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

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Leishmaniasis in Desert Storm Troops

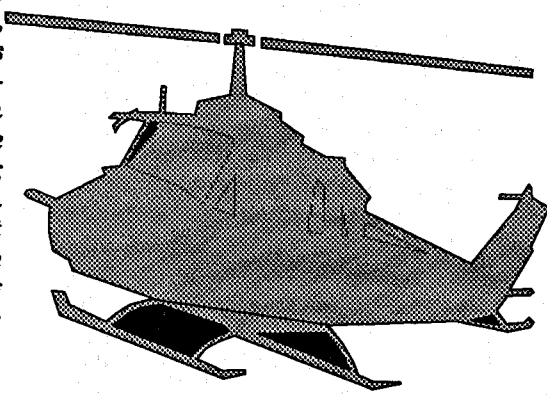
Answers to Frequently Asked Questions

In mid-November the Department of Defense (DOD) announced that it would defer accepting blood donations from service personnel returning from the Persian Gulf region because leishmaniasis had been confirmed in several servicemembers. Due to the large number of reservists involved in Operation Desert Storm, many of the questions raised by this announcement were directed to non-military physicians and local health departments. What follows are the answers to many of those questions; responses are taken largely from statements issued by the Department of Defense, the Centers for Disease Control (CDC), the Food and Drug Administration (FDA), and the American Association of Blood Banks (AABB).

What is leishmaniasis?

Leishmaniasis is a protozoan infection that exists in two major clinical forms: a cutaneous or mucocutaneous form ("Baghdad boil"), and a visceral form ("Kala-azar"). Infection occurs in southwest Asia and certain other parts of the world, but is very rarely seen in the United States. In the Old World the cutaneous form is caused primarily by *Leishmania tropica* and *L. major*, while the visceral form is caused primarily by *L. donovani*.

This traditional distinction is blurred by the recent findings of a viscerotropic form due to *L. tropica* among military personnel who deployed to southwest asia (SWA) during the gulf war. In seven cases of *L. tropica* infection diagnosed at Walter Reed Army Medical Center (WRAMC), patients were free of cutaneous lesions but the parasite was recovered from the bone marrow. Fifteen gulf-related cases of the traditional cutaneous form (skin lesions and temporary fever) due to *L. tropica* were also diagnosed and treated at WRAMC.



How many servicemembers are infected?

Only these 22 servicemembers, out of a half million deployed to the gulf, have been found to be infected with *Leishmania*. Military medical personnel are now trying to determine how prevalent the disease may be among returning servicemembers. Although DOD physicians believe the number of cases is small, they want to ensure that all cases are quickly detected and treated.

What are the clinical manifestations?

Cutaneous leishmaniasis of the Old World usually presents with one or more skin lesions on exposed surfaces of the body two to eight weeks following sandfly bites. Lesions begin as small (2-5 mm) erythematous papules which enlarge over time to become nodules 1-2 cm in diameter. A central crust eventually falls off leaving a painless ulcer which heals after several years, leaving a scar.

Development of a papule at the site of a sandfly bite within days of exposure is the earliest manifestation of visceral leishmaniasis. Two to six months later, systemic manifestations begin insidiously with fever, weight loss, hepatosplenomegaly, and lymphadenopathy. Late manifestations include anemia, bleeding tendencies, and jaundice. Untreated, the infection may be fatal.

The clinical spectrum for the newly recognized viscerotropic form of *L. tropica* infection was variable and nonspecific. Four of the six symptomatic cases had an acute syndrome which included a high fever with rigors and malaise, accompanied by

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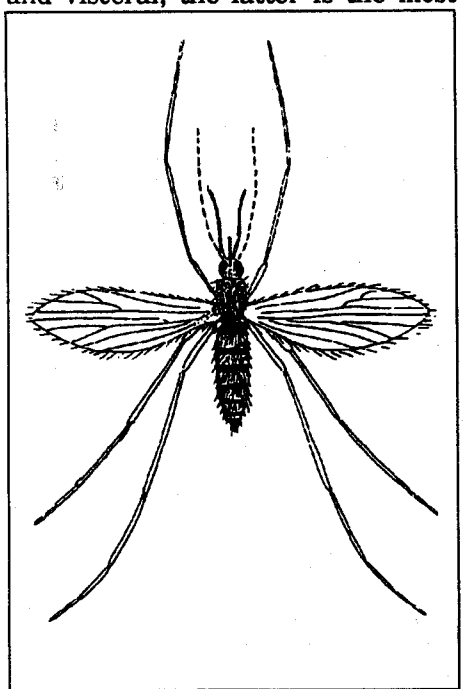
mild anemia and low grade elevation of liver enzymes (AST and ALT). Two cases had a subacute onset, presenting with gastrointestinal complaints which included watery, fecal-leucocyte-negative diarrhea (of small volumes), nausea, and non-focal abdominal pain that evolved over time to left upper quadrant pain with hepatosplenomegaly. Headaches and chronic irritating cough were also seen in some cases. One of the seven cases was completely asymptomatic and diagnosed on the basis of epidemiologic follow-up of an index case. The incubation period was difficult to accurately measure. However, in these cases, the onset of symptoms varied from weeks to months after leaving SWA.

Based on the current cases, the clinical appearance is much less severe (in immunocompetent individuals) than that seen in classical visceral leishmaniasis (kala-azar) caused by *L. donovani*. The natural history of this new syndrome is not known. The fact that this has not been clinically apparent in the many travelers to and inhabitants of that region suggests that infections are rare, and/or largely subclinical.

How is infection diagnosed?

Of the two clinical forms of leishmaniasis, cutaneous/mucocutaneous and visceral, the latter is the most difficult to diagnose. Biopsy of liver, spleen, or bone marrow is usually needed to demonstrate the parasite in tissue. In the viscerotropic cases investigated by Walter Reed Army Institute for Research, smears of the aspirate were negative by giemsa stain, but the organism was detected using anti-*Leishmania* monoclonal antibodies tagged with fluorescein.

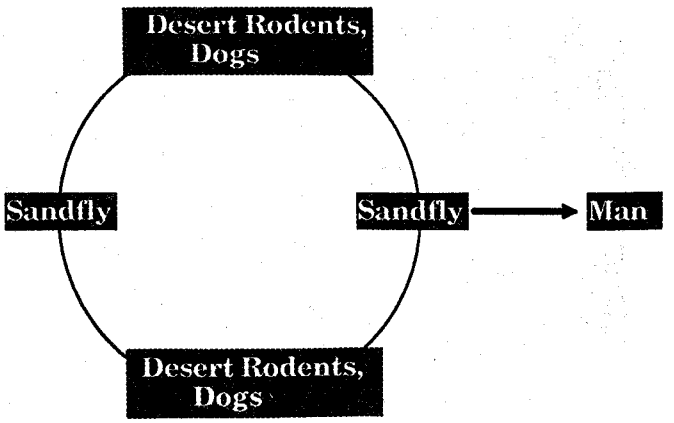


Sketch of a sandfly (*Phlebotomus* sp.), length ~2-3 mm. Courtesy of CDC.

Serum antibody detection is a useful adjunct for diagnosing visceral leishmaniasis but is less useful for cutaneous leishmaniasis. However, there is no commercially available serologic test currently available in the United States to confirm infection. Both the CDC and DOD use the immunofluorescent antibody (IFA) test for detection of anti-*Leishmania* antibodies. The IFA is helpful in differentiating leishmaniasis from other clinically similar conditions (in patients with suggestive signs and symptoms of *Leishmania* infection, a serum IFA ≥1:32 suggests infection) but cannot determine the species of *Leishmania*, which is often necessary for selecting appropriate therapy. False positives occur in patients with antibodies to *Trypanosoma cruzi*. At best, the specificity of IFA is 75% for both visceral and cutaneous disease. Based on very limited data, the sensitivity for visceral disease is roughly estimated to range from 80-90%, whereas the sensitivity for cutaneous disease is no better than 50%.

Should all returning service personnel be tested?

The CDC is not currently recommending routine serologic screening for leishmaniasis in any asymptomatic person, regardless of their travel history. Persons who have chronic skin lesions and/or unexplained febrile illnesses after returning from the Persian Gulf area should seek the advice of their personal physician or a specialist in infectious diseases.



How is infection transmitted?

The infection is spread primarily by bites from sandflies (*Phlebotomus* sp.) common to many parts of the world outside the U.S. Man is an incidental host. Transmission does not occur through sexual intercourse or person-to-person contact. Only five reported cases of leishmaniasis have ever been associated with blood transfusions worldwide, and in at least three of these cases the transfusions were received by children whose immune systems had not yet fully developed. These bloodborne infections were all due to *L. donovani*, not *L. tropica*. Thus, *L. tropica* is very unlikely to be present in blood donated for transfusion in the United States.

Which servicemembers are at greatest risk for this new form of leishmaniasis?

Epidemiologic risk factors for this viscerotropic form are not well defined at this time. The seven reported cases were in soldiers who were members of several different army units widely scattered throughout the SWA theater of operations in both field and urban settings. Navy, marine, air force and civilian personnel who were stationed within the theater of operations are presently considered to have been at risk of exposure.

How is infection treated?

The treatment of choice is sodium stibogluconate (Pentostam), an investigational new drug (IND) pro-

duced by Wellcome Trust of Great Britain. It is available under protocol to military physicians at WRAMC through Walter Reed Army Institute for Research, Washington, DC and to civilian physicians from the CDC, Atlanta, Georgia (see below).

Five of the seven cases with viscerotropic infection were treated with sodium stibogluconate. In two of these five cases, treatment was discontinued early because of thrombocytopenia. Following treatment, all five patients recovered, returned to duty and are being followed. A sixth case was asymptomatic and therefore not treated with sodium stibogluconate, but is being followed closely. The seventh and most recent case is still under care at WRAMC.

To obtain sodium stibogluconate for the treatment of parasitologically confirmed cases of leishmaniasis in non-DOD individuals, please call Ms. Susan Stokes or Mr. John Becher, CDC Drug Service: daytime 404/639-3670; evenings, weekends, holidays 404/639-2888.

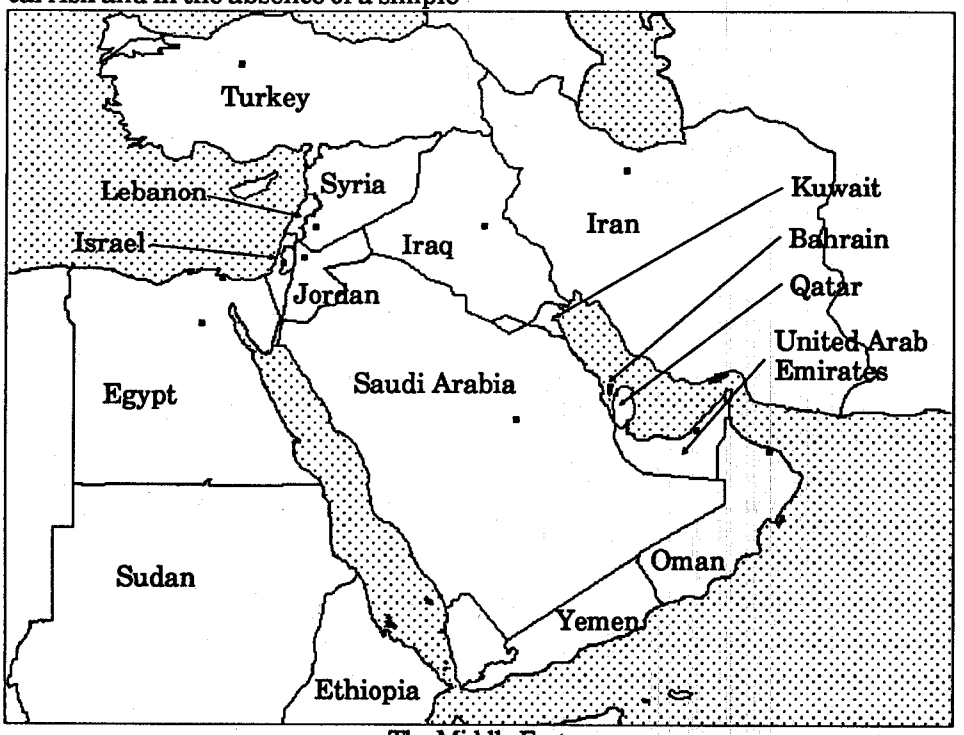
May returning service personnel donate blood?

Although no case of transfusion-associated transmission has been reported with *L. tropica*, these viscerotropic cases suggest a theoretical risk exists. Therefore, as a conservative safety precaution due to this theoretical risk and in the absence of a simple screening test, the Assistant Secretary of Defense (Health Affairs) has directed military services to defer until further notice all personnel from blood donation who were stationed in Saudi Arabia, Kuwait, Iraq, Bahrain, Qatar, United Arab Emirates, Oman and Yemen from 1 August 1990 and thereafter. The Department of Defense operates the Armed Services Blood Program separately from the general blood supply, drawing nearly all of its blood donations from military personnel.

The AABB has issued a similar statement for civilians who were in the same area, recommending deferral of donors of transfusable blood components until January 1, 1993. Donors of plasma intended for further manufacture need not be similarly deferred.

Blood products already collected from gulf war returnees currently in the inventory are not being withdrawn because of the very low risk of contamination balanced against the risk of a sudden shortfall of critical blood supplies. Under current procedures, donors who were symptomatic or blood units with an elevated ALT level would have already been excluded. None of the identified cases has donated blood and all patients with any form of leishmaniasis are permanently deferred from future donations. A blood donation history will be taken from any future case and, if positive, a complete lookback for that case will be conducted. The This delay will enable medical researchers to determine the level of additional infections among the exposed population and will also allow them to develop a screening test for infection.

When further information becomes available on the actual risk of transmission of *L. tropica* via transfusion, these recommendations may be modified. Although FDA and other Public Health Service agencies are carefully monitoring this situation, FDA believes that this treatable disease is unlikely to pose any significant threat to the blood supply or the public health.



The Middle East.

To whom should suspected cases be reported?

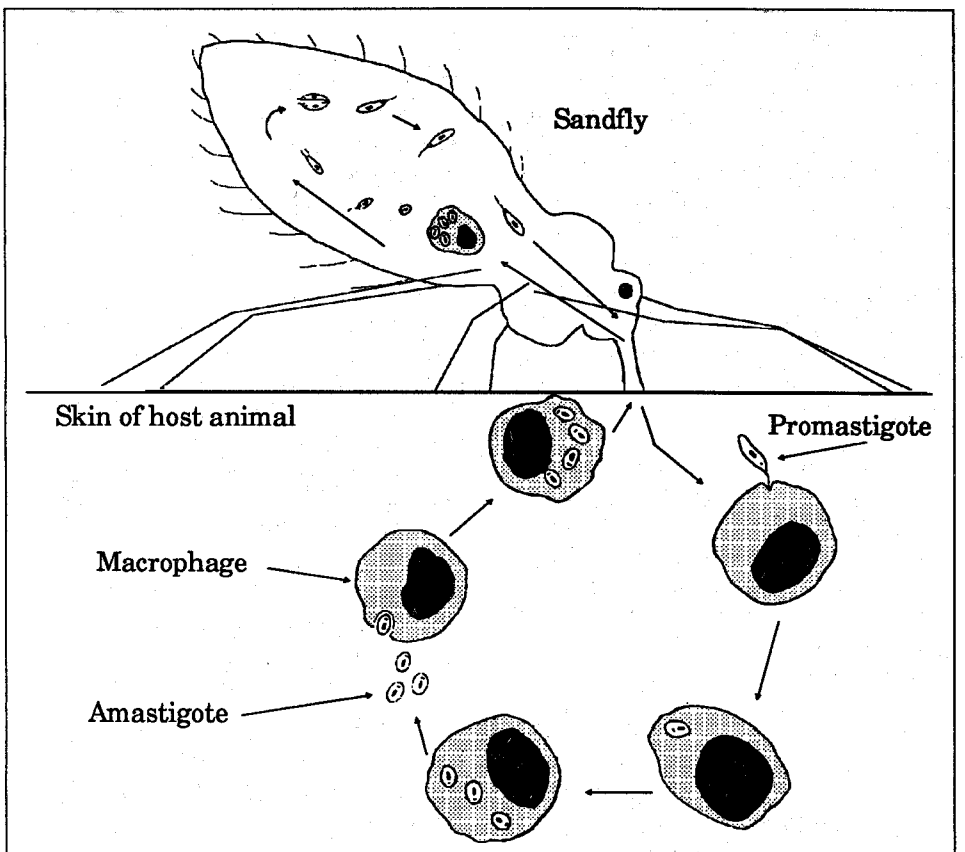
Any physician who suspects leishmaniasis involving DOD service personnel should contact the appropriate service infectious disease consultant.

- **U.S. Air force:** Gregory Melcher, MD, Maj, USAF, Wilford Hall Medical Center, Lackland Air Force Base, San Antonio, TX 78236, commercial Tel: 512/670-7444; DSN: 554-7444; Fax: 512/675-0173.
- **U.S. Navy/Marines:** Edward Oldfield, MD, Capt, USN, Naval Hospital, San Diego, CA 92134, commercial Tel: 619/532-7475; DSN: 522-7475; Fax: 619/532-2478.
- **U.S. Army:** Col. Charles Oster, MD, Infectious Disease Service Walter Reed Army Medical Center, Washington, DC 20307, 202/576-0585 (or -0586).

Any physician who suspects leishmaniasis involving non-DOD personnel should contact the appropriate local health department or the Office of Epidemiology, Virginia Department of Health (804/786-6261) and a report will be forwarded to CDC.

Where can one get additional information?

Questions from physicians and other health care professionals regarding transfusion-related clinical and scientific issues should be directed to FDA: Dr. John Finlayson, Acting Director, Hematology 301/496-0952; or Anne Hoppe, Acting



Based on Zaman V. Atlas of Medical Parasitology. Lea & Febiger, Philadelphia, 1980:45-57.

Life Cycle of Leishmania. Promastigote form is injected into skin by sandfly. These enter macrophage cells, and become amastigotes. Vector ingests infected host cells.

Director, Transfusion Services 301/227-6700.

Questions from physicians and other health care professionals regarding clinical diagnosis and management of DOD active duty military personnel and their dependents should be directed to the service-specific consultant listed above in the section on reporting. Other DOD points of contact (Office of the Surgeon General): Col. Peake 703/756-0141; Col. Erdtmann 703/756-0125; Col. Tomlinson 703/756-0135.

Questions from physicians and other health care professionals regarding the diagnosis and clinical management of suspected cases of leishmaniasis in persons not affiliated with the DOD may be directed to CDC: Dr. Barbara Herwaldt, Dr. Dennis Juranek, or Dr. Ralph Bryan National Center for Infectious Diseases, Division of Parasitic Diseases, Parasitic Diseases Branch 404/488-4050.

For questions specifically relating to serodiagnosis and culture of *Leishmania* sp., please call: Mr. Frank Steurer, National Center for Infectious Diseases, Division of Parasitic Diseases, Parasitic Diseases Branch 404/488-4414 (or -4415).

Questions from the press and general public regarding issues related to transfusion should be directed to:

- AABB: Ms. Marcia Lane 703/528-8200, Ext. 255.
- FDA: Mr. Brad Stone, or Ms. Faye Peterson 301/443-3285.
- DOD: Ms. Susan Hansen (media info) 703/695-0192.
- DOD: (public info) 703/697-5737.

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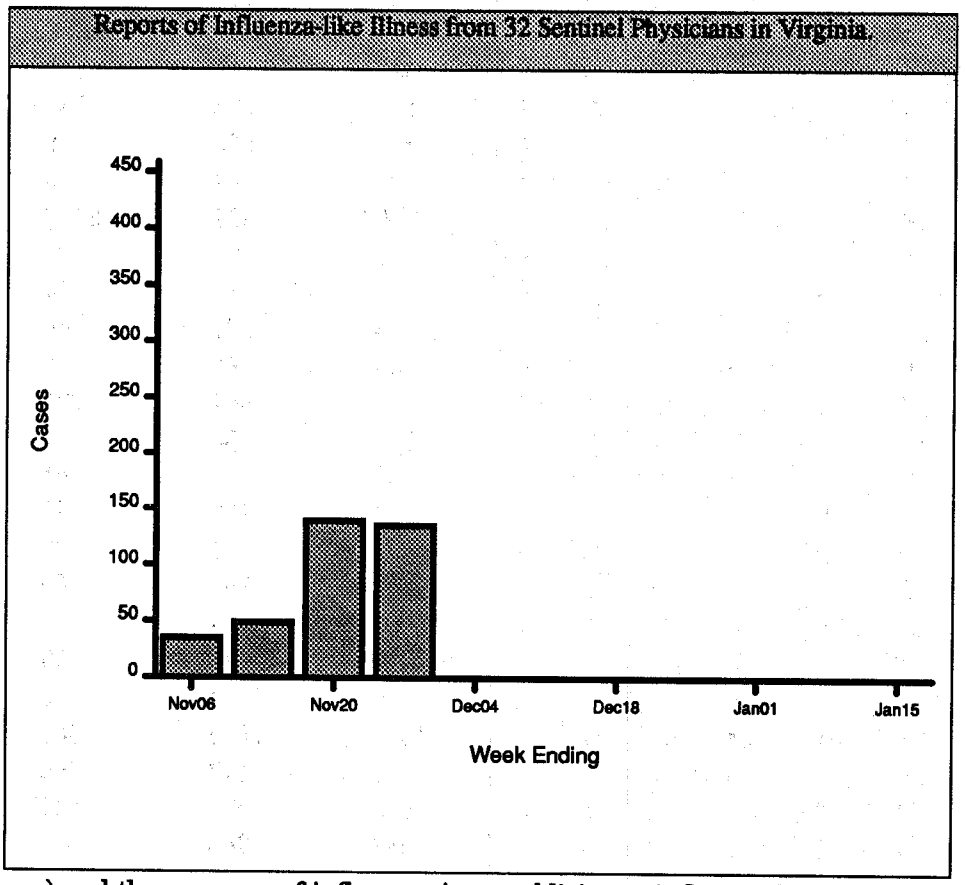
CDC Discontinues Distribution of Primaquine

CDC has been advised that the U.S. manufacturer (Winthrop Pharmaceuticals, New York) has resumed production of primaquine phosphate, the antimalarial drug that decreases the risk for relapses from *Plasmodium vivax* and *P. ovale*. Therefore, primaquine will no longer be available from the CDC Drug Service.

Influenza A isolated in Virginia

Influenza A virus has been isolated from two Virginia residents seen at the University of Virginia in Charlottesville. A confirmation of influenza A in Virginia was expected based on increased reports of flu-like disease throughout the state (see figure) and the presence of influenza A in the neighboring states of North Carolina and Tennessee.



Identification of the type of influenza virus that is circulating is important. Amantadine, an anti-viral drug, is available for reducing the severity of or preventing influenza A, but not influenza B. In the early stages of an influenza A outbreak in a facility where high-risk persons reside, the administration of amantadine to residents and employees can reduce the spread of infection.

This marks an unusually early start for the influenza season. This early start and attendant widespread publicity on influenza have led to an increased demand for vaccine. Although some shortages have been reported, enough vaccine should be available for the groups at risk for severe illness.

The groups who should receive vaccine include persons 65 years and older, residents of nursing homes and other chronic care facilities, adults and children with chronic disorders of the respiratory and cardiovascular systems, adults and children with chronic metabolic diseases and diseases that cause immunosuppression, and children up to the age of 18 who are receiving long term aspirin therapy.

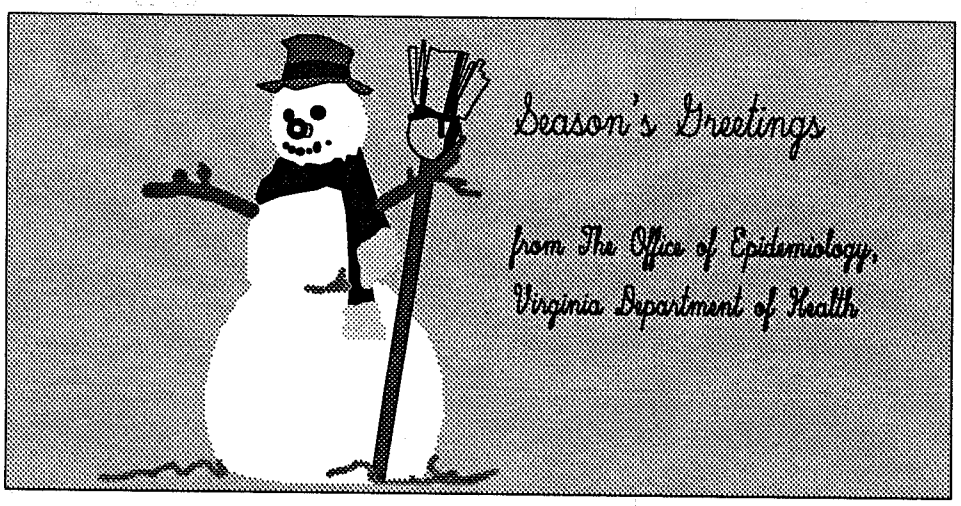
Persons fitting the target groups mentioned above should contact their private physicians or local health departments regarding the availability of vaccine.

People with influenza usually have a sudden onset of fever, muscle aches, headache, sore throat, and nonproductive cough. Unlike other common respiratory infections, influenza can cause severe debility lasting several days to a week. More severe illness can occur if pneumonia develops. Evidence suggests that influenza is not the only virus circulating at this time. Increased absenteeism from schools and work may also be due to a variety of less serious viral illnesses. The presence of other viruses has been confirmed by laboratory tests on patients in Virginia and surrounding states.

Reported by Amy S. Bloom, MD, and Suzanne R. Jenkins, VMD, MPH, Office of Epidemiology, VDH.

Meningococcal Meningitis at Lynchburg College

Two cases of meningitis due to *Neisseria meningitidis* serogroup C have been reported from Lynchburg College in Lynchburg, Virginia. The first case was in a student with onset on October 3; the second case was in an infirmary nurse with onset on November 14. The nurse had not been a contact of the first case. Close contacts of both cases were given antimicrobial prophylaxis with rifampin. The College has recently elected to offer meningococcal polysaccharide vaccine (serogroups A, C, Y, and W-135) to any student who wishes to receive it. The Office of Epidemiology, Virginia Department of Health, is not recommending that anyone outside the Lynchburg College community receive prophylaxis or immunization against *N. meningitidis*. To date in 1991, there have been a total of 32 reports of meningococcal infection in Virginia, and 4 (12.5%) of these have been due to serogroup C. This compares with 52 cases reported for the same period in 1990, of which 8 (15.4%) were due to serogroup C.



Cases of Selected Notifiable Diseases, Virginia, November 1 through November 30, 1991.

Disease	Total Cases Reported This Month						Total Cases Reported to Date in Virginia		
		Regions							
	State	NW	N	SW	C	E	This Yr	Last Yr	5 Yr Avg
AIDS	29	0	14	2	10	3	629	582	331
Campylobacter	76	18	16	16	16	10	602	533	594
Gonorrhea*	1662	-	-	-	-	-	16938	17441	15727
Hepatitis A	23	3	10	4	2	4	179	283	258
Hepatitis B	19	2	3	4	5	5	203	236	348
Hepatitis NANB	5	0	2	1	1	1	30	42	59
Influenza	16	0	1	2	13	0	706	811	2140
Kawasaki Syndrome	1	0	0	0	1	0	24	24	21
Legionellosis	3	0	1	1	1	0	16	13	14
Lyme Disease	16	4	2	4	2	4	143	122	46
Measles	0	0	0	0	0	0	30	86	78
Meningitis, Aseptic	27	2	13	3	4	5	407	344	295
Meningitis, Bacterial~	11	4	1	1	3	2	121	136	171
Meningococcal Infections	1	0	1	0	0	0	32	52	61
Mumps	6	0	0	0	4	2	61	103	96
Pertussis	4	2	1	0	0	1	24	24	35
Rabies in Animals	19	4	5	2	2	6	240	188	260
Reye Syndrome	0	0	0	0	0	0	2	1	1
Rocky Mountain Spotted Fever	1	0	0	1	0	0	19	24	26
Rubella	0	0	0	0	0	0	0	1	3
Salmonellosis	138	24	34	14	32	34	1241	1332	1487
Shigellosis	34	4	13	11	3	3	368	147	255
Syphilis (1° & 2°)*	68	0	11	4	18	35	843	891	511
Tuberculosis	15	3	0	2	1	9	289	360	361

Localities Reporting Animal Rabies: Augusta 1 skunk; Bath 1 skunk; Fairfax 2 raccoons; Goochland 1 raccoon; Isle of Wight 1 raccoon; King George 1 skunk; Loudoun 3 raccoons; Newport News 3 raccoons; Prince Edward 1 cat; Pulaski 1 skunk; Rockingham 1 skunk; Russell 1 skunk; Suffolk 1 raccoon; York 1 raccoon.

Occupational Illnesses: Asbestosis 8; Carpal Tunnel Syndrome 38; Coal Workers' Pneumoconiosis 22; Loss of Hearing 7; Mesothelioma 1; Repetitive Motion Disorder 4.

*Total now includes military cases to make the data consistent with reports of the other diseases.
~Other than meningococcal

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