disease prevention news

October 28, 1996 Vol. 56, No. 22

ACE Implicated in *Mycobacterium Abscessus* Infections

On August 12, 1996, the Centers for Disease Control and Prevention notified the Texas Department of Health (TDH) Infectious Disease Epidemiology and Surveillance Division (IDEAS) of a hazard posed by an injectable product contaminated with Mycobacterium abscessus. ***Adrenal Cortex Extract (ACE)*** *has been implicated in at least 54 cases of abscesses following intramuscular injections.*

On August 24, 1996, the Arizona Department of Health Services notified TDH that 8 practitioners, 2 distributors, and 2 pharmacies in 10 Texas cities had received vials of ACE (Table 1). It is possible that this product was distributed in other cities that are yet to be identified. In response to this notification, IDEAS faxed an alert to hospital infection control practitioners and laboratory directors throughout the state. Since 80% of all Texas *M. tuberculosis* isolates are confirmed at the TDH Laboratory, a computer search of laboratory records was done to identify individuals with *M. abscessus* wound infections.

Case Report

In response to the faxed alert, a physician submitted a case report on a patient with *M. abscessus* infection at an injection site. Prior to onset of her symptoms, this patient had received 6 injections at the office of 1 of the 8 providers who had received ACE vials. However, her records did not specify that she had received any ACE injections.

The patient is a 74-year-old white woman who previously had been healthy. In mid-May she developed back pain radiating to the left leg and particularly to her left hip. She was initially seen by a doctor who manipulated her hip and injected her back with procainamide hydrochloride and calcium in 3 places on 2 different occasions. The patient subsequently developed severe erythema and ulceration where the injections had been given.

On June 19 she was referred to a doctor who gave her a 20-day course of ciprofloxacin and prednisone. A magnetic resonance imaging (MRI) exam of her lumbar spine revealed multilevel discogenic disease with osteoarthritis and a slight posterior herniation of a disc at the L5-Sl level.

When she failed to improve on the prescribed therapy, she was referred to an orthopedic surgeon and a plastic surgeon. On July 11 she was placed on trimethoprim/sulfamethoxazole with wound care. About this time the wound over her lumbosacral spine was noted to be elliptical and about 10 centimeters long. Superficial cultures of the wound showed no growth and a gram stain was negative for organisms.

The patient was then referred to an infectious disease specialist. An acid-fast stain, performed on a swab of the lumbosacral wound on July 24, was also negative for organisms. On July 29 rapidly growing acid fast bacilli were isolated on culture media and identified as *M. abscessus.* The organism was resistant to ciprofloxacin, doxycycline, minocycline, and sulfamethoxazole. On physical exam August 8, she still had the large draining wound on her lower back; she had also developed a second draining lesion on the left buttock and an erythematous lesion on the right buttock.

Discussion

This case illustrates the difficulties inherent in treating *M. abscessus* infection. *M. abscessus* is an acid-fast rod that resembles diptheroids on

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Also in this issue:

gram stain. *M. abscessus* (which may appear in a laboratory report as "*M. chelonei* complex") is a rapidly growing mycobacteria which usually grows well on routine laboratory media and takes from 2 to 30 days for primary isolation. Appropriate collection of specimens for culture is paramount to diagnosis. The skin should be cleansed with alcohol before the needle aspiration is performed. Three to 5 milliliters of exudate, transudate, or drainage should be collected aseptically in a sterile container and diluted in 3 to 5 mL of sterile distilled water or nonbacteriostatic saline. If the volume is insufficient for needle aspiration, the specimen should be collected on a swab, and placed in 3 to 5 mL of physiologic saline. If immediate processing (within a few hours) is not possible, the culture material should be refrigerated and transported to the laboratory overnight at ambient temperature. Specimens should be labeled "rule out *M. abscessus.*" Any tissue specimen submitted to a laboratory must be thoroughly ground in the grinder or minced with sterile scissors before being cultured. If gross contamination with normal flora is suspected, digestion and decontamination with N-acetyl-L-cysteine-NaOH should be performed to facilitate the recovery of mycobacteria, following protocol recommended in the CDC handbook, *Public Health Mycobacteriology*.

Table 1. Known Distribution of Adrenal Cortex Extract to Cities in Texas

City	No.* receiving ACE vials
Abilene	1
Austin	2
Dallas	3
El Paso	1
Fort Worth	1
Grapevine	1
Irving	1
Mesquite	1
Plano	1

*practitioners, distributors, and pharmacies

Although healthy persons can develop infections with this organism, *M. abscessus* disease may be especially severe in immunosuppressed persons. *M. abscessus* skin and soft tissue infections are often acquired by inoculation or injection and usually manifested as acute inflammatory reactions with suppuration; they are easily mistaken for pyogenic abscesses. Most occur within one month of exposure, although incubation periods may be as long as one year. Chronic inflammation, ulceration, and sinus tract formation may occur.

Drainage is always indicated, and surgery, with excision of the involved tissues, may be indicated. Since the rapidly growing mycobacteria vary widely in their antibiotic susceptibilities, antimicrobial sensitivity tests should always be done. Most isolates are sensitive to clarithromycin, amikacin, and cefoxitin; some are sensitive to erythromycin, and all are resistant to cephamycins. Clarithromycin 500 milligrams, twice a day (BID), for 3 to 6 months, combined with excisional surgery, appears to offer a good chance for cure in most cases of localized disease in normal hosts. Prolonged antibiotic therapy and removal of all infected material (including prosthetic devices) may be required in cases of deep-seated infections or in immunocompromised hosts. **Expert consultation should be sought to assist in the management of these cases.**

On August 30, 1996, the FDA issued a Class 1 voluntary recall of the Adrenal Cortex Extract. This biologic comes in 30 mL multidose vials and is distributed by Phyne Pharmaceuticals under the Hallmark Labs label. Samples of Adrenal Cortex Extract with the Hallmark Labs label have been found to contain *M. abscessus.* Since April 1996 epidemiologic evidence has implicated this product in at least 54 cases of injection-site abscesses. Although it has been promoted for a wide variety of uses including weight loss, burn treatment, and treatment of substance abuse, Adrenal Cortex

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Extract is not approved for use by the FDA for any indication. It is usually derived from the adrenal glands of cattle, sheep, or swine. There have been reports from other states that in some instances ACE has been mixed with other drugs such as vitamins and injected. Patients receiving such concoctions may be unaware that they have gotten ACE. The product could also be improperly labeled and contain indications for use that might expose immunocompromised patients to increased risk of a mycobacterial infection.

This drug is not approved by the Food and Drug Administration. Patients who received the drug should be notified by the health care provider who administered or distributed the drug to them. Providers should inform their patients that they may have received a contaminated drug and inquire about inflammation or other signs of infection at injections sites. **Any health care providers administering ACE should stop using it immediately.** Health care providers who purchased the drug should turn the drug into the FDA. Information on how and where to turn in the drug is available by calling the FDA at (714) 667-7416.

Three additional cases have been reported since this article was written. In Texas, cases of apparent *M. abscessus* infection should be reported to the local health department or to the (IDEAS) Division at (800) 252-8239, press 1, or (512) 458-7676. In addition to this DPN article, the TDH internet web site contains a section on *Mycobacterium abscesses* that includes simplified information for the general public. The internet address is http://www.tdh.state.tx.us/mycobac.htm

Adrenal Cortex Extract is not approved for use by the FDA for any indication.

Prepared by Beverly Ray, RN, CIC, TDH (IDEAS) Division

Acknowledgement: The author would like to thank the following people for providing essential information for this report: Edward Goodman, MD, Chief of Infectious Disease at Presbysterian Hospital of Dallas; Eliane Haron, MD, private practice in Dallas; Cynthia Culmo, RS, Division Director, and Angela Bensel, RPh, Program Director, of the TDH Division of Drugs and Medical Devices; Denise Dunbar of the TDH Microbiological Services Division; and David E. Griffith, MD, and Richard J. Wallace, Jr., MD, of the University of Texas Health Center at Tyler.

Wound Botulism

Case Report

A probable case of botulism in a 49-year-old Dallas County woman was reported to the Texas Department of Health (TDH) in 1995. She had had a left mastectomy on May 10, 1995 and had completed her last course of chemotherapy on September 15. On September 30, she sustained a cat bite to her left thumb. The next day cellulitis developed at the site of the cat bite, and movement in the left thumb and index finger was impaired. She was hospitalized on October 2 for wound debridement and for intravenous antibiotics for a suspected *Pasteurella multocida* infection. On admission, her white blood cell count was 1,500 cubic millimeters, with 29% band forms and 25% polymorphonuclear cells.

Her wound initially improved, but by October 10 she complained of increased pain in her left arm. On October 12 she developed double vision, slurred speech, drooping eyelids, difficulty in swallowing, a decreased gag reflex, and chest pain on her left side. A series of neurologic examinations revealed findings consistent with a progressive, descend-

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ing flaccid paralysis. Axial and cranial magnetic resonance imaging (MRI), cranial angiography, and two lumbar punctures were normal. An edrophonium bromide (Tensilon®) test was negative.

On October 16 the patient exhibited decreasing respiratory vital capacities (1.0 liter forced vital capacity) and was admitted to the intensive care unit. She was examined by a neurologist and an infectious disease specialist; they determined that her neurologic findings were consistent with *Clostridium botulinum* infection. Botulism serologies as well as anaerobic wound cultures were submitted to the hospital and TDH labs. The patient received 2 doses of botulism antitoxin on October 17.

Consider Wound Botulism When...

- Clinical symptoms are compatible with *C. botulinum* intoxication,
- The patient has a history of injecting drug use, or
- The patient's food history does not identify a source for foodborne botulism.

Although laboratory confirmation by serum toxin detection and/or wound culture is preferred, lack of confirmation should not delay the administration of antitoxin to a patient with a clinically compatible illness.

Although botulism toxin assays of the patient's blood and stool were negative, and anaerobic wound cultures never grew *C. botulinum*, the patient's incubation period, symptomatology, and the electromyogram (EMG) results supported the diagnosis. In addition to the botulism antitoxin, she received steroid therapy and plasmapheresis. (The plasmapheresis was done because there was a remote possibility that the woman could have had a rare Guillain-Barre variant.) She began to recover and on November 8 was transferred to a Dallas rehabilitation facility in stable condition.

Discussion

Wound botulism is a rare illness that occurs after spores of *C. botulinum* have germinated in a wound and have produced botulinal toxin, which then causes a descending, symmetric flaccid paralysis. Because the syndrome appears after spore germination, the average incubation period is 10 days.[1]

Wound botulism accounted for 11 (21%) of the 53 adult botulism cases reported to CDC in 1994 . All 11 cases occurred in injecting drug users in California and many involved subcutaneous injection or "skin popping" of black tar heroin.[2] In 1995, 161 tests for adult wound botulism were performed by the California State Laboratory; 47 (29%) were laboratory confirmed. Of the 25 that were suggestive of wound botulism associated with black tar heroin use, 18 (72%) were laboratory confirmed. In many cases of wound botulism, a tissue sample cannot be obtained because the wound is very small or difficult to locate; the majority of cases are confirmed by serum toxin detection.

Black tar heroin, believed to be processed in Mexico, is a dark, gummy form of the drug. Its use is increasing and since 1993 has supplanted the use of traditional forms of heroin in California and other western states. "Skin popping" (subcutaneous injection) of heroin is common among chronic users who are either unable or reluctant to inject the drug intravenously. *C. botulinum* spores, which may either be in the heroin or in the liquid in which it is dissolved, are not destroyed by heating the heroin/liquid mixture. Inoculated into subcutaneous tissue, the spores can germinate and create toxin.[2]

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Wound botulism cases secondary to black tar heroin use could be occurring in Texas. According to the Texas Council on Alcohol and Drug Abuse (TCADA), black tar heroin has been one of the most commonly used forms of the drug in Texas for at least 25 years. Injection is the administration method of choice for the majority of Texas heroin users. A 1993 TCADA study of the male inmate population in Texas revealed that 8% of male heroin users had practiced the "skin popping" method.[3] The following year, a TCADA study of the female inmate population revealed that 12% of female heroin users had practiced the "skin popping" method.[4]

Diagnosis and Treatment

Botulism should be suspected in all patients with acute onset of flaccid paralysis with ophthalmoplegia, ptosis, or other cranial nerve dysfunction–particularly when the paralysis is descending, symmetric, and associated with a normal cerebrospinal fluid protein level. Such patients often have slurred or nasal speech and complain of blurred or double vision and difficulty in swallowing. A history of injecting drug use or a food history that does not identify a possible source for foodborne botulism should prompt consideration of wound botulism and elicitation of a thorough history. A meticulous physical examination for evidence of cellulitis or abscess is necessary because wounds containing *C. botulinum* may be small and initially unnoticed. The diagnosis is supported by either conventional EMG showing potentiation after supramaximal stimulation at 20-50 Hz, or single-fiber EMG showing increased jitter and blocking.[2] Because respiratory arrest poses the greatest threat to the patient's well-being, serial vital capacities should be followed.

For suspected cases of wound botulism, collect blood and tissue samples as early in the course of disease as possible. Send serum from 30cc of blood cold (preferably frozen) on dry ice. Procure a tissue sample (preferably by excision) from any evident wounds, including fracture sites. Keep tissue samples moist and place in a sterile petri dish; seal dish in an anaerobic transport pouch and ship cold but not frozen. Submit a stool sample if foodborne botulism is a possibility. Call Suzanne Barth at (512) 458-7214 prior to shipping samples to TDH.

Initial treatment decisions need not await neurologic or laboratory test results. Both risk of death and duration of hospitalization can be reduced by prompt administration of botulinal antitoxin. Wounds suspected of *C. botulinum* contamination should be widely debrided and irrigated, ideally after the administration of antitoxin.[2]

The Centers for Disease Control and Prevention releases botulism antitoxin only after consultation with state health officials. Suspected botulism cases must be reported **immediately** by phone; call (800) 705-8868.

Prepared by Mardi VanEgdom, TDH Infectious Disease Epidemiology and Surveillance Division and Robert Pinter, MD, Assistant Professor of Preventive Medicine, Internal Medicine, and Community Health, University of Texas Medical Branch (UTMB), Galveston.

Acknowledgment: The author acknowledges scientific, medical, and statistical information provided by Marta Ackers, MD, Foodborne and Diarrheal Diseases Branch, CDC; Steven G. Davis, MD, Norma B. Melamed, MD, Joseph Viroslav, MD, and John S. Webb, MD, St. Paul Medical Center; Jane Maxwell, MA, Director of the Research Department, TCADA; James McGee, MSPH, Botulism Diagnostic Laboratory, State of California Department of Health Services; and S. Benson Werner, MD, Chief, Disease Investigations, California Department of Health Services.

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3. Farabee D. Substance abuse among male inmates entering the Texas Department of Criminal Justice - Institutional Division: 1993. Texas Commission on Alcohol and Drug Abuse. Austin, October 1994.

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Red Tide in Laguna Madre

As of October 18, a red tide, or bloom, that began September 15 near Port Aranasas now extends from Matagorda Bay to the mouth of the Rio Grande River. A Texas Department of Health ban on the harvesting of oysters, clams, and mussels from these coastal waters is still in effect. The red discoloration of the water is due to an explosive growth of *Gymnodinium breve* (formerly called *Ptychodiscus brevis*), a dinoflagellate species of marine plankton. This single celled organism produces 2 heat-stable brevetoxins (A and B) which cause gill paralysis in vertebrate fish. Brevetoxins do not appear to harm shellfish but do bioaccumulate in these organisms, making them toxic to humans.

Consumption of oysters, clams, and mussels caught during a red tide can cause neurotoxic shellfish poisoning (NSP) in humans. While other seafood such as fish, crabs, and shrimp may die during blooms, they do not bioaccumulate the toxin. Caught alive, even from red-tide waters, these types of fish are safe to eat when cooked. Any type of seafood washed ashore should never be consumed.

There is no specific diagnostic laboratory test for NSP, so diagnosis is based on clinical evaluation of cases with relevant exposures. Onset of NSP symptoms usually occurs within 3 hours after ingestion of affected shellfish (range: 15 minutes to 18 hours after exposure). Symptoms are associated with progressive paresthesias which first affect the area around the mouth and later the pharynx, trunk, and limbs. Typical complaints include nausea, abdominal pains, diarrhea, dysphonia, ataxia, incoordination, headache, and generalized muscle weakness. A reversal of hot and cold temperature sensation, similar to that seen in ciguatera poisoning, has been reported. In cases of severe poisoning, dilated pupils, bradycardia, and, rarely, convulsions requiring respiratory support may also be seen.

No specific antitoxin is available, so treatment should be supportive in nature. Patients should be kept well hydrated, particularly if vomiting or diarrhea have been excessive. Patients with high levels of exposure may require brief hospitalization for observation. The illness is self-limiting, and symptoms generally subside in less than 24 hours with supportive therapy.

NSP should not be confused with paralytic shellfish poisoning (PSP), which is caused by a saxitoxin elaborated by a different dinoflagellate. PSP symptoms are similar, but far more severe: the characteristic neurologic symptoms can progress rapidly to respiratory paralysis and death. NSP is generally milder than either PSP or ciguatera poisoning, and human fatalities have not been documented.

During this incident, some tourists have complained of irritated eyes and respiratory problems. Vigorous mechanical action of the surf can cause aerosolization of the toxin. Brief human exposure to the airborne irritants may lead to an acute but rapidly reversible syndrome, characterized by conjunctival irritation, rhinorrhea, sneezing, and cough. Respiratory distress similar to an asthma attack has been reported. Irritative symptoms usually subside when the person leaves the affected area. During this bloom, however, individuals have complained that respiratory irritation continued for several hours to several days. Asthmatics and persons with prolonged exposure may be at increased risk of experiencing lingering effects.

To report suspected cases of human illness, call Richard A. Beauchamp, MD, of the TDH Bureau of Epidemiology, at (512) 458-7268. For further information regarding the status of this bloom and the safety of Gulf Coast seafood, contact Kirk Wiles of the TDH Seafood Safety Division at (512) 719-0215.

Perspectives in Public Health: Texas Department of Health (TDH) Quarterly CME Conference

On December 13, 1996, from 8:30 AM to 4:00 PM, the Texas Department of Health (TDH) will present its Perspectives in Public Health: TDH Quarterly CME Conference. Designed for public health and primary care physicians, the conference will be held at the TDH Headquarters in Austin, Texas. The program will consist of lectures supplemented by audiovisual slide presentations.

After attending this conference, the participants will be able to

- prevent, detect at an early stage, treat, control, or take remedial action against specific medical conditions that may adversely affect the health of individuals and populations in Texas;
- identify policies, processes, and products that promote and protect the health of people and preserve environmental quality; and
- establish relationships with other physicians concerned with public health and preventive medicine issues through dialogue with presenters and other participants.

Topics covered at the upcoming conference include

- Crisis Intervention in the Clinical Setting
  Tracy R. Gordy, MD, Private Practice, Neuropsychiatric Associates of Austin, Austin, Texas
- Update on Benign Prostatic Hypertrophy: Tales from the Butcher, the Baker, & the Icemaker
  Durwood E. Neal, Jr., MD, Associate Professor, Surgery/Urology, Microbiology and Internal Medicine, The University of Texas Medical Branch, Galveston, Texas
- The Treatment of Upper Respiratory Infections in Children
  Scott Dowell, MD, MPH, Childhood and Respiratory Diseases Branch, Division of Bacterial and Mycotic Diseases, Centers for Disease Control and Prevention, Atlanta, GA
- Life Outside the Bubble: Animal, Food, and Environmental Risks For Immunocompromised Persons
  Frederick J. Angulo, DVM, PhD, Medical Epidemiologist, Foodborne and Diarrheal Diseases Branch, National Center for Infectious Diseases, Project Officer, USDA/FDA/CDC Foodborne Diseases Project, Emerging Infections Program, Atlanta, GA
- Commissioner's Hour: Data and Outcomes
  John R. Lumpkin, MD, MPH, Director, Illinois Department of Public Health, Springfield, Illinois

The Texas Department of Health designates this educational activity for up to 6 hours in Category 1 credit towards the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

The Texas Department of Health is accredited by the Texas Medical Association to sponsor continuing education for physicians.

This program has been reviewed and is acceptable for 6 prescribed hours by the American Academy of Family Physicians.

For further information call: Public Health Professional Education - (800) 252-8239, press 4, or (512) 458-7677. To register, complete and return the registration form located on the back page of this issue.

Disease Prevention News (ISSN 1068-7920) is a free, biweekly publication of the Texas Department of Health, Public Health Professional Education, 1100 West 49th Street, Austin, TX 78756-3199, (512) 458-7677. Periodical postage paid at Austin, TX.
http://www.tdh.state.tx.us/dpnhome.htm
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POSTMASTER: Send address changes to Disease Prevention News, 1100 West 49th Street, Austin, TX 78756-3199.

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Lunch is included with all registration fees

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