VIRGINIA
EPIDEMIOLOGY BULLETIN

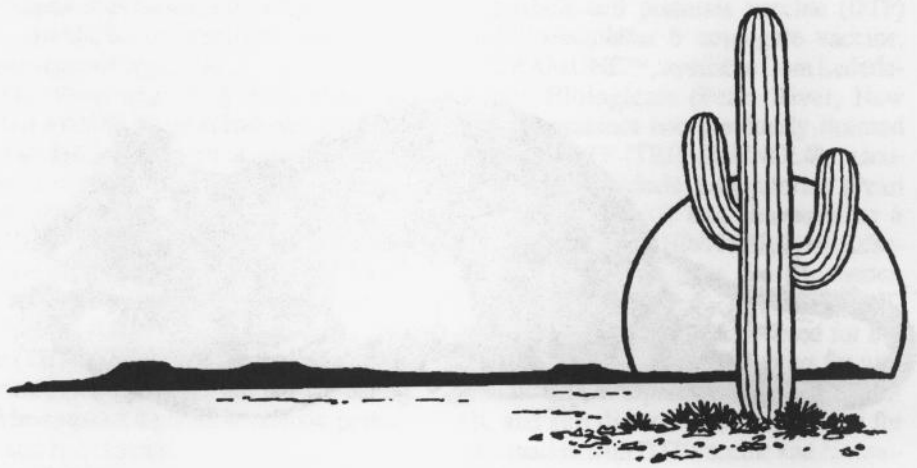
Robert B. Stroube, M.D., M.P.H., Commissioner
Grayson B. Miller, Jr., M.D., Epidemiologist
Editor: Carl W. Armstrong, M.D., F.A.C.P.

June, 1993

Volume 93, Number 6

Outbreak of Acute Illness – Southwestern United States, 1993*

Beginning in May 1993, cases of acute illness characterized by fever, myalgias, headache, and cough, followed by rapid development of respiratory failure, have been reported to the New Mexico Department of Health (NMDOH), Arizona Department of Health Services(ADHS), Colorado Department of Health (CDH), and Utah Department of Health (UDH). This report presents preliminary findings from an ongoing investigation of this problem, which suggest this illness is associated with a previously unrecognized hantavirus.

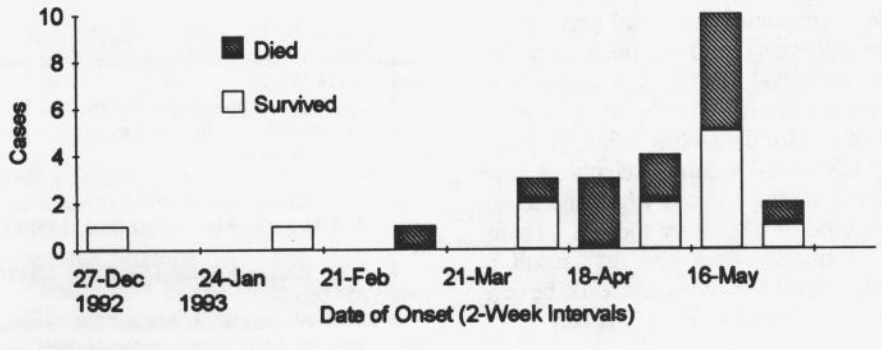


On May 14, the NMDOH was notified by the Office of the Medical Investigator that two persons living in the same household had died within 5 days of each other. Their illnesses were characterized by abrupt onset of fever, myalgias, headache, and cough, followed by the rapid development of respiratory failure. Tests for *Yersinia pestis* and other bacterial and viral pathogens were negative. After additional persons who had recently died following a similar clinical course were reported to the the NMDOH by the Indian Health Service (IHS), the ADHS, CDH, and UDH were contacted by the NMDOH seeking other possible cases.

To identify cases, public health officials established a provisional surveillance case definition of 1) radiographic evidence of unexplained bilateral pulmonary interstitial infiltrates with hypoxemia (arterial oxygen saturation of <90% while breathing room air) or 2) an autopsy finding of unexplained noncardiogenic pulmonary edema occurring during 1993. Through June 7, a total of 24 case-patients have been identified. Case-patients had onsets of illness beginning in December 1992; most (14) had onset in May (Figure 1). The most recent case-patient had onset of illness June 1. Case-patients resided in New Mexico (17), Arizona (five), Utah (one), and Colorado (one). Their median age was 34 years (range: 13-87 years; 17 were aged 18-50 years). Thirteen were male. Fourteen case-patients were American Indians, nine were white, and one was Hispanic. Twelve (50%) case-patients have died.

Clinical and autopsy specimens are being processed and analyzed by CDC. Preliminary results include detection of rising titers of antibodies to hantaviruses in paired serum specimens from two of the nine case-patients; elevated single anti-

Cases of Acute Illness, by 2-week Interval of Onset, Arizona, Colorado, New Mexico, and Utah, December 27, 1992-June 5, 1993



body titers were present in four other of the nine case-patients. The pattern of cross-reactivity to four different hantaviruses suggests that the infection is due to a previously unknown hantavirus. The NMDOH, ADHS, CDH, UDH, IHS, and CDC, with the assistance of the Navajo Nation Division of Health, are conducting intensive epidemiologic, laboratory, and environmental investigations to further define this unexplained illness cluster, determine the etiology of the illness, identify the source and mode of transmission, and develop prevention and control measures.

Editorial Note:

The preliminary laboratory findings of this investigation suggest a possible role for a hantavirus or related agent as a cause of this outbreak. Although this unexplained illness shares some clinical features with syndromes caused by hantaviruses, it lacks the prominent renal involvement and hemorrhagic manifestations previously reported with these agents.[1] Additional data are necessary to confirm these preliminary results. If verified, the role of this agent in the pathogenesis of the illnesses will require further study. Isolation of the first recognized hantavirus (Hantaan virus) was reported from Korea in 1978.[2] Although there are four recognized members (Hantaan, Puumala, Seoul, and Prospect Hill) of the genus Hantavirus of the family Bunyaviridae,[3] additional unidentified members likely exist. Hantaan, Puumala, and Seoul viruses are known human pathogens; Prospect Hill has not been associated with disease. Since the 1930s, epidemic and sporadic hantavirus-associated disease has been described throughout Eurasia, especially in Scandinavia and northeastern Asia. In the 1950s, thousands of United Nations military personnel were infected with hantaviruses during the Korean conflict;[1] more recently, transmission has been documented among U.S. military personnel training in Korea.[4] Hantaviruses have been isolated from rodents in the United States,[5] and serologic studies have documented human infections with hantaviruses.[6] However, acute disease associated with infection by pathogenic hantaviruses has not previously been reported in the Western Hemisphere.

The clinical manifestations of infection with these viruses vary; illness resulting from Hantaan virus infection generally includes fever, renal abnormalities, and in severe cases, shock, bleeding, and pulmonary edema.[1] The incubation period for the known pathogenic hantaviruses, although highly variable, generally ranges from 2 to 4 weeks.[3]

Rodents are the natural hosts for all known hantaviruses.[3] Humans are thought to be at risk for infection after exposure to rodent excreta, either through the aerosol route or direct inoculation. There is no evidence of person-to-person transmission for any of the known hantaviruses, nor has occupational transmission been documented to health-care workers. Laboratory workers practicing universal precautions while processing routine clinical materials (such as blood, urine, and respiratory specimens) are not considered to be at increased risk for hantavirus infection. However, laboratory-acquired infections have occurred among persons who handled infected wild or laboratory rodents.[7] Therefore, laboratory work that may result in propagation of hantaviruses should be conducted in a biosafety level 3 facility.[8]

No restriction of travel to areas affected by this outbreak is considered necessary; however, activities that may disrupt rodent burrows or result in contact with rodents or aerosolization of rodent excreta should be avoided. In the affected area, measures prudent for rodent control should be carried out in domestic settings, including wetting of rodent nests and dead rodents with disinfectant before their removal, securing foods from rodent access, and trapping rodents indoors. Broader measures to control rodents will be recommended once the specific rodent host(s) has been identified and the expected effects on the ecology of local rodent borne diseases, particularly plague, have been considered.

In one controlled study, intravenous administration of the antiviral drug ribavirin was effective in treating severe cases of hantavirus infection when administered early in the course of illness.[9] However, intravenous ribavirin is not licensed for use in the United States. Therefore, in the affected areas of the Southwest, clinicians considering use of ribavirin for treatment of potential cases should consult with their state health department.

The surveillance case definition used in this investigation is provisional. As additional information is gathered and the etiologic agent is characterized, the definition may require revision. Suspected cases should be reported immediately to public health authorities for further investigation. CDC has established a hotline to provide updated information on the unexplained illness outbreak and to report suspected cases; the number is (800)532-9929.

This cluster of unexplained acute illnesses in the Southwest illustrates the potential for new infectious disease problems to emerge at any time within the United States.[10] These diseases may emerge because of microbial adaptation, environmental disturbances or changes, or population shifts. Vigilance and surveillance are required to rapidly recognize and determine the etiology of these emerging microbial threats to health so that prevention and control strategies can be implemented.

References

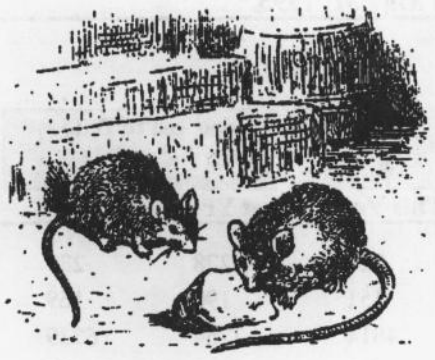
1. Sheedy JA, Froeb HF, Batson HA, et al. The clinical course of epidemic hemorrhagic fever. Am J Med 1954;16:619-28.

2. Lee HW, Lee PW, Johnson KM. Isolation of the etiologic agent of Korean hemorrhagic fever. J Infect Dis 1978;137:298-308.

3. McKee KT Jr, LeDuc JW, Peters CJ. Hantaviruses. In: Belshe RB, ed. Textbook of human virology, 2nd ed. St. Louis: Mosby Year Book, 1991:615-32.

4. CDC. Korean hemorrhagic fever. MMWR 1988;37:87-90,95-6.

5. LeDuc JW, Smith GA, Johnson KM. Hantaan-like viruses from domestic rats captured in the United States. Am J Trop Med Hyg 1984;33:992-8.



6. Childs JE, Glass GE, Korch GW, et al. Evidence of human infection with a rat-associated hantavirus in Baltimore, Maryland. Am J Epidemiol 1988;127:875-8.

7. Desmyter J, LeDuc JW, Johnson KM, Brasseur F, Deckers C, van Ypersele de Strihou C. Laboratory rat associated outbreak of haemorrhagic fever with renal syndrome due to Hantaan-like virus in Belgium. Lancet 1983;2:1445-8.

8. CDC/National Institutes of Health. Biosafety in microbiological and biomedical laboratories. 2nd ed. Atlanta: US Department ofHealth and Human Services, CDC, 1988; DHHS publication no.(CDC)88-8395.

9. Huggins JW, Hsiang CM, Cosgriff TM, et al. Prospective, double-blind, concurrent, placebo-controlled clinical trial of intravenous ribavirin therapy for hemorrhagic fever with renal syndrome. J Infect Dis 1991;164:119-27.

10. Lederberg J, Shope RE, Oaks SC Jr, eds. Emerging infections: microbial threats to health in the United States. Washington, DC: National Academy Press, 1992.

**Reprinted from MMWR 1993;42:421-424.*

Announcing the Fourth National Research Conference on Pesticides:

"New Directions in Pesticide Research, Development, Management, and Policy."

- Where: Hyatt Richmond, Richmond, Virginia.
- Sponsor: the Virginia Water Resources Research Center, Virginia Polytechnic Institute and State University.
- For further information and registration: contact Dr. Diana L. Weigmann, Interim Director, Virginia Water Resources Research Center, Virginia Polytechnic Institute and State University, 617 North Main Street, Blacksburg, Virginia 24060-3397, phone: (703) 231-8039.

New *Haemophilus* b Conjugate Vaccine and a Combined Diphtheria-Tetanus-Pertussis and *Haemophilus* b Conjugate Vaccine Approved*

Haemophilus influenzae type b (Hib) conjugate vaccines have been recommended for use in infants since 1990, and their routine use in infant vaccination has contributed to the substantial decline in the incidence of Hib disease in the United States. Vaccines against diphtheria, tetanus, and pertussis during infancy and childhood have been administered routinely in the United States since the late 1940s and have been associated with a greater than 90% reduction in morbidity and mortality associated with infection by these organisms. Because of the increasing number of vaccines now routinely recommended for infants, a high priority is the development of combined vaccines that allow simultaneous administration with fewer separate injections.

The Food and Drug Administration (FDA) recently licensed two new products for vaccinating children against these diseases: 1) the *Haemophilus* b conjugate vaccine (tetanus toxoid conjugate, ActHIB™),† for vaccination against Hib disease only and 2) a combined diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTP) and Hib conjugate vaccine (TETRAMUNE™), a combination of vaccines formulated for use in vaccinating children against diphtheria, tetanus, pertussis, and Hib disease.

ActHIB™

On March 30, 1993, the FDA approved a new *Haemophilus* b conjugate vaccine, polyribosylribitol phosphate-tetanus toxoid conjugate (PRP-T), manufactured by Pasteur Merieux Serum et Vaccins and distributed as ActHIB™ by Connaught Laboratories, Inc. (Swiftwater, Pennsylvania). This vaccine has been licensed for use in infants in a three-dose primary vaccination series administered at ages 2, 4, and 6 months. Previously unvaccinated infants 7-11 months of age should receive two doses 2 months apart. Previously unvaccinated children 12-14 months of age should receive one dose. A booster dose administered at 15 months of age is recommended for all children. Previously unvaccinated children 15-59 months of age should receive a single dose and do not require a booster. More than 90% of infants receiving a primary vaccination series of ActHIB™ (consecutive doses at 2, 4, and 6 months of age) develop a geometric mean liter of anti-*Haemophilus* b polysaccharide antibody >1 μg/mL. This response is similar to that of infants who receive recommended series of previously licensed *Haemophilus* b conjugate vaccines for which efficacy has been demonstrated in prospective trials. Two U.S. efficacy trials of PRP-T were terminated early because of the concomitant licensure of other *Haemophilus* b conjugate vaccines for use in infants. In these studies, no cases of invasive Hib disease were detected in approximately 6000 infants vaccinated with PRP-T. These and other studies suggest that the efficacy of PRP-T vaccine will be similar to that of the other licensed Hib vaccines.

TETRAMUNE™

On March 30, 1993, the FDA approved a combined diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTP) and *Haemophilus* b conjugate vaccine. TETRAMUNE™, available from Lederle-Praxis Biologicals (Pearl River, New York), combines two previously licensed products, DTP (TRIIMMUNOL®, manufactured by Lederle Laboratories [Pearl River, New York]) and *Haemophilus b* conjugate vaccine (HibTITER®, manufactured by Praxis Biologics, Inc. [Rochester, New York]).

This vaccine has been licensed for use in children aged 2 months-5 years for protection against diphtheria, tetanus, pertussis, and Hib disease when indications for vaccination with DTP vaccine and *Haemophilus* b conjugate vaccine coincide. Based on demonstration of comparable or higher antibody responses to each of the components of the two vaccines, TETRAMUNE™ is expected to provide protection against Hib, as well as diphtheria, tetanus, and pertussis, equivalent to that of already licensed formulations of other DTP and *Haemophilus* b vaccines.

The Advisory Committee for Immunization Practices (ACIP) recommends that all infants receive a primary series of one of the licensed *Haemophilus* b conjugate vaccines beginning at 2 months of age and a booster dose at age 12-15 months. The ACIP also recommends that all infants receive a four-dose primary series of diphtheria and tetanus toxoids and pertussis vaccine at 2, 4, 6, and 15-18 months of age, and a booster dose at 4-6 years. A complete statement regarding recommendations for use of ActHIB™ and TETRAMUNE™ is being developed.

**Adapted from MMWR 1993;42:296-298.*

†Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Public Health Service or the U.S. Department of Health and Human Services.

Cases of Selected Notifiable Diseases, Virginia, May 1 through May 31, 1993.*

Disease	Total Cases Reported This Month						Total Cases Reported to Date in Virginia		
	State	Regions NW	N	SW	C	E	This Yr	Last Yr	5 Yr Avg
AIDS	101	10	41	9	31	10	824	278	230
Campylobacteriosis	43	3	7	8	18	7	151	190	169
Gonorrhea†	1388	-	-	-	-	-	4814	7764	6739
Hepatitis A	8	2	5	1	0	0	60	47	106
Hepatitis B	17	0	5	3	3	6	65	81	99
Hepatitis NANB	7	2	1	4	0	0	19	15	19
Influenza	0	0	0	0	0	0	867	122	1147
Kawasaki Syndrome	3	0	1	0	0	2	13	10	10
Legionellosis	0	0	0	0	0	0	2	10	6
Lyme Disease	11	2	6	1	1	1	16	19	15
Measles	0	0	0	0	0	0	1	6	41
Meningitis, Aseptic	17	4	6	1	1	5	73	77	68
Meningitis, Bacterial‡	17	0	3	4	2	8	43	66	72
Meningococcal Infections	7	0	1	0	5	1	20	34	27
Mumps	1	0	1	0	0	0	14	20	48
Pertussis	3	0	0	0	2	1	9	4	8
Rabies in Animals	52	24	4	9	10	5	155	116	120
Reye Syndrome	0	0	0	0	0	0	0	0	1
Rocky Mountain Spotted Fever	1	1	0	0	0	0	1	0	1
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	77	13	19	14	15	16	298	291	358
Shigellosis	61	4	2	0	33	22	157	73	126
Syphilis (1° & 2°)†	51	1	6	7	6	31	259	344	315
Tuberculosis	35	3	9	7	7	9	176	116	131

Localities Reporting Animal Rabies: Albermarle 1 bat; Amelia 1 fox; Augusta 1 cow, 1 fox, 2 skunks; Caroline 1 cat; Charlotte 1 skunk; Essex 1 raccoon; Fairfax 1 raccoon; Fauquier 1 fox, 2 raccoons; Floyd 2 raccoons, 1 skunk; Frederick 2 foxes; Fredericksburg 1 cat; Hanover 3 raccoons, 1 skunk; Henrico 1 bat, 1 raccoon; King William 2 raccoons; Loudoun 3 raccoons; Louisa 1 skunk; Lunenburg 1 raccoon; Madison 1 cow; Montgomery 1 fox; Northumberland 1 raccoon; Orange 1 fox, 1 raccoon; Page 1 skunk; Prince George 1 raccoon; Pulaski 2 raccoons; Roanoke County 1 bat; Rockingham 2 raccoons; Shenandoah 1 raccoon; Stafford 2 raccoons, 1 skunk; Virginia Beach 1 raccoon; Warren 1 bat; Wythe 1 cow, 1 raccoon.

Occupational Illnesses: Asbestosis 18; Carpal Tunnel Syndrome 66; Coal Workers' Pneumoconiosis 15; Lead Poisoning 2; Loss of Hearing 13; Repetitive Motion Disorder 1; Silicosis 1.

*Data for 1993 are provisional. †Total now includes military cases to make the data consistent with reports of the other diseases. ‡Other than meningococcal.

Published monthly by the
VIRGINIA HEALTH DEPARTMENT
Office of Epidemiology
P.O. Box 2448
Richmond, Virginia 23218

Telephone: (804) 786-6261

VDH VIRGINIA DEPARTMENT OF HEALTH
Protecting You and Your Environment

Bulk Rate
U.S. POSTAGE
PAID
Richmond, Va.
Permit No. 936