



MORBIDITY AND MORTALITY WEEKLY REPORT

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Current Trends

Update: Influenza Activity — United States and Worldwide, and Composition of the 1993–94 Influenza Vaccine

In collaboration with the World Health Organization (WHO) international collaborating laboratories and with state and local health departments in the United States, CDC conducts surveillance to monitor influenza activity and to detect antigenic changes in the circulating strains of influenza viruses. This report summarizes surveillance for influenza in the United States and worldwide during the 1992–93 season and describes the composition of the 1993–94 influenza vaccine.

United States

During the 1992–93 influenza season, influenza activity in the United States began in October and increased gradually from December through late February. Recent reports suggest that activity may be declining in some areas. The number of isolates and the ratio of specimens positive for influenza to total specimens submitted for respiratory virus testing declined slightly during late February and early March. Weekly reports by state and territorial epidemiologists indicated increasing levels of influenzalike illness (ILI) from December through late February and a slight decline from late February through early March.

From October through January, influenza B viruses predominated and outbreaks were reported primarily among school-aged persons; outbreak activity reported among older adults was limited, and no excess occurred in influenza-associated mortality. Recent increased circulation of influenza A(H3N2) viruses has been associated with reports of increasing numbers of culture-confirmed outbreaks in nursing homes and other chronic-care facilities.

From September 27, 1992, through March 6, 1993, 1791 (86%) of the 2087 influenza virus isolates reported by the WHO collaborating laboratories in the United States were influenza type B. Influenza B viruses isolated in the United States this season have been antigenically similar to the B/Panama/45/90 virus included in the 1992–93 influenza vaccine. However, the proportion of influenza type A viruses has steadily increased since mid-January. From September 27, 1992, through January 16, 1993, 10 (2%) of the 578 influenza viruses reported were influenza type A compared with 144 (14%) of the 1026 viruses reported for January 17 through February 13 and

Influenza Activity — Continued

142 (29%) of the 483 viruses reported for February 14 through March 6. Of the 296 influenza A viruses isolated, 22 (7%) were subtyped as A(H1N1) and 115 (39%) as A(H3N2); 159 (54%) have not yet been subtyped. Of the influenza A(H3N2) viruses isolated in the United States this season and characterized at CDC, six were antigenically similar to the vaccine strain A/Beijing/353/89, and 28 were similar to the antigenic variant A/Beijing/32/92 (Table 1).

The proportion of deaths associated with pneumonia and influenza to total deaths reported through CDC's 121-city mortality reporting system exceeded the epidemic threshold for 1 week (ending February 20) but remained below the epidemic threshold for the following 2 weeks.

Worldwide

Influenza activity worldwide has occurred at moderate levels during the 1992–93 season. Influenza viruses have been isolated in association with sporadic activity and outbreaks in Asia, Europe, and North America. Although most activity has been associated with influenza B viruses, influenza A(H3N2) viruses were also isolated during periods of sporadic activity or outbreaks in 21 countries. Isolation of influenza A(H1N1) viruses has been rare.

Influenza B viruses were first reported in France, Japan, and the United States during October 1992 and predominated in all countries reporting influenza during the first months of the season. They remain the most common and widespread viruses isolated in Europe and North America. Influenza B viruses have been isolated in association with outbreaks among schoolchildren in China, Hungary, Japan, Sweden, the United Kingdom, and the United States. Other countries reporting isolation of influenza B viruses include Belgium, Bulgaria, Canada, Croatia, the Czech Republic, Denmark, Finland, France, Germany, Hong Kong, Israel, Italy, Lithuania, the Netherlands, Norway, Portugal, Romania, the Russian Federation, Singapore, the Slovak Republic, Spain, Switzerland, Taiwan, and Thailand.

Although influenza A(H3N2) viruses have been isolated less frequently worldwide, they were first reported in November 1992 during sporadic activity or small outbreaks in Japan, Sweden, and the United States. Japan subsequently reported culture-confirmed widespread outbreaks during December 1992 and January and February 1993. Influenza A(H3N2) viruses were isolated during outbreaks in northern China during late December and January. As of late February, influenza A(H3N2) viruses had

TABLE 1. Hemagglutination-inhibition titers of influenza A(H3N2) viruses with serum specimens from infected ferrets*

	Ferret antiserum						
Viral antigen	A/Beijing/353/89	A/Beijing/32/92					
Reference antigen							
A/Beijing/353/89	320	80					
A/Beijing/32/92	40	320					
Recent isolates							
A/Stockholm/01/93	40	320					
A/Sapporo/304/92	20	320					
A/New York/04/93	40	320					

^{*}A fourfold difference in hemagglutination-inhibition titers with two viruses is normally indicative of antigenic variation between viruses.

Influenza Activity — Continued

also been isolated in Belgium, Bulgaria, Canada, Croatia, the Czech Republic, Finland, France, Germany, Indonesia, Italy, the Netherlands, Norway, Romania, the Russian Federation, Singapore, Spain, and the United Kingdom.

Influenza A(H1N1) viruses have been isolated during periods of sporadic activity in Canada, France, the Netherlands, the United Kingdom, and the United States.

Composition of the 1993-94 Vaccine

For the 1993–94 influenza season, the Food and Drug Administration Vaccines and Related Biologicals Advisory Committee (VRBAC) has recommended that the trivalent influenza vaccine for the United States contain A/Texas/36/91-like(H1N1), A/Beijing/32/92-like(H3N2), and B/Panama/45/90-like viruses. This recommendation was based on the antigenic analysis of recently isolated influenza viruses, the patterns of spread of antigenic variants, and the antibody response of persons previously vaccinated with the 1992–93 influenza vaccine.

More than 300 influenza B viruses isolated worldwide since October 1992 have been characterized antigenically. All are similar to the B/Panama/45/90 vaccine strain, and to the closely related variant B/Qingdao/102/91 (1). Vaccines containing B/Panama/45/90-like viruses induced antibodies with similar frequency and titer to the vaccine virus and to representative recent isolates. Therefore, for the 1993–94 vaccine, the VRBAC recommended retaining the current B/Panama/45/90-like vaccine strain.

Although viruses similar to the A/Beijing/353/89 vaccine strain continue to be isolated, antigenic analysis of influenza A(H3N2) viruses indicates that many recently isolated strains from Asia, Europe, and North America are similar to the antigenic variant A/Beijing/32/92 (Table 1). Vaccines containing A/Beijing/353/89-like antigen induced a good response to this vaccine strain. In contrast, this vaccine induced lower and less frequent antibody responses to recent A(H3N2) isolates, such as A/Beijing/32/92, than to the A/Beijing/353/89 vaccine strain (Table 2). Therefore, the VRBAC recommended changing the influenza A(H3N2) vaccine component to an A/Beijing/32/92-like strain for the 1993–94 season.

Although the number of isolates of influenza A(H1N1) viruses has been limited, all those characterized have been closely related to the reference strains A/Taiwan/1/86 or A/Texas/36/91 (2). Antibody induced by vaccination with the A/Texas/36/91 vaccine component induced good immune responses to the vaccine strain and to representative recent isolates. Thus, the VRBAC recommended retaining the A/Texas/36/91-like vaccine strain for the 1993–94 vaccine.

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Influenza Activity — Continued

Editorial Note: The recent increase in influenza A activity in the United States indicates a continuing need for surveillance, including culture of specimens from patients with ILI. Although the severity and types of future influenza epidemics cannot be predicted reliably, the recent increased isolation of variant type A(H3N2) viruses suggests that such viruses may predominate during the 1993–94 influenza season.

Strains to be included in the influenza vaccine for the United States are selected from January through March each year to meet the production schedule required for the manufacture, quality control, and distribution of the more than 40 million doses of vaccine before the next influenza season. Specific recommendations for the use of the newly constituted influenza vaccine will be made by the Public Health Service Advisory Committee on Immunization Practices and published in the *MMWR Recommendations and Reports* during May 1993.

TABLE 2. Hemagglutination-inhibition (HI) antibody responses to the A/Beijing/353/89 (H3N2) component of the influenza vaccine*

Age group	No. persons	Virus strain	Prevaccina- tion GMT [†]	Postvaccina- tion GMT	% With HI titer ≥40
4–52 mos	21	A/Beijing/353/89	28	72	86
		A/Beijing/32/92	<20	23	43
17–25 yrs	30	A/Beijing/353/89	15	156	93
_		A/Beijing/32/92	8	43	63
Elderly	65	A/Beijing/353/89	21	47	78
(mean age: 85 yrs)		A/Beijing/32/92	9	16	30

 $^{^*}$ Volunteers received trivalent vaccine from the 1991–92 or 1992–93 seasons containing 15 μ g of the A/Beijing/353/89 (H3N2) component.

Sources of serum: University of Colorado, Denver; Goodwin House, Inc., Alexandria, Virginia.

References

- 1. World Health Organization. Recommended composition of influenza virus vaccines for use in the 1993–94 season. Wkly Epidemiol Rec 1993;68:57–60.
- 2. CDC. Update: influenza activity—United States, 1991–92 season. MMWR 1992;41:63–5.

Epidemiologic Notes and Reports

Malaria in Montagnard Refugees — North Carolina, 1992

Refugee groups emigrating from some areas of the world may have increased prevalences of exotic and potentially life-threatening diseases, challenging the diagnostic and case-management capacities of local and state health departments. This report summarizes efforts by public health officials and clinical health-care providers to diagnose and manage cases of malaria among a group of 402 Montagnard refugees who resettled to three counties in North Carolina in November 1992.

Since 1976, this group of Montagnard refugees has lived in a remote, densely forested area along the Cambodian-Vietnamese border where transmission of *Plasmodium vivax* and multidrug-resistant *P. falciparum* is intense. Before immigrat-

[†]Geometric mean titer.

Malaria — Continued

ing to the United States, the Montagnards spent 1 month in Phnom Penh, Cambodia, where they received routine physical examinations and screenings for human immunodeficiency virus, syphilis, tuberculosis, and other excludable physical and mental conditions. Of the 402 persons in this group, 299 (74%) were male, and 80 (20%) were children aged <10 years. Members of the group were resettled in Guilford County (175), Mecklenburg County (159), and Wake County (68). Within 1 month of arrival, one Montagnard died (from empyema and gram-negative sepsis), 16 were hospitalized, and 36 had illnesses requiring emergency medical assessment. Five cases of malarial illness were reported among members of the group in one county.

Because an initial assessment among 20 persons detected a 35% prevalence of parasitemia with either *P. falciparum* or *P. vivax*, all Montagnards were screened using quantitative buffy coat (QBC*) evaluation followed by thick and thin blood-smear examination. Self-reported history of fever was recorded at the time of blood collection to determine the association between fever and parasitemia among this group.

Of the 376 persons for whom QBC and/or thick-smear results were available, 178 (47%) were infected with one or more species of *Plasmodium*; 25 persons had been treated previously or were unavailable for screening. Among infected persons, 93 (52%) had *P. falciparum*, 71 (40%) had *P. vivax*, and five (3%) had *P. malariae*; 35 (20%) had *Plasmodium* parasites of unknown species. Infections with more than one species of *Plasmodium* were documented in 39 (22%) parasitemic persons. Among 161 persons with slide-positive malaria for whom a fever history was recorded, 27 (17%) reported having fever since arriving in the United States, suggesting a high level of acquired immunity to malarial illness among this group.

Because of the high prevalence of asymptomatic infection, all 402 members of the group were treated with halofantrine (Halfan*). Halofantrine was administered because *P. falciparum* strains from Southeast Asia are commonly resistant to other available antimalarials, including partial resistance to quinine. Halofantrine is highly effective against the blood stage of malaria parasites but has no effect on the liver stage of *P. vivax* (hypnozoites), which can produce malaria relapses for 3–5 years after initial infection. The risk for *P. vivax* relapse can be decreased by treating infected persons with primaquine (the only available antimalarial that is active against hypnozoites); however, because primaquine can cause severe hemolytic anemia in patients deficient in the red blood cell enzyme glucose-6-phosphate dehydrogenase (G6PD), all refugees for whom primaquine was indicated were screened for G6PD deficiency. Of 358 persons screened, 11 (3%) had G6PD deficiency of sufficient severity to preclude the use of primaquine.

After treatment, group sessions were held to inform the Montagnards, community leaders, and the staff of the sponsoring agencies about the risk for malaria relapse and the importance of early diagnosis and treatment. In addition, guidelines for the proper diagnosis and treatment of malaria were disseminated to selected health-care providers.

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

Malaria — Continued

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Editorial Note: The resettlement of the Montagnard refugees within 2 months of leaving an area of intense malaria transmission, without screening or presumptive treatment for malaria parasitemia, resulted in higher levels of malaria infection than previously seen in Southeast Asian refugees on arrival to the United States. This high prevalence might have been anticipated, because 25%–49% of persons entering Thai refugee camps from forested regions of Cambodia in the early 1980s were parasitemic (1,2). Unlike the Montagnards, these refugees typically remained in temporary resettlement camps in Asia for 4–5 months before arrival in the United States. Although the primary purpose of these camps was to provide cultural information and language training before immigration, this period also provided an opportunity to detect and treat malaria and other medical conditions. As a result, in 1980, among 3433 Indochinese (Laotian, Cambodian, and Vietnamese) refugees resettled in the United States, the prevalence of parasitemia was less than 2% (3).

Malaria was one of many health problems among these refugees; however, requirements for diagnosis, treatment, and management of malaria exceeded the capacity of the local and state health departments, many of which are neither staffed nor funded to provide primary health care. County health departments estimated that as long as 14 weeks would be needed to complete initial medical screening of the refugees, and the capacity of the state laboratory was exceeded by the need to rapidly process nearly 40 times the annual expected number of malaria slides. Even with technical assistance from CDC, malaria-specific screening and treatment procedures required 8 weeks for completion.

Although mosquitoes capable of transmitting malaria exist in North Carolina, local transmission of malaria is unlikely for at least three reasons. First, these Montagnard refugees arrived in November, when temperatures were low enough to preclude survival of anopheline mosquitoes. Second, when warmer ambient temperatures enable increases in the mosquito population, the housing conditions (including the presence of window screens) for persons in this group substantially decrease the likelihood that parasitemic persons will be exposed to anopheline mosquitoes. In recent periods, local transmission in the United States has occurred only when large groups of infected persons have resided outdoors or in substandard housing (e.g., migrant workers encamped in southern California [4]). Finally, any theoretical risk of local transmission in this setting will be further diminished by the presumptive treatment of all members of the resettled group, ongoing case detection and treatment of relapses, and administration of antimalarials to prevent relapses.

Expertise for prompt and accurate diagnosis of malaria and other exotic but potentially life-threatening medical problems in a large number of persons is limited in most local and state health departments (5). As a result, laboratory services and personnel can be quickly overwhelmed. Refugees who immigrate to the United States from tropical areas, among whom prevalences of malaria or other infectious diseases may be high, should receive medical screening and appropriate treatment under well-controlled conditions before departing for the United States. When this is not possible, medical personnel, laboratory support services, and other resources should be made

Malaria — Continued

available to local and state health departments to ensure adequate and timely health care.

References

- 1. Glass RI, Nieburg P, Cates W Jr, et al. Rapid assessment of health status and preventive-medicine needs of newly arrived Kampuchean refugees—Sakaeo, Thailand. Lancet 1980; 1:868–72.
- 2. CDC. Health status of Kampuchean refugees—Khao I-Dang. MMWR 1979;28:569-70.
- 3. Guerrero IC, Chin W, Collins WE. A survey of malaria in Indochinese refugees arriving in the United States, 1980. Am J Trop Med Hyg 1982;31:897–901.
- 4. Maldonado YA, Nahlen BL, Roberto RR, et al. Transmission of *Plasmodium vivax* malaria in San Diego County, California, 1986. Am J Trop Med Hyg 1990;42:3–9.
- 5. Lederberg J, Shope RE, Oaks SC, eds. Institute of Medicine. Emerging infections: microbial threats to health in the U.S. Washington, DC: National Academy Press, 1992:137.

Current Trends

Inability of Retroviral Tests to Identify Persons with Chronic Fatigue Syndrome, 1992

Chronic fatigue syndrome (CFS) is characterized by prolonged, debilitating fatigue (1). Although the cause of CFS unknown, CDC and researchers in other organizations have been investigating whether infection with a previously unidentified retrovirus might be an etiologic factor. Based on reports suggesting that retroviral infection with a human T-lymphotropic virus type 2 (HTLV-II)-like retrovirus or a spumavirus might be associated with CFS (2,3), some research and commercial laboratories developed assays to test specimens from persons with CFS. Even though the hypothesized association between infection with retroviruses and CFS has not been confirmed, these tests are used commonly to evaluate patients with CFS. This report summarizes the findings of a controlled, blinded study conducted in 1992 to determine whether three retroviral tests can distinguish serologically between patients with CFS (i.e., case-patients) and healthy controls.

Blood samples were obtained from 68 case-patients from four study populations (northern New Jersey [n=29 and n=14]; Charlotte, North Carolina [n=10]; and Lyndon-ville, New York [n=15 adolescents aged 11–21 years]*) whose illnesses met the published case definition for CFS (1). For each of the 68 CFS case-patients, one healthy convenience control was selected from the same geographic area and matched for age, sex, and race. † Specimens were assigned random code numbers so those from case-patients could not be distinguished from those of controls.

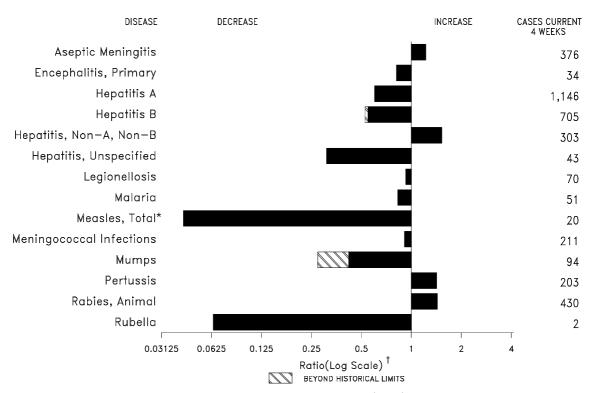
Blood samples from case-patients and controls were sent to two laboratories that had developed retroviral tests based on previous reports (2,3). Laboratory A performed testing with an original polymerase chain reaction (PCR) assay and a modification of the same assay (developed using the methodology that revealed nucleic acid sequences suggestive of an HTLV-II-like retrovirus). Laboratory B performed testing by culturing lymphocytes to identify the foamy cell cytopathic effect that is

(Continued on page 189)

†Case-patient's were matched because ČFS occurs primarily among white women (average age at onset: 30.2 years) (4).

^{*}Case-patients from the other three study populations were aged 18–62 years (median age for all study populations combined: 37.5 years).

FIGURE I. Notifiable disease reports, comparison of 4-week totals ending March 13, 1993, with historical data — United States



^{*}The large apparent decrease in reported cases of measles(total) reflects dramatic fluctuations in the historical baseline.

TABLE I. Summary — cases of specified notifiable diseases, United States, cumulative, week ending March 13, 1993 (10th Week)

	Cum. 1993		Cum. 1993
AIDS* Anthrax Botulism: Foodborne Infant Other Brucellosis Cholera Congenital rubella syndrome Diphtheria Encephalitis, post-infectious Gonorrhea Haemophilus influenzae (invasive disease)† Hansen Disease	10,300 - 1 10 1 9 4 1 - 28 71,155 228	Measles: imported indigenous Plague Poliomyelitis, Paralytic [§] Psittacosis Rabies, human Syphilis, primary & secondary Syphilis, congenital, age < 1 year Tetanus Toxic shock syndrome Trichinosis Tuberculosis Tularemia	4 43 - 13 - 5,345 - 3 47 6 2,566
Leptospirosis Lyme Disease	16 10 419	Typhoid fever Typhus fever, tickborne (RMSF)	56 20

[†]Ratio of current 4-week total to mean of 15 4-week totals (from previous, comparable, and subsequent 4-week periods for the past 5 years). The point where thehatched area begins is based on the mean and two standard deviations of these 4-week totals.

^{*}Updated monthly: last update February 27, 1993.

Of 210 cases of known age, 77 (37%) were reported among children less than 5 years of age.

No cases of suspected poliomyelitis have been reported in 1993; 4 cases of suspected poliomyelitis were reported in 1992; 6 of the 9 suspected cases with onset in 1991 were confirmed; all were vaccine associated.

TABLE II. Cases of selected notifiable diseases, United States, weeks ending March 13, 1993, and March 7, 1992 (10th Week)

		Aseptic	Enceph						/iral), by	tvpe		
Reporting Area	AIDS*	Menin- gitis	Primary	Post-in- fectious	Gono	rrhea	Α	В	NA,NB	Unspeci- fied	Legionel- losis	Lyme Disease
J	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1992	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993
UNITED STATES	10,300	1,173	98	28	71,155	86,714	3,704	1,860	766	114	204	419
NEW ENGLAND	679	27	3	-	1,691	2,116	134	85	1	2	8	47
Maine N.H.	8 47	4 2	1	-	13 9	24 31	4 2	1 11	-	-	1	- 5
Vt.	3	2	-	-	9	2	2	1	-	-	-	-
Mass. R.I.	403 29	15 4	2	-	637 82	779 153	79 32	63 9	1	2	6 1	14 14
Conn.	189	-	-	-	941	1,127	15	-	-	-	-	14
MID. ATLANTIC	2,506	99	3	3	6,664	8,841	182	203	43	3	41	287
Upstate N.Y. N.Y. City	236 1,841	52 5	-	1	1,144 1,541	569 4,574	69 10	61 1	20	1 -	7	171 -
N.J. Pa.	195 234	42	3	2	1,485 2,494	1,176	72 31	70 71	16 7	2	7 27	16 100
E.N. CENTRAL	787	42 177	28	6	15,094	2,522 17,790	469	205	156	2	67	4
Ohio	137	65	11	-	4,802	5,475	81	53	15	-	37	4
Ind. III.	277 106	31 22	2 2	2	1,595 4,758	1,760 5,151	278 62	43 17	3 2	- 1	14	-
Mich.	224	55	11	4	3,219	4,686	45	91	133	i	16	-
Wis.	43	4	2	-	720	718	3	1	3	-	-	-
W.N. CENTRAL Minn.	377 209	61 5	2 2	-	3,495 320	6,177 603	629 78	143 9	35 1	2 1	10	10 1
Iowa	40	18	-	-	329	326	5	5	2	i		i
Mo. N. Dak.	40	17 1	-	-	2,023 10	4,091 19	429 10	113	22	-	2	-
S. Dak.	17	3	-	-	31	45	8	-	-	-	-	-
Nebr. Kans.	26 45	1 16	-	-	- 782	8 1,085	70 29	3 13	6 4	-	6 2	8
S. ATLANTIC	2,357	307	16	13	20,049	27,110	229	306	114	23	29	45
Del. Md.	120 222	2 23	1 5	-	275	324	2 35	28	39 4	- 1	5 13	29 7
D.C.	176	23 8	- -	-	3,203 1,262	3,204 1,602	1	65 5	-	-	3	1
Va. W. Va.	20 3	39 4	5 4	3	1,239 130	3,962 181	32	23 5	4 2	11 3	-	3 1
N.C.	57	18	1	-	5,108	3,526	10	24	11	-	2	3
S.C. Ga.	54 268	2 21	-	-	1,353 2,791	2,302 12,009	3 29	7 24	- 19	-	2	-
Fla.	1,437	190	-	10	4,688	12,007	117	125	35	8	4	1
E.S. CENTRAL	613	81	5	1	8,289	8,871	52	209	189	-	13	3
Ky. Tenn.	53 196	38 19	1 4	1	936 2,578	952 2,830	30 11	19 167	3 182	-	2 9	2
Ala.	230	19	-	-	2,821	3,063	9	21	3	-	-	1
Miss. W.S. CENTRAL	134	5	- 9	-	1,954	2,026	2	2 145	1	-	2	-
W.S. CENTRAL Ark.	950 127	40 7	-	-	9,240 1,121	8,745 1,784	216 10	145 13	24 2	20	6	3 1
La.	172	1	-	-	2,012 549	1,492	8	18	10 9	- 1	1 5	-
Okla. Tex.	108 543	32	3 6	-	5,558	978 4,491	21 177	25 89	3	19	-	2
MOUNTAIN	695	58	5	3	1,956	2,220	737	116	58	25	17	2
Mont. Idaho	3 20	2	-	1	13 20	14 23	37 59	4 8	-	1	- 1	-
Wyo.	18	-	-	-	14	6	4	4	16	-	2	2
Colo. N. Mex.	303 78	16 11	2 1	2	629 208	922 175	207 53	13 52	10 18	16 -	1	-
Ariz.	31	16	2	-	683	683	220	23	6	5	5	-
Utah Nev.	77 165	1 12	-	-	45 344	41 356	146 11	3 9	6 2	3	1 7	-
PACIFIC Wash.	1,336 85	323	27	2	4,677 726	4,844 693	1,056 103	448 34	146 22	37 2	13 2	18
Oreg.	88	-	-	-	271	291	31	13	3	-	-	- -
Calif. Alaska	1,149 4	307 3	24 2	2	3,502 101	3,640 121	739 163	394 3	119	34	10	18
Hawaii	10	13	1	-	77	99	20	4	2	1	1	-
Guam		-	-	-	11	21	-	-	-	-	-	-
P.R. V.I.	522 33	15 -	-	-	88 19	15 13	6	44 1	3	-	-	-
Amer. Samoa	-	-	-	-	5	5	3	-	-	-	-	-
C.N.M.I.	-	2	-	-	11	5	-	-	-	-	-	-

N: Not notifiable

U: Unavailable

C.N.M.I.: Commonwealth of Northern Mariana Islands

^{*}Updated monthly; last update February 27, 1993.

TABLE II. (Cont'd.) Cases of selected notifiable diseases, United States, weeks ending March 13, 1993, and March 7, 1992 (10th Week)

			Measle	s (Rube	eola)		Menin-									
Reporting Area	Malaria	Indig	enous	Impo	orted*	Total	gococcal Infections	Mu	mps	F	Pertussis	S		Rubella	1	
	Cum. 1993	1993	Cum. 1993	1993	Cum. 1993	Cum. 1992	Cum. 1993	1993	Cum. 1993	1993	Cum. 1993	Cum. 1992	1993	Cum. 1993	Cum. 1992	
UNITED STATES	5 131	3	43	1	4	336	464	19	280	84	466	212	-	16	30	
NEW ENGLAND		1	23	-	1	4	34	-	2	55	135	15	-	1	4	
Maine N.H.	2	-	-	-	-	-	3 5	-	-	- 51	3 102	1 4	-	1	-	
Vt. Mass.	- 9	1 -	20	-	1 -	2	4 18	-	1	2	12 13	10	-	-	-	
R.I. Conn.	1 8	-	3	-	-	2	4	-	1	2	1 4	-	-	-	4	
MID. ATLANTIC	17	-	-	-	-	68	51	1	32	4	79	40	-	2	3	
Upstate N.Y. N.Y. City	9 2	-	-	-	-	18 21	22 3	1	12	3	29	16 3	-	-	2	
N.J. Pa.	3	-	-	-	-	29	7 19	-	1 19	- 1	11 39	15 6	-	1 1	1	
E.N. CENTRAL	12	-	-	-	-	4	73	2	62	12	77	22	-	-	5	
Ohio Ind.	4	-	-	-	-	3	22 16	2	26	9 2	57 9	3	-	-	-	
III.	3	-	-	-	-	-	23	-	17	-	4	5	-	-	5	
Mich. Wis.	2	-	-	-	-	1	11 1	-	19 -	1 -	6 1	1 7	-	-	-	
W.N. CENTRAL Minn.	1	-	-	-	-	3	24 2	1	11	1	19	16 2	-	1	1	
Iowa	1	-	-	-	-	-	3	-	2	-	-	1	-	-	-	
Mo. N. Dak.	-	-	-	-	-	-	9 -	1 -	6 3	-	8 1	8 2	-	1 -	-	
S. Dak. Nebr.	-	-	-	-	-	-	2	-	-	-	1 3	1 2	-	-	-	
Kans.	-	-	-	-	-	-	8	-	-	1	6	-	-	-	1	
S. ATLANTIC Del.	28 1	-	8	-	2	32	91 1	1	38 1	3	24	26	-	1	3	
Md. D.C.	5 5	-	-	-	1	3	7 4	-	16	1	15	10	-	-	- 1	
Va.	2	-	-	-	1	5	7	1	10	1	2	2	-	-	-	
W. Va. N.C.	9	-	-	-	-	3	2 14	-	2	-	1	6	-	-	-	
S.C. Ga.	2	-	-	-	-	-	10 32	-	1	-	3	6	-	-	-	
Fla.	4	-	8	-	-	21	14	-	8	1	3	2	-	1	2	
E.S. CENTRAL Ky.	3 -	-	-	-	-	129 113	33 6	3 -	12	4	17 3	1	-	-	-	
Tenn. Ala.	2	-	-	-	-	-	11 11	3	7 5	4	9 5	- 1	-	-	-	
Miss.	1	-	-	-	-	16	5	-	-	-	-	-	-	-	-	
W.S. CENTRAL Ark.	4 1	-	1	-	-	62	28 2	7 1	44 3	-	7	8	-	1	-	
La. Okla.	- 1	-	1	-	-	-	5 3	-	5 2	-	- 7	- 5	-	- 1	-	
Tex.	2	-	-	-	-	62	18	6	34	-	-	-	-	-	-	
MOUNTAIN Mont.	6 1	-	3	-	-	1	42 4	1	27	3	32	27	-	2	-	
Idaho Wyo.	-	-	-	-	-	- 1	1 1	- 1	3 1	1	5 1	4	-	1	-	
Colo.	3	-	2	-	-	-	5	-	4	-	11	12	-	-	-	
N. Mex. Ariz.	2	-	1	-	-	-	2 28	N -	N 13	1 1	12 3	8 -	-	-	-	
Utah Nev.	-	-	-	-	-	-	1	-	3	-	-	3	-	1	-	
PACIFIC Wash.	40 2	2	8	1	1	33 7	88 12	3	52 6	2	76 5	57 7	-	8	14	
Oreg. Calif.	2 35	-	2	-	-	- 17	11 58	N 3	N 39	2	- 66	4 44	-	1 4	- 14	
Alaska Hawaii	- 1	2	- 6	- 1§	- 1	9	4 3	-	2 5	-	1 4	2	-	1 2	-	
Guam	-	∠ U	-	U I3	-	4	-	- U	2	- U	-	-	U	_	-	
P.R. V.I.	-	-	37	-	-	30	3	- -	- 1	-	-	2	- -	-	-	
Amer. Samoa C.N.M.I.	-	U	1	U	-	-	- -	U -	4	U	-	-	U -	-	-	

^{*}For measles only, imported cases include both out-of-state and international importations. N: Not notifiable U: Unavailable † International § Out-of-state

TABLE II. (Cont'd.) Cases of selected notifiable diseases, United States, weeks ending March 13, 1993, and March 7, 1992 (10th Week)

Reporting Area		hilis Secondary)	Toxic- Shock Syndrome	Tuber	culosis	Tula- remia	Typhoid Fever	Typhus Fever (Tick-borne) (RMSF)	Rabies, Animal
grada	Cum. 1993	Cum. 1992	Cum. 1993	Cum. 1993	Cum. 1992	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993
UNITED STATES	5,345	6,387	47	2,566	2,950	11	56	20	1,089
NEW ENGLAND	85	142	5	29	26	-	7	2	220
Maine N.H.	2 2	- 9	- 1	3	-	-	-	-	- 5
Vt.	-	-	-	-	-	-	-	-	4
Mass. R.I.	45 2	60 9	4	6	23	-	5 -	2	62 -
Conn.	34	64	-	20	3	-	2	-	149
MID. ATLANTIC Upstate N.Y.	384 46	880 56	9 5	545 30	739 104	-	6 2	2	384 275
N.Y. City	249	459	-	361	400	-	2	-	-
N.J. Pa.	73 16	133 232	4	80 74	109 126	-	1 1	2	73 36
E.N. CENTRAL	785	864	14	327	336	2	5	-	4
Ohio Ind.	241 77	105 43	9 1	44 33	63 30	- 1	2 1	-	-
III.	266	373	-	175	156	-	1	-	-
Mich. Wis.	135 66	190 153	4	62 13	77 10	1 -	1 -	-	4
W.N. CENTRAL	293	209	4	40	75	2	-	-	62
Minn. Iowa	14 21	16 4	1 2	- 5	26 6	-	-	-	13 8
Mo.	233	157	-	22	28	1	-	-	1
N. Dak. S. Dak.	-	1 -	-	4	2 6	-	-	-	13 4
Nebr. Kans.	- 25	1 30	- 1	2 7	1 6	- 1	-	-	1 22
S. ATLANTIC	1,542	1,540	6	344	575	-	8	2	301
Del.	24	42	-	-	9	-	-	-	30
Md. D.C.	78 164	148 106	-	63 21	54 26	-	2	-	85 3
Va. W. Va.	119 6	123 3	-	10	77 15	-	1	-	62 9
N.C.	437	448	2	73	72	-	-	2	7
S.C. Ga.	163 261	249 421	-	51 126	55 114	-	1	-	22 83
Fla.	290	-	4	-	153	-	4	-	-
E.S. CENTRAL Ky.	680 57	933 26	1	173 54	199 62	3	1	3 2	14 1
Tenn.	182	194	1	-	-	2	-	-	-
Ala. Miss.	172 269	473 240	-	93 26	75 62	1 -	1 -	1	13 -
W.S. CENTRAL	1,298	948	-	177	203	2	1	11	56
Ark. La.	170 482	136 473	-	16 -	19 7	1	- 1	- -	2
Okla. Tex.	72 574	55 284	-	9 152	25 152	- 1	-	11	11 43
MOUNTAIN	47	109	2	66	72	'	1	-	43 12
Mont.	-	2	-	-	-	-	-	-	2
ldaho Wyo.	- 1	1 -	-	-	6	-	-	-	2
Colo. N. Mex.	18 10	20 11	1	-	5 14	-	-	-	2
Ariz.	18	40	-	44	25	-	1	-	6
Utah Nev.	-	1 34	1 -	8 14	6 16	-	-	- -	-
PACIFIC	231	762	6	865	725	2	27	-	36
Wash. Oreg.	11 14	23 12	-	42 10	37 8	-	-	-	-
Calif.	205	724	6	759	622	2	25	-	28
Alaska Hawaii	1	3	-	3 51	15 43	-	2	-	8
Guam	-	1	-	1	10	-	-	-	-
P.R. V.I.	101 11	24 11	-	2	24 1	-	-	-	12
Amer. Samoa	-	-	-	1	-	-	-	-	-
C.N.M.I.	=	1	=	1	4	-	-	-	-

U: Unavailable

TABLE III. Deaths in 121 U.S. cities,* week ending March 13, 1993 (10th Week)

	All Causes, By Age (Years) Post All Causes, By Age (Years) Post														
Donarting Area		All Cau	ses, By	/ Age (\	(ears)	1	P&I [†]	Donorting Area		All Cau	ises, By	/ Age (Y	ears)		P&I [†]
Reporting Area	All Ages	≥65	45-64	25-44	1-24	<1	Total	Reporting Area	All Ages	≥65	45-64	25-44	1-24	<1	Total
NEW ENGLAND Boston, Mass. Bridgeport, Conn. Cambridge, Mass. Fall River, Mass. Hartford, Conn. Lowell, Mass. Lynn, Mass. New Haven, Conn. Providence, R.I. Somerville, Mass. Springfield, Mass. Waterbury, Conn. Worcester, Mass. MID. ATLANTIC Albany, N.Y. Allentown, Pa. Buffalo, N.Y. Camden, N.J. Elizabeth, N.J.		639 155 53 160 27 51 25 14 49 43 40 6 49 34 77 1,888 55 52 73 22 23	5 5 14 5 3 2 9	56 19 1 1 1 9 3 1 4 9 1 1 1 5 272 3 2 2 4 3	12 5 1 1 1 1 1 5 7 2 1 1 2	15 8 1 - - - 1 5 84 2	100 42 7 3 6 1 1 1 1 2 4 3 14 195 5 1 2	S. ATLANTIC Atlanta, Ga. Baltimore, Md. Charlotte, N.C. Jacksonville, Fla. Miami, Fla. Norfolk, Va. Richmond, Va. Savannah, Ga. St. Petersburg, Fla. Tampa, Fla. Washington, D.C. Wilmington, Del. E.S. CENTRAL Birmingham, Ala. Chattanooga, Tenn. Knoxville, Tenn. Lexington, Ky. Memphis, Tenn. Mobile, Ala. Montgomery, Ala.	183 U 25 882 105	877 106 219 67 79 67 38 60 50 57 119 U 15 605 56 34 66 170 65 42	260 45 62 24 19 19 12 14 13 10 37 U 5 177 27 7 14 22 41 18 15	165 29 53 9 8 19 8 11 4 3 18 U 3 52 10 1 1 3 7 18	46 2 16 3 6 7 3 3 1 1 4 U	41 10 14 4 22 3 3 3 3 U - 22 5 1 3 3 9 1	87 10 33 3 6 2 3 5 4 4 4 13 U 4 84 3 11 12 15 30 10 11
Erie, Pa.§ Jersey City, N.J. New York City, N.Y. Newark, N.J. Paterson, N.J. Philadelphia, Pa. Pittsburgh, Pa.§ Reading, Pa. Rochester, N.Y. Schenectady, N.Y. Scranton, Pa.§ Syracuse, N.Y. Trenton, N.J. Utica, N.Y. Yonkers, N.Y.	42 67 1,567 83 31 222 111 8 157 29 25 86 42 23	33 40 1,034 37 15 121 78 5 125 23 20 60 34 20 36	6 14 286 20 7 46 23 5 5 5 23 2 1 5	2 11 185 17 5 19 4 1 4 1 - 3 2 2 2	32 4 2 7 4 - 2 - 1	1 2 30 5 2 29 2 - 3 - - - 1	3 2 91 21 2 13 12 1 16 3 3 2 1 8	Nashville, Tenn. W.S. CENTRAL Austin, Tex. Baton Rouge, La. Corpus Christi, Tex Dallas, Tex. El Paso, Tex. Ft. Worth, Tex. Houston, Tex. Little Rock, Ark. New Orleans, La. San Antonio, Tex. Shreveport, La. Tulsa, Okla. MOUNTAIN	150 1,696 68 65	104	33 338 13 13 14 49 9 28 82 17 33 35 20 25	10 177 9 3 3 38 9 12 50 8 17 16 5 7	3 67 3 2 - 14 3 6 19 4 6 4 4 2 2 27	49 1 2 8 2 2 9 12 4 1 5 3	12 110 5 5 1 16 4 6 32 8 13 9 11
E.N. CENTRAL Akron, Ohio Canton, Ohio Chicago, III. Cincinnati, Ohio Cleveland, Ohio Columbus, Ohio Dayton, Ohio Detroit, Mich. Evansville, Ind. Fort Wayne, Ind. Grand Rapids, Mic Indianapolis, Ind. Madison, Wis. Peoria, III. Rockford, III. South Bend, Ind. Toledo, Ohio Youngstown, Ohio W.N. CENTRAL Des Moines, Iowa Duluth, Minn. Kansas City, Kans. Kansas City, Kans. Kansas City, Kans. Kansas City, Mo. Lincoln, Nebr. Minneapolis, Minn Omaha, Nebr. St. Louis, Mo. St. Paul, Minn. Wichita, Kans.	172 35 161 53 54 61 114 69 807 59 27 48 128 33	1,431 52 188 207 93 92 U 1129 43 53 6 6 74 124 26 111 35 89 61 587 44 22 34 85 26 112 51 26 54	27 63 8 11 6 10 26 6 35 11 21 2 7 2 27 6 11 11 24	203 4 3 99 15 U 4 27 1 10 4 1 1 4 4 1 1 1 3 5 5 3 1 4 1 1 3 1 4 1 1 3 1 4 1 1 1 1 1 1 1 1 1 1 1 1 1	113 42 60 26 60 12 11 16 42 33 22 20 31 24 51 11	35 1 - 6 6 1 3 U - 4 4 1 1 3 3 - 2 2 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	140 4 15 9 4 U 12 14 18 6 8 4 12 6 7 7 1 1 1 2 4 6 7 7 1 1 2 6 7 7 1 1 2 6 7 7 1 1 2 6 7 7 7 1 1 2 6 7 7 7 7 7 7 7 7 7 7 7 7 7	Albuquerque, N.M. Colo. Springs, Colo Denver, Colo. Las Vegas, Nev. Ogden, Utah Phoenix, Ariz. Pueblo, Colo. Salt Lake City, Utar Tucson, Ariz. PACIFIC Berkeley, Calif. Fresno, Calif. Glendale, Calif. Honolulu, Hawaii Long Beach, Calif. Los Angeles, Calif. Pasadena, Calif. Portland, Oreg. Sacramento, Calif. San Diego, Calif. San Francisco, Cali San Jose, Calif. Santa Cruz, Calif. Seattle, Wash. Spokane, Wash. Tacoma, Wash. TOTAL	0. 61 94 180 27 173 21 1 91 115 2,370 16 120 28 78 96 652 27 179 194	80 46 61 110 21 108 15 61 81 1,563 9 71 23 48 62 399 18 124 140 119 124 139 36 128 44 79	11 7 19 46 3 3 4 11 22 404 4 24 2 113 4 28 23 37 31 40 8 29 11 15	8 3 9 20 3 17 2 12 7 258 2 11 10 11 92 5 17 19 25 26 10 1 1 21 25 5	5 4 1 3 6 5 3 74 1 7 1 2 30 4 9 6 5 7	1 1 1 4 - 8 2 2 2 2 59 - 7 - 2 4 8 - 1 6 6 8 1 1 6 6 1 1 1 6 1 1 1 1 1 1 1 1	4 11 10 1 21 27 7 152 2 7 3 8 7 28 2 11 20 15 4 16 6 11 7 5

^{*}Mortality data in this table are voluntarily reported from 121 cities in the United States, most of which have populations of 100,000 or more. A death is reported by the place of its occurrence and by the week that the death certificate was filed. Fetal deaths are not

included.

Pneumonia and influenza.

Because of changes in reporting methods in these 3 Pennsylvania cities, these numbers are partial counts for the current week. Complete counts will be available in 4 to 6 weeks.

Total includes unknown ages.

U: Unavailable.

Chronic Fatigue Syndrome — Continued

characteristic of a spumavirus. For the 29 case-patients and controls from New Jersey, samples were sent to laboratory A only; samples from all other case-patients and controls were sent to both laboratories A and B.

Previous retroviral tests performed at laboratory A (using their original PCR assay) were positive for all CFS case-patients from New Jersey. Other previous retroviral tests (performed at the research laboratory that reported finding an association between retroviral infection and CFS [2]) were positive for the 15 case-patients from New York. Of the 10 case-patients from North Carolina, six had been tested previously for retroviral infection; of these, four were positive.

None of the three assays could differentiate between case-patients and controls in either the combined study population or any of the individual study populations (Table 1). Both the original PCR assay from laboratory A and the cell-culture assay from laboratory B were positive for 59% and nearly 50%, respectively, of the case-patients and controls. The modified assay from laboratory A was negative for nearly all the case-patients (90%) and controls (96%).

Reported by: WJ Gunn, PhD, Arlington Associates, Lilburn, Georgia. AL Komaroff, MD, Brigham and Women's Hospital, DS Bell, MD, Harvard Univ Medical School, Boston; DB Connell, PhD, Abt Associates, Cambridge, Massachusetts. SM Levine, MD, Beth Israel Hospital, New York City. PR Cheney, MD, Cheney Clinic, Charlotte, North Carolina. Div of Viral and Rickettsial Diseases, National Center for Infectious Diseases, CDC.

Editorial Note: CFS has emerged as an important social and public health issue in the United States (3). Many of the complexities associated with this issue relate to diagnosis and reflect the inability of investigators to identify pathognomonic findings for CFS. In particular, CFS is primarily diagnosed by identifying specific symptoms reported by the patient and by excluding other potential causes of prolonged fatigue (3).

TABLE 1. Results of retroviral testing of chronic fatigue syndrome case-patients and controls — four study populations, 1992

		(% Positive, by assa	у
		Labora	atory A	Laboratory B
Study population	Sample size	Polymerase chain reaction, original	Polymerase chain reaction, modified	Culture for foamy cell cytopathic effect
New Jersey				
Cases	29	52%	0	*
Controls	29	59%	0	*
New Jersey				
Cases	14	57%	0	50%
Controls	14	71%	0	43%
New York				
Cases	15	60%	6%	40%
Controls	15	53%	6%	60%
North Carolina				
Cases	10	80%	10%	50%
Controls	10	50%	0	40%
Total population				
Cases	68	59%	3%	46% [†]
Controls	68	59%	1%	49 %†

^{*}Not tested; these specimens were not sent to laboratory B. †n=39.

Chronic Fatigue Syndrome — Continued

In April 1991, researchers reported finding nucleic acid sequences suggesting the presence of an HTLV-II-like retrovirus in lymphocytes of persons with CFS but not in healthy controls (2). Evidence suggesting the presence of a spumavirus—a retrovirus subfamily—in specimens from CFS patients also was reported in 1991 (3). These and other reports suggesting that retroviral infection might be associated with CFS have prompted investigations by institutions and have resulted in the use of retroviral testing to evaluate patients for CFS. Despite these efforts, the suggested association of retroviral infection with CFS has not been confirmed.

The study described in this report is the first controlled, blinded trial to examine the ability of these retroviral tests (i.e., PCR assay, PCR modified assay, and culture for foamy cell cytopathic effect) to distinguish CFS case-patients from controls. The findings from this study do not support the hypothesized association between infection with retroviruses and CFS and are consistent with findings from other studies assessing evidence of retroviral infection (5–10).

Although previously unidentified retroviral agents might be etiologic factors or cofactors for CFS, no scientific basis exists for the use of retroviral testing to confirm the diagnosis of CFS. Diagnostic testing of patients with suspected CFS should be done solely to exclude other diagnoses (11).

References

- 1. Holmes GP, Kaplan JE, Gantz NM, et al. Chronic fatigue syndrome: a working case definition. Ann Intern Med 1988;108:387–9.
- 2. DeFreitas E, Hilliard B, Cheney PR, et al. Retroviral sequences related to human T-lymphotrophic virus type II in patients with chronicfatigue immune dysfunction syndrome. Proc Natl Acad Sci USA 1991;88:2922–6.
- 3. Palca J. On the track of an elusive disease. Science 1991; 254:1726-8.
- 4. Gunn WJ, Connell DB, Randall B. Epidemiology of chronic fatigue syndrome: the Centers for Disease Control and Prevention study. In: Bock GR, Whelan J, eds. Proceedings of the CIBA Foundation Symposium 173: chronic fatigue syndrome. Chichester, West Sussex, England: John Wiley and Sons, 1993:88-101.
- Khan AS, Heneine WM, Chapman LE, et al. Assessment of a retrovirus sequence and other possible risk factors for the chronic fatigue syndrome in adults. Ann Intern Med 1993;118:241– 5.
- Folks T, Heneine W, Khan A, Woods T, Chapman L, Schonberger L. Investigation of retroviral involvement in chronic fatigue syndrome. In: Bock GR, Whelan J, eds. Proceedings of the CIBA Foundation Symposium 173: chronic fatigue syndrome. Chichester, West Sussex, England: John Wiley and Sons, 1993:160–75.
- 7. Heneine W, Woods TC, Sinha HD, et al. Absence of evidence forinfection with known human and animal retroviruses in patients with chronic fatigue syndrome. Clin Infect Dis (in press).
- 8. Gow JW, Simpson K, Rethwilm A, et al. Search for retrovirus in the chronicfatigue syndrome. J Clin Pathol 1992;45:11–14.
- 9. Landy AL, Jessop C, Lennette ET, Levy JA. Chronic fatigue syndrome: clinical condition associated with immune activation. Lancet 1991;338:707–12.
- 10. Schluederberg A, Straus SE, Peterson P, et al. Chronicfatigue syndrome research: definition and medical outcome assessment. Ann Intern Med 1992;117:325–31.
- 11. Schluederberg A, Straus S, Peterson P, et al. Chronic fatigue syndrome research. Ann Intern Med 1992;117:325–31.

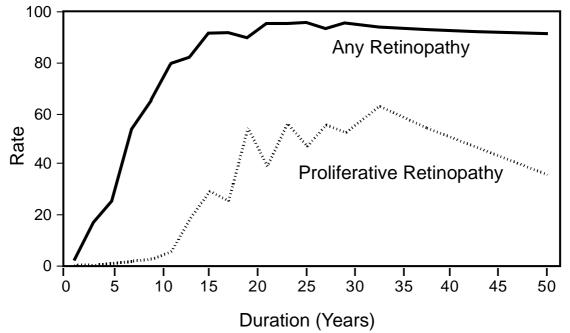
Effectiveness in Disease and Injury Prevention

Public Health Focus: Prevention of Blindness Associated with Diabetic Retinopathy

Each year in the United States, as many as 40,000 new cases of blindness occur among persons with diabetes (CDC, unpublished data, 1993). Diabetes is the leading cause of new blindness among U.S. adults aged 20–74 years (1). In addition, persons with diabetes are 25 times more likely than the general population to become blind. Most of this blindness in persons with diabetes results from diabetic retinopathy, a disorder characterized by microvascular changes and hemorrhage in the retina. Seven million persons in the United States have diabetes, and diabetic retinopathy will affect the majority during their lifetimes. This report summarizes information regarding the efficacy, effectiveness, and cost-effectiveness of screening for diabetic retinopathy.

The National Diabetes Data Group recognizes two major types of diabetes: insulindependent diabetes mellitus (IDDM) and noninsulin-dependent diabetes mellitus (NIDDM). Retinopathy occurs most frequently and severely among persons with IDDM (Figure 1), who represent approximately 5%–10% of all persons with diabetes (2). The prevalence of any diabetic retinopathy in this group is low immediately after diagnosis but increases to more than 90% after 15 years. The prevalence of proliferative diabetic retinopathy among persons with IDDM is negligible until 5 years' duration and increases to approximately 60% after 20 years. Among persons with IDDM, the prevalence of clinically significant macular edema (CSME) increases from less than 5% at short durations following diagnosis to more than 20% at 25 years' duration.

FIGURE 1. Prevalence* of retinopathy in persons with insulin-dependent diabetes mellitus, by duration of diabetes — Wisconsin Epidemiological Study of Diabetic Retinopathy, 1980–1982



^{*}Rate per 100 persons with insulin-dependent diabetes mellitus. Source: Reference 2. Adapted with permission.

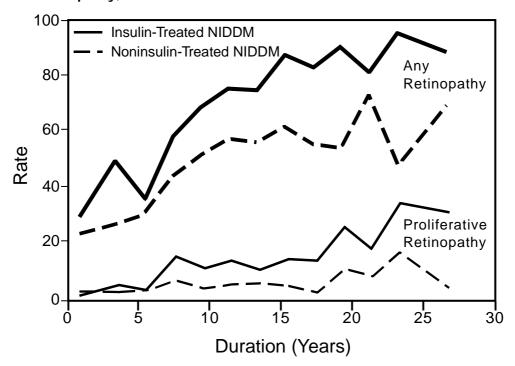
Approximately one third of all persons with NIDDM have insulin-treated diabetes. The prevalence of any retinopathy among persons with insulin-treated NIDDM steadily increases from 10%–30% at initial diagnosis to 90% at 25 years' duration (Figure 2); the prevalence of proliferative diabetic retinopathy increases from 2% at the time of diagnosis to approximately 20% after 20 years' duration. The prevalence of CSME is negligible at short durations following diagnosis but increases to more than 10% after 25 years.

Approximately half of all persons with diabetes have NIDDM treated by diet or oral hypoglycemic agents. The prevalence of any retinopathy among persons with non-insulin-treated NIDDM increases from 10%–20% at diagnosis to more than 60% at 20 years' duration. The prevalence of proliferative diabetic retinopathy increases from 2% at diagnosis to approximately 5% after 20 years' duration (Figure 2). The incidence and rate of progression of retinopathy are lowest among persons in this group. The prevalence of CSME in this group increases from less than 3% at short durations following diagnosis to more than 10% after 25 years.

Efficacy/Effectiveness

Prospective clinical trials indicate that laser photocoagulation therapy is effective in reducing the risk of visual impairment (3,4). Panretinal laser photocoagulation can reduce the risk of severe visual loss by at least 60% in some persons with diabetes (5). An annual eye examination can identify diabetic retinopathy early and permit timely treatment to prevent loss of vision and possible blindness (6). However, about half of

FIGURE 2. Prevalence* of retinopathy in persons with noninsulin-dependent diabetes mellitus (NIDDM), by duration of diabetes — Wisconsin Epidemiological Study of Diabetic Retinopathy, 1980–1982



^{*}Rate per 100 persons with noninsulin-dependent diabetes mellitus (NIDDM). Source: Reference 2. Adapted with permission.

persons with diabetes had not had a dilated eye examination in the preceding year (7).

Efficacy of Screening

The sensitivity of ophthalmoscopy in screening to identify diabetic retinopathy increases with the health-care provider's training and experience in performing eye examinations (8). Sensitivity of ophthalmoscopy performed by ophthalmologists, optometrists, trained ophthalmic technicians, and other health-care providers ranges from 50%–100% (9,10).

Retinal photography is a standard technique for examining eyes that have been pharmacologically (mydriatically) dilated or physiologically (nonmydriatically) dilated. Seven-field stereo retinal photography is both 100% sensitive and specific for diagnosing diabetic retinopathy and is the standard for evaluating severity of retinopathy in clinical trials and epidemiologic studies. Because stereo retinal photography is laborintensive and expensive, other modes for screening have been tested and compared. Both mydriatic and nonmydriatic retinal photography, using wider angle lenses and fewer fields, have tested favorably.

Cost-Effectiveness of Screening

For working-aged persons in the United States (i.e., persons aged 21–64 years), the federal budgetary cost of one person-year of blindness has been estimated at \$11,896 (11). Economic evaluations indicate that screening for diabetic retinopathy costs less than the cost of one person-year of blindness. Findings from one study (12) indicate that biannual and annual screening programs for persons with IDDM and NIDDM are cost-effective. Specifically, this study evaluated the cost-effectiveness of annual or biannual screening using three different diagnostic strategies (i.e., ophthalmoscopy and retinal photography with and without dilation) (Table 1). Each of the six strategies was compared with the baseline costs and consequences of the natural disease progression. The impact of treatment with laser and vitrectomy was added to natural progression as part of the modeling. A limitation of this study was that the model did not include the incidental benefits of detecting and treating cataract, glaucoma, and macular edema.

A second study evaluated the cost-effectiveness of different screening protocols for diabetic retinopathy among persons with IDDM (13) and focused on the effectiveness of eye examinations at three (6-, 12-, and 24-month) intervals, with and without the performance of seven-field stereo retinal photography. Assumptions included a sight-year cost of \$6300 (based on Social Security data), an annual cost of \$3150 for sight loss associated with macular edema, and an average age at onset of 12.5 years. Based on these assumptions, and by varying the strategies, \$62 million-\$109 million and 71,000-85,000 sight-years would be saved annually in the United States.

Reported by: Div of Diabetes Translation, National Center for Chronic Disease Prevention and Health Promotion, CDC.

Editorial Note: The findings in this report indicate that screening for diabetic retinopathy is both effective for preventing blindness and cost-effective. This prevention effort requires improvements in timeliness of screening, case-finding, and entry into the health-care system. To initiate treatment, all persons with diabetes (except those with IDDM of less than 5 years' duration) should receive an annual dilated eye exami-

TABLE 1. Projected costs and benefits of annual screening strategies for three 1000-person cohorts* followed more than 60 years†

Program strategy	Total sight- years	Sight- years gained	Total costs	Marginal costs§
Younger-onset cohort with ≥5 years of diabetes				
Natural disease progression (no care)	11,481	0	\$5,610,634	0
Annual ophthalmoscopic screening Annual nonmydriatic camera photo-	11,784	303	\$4,513,870	(\$1,096,765)
graphic screening Annual mydriatic camera photographic	11,795	314	\$4,574,381	(\$1,036,253)
screening	11,800	319	\$4,589,565	(\$1,021,069)
Older-onset cohort taking insulin				
Natural disease progression (no care)	6,893	0	\$1,714,690	0
Annual ophthalmoscopic screening Annual nonmydriatic camera photo-	6,950	58	\$1,657,795	(\$56,895)
graphic screening Annual mydriatic camera photographic	6,954	61	\$1,723,279	\$8,589
screening	6,956	62	\$1,747,539	\$32,849
Older-onset cohort not taking insulin				
Natural disease progression (no care)	6,708	0	\$ 869,550	0
Annual ophthalmoscopic screening Annual nonmydriatic camera photo-	6,727	19	\$ 896,821	\$27,270
graphic screening Annual mydriatic camera photographic	6,728	20	\$ 972,224	\$102,674
screening	6,729	21	\$1,006,900	\$137,350

^{*}For each cohort, the strategies are ordered in increasing effectiveness as measured by sightyears gained.

nation performed by a trained provider and should receive appropriate referral and treatment.

To reduce blindness associated with diabetic retinopathy, public health and clinical health-care providers must identify and treat high-risk persons before loss of vision. Diabetes-control programs are effective in identifying and treating persons at high risk for vision loss (14). Tertiary prevention in the form of laser treatment for proliferative diabetic retinopathy and macular edema is available in all states and most areas. Ongoing investigations are assessing whether effective control of hyperglycemia will ensure secondary prevention of diabetic retinopathy and blindness.

References

- 1. National Society to Prevent Blindness. Visual problems in the U.S. data analysis definitions. Data Sources, Detailed Data Tables, Analysis, Interpretation. New York: National Society to Prevent Blindness, 1980:1–46.
- 2. Klein R, Klein BEK, Moss SE. The Wisconsin Epidemiological Study of Diabetic Retinopathy: a review. Diabetes Metab Rev 1989;5:5559–70.
- 3. Diabetic Retinopathy Study Research Group. Photocoagulation treatment of proliferative diabetic retinopathy: clinical application of Diabetic Retinopathy Study (DRS) findings, DRS report no. 8. Ophthalmology 1981;88:583–600.
- 4. Early Treatment Diabetic Retinopathy Study Research Group. Treatment techniques and clinical guidelines for photocoagulation of diabetic macular edema. Ophthalmology 1987; 94:761–74.

[†]The columns labeled "sight-years gained" and "marginal costs" refer to the difference between sight-year totals and cost totals and costs reported for natural disease progression (no care) for each cohort.

[§]Cost-savings are shown in parentheses. Costs not in parentheses represent net expenditures.

- 5. Ferris FL. How effective are treatments for diabetic retinopathy? JAMA 1993;269:1290-1.
- CDC. The prevention and treatment of complications of diabetes mellitus: a guide for primary care practitioners. Atlanta: US Department of Health and Human Services, Public Health Service, ice, 1991.
- 7. Brechner RJ, Harris M, Cowie K. Eyes and diabetes—who's getting care? The National Health Interview Survey Diabetes Supplement 1989. Diabetes 1992;41(suppl 1):7A.
- 8. Singer DE, Nathan DM, Fogel HA, Schachat AP. Screening for diabetic retinopathy. Ann Intern Med 1992;116:660–771.
- 9. Nathan DM, Fogel HA, Godine JE. Role of diabetologist in evaluating diabetic retinopathy. Diabetes Care 1991;14:26–33.
- 10. Moss SE, Klein R, Kessler SD, Richie KA. Comparison between ophthalmoscopy and fundus photography in determining severity of diabetic retinopathy. Ophthalmology 1985;92:62–7.
- 11. Chiang YP, Bassi LJ, Javitt JC. Federal budgetary costs of blindness. Millbank Quarterly 1990;70:319–40.
- 12. Dasbach EJ, Fryback DG, Newcomb PA, Klein R, Klein BEK. Cost-effectiveness strategies for detecting diabetic retinopathy. Med Care 1991;29:20–38.
- 13. Javitt JC, Canner JK, Frank RG, Steinwachs DM, Sommer A. Detecting and treating retinopathy in patients with type 1 diabetes mellitus. Ophthalmology 1990;97:483–95.
- 14. Will JC, German RR, Michael S, Durth D. Compliance in eye disease screening programs. Diabetes 1991;40(suppl 1):351A.

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