June 1999 volume 15 number 6

Georgia Epidemiology Report

Division of Public Health
http://health.state.ga.us

The Georgia Epidemiology Report is a publication of the Epidemiology Section of the Epidemiology and Prevention Branch, Division of Public Health, Georgia Department of Human Resources

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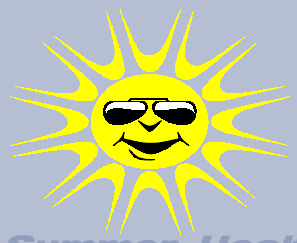

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Infectious diseases potentially associated with bioterrorism or intentional transmission

Editor's Note: Additions to the Notifiable Disease List (effective July 1, 1999). Seven diseases—plague, tularemia, Q fever, cyclosporiasis, yersiniosis, ehrlichiosis, and infection with Staphylococcus aureus with reduced susceptibility to vancomycin—have been added to the Notifiable Diseases List for Georgia, effective immediately. The first three are considered potential weapons of bioterrorism, and are discussed below, while the remaining four newly notifiable diseases will be described in another issue later in 1999.

Several recent events have focused public attention on the potential for infectious agents to be used in terrorist attacks. Biological agents and toxins are relatively easy to obtain, inexpensive, and difficult to detect. Advanced bioweapons programs in Iraq were revealed following the Persian Gulf War. A large biological weapons program was active in the Union of Soviet Socialist Republics (USSR) well into the 1980's, and little information about the supplies and scientists involved, or their current whereabouts, is available. The apocalyptic religious cult Aum Shinrikyo attempted to disseminate anthrax and botulinum toxin in Tokyo in the 1990's, and attempted to obtain the Ebola virus, before turning to the chemical agent sarin as a weapon. In the United States (US), several anti-government groups and individuals have planned the use of or successfully obtained biological agents and toxins such as plague and ricin. In response, several laws and appropriations dealing with bioterrorism have been enacted by the U.S. Congress. Federal authorities have recommended that local and State health departments improve and enhance surveillance and response capacity for diseases with potential for intentional transmission.

No bioterrorist event has occurred in Georgia, although hoaxes involving letters declaring to contain anthrax have occurred. Bioterrorism preparedness has become an important public health function, and is similar to planning for natural disasters, chemical or radiologic accidents, or pandemic influenza. A major component of bioterrorism preparedness is providing information for health care providers about the diseases that might be involved, and developing or enhancing reporting systems. The Centers for Disease Control and Prevention (CDC) have recommended that potential bioterrorism agents, such as plague, tularemia, Q fever, anthrax, brucellosis, smallpox and botulism, be designated as notifiable diseases. The common link among these infectious agents is their ability to be intentionally transmitted by aerosol. All except smallpox and botulism are zoonoses, meaning that disease is normally acquired from animals, which may also show signs of infection. Therefore, documented infection in persons who do not have known occupational, domestic or recreational exposures may be one clue that intentional transmission has occurred. A brief overview of the natural course of infection with plague, tularemia, and Q fever is presented in this issue.

1) Plague

Plague is a life-threatening disease caused by the gram negative bacterium *Yersinia pestis*. Transmission to humans occurs by the bite of animal fleas (usually rodent), by direct exposure to infected tissues, or via respiratory droplets from infected humans or animals. Persons with **bubonic** plague typically have an abrupt onset of fever, rigors,

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headache and myalgia beginning 2 to 8 days after exposure, concomitant with or followed shortly by severe pain and enlargement in regional lymph nodes (buboes) that drain the site of inoculation. Only a minority will have a skin lesion or visible bite at time of presentation. **Bubonic** plague may quickly progress to bacteremia and severe illness, or the disease may present only as a septicemia. **Pneumonic** plague has a shorter incubation period (2-3 days) and presents as a patchy bronchopneumonia that quickly progresses to respiratory failure and shock. The mortality rate for untreated **bubonic** plague approaches 50%; the mortality rate for untreated **pneumonic** or septicemic plague, and for those whose diagnosis is delayed beyond 18 hours, is considerably higher. Failure to consider the diagnosis, leading to delays in appropriate treatment, is common among U.S. patients.

Diagnosis (Table 1) is usually made by culture of tissue, blood, bubo aspirate or sputum. The organism grows slowly on culture media, and the optimal growth temperature is 28° C rather than the 37° used for most bacteria. *Y. pestis* may be seen in stained tissue preparations or bubo aspirates. For patients with bacteremia, a Wright stain of buffy coat preparations may demonstrate a characteristic bipolar staining pattern of the organisms within blood leukocytes. A fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen also is confirmatory. The Georgia State Public Health Laboratory offers culture diagnosis.

Aminoglycosides, chloramphenicol, tetracycline, and sulfa drugs all have activity against *Y. pestis*, although streptomycin is the drug of choice. Penicillin and cephalosporin-based antibiotics are ineffective. Chemoprophylaxis with chloramphenicol or tetracycline is recommended only for contacts of persons with **pneumonic** plague. Strict isolation for at least 48 hours after initiation of treatment is necessary for persons with **pneumonic** plague, as person-to-person transmission is possible. A vaccine is available but offers protection only against **bubonic** plague.

Plague is rare in the U.S. with fewer than 400 cases since 1943, and no person-to-person transmission has been documented since the 1920's. It has been decades since a case was identified in Georgia. However, the disease remains endemic in some western states, especially New Mexico, Arizona, California and Colorado. Plague should be suspected when travelers to these areas or possible victims of bioterrorism present with severe, systemic illness.

2) Tularemia

Tularemia is caused by the gram negative bacterium *Francisella tularensis*. The organism infects a remarkable variety of animal species, including mammals, birds, amphibians and fish. Tularemia can be acquired by humans through contact with infected animal tissues, or by a bite from an infected tick or deerfly. Inhalation of contaminated dusts and ingestion of contaminated material are less common routes of transmission. Mosquitoes are also an important vector in Scandinavian countries. Hunting or handling wild mammals, especially rabbits, is a risk factor for tularemia. The organism is killed by thorough cooking, but survives freezing. Person-to-person transmission has not been documented.

The incubation period from exposure to clinical symptoms ranges from 1 to 14 days, depending upon the inoculum size and route. At least 6 distinct clinical syndromes for patients with tularemia are recognized. The most common is an ulceroglandular syndrome with painful, enlarged lymph nodes draining from the ulcerated site of inoculation (tick bite or laceration). The glandular form is similar, but a primary ulcer is not present. An oropharyngeal form, with painful pharyngitis, vomiting and abdominal pain, may follow ingestion. The typhoidal form presents as a primary septicemia, or fever of unknown origin, and usually follows inhalation or ingestion. An oculoglandular form results from inoculation into the conjunctiva. Finally, a pleuropulmonary form may follow inhalation exposures. All forms of tularemia are frequently complicated by pneumonitis, and without early recognition and treatment of disease, mortality rates may be as high as 30%. Treatment with aminoglycosides, tetracycline, doxycycline or chloramphenicol is effective, but streptomycin is the drug of choice. An investigational vaccine has been developed but is not widely available.

Tularemia is usually diagnosed (Table 1) by demonstrating a fourfold rise in serum antibody titer to *F. tularensis* antigen between acute- and convalescent-phase specimens. Laboratory culture of *F. tularensis* poses a significant risk to laboratory workers, and should only be attempted by trained personnel in specialized facilities. The Georgia State Public Health Laboratory offers culture diagnosis. The circumstances necessary for natural transmission to humans are present in Georgia, and several cases have been diagnosed in recent years. Tularemia should be suspected when persons with wild animal or tick exposures or possible victims of bioterrorism present with fever or pneumonia.

3) Q fever

Q fever is caused by the rickettsial bacterium *Coxiella burnetii.* The odd name for this disease is derived from it being listed as "? fever" by investigators earlier in this century, who could not isolate the cause of the disease. *C. burnettii* normally infects sheep, goats, and cattle, especially their placental tissues, but can cause illness in a wide variety of mammals. Parturient cats (cats that are birthing) have been implicated in several outbreaks. The organisms are highly infectious, and are easily inhaled in contaminated aerosols or dusts (which may travel great distances from their origin), or from infected animal tissue. Unpasteurized cheese may also transmit disease. Person-to-person transmission is very unusual, but has been reported after exposure to infected human tissue, or the laundry of infected persons. *C. burnettii* is very resistant to drying and chemical agents and may remain viable in dust for months.

Following a long incubation period of 2 to 6 weeks, Q fever most commonly presents as an "atypical pneumonia" syndrome. An abrupt onset of high fever, chills and severe headache is typical, and hepatomegaly or splenomegaly is common. Serum aminotransferases are usually elevated and a syndrome resembling acute viral hepatitis may occur. Unlike most rickettsial diseases, a rash is not usually observed. The disease is often self-limited, but treatment with tetracycline or doxycycline may shorten the course and is advised. Chronic Q fever develops in a few patients, presenting as "culture-negative" endocarditis. No vaccine is commercially available.

Q fever is usually diagnosed (Table 1) by demonstrating a fourfold rise between acute- and convalescent-phase specimens in serum antibody titer to *C. burnettii* antigen. Laboratory culture of *C. burnettii* poses a significant risk to laboratory workers, and is not advised. Serologic testing is offered by the Georgia State Public Health Laboratory. Several cases of Q fever have been diagnosed in Georgia in recent years, and Q fever should be considered when a person with animal exposures or a possible victim of bioterrorism present with pneumonia and/or hepatitis.

Suspected cases of plague, tularemia or Q fever should be reported immediately to the Georgia Division of Public Health, Epidemiology and Prevention Branch, at 404-657-2588.

This article was contributed by Anthony Fiore, M.D., M.P.H.

Additional Readings:

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Table 1: Diagnostic criteria for plague, tularemia, and Q fever

PLAGUE	
Presumptive	Elevated serum antibody titer to *Y. pestis* fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination *or* Detection of F1 antigen in a clinical specimen by fluorescent assay
Confirmatory	Isolation of *Y. pestis* from a clinical specimen *or* Fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen
TULAREMIA	
Presumptive	Elevated serum antibody titer to F. tularensis antigen (without documented fourfold or greater change) in a patient with no history of tularemia vaccination *or* Detection of *F. tularensis* in a clinical specimen by fluorescent assay
Confirmatory	Isolation of *F. tularensis* in a clinical specimen *or* Fourfold or greater change in serum antibody to *F. tularensis* antigen
Q FEVER	
Presumptive	Elevated serum antibody titer to *C. burnettii* antigen (without documented fourfold or greater change) in a patient with no history of Q fever vaccination *or* Detection of *C. burnettii* in a clinical specimen by fluorescent assay
Confirmatory	Isolation of *C. burnettii* in a clinical specimen *or* Fourfold or greater change in serum antibody to *C. burnettii* antigen

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June 1999 **Volume 15 Number 6**

Reported Cases of Selected Notifiable Diseases in Georgia Profile* for March 1999

Selected Notifiable Diseases	Total Reported for March 1999	Previous 3 Months Total Ending in March			Previous 12 Months Total Ending in March		
	1999	1997	1998	1999	1997	1998	1999
Campylobacteriosis	39	113	130	155	745	783	798
Chlamydia genital infection	1271	3284	6081	4023	13631	18993	23192
Cryptosporidiosis	22	8	27	53	88	93	178
E. coli O157:H7	0	14	2	1	49	34	81
Giardiasis	65	214	208	258	873	910	1268
Gonorrhea	911	4342	4942	3168	18907	19141	18897
Haemophilus influenzae (invasive)	6	18	20	21	49	44	70
Hepatitis A (acute)	54	112	199	140	471	850	829
Hepatitis B (acute)	10	30	82	39	83	276	166
Legionellosis	0	0	0	0	2	6	8
Lyme Disease	0	1	2	0	2	10	3
Meningococcal Disease (invasive)	5	35	45	19	124	117	76
Mumps	0	5	0	0	13	6	2
Pertussis	4	8	3	7	37	13	42
Rubella	0	0	0	0	0	0	0
Salmonellosis	70	242	207	255	1449	1345	1907
Shigellosis	22	253	230	70	1246	1181	990
Syphilis - Primary	7	43	32	23	187	150	111
Syphilis - Secondary	2	97	57	43	454	323	219
Syphilis - Early Latent	38	331	237	159	1306	1029	705
Syphilis - Other**	17	381	223	84	1165	1074	656
Syphilis - Congenital	1	5	0	4	29	16	16
Tuberculosis	43	189	138	112	761	644	605

* The cumulative numbers in the above table reflect the date the disease was first diagnosed rather than the date the report was received at the state office, and therefore are subject to change over time due to late reporting. The 3 month delay in the disease profile for a given month is designed to minimize any changes that may occur. This method of summarizing data is expected to provide a better overall measure of disease trends and patterns in Georgia.

** Other syphilis includes latent (unknown duration), late latent, late with symptomatic manifestations, and neurosyphilis.

AIDS Profile Update

Report Period	Total Cases Reported *		Percent Female	Risk Group Distribution (%)						Race Distribution (%)		
				MSM	IDU	MSM&IDU	HS	Blood	Unknown	White	Black	Other
Latest 12 Months:												
4/98 - 3/99	1291	20.4	36.8	15.2	4.9	13.1	0.8	29.1	23	74.5	2.5	
Five Years Ago:												
4/93 - 3/94	1944	15.7	44.8	22.4	5.6	13	1.1	13.1	31.6	66.5	1.9	
Cumulative:												
7/81 - 3/99	20322	15.4	50.6	19.2	5.8	12.2	1.9	10.3	38	59.9	2.1	

MSM - Men having sex with men **IDU - Injection drug users** **HS - Heterosexual**

* Case totals are accumulated by date of report to the Epidemiology Section