Opening the lesions with the blunt edge of a sterile scalpel and harvesting the fluid with a sterile swab should obtain vesicular fluid. The swab(s) should be placed in a cryo-safe 1-2 ml gasketed vial (the gasket on the vial prevents gas exchange, e.g., carbon dioxide vapors from dry ice, which can acidify samples). Scabs can be removed with forceps and also placed in a gasketed vial. The vial should not contain any transport medium. In addition, a droplet of vesicular fluid can be placed on a clean microscopic slide and allowed to air dry in a safe location. The slides should be placed in an airtight container. Specimens from different patients should not be mixed together. All specimens should be safely secured for shipping. Specimens will be tested at the CDC's Biosafety Level 4 reference laboratory using the following tests:
    - **Light or Electronic Microscopy -** Scrapings of vesicular lesions can be examined by electron microscopy for characteristic brick-shaped virions. This method does not distinguish variola from vaccinia, monkeypox or cowpox.
    - **Viral cultures –** Requires isolation of virus and characterization of its growth on chorioallantoic membrane or cell culture.

Other Testing

Polymerase chain reaction and restriction fragment length polymorphisms (RFLP) diagnostic techniques promise a more accurate and less cumbersome method of identifying variola virus. These techniques are currently only available at national reference laboratories, such as the CDC.

Handling Laboratory Specimens

All other laboratory tests should be performed in Biological Safety Level 2 cabinets and blood cultures should be maintained in a closed system. Laboratory staff handling specimens from persons who might have smallpox must wear surgical gloves, protective gowns and shoe covers. Every effort should be made to avoid splashing or creating an aerosol, and protective eye wear and masks should be worn if work cannot be done in a Biological Safety Level 2 cabinet. A full-face mask respirator with a HEPA (high efficiency particulate air) filter is an acceptable, but cumbersome, alternative to masks and protective eye wear. Laboratories working with a large amount of viral organisms should use Biological Safety Level 3 cabinets.

Accidental spills of potentially contaminated material should be decontaminated immediately by covering liberally with a disinfectant solution (1% sodium hypochlorite or sodium hydroxide (0.1N)). All biohazardous waste should be decontaminated by autoclaving. Contaminated equipment or instruments may be decontaminated with a hypochlorite solution, 1% peracetic acid, formaldehyde, ethylene oxide, copper irradiation, or other O.S.H.A. approved solutions, or by autoclaving or boiling for 10 minutes.

TREATMENT

- Supportive care is the mainstay of therapy.
- Currently, there are no anti-viral drugs of proven efficacy. Although, adefovir, dipivoxil, cidofovir and

ribavirin have significant in vitro antiviral activity against poxviruses, their efficacy as therapeutic agents for smallpox is currently uncertain. Cidofovir is FDA-licensed and shows the most promise in animal models.

ISOLATION OF PATIENTS

- Smallpox is transmissible from person-to-person by exposure to respiratory secretions (particularly from coughing patients), contact with pox lesions and by fomites (although not efficiently). All staff should observe both Airborne and Contact Precautions, in addition to Standard Precautions, when caring for patients with suspected or confirmed smallpox.
- Patients should be placed in a closed-door, negative pressure room with 6 to 12 air exchanges per hour and HEPA filtration of exhausted air. Patients with smallpox should be placed on strict isolation from the onset of eruptive exanthem until all pox scabs have separated (generally 14-28 days). Healthcare workers and others entering the room should wear appropriate respiratory protection; respiratory masks should meet the minimal NIOSH standard for particulate respirators (N95). Healthcare provides should wear clean gloves and gowns for all patient contact.
- In the event of a large-scale smallpox outbreak due to a bioterrorist attack, there may be massive numbers of victims. In this case, there may be a need to cohort patients due to limited availability of respiratory isolation rooms. If this is done, then all patients should receive smallpox vaccine or vaccine immune globulin within 3 days of exposure, if available, in the event that some of these patients are misdiagnosed with smallpox.
- All healthcare workers providing direct patient care to persons with smallpox should be vaccinated. If vaccine is unavailable, then only staff who previously received smallpox vaccine (*e.g., persons born before 1972 or persons who were in the military before 1989*) should be caring for patients with smallpox.

DISPOSAL OF INFECTIOUS WASTE

- Use of tracking forms, containment, storage, packaging, treatment and disposal methods should be based upon the same rules as all other regulated medical wastes.

AUTOPSY AND HANDLING OF CORPSES

- All postmortem procedures are to be performed using Universal Precautions. In addition, due to concerns about aerosolization of the virus, personnel should use particulate respirators as recommended under Strict Isolation precautions.
- All persons performing or assisting in postmortem procedures must wear mandated P.P.E. (personal protective equipment) as delineated by O.S.H.A. guidelines.
- Instruments should be autoclaved or sterilized with a 10% bleach solution or other solutions approved by O.S.H.A. Surfaces contaminated during postmortem procedures should be decontaminated with an appropriate chemical germicide such as 10% hypochlorite or 5% phenol (carbolic acid).

MANAGEMENT OF EXPOSED PERSONS

- An exposed person is defined as a person who has been in close personal contact with a patient with suspect or confirmed smallpox. Close personal contact includes persons residing in the same household with the case-patient or persons with face-to-face contact with the case AFTER the case developed febrile illness. (During outbreaks in Europe in the 1960's, up to 10-20 secondary cases occurred after exposure to a single case-patient, if vaccination efforts were delayed.)
- **Quarantine:** All exposed persons should be placed in strict quarantine with respiratory isolation for 17 days

after last contact with suspect or confirmed smallpox case(s). In the setting of a large outbreak due to bioterrorism, this may not be possible - in which case, quarantine of exposed persons in their home with a daily fever watch may be an alternative public health measure.

- **Vaccination:** In the United States, the smallpox vaccine supply is overseen by the CDC. The Wyeth vaccine (using the New York Board of Health vaccinia strain) is freeze-dried in multidose vials (50 doses per vial) at 20 ^{o}C. Vaccine Indications: All exposed persons, including all household and face-toface contacts of patients, should be vaccinated immediately, if vaccine is available. Additionally, all health care workers that might care for smallpox patients, emergency personnel who might transport patients, and mortuary staff should be vaccinated, if vaccine is available. Vaccination is most effective at protecting against smallpox if given within 3 days of exposure. Methodology: A bifurcated needle is inserted into an ampule of reconstituted vaccine and, on withdrawal, a droplet of vaccine is held by capillarity between the two tines. The needle is held at right angles to the skin, the wrist of the vaccinator rests against the arm. Fifteen up and down (perpendicular) strokes of the needle are rapidly made in an area of 5-mm diameter. The strokes should be sufficiently vigorous so that a trace of blood appears at the vaccination site after 15-30 seconds. Excess vaccine should be wiped from the site with gauze (gauze should be discarded into a hazardous waste receptacle) and the site covered with a loose, non-occlusive bandage.

EVALUATION OF VACCINE RESPONSE

- Primary vaccine response (never previously vaccinated): Day 3: A red papule appears at the vaccination site Day 5: Papule becomes vesicular Day 7: A whitish, umbilicated, multilocular pustule develops, containing turbid lymph and surrounded by an erythematous areola which may expand further for 3 days. Fever during days 4-14, particularly for children, is common. The pustule dries and falls off after about 3 weeks.
- Re-immunization response (those previously vaccinated): May react as described above, or may have a papule surrounded by erythema that peaks between 3 and 7 days. A response that peaks within 48 hours is a hypersensitivity reaction; patients with this reaction should be revaccinated.

CONTRAINDICATIONS TO VACCINATION

- Eczema or other exfoliative skin condition (*e.g., atopic dermatitis, burns, impetigo*)
- Leukemia, lymphoma, generalized malignancy or chemotherapy with alkylating agents, antimetabolites, radiation or high dose corticosteroids
- HIV infection or AIDS
- Hereditary immune deficiency disorders
- Pregnant women
- Life-threatening allergy to polymyxin B, streptomycin, tetracycline or neomycin.
- In the setting of a large bioterrorist attack, the risk of vaccination must be weighed against the likelihood of acquiring infection. If VIG (vaccinia immune globulin) is available, those in close personal contact with a smallpox case AND with a clear contraindication to vaccine may receive vaccine PLUS VIG (0.3 ml/kg of body weight) simultaneously within the first week following exposure.

POTENTIAL SIDE EFFECTS OF VACCINATION

- Side effects include: low grade fever, lymphadenopathy, autoinoculation, secondary inoculation, ocular vaccinia, urticarial rash, Stevens-Johnson syndrome, generalized vaccinia (3 per 10,000 vaccinations occurring from 6-9 days after vaccination), eczema vaccinatum, progressive vaccinia (1 per million vaccinations) and postvaccinial encephalitis (3 per million primary vaccinations occurring from 8-15 days after vaccination).

MEDICAL MANAGEMENT GUIDELINES FOR SMALLPOX
• **Severe vaccine complications should be treated with VIG (0.6 ml/kg body weight). The dose should be administered intramuscularly in 2 divided doses over a 24 to 36 hour period. The dose can be repeated in 2-3 days, if needed.**

SMALLPOX FACT SHEET

Smallpox Overview

The Disease

Smallpox is a serious, contagious, and sometimes fatal infectious disease. There is no specific treatment for smallpox disease, and the only prevention is vaccination. The name *smallpox* is derived from the Latin word for "spotted" and refers to the raised bumps that appear on the face and body of an infected person.

There are two clinical forms of smallpox. Variola major is the severe and most common form of smallpox, with a more extensive rash and higher fever. There are four types of variola major smallpox: ordinary (the most frequent type, accounting for 90% or more of cases); modified (mild and occurring in previously vaccinated persons); flat; and hemorrhagic (both rare and very severe). Historically, variola major has an overall fatality rate of about 30%; however, flat and hemorrhagic smallpox usually are fatal. Variola minor is a less common presentation of smallpox, and a much less severe disease, with death rates historically of 1% or less.

Smallpox outbreaks have occurred from time to time for thousands of years, but the disease is now eradicated after a successful worldwide vaccination program. The last case of smallpox in the United States was in 1949. The last naturally occurring case in the world was in Somalia in 1977. After the disease was eliminated from the world, routine vaccination against smallpox among the general public was stopped because it was no longer necessary for prevention.

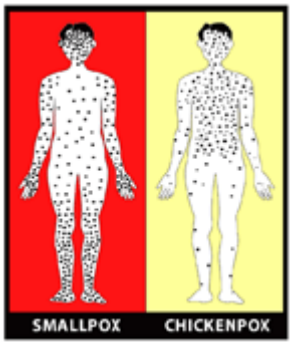
Where Smallpox Comes From

Smallpox is caused by the variola virus that emerged in human populations thousands of years ago. Except for laboratory stockpiles, the variola virus has been eliminated. However, in the aftermath of the events of September and October, 2001, there is heightened concern that the variola virus might be used as an agent of bioterrorism. For this reason, the U.S. government is taking precautions for dealing with a smallpox outbreak.

Transmission

Generally, direct and fairly prolonged face-to-face contact is required to spread smallpox from one person to another. Smallpox also can be spread through direct contact with infected bodily fluids or contaminated objects such as bedding or clothing. Rarely, smallpox has been spread by virus carried in the air in enclosed settings such as buildings, buses, and trains. Humans are the only natural hosts of variola. Smallpox is not known to be transmitted by insects or animals.

A person with smallpox is sometimes contagious with onset of fever (prodrome phase), but the person becomes most contagious with the onset of rash. At this stage the infected person is usually very sick and not able to move around in the community. The infected person is contagious until the last smallpox scab falls off.

Smallpox Disease	
Incubation Period **(Duration: 7 to 17 days)** ***Not contagious***	**Exposure to the virus** is followed by an incubation period during which people do not have any symptoms and may feel fine. This incubation period averages about 12 to 14 days but can range from 7 to 17 days. During this time, people are not contagious.
Initial Symptoms ***(Prodrome)*** **(Duration: 2 to 4 days)** ***Sometimes contagious****	The **first symptoms** of smallpox include fever, malaise, head and body aches, and sometimes vomiting. The fever is usually high, in the range of 101 to 104 degrees Fahrenheit. At this time, people are usually too sick to carry on their normal activities. This is called the *prodrome* phase and may last for 2 to 4 days.
Early Rash **(Duration: about 4 days)** ***Most contagious*** **Rash distribution:**  	A **rash emerges** first as small red spots on the tongue and in the mouth. These spots develop into sores that break open and spread large amounts of the virus into the mouth and throat. At this time, the person becomes **most contagious**. Around the time the sores in the mouth break down, a rash appears on the skin, starting on the face and spreading to the arms and legs and then to the hands and feet. Usually the rash spreads to all parts of the body within 24 hours. As the rash appears, the fever usually falls and the person may start to feel better. By the third day of the rash, the rash becomes raised bumps. By the fourth day, the bumps fill with a thick, opaque fluid and often have a depression in the center that looks like a bellybutton. (This is a major distinguishing characteristic of smallpox.) Fever often will rise again at this time and remain high until scabs form over the bumps.
Pustular Rash **(Duration: about 5 days)** ***Contagious***	The bumps become **pustules**—sharply raised, usually round and firm to the touch as if there's a small round object under the skin. People often say the bumps feel like BB pellets embedded in the skin.
Pustules and Scabs **(Duration: about 5 days)** ***Contagious***	The pustules begin to form a crust and then **scab**. By the end of the second week after the rash appears, most of the sores have scabbed over.
Resolving Scabs **(Duration: about 6 days)** ***Contagious***	The scabs begin to fall off, leaving marks on the skin that eventually become pitted **scars**. Most scabs will have fallen off three weeks after the rash appears. The person is contagious to others until all of the scabs have fallen off.
Scabs resolved ***Not contagious***	Scabs have fallen off. Person is no longer contagious.

*Smallpox may be contagious during the *prodrome* phase, but is most infectious during the first 7 to 10 days following rash onset.

For more information, visit www.cdc.gov/smallpox, or call CDC at 800-CDC-INFO (English and Spanish) or 888-232-6348 (TTY).

August 9, 2004

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION
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BIOTERRORISM: TULAREMIA

EPIDEMIOLOGY

- Highly infectious after aerosolization.
- Infectious dose can be as low as 10-15 organisms.
- Person-to-person transmission does not occur.

CLINICAL

- Incubation period is 3-6 days (ranges 1-21 days).
- Aerosolization would most likely result in typhoidal tularemia, with pneumonic involvement.
- Typhoidal tularemia is a nonspecific illness, with fever, headache, malaise and non-productive cough (mortality rates can be as high as 30-60%).
- Diagnosis requires high index of suspicion given nonspecific presentation.

LABORATORY DIAGNOSIS

- Bacterial cultures should be handled in a Biosafety Level 3 facility; isolation of organism can otherwise put laboratory workers at risk.
- Organism is difficult to culture and grows poorly on standard media; cysteine-enriched media is required.
- Serology is most commonly used for diagnosis.

PATIENT ISOLATION

- Standard precautions. Respiratory isolation not required.

TREATMENT

- Streptomycin (7.5 mg/kg IM q 12 hours x 10-14 days) or gentamicin (3-5 mg/kg/day IV or IM qd in 3 divided doses x 10-14 days) are the preferred antibiotics.
- Tetracyclines are alternative choices, although they are bacteriostatic and associated with higher relapse rates and must be continued for at least 14 days.

PROPHYLAXIS

- Antibiotic prophylaxis is most effective if begun within 24 hours after exposure to aerosol.
- Tetracyclines are recommended for 14 days.

Medical Management Guidelines for Bioterrorism Agents

MEDICAL MANAGEMENT GUIDELINES FOR TULAREMIA

For more information go to: http://emergency.cdc.gov/agent/tularemia/diagnosis.asp

BACKGROUND INFORMATION

- Tularemia is a zoonotic disease caused by Francisella tularensis, a gram-negative intracellular coccobacillus. F. tularensis has several biovars; F. tularensis biovar tularensis is the most common naturally-occurring isolate in the United States.
- The organism is primarily recovered from lagomorphs (rabbits), rodents and arthropods (ticks and deer flies) in the United States and from water, mosquitoes and aquatic mammals outside the United States. The rabbit is the vertebrate most commonly associated with tularemia in North America. In recent years, the reported incidence of tularemia has declined to less than 200 cases per year in the United States.

ROUTE OF EXPOSURE/TRANSMISSION/USE AS A BIOTERRORISM AGENT

- Tularemia is acquired under natural conditions by direct inoculation (such as an arthropod bite), animal contact such as skinning or eating infected animals, or via the airborne route. (Domestic cats have occasionally transmitted tularemia by bites or scratches.) F. tularensis may survive for prolonged periods in water, mud and animal carcasses; even if frozen Francisella tularensis is highly infectious. After aerosolization, 10-50 virulent organisms given by aerosol can cause infection in humans, and as few as 10 organisms can cause infection when administered percutaneously. In the event of a bioterrorist attack, aerosolization would be the most likely route of infection.
- Tularemia transmission from patient-to-patient has never been reported, even among patients with tularemia pneumonia. Persons exposed to an aerosol of Francisella tularensis do not present a risk for secondary infection of others or for re-aerosolization of the organism.

Use as a Bioterrorism Agent

- Weaponized by the United States military during the biologic offensive program in the 1950s-1960s.
- Highly infectious after aerosolization; infectious dose can be as low as 10 to 50 microorganisms if inhaled.
- Aerosolized F. tularensis would cause typhoidal tularemia (a nonspecific, febrile illness), with high mortality rates (30-60%) if untreated.

CLINICAL MANIFESTATIONS

- During an act of bioterrorism, release of an aerosol will be the most likely route of transmission with typhoidal tularemia the most likely clinical presentation.
- There are several different classification systems for clinical tularemia. The most straightforward classifies tularemia into ulceroglandular (75% of patients) and typhoidal (25% of patients).

- **Ulceroglandular** disease involves lesions on the skin or mucous membranes (including conjunctiva), lymph nodes larger than 1 cm, or both.
- In **typhoidal** tularemia, the lymph nodes are usually smaller than 1 cm and no skin or mucous membrane lesions are present--this form is more commonly associated with pneumonia and has a higher mortality rate.

Typhoidal Tularemia

- An acute, nonspecific febrile illness associated with F. tularensis that is **not** associated with prominent lymphadenopathy.
- Typhoidal tularemia is mainly due to inhalation of infected aerosols. **Most likely form during an act of bioterrorism.**
- **Incubation period**: 3 - 6 days (range 1-21 days)
- **Symptoms -**prominent symptoms include:
    - Fever with chills
    - Headache
    - Myalgias
    - Sore throat
    - Anorexia
    - Nausea
    - Vomiting
    - Diarrhea (can be a major component of illness, generally watery stool not bloody)
    - Abdominal pain
    - Cough
- Patients may develop a sepsis syndrome with hypotension, adult respiratory distress syndrome, renal failure, disseminated intravascular coagulation and shock.
- **Pleuropulmonary disease** (pneumonic tularemia) is common with pulmonary infiltrates or pleural effusions seen in up to 45% of typhoidal tularemia cases. A patchy, alveolar process is most often seen on chest x-ray. Patients may develop acute respiratory distress syndrome and require mechanical ventilation.

Ulceroglandular Tularemia

- Generally due to inoculation of the organism into the skin or mucous membranes.
- **Incubation period:** 3 - 6 days (range 1 - 21 days)
- **Symptoms**
    - Local papule develops at the inoculation site, with progression to a pustule then an ulcer within several days. Lymphadenopathy develops in 85% of patients. Nodes are usually tender and 0.5-10 cm in diameter (mean 2 cm). Enlarged nodes may become fluctuant, drain spontaneously or persist for months to years.
    - A cutaneous ulcer occurs in 60% of cases. Ulcers are usually singular and 0.4-3.0 cm in diameter, with heaped-up borders. Ulcers are almost always accompanied by regional

lymphadenopathy.

- In addition, the following symptoms may be present (in decreasing order of likelihood of appearance):
    - Fever (present in 85% of patients)
    - Chills
    - Headache
    - Cough
    - Myalgia
    - Chest pain
    - Vomiting
    - Arthralgia
    - Sore throat
    - Abdominal pain
    - Diarrhea
    - Dysuria
    - Back pain
    - Stiff neck
- Ulceroglandular tularemia can also be complicated by pleuropulmonary disease or pharyngeal involvement.
- Pharyngeal tularemia (via ingestion of contaminated food, water or droplets) is associated with severe throat pain, exudative pharyngitis and often pharyngeal ulcerations.

LABORATORY DIAGNOSIS

- **Routine laboratory work must be done in Biosafety Level 2 facilities. However, handling of bacterial cultures once the organism is identified should be done in Biosafety Level 3 facilities If tularemia is suspected, please call the Santa Clara County Public Health Laboratory at 408-885-4272 to arrange for submission of specimens for testing. After hours, please call 408-299-2501.**
- The diagnosis of tularemia requires a high index of suspicion since the disease often presents with very nonspecific symptoms. The diagnosis can be made by recovery of the organism from blood, ulcers, conjunctival exudates, sputum, pleural fluid, lymph nodes, gastric washings and pharyngeal exudates. Since the organism is difficult to isolate and constitutes a potential danger to laboratory personnel, serologic evidence of infection in a patient with a compatible clinical syndrome is commonly used for diagnosis.

Culture

- F. tularensis grows poorly on standard media. It forms small, smooth, opaque colonies when grown on media containing cysteine or other sulfhydryl compounds (e.g., glucose cysteine blood agar or thioglycollate broth) at 37C. The organism has also been isolated from automated radiometric detection systems if the media is subcultured on chocolate agar. The bacteria grows slowly; some strains may require up to 2-3 weeks to develop visible colonies.
- **Notify the clinical laboratory in advance of submitting specimens for culture which may contain F. tularensis, since isolation of the organism can put laboratory workers at risk for infection.**

MEDICAL MANAGEMENT GUIDELINES FOR TULAREMIA

Serology

- Antibody detection assays include tube agglutination, microagglutination and ELISA. Significant antibody does not appear until the end of the second week of illness, peaks at 4-5 weeks, and can persist for more than a decade. A single titre (by tube agglutination) of > 1:160 is a presumptive positive; a four-fold rise is required for a definitive serologic diagnosis. ELISA and microagglutination tests may be more sensitive than tube agglutination. Antibodies may cross-react with Brucella spp., Proteus 0X19 and Yersinia spp. but dithiothreitol treatment of the serum will eliminate most of these reactions. Serology testing is available through national reference laboratories.

HANDLING LABORATORY SPECIMENS

- Tularemia is the third most commonly reported laboratory-associated bacterial infection. Cases have occurred among clinical laboratorians working with bacterial cultures. Laboratory staff handling specimens from persons who are suspected of having tularemia must wear face masks with eye protection, surgical gloves, protective gowns, and shoe covers --- especially when working with pure bacterial cultures. Laboratory tests (such as serological examinations and staining of impression smears) can be performed in Biological Safety Level 2 cabinets.
- **Blood cultures should be maintained in a closed system and clinical isolates from blood or any other site should be handled in Biological Safety Level 3 cabinets.**
- Every effort should be made to avoid splashing or creating an aerosol. Biosafety Level 3 practices and facilities should be used for inoculation, incubation, centrifugation and harvesting of cell cultures and the manipulation of infected tissues.
- Accidental spills of potentially contaminated material should be decontaminated immediately by covering liberally with a disinfectant solution (0.1% sodium hypochlorite or sodium hydroxide (0.1N)). All biohazardous waste should be decontaminated by autoclaving. Contaminated equipment or instruments may be decontaminated with a hypochlorite solution, hydrogen peroxide, peracetic acid, 1% glutaraldehyde solution, formaldehyde, ethylene oxide, copper irradiation, or other O.S.H.A. approved solutions, or by autoclaving or boiling for 10 minutes.

TREATMENT

- The treatment of choice for all forms of tularemia except meningitis is streptomycin; gentamicin is an acceptable alternative. For both drugs, dosages must be adjusted for renal insufficiency.
- **Gentamicin is safe during pregnancy; avoid streptomycin due to its association with irreversible deafness in children exposed in utero.**
- **Streptomycin**: Adult dosage is 0.5-1.0 gm (7.5 mg/kg) intramuscularly every 12 hours for 10-14 days. In very sick patients, streptomycin may be give at 15 mg/kg intramuscularly every 12 hours for 10-14 days. **Pediatric dose**: 15 mg/kg intramuscularly every 12 hours for 10-14 days.

ALTERNATIVE TREATMENTS:

- Gentamicin: 3-5 mg/kg/day intravenously or intramuscularly in three divided doses, with a peak serum

level of at least 5 ug/ml desirable. Continue for 10-14 days.

  - Pediatric dose: 2.5 mg/kg intravenously or intramuscularly every 8 hours for 10-14 days

- Tetracycline and chloramphenicol are bacteriostatic and associated with high relapse rates. These agents must be continued for a minimum of 14 days. Tetracycline: 2 grams /day IV or orally in four divided doses or doxycycline 100 mg IV or orally twice a day for at least 14 days.

  - Pediatric dose: [Not recommended for children less than 9 years, pregnant or lactating women] If > 45 kg, give adult dosage of doxycycline; if less than 45 kg, give 2.2 mg/kg twice a day. Tetracycline at 30 mg/kg/day orally, to a maximum of 2 grams/day, in four divided doses for at least 14 days.

- Chloramphenicol should generally not be used due to the availability of effective alternatives with fewer serious side effects.

- Additional agents with favorable in vitro susceptibility tests but limited clinical data on efficacy include: fluroquinolones (except cinoxacin), erythromycin (resistant strains of F. tularensis have been identified), and rifampin. Penicillin and cephalosporins are not effective and should not be used to treat tularemia.

COMPLICATION OF TULAREMIA - MENINGITIS

A rare complication of tularemia, meningitis requires special attention with regard to therapy as the penetration of streptomycin or gentamicin into the CSF is suboptimal. The treatment of meningeal infection should include combination therapy with chloramphenicol plus streptomycin or possibly a third-generation cephalosporin plus streptomycin (limited data available on efficacy).

ISOLATION OF PATIENTS

- Tularemia is not transmissible from person-to-person. Standard precautions should be followed for all patients --respiratory isolation rooms are not required. Ulcers or wounds in patients with tularemia should be covered and contact isolation maintained as F. tularensis can be isolated from such lesions for one month or longer.

DISPOSAL OF INFECTIOUS WASTE

- Use of tracking forms, containment, storage, packaging, treatment and disposal methods should be based upon the same rules as all other regulated medical wastes.

AUTOPSY AND HANDLING OF CORPSES

- **All postmortem procedures are to be performed using Respiratory Precautions.**
- Efforts should be made to avoid aerosolization.
- All persons performing or assisting in postmortem procedures must wear mandated P.P.E. (personal

protective equipment) as delineated by O.S.H.A. guidelines.

- Instruments should be autoclaved or sterilized with a 10% bleach solution or other solutions approved by O.S.H.A. Surfaces contaminated during postmortem procedures should be decontaminated with an appropriate chemical germicide such as 10% hypochlorite or 5% phenol (carbolic acid).

MANAGEMENT OF EXPOSED PERSONS

- An exposed person is defined as a person who has been exposed to the release of a Francisella tularensis-containing aerosol.

Post-Exposure Prophylaxis

- Antibiotic prophylaxis should begin as soon as possible after exposure and is **most effective if begun within 24 hours**.
- Limited data suggests that tetracyclines may be effective:
    - Tetracycline 500 mg orally in 4 divided doses for 14 days
    - Doxycycline 100mg orally twice daily for 14 days

Pediatric Patients And Pregnant Women

- Although tetracyclines are not generally recommended for children under age 9 or for pregnant women, the risk of developing tularemia may outweigh these limitations. Floroquinolones are a potential alternative for prophylaxis.
- **Doxycycline:**
    - If > 45 kg - 100 mg orally every 12 hours
    - If $\leq$ 45 kg - 2.2 mg/kg orally every 12 hours
- If antibiotic prophylaxis is not started within 24 hours of exposure, then exposed persons should be instructed to begin a fever watch and seek medical care if temperature exceeds 38.5 ^{o}C.

FACT SHEET

Key Facts About Tularemia

This fact sheet provides important information that can help you recognize and get treated for tularemia. For more detailed information, please visit the Centers for Disease Control and Prevention (CDC) Tularemia Web site (www.bt.cdc.gov/agent/tularemia).

What is Tularemia?

Tularemia is a potentially serious illness that occurs naturally in the United States. It is caused by the bacterium *Francisella tularensis* found in animals (especially rodents, rabbits, and hares).

What are the Symptoms of Tularemia?

Symptoms of tularemia could include:

- sudden fever
- chills
- headaches
- diarrhea
- muscle aches
- joint pain
- dry cough
- progressive weakness

People can also catch pneumonia and develop chest pain, bloody sputum and can have trouble breathing and even sometimes stop breathing.

Other symptoms of tularemia depend on how a person was exposed to the tularemia bacteria. These symptoms can include ulcers on the skin or mouth, swollen and painful lymph glands, swollen and painful eyes, and a sore throat.

How Does Tularemia Spread?

People can get tularemia many different ways:

- being bitten by an infected tick, deerfly or other insect
- handling infected animal carcasses
- eating or drinking contaminated food or water
- breathing in the bacteria, *F. tularensis*

Tularemia is not known to be spread from person to person. People who have tularemia do not need to be isolated. People who have been exposed to the tularemia bacteria should be treated as soon as possible. The disease can be fatal if it is not treated with the right antibiotics.

How Soon Do Infected People Get Sick?

Symptoms usually appear 3 to 5 days after exposure to the bacteria, but can take as long as 14 days.

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What Should I Do if I Think I Have Tularemia?

Consult your doctor at the first sign of illness. Be sure to let the doctor know if you are pregnant or have a weakened immune system.

How Is Tularemia Treated?

Your doctor will most likely prescribe antibiotics, which must be taken according to the directions supplied with your prescription to ensure the best possible result. Let your doctor know if you have any allergy to antibiotics.

A vaccine for tularemia is under review by the Food and Drug Administration and is not currently available in the United States.

What Can I Do To Prevent Becoming Infected with Tularemia?

Tularemia occurs naturally in many parts of the United States. Use insect repellent containing DEET on your skin, or treat clothing with repellent containing permethrin, to prevent insect bites. Wash your hands often, using soap and warm water, especially after handling animal carcasses. Be sure to cook your food thoroughly and that your water is from a safe source.

Note any change in the behavior of your pets (especially rodents, rabbits, and hares) or livestock, and consult a veterinarian if they develop unusual symptoms.

Can Tularemia Be Used As a Weapon?

Francisella tularensis is very infectious. A small number (10-50 or so organisms) can cause disease. If F. tularensis were used as a weapon, the bacteria would likely be made airborne for exposure by inhalation. People who inhale an infectious aerosol would generally experience severe respiratory illness, including life-threatening pneumonia and systemic infection, if they are not treated. The bacteria that cause tularemia occur widely in nature and could be isolated and grown in quantity in a laboratory, although manufacturing an effective aerosol weapon would require considerable sophistication.

What is CDC Doing About Tularemia?

The CDC operates a national program for bioterrorism preparedness and response that incorporates a broad range of public health partnerships. Other things CDC is doing include:

- Stockpiling antibiotics to treat infected people
- Coordinating a nation-wide program where states share information about tularemia
- Creating new education tools and programs for health professionals, the public, and the media.

For more information, visit www.bt.cdc.gov/agent/tularemia, or call the CDC public response hotline at (888) 246-2675 (English), (888) 246-2857 (Español), or (866) 874-2646 (TTY)

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BIOTERROISM: VIRAL HEMMORHAGIC FEVERS

ETIOLOGIC AGENTS

The following agents can all cause viral hemmorhagic fever (VHF)

- Arenaviradae (Lassa, Junin, Machupo, Guanarito, and Sabia),
- Filoviradae (Marburg and Ebola),
- Bunyaviradae (Congo-Crimean hemmorhagic fever virus and hantaviruses)
- Flaviradae (yellow fever and Dengue)

EPIDEMIOLOGY

- Highly infectious after aerosolization.
- Infectious dose can be as low as 1-10 organisms.
- Risk of person-to-person transmission depends on virus.

CLINICAL

- Incubation period is 4 – 21 days, depending on virus.
- Clinical presentation would vary by viral agent; however, dominant clinical features of all are a consequence of microvascular damage and changes in vascular permeability.
- Fever, myalgia, and prostration may evolve to shock, generalized mucous membrane hemmorhage, and neurologic, hematopoietic, or pulmonary involvement.

LABORATORY DIAGNOSIS

- Viral isolation should be handled in a Biosafety Level 3 or 4 facility and may take 3 – 10 days.
- ELISA or reverse transcriptase PCR available for most VHF viruses.

PATIENT ISOLATION

- Isolation room with contact precautions.

TREATMENT

- Ribavirin (30 mg/kg IV x 1, then 15 mg/kg IV q 6 h x 4 days, 7.5 mg/kg IV q 8 x 6 days) may be helpful for Congo-Crimean hemorrhagic fever or arenaviruses.

PROPHYLAXIS

- Licensed vaccine available only for yellow fever.

MEDICAL MANAGEMENT GUIDELINES FOR VIRAL HEMMORHAGIC FEVERS

For more information go to: http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/vhf.htm

BACKGROUND INFORMATION

- Viral hemorrhagic fevers (VHFs) refer to a group of illnesses that are caused by several distinct families of viruses. In general, the term "viral hemorrhagic fever" is used to describe a severe multisystem syndrome (multisystem in that multiple organ systems in the body are affected).
- Characteristically, the overall vascular system is damaged, and the body's ability to regulate itself is impaired. These symptoms are often accompanied by hemorrhage (bleeding); however, the bleeding is itself rarely life-threatening. While some types of hemorrhagic fever viruses can cause relatively mild illnesses, many of these viruses cause severe, life-threatening disease.

ROUTE OF EXPOSURE/TRANSMISSION

- VHFs are caused by viruses of four distinct families: arenaviruses, filoviruses, bunyaviruses, and flaviviruses. Each of these families share a number of features:
  - They are all RNA viruses, and all are covered, or enveloped, in a fatty (lipid) coating.
  - Their survival is dependent on an animal or insect host, called the natural reservoir.
  - The viruses are geographically restricted to the areas where their host species live.
  - Humans are not the natural reservoir for any of these viruses. Humans are infected when they come into contact with infected hosts. However, with some viruses, after the accidental transmission from the host, humans can transmit the virus to one another.
  - Human cases or outbreaks of hemorrhagic fevers caused by these viruses occur sporadically and irregularly. The occurrence of outbreaks cannot be easily predicted.
- With a few noteworthy exceptions, there is no cure or established drug treatment for VHFs.
- In rare cases, other viral and bacterial infections can cause a hemorrhagic fever; scrub typhus is a good example.

CLINICAL MANIFESTATIONS, TREATMENT AND SPECIMEN HANDLING/SUBMITTING INFORMATION

- Go to http://www.cdc.gov/ncidod/dvrd/spb/mnpages/disinfo.htm for information on sixteen (16) viral hemorrhagic fevers.

Viral Hemorrhagic Fevers

Fact Sheet

What are viral hemorrhagic fevers?

Viral hemorrhagic fevers (VHFs) refer to a group of illnesses that are caused by several distinct families of viruses. In general, the term "viral hemorrhagic fever" is used to describe a severe multisystem syndrome (multisystem in that multiple organ systems in the body are affected). Characteristically, the overall vascular system is damaged, and the body's ability to regulate itself is impaired. These symptoms are often accompanied by hemorrhage (bleeding); however, the bleeding is itself rarely life-threatening. While some types of hemorrhagic fever viruses can cause relatively mild illnesses, many of these viruses cause severe, life-threatening disease.

The Special Pathogens Branch (SPB) primarily works with hemorrhagic fever viruses that are classified as biosafety level four (BSL-4) pathogens. A list of these viruses appears in the SPB disease information index. The Division of Vector-Borne Infectious Diseases, also in the National Center for Infectious Diseases, works with the non-BSL-4 viruses that cause two other hemorrhagic fevers, dengue hemorrhagic fever and yellow fever.

How are hemorrhagic fever viruses grouped?

VHFs are caused by viruses of four distinct families: arenaviruses, filoviruses, bunyaviruses, and flaviviruses. Each of these families share a number of features:

- They are all RNA viruses, and all are covered, or enveloped, in a fatty (lipid) coating.
- Their survival is dependent on an animal or insect host, called the natural reservoir.
- The viruses are geographically restricted to the areas where their host species live.
- Humans are not the natural reservoir for any of these viruses. Humans are infected when they come into contact with infected hosts. However, with some viruses, after the accidental transmission from the host, humans can transmit the virus to one another.
- Human cases or outbreaks of hemorrhagic fevers caused by these viruses occur sporadically and irregularly. The occurrence of outbreaks cannot be easily predicted.
- With a few noteworthy exceptions, there is no cure or established drug treatment for VHFs.

In rare cases, other viral and bacterial infections can cause a hemorrhagic fever; scrub typhus is a good example.

What carries viruses that cause viral hemorrhagic fevers?

Viruses associated with most VHFs are zoonotic. This means that these viruses naturally reside in an animal reservoir host or arthropod vector. They are totally dependent on their hosts for replication and overall survival. For the most part, rodents and arthropods are the main reservoirs for viruses causing VHFs. The multimammate rat, cotton rat, deer mouse, house mouse, and other field rodents are examples of reservoir hosts. Arthropod ticks and mosquitoes serve as vectors for some of the illnesses. However, the hosts of some viruses remain unknown -- Ebola and Marburg viruses are well-known examples.

Where are cases of viral hemorrhagic fever found?

Taken together, the viruses that cause VHFs are distributed over much of the globe. However, because each virus is associated with one or more particular host species, the virus and the disease it causes are usually seen only where the host species live(s). Some hosts, such as the rodent species carrying several of the New World arenaviruses, live in geographically restricted areas. Therefore, the risk of getting VHFs caused by these viruses is restricted to those areas. Other hosts range over continents, such as the rodents that carry viruses which cause various forms of hantavirus pulmonary syndrome (HPS) in North and South America, or the different set of rodents that carry viruses which cause hemorrhagic fever with renal syndrome (HFRS) in Europe and Asia. A few hosts are distributed nearly worldwide, such as the common rat. It can carry Seoul virus, a cause of HFRS; therefore, humans can get HFRS anywhere where the common rat is found.

While people usually become infected only in areas where the host lives, occasionally people become infected by a host that has been exported from its native habitat. For example, the first outbreaks of Marburg hemorrhagic fever, in Marburg and Frankfurt, Germany, and in Yugoslavia, occurred when laboratory workers handled imported monkeys infected with Marburg virus. Occasionally, a person becomes infected in an area where the virus occurs naturally and then travels elsewhere. If the virus is a type that can be transmitted further by person-to-person contact, the traveler could infect other people. For instance, in 1996, a medical professional treating patients with Ebola hemorrhagic fever (Ebola HF) in Gabon unknowingly became infected. When he later traveled to South Africa and was treated for Ebola HF in a hospital, the virus was transmitted to a nurse. She became ill and died. Because more and more people travel each year, outbreaks of these diseases are becoming an increasing threat in places where they rarely, if ever, have been seen before.

How are hemorrhagic fever viruses transmitted?

Viruses causing hemorrhagic fever are initially transmitted to humans when the activities of infected reservoir hosts or vectors and humans overlap. The viruses carried in rodent reservoirs are transmitted when humans have contact with urine, fecal matter, saliva, or other body excretions from infected rodents. The viruses associated with arthropod vectors are spread most often when the vector mosquito or tick bites a human, or when a human crushes a tick. However, some of these vectors may spread virus to animals, livestock, for example. Humans then become infected when they care for or slaughter the animals.

Some viruses that cause hemorrhagic fever can spread from one person to another, once an initial person has become infected. Ebola, Marburg, Lassa and Crimean-Congo hemorrhagic fever viruses are examples. This type of secondary transmission of the virus can occur directly, through close contact with infected people or their body fluids. It can also occur indirectly, through contact with objects contaminated with infected body fluids. For example, contaminated syringes and needles have played an important role in spreading infection in outbreaks of Ebola hemorrhagic fever and Lassa fever.

What are the symptoms of viral hemorrhagic fever illnesses?

Specific signs and symptoms vary by the type of VHF, but initial signs and symptoms often include marked fever, fatigue, dizziness, muscle aches, loss of strength, and exhaustion. Patients with severe cases of VHF often show signs of bleeding under the skin, in internal organs, or from body orifices like the mouth, eyes, or ears. However, although they may bleed from many sites around the body, patients rarely die because of blood loss. Severely ill patient cases may also show shock, nervous system malfunction, coma, delirium, and seizures. Some types of VHF are associated with renal (kidney) failure.

How are patients with viral hemorrhagic fever treated?

Patients receive supportive therapy, but generally speaking, there is no other treatment or established cure for VHFs. Ribavirin, an anti-viral drug, has been effective in treating some individuals with Lassa fever or HFRS. Treatment with convalescent-phase plasma has been used with success in some patients with Argentine hemorrhagic fever.

How can cases of viral hemorrhagic fever be prevented and controlled?

With the exception of yellow fever and Argentine hemorrhagic fever, for which vaccines have been developed, no vaccines exist that can protect against these diseases. Therefore, prevention efforts must concentrate on avoiding contact with host species. If prevention methods fail and a case of VHF does occur, efforts should focus on preventing further transmission from person to person, if the virus can be transmitted in this way. Because many of the hosts that carry hemorrhagic fever viruses are rodents, disease prevention efforts include:

- controlling rodent populations;
- discouraging rodents from entering or living in homes or workplaces;
- encouraging safe cleanup of rodent nests and droppings.

For hemorrhagic fever viruses spread by arthropod vectors, prevention efforts often focus on community-wide insect and arthropod control. In addition, people are encouraged to use insect repellant, proper clothing, bednets, window screens, and other insect barriers to avoid being bitten.

For those hemorrhagic fever viruses that can be transmitted from one person to another, avoiding close physical contact with infected people and their body fluids is the most important way of controlling the spread of disease. Barrier nursing or infection control techniques include isolating infected individuals and wearing protective clothing. Other infection control recommendations include proper use, disinfection, and disposal of instruments and equipment used in treating or caring for patients with VHF, such as needles and thermometers.

In conjunction with the World Health Organization, CDC has developed practical, hospital-based guidelines, titled: *Infection Control for Viral Haemorrhagic Fevers In the African Health Care Setting*. The manual can help health-care facilities recognize cases and prevent further hospital-based disease transmission using locally available materials and few financial resources.

What needs to be done to address the threat of viral hemorrhagic fevers?

Scientists and researchers are challenged with developing containment, treatment, and vaccine strategies for these diseases. Another goal is to develop immunologic and molecular tools for more rapid disease diagnosis, and to study how the viruses are transmitted and exactly how the disease affects the body (pathogenesis). A third goal is to understand the ecology of these viruses and their hosts in order to offer preventive public health advice for avoiding infection.

CHEMICAL EMERGENCIES: NERVE AGENTS

Tabun (GA); Sarin (GB); Soman (GD); and VX

ROUTES OF EXPOSURE

- Inhalation
- Skin or eye contact
- Ingestion

CLINICAL HEALTH EFFECTS

Acute Exposure

- Nerve agents alter cholinergic synaptic transmission at neuroeffector junctions at skeletal myoneural junctions and autonomic ganglia (nicotinic effects), and in the CNS. Initial symptoms depend on the dose and route of exposure.
- Muscarinic effects include pinpoint pupils; blurred or dim vision; conjunctivitis; eye and head pain; hypersecretion by salivary, lacrimal, sweat, and bronchial glands; narrowing of the bronchi; nausea, vomiting, diarrhea, and crampy abdominal pains; urinary and fecal incontinence; and slow heart rate.
- Nicotinic effects include skeletal muscle twitching, cramping, and weakness.
- Relatively small to moderate vapor exposure causes pinpoint pupils, rhinorrhea, bronchoconstriction, excessive bronchial secretions, and slight to moderate dyspnea.

Central Nervous System (CNS)

- Nerve agents cause behavioral and psychological changes in humans. CNS effects include irritability, nervousness, fatigue, insomnia, memory loss, impaired judgment, slurred speech, and depression. High exposures may produce loss of consciousness, seizures, and apnea.

Respiratory

- Inhalation of nerve agent vapors causes respiratory tract effects within seconds to minutes. Symptoms include excessive rhinorrhea and bronchial secretions, chest tightness, and difficulty breathing due to constriction of bronchial muscles and mucous secretions. Respiratory failure may occur due to CNS depression.

Cardiovascular

- Vagal stimulation may produce bradycardia, but pulse rate may be increased due to ganglionic stimulation, and the effects of hypoxia. Bradyarrhythmias and hypertension may occur.

Gastrointestinal

- Abdominal pain, nausea and vomiting are common manifestations of exposure by any route but may be the first systemic effects from liquid exposure on skin. If these symptoms occur within an hour of dermal exposure, severe intoxication is indicated. Diarrhea and fecal incontinence may also occur.

Skeletal muscles

- Nerve agents stimulate skeletal muscle producing fasciculations and twitching leading to fatigue and flaccid paralysis. Muscle twitching/fasciculations are clinical identifiers that indicate possible nerve agent exposure.

Metabolic

- Profuse sweating may occur.

Ocular

- Symptoms may occur from local effects of vapor exposure and from systemic absorption. Pinpoint pupils and spasm of the muscle of visual accommodation (i.e., ciliary muscle) leading to blurred and dim vision, aching pain in the eye, and conjunctivitis are typical effects.

Potential Sequelae

- CNS effects such as fatigue, irritability, nervousness and impairment of memory may persist for as long as 6 weeks after recovery from acute effects.

LABORATORY TESTS

- Routine laboratory studies for all admitted patients include CBC, glucose, and serum electrolyte determinations.
- Chest X-ray and pulse oximetry (or ABG measurements) are recommended for severe exposures.
- Symptomatic and asymptomatic patients suspected of significant exposure should have determinations of red blood cell (RBC) cholinesterase activity, the most useful test for nerve agent poisoning.

EXPOSURE/CONTAMINATION:

- Persons whose skin or clothing is contaminated with nerve agent can contaminate rescuers by direct contact or through off-gassing vapor.
- Persons whose skin is exposed only to nerve agent vapor pose no risk of secondary contamination; however, clothing can trap vapor.

TREATMENT:

- ACUTE EXPOSURE: When possible, atropine and 2-PAM Cl should be given under medical supervision to symptomatic patients who have known or strongly suspected nerve agent toxicity. Patients who are comatose, hypotensive, or seizing or have cardiac dysrhythmias should be treated according to advanced life support (ALS) protocols.
- EYE – Severity of miosis cannot be used as an indicator of the amount of exposure or effectiveness of the antidotes. Maximum miosis may not occur until an hour or more after exposure. If severe eye pain or nausea and vomiting occur, consider topical administration of atropine or homatropine.
- SKIN – Skin must be decontaminated within minutes following exposure to nerve agent. Because of the high toxicity, rapid absorption, and volatility, it is unlikely that a patient brought to a medical facility will have nerve agent on the skin. However, some nerve agent may remain in the hair or clothing and should be decontaminated if not previously done.
- INHALATION – Ventilatory support is essential. Suction secretions from the nose, mouth, and respiratory tract. Resistance to ventilation is expected due to bronchial constriction and spasm; lessens after administration of atropine.

- INGESTION - Do not induce emesis because of the risk of pulmonary aspiration of gastric contents which may result from abrupt respiratory arrest, seizures, or vomiting. If the patient is alert and charcoal has not been given previously, administer slurry of activated charcoal. If the patient's condition is evaluated within 30 minutes after ingestion, consider gastric lavage.

DISPOSITION/FOLLOWUP

- Patients exposed to nerve agent vapor that have only miosis and/or mild rhinorrhea when they reach the medical facility do not need to be admitted. All other patients who have had exposure to nerve agent should be hospitalized and observed closely.
- Patients who have severe exposure should be evaluated for persistent CNS sequelae.
- Patients should be advised to avoid organophosphate insecticide exposure until sequential RBC cholinesterase activity (measured at weekly to monthly intervals) has stabilized in the normal range.

Medical Management Guidelines for Nerve Agents

MEDICAL MANAGEMENT GUIDELINES FOR

Nerve Agents

Tabun (GA); Sarin (GB); Soman (GD); and VX

For further information go to: http://www.atsdr.cdc.gov/MMG/MMG.asp?id=523&tid=93

To report chemical spills: Chemtrec – http://www.chemtrec.com/responder/resources/Pages/erfaqs.aspx

BACKGROUND INFORMATION

Nerve agents are the most toxic of the known chemical warfare agents. They are chemically similar to organophosphate pesticides and exert their biological effects by inhibiting acetylcholinesterase enzymes. G-type agents are clear,colorless, and tasteless liquids that are miscible in water and most organic solvents. GB is odorless and is the most volatile nerve agent; however, it evaporates at about the same rate as water. GA has a slightly fruity odor, and GD has a slight camphor-like odor. VX is a clear, amber-colored, odorless, oily liquid. It is miscible with water and soluble in all solvents. It is the least volatile nerve agent.

SYNONYMS

GA: ethyl dimethylamidocyanophosphate; ethyl N,N-dimethylphosphoramidocyanidate; ethyl dimethyl-phosphoramidocyanidate; dimethylaminoethoxy-cyanophosphine oxide; dimethylamidoethoxy-phosphoryl cyanide; EA1205; dimethylphosphora-midocyanidic acid ethyl ester; GB: isopropyl methylphosphonofluoridate; isopropoxymethyl-phosphoryl fluoride; trilone; MFI; TL1 618; isopropyl-methanefluorophosphonate; T144; T2106; fluoro-(isopropoxy) methylphosphine oxide; methylisopro-poxyfluorophosphine oxide; zarin; GD: pinacolyl methylphosphonofluoridate; 1,2,2-trimethylpropyl methylphosphonofluoridate; methylpinacolyloxy-fluorophosphine oxide; pinacolyloxymethylphosphonyl fluoride; pinacolylmethylfluorophosphonate; 1,2,2-trimethylpropoxyfluoro(methyl)phosphine oxide; pinacolyl methylphosphonyl fluoride; VX: O-ethyl S-

EXPOSURE/CONTAMINATION

- Persons whose skin or clothing is contaminated with nerve agent can contaminate rescuers by direct contact or through off-gassing vapor. Persons whose skin is exposed only to nerve agent vapor pose no risk of secondary contamination; however, clothing can trap vapor.

(2-diisopropylaminoethyl) methylphosphonothiolate; methylphosphonothioic acid; S-2-diisopropylamino)ethyl O-ethyl methylphosphonothioate; O-ethyl S-(2-diisopropylaminoethyl)methylphosphonothioate; O-ethyl S-(2-diisopropoylaminoethyl) methylthiolphosphonoate; O-ethyl S-diisopropylaminoethyl methylphosphonothiolate.	

ROUTES OF EXPOSURE

Inhalation

- Nerve agents are readily absorbed from the respiratory tract. Rhinorrhea and tightness in the throat or chest begin within seconds to minutes after exposure. Nerve agent vapors are heavier than air. Odor does not provide adequate warning of detection. The estimated LCt50 (the product of concentration 50 times time that is lethal to 50% of the exposed population by inhalation) ranges from 10 mg-min/m_3 for VX to 400 mg-min/m_3 for GA.

Skin/Eye Contact

- Nerve agent liquids are readily absorbed from the skin and eyes. Vapors are not absorbed through the skin except at very high concentrations. Ocular effects may result from both direct contact and systemic absorption. The nature and timing of symptoms following dermal contact with liquid nerve agents depend on exposure dose; effects may be delayed for several hours. As little as one drop of VX on the skin can be fatal and 1 to 10 mL of GA, GB, or GD can be fatal.

Ingestion

- Ingestion of nerve agents is expected to be relatively rare compared to inhalation exposure or skin contact; however, they are readily absorbed from the GI tract and are highly toxic.

HEALTH EFFECTS

Acute Exposure

- Nerve agents alter cholinergic synaptic transmission at neuroeffector junctions (muscarinic effects), at skeletal myoneural junctions and autonomic ganglia (nicotinic effects), and in the CNS. Initial symptoms depend on the dose and route of exposure.
- Muscarinic effects include pinpoint pupils; blurred or dim vision; conjunctivitis; eye and head pain; hypersecretion by salivary, lacrimal, sweat, and bronchial glands; narrowing of the bronchi; nausea, vomiting, diarrhea, and crampy abdominal pains; urinary and fecal incontinence; and slow heart rate.
- Nicotinic effects include skeletal muscle twitching, cramping, and weakness. Nicotinic stimulation can obscure certain muscarinic effects and produce rapid heart rate and high blood pressure.
- Relatively small to moderate vapor exposure causes pinpoint pupils, rhinorrhea, bronchoconstriction, excessive bronchial secretions, and slight to moderate dyspnea. Mild to moderate dermal exposure results in sweating and muscular fasciculations at the site of contact, nausea, vomiting, diarrhea, and weakness. The onset of these mild to moderate signs and symptoms following dermal exposure may be delayed for as long as 18 hours. Higher exposures (any route) cause loss of consciousness, seizures, muscle fasciculations, flaccid paralysis, copious secretions, apnea, and death.
- Children do not always respond to chemicals in the same way that adults do. Different protocols for managing their care may be needed

Central Nervous System (CNS)

- Nerve agents cause behavioral and psychological changes in humans. CNS effects include irritability, nervousness, fatigue, insomnia, memory loss, impaired judgment, slurred speech, and depression. High exposures may produce loss of consciousness, seizures, and apnea.

Respiratory

- Inhalation of nerve agent vapors causes respiratory tract effects within seconds to minutes. Symptoms include excessive rhinorrhea and bronchial secretions, chest tightness, and difficulty breathing due to constriction of bronchial muscles and mucous secretions. Respiratory failure may occur due to CNS depression.

Cardiovascular

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Metabolic

- Profuse sweating may occur.

Ocular

- Symptoms may occur from local effects of vapor exposure and from systemic absorption. Pinpoint pupils and spasm of the muscle of visual accommodation (i.e., ciliary muscle) leading to blurred and dim vision, aching pain in the eye, and conjunctivitis are typical effects.

Potential Sequelae

- CNS effects such as fatigue, irritability, nervousness and impairment of memory may persist for as long as 6 weeks after recovery from acute effects. Although exposure to some organophosphate compounds may cause a delayed mixed sensory-motor peripheral neuropathy, there are no reports of this condition among humans exposed to nerve agents.

ABC REMINDERS

- Evaluate and support the airway, breathing, and circulation.
- If the patient is apneic, give antidotes immediately. Administer atropine (2 mg for adults and 0.05 to 0.1 mg/kg for children) every 5 to 10 minutes until dyspnea, resistence to ventilation, and secretions are minimized.Intubate the trachea in cases of respiratory compromise. Suctioning may be required for excessive bronchial secretions.
- If the patient's condition precludes intubation, surgically create an airway.
- **In a severely exposed casualty (unconscious, gasping, or not breathing), the antidotes will be required to allow ventilation**.
- Maintain adequate circulation. Establish intravenous access if necessary. Attach a cardiac monitor, as needed.

TREATMENT/ANTIDOTE – ACUTE EXPOSURE

- When possible, atropine and 2-PAM Cl should be given under medical supervision to symptomatic

patients who have known or strongly suspected nerve agent toxicity

- Patients who are comatose, hypotensive, or seizing or have cardiac dysrhythmias should be treated according to advanced life support (ALS) protocols. Diazepam (5 to 10 mg in adults and 0.2 to 0.5 mg/kg in children) should be used to control convulsions. Lorazepam or other benzodiazepines may be used but barbiturates, phenytoin, and other anticonvulsants are not effective.
- Patients exposed to vapor who have miosis and rhinorrhea will need no care unless
    - (a) they have eye or head pain or nausea and vomiting; under these circumstances topical atropine or homatropine in the eye should relieve the symptoms and the patient can be discharged within an hour or so; or
    - (b) the rhinorrhea is very severe; under these circumstances, atropine IM (2 mg in adults and 0.05 mg/kg in children) should relieve this and the patient can be discharged in an hour or so.
- Topical atropine and homatropine should not be used routinely for miosis because they cause visual impairment for about 24 hours. See Table 4 for other antidote and treatment recommendations..

TREATMENT – INHALATION EXPOSURE

- Ventilatory support is essential.
- Following low-dose exposure, administration of antidotes and supplemental oxygen may be adequate.
- Suction secretions from the nose, mouth, and respiratory tract.
- Marked resistance to ventilation is expected due to bronchial constriction and spasm. Resistance lessens after administration of atropine.

TREATMENT - SKIN EXPOSURE

- Skin must be decontaminated within minutes following exposure to nerve agent. Because of the high toxicity, rapid absorption, and volatility, it is unlikely that a patient brought to a medical facility will have nerve agent on the skin. However, some nerve agent may remain in the hair or clothing and should be decontaminated if not previously done.

TREATMENT – EYE EXPOSURE

- Severity of miosis cannot be used as an indicator of the amount of exposure or effectiveness of the antidotes. Maximum miosis may not occur until an hour or more after exposure.
- If severe eye pain or nausea and vomiting occur, protect eyes from bright light and consider topical administration of atropine or homatropine.
- Test visual acuity.

TREATMENT - INGESTION

- Do not induce emesis because of the risk of pulmonary aspiration of gastric contents which may result from abrupt respiratory arrest, seizures, or vomiting.
- If the patient is alert and charcoal has not been given previously, administer a slurry of activated charcoal.

If the patient's condition is evaluated within 30 minutes after ingestion, consider gastric lavage. (Gastric contents should be considered potentially hazardous by skin contact or inhalation and should be quickly isolated).

LABORATORY TESTS

- Routine laboratory studies for all admitted patients include CBC, glucose, and serum electrolyte determinations.
- Chest X-ray and pulse oximetry (or ABG measurements) are recommended for severe exposures.

- Symptomatic and asymptomatic patients suspected of significant exposure should have determinations of red blood cell (RBC) cholinesterase activity, the most useful test for nerve agent poisoning. Severe symptoms of toxicity are usually present when more than 70% of RBC cholinesterase is inhibited. However, there is no correlation between cholinesterase activity and severity of topical signs and symptoms (e.g., miosis, rhinorrhea, dyspnea). If this test is not available, plasma cholinesterase can be measured.

DISPOSITION AND FOLLOW-UP

- Patients exposed to nerve agent vapor who have only miosis and/or mild rhinorrhea when they reach the medical facility do not need to be admitted. All other patients who have had exposure to nerve agent should be hospitalized and observed closely.
- Patients who have severe exposure should be evaluated for persistent CNS sequelae.
- Patients should be advised to avoid organophosphate insecticide exposure until sequential RBC cholinesterase activity (measured at weekly to monthly intervals) has stabilized in the normal range, a process that may take 3 to 4 months after severe poisoning.

DELAYED EFFECTS

- Effects from skin exposure to liquid nerve agent may not develop for up to 18 hours following exposure. Patients who have inhalation exposure and who complain of chest pain, chest tightness, or cough should be observed and examined periodically for 6 to 12 hours to detect delayed-onset bronchitis, pneumonia, pulmonary edema, or respiratory failure.
- Formaldehyde poisoning can cause permanent alterations of nervous system function, including problems with memory, learning, thinking, sleeping, personality changes, depression, headache, and sensory and perceptual changes.

PATIENT RELEASE

Provide patient information sheet.

Nerve Agents
Patient Information Sheet

This handout provides information and follow-up instructions for persons who have been exposed to nerve agents.

What are nerve agents?
Nerve agents are chemical warfare agents, similar to but much more potent than organophosphate insecticides. They are colorless to amber-colored, tasteless liquids that may evaporate to create a gas. GB and VX are odorless, while GA has a slight fruity odor, and GD has a slight camphor odor.

What immediate health effects can result from exposure to nerve agents?
Nerve agents are extremely toxic chemicals that attack the nervous system. As little as one drop to a few milliliters of nerve agent contacting the skin can cause death within 15 minutes. Nerve agent exposure can cause runny nose, sweating, blurred vision, headache, difficulty breathing, drooling, nausea, vomiting, muscle cramps and twitching, confusion, convulsions, paralysis, and coma. Symptoms occur immediately if you inhale nerve agent vapor but may be delayed for several hours if you get nerve agent liquid on your skin.

Can nerve agent poisoning be treated?
There are antidotes for nerve agent poisoning but they must be administered quickly after exposure. Immediate decontamination is critical and hospitalization may be needed.

Are any future health effects likely to occur?
Complete recovery may take several months. After a severe exposure with prolonged seizures, permanent damage to the central nervous system is possible.

What tests can be done if a person has been exposed to nerve agents?
Activity of a blood enzyme called acetylcholinesterase can be measured to assess exposure and recovery.

Where can more information about nerve agents be found?
More information about nerve agents can be obtained from your regional poison control center; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in toxicology or occupational and environmental health. Ask the person who gave you this form for help locating these telephone numbers.

Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

[ ] Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 24 hours, especially:

- dizziness, loss of coordination, loss of memory
- coughing, wheezing, or shortness of breath
- nausea, vomiting, cramps, or diarrhea
- muscle weakness or twitching
- blurred vision

[ ] No follow-up appointment is necessary unless you develop any of the symptoms listed above.
[ ] Call for an appointment with Dr. _____ in the practice of _____. When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.
[ ] Return to the Emergency Department/ _____ Clinic on (date) _____at __ _____ AM/PM for a follow-up examination.
[ ] Do not perform vigorous physical activities for 1 to 2 days.
[ ] You may resume everyday activities including driving and operating machinery.
[ ] Do not return to work for _____ days.
[ ] You may return to work on a limited basis. See instructions below.
[ ] Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.
[ ] Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.
[ ] Avoid taking the following medications: _____
[ ] You may continue taking the following medication(s) that your doctor(s) prescribed for you: __
_____
_____
[ ] Other instructions: _____
_____
_____

- Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.

- You or your physician can get more information on the chemical by contacting: _____ _____ or _____, or by checking out the following Internet Web sites: _____; _____.

Signature of patient _____ Date _____

Signature of physician _____ Date_____

CHEMICAL EMERGENCIES: BLISTER AGENTS

LEWISITE (L)($C_2H_2ASCL_3$)
MUSTARD-LEWISITE MIXTURE (HL)

ROUTES OF EXPOSURE

- Inhalation
- Skin or eye contact
- Ingestion (uncommon)

CLINICAL:

Dermal

- Lewisite liquid or vapor produces pain and skin irritation within seconds to minutes after contact.
- The Lewisite blister starts as a small blister in the center of the erythematous area and expands to include the entire inflamed area.
- Mustard-Lewisite Mixture also produces pain and irritation immediately, and erythema within 30 minutes. Blistering is delayed for hours and tends to cover the entire area of reddened skin.

Ocular

- Lewisite vapor causes pain and blepharospasm on contact. Edema of the conjunctiva and eyelids follows, and the eyes may be swollen shut within an hour. With high doses, corneal damage and iritis may follow.
- Liquid Lewisite causes severe eye damage on contact.
- Mustard-Lewisite Mixture also causes ocular effects extremely rapidly. Lacrimation, photophobia, and inflammation of the conjunctiva and cornea may occur.

Respiratory

- Lewisite and Mustard-Lewisite Mixture are extremely irritating to the respiratory tract mucosa.
- Burning nasal pain, epistaxis, sinus pain, laryngitis, cough and dyspnea may occur.
- Necrosis can cause pseudomembrane formation and local airway obstruction.
- Pulmonary edema may occur following exposure to high concentrations.

Gastrointestinal

- Ingestion or inhalation of Lewisite may cause nausea and vomiting.
- Ingestion of Mustard-Lewisite Mixture produces severe stomach pains, vomiting, and bloody stools after a 15-20 minute latency period.

Cardiovascular

- High-dose exposure to Lewisite may cause "Lewisite shock," a condition resulting from increased capillary permeability and subsequent intravascular fluid loss, hypovolemia, and organ congestion.

LABORATORY DIAGNOSIS:

- Routine laboratory studies should be done for all patients requiring admission. These include CBC, glucose, serum electrolytes, and liver and kidney function tests.
- Chest radiography and pulse oximetry (or arterial blood gases measurements) are recommended for severe inhalation exposure or if pulmonary aspiration is suspected.

EXPOSURE:

- Persons whose skin or clothing is contaminated with liquid Lewisite or Mustard-Lewisite Mixture can contaminate rescuers by direct contact or through off-gassing vapor.

TREATMENT:

- ANTIDOTE - British Anti-Lewisite (BAL) can be given by intramuscular injection as an antidote for systemic effects but has no effect on the local lesions of the skin, eyes, or airways.
- Treatment consists primarily of supportive care.
- EYE – For conjunctivitis, topical analgesics. For lesions, topical mydriatic (e.g., atropine), topical antibiotics. Some authorities feel that topical steroids (used within the first 24 hours only) may reduce inflammation.
- SKIN – Systemic analgesics, topical antibiotics, systemic antibiotics. Patients with 2^{nd} & 3^{rd} degree burns should be transferred to a burn unit.
- INHALATION – Mild non-productive cough, irritation of the nose and sinuses, and/or a sore throat steam vaporizer, lozenges. More severe effects, intubation and oxygen-assisted ventilation, as necessary, and admit to the Critical Care Unit once decontamination has been assured.
- INJESTION - **Do not induce emesis.** Treat nausea and vomiting with anti-emetics

DISPOSITION/FOLLOWUP

- Patients who have skin, eye, or airway signs and symptoms will require hospitalization.
- Skin burns take up to 18 hours to fully develop.
- Chemical pneumonitis may begin within 24 hours or up to 3 days after inhalation exposure.
- A patient who initially had mild symptoms should be observed for at least 18 to 24 hours after exposure. If no further symptoms develop and there is no significant progression, the patient may be discharged.
- Discharged patients should be advised to rest and to seek medical care promptly if symptoms develop.
- Follow-up laboratory evaluation of bone marrow, hepatic, and renal function should be arranged for severely exposed patients until they are completely recovered.

Medical Management Guidelines for Blister Agents/Vesicants

MEDICAL MANAGEMENT GUIDELINES FOR
Lewisite (L)($C_2H_2AsCl_3$)
Mustard-Lewisite Mixture (HL)

For further information go to: http://www.atsdr.cdc.gov/MMG/MMG.asp?id=922&tid=190

To report chemical spills: Chemtrec – http://www.chemtrec.com/responder/resources/Pages/erfaqs.aspx

BACKGROUND INFORMATION

SYNONYMS FOR LEWISITE: L, arsine (2-chlorovinyl) dichloro-, arsenous dichloride (2-chloroethenyl)-, chlorovinylarsine dichloride, 2-chlorovinyldichloroarsine, beta-chlorovinyldichloroarsine, dichloro-(2-chlorovinyl)arsine, EA1034.

SYNONYMS FOR MUSTARD-LEWISITE include HL and Sulfur Mustard/Lewisite.

Lewisite is an organic arsenical known for its vesicant properties. Pure Lewisite is an oily, colorless liquid, while impure Lewisite is amber to black. It remains a liquid at low temperatures and is persistent in colder climates. It has the odor of geraniums.

Mustard-Lewisite Mixture is a liquid mixture of distilled Mustard (HD) and Lewisite. Due to its low freezing point, the mixture remains a liquid in cold weather and at high altitudes. The mixture with the lowest freezing point consists of 63% Lewisite and 37% Mustard. It has a garlic-like odor.

EXPOSURE/CONTAMINATION

Persons whose skin or clothing is contaminated with liquid Lewisite or Mustard-Lewisite Mixture can contaminate rescuers by direct contact or through off-gassing vapor.

ROUTES OF EXPOSURE

Inhalation

- Exposure to Lewisite vapor at a concentration of 8 mg-min/m©ø causes immediate burning pain of the respiratory tract. Its odor is noted at about 20 mg-min/m©ø. The LCt_{50} (the product of concentration times time that is lethal to 50% of the exposed population by inhalation) is approximately 1,500 mg-min/m©ø.
- Exposure to Mustard-Lewisite Mixture vapor induces immediate respiratory tract irritation and severe inflammation after a few hours latency period. Both agents are readily absorbed from the lungs.

Skin/Eye Contact

- Absorption may occur after skin or eye contact with liquid or vapor Lewisite.
- Absorption across the skin begins within minutes. Vesication is caused by about 14 ¥ìg of liquid, and the LD_{50} of liquid on the skin is about 30-50 mg/kg.
- Liquid Lewisite causes severe eye damage within minutes of contact.
- The vapor also acts quickly, with pain on contact, followed by edema of the conjunctiva and eyelids, and iritis and corneal damage with high doses.
- Systemic absorption may occur following skin or eye exposure to liquid or vapor Mustard-Lewisite Mixture. The mixture causes immediate stinging pain of the skin, with blistering delayed for hours. Graying of the skin will follow within a very short time if exposure is from liquid (because of Lewisite).
- Erythema and blisters will appear earlier than from mustard alone.

- Exposure of the eyes to Mustard-Lewisite Mixture produces lacrimation and inflammation of the conjunctiva and cornea.
- After exposure to low amounts of Lewisite or to the mixture, temporary loss of eyesight may occur because of blepharospasm or eyelid edema.
- After exposure to high amounts, permanent loss of sight may occur because of corneal damage; however, this is unusual.

Ingestion

Ingestion of either Lewisite or Mustard-Lewisite Mixture is an uncommon route for exposure but can lead to local effects and systemic absorption.

HEALTH EFFECTS

Acute Exposure

- Lewisite damages skin, eyes, and airways by direct contact. It inhibits many enzymes, in particular those with thiol groups, such as pyruvic oxidase, alcohol dehydrogenase, succinic oxidase, hexokinase, and succinic dehydrogenase.
- The exact mechanism by which Lewisite damages cells is not known. Mustard-Lewisite Mixture shares the vesicant properties of Lewisite and the DNA alkylation and cross-linking properties of mustard.

Dermal

- Lewisite liquid or vapor produces pain and skin irritation within seconds to minutes after contact. For liquid Lewisite, erythema occurs within 15 to 30 minutes after exposure and blisters start within several hours, developing fully by 12-18 hours. For the vapor, response times are a little longer. The Lewisite blister starts as a small blister in the center of the erythematous area and expands to include the entire inflamed area. Mustard-Lewisite Mixture also produces pain and irritation immediately, and erythema within 30 minutes. Blistering is delayed for hours and tends to cover the entire area of reddened skin.

Ocular

- Lewisite vapor causes pain and blepharospasm on contact. Edema of the conjunctiva and eyelids follows, and the eyes may be swollen shut within an hour. With high doses, corneal damage and iritis may follow.
- Liquid Lewisite causes severe eye damage on contact.
- Mustard-Lewisite Mixture also causes ocular effects extremely rapidly. Lacrimation, photophobia, and inflammation of the conjunctiva and cornea may occur.

Respiratory

- Lewisite and Mustard-Lewisite Mixture are extremely irritating to the respiratory tract mucosa.
- Burning nasal pain, epistaxis, sinus pain, laryngitis, cough and dyspnea may occur.
- Necrosis can cause pseudomembrane formation and local airway obstruction.
- Pulmonary edema may occur following exposure to high concentrations.

Gastrointestinal

- Ingestion or inhalation of Lewisite may cause nausea and vomiting.
- Ingestion of Mustard-Lewisite Mixture produces severe stomach pains, vomiting, and bloody stools after a 15-20 minute latency period.

Cardiovascular

- High-dose exposure to Lewisite may cause "Lewisite shock," a condition resulting from increased capillary permeability and subsequent intravascular fluid loss, hypovolemia, and organ congestion.

Hepatic

- Hepatic necrosis may occur due to shock and hypoperfusion following exposure to high levels of Lewisite.

Renal

- Exposure to high levels of Lewisite may cause decreased renal function secondary to hypotension.

Hematopoietic

- Systemic absorption of Mustard-Lewisite Mixture may induce bone marrow suppression and an increased risk for fatal complicating infections.

Potential Sequelae

Chronic respiratory and eye conditions may persist following exposure to large amounts of Lewisite or Mustard-Lewisite Mixture

ABC REMINDERS

- Evaluate and support the airway, breathing, and circulation.
- Intubate the trachea in cases of respiratory compromise. If the patient's condition precludes intubation, surgically create an airway.
- Establish intravenous access and continuously monitor cardiac rhythm in seriously ill patients.
- Treat patients who have bronchospasm with bronchodilators.

Patients who are comatose or hypotensive, or have seizures or ventricular dysrhythmias due to other exposures or trauma should be treated in the conventional manner.

ANTIDOTES

- British Anti-Lewisite (BAL) can be given by intramuscular injection as an antidote for systemic effects but has no effect on the local lesions of the skin, eyes, or airways. Treatment consists primarily of supportive care.
- British Anti-Lewisite (BAL), also called Dimercaprol, is a chelating agent shown to reduce systemic effects from Lewisite exposure. Due to toxic side effects, **BAL should be administered only to patients who have signs of shock or significant pulmonary injury.**
- Chelation therapy should be performed only by trained personnel. Consultation with the regional poison control center is recommended. The standard dosage regimen is 3 to 5 mg/kg IM every 4 hours for four doses. This regimen can be adjusted depending on the severity of the exposure and the symptoms. Contraindications to BAL include pre-existing renal disease, pregnancy (except in life threatening circumstances) and concurrent use of medicinal iron.
- Alkalization of the urine stabilizes the Dimercaprol-metal complex and has been proposed to protect the kidneys during chelation therapy. If acute renal insufficiency develops, hemodialysis should be considered to remove the Dimercaprol-arsenic complex. Side effects of BAL administered at 3 mg/kg are mostly pain at the injection site. At 5 mg/kg, the effects may include nausea; vomiting; headache; burning sensation of the lips, mouth, throat, and eyes; lacrimation; rhinorrhea; salivation; muscle aches; burning and tingling in the extremities; tooth pain; diaphoresis; chest pain; anxiety; and agitation.

TREATMENT - SKIN EXPOSURE

- A small area of erythema beginning later than 12 hours after exposure is unlikely to progress to a significant lesion. The patient should be examined, treated with a soothing lotion and a systemic analgesic, sent home, and instructed to return if progression occurs.
- A patient with a significant area of erythema or one seen earlier with a significant area of erythema with or without blistering should be admitted for further evaluation.
- Most burns are second degree although third degree burns may occur after liquid exposure. In general, small blisters (i.e., <1 cm) should remain roofed and larger ones (i.e., >1 cm) should be unroofed. This is a

Lewisite and Mustard-Lewisite Mixture
Patient Information Sheet

This handout provides information and follow-up instructions for persons who have been exposed to Lewisite or Mustard-Lewisite Mixture.

What are Lewisite and Mustard-Lewisite Mixture?
Lewisite is a chemical warfare agent that was first produced in 1918. It has not been used in warfare, although it may be stockpiled by some countries. Mustard-Lewisite Mixture is a mixture of Lewisite and Mustard. It was developed to achieve a lower freezing point for ground dispersal and aerial spraying.

What immediate health effects can be caused by exposure to Lewisite and Mustard-Lewisite Mixture?
Lewisite and Mustard-Lewisite Mixture produce pain and skin irritation immediately after exposure. Both compounds cause skin blisters and damage to the airways and eyes. They are also extremely irritating to the eyes, skin, nose, and throat. Exposure to very high levels may result in kidney and liver damage. Mustard-Lewisite Mixture can also damage the immune system.

Can Lewisite and Mustard-Lewisite poisoning be treated?
Immediate decontamination reduces symptoms. Intramuscular injection of British Anti-Lewisite (BAL) may be used to treat severe conditions but will not prevent lesions on the skin, eye, or airways. Persons who have been exposed to large amounts of Lewisite and Mustard-Lewisite Mixture will need to be hospitalized.

Are any future health effects likely to occur?
Adverse health effects, such as chronic respiratory diseases, may occur from exposure to high levels of these agents. Severe damage to the eye may be present for a long time after the exposure.

What tests can be done if a person has been exposed to Lewisite or Mustard-Lewisite?
There is no specific test to confirm exposure to Lewisite or Mustard-Lewisite Mixture; however, measurement of arsenic in the urine may help to identify exposure.

Where can more information about Lewisite or Mustard-Lewisite be found?
More information about Lewisite and Mustard-Lewisite Mixture can be obtained from your regional poison control center; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in toxicology or occupational and environmental health. Ask the person who gave you this form for help locating these telephone numbers.

Lewisite and Mustard-Lewisite Mixture
Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

[ ] Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 24 hours, especially:

- coughing, wheezing, shortness of breath, or discolored sputum
- increased pain or discharge from injured eyes
- increased redness, pain, or a pus-like discharge from injured skin; fever; or chills

[ ] No follow-up appointment is necessary unless you develop any of the symptoms listed above.
[ ] Call for an appointment with Dr. _____ in the practice of _____. When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.
[ ] Return to the Emergency Department/ _____ Clinic on (date) _____at _____ AM/PM for a follow-up examination.
[ ] Do not perform vigorous physical activities for 1 to 2 days.
[ ] You may resume everyday activities including driving and operating machinery.
[ ] Do not return to work for _____ days.
[ ] You may return to work on a limited basis. See instructions below.
[ ] Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.
[ ] Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.
[ ] Avoid taking the following medications: _____
[ ] You may continue taking the following medication(s) that your doctor(s) prescribed for you: _____
_____
_____
[ ] Other instructions: _____
_____
_____

- Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.

- You or your physician can get more information on the chemical by contacting: _____ _____ or _____, or by checking out the following Internet Web sites: _____; _____.

Signature of patient _____ Date _____

Signature of physician _____ Date_____

controversial issue, but many feel that the roof will eventually come off anyway. The denuded area should be irrigated two or three times a day using a whirlpool.

- If the lesion is large (the patient should be given ample amounts of a systemic analgesic beforehand). This should be followed by liberal application of a topical antibiotic. Skin lesions may take many months to heal. Fluids are not lost as they are in thermal burns, and fluid replacement should be according to the general needs of the patient and not according to "burn therapy" formulas.
- Systemic antibiotics should be used when there are signs of infection and a culture indicates the responsible organism. Patients with a large area of second or third degree burns should be transferred to a Burn Unit for further care and reverse isolation.

TREATMENT - INGESTION EXPOSURE

Do not induce emesis. Treat nausea and vomiting with anti-emetics.

LABORATORY TESTS

Routine laboratory studies should be done for all patients requiring admission. These include CBC, glucose, serum electrolytes, and liver and kidney function tests. Consider monitoring hourly fluid intake and output. Chest X-ray and pulse oximetry (or ABG measurements) are recommended for all patients with inhalation exposures. Since Lewisite contains arsenic, urinary arsenic excretion may be helpful if the diagnosis is in doubt. A test for urine thiodiglycol, a metabolite of mustard, can be performed at specialized laboratories, but is not a routine laboratory measure.

DISPOSITION AND FOLLOW-UP

- Patients who have skin, eye, or airway signs and symptoms will require hospitalization, as discussed above.
- Follow-up laboratory evaluation of bone marrow, hepatic, and renal function should be arranged for severely exposed patients until they are completely recovered. Patients who have mild skin burns or corneal lesions should be reexamined within 24 hours.

DELAYED EFFECTS

Skin burns take up to 18 hours to fully develop. Chemical pneumonitis may begin within 24 hours or up to 3 days after inhalation exposure. Significant systemic absorption of Mustard-Lewisite Mixture may produce a fall in the leukocyte count beginning on days 3 through 5. Erythrocytes and thrombocytes may subsequently fall if bone marrow damage is severe and in this case the risk of life-threatening infection rises.

PATIENT RELEASE

A patient who initially had mild symptoms should be observed for at least 18 to 24 hours after exposure. If no further symptoms develop and there is no significant progression, the patient may be discharged. Discharged patients should be advised to rest and to seek medical care promptly if symptoms develop.

CHEMICAL EMERGENCIES: BLISTER AGENTS

SULFUR MUSTARD AGENT H OR HD ($C_4H_8CL_2S$) SULFUR MUSTARD AGENT HT

ROUTES OF EXPOSURE

- Inhalation
- Skin or eye contact
- Ingestion (uncommon)
- Skin, eye, and airway exposure to vapor sulfur mustard and skin and eye exposure to liquid mustard may cause systemic toxicity. The lethal dose is about 100 mg/kg or 1 to 1.5 teaspoons of liquid.

CLINICAL:

Health Effects

- Sulfur mustards are vesicants causing skin, eye, and respiratory tract injury. Although these agents cause cellular changes within minutes of contact, the onset of pain and other clinical effects are delayed for 1 to 24 hours. Thus, patients arriving immediately from the scene of exposure are not likely to have signs and symptoms.

- Sulfur mustards are alkylating agents that may cause bone marrow suppression and neurologic and gastrointestinal toxicity.

Skin/Eye Contact

- Direct skin exposure to sulfur mustards causes erythema and blistering. Generally, a pruritic rash will develop within 4 to 8 hours followed by blistering 2 to 18 hours later.
- Mustard vapor and liquid are absorbed through the eyes, skin, and mucous membranes. Clinical effects do not occur until hours after exposure.

Ingestion

- Ingestion may cause local effects and systemic absorption.

Ocular

- Sulfur mustard vapor or liquid may cause intense conjunctival and scleral pain, swelling, lacrimation, blepharospasm, and photophobia; however, these effects do not appear for an hour or more.
- Miosis due to cholinergic effects may occur. High concentrations of vapor or liquid can cause corneal edema, perforation, blindness, and later scarring.

Respiratory

- Dose-dependent inflammatory reactions in the upper and lower airway begin to develop several hours after exposure and progress over several days.
- Burning nasal pain, epistaxis, sinus pain, laryngitis, loss of taste and smell, cough, wheezing, and dyspnea may occur.

- Necrosis of respiratory epithelium can cause pseudomembrane formation and local airway obstruction.

Gastrointestinal

- Ingestion may cause chemical burns of the GI tract and cholinergic stimulation.
- Nausea and vomiting may occur following ingestion or inhalation.
- Nausea, vomiting, and diarrhea occurring several days after exposure indicates damage to the GI tract and thus is a poor prognostic sign.

Central Nervous System (CNS)

- High doses of sulfur mustards can cause hyperexcitability, convulsions, and insomnia.

Hematopoietic

- Systemic absorption of sulfur mustard may induce bone marrow suppression and an increased risk for fatal complicating infections, hemorrhage, and anemia.

LABORATORY DIAGNOSIS:

- Routine laboratory studies for admitted patients include glucose, serum electrolytes, and daily CBC.
- Chest x-ray and pulse oximetry (or ABG measurement) should be done frequently on all patients with inhalation effects.
- A test for urinary thioglycol (a metabolite of mustard) can be performed at specialized laboratories, but is not a routine laboratory measure.

EXPOSURE:

- People whose skin or clothing is contaminated with sulfur mustard can contaminate rescuers by direct contact or through off-gassing vapor.

TREATMENT:

- Decontamination of all potentially exposed areas within minutes after exposure is the only effective means of decreasing tissue damage.
- Thus, by the time a patient arrives in the emergency department, decontamination can only prevent secondary exposure to medical staff; it does not limit the patient's injury.
- Treatment consists primarily of supportive care.
- ANTIDOTE – There is no antidote for sulfur mustard toxicity.
- EYE – For conjunctivitis, topical analgesics. For lesions, topical mydriatic (e.g., atropine), topical antibiotics. Some authorities feel that topical steroids (used within the first 24 hours only) may reduce inflammation.
- SKIN – Systemic analgesics, topical antibiotics, systemic antibiotics. Patients with 2nd & 3rd degree burns should be transferred to a burn unit. Blister fluid does not contain mustard or other toxic substances. Skin lesions may take many months to heal.
- INHALATION – Mild non-productive cough, irritation of the nose and sinuses, and/or a sore throat steam vaporizer, lozenges. More severe effects, intubation and oxygen-assisted ventilation, as necessary, and admit to the Critical Care Unit once decontamination has been assured. Daily sputum cultures and systemic antibiotics with signs of infection and an identified organism. A chemical pneumonitis may occur in the first several days.
  INJESTION – **Do not induce emesis**. Cautious orogastric lavage might remove ingested material. There is no evidence that activated charcoal is beneficial.

- BONE MARROW - Transfusions may be useful. Treatment with granulocyte colony-stimulating factor (GCSF) has been successful experimentally with nitrogen mustard.
- **DISPOSITION/FOLLOWUP**
- Patients with moderate to severe exposures will require hospitalization, as described above.
- Follow-up evaluation of respiratory, neurological, and bone marrow function should be arranged for severely exposed patients.

Medical Management Guidelines for Blister Agents/Vesicants

MEDICAL MANAGEMENT GUIDELINES FOR

SULFUR MUSTARD AGENT H OR HD ($C_4H_8CL_2S$)

SULFUR MUSTARD AGENT HT

For further information go to: http://www.atsdr.cdc.gov/MMG/MMG.asp?id=924&tid=191

To report chemical spills: Chemtrec – http://www.chemtrec.com/responder/resources/Pages/erfaqs.aspx

BACKGROUND INFORMATION

SYNONYMS:

H and HD: Bis(2-chloroethyl) sulfide; bis(beta-chloroethyl) sulfide; di-2-chloroethyl sulfide; 1-chloro-2(beta-chloroethylthio)ethane; 2,2'-dichloroethyl sulfide; sulfur mustard; Iprit; Kampstoff "Lost"; mustard gas; senfgas, S-yperite; yellow cross liquid; yperite

HT: Mixture of bis(2-chloroethyl) sulfide and bis[2-(2-chloroethylthio)-ethyl]ether

Sulfur mustards are vesicants and alkylating agents. They are colorless when pure but are typically a yellow to brown oily substance with a slight garlic or mustard odor. H contains about 20 to 30% impurities (mostly sulfur); distilled mustard is known as HD and is nearly pure; HT is a mixture of 60% HD and 40% agent T (a closely related vesicant with a lower freezing point). Sulfur mustards evaporate slowly. They are very sparingly soluble in water but are soluble in oils, fats, and organic solvents. They are stable at ambient temperatures but decompose at temperatures greater than 149¨¬C.

EXPOSURE/CONTAMINATION

People whose skin or clothing is contaminated with sulfur mustard can contaminate rescuers by direct contact or through off-gassing vapor.

ROUTES OF EXPOSURE

INHALATION

Sulfur mustards are readily absorbed from the respiratory tract; injury develops slowly and intensifies over several days. The odor of sulfur mustards does not provide adequate warning of detection. The LCt_{50} (the product of concentration times time that is lethal to 50% of the exposed population by inhalation) is approximately 1,500 mg-min/m_3. The vapors are heavier than air. When inhaled, these agents may cause systemic effects. The estimated Ct for airway injury is 100 to 200 mg-min/m_3.

SKIN/EYE CONTACT

Mustard vapor and liquid are absorbed through the eyes, skin, and mucous membranes. Clinical effects do not occur until hours after exposure. The median incapacitating dose for the vapor is 200 mg-min/m_3. A Ct of 12 to 70 mg-min/m_3 produces eye lesions. Direct contact with the liquid can cause skin and eye burns that develop an hour or more after exposure. A 10 ¥ìg droplet is capable of producing blisters. Skin, eye, and airway exposure to vapor sulfur mustard and skin and eye exposure to liquid mustard may cause systemic toxicity. The lethal dose is about

MEDICAL MANAGEMENT GUIDELINES FOR

SULFUR MUSTARD AGENT H OR HD ($C_4H_8CL_2S$)

SULFUR MUSTARD AGENT HT

100 mg/kg or 1 to 1.5 teaspoons of liquid.

INGESTION

Ingestion may cause local effects and systemic absorption.

HEALTH EFFECTS: ACUTE EXPOSURE

- Sulfur mustards are vesicants causing skin, eye, and respiratory tract injury. Although these agents cause cellular changes within minutes of contact, the onset of pain and other clinical effects are delayed for 1 to 24 hours. Thus, patients arriving immediately from the scene of exposure are not likely to have signs and symptoms.
- Sulfur mustards are alkylating agents that may cause bone marrow suppression and neurologic and gastrointestinal toxicity.
- Sulfur mustards are vesicants and alkylating agents; however, the biochemical mechanisms of action are not clearly understood. They are highly reactive and combine rapidly with proteins, DNA, or other molecules. Therefore, within minutes following exposure intact mustard or its reactive metabolites are not found in tissue or biological fluids. Sulfur mustards also have cholinergic activity, stimulating both muscarinic and nicotinic receptors. The onset of clinical symptoms and their time of onset depend on the severity of exposure. The death rate from exposure to sulfur mustard is low (2 to 3% during World War I). Death usually occurs between the 5^{th} and 10^{th} day due to pulmonary insufficiency complicated by infection due to immune system compromise.

HEALTH EFFECTS: OCULAR

- The eye is the most sensitive tissue to sulfur mustard effects. Sulfur mustard vapor or liquid may cause intense conjunctival and scleral pain, swelling, lacrimation, blepharospasm, and photophobia; however, these effects do not appear for an hour or more.
- Miosis due to cholinergic effects may occur. High concentrations of vapor or liquid can cause corneal edema, perforation, blindness, and later scarring.

HEALTH EFFECTS: DERMAL

- Direct skin exposure to sulfur mustards causes erythema and blistering. Generally, a pruritic rash will develop within 4 to 8 hours followed by blistering 2 to 18 hours later. Contact with the vapor may result in first and second degree burns, while contact with the liquid typically produces second and third degree chemical burns. An area of burn covering 25% or more of the body surface area may be fatal.

HEALTH EFFECTS: RESPIRATORY

- Dose-dependent inflammatory reactions in the upper and lower airway begin to develop several hours after exposure and progress over several days. Burning nasal pain, epistaxis, sinus pain, laryngitis, loss of taste and smell, cough, wheezing, and dyspnea may occur. Necrosis of respiratory epithelium can cause pseudomembrane formation and local airway obstruction.

MEDICAL MANAGEMENT GUIDELINES FOR
SULFUR MUSTARD AGENT H OR HD ($C_4H_8CL_2S$)
SULFUR MUSTARD AGENT HT

HEALTH EFFECTS: GASTROINTESTINAL

- Ingestion may cause chemical burns of the GI tract and cholinergic stimulation. Nausea and vomiting may occur following ingestion or inhalation. Early nausea and vomiting is usually transient and not severe. Nausea, vomiting, and diarrhea occurring several days after exposure indicates damage to the GI tract and is a poor prognostic sign.

HEALTH EFFECTS: CENTRAL NERVOUS SYSTEM (CNS)

- High doses of sulfur mustards can cause hyperexcitability, convulsions, and insomnia.

HEALTH EFFECTS: HEMATOPOIETIC

- Systemic absorption of sulfur mustard may induce bone marrow suppression and an increased risk for fatal complicating infections, hemorrhage, and anemia.

ABC REMINDERS

- Evaluate and support the airway, breathing, and circulation.
- Intubate the trachea in cases of respiratory compromise. If the patient's condition precludes intubation, surgically create an airway.
- Treat patients who have bronchospasm with bronchodilators.
- Patients who are comatose or hypotensive, or have seizures or ventricular dysrhythmias due to other exposures or trauma should be treated in the conventional manner.
- Establish intravenous access and continuously monitor cardiac rhythm in seriously ill patients.

ANTIDOTES

- There is no antidote for sulfur mustard toxicity. Decontamination of all potentially exposed areas within minutes after exposure is the only effective means of decreasing tissue damage. Thus, by the time a patient arrives in the emergency department, decontamination can only prevent secondary exposure to medical staff; it does not limit the patient's injury. Medical treatment is supportive.

TREATMENT: EYE EXPOSURE

- Mild conjunctivitis beginning more than 12 hours after exposure is unlikely to progress to a severe lesion. The patient should have a thorough eye examination (including a test for visual acuity). The patient should be treated with a soothing eye solution, such as Visine or Murine, sent home, and told to return if there is worsening.
- Conjunctivitis beginning earlier and other effects such as lid swelling and signs/symptoms of inflammation indicate a need for inpatient care and observation.
- Eye lesions range from conjunctivitis to involvement of the entire eye including cornea and lids. Erosion of or perforation of the cornea may occur with very severe exposure to liquid, but this is rare. Readily available eye solutions may suffice for conjunctivitis.
- More severe lesions should be treated with a topical mydriatic (e.g., atropine), topical antibiotics, and

vaseline or similar substance applied to the lid edges several times a day.

- Topical analgesics should be used only for an initial examination (including slit lamp and a test of visual acuity), but not after. Pain should be controlled with systemic analgesics. Once the lid edema and blepharospasm subside and the eyes are open, dark glasses may reduce the discomfort of photophobia.
- Some authorities feel that topical steroids (used within the first 24 hours only) may reduce inflammation.

TREATMENT: SKIN EXPOSURE

- A small area of erythema beginning later than 12 hours after exposure is unlikely to progress to a significant lesion. The patient should be examined, treated with a soothing lotion, sent home, and instructed to return if progression occurs.
- A patient with a significant area of erythema or one seen earlier with a significant area of erythema with or without blistering should be admitted for further evaluation.
- Most burns are second degree although third degree burns may occur after liquid exposure. In general, small blisters (i.e., <1cm) remain roofed and larger ones (i.e., >1cm) should be unroofed. This is a controversial issue, but many feel that the roof will eventually come off anyway.
- Blister fluid does not contain mustard or other toxic substances.
- The denuded area should be irrigated two or three times a day using a whirlpool if the lesion is large (the patient should be given ample amounts of a systemic analgesic beforehand). This should be followed by liberal application of a topical antibiotic.
- Skin lesions may take many months to heal.
- Fluids are not lost as they are in thermal burns, and fluid replacement should be according to the general needs of the patient and not according to "burn therapy" formulas.
- Systemic antibiotics should be used when there are signs of infection and a culture indicates the responsible organism.
- Patients with a large area of second or third degree burns should be transferred to a Burn Unit for further care and reverse isolation.

TREATMENT: INHALATION EXPOSURE

- A patient with a mild, non-productive cough, irritation of the nose and sinuses, and/or a sore throat that began later than 12 hours after exposure should be told to use a cool steam vaporizer and lozenges or cough drops and sent home with instructions to return if the symptoms worsen.
- Patients with more severe effects (laryngitis, shortness of breath, a productive cough) seen at any time postexposure should be admitted directly to the Critical Care Unit once decontamination has been assured. Those with less severe effects should be admitted to a routine care ward.
- Airway damage may range from irritation of the nose and sinuses, to pharyngitis, to destruction of the airway mucosa from the upper airways to the smallest bronchiole. Airway damage is a common cause of death. Upper airway irritation (nose, sinuses, pharynx) may benefit from cool steam inhalation and cough drops or lozenges.
- A patient with signs of airway damage below the pharynx should be provided with oxygen- assisted ventilation as necessary (with PEEP); at the first sign of damage of the larynx or below, the patient should

be intubated and transferred to the Critical Care Unit.

- Bronchodilators should be used if there are signs of bronchoconstriction; steroids might be used if the usual bronchodilators are not effective, but otherwise steroids are not of proven value.
- Daily sputum cultures should be done and systemic antibiotics should be begun with signs of infection and an identified organism. A chemical pneumonitis may occur in the first several days with infiltrates on X-ray, an increase in WBC, and a fever, but this is generally sterile. Organisms generally are not the cause until the third or fourth day postexposure, and antibiotics should not be used prophylactically.
- Patients with airway damage below the pharynx should be managed on the Critical Care Unit by a physician experienced in the management of complicated pulmonary and airway injuries.

TREATMENT: INGESTION EXPOSURE

- **Do not induce emesis**. If a large dose has been ingested and the patient's condition is evaluated within 30 minutes after ingestion, cautious orogastric lavage might remove ingested material. However, the risk of potential bleeding and perforation must be considered. There is no evidence that activated charcoal is beneficial.

TREATMENT: BONE MARROW

- If the bone marrow has been damaged, the white blood cell count in the peripheral blood will start to decrease at about days 3 to 5 after exposure. This decrease may be followed by a decrease in red blood cells and platelets. Often, this decrease is not marked and the marrow recovers.
- Transfusions may be useful. Treatment with granulocyte colony-stimulating factor (GCSF) has been successful experimentally with nitrogen mustard.
- Marrow transplants have not been attempted, but might be useful.
- A patient with a marked decrease in white blood cell count should be transferred to an Oncology or Burn Unit for reverse isolation.

LABORATORY TESTS

- Routine laboratory studies for admitted patients include glucose, serum electrolytes, and daily CBC. Chest x-ray and pulse oximetry (or ABG measurement) should be done frequently on all patients with inhalation effects. A test for urinary thioglycol (a metabolite of mustard) can be performed at specialized laboratories, but is not a routine laboratory measure.

DISPOSITION AND FOLLOW-UP

- Patients with moderate to severe exposures will require hospitalization, as described above.
- Follow-up evaluation of respiratory, neurological, and bone marrow function should be arranged for severely exposed patients.

DELAYED EFFECTS

- Significant systemic absorption of sulfur mustard may produce a fall in the leukocyte count beginning on

days 3 to 5.

- Erythrocytes and thrombocytes may subsequently fall if bone marrow damage is severe and in this case the risk of life-threatening infection rises.

PATIENT RELEASE

Patients who have sustained mild exposure may be discharged. Discharged patients should be advised to rest and to seek medical care promptly if symptoms progress.

Blister Agents
Sulfur Mustard (H, HD, and HT)
Patient Information Sheet

This handout provides information and follow-up instructions for persons who have been exposed to sulfur mustard.

What are sulfur mustards?
Sulfur mustards are yellowish to brown liquids that have been used as chemical warfare agents since 1917.

What immediate health effects can result from exposure to sulfur mustards?
Sulfur mustards produce blistering and cell damage, but symptoms are delayed for hours. They cause damage to the skin, eyes, and respiratory tract. The eyes are the most sensitive. Nausea and vomiting may occur within the first few hours after exposure. Skin rashes, blisters, and lung damage may develop within a few hours of exposure but may take 12 to 24 hours to develop. Sulfur mustard can also suppress the immune system.

Can sulfur mustard poisoning be treated?
There is no antidote for sulfur mustard, but its effects can be treated and most exposed people recover. Immediate decontamination reduces symptoms. People who have been exposed to large amounts of sulfur mustard will need to be treated in a hospital.

Are any future health effects likely to occur?
Adverse health effects, such as chronic respiratory diseases, may occur from exposure to high levels of these agents. Severe damage to the eyes and skin may be present for a long time following the exposure.

What tests can be done if a person has been exposed to sulfur mustards?
There are no routine tests to determine if someone has been exposed to sulfur mustard. Thiodiglycol (a break-down product of mustard) may be detected in the urine up to 2 weeks following exposure; however, this test is available only in several specialized laboratories.

Where can more information about sulfur mustards be found?
More information about sulfur mustard can be obtained from your regional poison control center; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in toxicology or occupational and environmental health. Ask the person who gave you this form for help locating these telephone numbers.

Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

[ ] Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 24 hours, especially:

- coughing, wheezing, shortness of breath, or discolored sputum
- increased pain or discharge from injured eyes
- increased redness, pain, or a pus-like discharge from injured skin
- fever or chills

[ ] No follow-up appointment is necessary unless you develop any of the symptoms listed above.
[ ] Call for an appointment with Dr. _____ in the practice of _____. When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.
[ ] Return to the Emergency Department/ _____ Clinic on (date) _____at ___ _____ AM/PM for a follow-up examination.
[ ] Do not perform vigorous physical activities for 1 to 2 days.
[ ] You may resume everyday activities including driving and operating machinery.
[ ] Do not return to work for _____ days.
[ ] You may return to work on a limited basis. See instructions below.
[ ] Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.
[ ] Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.
[ ] Avoid taking the following medications: _____
[ ] You may continue taking the following medication(s) that your doctor(s) prescribed for you: __
_____
_____
[ ] Other instructions: _____
_____
_____

- Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.

- You or your physician can get more information on the chemical by contacting: _____ _____ or _____, or by checking out the following Internet Web sites: _____; _____.

Signature of patient _____ Date _____

Signature of physician _____ Date_____

CHEMICAL EMERGENCIES: BLOOD AGENTS

HYDROGEN CYANIDE (HCN)

ROUTES OF EXPOSURE

- Inhalation
- Skin/Eye Contact
- Ingestion

CLINICAL:

- Hydrogen cyanide poisoning is marked by abrupt onset of profound toxic effects that may include syncope, seizures, coma, gasping respirations, and cardiovascular collapse, causing death within minutes.
- Patients exposed to hydrogen cyanide can survive with supportive care and rapid administration of specific antidotes.
- ANTIDOTE: Patients who have signs or symptoms of significant systemic toxicity should be evaluated for antidotal treatment. In the United States, antidotes for cyanide include amyl nitrite perles and intravenous infusions of sodium nitrite and sodium thiosulfate, which are packaged in the cyanide antidote kit.

Central Nervous System (CNS)

- CNS signs and symptoms usually develop rapidly. Initial symptoms are nonspecific and include excitement, dizziness, nausea, vomiting, headache, and weakness. As poisoning progresses, drowsiness, tetanic spasm, lockjaw, convulsions, hallucinations, loss of consciousness, and coma may occur.

Cardiovascular

- Abnormal heartbeat can occur in cases of severe poisoning. Slow heartbeat, intractable low blood pressure, and death may result. High blood pressure and a rapid heartbeat may be early, transient findings.

Respiratory

- After systemic poisoning begins, victims may complain of shortness of breath and chest tightness. Pulmonary findings may include rapid breathing and increased depth of respirations.
- As poisoning progresses, respirations become slow and gasping; a bluish skin color may or may not be present. Accumulation of fluid in the lungs may develop.
- Children may be more vulnerable to gas exposure because of relatively increased minute ventilation per kg and failure to evacuate an area promptly when exposed.

Metabolic

- An anion-gap, metabolic acidosis occurs in severe poisoning from increased blood levels of lactic acid.
- Because of their higher metabolic rates, children may be more vulnerable to toxicants interfering with basic metabolism.

Dermal

- Dermal absorption can occur, leading to systemic toxicity. Absorption occurs more readily at high ambient temperature and relative humidity. Because of their relatively larger surface area: body weight ratio, children are more vulnerable to toxicants absorbed through the skin.

Ocular

- When splashed in the eye, hydrogen cyanide can cause eye irritation and swelling.

LABORATORY DIAGNOSIS:

- The diagnosis of acute cyanide toxicity is primarily a clinical one (based on rapid onset of CNS toxicity and cardiorespiratory collapse).
- Laboratory testing is useful for monitoring the patient and evaluating complications. Routine laboratory studies for all exposed patients include CBC, blood glucose, and electrolyte determinations.

EXPOSURE/CONTAMINATION:

- Hospital personnel in an enclosed area can be secondarily contaminated by vapor off-gassing from heavily soaked clothing or skin, or from toxic vomitus.
- Avoid dermal contact with cyanide-contaminated patients or with gastric contents of patients who may have ingested cyanide-containing materials.
- Patients do not pose secondary contamination risks after contaminated clothing is removed and the skin is washed.

TREATMENT

- ANTIDOTE - Amyl nitrite perles and intravenous infusions of sodium nitrite and sodium thiosulfate, which are packaged in the cyanide antidote kit. Treatment consists primarily of supportive care.

TREATMENT – INGESTION EXPOSURE

- **Do not induce emesis.**
- If the victim is symptomatic, immediately institute emergency life support measures including the use of a cyanide antidote kit (see *Antidotes* and *Other Treatments*). If the victim is alert, asymptomatic, has a gag reflex, and it has not been done previously, perform gastric lavage and give activated charcoal as soon as possible. Administer a slurry of activated charcoal at 1 gm/kg (usual adult dose 60-90 g, child dose 25-50 g). A soda can and a straw may be of assistance when offering charcoal to a child.

DISPOSITION/FOLLOWUP

- Consider hospitalizing patients who have histories of significant exposure and are symptomatic.
- Whenever infusions from the cyanide antidote kit are used, the patient should be admitted to the intensive care unit.
- Survivors of a serious exposure should be evaluated for ischemic damage to the brain and heart. Patients who have serious systemic cyanide poisoning may be at risk for CNS sequelae including Parkinsonian-like syndromes; they should be monitored for several weeks to months.
- Obtain the name of the patient's primary care physician so that the hospital can send a copy of the ED visit to the patient's doctor.
- Patients who have corneal injuries should be reexamined within 24 hours.

Medical Management Guidelines for Blood Agents

MEDICAL MANAGEMENT GUIDELINES FOR

Hydrogen Cyanide (HCN)

Cyanogen chloride (CK),Hydrogen cyanide (AC),Potassium cyanide (KCN),Sodium cyanide (NaCN)

For further information go to: http://www.atsdr.cdc.gov/MMG/MMG.asp?id=1073&tid=19

To report chemical spills: Chemtrec – http://www.chemtrec.com/responder/resources/Pages/erfaqs.aspx

BACKGROUND INFORMATION

At temperatures below 78ºF, hydrogen cyanide is a colorless or pale-blue liquid (hydrocyanic acid); at higher temperatures, it is a colorless gas. Hydrogen cyanide is very volatile, producing potentially lethal concentrations at room temperature. The vapor is flammable and potentially explosive. Hydrogen cyanide has a faint, bitter almond odor and a bitter, burning taste. It is soluble in water and is often used as a 96% aqueous solution.

SYNONYMS FOR HYDROGEN CYANIDE:

Synonyms include formonitrile. Aqueous solutions are referred to as hydrocyanic acid and prussic acid.

EXPOSURE/CONTAMINATION

Hospital personnel in an enclosed area can be secondarily contaminated by vapor off-gassing from heavily soaked clothing or skin, or from toxic vomitus. Avoid dermal contact with cyanide-contaminated patients or with gastric contents of patients who may have ingested cyanide-containing materials. Patients do not pose secondary contamination risks after contaminated clothing is removed and the skin is washed.

ROUTES OF EXPOSURE

Inhalation

- Hydrogen cyanide is readily absorbed from the lungs; symptoms of poisoning begin within seconds to minutes. The odor of hydrogen cyanide is detectable at 2-10 ppm (OSHA PEL = 10 ppm), but **does not provide adequate warning of hazardous concentrations**. Perception of the odor is a genetic trait (20% to 40% of the general population cannot detect hydrogen cyanide); also, rapid olfactory fatigue can occur. Hydrogen cyanide is lighter than air.
- Children exposed to the same levels of hydrogen cyanide as adults may receive larger doses because they have greater lung surface area: body weight ratios and increased minute volumes:weight ratios.

Skin/Eye Contact

- Exposure to hydrogen cyanide can cause skin and eye irritation. More importantly, skin or eye absorption is rapid and contributes to systemic poisoning. After skin exposure, onset of symptoms may be immediate or delayed for 30 to 60 minutes. Most cases of toxicity from dermal exposure have been from industrial accidents involving partial immersion in liquid cyanide or cyanide solutions or from contact with molten cyanide salts, resulting in large surface-area burns.
- Children are more vulnerable to toxicants absorbed through the skin because of their relatively larger surface area:body weight ratio.

Ingestion

- Ingestion of hydrogen cyanide solutions or cyanide salts can be rapidly fatal.

HEALTH EFFECTS

Acute Exposure

- Hydrogen cyanide poisoning is marked by abrupt onset of profound toxic effects that may include syncope, seizures, coma, gasping respirations, and cardiovascular collapse, causing death within minutes.
- In humans, cyanide combines with the ferric ion in mitochondrial cytochrome oxidase, preventing electron transport in the cytochrome system and bringing oxidative phosphorylation and ATP production to a halt. The inhibition of oxidative metabolism puts increased demands on anaerobic glycolysis, which results in lactic acid production and may produce severe acid-base imbalance. The CNS is particularly sensitive to the toxic effects of cyanide, and exposure to hydrogen cyanide generally produces symptoms within a short period of time.
- Children do not always respond to chemicals in the same way that adults do. Different protocols for managing their care may be needed.
- Patients exposed to hydrogen cyanide can survive with supportive care and rapid administration of specific antidotes.

Central Nervous System (CNS)

- CNS signs and symptoms usually develop rapidly. Initial symptoms are nonspecific and include excitement, dizziness, nausea, vomiting, headache, and weakness. As poisoning progresses, drowsiness, tetanic spasm, lockjaw, convulsions, hallucinations, loss of consciousness, and coma may occur.

Cardiovascular

- Abnormal heartbeat can occur in cases of severe poisoning. Slow heartbeat, intractable low blood pressure, and death may result. High blood pressure and a rapid heartbeat may be early, transient findings.

Respiratory

- After systemic poisoning begins, victims may complain of shortness of breath and chest tightness. Pulmonary findings may include rapid breathing and increased depth of respirations.
- As poisoning progresses, respirations become slow and gasping; a bluish skin color may or may not be present. Accumulation of fluid in the lungs may develop.
- Children may be more vulnerable to gas exposure because of relatively increased minute ventilation per kg and failure to evacuate an area promptly when exposed.

Metabolic

- An anion-gap, metabolic acidosis occurs in severe poisoning from increased blood levels of lactic acid.
- Because of their higher metabolic rates, children may be more vulnerable to toxicants interfering with basic metabolism.

Dermal

- Dermal absorption can occur, leading to systemic toxicity. Absorption occurs more readily at high ambient temperature and relative humidity.
- Because of their relatively larger surface area:body weight ratio, children are more vulnerable to toxicants absorbed through the skin.

Ocular

- When splashed in the eye, hydrogen cyanide can cause eye irritation and swelling. Eye contact with cyanide salts has produced systemic symptoms in experimental animals.

Potential Sequelae

- Survivors of severe exposure may suffer brain damage due to a direct action on neurons, or to lack of oxygen, or possibly due to insufficient blood circulation. Cases of neurologic sequelae such as personality

changes, memory deficits, disturbances in voluntary muscle movements, and the appearance of involuntary movements (i.e., extrapyramidal syndromes) have been reported.

ABC REMINDERS

- Evaluate and support airway, breathing, and circulation. In cases of respiratory compromise secure airway and respiration via endotracheal intubation. If not possible, surgically create an airway.
- Continuously monitor cardiac rhythm.
- Patients who are in shock or have seizures should be treated according to ALS protocols. These patients or those who have dysrhythmias may be seriously acidotic; consider giving 1 mEq/kg intravenous sodium bicarbonate

ANTIDOTES

- Patients who have signs or symptoms of significant systemic toxicity should be evaluated for antidotal treatment. In the United States, antidotes for cyanide include amyl nitrite perles and intravenous infusions of sodium nitrite and sodium thiosulfate, which are packaged in the cyanide antidote kit.
- If one dose of the antidotes from the kit has been administered previously by prehospital personnel and inadequate clinical response has occurred, a second dose of one-half the initial amounts may be given 30 minutes after the initial dose. Further doses should be guided by the patient's clinical condition and not by the percentage of methemoglobin induced. The usual methods of monitoring methemoglobin levels are unreliable in cases of cyanide poisoning and may seriously underestimate the levels of inactive hemoglobin.
- Amyl nitrite perles should be broken onto a gauze pad and held under the nose, over the Ambu-valve intake, or placed under the lip of the face mask. Inhale for 30 seconds every minute and use a new perle every 3 minutes if sodium nitrite infusions will be delayed.
- If the patient has not responded to oxygen and amyl nitrite treatment, infuse sodium nitrite intravenously as soon as possible. The usual adult dose is 10 mL of a 3% solution (300 mg) infused over absolutely no less than 5 minutes; the average pediatric dose is 0.12 to 0.33 mL/kg body weight up to 10 mL infused as above. Monitor blood pressure during sodium nitrite administration, and slow the rate of infusion if hypotension develops.
- Next, infuse sodium thiosulfate intravenously. The usual adult dose is 50 mL of a 25% solution (12.5 g) infused over 10 to 20 minutes; the average pediatric dose is 1.65 mL/kg of a 25% solution. Repeat one-half of the initial dose 30 minutes later if there is an inadequate clinical response.
- Amyl nitrite and sodium nitrite oxidize the ferrous iron of hemoglobin to methemoglobin. Methemoglobin levels should not exceed 20%. Repeat treatment with nitrite and thiosulfate as required.
- The efficacy of hyperbaric oxygen in cyanide poisoning is unproven. It has been reported to be useful in severe cases of smoke inhalation combined with exposure to hydrogen cyanide and carbon monoxide.

TREATMENT – INGESTION EXPOSURE

- **Do not induce emesis.**
- If the victim is symptomatic, immediately institute emergency life support measures including the use of a cyanide antidote kit (see *Antidotes* and *Other Treatments*). If the victim is alert, asymptomatic, has a gag reflex, and it has not been done previously, perform gastric lavage and give activated charcoal as soon as possible. Because cyanide absorption from the gut is rapid, the usefulness of activated charcoal will depend on how quickly after ingestion it can be administered.
- Administer a slurry of activated charcoal at 1 gm/kg (usual adult dose 60-90 g, child dose 25-50 g). A soda can and a straw may be of assistance when offering charcoal to a child.
- Toxic vomitus or gastric washings should be isolated (e.g., by attaching the lavage tube to isolated wall

suction or another closed container).

LABORATORY TESTS

- The diagnosis of acute cyanide toxicity is primarily a clinical one (based on rapid onset of CNS toxicity and cardiorespiratory collapse). Laboratory testing is useful for monitoring the patient and evaluating complications. Routine laboratory studies for all exposed patients include CBC, blood glucose, and electrolyte determinations. Additional studies for patients exposed to hydrogen cyanide include ECG monitoring, determinations of serum lactate, chest radiography, and pulse oximetry (or ABG measurements).
- In severe poisonings, venous blood is oxygenated and has a bright red color. Elevated venous PO_2 and venous percent O_2 saturation occurs, narrowing the gap between arterial and central venous PO_2 or percent O_2 saturation.
- After treatment with nitrites, serum methemoglobin levels may be monitored. However, the usual methods of monitoring methemoglobin levels are unreliable in cases of cyanide poisoning and may seriously underestimate the levels of inactive hemoglobin. Alternative methods exist, but may not be available. Whole blood cyanide tests generally require several hours and cannot be used to guide emergency treatment. However, blood cyanide levels may be useful in documenting exposure.

DISPOSITION AND FOLLOW-UP

- Consider hospitalizing patients who have histories of significant exposure and are symptomatic.
- Whenever infusions from the cyanide antidote kit are used, the patient should be admitted to the intensive care unit.
- Obtain the name of the patient's primary care physician so that the hospital can send a copy of the ED visit to the patient's doctor.
- Survivors of a serious exposure should be evaluated for ischemic damage to the brain and heart. Patients who have serious systemic cyanide poisoning may be at risk for CNS sequelae including Parkinsonian-like syndromes; they should be monitored for several weeks to months.
- Patients who have corneal injuries should be reexamined within 24 hours.

DELAYED EFFECTS

- Patients who have ingested hydrogen cyanide solutions or patients who have direct skin or eye contact should be observed in the Emergency Department for at least 4 to 6 hours.

PATIENT RELEASE

Patients who remain asymptomatic 4 to 6 hours after exposure may be discharged with instructions to seek medical care promptly if symptoms develop.

Hydrogen Cyanide
Patient Information Sheet

This handout provides information and follow-up instructions for persons who have been exposed to hydrogen cyanide.

What is hydrogen cyanide?
At room temperature, hydrogen cyanide is a volatile, colorless-to-blue liquid (also called hydrocyanic acid). It rapidly becomes a gas that can produce death in minutes if breathed. Hydrogen cyanide is used in making fibers, plastics, dyes, pesticides, and other chemicals, and as a fumigant to kill rats. It is also used in electroplating metals and in developing photographic film.

What immediate health effects can be caused by exposure to hydrogen cyanide?
Breathing small amounts of hydrogen cyanide may cause headache, dizziness, weakness, nausea, and vomiting. Larger amounts may cause gasping, irregular heartbeats, seizures, fainting, and even rapid death. Generally, the more serious the exposure, the more severe the symptoms. Similar symptoms may be produced when solutions of hydrogen cyanide are ingested or come in contact with the skin.

Can hydrogen cyanide poisoning be treated?
The treatment for cyanide poisoning includes breathing pure oxygen, and in the case of serious symptoms, treatment with specific cyanide antidotes. Persons with serious symptoms will need to be hospitalized.

Are any future health effects likely to occur?
A single small exposure from which a person recovers quickly is not likely to cause delayed or long-term effects. After a serious exposure, a patient may have brain or heart damage.

What tests can be done if a person has been exposed to hydrogen cyanide?
Specific tests for the presence of cyanide in blood and urine generally are not useful to the doctor. If a severe exposure has occurred, blood and urine analyses and other tests may show whether the brain or heart has been injured. Testing is not needed in every case.

Where can more information about hydrogen cyanide be found?
More information about hydrogen cyanide can be obtained from your regional poison control center; your state, county, or local health department; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in occupational and environmental health. If the exposure happened at work, you may wish to discuss it with your employer, the Occupational Safety and Health Administration (OSHA), or the National Institute for Occupational Safety and Health (NIOSH). Ask the person who gave you this form for help in locating these telephone numbers.

Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

[ ] Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 24 hours, especially:

- difficulty breathing, shortness of breath, or chest pain
- confusion or fainting
- increased pain or a discharge from your eyes
- increased redness, pain, or a pus-like discharge in the area of a skin burn

[ ] No follow-up appointment is necessary unless you develop any of the symptoms listed above.
[ ] Call for an appointment with Dr. _____ in the practice of _____. When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.
[ ] Return to the Emergency Department/ _____ Clinic on (date) _____at ___ _____ AM/PM for a follow-up examination.
[ ] Do not perform vigorous physical activities for 1 to 2 days.
[ ] You may resume everyday activities including driving and operating machinery.
[ ] Do not return to work for _____ days.
[ ] You may return to work on a limited basis. See instructions below.
[ ] Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.
[ ] Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.
[ ] Avoid taking the following medications: _____
[ ] You may continue taking the following medication(s) that your doctor(s) prescribed for you: __
_____
_____
[ ] Other instructions: _____
_____
_____

- Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.

- You or your physician can get more information on the chemical by contacting: _____ _____ or _____, or by checking out the following Internet Web sites: _____; _____.

Signature of patient _____ Date _____

Signature of physician _____ Date _____

CHEMICAL EMERGENCIES: BLOOD AGENTS

ARSINE (AsH_3)

ROUTES OF EXPOSURE

- Inhalation
- Skin or eye contact
- Ingestion

CLINICAL

- After absorption by the lungs, arsine enters red blood cells (RBC) where different processes may contribute to hemolysis and impairment of oxygen transport. Arsine preferentially binds to hemoglobin, and is oxidized to an arsenic dihydride intermediate and elemental arsenic, both of which are hemolytic agents.
- Pre-existing cardiopulmonary or renal conditions, iron deficiency, and/or pre-existing anemia may result in more severe outcomes if hemolysis occurs.

Hematologic

- Acute intravascular hemolysis develops within hours and may continue for up to 96 hours. Haptoglobin levels decline rapidly. Free hemoglobin levels in plasma rise (levels greater than 2 g/dL have been reported). Anemia develops; the peripheral smear shows variation in the size of the red blood cells, irregularly shaped blood cells, red-cell fragments, components that have an affinity for basic dyes, Heinz bodies, and ghost cells. The bone marrow usually shows no abnormalities. Coombs and Ham tests are negative, and RBC fragility is normal.
- Methemoglobinemia can be of concern in infants up to 1 year old. Children may be more vulnerable to loss of effectiveness of hemoglobin because of their relative anemia compared to adults.

Respiratory

- Difficult breathing is among the early symptoms of arsine poisoning. A garlic odor may be present on the breath. Delayed accumulation of fluid in the lungs may occur after massive exposure. Dyspnea may be due to lack of oxygen secondary to hemolysis.
- Children may be more vulnerable because of increased minute ventilation per kg and failure to evacuate an area promptly when exposed.

Renal

- Kidney failure due to acute tubular destruction is a significant sequela of arsine exposure. Urinalysis shows large amounts of protein and free hemoglobin usually without intact RBCs. Urine may be colored (e.g., brown, red, orange, or greenish). Decreased urinary output may develop within 24 to 48 hours.

Gastrointestinal

- Nausea, vomiting, and crampy abdominal pain are among the first signs of arsine poisoning. Onset varies from a few minutes to 24 hours after exposure.

Dermal

- The characteristic bronze tint of the skin caused by arsine toxicity is induced by hemolysis and may be caused by hemoglobin deposits. This is not true jaundice which can occur in severe cases.
- Contact with the liquid (compressed gas) can cause frostbite.

Cardiovascular

- Hypotension may occur with severe exposures. EKG changes and dysrhythmias associated with hypocalaemia can occur.

Hepatic

- Right upper quadrant pain, hepatomegaly, elevated serum globulin, elevated liver enzymes and prolonged prothrombin time have been observed.

Musculoskeletal

- Skeletal muscle injury or necrosis have been reported. Muscle pain and twitches, myoglobinuria, elevated levels of serum creatine phosphokinase (CPK) and aldolase have been observed.

Ocular

- Red staining of the conjuctiva may be an early sign of arsine poisoning.

LABORATORY DIAGNOSIS:

- If significant exposure is a possibility and transfusion is considered, obtain a blood sample for type and screen.
- Laboratory tests to determine hemolysis include CBC with peripheral smear, urinalysis, and plasma free hemoglobin and haptoglobin analyses.
- Other useful studies include renal-function tests (e.g., BUN, creatinine), and determinations of serum electrolytes and bilirubin levels.

EXPOSURE:

- Persons exposed to arsine pose no serious risks of secondary contamination to personnel outside the Hot Zone.

TREATMENT:

- If massive exposure is suspected or if the patient is hypotensive, ensure adequate hydration by infusing intravenous saline or lactated Ringer's solution. Monitor fluid balance and avoid fluid overload if renal failure supervenes; monitor plasma electrolytes to detect disturbances (particularly hyperkalemia) as early as possible. Monitor hematocrit.
- Because of possible severe hemolysis ensure adequate oxygenation by arterial blood gas measurement or pulse oxygenation monitoring. The use of diuretics such as furosimide to maintain urinary flow is an important consideration and should be performed under medical base control.
- EYE – In case of frostbite injury, ensure that thorough warming with lukewarm water or saline has been completed. Examine the eyes for corneal damage and treat appropriately. Immediately consult an ophthalmologist for patients who have corneal injuries.
- SKIN – In case of frostbite injury, irrigate with lukewarm (42ºC) water according to standard treatment
- INHALATION – Administer supplemental oxygen by mask to patients who have respiratory symptoms. Treat patients who have bronchospasm with aerosolized bronchodilators. Consider racemic epinephrine aerosol

for children who develop stridor. If hemolysis develops, initiate urinary alkalinization. Consider hemodialysis if renal failure is severe

DISPOSITION/FOLLOWUP

- Decisions to admit or discharge a patient should be based on exposure history, physical examination, and test results.
- Obtain the name of the patient's primary care physician so that the hospital can send a copy of the ED visit to the patient's doctor.
- All patients should have repeat urine and blood laboratory tests in 12 to 24 hours. Patients who have corneal injuries should be reexamined within 24 hours.
- If severe hemolysis has occurred, anemia may persist for several weeks.
- Polyneuropathy and alteration in mental status are reported to have followed arsine poisoning after a latency of 1 to 6 months.
- Patients should be evaluated periodically by their physician for several months; these examinations should include hematological and urinalysis tests.

Medical Management Guidelines for Blood Agents

MEDICAL MANAGEMENT GUIDELINES FOR

Arsine (AsH_3)

For further information go to: http://www.atsdr.cdc.gov/MHMI/mmg169.html

To report chemical spills: Chemtrec – http://www.chemtrec.com/responder/resources/Pages/erfaqs.aspx

BACKGROUND INFORMATION

Arsine is a colorless, flammable, and highly toxic gas. It has a garlic-like or fishy odor that can be detected at concentrations of 0.5 ppm and above. Because arsine is nonirritating and produces no immediate symptoms, persons exposed to hazardous levels may be unaware of its presence. Arsine is water soluble. It is generally shipped in cylinders as a liquefied compressed gas. Exposure frequently occurs when arsine gas is generated while metals or crude ores containing arsenic impurities are treated with acid and this is a common source of exposure.

SYNONYMS FOR ARSINE: Synonyms include arsenic hydride, arsenic trihydride, arseniuretted hydrogen, arsenious hydride, hydrogen arsenide, and SA.

EXPOSURE/CONTAMINATION

Persons exposed to arsine pose no serious risks of secondary contamination to personnel outside the Hot Zone.

ROUTES OF EXPOSURE

Inhalation

- Inhalation is the major route of exposure. The odor threshold of arsine is 10-fold greater than the OSHA permissible exposure limit. **Odor is not an adequate indicator of arsine's presence and does not provide reliable warning of hazardous concentrations**. Arsine is heavier than air and hazardous concentrations may develop quickly in enclosed, poorly ventilated, or low-lying areas. Initial symptoms (malaise, dizziness, nausea, abdominal pain, and dyspnea) may develop within several hours of exposure to 3 ppm of arsine.
- Children exposed to the same levels of arsine as adults may receive larger dose because they have greater lung surface area:body weight ratios and increased minute volumes:weight ratios. In addition, they may be exposed to higher levels than adults in the same location because of their short stature and the higher levels of arsine found nearer to the ground.

Skin/Eye Contact

- There is little information about direct toxic effects of arsine on the skin or eyes, or about absorption through the skin. Exposure to liquid arsine (the compressed gas) can result in frostbite.

Ingestion

- Ingestion of arsine itself is unlikely because it is a gas at room temperature. However, metal arsenides are solids that can react with acidic gastric contents, releasing arsine gas in the stomach.

HEALTH EFFECTS

Acute Exposure

- After absorption by the lungs, arsine enters red blood cells (RBC) where different processes may contribute to hemolysis and impairment of oxygen transport. Inhibition of catalase may lead to accumulation of hydrogen peroxide which, as an oxidizer, destroys red cell membranes and may contribute to arsine-induced conversion of Fe^{+2} to Fe^{+3}, which also impairs oxygen transport. Arsine preferentially binds to hemoglobin, and is oxidized to an arsenic dihydride intermediate and elemental arsenic, both of which are hemolytic agents.
- Arsine toxicity involves depletion of reduced glutathione. Therefore, people deficient in the enzyme glucose-6-phosphate-dehydrogenase (G6PD) are more susceptible to hemolysis following arsine exposure.
- Pre-existing cardiopulmonary or renal conditions, iron deficiency, and/or pre-existing anemia may result in more severe outcomes if hemolysis occurs.
- Contact with the skin or eyes does not result in systemic toxicity. Ingestion of arsine is unlikely, but ingestion of metallic arsenides can lead to arsine gas production and toxicity.

Hematologic

- Acute intravascular hemolysis develops within hours and may continue for up to 96 hours. Haptoglobin levels decline rapidly. Free hemoglobin levels in plasma rise (levels greater than 2 g/dL have been reported). Anemia develops; the peripheral smear shows variation in the size of the red blood cells, irregularly shaped blood cells, red-cell fragments, components that have an affinity for basic dyes, Heinz bodies, and ghost cells. The bone marrow usually shows no abnormalities. Coombs and Ham tests are negative, and RBC fragility is normal.
- Methemoglobinemia can be of concern in infants up to 1 year old. Children may be more vulnerable to loss of effectiveness of hemoglobin because of their relative anemia compared to adults.

Respiratory

- Difficult breathing is among the early symptoms of arsine poisoning. A garlic odor may be present on the breath. Delayed accumulation of fluid in the lungs may occur after massive exposure. Dyspnea may be due to lack of oxygen secondary to hemolysis.
- Children may be more vulnerable because of increased minute ventilation per kg and failure to evacuate an area promptly when exposed.

Renal

- Kidney failure due to acute tubular destruction is a significant sequela of arsine exposure. Hemoglobin in the urine is thought to be the major cause of damage to the kidneys; however, a direct toxic effect of arsine or deposition of the arsine-hemoglobin-haptoglobin complex may also play a role. Urinalysis shows large amounts of protein and free hemoglobin usually without intact RBCs. Urine may be colored (e.g., brown, red, orange, or greenish). Decreased urinary output may develop within 24 to 48 hours.

Gastrointestinal

- Nausea, vomiting, and crampy abdominal pain are among the first signs of arsine poisoning. Onset varies from a few minutes to 24 hours after exposure.

Dermal

- The characteristic bronze tint of the skin caused by arsine toxicity is induced by hemolysis and may be caused by hemoglobin deposits. This is not true jaundice which can occur in severe cases.
- Contact with the liquid (compressed gas) can cause frostbite.

Cardiovascular

- Hypotension may occur with severe exposures. EKG changes and dysrhythmias associated with hypocalaemia can occur.

Hepatic

- Right upper quadrant pain, hepatomegaly, elevated serum globulin, elevated liver enzymes and prolonged prothrombin time have been observed.

Musculoskeletal

- Skeletal muscle injury or necrosis have been reported. Muscle pain and twitches, myoglobinuria, elevated levels of serum creatine phosphokinase (CPK) and aldolase have been observed.

Ocular

- Red staining of the conjuctiva may be an early sign of arsine poisoning.

ABC REMINDERS

- Evaluate and support airway, breathing, and circulation. Establish intravenous access in symptomatic patients. Monitor cardiac rhythm.
- Monitor fluid balance carefully to avoid fluid overload if renal failure supervenes; monitor plasma electrolytes to detect disturbances (particulary hyperkalemia) as early as possible, and monitor hematocrit.
- Patients who are comatose or hypotensive should be treated in the conventional manner.
- Consider dopamine for hypotension or oligonuria, or norepinephrine in cases of severe resistant shock.
- Observe patients who have inhaled arsine for up to 24 hours. Follow up as clinically indicated..

TREATMENT – ACUTE EXPOSURE

Yellow highlighted text is from field treatment section (Advanced Treatment) – need to determine if it is covered in the ER section – need to decipher it. Maybe the panel can help?

- If massive exposure is suspected or if the patient is hypotensive, ensure adequate hydration by infusing intravenous saline or lactated Ringer's solution. For adults, bolus 1,000 mL/hour if blood pressure is under 80 mm Hg; if systolic pressure is over 90 mm Hg, an infusion rate of 150 to 200 mL/hour is sufficient. For children with compromised perfusion administer a 20 mL/kg bolus of normal saline over 10 to 20 minutes, then infuse at 2 to 3 mL/kg/hour. Monitor fluid balance and avoid fluid overload if renal failure supervenes; monitor plasma electrolytes to detect disturbances (particularly hyperkalemia) as early as possible. Monitor hematocrit.
- Because of possible severe hemolysis ensure adequate oxygenation by arterial blood gas measurement or pulse oxygenation monitoring. The use of diuretics such as furosimide to maintain urinary flow is an important consideration and should be performed under medical base control.

TREATMENT – INHALATION EXPOSURE

- Administer supplemental oxygen by mask to patients who have respiratory symptoms. Treat patients who have bronchospasm with aerosolized bronchodilators. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Also consider the health of the myocardium before choosing which type of bronchodilator should be administered. Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). Arsine poisoning is not known to pose additional risk during the use of bronchial or cardiac sensitizing agents.
- Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25-0.75 mL of 2.25% racemic epinephrine solution in 2.5 cc water, repeat every 20 minutes as needed cautioning for myocardial variability.
- If hemolysis develops, initiate urinary alkalinization. Add 50 to 100 mEq of sodium bicarbonate to one liter of 5% dextrose in 0.25 normal saline and administer intravenously at a rate that maintains urine output at 2 to 3 mL/kg/hour. Maintain alkaline urine (i.e., pH >7.5) until urine is hemoglobin free. Closely monitor serum electrolytes, calcium, BUN, creatinine, hemoglobin, and hematocrit.
- Consider hemodialysis if renal failure is severe. (Although hemodialysis will assist the patient who has renal

failure, it will not effectively remove the arsine-hemoglobin or arsine-haptoglobin complexes deposited in the renal tubules.) Blood transfusions may be necessary if hemolysis causes severe anemia.

TREATMENT - SKIN EXPOSURE

- In case of frostbite injury, irrigate with lukewarm (42ºC) water according to standard treatment.

TREATMENT – EYE EXPOSURE

- In case of frostbite injury, ensure that thorough warming with lukewarm water or saline has been completed. Examine the eyes for corneal damage and treat appropriately. Immediately consult an ophthalmologist for patients who have corneal injuries.

LABORATORY TESTS

- If significant exposure is a possibility and transfusion is considered, obtain a blood sample for type and screen. Laboratory tests to determine hemolysis include CBC with peripheral smear, urinalysis, and plasma free hemoglobin and haptoglobin analyses. Other useful studies include renal-function tests (e.g., BUN, creatinine), and determinations of serum electrolytes and bilirubin levels.
- Consider monitoring urinary arsenic excretion to assess the severity of poisoning. Note that the amount of arsine that must be absorbed to cause significant poisoning may not be large.

DISPOSITION AND FOLLOW-UP

- Decisions to admit or discharge a patient should be based on exposure history, physical examination, and test results.
- Obtain the name of the patient's primary care physician so that the hospital can send a copy of the ED visit to the patient's doctor.
- All patients should have repeat urine and blood laboratory tests in 12 to 24 hours. Patients who have corneal injuries should be reexamined within 24 hours.
- If severe hemolysis has occurred, anemia may persist for several weeks.
- Polyneuropathy and alteration in mental status are reported to have followed arsine poisoning after a latency of 1 to 6 months. Patients should be evaluated periodically by their physician for several months; these examinations should include hematological and urinalysis tests.

DELAYED EFFECTS

- All patients who have suspected arsine exposure should be carefully observed for 24 hours, including hourly urine output. Onset of hemolysis may be delayed for up to 24 hours, and acute renal failure may not become evident for as long as 72 hours after exposure.

PATIENT RELEASE

Patients who have no signs of hemolysis may be discharged after 24 hours of observation with instructions to seek medical care promptly if symptoms develop. Released patients should also be instructed to rest and to drink plenty of fluids.

Arsine
Patient Information Sheet

This handout provides information and follow-up instructions for persons who have been exposed to arsine.

What is arsine?
Arsine is a colorless, flammable gas that does not burn the eyes, nose, or throat. At high concentrations it has a garlic-like or fishy smell, but a person can be exposed to a hazardous concentration of arsine and may not be able to smell it. Arsine is widely used in the manufacturing of fiberoptic equipment and computer microchips. It is sometimes used in galvanizing, soldering, etching, and lead plating. Certain ores or metals may contain traces of arsenic. If water or acid contacts these ores or metals, they may release arsine gas at hazardous levels.

What immediate health effects can result from arsine exposure?
Breathing in arsine gas can be very harmful, even in small quantities. The main effect of arsine poisoning is to destroy red blood cells, causing anemia (lack of red blood cells) and kidney damage (from circulating red-blood-cell debris). Initially, exposed individuals may feel relatively well. Within hours after a serious exposure, the victim may develop headache, weakness, shortness of breath, and back or stomach pain with nausea and vomiting; the urine may turn a dark red, brown or greenish color. The skin may become yellow or bronze in color, the eyes red or green. Generally, the more serious the exposure, the worse the symptoms. Although arsine is related to arsenic, it does not produce the usual signs and symptoms of arsenic poisoning.

Can arsine poisoning be treated?
There is no antidote for arsine, but its effects can be treated. A doctor may give the exposed patient fluids through a vein to protect the kidneys from damage. For severe poisoning, blood transfusions and cleansing of the blood (hemodialysis) may be needed to prevent worsening kidney damage.

Are any future health effects likely to occur?
After a serious exposure, symptoms usually begin within 2–24 hours (see the *Follow-up Instructions*). Most people do not develop long-term effects from a single, small exposure to arsine. In rare cases, permanent kidney damage or nerve damage has developed after a severe exposure. Repeated exposures to arsine over a long period of time might cause skin or lung cancer, but this has not been studied.

What tests can be done if a person has been exposed to arsine?
Specific tests can show the amount of arsenic in urine, but this information may or may not be helpful to the doctor. Standard tests of blood, urine, and other measures of health may show whether exposure has caused serious injury to the lungs, blood cells, kidneys, or nerves. Since toxic effects of arsine poisoning may be delayed, testing should be done in all cases of suspected exposure to arsine.

Where can more information about arsine be found?
More information about arsine can be obtained from your regional poison control center; your state, county, or local health department; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in occupational and environmental health. If the exposure happened at work, you may wish to discuss it with your employer, the Occupational Safety

and Health Administration (OSHA), or the National Institute for Occupational Safety and Health (NIOSH). Ask the person who gave you this form for help in locating these telephone numbers.

Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

[ ] Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 24–72 hours, especially:
- unusual fatigue or weakness
- shortness of breath
- abnormal urine color (red or brown)
- stomach pain or tenderness
- unusual skin color (yellow or bronze)

[ ] No follow-up appointment is necessary unless you develop any of the symptoms listed above.
[ ] Call for an appointment with Dr. _____ in the practice of _____. When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.
[ ] Return to the Emergency Department/ _____ Clinic on (date) _____at _____ AM/PM for a follow-up examination.
[ ] Do not perform vigorous physical activities for 1 to 2 days.
[ ] You may resume everyday activities including driving and operating machinery.
[ ] Do not return to work for _____ days.
[ ] You may return to work on a limited basis. See instructions below.
[ ] Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.
[ ] Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.
[ ] Avoid taking the following medications: _____
[ ] You may continue taking the following medication(s) that your doctor(s) prescribed for you: _____
_____
_____
[ ] Other instructions: _____
_____
_____

- Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.

- You or your physician can get more information on the chemical by contacting: _____ _____ or _____, or by checking out the following Internet Web sites: _____; _____.

Signature of patient _____ Date _____

Signature of physician _____ Date _____

CHEMICAL EMERGENCIES: PULMONARY INTOXICANTS

AMMONIA (NH_3)

ROUTE OF EXPOSURE:

- Inhalation
- Skin or eye contact

CLINICAL:

- Nasopharyngeal and tracheal burns
- Bronchiolar and alveolar edema
- Airway destruction resulting in respiratory distress or failure.
- Serious corrosive injury
- Skin burns
- Permanent eye damage or blindness.

LABORATORY DIAGNOSIS:

- Routine laboratory studies for all exposed patients include CBC, glucose, and electrolyte determinations.
- Chest radiography and pulse oximetry (or arterial blood gases measurements) are recommended for severe inhalation exposure or if pulmonary aspiration is suspected.

EXPOSURE:

- Persons exposed only to ammonia **gas** do not pose significant risks of secondary contamination to personnel outside the Hot Zone.
- Persons whose clothing or skin is contaminated with **liquid** ammonium hydroxide can secondarily contaminate response personnel by direct contact or through off-gassing ammonia vapor.

TREATMENT:

- Evaluate and support airway, breathing, and circulation.
- Administer supplemental oxygen by mask to patients who have respiratory symptoms.
- Watch for signs of laryngeal edema and airway compromise.
- In cases of respiratory compromise, secure airway and respiration via endotracheal intubation. If not possible, surgically secure an airway.
- Treat patients who have bronchospasm with aerosolized bronchodilators
- Cardiac sensitizing agents may be appropriate
- Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25-0.75 mL of 2.25% racemic epinephrine solution in water, repeat every 20 minutes as needed cautioning for myocardial variability.
- Patients who are comatose, hypotensive or have seizures should be treated in the conventional manner.

DISPOSITION/FOLLOWUP

Consider hospitalizing patients who:

- Have evidence of respiratory distress or
- Significant skin burns or who
- Have ingested an ammonia solution.

MEDICAL MANAGEMENT OF CHEMICAL AGENTS

Respiratory Agents (Choking/Lung/Pulmonary; agents which cause severe irritation or swelling of the respiratory tract)

MEDICAL MANAGEMENT GUIDELINES FOR AMMONIA (NH_3)

For Further Information Go To http://www.atsdr.cdc.gov/MMG/MMG.asp?id=7&tid=2
To report chemical spills: Chemtrec – http://www.chemtrec.com/responder/resources/Pages/erfaqs.aspx

BACKGROUND INFORMATION:

Synonyms include ammonia gas, anhydrous ammonia, and liquid ammonia. Aqueous solutions are referred to as aqueous ammonia, ammonia solution, and ammonium hydroxide.

Children exposed to the same levels of ammonia vapor as adults may receive larger dose because they have greater lung surface area: body weight ratios and increased minute volumes: weight ratios. In addition, they may be exposed to higher levels because of their short stature and the higher levels of ammonia vapor found nearer to the ground.

EXPOSURE/CONTAMINATION

- Persons exposed only to ammonia **gas** do not pose significant risks of secondary contamination to personnel outside the Hot Zone. Persons whose clothing or skin is contaminated with **liquid** ammonium hydroxide can secondarily contaminate response personnel by direct contact or through off-gassing ammonia vapor.
- Hospital personnel in an enclosed area can be secondarily contaminated by vapor off-gassing from heavily soaked clothing or from the vomitus of victims who have ingested ammonia.

ROUTES OF EXPOSURE:

INHALATION

Inhalation of ammonia may cause nasopharyngeal and tracheal burns, bronchiolar and alveolar edema, and airway destruction resulting in respiratory distress or failure.

Children exposed to the same levels of ammonia vapor as adults may receive larger dose because they have greater lung surface area: body weight ratios and increased minute volumes: weight ratios. They may be exposed to higher levels because of their short stature and the higher levels of ammonia vapor found nearer to the ground.

SKIN/EYE CONTACT

The extent of injury produced by exposure to ammonia depends on the duration of the exposure and the concentration of the gas or liquid. Even low airborne concentrations (100 ppm) of ammonia may produce rapid eye and nose irritation. Higher concentrations may cause severe eye injury. Contact with concentrated ammonia solutions, such as some industrial cleaners (25%), may cause serious corrosive injury, including skin burns, permanent eye damage, or blindness. Contact with liquefied ammonia can cause frostbite injury.

Children are more vulnerable to toxicants that affect the skin because of their relatively larger surface area:body weight ratio.

The full extent of damage to the eyes may not be clear until up to 1 week after the injury is sustained.

INGESTION

Ingestion of ammonium hydroxide, while uncommon, results in corrosive damage to the mouth, throat, and stomach. Ingestion of ammonia does not normally result in systemic poisoning.

1. ABC REMINDERS

- Evaluate and support airway, breathing, and circulation.
- Administer supplemental oxygen by mask to patients who have respiratory symptoms.
- Watch for signs of laryngeal edema and airway compromise.
- Children may be more vulnerable to corrosive agents than adults because of the smaller diameter of their airways.
- In cases of respiratory compromise, secure airway and respiration via endotracheal intubation. If not possible, surgically secure an airway.
- Treat patients who have bronchospasm with aerosolized bronchodilators. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Also consider the health of the myocardium before choosing which type of bronchodilator should be administered.
- Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). Ammonia poisoning is not known to pose additional risk during the use of bronchial or cardiac sensitizing agents.
- Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25-0.75 mL of 2.25% racemic epinephrine solution in water, repeat every 20 minutes as needed cautioning for myocardial variability.
- Patients who are comatose, hypotensive or have seizures should be treated in the conventional manner. Manage hypotension and shock with intravenous fluids (use caution when pulmonary edema is present); pressor agents may be required.

TREATMENT: GENERAL

- Monitor fluid and electrolyte balance and restore if abnormal. Fluids should be administered cautiously to patients with pulmonary edema.

TREATMENT: SKIN EXPOSURE

- If ammonia gas or solution was in contact with the skin, chemical burns may result; treat as thermal burns.

TREATMENT: EYE EXPOSURE

- Continue irrigation for at least 15 minutes or until the pH of the conjunctival fluid has returned to normal. Test visual acuity. Examine the eyes for corneal damage and treat appropriately. Immediately consult an ophthalmologist for patients who have severe corneal injuries.

TREATMENT: INGESTION EXPOSURE

- **Do not induce emesis** because this may re-expose the esophagus and mouth to the caustic substance.
- Do not administer activated charcoal. Do not perform gastric lavage or attempt neutralization after ingestion. If not given during decontamination, give 4 to 8 ounces of water by mouth to dilute stomach contents.
- Consider endoscopy to evaluate the extent of gastrointestinal-tract injury. Extreme throat swelling may require endotracheal intubation or cricothyroidotomy.

ANTIDOTES

- There is no specific antidote for ammonia poisoning.
- Although administration of corticosteroids to limit esophageal scarring is recommended by some toxicologists, this treatment is unproven and may be harmful in patients who have perforation or serious infection.
- Hemodialysis is not effective.

LABORATORY TESTS

- Routine laboratory studies for all exposed patients include CBC, glucose, and electrolyte determinations.
- Chest radiography and pulse oximetry (or arterial blood gases measurements) are recommended for severe inhalation exposure or if pulmonary aspiration is suspected.
- No specific biologic test for ammonia exposure exists.

DISPOSITION AND FOLLOW-UP

- Consider hospitalizing patients who:
  - Have evidence of respiratory distress or
  - Significant skin burns or who
  - Have ingested an ammonia solution.
- Obtain the name of the patient's primary care physician so that the hospital can send a copy of the ED visit to the patient's doctor.
- Patients with mild to moderate skin burns should be reexamined within 24 hours.
- Patients who have eye injuries should be reexamined by an ophthalmologist in 24 hours.

DELAYED EFFECTS

- Pulmonary injury may continue to evolve over 18 to 24 hours. Residual bronchoconstriction, bronchiectasis and small airway disease may occur, and chronic obstructive pulmonary disease can develop. Patients exposed by inhalation who are initially symptomatic should be observed carefully and reexamined periodically. Pulmonary function tests should be repeated on an annual basis. Patients who develop pulmonary edema should be admitted to an intensive care unit.
- Acute ocular exposure to ammonia may result in persistent intraocular pressure, cataract formation, and glaucoma with significant reduction in visual acuity.

PATIENT RELEASE

Patients who are asymptomatic following exposure or who experienced mild symptoms that have been treated may be released and advised to seek medical care promptly if symptoms recur or develop. Cigarette smoking may exacerbate pulmonary injury and should be discouraged for 72 hours after exposure.

Ammonia
Patient Information Sheet

This handout provides information and follow-up instructions for persons who have been exposed to ammonia gas or ammonium hydroxide solution.

What is ammonia?
Ammonia is a colorless, highly irritating gas with a sharp, suffocating odor. It easily dissolves in water to form a caustic solution called ammonium hydroxide. It is not highly flammable, but containers of ammonia may explode when exposed to high heat. About 80% of the ammonia produced is used in fertilizers. It is also used as a refrigerant and in the manufacture of plastics, explosives, pesticides, and other chemicals. It is found in many household and industrial-strength cleaning solutions.

What immediate health effects can result from ammonia exposure?
Most people are exposed to ammonia from breathing the gas. They will notice the pungent odor and experience burning of the eyes, nose, and throat after breathing even small amounts. With higher doses, coughing or choking may occur. Exposure to high levels of ammonia can cause death from a swollen throat or from chemical burns to the lungs. Skin contact with ammonia-containing liquids may cause burns. Eye exposure to concentrated gas or liquid can cause serious corneal burns or blindness. Drinking a concentrated ammonia solution can cause burns to the mouth, throat, and stomach. Generally, the severity of symptoms depends on the degree of exposure.

Can ammonia poisoning be treated?
There is no antidote for ammonia poisoning, but ammonia's effects can be treated, and most people recover. Persons who have experienced serious signs and symptoms (such as severe or persistent coughing or burns in the throat) may need to be hospitalized.

Are any future health effects likely to occur?
A single small exposure from which a person recovers quickly is not likely to cause delayed or long-term effects. After a severe exposure, injury to the eyes, lungs, skin, or digestive system may continue to develop for 18 to 24 hours, and serious delayed effects, such as gastric perforation, chronic pulmonary obstructive disease, or glaucoma, are possible.

What tests can be done if a person has been exposed to ammonia?
Specific tests for the presence of ammonia in blood or urine generally are not useful to the doctor. If a severe exposure has occurred, blood and urine analyses, chest x-rays, and other tests may show whether the lungs have been injured. Testing is not needed in every case. If ammonia contacts the eyes, the doctor may put a special dye in the eyes and examine them with a magnifying lamp.

Where can more information about ammonia be found?
More information about ammonia can be obtained from your regional poison control center; your state, county, or local health department; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in occupational or environmental health. If the exposure happened at work, you may wish to discuss it with your employer, the Occupational Safety and Health Administration (OSHA), or the National Institute for Occupational Safety and Health (NIOSH). Ask the person who gave you this form for help in locating these telephone numbers.

Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

[ ] Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 24 hours, especially:
- coughing
- difficulty breathing or shortness of breath
- wheezing or high-pitched voice
- chest pain or tightness
- increased pain or a discharge from exposed eyes
- increased redness or pain or a pus-like discharge in the area of a skin burn
- stomach pain or vomiting

[ ] No follow-up appointment is necessary unless you develop any of the symptoms listed above.
[ ] Call for an appointment with Dr. _____ in the practice of _____. When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.
[ ] Return to the Emergency Department/ _____ Clinic on (date) _____ at _____ AM/PM for a follow-up examination.
[ ] Do not perform vigorous physical activities for 1 to 2 days.
[ ] You may resume everyday activities including driving and operating machinery.
[ ] Do not return to work for _____ days.
[ ] You may return to work on a limited basis. See instructions below.
[ ] Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.
[ ] Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.
[ ] Avoid taking the following medications: _____
[ ] You may continue taking the following medication(s) that your doctor(s) prescribed for you: _____
_____
_____
[ ] Other instructions: _____
_____
_____

- Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.
- You or your physician can get more information on the chemical by contacting: _____ _____ or _____, or by checking out the following Internet Web sites: _____; _____.

Signature of patient _____ Date _____

Signature of physician _____ Date _____

CHEMICAL EMERGENCIES: PULMONARY INTOXICANTS

CHLORINE (NH_3)

ROUTE OF EXPOSURE

- Inhalation
- Skin or eye contact
- Ingestion

CLINICAL HEALTH EFFECTS:

Respiratory:

- Eye and nasal irritation, sore throat, coughing
- Respiratory distress, airway obstruction, pulmonary edema
- Immediate onset of rapid breathing, blue discoloration of the skin, wheezing, rales, hemoptysis.
- Pulmonary injury may progress over several hours. Lung collapse may occur.
- Reactive airways dysfunction syndrome (RADS), a chemical irritant-induces type of asthma.

Cardiovascular:

- Tachycardia & initial hypertension followed by hypotension.
- With massive chlorine inhalation, excess of chloride ions in the blood causing acid-base imbalance.

Metabolic

- Acidosis, Acid-Base imbalance
- Children more vulnerable to toxicants interfering with base metabolism

Dermal

- Skin irritation, burning pain, inflammation and blisters.
- Liquefied chlorine can result in frostbite injury

Ocular

- Burning discomfort, spasmodic blinking, involuntary closing of eyelids, redness, conjunctivitis and tearing. Corneal burns at high concentrations

LABORATORY DIAGNOSIS:

- Routine laboratory studies for all exposed patients include CBC, glucose, and electrolyte determinations.
- Patients who have respiratory complaints may require pulse oximetry (or ABG measurements) and chest radiography.
- Massive inhalation may be complicated by hyperchloremic metabolic acidosis; in addition to electrolytes, monitor blood pH.

EXPOSURE:

- Hospital personnel are at minimal risk of secondary contamination from patients exposed only to chlorine **gas**.
- Clothing or skin soaked with industrial-strength bleach or similar solutions may be corrosive to

personnel
and may release harmful chlorine gas.

TREATMENT:

- Evaluate and support airway, breathing, and circulation. Administer supplemental oxygen by mask.
- In cases of respiratory compromise secure airway and respiration via endotracheal intubation. If not possible, surgically secure an airway.
- Treat patients who have bronchospasm with aerosolized bronchodilators.
- Cardiac sensitizing agents may be appropriate. Chlorine poisoning is not known to pose additional risk during the use of bronchial or cardiac sensitizing agents.
- Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25-0.75 mL of 2.25% racemic epinephrine solution in 2.5 cc water, repeat every 20 minutes as needed cautioning for myocardial variability.
- Patients who are comatose, hypotensive, or having seizures or cardiac arrhythmias treated in the conventional manner.

DISPOSITION/FOLLOWUP

Consider hospitalizing patients who have a suspected significant exposure or have eye burns or serious skin burns.

Medical Management Guidelines for Chemical Agents

Respiratory Agents (Choking/Lung/Pulmonary; agents which cause severe irritation or swelling of the respiratory tract)

MEDICAL MANAGEMENT GUIDELINES FOR
CHLORINE (CL_2)

For Further Information Go To http://www.atsdr.cdc.gov/MMG/MMG.asp?id=198&tid=36
To report chemical spills: Chemtrec – http://www.chemtrec.com/responder/resources/Pages/erfaqs.aspx

BACKGROUND INFORMATION

- Synonyms include molecular chlorine.
- At room temperature, chlorine is a yellow-green gas with a pungent irritating odor. Under increased pressure or at temperatures below -30ºF, it is a clear, amber-colored liquid. It is generally shipped in steel cylinders as a compressed liquid.
- Chlorine is only slightly soluble in water, but on contact with moisture it forms hypochlorous acid (HClO) and hydrochloric acid (HCl); the unstable HClO readily decomposes, forming oxygen free radicals. Because of these reactions, water substantially enhances chlorine's oxidizing and corrosive effects.
- Alternatively, chlorine may be converted to hypochlorous acid which can penetrate cells and react with cytoplasmic proteins to form N-chloro derivatives that destroy cell structure.
- Symptoms may be apparent immediately or delayed for a few hours.

EXPOSURE/CONTAMINATION

- Hospital personnel are at minimal risk of secondary contamination from patients who have been exposed only to chlorine **gas**.
- However, clothing or skin soaked with industrial-strength bleach or similar solutions may be corrosive to personnel and may release harmful chlorine gas.

ROUTES OF EXPOSURE:

INHALATION

Most exposures to chlorine occur by inhalation. Chlorine's odor or irritant properties are discernible by most individuals at 0.32 ppm which is less than the OSHA permissible exposure limit (PEL) of 1 ppm. Chlorine is heavier than air and may cause asphyxiation in poorly ventilated, enclosed, or low-lying areas.

Children are at increased risk for exposure to inhaled toxicants because they have a greater lung surface area: body weight ratio and an increased minute volume: weight ratio. Children may be more vulnerable to corrosive agents than adults because of the smaller diameter of their airways. Children also may be at increased risk because of their short stature, when higher concentrations of the chemical are found at low-lying areas.

SKIN/EYE CONTACT

- Direct contact with liquid chlorine or concentrated vapor causes severe chemical burns, leading to cell death and ulceration.

INGESTION

- Ingestion is unlikely to occur because chlorine is a gas at room temperature.
- Solutions that are able to generate chlorine (e.g., sodium hypochlorite solutions) may cause

corrosive injury if ingested.

HEALTH EFFECTS

ACUTE EXPOSURE- RESPIRATORY

- Chlorine is water soluble and therefore, primarily removed by the upper airways. Exposure to low concentrations of chlorine (1 to 10 ppm) may cause eye and nasal irritation, sore throat, and coughing.
- Inhalation of higher concentrations of chlorine gas (>15 ppm) can rapidly lead to respiratory distress with airway constriction and accumulation of fluid in the lungs (pulmonary edema).
- Patients may have immediate onset of rapid breathing, blue discoloration of the skin, wheezing, rales or hemoptysis.
- In symptomatic patients, pulmonary injury may progress over several hours. Lung collapse may occur. The lowest lethal concentration for a 30-minute exposure has been estimated as 430 ppm.
- Exposure to chlorine can lead to reactive airways dysfunction syndrome (RADS), a chemical irritant-induced type of asthma.

CARDIOVASCULAR

- Tachycardia and initial hypertension followed by hypotension may occur. After severe exposure, cardiovascular collapse may occur from lack of oxygen.

METABOLIC

- Acidosis may result from insufficient oxygenation of tissues. An unusual complication of massive chlorine inhalation is an excess of chloride ions in the blood, causing an acid-base imbalance.
- Because of their higher metabolic rates, children may be more vulnerable to toxicants interfering with basic metabolism.

DERMAL

- Chlorine irritates the skin and can cause burning pain, inflammation, and blisters. Exposure to liquefied chlorine can result in frostbite injury.

OCULAR

- Low concentrations in air can cause burning discomfort, spasmodic blinking or involuntary closing of the eyelids, redness, conjunctivitis, and tearing. Corneal burns may occur at high concentrations.

ABC REMINDERS

- Evaluate and support airway, breathing, and circulation. Children may be more vulnerable to corrosive agents than adults because of the smaller diameter of their airways.
- Administer supplemental oxygen by mask to patients who have respiratory symptoms.
- In cases of respiratory compromise secure airway and respiration via endotracheal intubation. If not possible, surgically secure an airway.
- Treat patients who have bronchospasm with aerosolized bronchodilators. The use of bronchial sensitizing agents in situations of multiple chemical exposures may pose additional risks. Consider the health of the myocardium before choosing which type of bronchodilator should be administered.
- Cardiac sensitizing agents may be appropriate; however, the use of cardiac sensitizing agents after exposure to certain chemicals may pose enhanced risk of cardiac arrhythmias (especially in the elderly). Chlorine poisoning is not known to pose additional risk during the use of bronchial or cardiac sensitizing agents.
- Consider racemic epinephrine aerosol for children who develop stridor. Dose 0.25-0.75 mL of 2.25%

racemic epinephrine solution in 2.5 cc water, repeat every 20 minutes as needed cautioning for myocardial variability.
- Patients who are comatose, hypotensive, or having seizures or cardiac arrhythmias should be treated in the conventional manner.

ANTIDOTES
- There is no specific antidote for chlorine.
- Treatment is supportive.

TREATMENT:GENERAL
- Establish intravenous access in seriously ill patients if this has not been done previously.
- Continuously monitor cardiac rhythm.

TREATMENT: EYE EXPOSURE
- Chlorine-exposed eyes should be irrigated for at least 15 minutes.
- Test visual acuity and examine the eyes for corneal damage and treat appropriately.
- Immediately consult an ophthalmologist for patients who have corneal injuries.

TREATMENT: SKIN EXPOSURE
- If concentrated chlorine gas or chlorine-generating solutions contact the skin, chemical burns may occur; treat as thermal burns.
- If the liquefied compressed gas is released and contacts the skin, frostbite may result. If a victim has frostbite, treat by rewarming affected areas in a water bath at a temperature of 102 to 108ºF (40 to 42ºC) for 20 to 30 minutes and continue until a flush has returned to the affected area.
- Because of their larger surface area:body weight ratio children are more vulnerable to toxicants absorbed through the skin.

LABORATORY TESTS

The diagnosis of acute chlorine toxicity is primarily clinical, based on respiratory difficulties and irritation. However, laboratory testing is useful for monitoring the patient and evaluating complications.
- Routine laboratory studies for all exposed patients include CBC, glucose, and electrolyte determinations.
- Patients who have respiratory complaints may require pulse oximetry (or ABG measurements) and chest radiography.
- Massive inhalation may be complicated by hyperchloremic metabolic acidosis; in addition to electrolytes, monitor blood pH.

DISPOSITION AND FOLLOW-UP
- Consider hospitalizing patients who have a suspected significant exposure or have eye burns or serious skin burns.
- Obtain the name of the patient's primary care physician so that the hospital can send a copy of the ED visit to the patient's doctor.
- Follow up is recommended for all hospitalized patients because long-term respiratory problems can result. Respiratory monitoring is recommended until the patient is symptom-free. Chlorine-induced reactive airways dysfunction syndrome (RADS) has been reported to persist from 2 to 12 years.
- Patients who have skin or corneal injury should be re-examined within 24 hours.

DELAYED EFFECTS

- Symptomatic patients complaining of persistent shortness of breath, severe cough, or chest tightness should be admitted to the hospital and observed until symptom-free.
- Pulmonary injury may progress for several hours.

PATIENT RELEASE

Asymptomatic patients and those who experienced only minor sensations of burning of the nose, throat, eyes, and respiratory tract, slight cough, may be released. In most cases, these patients will be free of symptoms in an hour or less. They should be advised to seek medical care if symptoms develop or recur.

Ammonia
Patient Information Sheet

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What is ammonia?
Ammonia is a colorless, highly irritating gas with a sharp, suffocating odor. It easily dissolves in water to form a caustic solution called ammonium hydroxide. It is not highly flammable, but containers of ammonia may explode when exposed to high heat. About 80% of the ammonia produced is used in fertilizers. It is also used as a refrigerant and in the manufacture of plastics, explosives, pesticides, and other chemicals. It is found in many household and industrial-strength cleaning solutions.

What immediate health effects can result from ammonia exposure?
Most people are exposed to ammonia from breathing the gas. They will notice the pungent odor and experience burning of the eyes, nose, and throat after breathing even small amounts. With higher doses, coughing or choking may occur. Exposure to high levels of ammonia can cause death from a swollen throat or from chemical burns to the lungs. Skin contact with ammonia-containing liquids may cause burns. Eye exposure to concentrated gas or liquid can cause serious corneal burns or blindness. Drinking a concentrated ammonia solution can cause burns to the mouth, throat, and stomach. Generally, the severity of symptoms depends on the degree of exposure.

Can ammonia poisoning be treated?
There is no antidote for ammonia poisoning, but ammonia's effects can be treated, and most people recover. Persons who have experienced serious signs and symptoms (such as severe or persistent coughing or burns in the throat) may need to be hospitalized.

Are any future health effects likely to occur?
A single small exposure from which a person recovers quickly is not likely to cause delayed or long-term effects. After a severe exposure, injury to the eyes, lungs, skin, or digestive system may continue to develop for 18 to 24 hours, and serious delayed effects, such as gastric perforation, chronic pulmonary obstructive disease, or glaucoma, are possible.

What tests can be done if a person has been exposed to ammonia?
Specific tests for the presence of ammonia in blood or urine generally are not useful to the doctor. If a severe exposure has occurred, blood and urine analyses, chest x-rays, and other tests may show whether the lungs have been injured. Testing is not needed in every case. If ammonia contacts the eyes, the doctor may put a special dye in the eyes and examine them with a magnifying lamp.

Where can more information about ammonia be found?
More information about ammonia can be obtained from your regional poison control center; your state, county, or local health department; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in occupational or environmental health. If the exposure happened at work, you may wish to discuss it with your employer, the Occupational Safety and Health Administration (OSHA), or the National Institute for Occupational Safety and Health (NIOSH). Ask the person who gave you this form for help in locating these telephone numbers.

Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

[ ] Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 24 hours, especially:
- coughing
- difficulty breathing or shortness of breath
- wheezing or high-pitched voice
- chest pain or tightness
- increased pain or a discharge from exposed eyes
- increased redness or pain or a pus-like discharge in the area of a skin burn
- stomach pain or vomiting

[ ] No follow-up appointment is necessary unless you develop any of the symptoms listed above.
[ ] Call for an appointment with Dr. _____ in the practice of _____. When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.
[ ] Return to the Emergency Department/ _____ Clinic on (date) _____ at _____ AM/PM for a follow-up examination.
[ ] Do not perform vigorous physical activities for 1 to 2 days.
[ ] You may resume everyday activities including driving and operating machinery.
[ ] Do not return to work for _____ days.
[ ] You may return to work on a limited basis. See instructions below.
[ ] Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.
[ ] Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.
[ ] Avoid taking the following medications: _____
[ ] You may continue taking the following medication(s) that your doctor(s) prescribed for you: _____
_____
_____
[ ] Other instructions: _____
_____
_____

- Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.
- You or your physician can get more information on the chemical by contacting: _____ _____ or _____, or by checking out the following Internet Web sites: _____; _____.

Signature of patient _____ Date _____

Signature of physician _____ Date _____

CHEMICAL EMERGENCIES: PULMONARY INTOXICANTS

PHOSGENE OXIME ($CHCL_2NO$)

ROUTES OF EXPOSURE

- Inhalation
- Skin or eye contact
- Ingestion (uncommon)

CLINICAL:

Health Effects

- Direct contact with phosgene oxime results in immediate pain, irritation, and tissue necrosis. Inhalation and systemic absorption may result in pulmonary edema, necrotizing bronchiolitis, and pulmonary thrombosis.

Skin/Eye Contact

- Pain and local tissue destruction occur immediately on contact with skin, eyes and mucous membranes.

Ingestion

- No human data are available. Animal studies suggest phosgene oxime may induce hemorrhagic inflammatory lesions in the gastrointestinal tract.

Ocular

- Contact with the eyes may result in severe pain, conjunctivitis, and keratitis.

Dermal

- Direct skin exposure to any form of phosgene oxime causes immediate pain and blanching with an erythematous ring. After 30 minutes a wheal occurs followed by necrosis. Extreme pain may persist for days.
- Absorption through the skin can cause pulmonary edema.

Respiratory

- Phosgene oxime produces immediate irritation to the upper respiratory tract.
- Inhalation and systemic absorption may cause pulmonary edema, necrotizing bronchiolitis and pulmonary thrombosis.

LABORATORY DIAGNOSIS:

- Routine laboratory studies should be done for all patients requiring admission. These include CBC, glucose, serum electrolytes, liver enzymes, and kidney function tests.
- Chest X-ray and pulse oximetry (or ABG measurements) are recommended for inhalation exposures.

EXPOSURE:

- Persons whose clothing or skin is contaminated with liquid or solid phosgene oxime can cause secondary contamination by direct contact or through off-gassing vapor.
- Persons exposed only to phosgene oxime vapor pose no risk of secondary contamination.

TREATMENT:

- ANTIDOTE – There is no antidote for sulfur mustard toxicity.
- EYE – Mild conjunctivitis beginning more than 12 hours after exposure is unlikely to progress to a severe lesion. Mild conjunctivitis treat with a soothing eye solution such as Visine or Murine.
- Lesions more severe than conjunctivitis may be treated with a topical mydriatic (e.g., atropine), topical antibiotics, and vaseline or similar substance applied to the lid edges several times a day. Pain may be controlled with systemic analgesics.
- SKIN – If the skin was in contact with phosgene oxime, treat tissue damage in the same manner as for any corrosive lesion. If the burned area is large, the patient should be transferred to a Burn Unit with reverse isolation. Systemic antibiotics should be used when there are signs of infection and a culture indicates the responsible organism.

- INHALATION – Patients with minor upper-respiratory symptoms (nose, sinus, pharyngitis) should be admitted to a routine care ward for treatment. Pulmonary edema may develop several hours after exposure. Patients with symptoms or signs of severe respiratory injury should be admitted to the Critical Care Unit for treatment in a conventional manner for non-cardiac pulmonary edema.
- INJESTION – **Do not induce emesis**. Treat nausea and vomiting with antiemetics

DISPOSITION/FOLLOWUP

- Patients with moderate to severe exposures will require hospitalization, as described above.
- Patients who have mild skin burns should be reexamined within 24 hours.

Medical Management Guidelines for Phosgene Oxime

MEDICAL MANAGEMENT GUIDELINES FOR PHOSGENE OXIME ($CHCL_2NO$)

For more information go to: http://www.atsdr.cdc.gov/MMG/MMG.asp?id=1010&tid=213

To report chemical spills: Chemtrec – http://www.chemtrec.com/responder/resources/Pages/erfaqs.aspx

BACKGROUND INFORMATION:

- Synonyms include dichloroformoxime; CX.
- Phosgene oxime is an urticant or nettle agent. It is one of the least well studied chemical warfare agents; therefore, specific information is limited. Pure phosgene oxime is a colorless, crystalline solid; however, the munitions grade compound is a yellowish-brown liquid. The solid material can release enough vapor to cause symptoms. Post World War II studies indicate that concentrations below 8% cause no or inconsistent effects.
- Phosgene Oxime is readily absorbed by the skin causing an immediate corrosive lesion. Ocular and pulmonary exposure may cause incapacitating inflammation, systemic absorption and death.

EXPOSURE/CONTAMINATION:

Persons whose clothing or skin is contaminated with liquid or solid phosgene oxime can cause secondary contamination by direct contact or through off-gassing vapor. Persons exposed only to phosgene oxime vapor pose no risk of secondary contamination.

ROUTES OF EXPOSURE:

INHALATION

- Inhaled phosgene oxime is extremely irritating to the upper airways and causes pulmonary edema. Irritation occurs with exposures to 0.2 mg-min/m³ and becomes unbearable at 3 mg-min/m³. The estimated LCt_{50} (the product of concentration times time that is lethal to 50% of the exposed population by inhalation) is 1,500 to 2,000 mg-min/m³.

SKIN/EYE CONTACT

- Pain and local tissue destruction occur immediately on contact with skin, eyes and mucous membranes. Phosgene oxime is rapidly absorbed from the skin and eyes and may result in systemic toxicity. The LD_{50} for skin exposure is estimated as 25 mg/kg.

INGESTION

No human data are available. Animal studies suggest phosgene oxime may induce hemorrhagic inflammatory lesions in the gastrointestinal tract.

HEALTH EFFECTS: ACUTE EXPOSURE

- Direct contact with phosgene oxime results in immediate pain, irritation, and tissue necrosis. Inhalation and systemic absorption may result in pulmonary edema, necrotizing bronchiolitis, and pulmonary thrombosis.
- Phosgene oxime is known to cause more severe tissue damage than vesicants and other urticants but it has not been well studied and the mechanism of action is unknown.
- Phosgene oxime is an urticant or nettle agent capable of producing erythema, wheals, and urticaria. It is considered a corrosive agent because it causes extensive tissue damage. The skin effects are similar to those caused by strong acids; however, the mechanism of action is unknown.

MEDICAL MANAGEMENT GUIDELINES FOR PHOSGENE OXIME ($CHCL_2NO$)

HEALTH EFFECTS: OCULAR

- Contact with the eyes may result in severe pain, conjunctivitis, and keratitis.

HEALTH EFFECTS: DERMAL

- Direct skin exposure to any form of phosgene oxime causes immediate pain and blanching with an erythematous ring. After 30 minutes a wheal occurs followed by necrosis. Extreme pain may persist for days. Absorption through the skin can cause pulmonary edema.

HEALTH EFFECTS: RESPIRATORY

- Phosgene oxime produces immediate irritation to the upper respiratory tract. Inhalation and systemic absorption may cause pulmonary edema, necrotizing bronchiolitis and pulmonary thrombosis.

HEALTH EFFECTS: GASTROINTESTINAL

There are no human data; however, animal studies suggest that hemorrhagic inflammatory lesions may occur throughout the gastrointestinal tract.

ABC REMINDERS:

- Evaluate and support the airway, breathing, and circulation. Intubate the trachea in cases of respiratory compromise. If the patient's condition precludes intubation, surgically create an airway.
- Treat patients who have bronchospasm with bronchodilators.
- Patients who are comatose or hypotensive, or have seizures or ventricular dysrhythmias due to other exposures or trauma should be treated in the conventional manner.

ANTIDOTE:

There is no antidote for phosgene oxime toxicity. Treatment consists of supportive measures.

TREATMENT: INHALATION EXPOSURE

- Patients with minor upper-respiratory symptoms (nose, sinus, pharyngitis) should be admitted to a routine care ward for treatment. Pulmonary edema may develop several hours after exposure.
- Patients with symptoms or signs of severe respiratory injury should be admitted to the Critical Care Unit for treatment in a conventional manner for non-cardiac pulmonary edema.

TREATMENT: SKIN EXPOSURE

- If the skin was in contact with phosgene oxime, treat tissue damage in the same manner as for any corrosive lesion.
- If the burned area is large, the patient should be transferred to a Burn Unit with reverse isolation. Most burns are second degree although third degree burns may occur after liquid exposure.
- The denuded area should be irrigated two or three times a day using a whirlpool if the lesion is large (the patient should be given ample amounts of a systemic analgesic beforehand). This should be followed by liberal application of a topical antibiotic. Skin lesions may take many months to heal.
- Systemic antibiotics should be used when there are signs of infection and a culture indicates the responsible organism.

TREATMENT: EYE EXPOSURE

- Mild conjunctivitis beginning more than 12 hours after exposure is unlikely to progress to a severe

lesion.

- The patient should have a thorough eye examination (including a test for visual acuity), treatment with a soothing eye solution such as Visine or Murine, and be advised to return if there is worsening.
- Conjunctivitis beginning earlier and other effects such as lid swelling and signs/symptoms of inflammation indicate need for inpatient care and observation.
- Lesions more severe than conjunctivitis may be treated with a topical mydriatic (e.g., atropine), topical antibiotics, and vaseline or similar substance applied to the lid edges several times a day.
- Consult an ophthalmologist for patients with severe corneal injuries.
- Topical analgesics should be used only for an initial examination (including slit lamp and a test of visual acuity), but not after.
- Pain may be controlled with systemic analgesics. Once the lid edema and blepharospasm subside and the eyes are open, dark glasses may reduce the discomfort of photophobia.

TREATMENT: INGESTION EXPOSURE

Do not induce emesis. Treat nausea and vomiting with antiemetics.

LABORATORY TESTS

- Routine laboratory studies should be done for all patients requiring admission. These include CBC, glucose, serum electrolytes, liver enzymes, and kidney function tests.

Chest X-ray and pulse oximetry (or ABG measurements) are recommended for inhalation exposures.

DISPOSITION AND FOLLOW-UP

- Patients with moderate to severe exposures will require hospitalization, as discussed above.
- Patients who have mild skin burns should be reexamined within 24 hours.

Delayed Effects Patient Release

Patients with no symptoms may be discharged. Discharged patients should be advised to rest and to seek medical care promptly if symptoms develop.

Phosgene Oxime ($CHCl_2NO$)
Patient Information Sheet

This handout provides information and follow-up instructions for persons who have been exposed to phosgene oxime.

What is phosgene oxime?
Phosgene oxime is a colorless, crystalline solid or a yellowish-brown liquid. It is classified as a urticant or nettle chemical warfare agent; however, it has not been used on the battlefield.

What immediate health effects can be caused by exposure to phosgene oxime?
Phosgene oxime causes immediate and painful skin and eye lesions. Inhalation causes fluid to accumulate in the lungs and severe bronchitis.

Can phosgene oxime poisoning be treated?
There is no antidote for phosgene oxime. Its effects can be treated in the same way as burns from other causes (e.g., strong acids). Exposed persons may need to be hospitalized.

Are any future health effects likely to occur?
There is no information evaluating future health effects.

What tests can be done if a person has been exposed to phosgene oxime?
There are no specific tests to confirm exposure.

Where can more information about phosgene oxime be found?
Phosgene oxime is one of the least well studied chemical warfare agents; therefore, specific information is limited. More information about phosgene oxime may be obtained from your regional poison control center; the Agency for Toxic Substances and Disease Registry (ATSDR); your doctor; or a clinic in your area that specializes in toxicology or occupational and environmental health. Ask the person who gave you this form for help locating these telephone numbers.

Follow-up Instructions

Keep this page and take it with you to your next appointment. Follow *only* the instructions checked below.

[ ] Call your doctor or the Emergency Department if you develop any unusual signs or symptoms within the next 24 hours, especially:

- coughing, wheezing, or shortness of breath
- increased pain or discharge from injured eyes
- increased redness, pain, or a pus-like discharge from injured skin

[ ] No follow-up appointment is necessary unless you develop any of the symptoms listed above.
[ ] Call for an appointment with Dr. _____ in the practice of _____. When you call for your appointment, please say that you were treated in the Emergency Department at _____ Hospital by _____ and were advised to be seen again in _____ days.
[ ] Return to the Emergency Department/ _____ Clinic on (date) _____ at _____ AM/PM for a follow-up examination.
[ ] Do not perform vigorous physical activities for 1 to 2 days.
[ ] You may resume everyday activities including driving and operating machinery.
[ ] Do not return to work for _____ days.
[ ] You may return to work on a limited basis. See instructions below.
[ ] Avoid exposure to cigarette smoke for 72 hours; smoke may worsen the condition of your lungs.
[ ] Avoid drinking alcoholic beverages for at least 24 hours; alcohol may worsen injury to your stomach or have other effects.
[ ] Avoid taking the following medications: _____
[ ] You may continue taking the following medication(s) that your doctor(s) prescribed for you: _____
_____
_____
[ ] Other instructions: _____
_____
_____

- Provide the Emergency Department with the name and the number of your primary care physician so that the ED can send him or her a record of your emergency department visit.

- You or your physician can get more information on the chemical by contacting: _____ _____ or _____, or by checking out the following Internet Web sites: _____; _____.

Signature of patient _____ Date _____

Signature of physician _____ Date _____

RADIOLOGICAL EMERGENCIES

RADIATION – ACUTE RADIATION SYNDROME

ROUTE OF EXPOSURE:

- Acute Radiation Syndrome (ARS) (sometimes known as radiation toxicity or radiation sickness) is an acute illness caused by irradiation of the entire body (or most of the body) by a high dose of penetrating radiation
  in a very short period of time (usually a matter of minutes).

CLINICAL:

- **Bone marrow syndrome** (sometimes referred to as hematopoietic syndrome) the full syndrome will usually occur with a dose between 0.7 and 10 Gy (70 – 1000 rads) though mild symptoms may occur as low as 0.3 Gy or 30 rads.
- **Gastrointestinal (GI) syndrome:** the full syndrome will usually occur with a dose greater than approximately 10 Gy (1000 rads) although some symptoms may occur as low as 6 Gy or 600 rads.
- **Cardiovascular (CV)/ Central Nervous System (CNS) syndrome:** the full syndrome will usually occur with a dose greater than approximately 50 Gy (5000 rads) although some symptoms may occur as low as 20 Gy or 2000 rads

STAGES OF ACUTE RADIATION SYNDROME

1. Prodromal stage (N-V-D stage): The classic symptoms for this stage are nausea, vomiting, as well as anorexia and possibly diarrhea (depending on dose), which occur from minutes to days following exposure.
   The symptoms may last (episodically) for minutes up to several days.
2. Latent stage: In this stage, the patient looks and feels generally healthy for a few hours or even up to a few weeks.
3. Manifest illness stage: In this stage symptoms depend on the specific syndrome and last from hours up to several months.
4. Recovery or death: Most patients who do not recover will die within several months of exposure.
   The recovery process lasts from several weeks up to two years.

DIAGNOSIS:

- The diagnosis of ARS can be difficult to make because ARS causes no unique disease. Also, depending on the dose, the prodromal stage may not occur for hours or days after exposure, or the patient may already be in the latent stage by the time they receive treatment.
- If a patient is known to have been or suspected of having been exposed to a large radiation dose, draw blood for CBC analysis with special attention to the lymphocyte count, every 2 to 3 hours during the first 8 hours after exposure (and every 4 to 6 hours for the next 2 days)
- If no radiation exposure is initially suspected, consider ARS in the differential diagnosis if a history exists

of nausea and vomiting that is unexplained by other causes. Other indications are bleeding, epilation, or white blood count (WBC) and platelet counts abnormally low a few days or weeks after unexplained nausea and vomiting.

TREATMENT:

- Secure ABCs (airway, breathing, circulation) and physiologic monitoring (blood pressure, blood gases, electrolyte and urine output) as appropriate.
- Treat major trauma, burns and respiratory injury if evident.
- In addition to the blood samples required to address the trauma, obtain blood samples for CBC (complete blood count), with attention to lymphocyte count, and HLA (human leukocyte antigen) typing prior to any initial transfusion and at periodic intervals following transfusion.
- Treat contamination as needed.
- If exposure occurred within 8 to 12 hours, repeat CBC, with attention to lymphocyte count, 2 or 3 more times (approximately every 2 to 3 hours) to assess lymphocyte depletion.

Medical Management Guidelines for
Acute Radiation Syndrome (ARS) and Cutaneous Radiation Syndrome (CRS)

For further information go to: http://www.bt.cdc.gov/radiation/arsphysicianfactsheet.asp

Technical assistance can be obtained from the Radiation Assistance Center/Training Site (REAC/TS) at (865) 576-3131 (M-F, 8 am to 4:30 pm EST) or (865) 576-1005 (after hours), or at http://www.orau.gov/reacts/ and from the Medical Radiobiology Advisory Team (MRAT) at (301) 295-0316.

Additional information can be obtained from the CDC Health Alert Network at http://www.emergency.cdc.gov or 1-800-31-3435.

Background Information

Acute Radiation Syndrome (ARS) (sometimes known as radiation toxicity or radiation sickness) is an acute illness caused by irradiation of the entire body (or most of the body) by a high dose of penetrating radiation in a very short period of time (usually a matter of minutes). The major cause of this syndrome is depletion of immature parenchymal stem cells in specific tissues. Examples of people who suffered from ARS are the survivors of the Hiroshima and Nagasaki atomic bombs, the firefighters that first responded after the Chernobyl Nuclear Power Plant event in 1986, and some unintentional exposures to sterilization irradiators.

The required conditions for ACUTE RADIATION SYNDROME (ARS) are:

- The radiation dose must be large (i.e., greater than 0.7 Gray (Gy)[1, 2] or 70 rads).
    - Mild symptoms may be observed with doses as low as 0.3 Gy or 30 rads.
- The dose usually must be external (i.e., the source of radiation is outside of the patient's body).
    - Radioactive materials deposited inside the body have produced some ARS effects only in extremely rare cases.
- The radiation must be penetrating (i.e., able to reach the internal organs).
    - High energy X-rays, gamma rays, and neutrons are penetrating radiations.
- The entire body (or a significant portion of it) must have received the dose[3].
    - Most radiation injuries are local, frequently involving the hands, and these local injuries seldom cause classical signs of ARS.
- The dose must have been delivered in a short time (usually a matter of minutes).
    - Fractionated doses are often used in radiation therapy. These are large total doses delivered in small daily amounts over a period of time. Fractionated doses are less effective at inducing ARS than a single dose of the same magnitude.

NOTES:

1. The Gray (Gy) is a unit of absorbed dose and reflects an amount of energy deposited into a mass of tissue (1 Gy = 100 rads). In this document, the referenced absorbed dose is that dose inside the patient's body (i.e., the dose that is normally measured with personal dosimeters).

2. The referenced absorbed dose levels in this document are assumed to be from beta, gamma, or x radiation. Neutron or proton radiation produces many of the health effects described herein at lower absorbed dose levels.

3. The dose may not be uniform, but a large portion of the body must have received more than 0.7 Gy (70 rads).

HEALTH EFFECTS

Acute Exposure:

The three classic ARS Syndromes are:

1. **Bone marrow syndrome** (sometimes referred to as hematopoietic syndrome) the full syndrome will usually occur with a dose between 0.7 and 10 Gy (70 – 1000 rads) though mild symptoms may occur as low as 0.3 Gy or 30 rads[4].
    - The survival rate of patients with this syndrome decreases with increasing dose. The primary cause of death is the destruction of the bone marrow, resulting in infection and hemorrhage.
2. **Gastrointestinal (GI) syndrome:** the full syndrome will usually occur with a dose greater than approximately 10 Gy (1000 rads) although some symptoms may occur as low as 6 Gy or 600 rads.
    - Survival is extremely unlikely with this syndrome. Destructive and irreparable changes in the GI tract and bone marrow usually cause infection, dehydration, and electrolyte imbalance. Death usually occurs within 2 weeks.
3. **Cardiovascular (CV)/ Central Nervous System (CNS) syndrome:** the full syndrome will usually occur with a dose greater than approximately 50 Gy (5000 rads) although some symptoms may occur as low as 20 Gy or 2000 rads.
    - Death occurs within 3 days. Death likely is due to collapse of the circulatory system as well as increased pressure in the confining cranial vault as the result of increased fluid content caused by edema, vasculitis, and meningitis.

NOTES

Although the dose ranges provided in this document apply to most healthy adult members of the public, a great deal of variability of radiosensitivity among individuals exists, depending upon the age and condition of health of the individual at the time of exposure. Children and infants are especially sensitive.

The four stages of ARS are:

5. Prodromal stage (N-V-D stage): The classic symptoms for this stage are nausea, vomiting, as well as anorexia and possibly diarrhea (depending on dose), which occur from minutes to days following exposure. The symptoms may last (episodically) for minutes up to several days.
6. Latent stage: In this stage, the patient looks and feels generally healthy for a few hours or even up to a few weeks.
7. Manifest illness stage: In this stage the symptoms depend on the specific syndrome (see Table 1) and last from hours up to several months.
8. Recovery or death: Most patients who do not recover will die within several months of exposure. The recovery process lasts from several weeks up to two years.

These stages are described in further detail in Table 1.

Table 1: Acute Radiation Syndromes

Syndrome	Dose[*]	Prodromal Stage	Latent Stage	Manifest Illness Stage	Recovery
Hematopoietic (Bone Marrow)	> 0.7 Gy (> 70 rads) ***(mild symptoms may occur as low as 0.3 Gy or 30 rads)***	• Symptoms are anorexia, nausea and vomiting. • Onset occurs 1 hour to 2 days after exposure. • Stage lasts for minutes to days.	• Stem cells in bone marrow are dying, although patient may appear and feel well. • Stage lasts 1 to 6 weeks.	• Symptoms are anorexia, fever, and malaise. • Drop in all blood cell counts occurs for several weeks. • Primary cause of death is infection and hemorrhage. • Survival decreases with increasing dose. • Most deaths occur within a few months after exposure.	• in most cases, bone marrow cells will begin to repopulate the marrow. • There should be full recovery for a large percentage of individuals from a few weeks up to two years after exposure. • death may occur in some individuals at 1.2 Gy (120 rads). • the LD50/60[‡] is about 2.5 to 5 Gy (250 to 500 rads)
Gastrointestinal (GI)	> 10 Gy (> 1000 rads) ***(some symptoms may occur as low as 6 Gy or 600 rads)***	• Symptoms are anorexia, severe nausea, vomiting, cramps, and diarrhea. • Onset occurs within a few hours after exposure. • Stage lasts about 2 days.	• Stem cells in bone marrow and cells lining GI tract are dying, although patient may appear and feel well. • Stage lasts less than 1 week.	• Symptoms are malaise, anorexia, severe diarrhea, fever, dehydration, and electrolyte imbalance. • Death is due to infection, dehydration, and electrolyte imbalance. • Death occurs within 2 weeks of exposure.	• the LD100[‡] is about 10 Gy (1000 rads)
Cardiovascular (CV)/ Central Nervous System (CNS)	> 50 Gy (5000 rads) ***(some symptoms may occur as low as 20 Gy or 2000 rads)***	• Symptoms are extreme nervousness and confusion; severe nausea, vomiting, and watery diarrhea; loss of consciousness; and burning sensations of the skin. • Onset occurs within	• Patient may return to partial functionality. • Stage may last for hours but often is less.	• Symptoms are return of watery diarrhea, convulsions, and coma. • Onset occurs 5 to 6 hours after exposure. • Death occurs within 3 days of exposure.	• No recovery is expected.

		minutes of exposure. • Stage lasts for minutes to hours.			

* The absorbed doses quoted here are “gamma equivalent” values. Neutrons or protons generally produce the same effects as gamma, beta, or X-rays but at lower doses. If the patient has been exposed to neutrons or protons, consult radiation experts on how to interpret the dose.
† The LD50/60 is the dose necessary to kill 50% of the exposed population in 60 days.
‡ The LD100 is the dose necessary to kill 100% of the exposed population

Cutaneous Radiation Syndrome (CRS)

The concept of cutaneous radiation syndrome (CRS) was introduced in recent years to describe the complex pathological syndrome that results from acute radiation exposure to the skin.

ARS usually will be accompanied by some skin damage. It is also possible to receive a damaging dose to the skin without symptoms of ARS, especially with acute exposures to beta radiation or X-rays. Sometimes this occurs when radioactive materials contaminate a patient's skin or clothes.

When the basal cell layer of the skin is damaged by radiation, inflammation, erythema, and dry or moist desquamation can occur. Also, hair follicles may be damaged, causing epilation. Within a few hours after irradiation, a transient and inconsistent erythema (associated with itching) can occur. Then, a latent phase may occur and last from a few days up to several weeks, when intense reddening, blistering, and ulceration of the irradiated site are visible.

In most cases, healing occurs by regenerative means; however, very large skin doses can cause permanent hair loss, damaged sebaceous and sweat glands, atrophy, fibrosis, decreased or increased skin pigmentation, and ulceration or necrosis of the exposed tissue.

PATIENT MANAGEMENT

Triage: If radiation exposure is suspected:

- Secure ABCs (airway, breathing, circulation) and physiologic monitoring (blood pressure, blood gases, electrolyte and urine output) as appropriate.
- Treat major trauma, burns and respiratory injury if evident.
- In addition to the blood samples required to address the trauma, obtain blood samples for CBC (complete blood count), with attention to lymphocyte count, and HLA (human leukocyte antigen) typing prior to any initial transfusion and at periodic intervals following transfusion.
- Treat contamination as needed.
- If exposure occurred within 8 to 12 hours, repeat CBC, with attention to lymphocyte count, 2 or 3 more times (approximately every 2 to 3 hours) to assess lymphocyte depletion.

DIAGNOSIS

The diagnosis of ARS can be difficult to make because ARS causes no unique disease. Also, depending on the dose, the prodromal stage may not occur for hours or days after exposure, or the patient may already be in the latent stage by the time they receive treatment, in which case the patient may appear and feel well when first assessed.

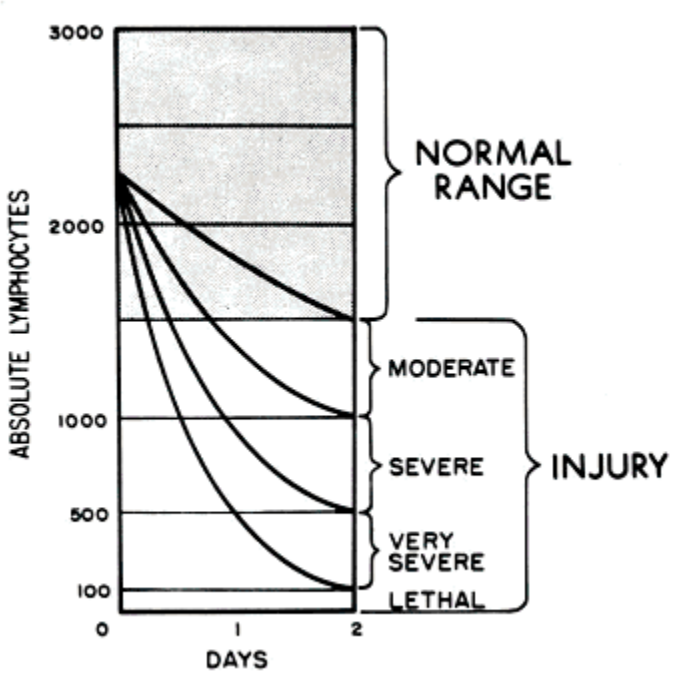
If a patient received more than 0.05 Gy (5 rads) and three or four CBCs are taken within 8 to 12 hours of the exposure, a quick estimate of the dose can be made (see Ricks, et. al. for details). If these initial blood counts are not taken, the dose can still be estimated by using CBC results over the first few days. It would be best to have radiation dosimetrists conduct the dose assessment, if possible.

If a patient is known to have been or suspected of having been exposed to a large radiation dose, draw blood for CBC analysis with special attention to the lymphocyte count, every 2 to 3 hours during the first 8 hours after exposure (and every 4 to 6 hours for the next 2 days). Observe the patient during this time for symptoms and consult with radiation experts before ruling out ARS.

If no radiation exposure is initially suspected, you may consider ARS in the differential diagnosis if a history exists of nausea and vomiting that is unexplained by other causes. Other indications are bleeding, epilation, or white blood count (WBC) and platelet counts abnormally low a few days or weeks after unexplained nausea and vomiting. Again, consider CBC and chromosome analysis and consultation with radiation experts to confirm diagnosis.

INITIAL TREATMENT AND DIAGNOSTIC EVALUATION

Treat vomiting[5], and repeat CBC analysis, with special attention to the lymphocyte count, every 2 to 3 hours for the first 8 to 12 hours following exposure (and every 4 to 6 hours for the following 2 or 3 days). Sequential changes in absolute lymphocyte counts over time are demonstrated below in the Andrews Lymphocyte Nomogram (see Figure 1). Precisely record all clinical symptoms, particularly nausea, vomiting, diarrhea, and itching, reddening or blistering of the skin. Be sure to include time of onset. Collect vomitus in the first few days for later analysis.



From: Andrews GA, Auxier JA, Lushbaugh CC. *The Importance of Dosimetry to the Medical Management of Persons Exposed to High Levels of Radiation.* In *Personal Dosimetry for Radiation Accidents*. Vienna : International Atomic Energy Agency; 1965.

TREATMENT

After consultation, begin the following (as indicated):

- Supportive care in a clean environment (if available, the use of a burn unit may be quite effective)
- Prevention and treatment of infections
- Stimulation of hematopoiesis by use of growth factors
- Stem cell transfusions or platelet transfusions (if platelet count is too low)
- Psychological support
- Careful observation for erythema (document locations), hair loss, skin injury, mucositis, parotitis, weight loss, or fever
- Confirmation of initial dose estimate using chromosome aberration cytogenetic bioassay when possible. Although resource intensive, this is the best method of dose assessment following acute exposures.
- Consultation with experts in radiation accident management

RADIOLOGICAL EMERGENCIES

RADIATION – CUTANEOUS RADIATION INJURY

ROUTE OF EXPOSURE:

- Injury to the skin and underlying tissues from acute exposure to a large external dose of radiation is referred to as cutaneous radiation injury (CRI). Acute radiation syndrome (ARS) will usually be accompanied by some skin damage; however, CRI can occur without symptoms of ARS.

CLINICAL:

- Early signs and symptoms of CRI are itching, tingling, or a transient erythema or edema without a history of exposure to heat or caustic chemicals.
- Exposure to radiation can damage the basal cell layer of the skin and result in inflammation, erythema, and dry or moist desquamation. In addition, radiation damage to hair follicles can cause epilation.
- The visible skin effects depend on the magnitude of the dose as well as the depth of penetration of the radiation.
- Unlike the skin lesions caused by chemical or thermal damage, the lesions caused by radiation exposures do not appear for hours to days following exposure, and burns and other skin effects tend to appear in cycles.
- The key treatment issues with CRI are infection and pain management.

STAGES OF CUTANEOUS RADIATION INJURY

- **Prodromal stage** (within hours of exposure)—This stage is characterized by early erythema (first wave of erythema), heat sensations, and itching that define the exposure area. The duration of this stage is from 1 to 2 days.
- **Latent stage** (1–2 days postexposure)—No injury is evident. Depending on the body part, the larger the dose, the shorter this period will last. The skin of the face, chest, and neck will have a shorter latent stage than will the skin of the palms of the hands or the soles of the feet.
- **Manifest illness stage** (days to weeks postexposure)—The basal layer is repopulated through proliferation of surviving clonogenic cells. This stage begins with main erythema (second wave), a sense of heat, and slight edema, which are often accompanied by increased pigmentation.
- **Third wave of erythema** (10–16 weeks postexposure, especially after beta exposure)—The exposed person experiences late erythema, injury to blood vessels, edema, and increasing pain. A distinct bluish color of the skin can be observed. Epilation may subside, but new ulcers, dermal necrosis, and dermal atrophy (and thinning of the dermis layer) are possible.
- **Late effects** (months to years postexposure; threshold dose ~10 Gy or 1000 rads)—Symptoms can vary from slight dermal atrophy (or thinning of dermis layer) to constant ulcer recurrence, dermal necrosis, and deformity.

DIAGNOSIS:

The signs and symptoms of CRI are as follows:

- Intensely painful burn-like skin injuries (including itching, tingling, erythema, or edema) without a history of exposure to heat or caustic chemicals
  Note : Erythema will not be seen for hours to days following exposure, and its appearance is cyclic.
- Epilation
- A tendency to bleed
- Possible signs and symptoms of ARS

EXPOSURE/CONTAMINATION

- On occasion a patient might also be contaminated with radioactive material. To address patient decontamination, please go to the following Web site: http://www.orau.gov/reacts/emergency.htm.

TREATMENT

- Localized injuries should be treated symptomatically as they occur, and radiation injury experts should be consulted for detailed information.
- Supportive care in a clean environment (a burn unit if one is available)
- Prevention and treatment of infections
- Use of the following:
  - Medications to reduce inflammation, inhibit protealysis, relieve pain, stimulate regeneration, and improve circulation
  - Anticoagulant agents for widespread and deep injury
- Pain management
- Psychological support

Medical Management Guidelines for
Cutaneous Radiation Injury (CRI)

For further information go to: http://www.bt.cdc.gov/radiation/criphysicianfactsheet.asp

Technical assistance can be obtained from the Radiation Assistance Center/Training Site (REAC/TS) at (865) 576-3131 (M-F, 8 am to 4:30 pm EST) or (865) 576-1005 (after hours), or at http://www.orau.gov/reacts/ and from the Medical Radiobiology Advisory Team (MRAT) at (301) 295-0316.

Additional information can be obtained from the CDC Health Alert Network at http://www.emergency.cdc.gov or 1-800-31-3435.

Background Information

Injury to the skin and underlying tissues from acute exposure to a large external dose of radiation is referred to as cutaneous radiation injury (CRI). Acute radiation syndrome (ARS) will usually be accompanied by some skin damage; however, CRI can occur without symptoms of ARS. This is especially true with acute exposures to beta radiation or low-energy x-rays, because beta radiation and low-energy x-rays are less penetrating and less likely to damage internal organs than gamma radiation is. CRI can occur with radiation doses as low as 2 Gray (Gy) or 200 rads [1] and the severity of CRI symptoms will increase with increasing doses. Most cases of CRI have occurred when people inadvertently came in contact with unsecured radiation sources from food irradiators, radiotherapy equipment, or well depth gauges. In addition, cases of CRI have occurred in people who were overexposed to x-radiation from fluoroscopy units.

Early signs and symptoms of CRI are itching, tingling, or a transient erythema or edema without a history of exposure to heat or caustic chemicals. Exposure to radiation can damage the basal cell layer of the skin and result in inflammation, erythema, and dry or moist desquamation. In addition, radiation damage to hair follicles can cause epilation. Transient and inconsistent erythema (associated with itching) can occur within a few hours of exposure and be followed by a latent, symptom-free phase lasting from a few days to several weeks. After the latent phase, intense reddening, blistering, and ulceration of the irradiated site are visible. Depending on the radiation dose, a third and even fourth wave of erythema are possible over the ensuing months or possibly years.

In most cases, healing occurs by regenerative means; however, large radiation doses to the skin can cause permanent hair loss, damaged sebaceous and sweat glands, atrophy, fibrosis, decreased or increased

NOTE:

Both the Gray (Gy) and the rad are units of absorbed dose and reflect the amount of energy deposited in a mass of tissue (1 Gy = 100 rads). In this document, the absorbed dose refers to that dose received by at least 10 cm 2 of the basal cell layer of the skin. The referenced absorbed dose levels in this document are assumed to be from beta, gamma, or x-radiation. Neutron or proton radiation produces many of the health effects described herein at lower absorbed dose levels.

skin pigmentation, and ulceration or necrosis of the exposed tissue.	
With CRI, it is important to keep the following things in mind: • The visible skin effects depend on the magnitude of the dose as well as the depth of penetration of the radiation. • Unlike the skin lesions caused by chemical or thermal damage, the lesions caused by radiation exposures do not appear for hours to days following exposure, and burns and other skin effects tend to appear in cycles. • The key treatment issues with CRI are infection and pain management.[2]	**NOTE:** On occasion a patient might also be contaminated with radioactive material. To address patient decontamination, please go to the following Web site: http://www.orau.gov/reacts/emergency.htm.
Stages and Grades of CRI CRI will progress over time in stages and can be categorized by grade, with characteristics of the stages varying by grade of injury, as shown in Table 1.(following) Appendix A gives a detailed description of the various skin responses to radiation, and Appendix B provides color photographs of examples of some of these responses. Appendix A follows, or use the link to the right. **Prodromal stage** (within hours of exposure)—This stage is characterized by early erythema (first wave of erythema), heat sensations, and itching that define the exposure area. The duration of this stage is from 1 to 2 days. **Latent stage** (1–2 days postexposure)—No injury is evident. Depending on the body part, the larger the dose, the shorter this period will last. The skin of the face, chest, and neck will have a shorter latent stage than will the skin of the palms of the hands or the soles of the feet. **Manifest illness stage** (days to weeks postexposure)—The basal layer is repopulated through proliferation of surviving clonogenic cells. This stage begins with main erythema (second wave), a sense of heat, and slight edema, which are often accompanied by increased pigmentation. The symptoms that follow vary from dry desquamation or ulceration to necrosis, depending on the severity of the CRI (see Table 1). **Third wave of erythema** (10–16 weeks postexposure, especially after beta exposure)—The exposed person experiences late erythema, injury to blood vessels, edema, and increasing pain. A distinct bluish color of the skin can be observed. Epilation may subside, but new ulcers, dermal necrosis, and dermal atrophy (and thinning of the dermis layer) are possible.	**SEE ALSO:** Appendix A – CDC website description - responses of the skin to radiation. See below for the same information on this document. Appendix B – CDC website photographs.

Late effects (months to years postexposure; threshold dose ~10 Gy or 1000 rads)—Symptoms can vary from slight dermal atrophy (or thinning of dermis layer) to constant ulcer recurrence, dermal necrosis, and deformity. Possible effects include occlusion of small blood vessels with subsequent disturbances in the blood supply (telangiectasia); destruction of the lymphatic network; regional lymphostasis; and increasing invasive fibrosis, keratosis, vasculitis, and subcutaneous sclerosis of the connective tissue. Pigmentary changes and pain are often present. Skin cancer is possible in subsequent years. **Recovery** (months to years)	

TABLE 1: GRADES OF CUTANEOUS RADIATION INJURY

Grade	Skin dose [*]	Prodromal stage	Latent stage	Manifest illness stage	Third wave of erythema [†]	Recovery	Late effects
I	> 2 Gy (200 rads) [‡]	1–2 days postexposure or not seen	no injury evident for 2–5 weeks postexposure [§]	• 2–5 weeks postexposure, lasting 20–30 days: redness of skin, slight edema, possible increased pigmentation • 6–7 weeks postexposure, dry desquamation	not seen	complete healing expected 28–40 days after dry desquamation (3–6 months postexposure)	• possible slight skin atrophy • possible skin cancer decades after exposure
II	> 15 Gy (1500 rads)	6–24 hours postexposure with immediate sensation of heat lasting 1–2 days	no injury evident for 1–3 weeks postexposure	• 1–3 weeks postexposure; redness of skin, sense of heat, edema, skin may turn brown • 5–6 weeks postexposure, edema of subcutaneous tissues and blisters with moist desquamation • possible epithelialization later	• 10–16 weeks postexposure, injury of blood vessels, edema, and increasing pain • epilation may subside, but new ulcers and necrotic changes are possible	healing depends on size of injury and the possibility of more cycles of erythema	• possible skin atrophy or ulcer recurrence • possible telangiectasia (up to 10 years postexposure) • possible skin cancer decades after exposure
III	> 40 Gy (4000 rads)	4–24 hours postexposure, with immediate pain or tingling	none or less than 2 weeks	• 1–2 weeks postexposure: redness of skin, blisters, sense of	• 10–16 weeks postexposure: injury of blood vessels, edema,	can involve ulcers that are extremely difficult to treat	• possible skin atrophy, depigmentation, constant ulcer recurrence, or

TABLE 1: GRADES OF CUTANEOUS RADIATION INJURY							
Grade	**Skin dose** *	**Prodromal stage**	**Latent stage**	**Manifest illness stage**	**Third wave of erythema** †	**Recovery**	**Late effects**
		lasting 1–2 days		heat, slight edema, possible increased pigmentation • followed by erosions and ulceration as well as severe pain	new ulcers, and increasing pain • possible necrosis	and that can require months to years to heal fully	deformity • possible occlusion of small vessels with subsequent disturbances in the blood supply, destruction of the lymphatic network, regional lymphostasis, and increasing fibrosis and sclerosis of the connective tissue • possible telangiectasia • possible skin cancer decades after exposure
IV	> 550 Gy (55,000 rads)	occurs minutes to hours postexposure, with immediate pain or tingling, accompanied by swelling	none	• 1–4 days postexposure accompanied by blisters • early ischemia (tissue turns white, then dark blue or black with substantial pain) in most severe cases • tissue becomes necrotic within 2 weeks following exposure, accompanied by substantial pain	does not occur due to necrosis of skin in the affected area	recovery possible following amputation of severely affected areas and possible skin grafts	• continued plastic surgery may be required over several years • possible skin cancer decades after exposure

* Absorbed dose to at least 10 cm 2 of the basal cell layer of the skin

† Especially with beta exposure

‡ The Gray (Gy) is a unit of absorbed dose and reflects an amount of energy deposited in a mass of tissue (1 Gy = 100 rads).

§ Skin of the face, chest, and neck will have a shorter latent phase than the skin of the palms of the hands and the skin of the feet.

CRI PATIENT MANAGEMENT - DIAGNOSIS

The signs and symptoms of CRI are as follows:

- Intensely painful burn-like skin injuries (including itching, tingling, erythema, or edema) without a history of exposure to heat or caustic chemicals
  Note : Erythema will not be seen for hours to days following exposure, and its appearance is cyclic.
- Epilation
- A tendency to bleed
- Possible signs and symptoms of ARS

As mentioned previously, local injuries to the skin from acute radiation exposure evolve slowly over time, and symptoms may not manifest for days to weeks after exposure. Consider CRI in the differential diagnosis if the patient presents with a skin lesion without a history of chemical or thermal burn, insect bite, or skin disease or allergy. If the patient gives a history of possible radiation exposure (such as from a radiography source, x-ray device, or accelerator) or a history of finding and handling an unknown metallic object, note the presence of any of the following: erythema, blistering, dry or wet desquamation, epilation, ulceration.

Regarding lesions associated with CRI be aware that,

- Days to weeks may pass before lesions appear;
- Unless patients are symptomatic, they will not require emergency care; and
- Lesions can be debilitating and life threatening after several weeks.
- Medical follow-up is essential, and victims should be cautioned to avoid trauma to the involved areas.

INITIAL TREATMENT

Localized injuries should be treated symptomatically as they occur, and radiation injury experts should be consulted for detailed information. Such information can be obtained from the Radiation Emergency Assistance Center/Training Site (REAC/TS) at www.orau.gov/reacts/ or (865) 576-1005.

As with ARS, if the patient also has other trauma, wounds should be closed, burns covered, fractures reduced, surgical stabilization performed, and definitive treatment given within the first 48 hours after injury. After 48 hours, surgical interventions should be delayed until hematopoietic recovery has occurred.

A baseline CBC and differential should be taken and repeated in 24 hours. Because cutaneous radiation injury is cyclic, areas of early erythema should be noted and recorded. These areas should also be sketched and photographed, if possible, ensuring that the date and time are recorded. The following should be initiated as indicated:

- Supportive care in a clean environment (a burn unit if one is available)
- Prevention and treatment of infections
- Use of the following:
  - Medications to reduce inflammation, inhibit protealysis, relieve pain, stimulate regeneration, and improve circulation
  - Anticoagulant agents for widespread and deep injury
- Pain management
- Psychological support

RECOMMENDATIONS FOR TREATMENT BY STAGE

The following recommendations for treatment by stage of the illness were obtained by summarizing recommendations from Ricks et al. (226) and Gusev et al. (231), but they do not represent official recommendations of CDC.

Prodromal Stage —Use antihistamines and topical antipruriginous preparations, which act against itch and also might prevent or attenuate initiation of the cycle that leads to the manifestation stage. Anti-inflammatory medications such as corticosteroids and topical creams, as well as slight sedatives, may prove useful.

Latent Stage —Continue anti-inflammatory medications and sedatives. At midstage, use proteolysis inhibitors, such as Gordox®.

Manifestation Stage —Use repeated swabs, antibiotic prophylaxis, and anti-inflammatory medications, such as Lioxasol®, to reduce bacterial, fungal, and viral infections

- Apply topical ointments containing corticosteroids along with locally acting antibiotics and vitamins.
- Stimulate regeneration of DNA by using Lioxasol® and later, when regeneration has started, biogenic drugs, such as Actovegin® and Solcoseril®.
- Stimulate blood supply in third or fourth week using Pentoxifylline® (contraindicated for patients with atherosclerotic heart disease).
- Puncture blisters if they are sterile, but do not remove them as long as they are intact.
- Stay alert for wound infection. Antibiotic therapy should be considered according to the individual patient's condition.
- Treat pain according to the individual patient's condition. Pain relief is very difficult and is the most demanding part of the therapeutic process.
- Debride areas of necrosis thoroughly but cautiously.

TREATMENT OF LATE EFFECTS

After immediate treatment of radiation injury, an often long and painful process of healing will ensue. The most important concerns are the following:

- Pain management
- Fibrosis or late ulcers
  Note : Use of medication to stimulate vascularization, inhibit infection, and reduce fibrosis may be effective. Examples include Pentoxifylline®, vitamin E, and interferon gamma. Otherwise, surgery may be required.
- Necrosis
- Plastic/reconstructive surgery
  Note : Surgical treatment is common. It is most effective if performed early in the treatment process. Full-thickness graft and microsurgery techniques usually provide the best results.
- Psychological effects, such as posttraumatic stress disorder
- Possibility of increased risk of skin cancer later in life

For Further Assistance

1. Technical assistance - Radiation Emergency Assistance Center/Training Site (REAC/TS) at **(865) 576-3131** (M-F, 8 AM to 4:30 PM EST) or **(865) 576-1005** (after hours), or at http://www.orau.gov/reacts/ , and from the Medical Radiobiology Advisory Team (MRAT) at **(301) 295-0316**.
2. CDC Health Alert Network at emergency.cdc.gov or **1-800-311-3435**.

APPENDIX A: RESPONSES OF THE SKIN TO RADIATION

Acute epidermal necrosis (time of onset: < 10 days postexposure; threshold dose: ~550 Gy or 55,000 rads)— Interphase death of postmitotic keratinocytes in the upper visible layers of the epidermis (may occur with high-dose, low-energy beta irradiation)

Acute ulceration (time of onset: < 14 days postexposure; threshold dose: ~20 Gy or 2000 rads)—Early loss of the epidermis— and to a varying degree, deeper dermal tissue—that results from the death of fibroblasts and endothelial cells in interphase

Dermal atrophy (time of onset: > 26 weeks postexposure; threshold dose: ~10 Gy or 1000 rads)— Thinning of the dermal tissues associated with the contraction of the previously irradiated area

Dermal necrosis (time of onset > 10 weeks postexposure; threshold dose: ~20 Gy or 2000 rads)— Necrosis of the dermal tissues as a consequence of vascular insufficiency

Dry desquamation (time of onset: 3–6 weeks postexposure; threshold dose: ~8 Gy or 800 rads)— Atypical keratinization of the skin caused by the reduction in the number of clonogenic cells within the basal layer of the epidermis

Early transient erythema (time of onset: within hours of exposure; threshold dose: ~2 Gray [Gy] or 200 rads)— Inflammation of the skin caused by activation of a proteolytic enzyme that increases the permeability of the capillaries

Epilation (time of onset: 14–21 days; threshold dose: ~3 Gy or 300 rads)— Hair loss caused by the depletion of matrix cells in the hair follicles

Late erythema (time of onset: 8–20 weeks postexposure; threshold dose: ~20 Gy or 2000 rads)— Inflammation of the skin caused by injury of blood vessels. Edema and impaired lymphatic clearance precede a measured reduction in blood flow.

Invasive fibrosis (time of onset: months to years postexposure; threshold dose: ~20 Gy or 2000 rads)— Method of healing associated with acute ulceration, secondary ulceration, and dermal necrosis that leads to scar tissue formation

Main erythema (time of onset: days to weeks postexposure; threshold dose: ~3 Gy or 300 rads)— Inflammation of the skin caused by hyperaemia of the basal cells and subsequent epidermal hypoplasia (see photos 1 and 2)

Moist desquamation (time of onset: 4–6 weeks postexposure; threshold dose: ~15 Gy or 1500 rads)— Loss of the epidermis caused by sterilization of a high proportion of clonogenic cells within the basal layer of the epidermis

Secondary ulceration (time of onset: > 6 weeks postexposure; threshold dose: ~15 Gy or 1500 rads)— Secondary damage to the dermis as a consequence of dehydration and infection when moist desquamation is severe and protracted because of reproductive sterilization of the vast majority of the clonogenic cells in the irradiated area

Telangiectasia (time of onset: > 52 weeks postexposure; threshold dose for moderate severity at 5 years: ~40 Gy or 4000 rads)— Atypical dilation of the superficial dermal capillaries