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Cryptosporidiosis

Case Report: A 42 year old hispanic man underwent cardiac transplantation. While on maintenance immunosuppressive therapy with cyclosporine, azathioprine, and prednisone, he developed low grade fever and profuse, hemorrhagic, watery diarrhea with up to 10-12 stools per day. There was an absence of abdominal pain, nausea, vomiting, and headache, and no loss of appetite occurred. Leukocytes were not seen on microscopy of a fecal specimen. Stool cultures for routine pathogens, including *Shigella, Salmonella, Campylobacter,* and *Yersinia,* were negative. A modified acid fast stain of stool demonstrated many organisms compatible with *Cryptosporidium* occysts. Treatment with spiramycin, a macrolide antibiotic, was followed by resolution of fever and a decrease in the number of stools.

Submitted by Lisa Oakley, M.D., Fellow in Infectious Diseases, Medical College of Virginia, Richmond.

Comment: Since 1976 when the first human case of cryptosporidiosis was reported in the United States, the number of reported cases has increased dramatically.[1] This is the result of more awareness of the disease by the medical community and improvement in techniques employed for its detection. In addition to the role of *Cryptosporidium* as an opportunistic pathogen in immunodeficient individuals (especially AIDS patients),[1,2] it has been associated with diarrheal disease in animal handlers,[3,4] identified as the cause of numerous day-care center outbreaks of diarrhea[4-7] and implicated in several waterborne outbreaks.[8] It now appears that it is a component of traveler's diarrhea[9] as well as a large contributor to diarrheal disease in developing countries.[10]

Cryptosporidium is a small (2-6μm) protozoan with a complex 6-stage life cycle that includes the development of thin walled, autoinfective oocysts and thick walled, environmentally resistant oocysts.[1,11] The presence of the autoinfective oocysts probably explains why a small number of ingested oocysts can produce a very heavy infection and why chronic cryptosporidiosis can continue for months or even years in an immunodeficient host.

Animals exposed to *Cryptosporidium* can resist infection, experience a self-limited infection with diarrhea, weight loss and/or anorexia or die shortly after becoming infected. A variety of animal species has been reported to be infected with *Cryptosporidium,* however the only horses reported with disease have been those with inherited combined immunodeficiency (Table 1).[1,11] The development of clinical manifestations in animals is dependent on species, age and immune status. In contrast to the disease in humans, there does not seem to be a chronic form of cryptosporidiosis in animals.

Humans infected with *Cryptosporidium* who have normal immune function may be either asymptomatic or experience short term, self-limiting disease. In immunodeficient individuals the disease is usually long term and becomes life threatening unless the immunodeficiency is reversed. Cryptosporidiosis is usually characterized by profuse, watery diarrhea without gross or microscopic blood.

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***Table 1. Animals reported to be infected with* Cryptosporidium.**

Laboratory Animals

Mice
Rabbits
Guinea pigs
Monkeys

Livestock

Calves
Lambs
Pigs
Goats
Foals

Pets

Dogs
Cats

Birds

Chickens
Turkeys
Peacocks
Geese
Parrots
Pheasants

Other

Snakes
Deer

Preventing Perinatal Transmission of the AIDS Virus.

The information and recommendations in this document are intended to assist health-care providers and state and local health departments in developing procedures to prevent perinatal transmission of human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV), the virus that causes acquired immunodeficiency syndrome (AIDS).

This document contains recommendations for providing counselling and, when indicated, testing for antibody to HTLV-III/LAV for women who are at increased risk of acquiring the virus and who are either pregnant or may become pregnant. It is important that these women know they are at risk, as well as know and understand their HTLV-III/LAV-antibody status, so they can make informed decisions to help prevent perinatally acquired HTLV-III/LAV.

Through counselling, uninfected women can learn how to avoid becoming infected, and infected women can choose to delay pregnancy until more is known about perinatal transmission of the virus. If already pregnant, infected women can be provided information for managing the pregnancy and caring for the child.

Currently available data indicate that most pediatric HTLV-III/LAV infections and AIDS are acquired perinatally from infected women, but additional studies are needed to better quantify the risk of transmission from an infected pregnant woman to the fetus or newborn.

The recommendations below pertain to women. However, men who are HTLV-III/LAV-antibody positive should also be counselled regarding the risks of sexual and perinatal transmission, so they can refer for counselling and testing their sex partners who may be pregnant or considering pregnancy.

BACKGROUND

Pediatric AIDS Cases due to Perinatal Transmission. As of December 1, 1985, 217 (1%) of the 15,172 AIDS cases

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Cryptosporidiosis

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Immunocompromised patients commonly have fluid losses of 3 liters per day (up to 17 liters per day has been reported).[1] Other signs and symptoms include mild, epigastric, cramping pain, nausea, vomiting, anorexia and in a few patients, mild fever. Routine blood tests are usually normal and radiographic and endoscopic exams normal or nonspecific.

Until recently, the identification of *Cryptosporidium* was made by light or electron microscopic examination of intestinal biopsies. Currently, stool examinations by experienced microscopists using specific stains (acid fast) and/or concentration techniques (Sheathers sugar flotation) give results as good as or better than those from intestinal biopsies.[1,11] The organisms are small and easily overlooked or confused with yeast; the person performing the exam should therefore be alerted that *Cryptosporidium* is suspected.

An effective treatment for either animals or humans is yet to be identified. Because *Cryptosporidium* apparently does not cause a chronic illness in animals, research on susceptible animals has concentrated on the efficacy of prophylactic treatment.[1] The only consistently successful intervention for humans has occurred when the underlying immune deficiency could be reversed. Although the improvement described in the above case report coincided with spiramycin therapy and there have been other such case reports, no controlled clinical trials have been published documenting efficacy against *Cryptosporidium*.[1,12,13]

Cryptosporidiosis should be considered in any differential diagnosis for diarrhea occurring in animals or humans, particularly in high risk groups such as animal handlers (including veterinarians and their staffs), children in day-care and immunocompromised individuals. The Division of Epidemiology would like to be informed of any laboratory confirmed case of human cryptosporidiosis. The Division of Consolidated Laboratory Services in the Virginia Department of General Services can process stool samples from patients with suspected infections.

Discussion by Suzanne R. Jenkins, V.M.D, M.P.H., Assistant State Epidemiologist, Virginia Department of Health.

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AIDS Virus

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reported to CDC occurred among children under 13 years of age. Sixty percent of these children are known to have died. These 217 cases represent only the more severe manifestations of HTLV-III/LAV infection. Less severe manifestations, often described as AIDS-related complex (ARC), are not reported to CDC, so the number of children with clinically significant illness attributable to HTLV-III/LAV infection is greater than the reported cases of pediatric AIDS. In addition, a number of infected children are probably asymptomatic.

Of the 217 reported pediatric AIDS patients, 165 (76%) have as their only known risk factor a mother belonging to a group with increased prevalence of HTLV-III/LAV infection. An additional 18% of the pediatric cases are attributable to transfusions of blood or blood products, while risk factor information is missing or incomplete on the remaining 6%. Of the 217 children with AIDS, 48% had mothers who were intravenous (IV) drug abusers; 17% had mothers who were born in Haiti; and 10% had mothers who were sex partners of either IV drug abusers or bisexual men.

Of the patients with perinatally acquired AIDS, 45% resided in New York City, while Florida and New Jersey accounted for an additional 32%.

Mechanisms of Perinatal Transmission. It is believed that HTLV-III/LAV is transmitted from infected women to their fetuses or offspring during pregnancy, during labor and delivery, or perhaps shortly after birth. Transmission of the virus during pregnancy or labor and delivery is demonstrated by two reported AIDS cases occurring in children who had no contact with their infected mothers after birth. One was delivered by Cesarean section (*1,2*).

Transmission of the virus after birth has been implicated in one case of HTLV-III/LAV infection in a child born to a mother reported to have acquired the infection from a postpartum blood transfusion. Since she breastfed the child for 6 weeks, the authors suggested breastfeeding as the possible mode of transmission (*3*). Recently, HTLV-III/LAV has been isolated from the breast milk of infected women (*4*).

Risk of Perinatal Transmission from Infected Mothers. The rate of perinatal transmission of HTLV-III/LAV from infected pregnant women is unknown; however, available data suggest a high rate. In one study of 20 infants born to infected mothers who had already delivered one infant with AIDS, 13 (65%) had serologic and/or clinical evidence of infection with HTLV-III/LAV several months after birth (*5,6*). Since these women were selected on the basis of having previously transmitted HTLV-III/LAV perinatally, this study may overestimate the average risk of transmission for all infected pregnant women.

Perinatal transmission from an infected mother to her newborn is not inevitable. Of three children born to women who became infected with HTLV-III/LAV by artificial insemination from an infected donor, all were in good health and negative for anti-

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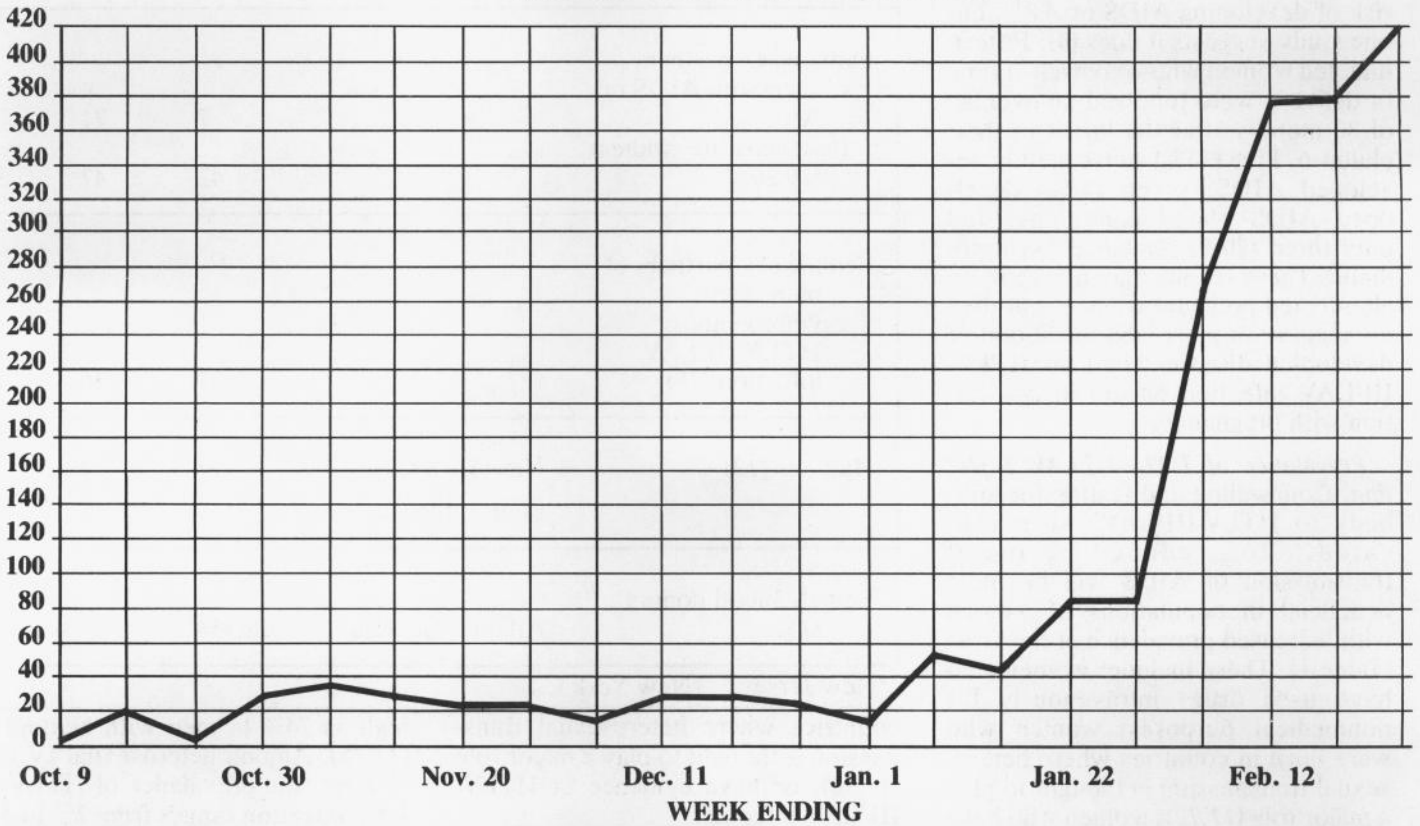
Influenza Surveillance Virginia 1985-86



In late January an outbreak of influenza-like illness was reported from all regions of Virginia by 33 participating sentinel physicians. The outbreak continued to peak in late February. Several laboratories reported isolating a number of influenza type B viruses. There were no isolations in Virginia of type A viruses reported during February. Nationally, many states have reported similar outbreaks, with type B and type A (H3N2) viruses causing the vast majority.

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body to the virus more than 1 year after birth (*7*). Another child, born to a woman who was already pregnant at the time of AIDS diagnosis and was demonstrated to be viremic, was seronegative, culture negative, and healthy at birth and at 4 months of age (*8*). In a retrospective study evaluating nine children under 5 years of age whose mothers were later diagnosed with AIDS, two (22%) had antibody to HTLV-III/LAV (*9*). The infection status of these women during pregnancy was unknown.

In these studies, the rate of transmission ranged from 0% (0/3) to 65% (13/20). Additional studies are needed to better define the rate of transmission and variables associated with it.

Risk of Illness among Infected Pregnant Women. Pregnancy is associated with suppression of cell-mediated immunity and increased susceptibility to some infections (*10*). The T-helper to T-suppressor ratio is decreased during normal pregnancy, being lowest in the third trimester, and returns to normal approximately 3 months postpartum (*10*). It is not known whether pregnancy increases an infected woman's risk of developing AIDS or ARC, but one study suggests it does (*6*). Fifteen infected women who were well at time of delivery were followed an average of 30 months after the births of their children. Five (33%) subsequently developed AIDS; seven (47%) developed AIDS-related conditions; and only three (20%) remained asymptomatic. These results may not apply to all infected pregnant women, but they do suggest an increased likelihood of developing disease when an HTLV-III/LAV infection occurs in association with pregnancy.

Prevalance of HTLV-III/LAV Infection. Counselling and testing for antibody to HTLV-III/LAV, when indicated, to reduce perinatal transmission of AIDS will be most beneficial in populations of women with increased prevalence of the virus (Table 1). These include: women who have used drugs intravenously for nonmedical purposes; women who were born in countries where heterosexual transmission is thought to play a major role (*11,12*); women who have engaged in prostitution; and women who are or have been sex partners of men who abuse IV drugs, are bisexual, have hemophilia, were born in countries where heterosexual transmission is thought to play a major role (*11,12*), or have evidence of HTLV-III/LAV infection.

TABLE 1. Prevalence of HTLV-III/LAV Antibody in Heterosexual Populations—United States

Populations	Location	No. tested	Prevalence (%)
Intravenous drug abusers *(16,17)*	New York City	274	59
	NJ* < 5 miles from NYC†	204	56
	NJ 5-10 miles from NYC	124	43
	NJ > 100 miles from NYC	55	2
	San Francisco	53	9
Persons with hemophilia *(13,14)*			
Factor VIII concentrate recipients		234	74
Factor IX concentrate recipients		36	39
Cryoprecipitate only recipients		15	40
Female prostitutes *(21)*	Seattle, Washington	92	5
	Miami, Florida	25	40
Female sex partners of men with AIDS or ARC (two separate studies) *(19,20)*		7	71
		42	47
Female sex partners of men with asymptomatic HTLV-III/LAV infection *(18)*		21	10
Haitians *(12)*	New York City	97	4
	Miami, Florida	129	8
Female blood donors *(15)*	Atlanta, Georgia	28,354	0.01

*New Jersey †New York City

The prevalence of antibody to HTLV-III/LAV in U.S. populations of men and women ranges from less than 0.01% in female blood donors to as high as 74% in men with hemophilia (*13-15*). Among heterosexual IV drug abusers, the prevalance of HTLV-III/LAV infection ranges from 2% to 59% in various geographic areas (*16,17*). Seroprevalance among the heterosexual partners of persons at increased risk for AIDS varies from 10% in fe-

male partners of asymptomatic, seropositive hemophilia patients to 71% in the female partners of men with AIDS or ARC (*18-20*). Among prostitutes, the HTLV-III/LAV antibody prevalance varies from 5% to 40%, depending on geographic area, with most of the women with positive tests relating histories of IV drug abuse (*21*). Among female blood donors in Atlanta, Georgia, who denied belonging to high-risk groups, 0.01% had repeatedly reactive enzyme-linked immunosorbent assays (ELISAs) followed by reactive Western blot tests (*15*).

Commercially available tests to detect antibody to HTLV-III/LAV are ELISAs using antigens derived from whole disrupted HTLV-III/LAV. When the ELISA is reactive on initial testing, it is standard procedure to repeat the test on the same specimen. Repeatedly reactive tests are highly sensitive and specific for antibody to HTLV-III/LAV. However, when the ELISA is used to screen populations in which the prevalence of infection is very low (such as blood donors or women not in high-risk groups), the proportion of repeatedly reactive results that are falsely positive will be higher. For that reason, an additional test, such as a Western blot, is recommended following repeatedly reactive ELISA results, especially in low-prevalence populations. In populations with high prevalence of infection (e.g. homosexual men or IV drug abusers), most repeatedly reactive ELISAs are reactive by Western blot or another test. For example, among 109 IV drug abusers whose sera were repeatedly reactive by ELISA, over 85% were reactive by Western blot (*22*). In contrast, in a low-prevalence population of 69 female blood donors whose sera were repeatedly reactive by ELISA, only 5% were reactive by Western blot (*15*).

Due to the seriousness of the implications of HTLV-III/LAV-antibody reactivity, it is recommended that repeatedly reactive ELISAs be followed by an additional test, such as the Western blot. Women with sera repeatedly reactive by ELISA and reactive by Western blot should have a thorough medical evaluation. HTLV-III/LAV has been isolated from a single specimen in 67%-95% of persons with specific antibody (*23,24*). Because infection has been demonstrated in asymptomatic persons, the presence of specific antibody should be considered presumptive evidence of current infection and infectiousness.

RECOMMENDATIONS

Women Who Should be Offered Counselling and Testing. *Counselling services and testing for antibody to HTLV-III/LAV should be offered to pregnant women and women who may become pregnant in the following groups:* (1) those who have evidence of HTLV-III/LAV infection; (2) those who have used drugs intravenously for nonmedical purposes; (3) those who were born in countries where heterosexual transmission is thought to play a major role (*11,12*); (4) those who have engaged in prostitution; (5) those who are or have been sex partners of: IV drug abusers, bisexual men, men with hemophilia, men who were born in countries where heterosexual transmission is thought to play a major role (*11,12*), or men who otherwise have evidence of HTLV-III/LAV infection. If data become available to show that HTLV-III/LAV-antibody prevalence is increased in other groups or settings, counselling and testing programs should be extended to include them. Routine counselling and testing of women who are not included in the above-mentioned groups is not recommended due to low prevalence of infection and concern about interpretation of test results in a low-prevalence population. However if a woman requests it, the service should be provided in accordance with these recommendations.

Settings for Offering Counselling and Testing. Counselling and testing for antibody to HTLV-III/LAV to prevent perinatal transmission is recommended in the setting of any medical service in which women at increased risk are commonly encountered. These include services for treating IV drug abuse (i.e., detoxification and methadone maintenance), comprehensive hemophilia treatment centers, sexually transmitted disease clinics, and clinics that serve female prostitutes. In addition, services related to reproduction, such as family planning and infertility services, gynecologic, premarital, or preconceptual examinations, and prenatal and obstetric services should also consider offering counselling and testing if high-risk women are seen at these facilities. Testing for antibody to HTLV-III/LAV should be performed with the woman's consent after counseiling is provided regarding risk factors for infection, the interpretation of test results, the risks of transmission, and the possible increased likelihood of disease among women infected with HTLV-III/LAV in association with pregnancy. The counselling and testing must be conducted in an environment in which confidentiality can be assured. In settings where confidential counselling and testing cannot be assured, information should be provided and referrals made to appropriate facilities.

Frequency of Testing. Detectable antibodies to HTLV-III/LAV may not develop until 2-4 months after exposure. This, and whether the woman is continuously exposed, should be taken into account when considering the need for, and frequency of, repeat testing. High-risk women should be offered counselling and testing before they become pregnant. During pregnancy, counselling and testing should be offered as soon as the woman is known to be pregnant. If the initial test is negative, repeat testing may be indicated near delivery to aid in the clinical management of the pregnant

woman and newborn. If this final test is negative and the mother's risk of exposure no longer exists, she may safely consider breastfeeding the child, and management of the child need not include the same concerns that would be appropriate if the woman had had a positive test or if she were at high risk and had not been tested at all.

Counselling Women with Positive Results. Women with virologic or serologic evidence of HTLV-Ill/LAV infection should be counselled regarding their own risk of AIDS and the risk of perinatal and sexual transmission of HTLV-Ill/LAV. Infected women should be counselled to refer their sex partners for counselling and testing. If the partners of these women are not infected, both members of the couple should be counselled on how they may modify their sexual practices to reduce the risk of HTLV-Ill/LAV transmission to the uninfected partner. In addition, the couple should be told not to donate blood, organs, or sperm and should be discouraged from using IV drugs and advised against sharing needles and syringes. When seeking medical or dental care for intercurrent illness, they should inform those responsible for their care of their positive antibody status so appropriate evaluation can be undertaken. Recommendations for providing information and advice to individuals infected with HTLV-Ill/LAV have been published (25).

Infected women should be advised to consider delaying pregnancy until more is known about perinatal transmission of the virus. Pregnant infected women may require additional medical and social support services due to an enhanced risk of opportunistic infections and psychosocial difficulties during and after pregnancy. Obstetric-care providers should be alert to signs and symptoms of HTLV-Ill/LAV and related opportunistic infections in these pregnant women and to the need for specialized medical care.

HTLV-Ill/LAV-infected women should be advised against breastfeeding to avoid postnatal transmission to a child who may not yet be infected. The child should receive follow-up pediatric evaluations to determine whether he/she has HTLV-Ill/LAV infection, and to diagnose and treat promptly any diseases that may be secondary to HTLV-Ill/LAV infection. Recommendations for educating and providing foster care for infected children have been published (26).

Counselling Women with Negative Test Results. A negative ELISA for HTLV-Ill/LAV antibody in women who have no clinical or laboratory evidence of HTLV-Ill/LAV infection is evidence that they have probably not been infected. However, uninfected women who have sex partners with evidence of HTLV-Ill/LAV infection or with an increased risk of becoming infected should be informed that sexual intercourse increases their risk of infection. These women should be informed of the risks associated with pregnancy if they become infected and advised to consider delaying pregnancy until more is known about perinatal transmission of the virus or until they are no longer considered to be at risk for acquiring the virus. In addition to preventing pregnancy, the consistent and proper use of condoms can offer some protection against HTLV-Ill/LAV infection.

High-risk women, even if seronegative, should be told not to donate blood or organs. To decrease their risk of becoming infected, IV drug abusers should be encouraged to seek treatment for their drug abuse. Persons counselling IV drug abusers should know that IV drug abuse is often strongly ingrained and compulsive. Despite educational efforts and encouragement for treatment, some addicts will continue to abuse drugs or relapse after treatment. If drug abuse continues, they should be advised not to share needles or syringes and to use only sterile equipment.

Additional Considerations. These recommendations will be revised as additional information becomes available. It is recognized that provision of the recommended professional counselling, HTLV-Ill/LAV-antibody testing and associated specialized medical services will take time to implement and may stress available resources, particularly in public facilities, which are most greatly affected. Health-care providers, social-service personnel, and others involved in educating and caring for HTLV-Ill/LAV-infected persons should be aware of the potential for social isolation and should be sensitive to the need for confidentiality. They should be familiar with federal and state laws, regulations, and policies that protect the confidentiality of clinical data and test results. Each institution should assure that specific mechanisms are in place to protect the confidentiality of all records and to prevent the misuse of information. Anonymous testing would not be appropriate if it prevents adequate counselling and medical follow-up evaluation.

Hospital precautions for managing infected women and infants should be patterned after those for caring for patients with HTLV-Ill/LAV infection (27,28). Additonal recommendations will follow.

DEVELOPMENT OF THESE RECOMMENDATIONS

The information and recommendations contained in this document were developed and compiled by CDC and the U.S. Public Health Service in consultation with individuals representing: the Conference of State and Territorial Epidemiologists, the Association of State and Territorial Health Officials, the American Public Health Association, the United States Conference of Local Health Officers, the American Medical Association, the American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, the Planned Parenthood Federation of America, the American Venereal Disease Association, the Division of Maternal and Child Health of the Health Resources and Services Administration, the National Institute on Drug Abuse of the Alcohol, Drug Abuse, and Mental Health Administration, the National Hemophilia Foundation, the Haitian Medical Association, the American Bar Foundation, and the Kennedy Institute of Ethics at Georgetown University. The consultants also included representatives of the departments of health of the areas with the largest number of perinatally transmitted pediatric AIDS cases: New York City, Florida, and New Jersey. These recommendations may not reflect the views of all individual consultants or the organizaitons they represent.

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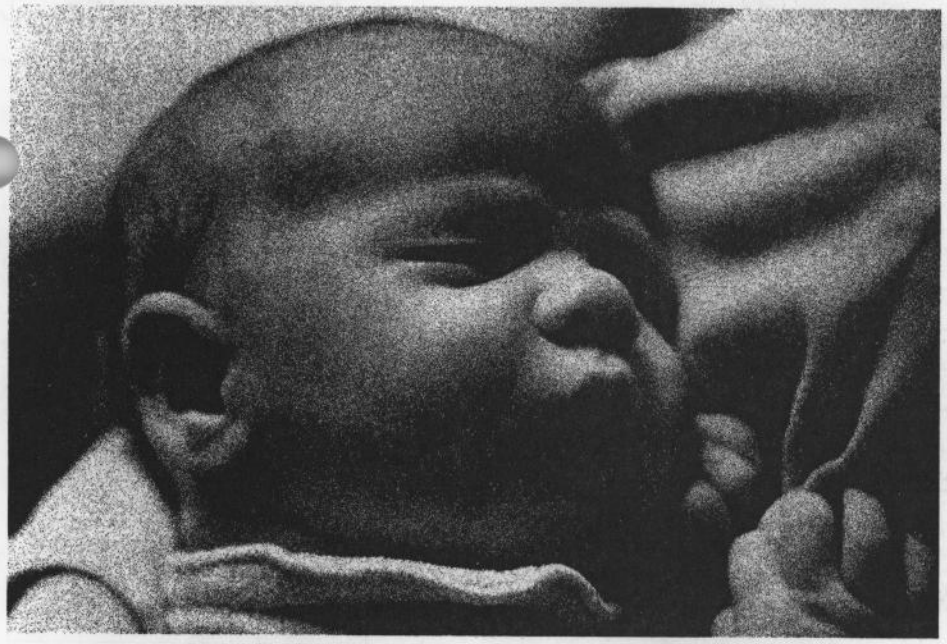

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Reprinted from MMWR 1985; 34:721-6, 731-2.

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Cases of selected notifiable diseases, Virginia, for the period February 1 through February 28, 1986

Disease	State				Mean 5 Year To Date	Regions				
	This Month	Last Month	Total to Date 1986	Total to Date 1985		This Month N.W.	N.	S.W.	C.	E.
Measles	0	0	0	0	3	0	0	0	0	0
Mumps	1	4	5	6	12	0	0	1	0	0
Pertussis	4	2	6	1	3	2	0	0	1	1
Rubella	0	0	0	0	1	0	0	0	0	0
Meningitis—Aseptic ↘ ↘	15	18	33	32	25	2	2	2	3	6
*Bacterial ↘ ↘	21	21	42	58	48	2	3	4	3	9
Hepatitis A (Infectious) ≠ ↘	10	4 3	14 13	50	30	2	5	1	1	1
B (Serum) ≠ ↘	29 30	24 23	53 52	105	79	3	10	11	23	3
Non-A, Non-B ≠ ↘	8 9	2	10 11	16	13	1	20	2	1	4 5
Salmonellosis	65	64	133	139	137	10	16	17	9	13
Shigellosis ↘	4	5	9	10	38	0	0	2	0	2
Campylobacter Infections ≠ ↘	27 26	28 27	55 53	59	41	4	5	5	6	7 6
Tuberculosis	28	7	36	27	—	4	2	10	7	5
Syphilis (Primary & Secondary)	28	54	82	50	88	0	7	3	4	15
Gonorrhea	1492	1279	2771	2674	3128	—	—	—	—	—
Rocky Mountain Spotted Fever ↘	0	0	0	0	0	0	0	0	0	0
Rabies in Animals	9	6	15	21	45	5	0	1	3	0
Meningococcal Infections ↘	6	2	8	11	13	0	1	1	1	3
Influenza	578	13	592	306	1080	383	17	148	30	0
Toxic Shock Syndrome ↘	0	2	2	0	1	0	1	0	0	1
Reyes Syndrome ↘	0	0	0	1	2	0	0	0	0	0
Legionellosis strange ↘	15 0	[redacted] 3	18 3	3	3	4 0	20	2 0	30	6 0
Kawasaki's Disease strange ↘	2	2 1	4 3	12	6	1	2 0	2 0	1 1	6 0
Other: Acquired Immunodeficiency Syndrome	24	21	45	9	—	0	11	3	6	4

Counties Reporting Animal Rabies: Caroline 1 raccoon; Shenandoah 1 skunk; Spotsylvania 1 raccoon; Warren 1 raccoon, 1 skunk; Lee 1 fox; Goochland 1 raccoon; Hanover 1 bovine, 1 raccoon.

Occupational Illnesses: Pneumoconioses 18; Carpal tunnel syndrome 17; Asbestosis 6; Poisoning, lead 4; Hearing loss 2; Silicosis 1.

*other than meningococcal

Leprosy
Malaria
> also strange

Σ Regions ≠ Feb total sometimes

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