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**By law, health care providers must report suspected or confirmed Anthrax to the local health department immediately (within 1 hr).**

**Even a single case of Anthrax is considered an outbreak and is a public health emergency.**

**To report: call SFDPH communicable disease control (24/7 Tel: 415-554-2830).**

**Upon receipt, SFDPH will initiate the public health response and can facilitate lab testing.**

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## AGENT

*Bacillus anthracis* is a large, gram-positive, spore-forming, aerobic, encapsulated, rod-shaped bacterium. In an environment rich in nutrients, the spores germinate and form bacteria. Conversely, when nutrients in the environment are exhausted, the bacteria form spores. Anthrax spores are resistant to drying, heat, ultraviolet light, gamma radiation, and some disinfectants. Spores can persist in soil for years, whereas anthrax bacteria survive poorly outside of mammalian hosts.

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## EPIDEMIOLOGY

### **Anthrax as a Biological Weapon**

Several countries have had anthrax weaponization programs in the past, including the USA. In 1979 an outbreak of anthrax in the Soviet Union resulted from accidental release of anthrax spores from a facility where weaponized anthrax was being produced. Of 77 reported human cases, all but 2 were inhalational, and there was an 86% fatality rate.

Anthrax was successfully used as a biological weapon in the USA in October 2001. Cases resulted from direct or indirect exposure to mail that was deliberately contaminated with anthrax spores. In total, 22 cases were identified, 11 with inhalational (5 fatal) and 11 with cutaneous anthrax.

As a result of this outbreak, the US Postal Service is deploying autonomous detection systems for anthrax (the Biohazard Detection System [BDS]) in select mail processing and distribution centers across the United States, including the US Postal Service Mail Processing and Distribution Center in San Francisco (see Environmental Testing, below).

**Aerosol release of weaponized spores is the most likely mechanism for use of anthrax as a biological weapon.** Weaponization for aerosol release generally involves use of highly

concentrated spores, treated to reduce clumping and reduce particle size, and potentially the use of antimicrobial-resistant or genetically modified strains to increase virulence or escape vaccine protection.

Deliberate contamination of food or water with anthrax spores also is a possibility. Spores remain stable in water for at least several days following inoculation. *B anthracis* spores are not destroyed by pasteurization, making contamination of milk another theoretical possibility.

### **Naturally Occurring Anthrax**

*B. anthracis* spores are found in soil in many areas of the world, including Bay Area counties with cattle grazing.

Anthrax is predominantly a disease of animals. Livestock or other herbivores acquire infection from consuming contaminated soil or feed. Anthrax in animals is endemic in many areas of the world. In the USA, anthrax outbreaks in animals occur sporadically. In 2001, an outbreak of bovine anthrax caused the death of 21 beef cattle in a rural section of Santa Clara County.

Naturally occurring anthrax in humans occurs after exposure to infected animals or contaminated animal products.

- Cutaneous anthrax generally occurs via contact with infected tissues of dead animals. Occupational exposures include butchering and processing of animal hides. In the USA, cutaneous anthrax represents 95% of naturally occurring cases. Since 1990, only two cases of naturally occurring anthrax have been reported in the USA; both had cutaneous disease, and neither case was in California.
- Gastrointestinal (GI) anthrax is associated with consumption of contaminated, undercooked meat.
- Inhalational anthrax results from contact with contaminated hair, wool, or hides, particularly during processing.

Person-to-person transmission of *B anthracis* does not occur with GI or inhalational anthrax, but has been reported rarely with cutaneous anthrax.

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## CLINICAL FEATURES

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Clinical manifestations of anthrax resulting from a bioweapons attack will depend on the method of dissemination. An aerosol release would result in most infected individuals presenting with symptoms of inhalational anthrax, with fewer having the cutaneous form. High-dose powder dissemination, as with contaminated mail, resulted in cases of both inhalational and cutaneous anthrax in the 2001 outbreak. A terrorist may develop cutaneous or inhalational anthrax after working with the agent.

The bacillus produces high levels of 2 toxins: edema toxin causes massive edema at the site of germination, and lethal toxin initiates the cascade of inflammatory mediators that leads to sepsis. High levels of toxin in the blood lead to death even if the bacteria are killed with antibiotics.

### **Inhalational Anthrax**

Inhalational anthrax is caused by inhalation of spores that reach the alveoli, undergo phagocytosis and travel to regional lymph nodes. The spores then germinate to become bacterial cells, which multiply in the lymphatic system and cause lymphadenitis of the mediastinal and peribronchial lymph nodes. The bacteria cause focal, hemorrhagic necrosis in the lungs, accompanied by intraalveolar edema and pleural effusion. Bacteria entering the bloodstream lead to septicemia, septic shock, and death.

<b>INHALATIONAL ANTHRAX: CLINICAL FEATURES</b>	
<b>Incubation Period</b>	2-7 days (up to 43 days or longer)
<b>Signs &amp; Symptoms</b>	<p>Illness often biphasic</p> <p>Initial Phase</p> <ul style="list-style-type: none"> <li>• Flu-like picture with mild, nonspecific respiratory illness, nonproductive cough, low-grade fever, malaise, myalgia</li> <li>• Occasionally abdominal pain, mild chest discomfort</li> </ul> <p>Acute Phase</p> <ul style="list-style-type: none"> <li>• Develops after 2-5 days of prodrome, occasionally preceded by 1-2 days of improvement</li> <li>• Severe respiratory distress, cyanosis</li> <li>• Profuse sweating</li> <li>• High fever</li> <li>• Progresses to shock, death in 24-36 hours if left untreated</li> </ul>
<b>Laboratory Findings</b>	<ul style="list-style-type: none"> <li>• Elevated WBC with left shift</li> <li>• Abnormal CXR: <ul style="list-style-type: none"> <li>~ Mediastinal widening</li> <li>~ Infiltrates, consolidation</li> <li>~ Pleural effusion</li> </ul> </li> <li>• Abnormal CT scan: <ul style="list-style-type: none"> <li>~ Mediastinal adenopathy, widening</li> <li>~ Pleural effusion</li> <li>~ Infiltrates, consolidation</li> </ul> </li> </ul>

### **Cutaneous Anthrax**

In cutaneous anthrax, spores or bacilli are introduced through preexisting skin breaks. Germination at the site of introduction leads to localized necrosis with eschar formation and soft-tissue or mucosal edema. Organisms are phagocytosed and carried to regional lymph nodes, often causing painful lymphadenopathy and lymphangitis. Septicemic complications of cutaneous anthrax occur in 10-20% of untreated cases.

<b>CUTANEOUS ANTHRAX: CLINICAL FEATURES</b>	
<b>Incubation Period</b>	1-7 days (up to 12 days)
<b>Signs &amp; Symptoms</b>	<p>Initial lesion</p> <ul style="list-style-type: none"> <li>• Begins as small, pruritic papule or vesicle</li> <li>• Lesions tend to occur on exposed areas of body (eg, face, hands, arms, neck)</li> <li>• By second day, papule ulcerates with central necrosis and drying</li> <li>• Painless</li> <li>• Localized, nonpitting edema develops, surrounding ulcerated area</li> <li>• Fine vesicles may encircle ulcer</li> </ul> <p>Lesion Progression</p> <ul style="list-style-type: none"> <li>• After 1 to 2 days, black eschar forms over ulcerated area</li> <li>• Lesion itself is painless (though regional adenopathy may be painful)</li> <li>• Eschar sloughs off after 12-14 days</li> <li>• Lesions resolve without complications or scarring in 80%-90% of patients</li> <li>• Nonpitting edema, lymphangitis, and painful lymphadenopathy may occur</li> <li>• Fever and malaise are common</li> <li>• Despite antibiotic treatment, the lesion will progress through all stages</li> <li>• Treatment is aimed at preventing systemic dissemination, as 10-20% of untreated cutaneous anthrax becomes systemic</li> </ul>
<b>Laboratory Findings</b>	<ul style="list-style-type: none"> <li>• WBC count often is normal or may be slightly elevated</li> <li>• Gram stain of lesion may reveal gram-positive rods; neutrophils are uncommon</li> </ul>

### **Gastrointestinal Anthrax**

GI anthrax results from ingestion of *B. anthracis* bacteria, such as may be found in poorly cooked meat from infected animals. The incubation period for GI anthrax is 1-7 days. Two clinical presentations have been described.

With intestinal anthrax, intestinal lesions occur and are followed by regional lymphadenopathy. Symptoms of intestinal anthrax are initially nonspecific and include nausea, vomiting, anorexia and fever. As disease progresses, abdominal pain, hematemesis and bloody diarrhea develop, occasionally accompanied by ascites. The patient may present with findings of an acute surgical abdomen. Hematogenous spread with resultant septicemia can occur.

In oropharyngeal anthrax, a mucosal ulcer occurs initially in the mouth or throat, associated with fever. This is followed by cervical edema and lymphadenopathy. Hematogenous spread with resultant septicemia can occur.

Gram stain of peritoneal fluid or oropharyngeal ulcers may show gram-positive rods. Elevated WBC with left shift may be present. *B anthracis* can be cultured from oropharyngeal swabs and stool specimens.

## **Anthrax Meningitis**

Anthrax meningitis may occur as a complication of cutaneous, inhalational, or GI anthrax. Symptoms of the primary site of infection usually will be present; however meningitis may be the presenting illness. Characteristic features of bacterial meningitis are usually present. A hemorrhagic meningoencephalitis is not uncommon.

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## **DIFFERENTIAL DIAGNOSIS**

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Because of its mild, nonspecific nature, a high index of suspicion is necessary to make the diagnosis of anthrax in the early stages. However, early diagnosis is desirable as prompt administration of antibiotics can be critical to patient survival.

### **Differential: Inhalational Anthrax**

Early disease mimics influenza and other respiratory infections. However nasal symptoms are typically not present and rapid diagnostic tests, such as nasopharyngeal swabs for detection of respiratory virus antigens, would typically be negative.

**Key features that distinguish inhalational anthrax from other conditions are:**

- **CXR is abnormal even during early stages of flu-like illness**
- **CXR or Chest CT show widened mediastinum and pleural effusion but minimal or no pneumonitis**

Other conditions to consider:

- Community-acquired pneumonia (e.g. bacterial, Mycoplasma, Chlamydia)
- Influenza
- Other viral pneumonia (e.g. RSV, CMV, hantavirus)
- Q fever
- Pneumonic plague
- Tularemia
- Primary mediastinitis
- Dissecting aortic aneurysm

### **Differential: Gastrointestinal Anthrax**

The differential diagnosis for the intestinal form of the disease includes:

- Any cause of acute abdomen
- Bacterial peritonitis
- Acute bacterial gastroenteritis (e.g. *Campylobacter*, *Shigella*, toxigenic *E. coli*, *Yersinia*)
- Typhoid fever
- Intestinal tularemia

The differential diagnosis for the oropharyngeal form of the disease includes:

- Streptococcal pharyngitis
- Infectious mononucleosis
- Enteroviral vesicular pharyngitis

- Herpetic pharyngitis
- Diphtheria
- Anaerobic pharyngitis (Vincent's angina)
- *Yersinia enterocolitica* pharyngitis
- Pharyngeal tularemia

### **Differential: Cutaneous Anthrax**

**Key features that distinguish cutaneous anthrax are:**

- **Painlessness of the lesion itself**
- **Large extent of local edema**

Other conditions to consider:

- Ecthyma gangrenosum
- Ulceroglandular tularemia
- Bubonic plague
- Staphylococcal or streptococcal cellulitis
- Brown recluse spider bite
- Necrotizing soft tissue infections, (e.g. group A Strep and Clostridia)
- Rickettsial pox
- Scrub typhus
- Necrotic herpes simplex infection

### **Differential: Anthrax Meningitis**

A key feature that distinguishes anthrax meningitis is bloody CSF containing gram-positive bacilli.

## LABORATORY DIAGNOSIS

The gold standard for anthrax diagnosis is direct culture of clinical specimens onto blood agar with demonstration of typical gram stain, motility, and biochemical features.

- For suspected cutaneous anthrax, collect a sterile sample for gram stain and culture from the fluid of an unroofed vesicle, or from the exudate of an ulcer or eschar. If there is no visible exudate, the edge of the eschar can be lifted with forceps and the fluid near the edge collected. A negative culture does not exclude the diagnosis of cutaneous anthrax.
- For suspected inhalational anthrax, collect sputum for gram stain and culture if sputum is being produced. Obtain blood for smear and culture. If pleural effusion is present, collect a specimen for gram stain and culture.

**If you are testing or considering testing for Anthrax, you should:**

- **IMMEDIATELY notify SFDPH Communicable Disease Control (24/7 Tel: 415-554-2830). SFDPH can authorize and facilitate testing, and will initiate the public health response as needed.**
- **Inform your lab that Anthrax is under suspicion. Labs may view gram-positive bacilli as contaminants and may not pursue further identification unless notified.**

- For suspected GI anthrax, obtain a stool specimen for culture (or a rectal swab from patients unable to produce stool). Obtain blood for smear and culture. If ascites is present, obtain a specimen for gram stain and culture.
- For suspected anthrax meningitis, obtain a CSF specimen for gram stain and culture and obtain blood for smear and culture.

Blood cultures should be obtained prior to antibiotic administration if possible, as they are positive nearly 100% of the time in inhalational anthrax but there is rapid sterilization of blood after a single dose of antibiotics.

Other diagnostic tests are under investigation or are available only at designated reference laboratories. These include serologic tests (useful for retrospective diagnosis), direct fluorescent antibody (DFA) testing, PCR-based assays, and immunohistochemistry methods. Reference lab testing is accessed via SFDPH. Specimens should be submitted to your clinical lab, which will coordinate with the SFDPH Public Health Lab as needed.

### **Testing for Exposure to Aerosolized Anthrax**

Nasal swab cultures have been used to study exposure to aerosolized anthrax in non-symptomatic patients. However, nasal swabs are not recommended for use in the clinical setting, as the sensitivity, specificity, and predictive value of nasal swab cultures is not known.

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## TREATMENT AND PROPHYLAXIS

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**These recommendations are current as of this document date. SFDPH will provide periodic updates as needed and situational guidance in response to events ([www.sfdph.org/cdcp](http://www.sfdph.org/cdcp)).**

### **Treatment of Confirmed or Suspected Anthrax**

This section refers to individuals with confirmed anthrax or who are ill with suspected anthrax.

The basic components of treatment for anthrax consist of hospitalization with intensive supportive care and IV antibiotics. Antimicrobials should be started immediately upon suspicion and prior to confirmation of the diagnosis. As susceptibility data will be delayed, initial antibiotics must be chosen empirically.

Recommendations for initial empiric therapy of confirmed or suspected inhalational, GI, or CNS anthrax are shown in the table below. Empiric therapy with at least 2 agents is recommended due to the potential for infection with strains of *B. anthracis* engineered to be penicillin- and/or tetracycline-resistant. Once susceptibilities are determined, the regimen may be further tailored, in consultation with an infectious disease specialist or in accordance with SFDPH recommendations.

INITIAL IV THERAPY FOR INHALATIONAL, GI, OR CNS ANTHRAX†	
Patient Category	Therapy Recommendation
Adults	Ciprofloxacin, 400 mg IV q12 hr †† <b>or</b> Doxycycline, 100 mg IV q12 hr** <b>and</b> One or two additional antimicrobials (agents with <i>in vitro</i> activity include rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, and clarithromycin)††
Children *	Ciprofloxacin, 10-15 mg/kg IV q12 hr, not to exceed 1 g/day†† <b>or</b> Doxycycline**: >8 yr and >45 kg: 100 mg IV q12 hr >8 yr and ≤45 kg: 2.2 mg/kg IV q12 hr ≤8 yr: 2.2 mg/kg every IV q12 hr <b>and</b> One or two additional antimicrobials (see agents listed above)††
Pregnant women *	Same as for nonpregnant adults
Immunocompromised	Same as for nonimmunocompromised persons and children
† Steroids may be considered an adjunct therapy for patients with severe edema and for meningitis based on experience with bacterial meningitis of other etiologies. * High death rates from infection outweigh the relative contraindications of doxycycline and fluoroquinolones in children and pregnant women. ** If meningitis is suspected, doxycycline may be less optimal because of poor CNS penetration. †† Because of concerns of beta-lactamases in <i>B. anthracis</i> isolates, penicillin and ampicillin should not be used alone. Consultation with an I.D. specialist is advised. <i>B. anthracis</i> strains are naturally resistant to sulfamethoxazole, trimethoprim, cefuroxime, cefotaxime sodium, aztreonam, and ceftazidime. †† If IV ciprofloxacin is not available, oral ciprofloxacin may be acceptable as it is rapidly and well absorbed from the GI tract with no substantial loss by first-pass metabolism. Maximum serum concentrations are attained 1-2 hours after oral dosing but may not be achieved if vomiting or ileus is present.	
Source: Working Group on Civilian Biodefense. Inglesby et al, JAMA 2002;287(17):2236-52	

After clinical improvement is noted, treatment can be switched to oral therapy with ciprofloxacin or doxycycline, based on susceptibilities and clinical considerations, at doses identical to the IV doses. **Therapy should be continued for a total duration of 60 days** because of the potential persistence of spores after an aerosol exposure.

Localized cutaneous anthrax can usually be treated with a single oral antibiotic, either ciprofloxacin or doxycycline, at doses equivalent to the IV doses shown above. Therapy should be continued for 60 days duration. If in addition to cutaneous lesions there are signs of systemic disease or extensive edema, or if lesions are present on the head or the neck, then the multi-drug IV regimen in the table above should be followed.

### **Prophylaxis of Persons Exposed but Without Symptoms**

Post-exposure prophylaxis is the administration of antibiotics, with or without vaccine, after suspected exposure to anthrax has occurred but before symptoms are present. (If symptoms are present, see section on treatment, above). In general, post-exposure prophylaxis is recommended

for those exposed to an air space where a suspicious material may have been aerosolized or which may be the source of an inhalational anthrax case. As there is no known person-to-person transmission of inhalational anthrax, prophylaxis should not be offered to contacts of cases, unless also exposed to the original source.

Post-exposure prophylaxis of potential inhalational anthrax consists of oral administration of either ciprofloxacin or doxycycline, at doses equivalent to the IV doses above. Therapy should be continued for 60 days duration. Patients treated for exposure should be informed of the importance of completing the full course of antibiotic prophylaxis regardless of the absence of symptoms.

Due to concerns about use of doxycycline or ciprofloxacin in children and about doxycycline use in pregnant women, the CDC has indicated that for prophylaxis, therapy can be switched to amoxicillin in these groups if the isolate is determined to be susceptible. Amoxicillin may also be considered for patients allergic to both ciprofloxacin and doxycycline.

### **Anthrax Vaccine**

The anthrax vaccine adsorbed (AVA) is available but only in limited supply that is controlled by federal authorities. It is an inactivated cell-free filtrate of an avirulent strain of *B. anthracis*. Local reactions and mild systemic reactions are common. Severe allergic reactions are rare (<1 per 100,000).

AVA is licensed for pre-exposure use to prevent cutaneous anthrax in healthy, non-pregnant adults 18-65 years of age who have a high likelihood of coming into contact with anthrax, including certain laboratory workers and animal processing workers. AVA is not currently licensed for post-exposure use, and must be given in this context under an FDA investigational drug protocol. The CDC may recommend its use for post-exposure prophylaxis under some circumstances. Research is underway on a new anthrax vaccine.

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## INFECTION CONTROL\*

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**These recommendations are current as of this document date. SFDPH will provide periodic updates as needed and situational guidance in response to events ([www.sfdph.org/cdcp](http://www.sfdph.org/cdcp)).**

There are no data to suggest that person-to-person transmission of inhalational or GI anthrax occurs. Therefore, **Standard Precautions** are considered adequate for patients with **inhalational** and/or **GI anthrax**. Patients do not require isolation rooms.

Person-to-person transmission has only rarely been reported for patients with cutaneous anthrax prior to the 2001 outbreak. Most authorities, including the Working Group on Civilian Biodefense, recommend **Standard Precautions** for patients with **cutaneous anthrax**.

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\* For description of Precautions, see chapter on Infection Control

Articles contaminated with infective material including bandages should be discarded, bagged and labeled before being sent for decontamination and reprocessing. Contaminated surfaces should be cleaned with a hospital-approved disinfectant or a 1:10 dilution of household bleach.

Decontamination of persons exposed to anthrax should involve:

- Removal of contaminated clothing. Clothing should be handled minimally to avoid aerosolization, stored in labeled plastic bags, and then laundered.
- Showering thoroughly with soap and water.

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## ENVIRONMENTAL TESTING

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New environmental sampling systems are currently in use to detect possible release of anthrax.

One such system, the Biohazard Detection System (BDS), has been deployed by the US Postal Service to assist with early detection of *B. anthracis* at mail processing and distribution centers across the USA. **A BDS system is now active at the main postal processing facility in San Francisco.** The BDS is a fully automated air-sampling system consisting of an aerosol collector, PCR cartridge and controller computer. Positive BDS signals will be confirmed by a public health reference lab. In the event of a positive signal, SFDPH has developed an emergency response plan in coordination with the Postal Service and other city emergency partners.

BioWatch is a federal program that continuously collects outdoor air samples, screening the environment for harmful aerosolized biological agents. **BioWatch sensors have been deployed in the San Francisco Bay Area.** Specialized air sampling devices are mounted on existing outdoor air quality monitors. The air sampling filters are retrieved and transported regularly to a local CDC-coordinated laboratory for PCR analysis. If a biological pathogen is detected, the laboratory performs a second PCR test for confirmation. A culture may also be initiated to assess viability and antimicrobial sensitivities. A confirmed positive result would initiate a major response from local, state, and federal agencies.

In the event of a positive signal from either the BDS or the BioWatch systems, updated information and instructions for San Francisco health care providers will be available at [www.sfdph.org/cdcp](http://www.sfdph.org/cdcp).

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## REFERENCES

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CDC. Additional options for preventive treatment for persons exposed to inhalational anthrax. MMWR 2001;50(50):1142

CDC. Considerations for distinguishing influenza-like illness from inhalational anthrax. MMWR 2001;50(44):984-6

CDC. Investigation of anthrax associated with intentional exposure and interim public health guidelines, October 2001. MMWR 2001;50(41):889-93

CDC. Investigation of bioterrorism-related anthrax and interim guidelines for clinical evaluation of persons with possible anthrax. MMWR 2001; 50(43):941-8

CDC. Investigation of bioterrorism-related anthrax and interim guidelines for exposure management and antimicrobial therapy, October 2001. MMWR 2001; 50(42): 909-19

CIDRAP. Anthrax: Current, comprehensive information on pathogenesis, microbiology, epidemiology, diagnosis, treatment, and prophylaxis. March 3, 2005.  
([www.cidrap.umn.edu/cidrap/content/bt](http://www.cidrap.umn.edu/cidrap/content/bt))

Inglesby TV et al, for the Working Group on Civilian Biodefense. Anthrax as a biological weapon, 2002: updated recommendations for management. JAMA 2002; 287(17): 2236-52

LA County DHS. Terrorism Agent Information and Treatment Guidelines for Clinicians and Hospitals. June 2003. ([labt.org/Zebra.asp](http://labt.org/Zebra.asp))

Swartz MN. Current Concepts: Recognition and management of anthrax—an update. N Engl J Med 2001 Jun; 345(22):1621-6.