Surveillance of Infectious Mononucleosis Cases by Use of Existing Data from State Laboratories

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THE DISCOVERY of Epstein-Barr virus (EBV) in association with Burkitt's lymphoma (BL) (*1*) and as the cause of infectious mononucleosis (IM) (*2,3*) has generated interest in anti-EBV immunization (*4,5*). If such a vaccine were to be developed, demonstration of its effectiveness would require a disease surveillance mechanism whereby patterns of IM could be monitored and compared in immunized and nonimmunized populations. Currently, no such surveillance mechanism exists, and relatively little information has been gathered on patterns of IM incidence in general populations (*6*). During a 2-year period, 1974–76, we explored the feasibility of using existing information on IM cases reported to State health department laboratories as a basis for ongoing surveillance of incidence patterns. The results of this effort are reported here.

Materials and Methods

The State laboratories of Connecticut, Georgia, Iowa, South Carolina, Virginia, and Wisconsin participated in the study. Each of these laboratories routinely used specific serologic tests for IM, and each was able to provide certain identifying information about individual serum specimens (table 1). Arrangements were made with each laboratory to supply the Centers for Disease Control (CDC) information on a monthly basis on each serum specimen positive for IM testing in whatever form was convenient for the laboratory. Coding, collation, and analysis of data were performed at CDC.

Although data available on individual specimens varied among the laboratories, depending on which items of information were requested from the local physicians who submitted specimens, all of the laboratories were able to provide at least the patient's age, sex, county of residence, and date of specimen collection (tables 1 and 2). Multiple specimens from one patient were usually identified only if those specimens had been submitted simultaneously. The data covered specimens collected over the 24 months from April 1, 1974, through March 31, 1976. Data from Georgia were available only through August 31, 1975. Connecticut, Georgia, South Carolina, and Wisconsin provided information on all serum specimens tested for IM, whether they were positive or negative.

Diagnostic procedures differed considerably among the participating laboratories (table 1). Five of the six relied on ox cell hemolysin titers—in three laboratories in combination with other tests (South Carolina, Virginia, and Wisconsin). Sheep red blood cell agglutination was used as a screening procedure in Iowa, Virginia, and Wisconsin. In Iowa, screening was followed by measurement of heterophile titers with guinea pig kidney absorption. The monospot test was used in South Carolina and Wisconsin. Testing for antibody against EBV was performed only in Wisconsin. Heterophile antibody titrations were conducted in Connecticut, Georgia, Iowa, and Wisconsin.

Results

Incidence. The number of tests performed by each laboratory is shown in table 2, according to test results. The numbers of specimens handled varied widely among the laboratories. Estimated crude annual incidence rates, calculated

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from these data, are shown in table 3. Obviously, completeness of case ascertainment by State laboratories over the 2 years differed greatly. In Connecticut and Wisconsin fairly complete ascertainment seems to have been achieved when their rates are compared with data from other population-based surveys of IM occurrence (*7,8*). Ascertainment was less complete in Iowa, Georgia, and Virginia and only fractional in South Carolina. Since numerators for these rates represent specimens tested and thus may include a certain number of repeat specimens for individual persons, the incidence values may well be falsely high.

As a further crude measure of the completeness of case reporting, the numbers of counties in each State with and without specimens submitted (whether positive or negative) were tabulated. Only Connecticut (100 percent of counties) and Wisconsin (92.8 percent of counties) approached complete representation. The other 4 States ranged between 39 and 52.8 percent of the counties represented. In Connecticut (*9*), crude county-specific annual rates ranged from 5.6 to 92.3 positive tests per 100,000 population (table 4). Although these variations may be the result of county differences in completeness of case reporting, they also may reflect differing socioeconomic, racial, and age patterns.

Age, sex, and race. The patterns by age, sex, and race for patients with positive tests were similar to those observed in other studies (*7, 8*). Positive specimens came most frequently from teenagers (ages 15–19 years); 68 percent of those who had positive specimens were under age 25 (table 5). Females outnumbered males by a ratio of 1:1.2, and they also became ill at a slightly younger age than males. However,

Table 1. Diagnostic procedures for infectious mononucleosis, titer criteria, and specimen data provided by participating laboratories

State laboratory and procedure	Positive titer criteria	Specimen data
Connecticut: microtiter ox cell	1:40+	Patient's age, sex, county of residence, date of specimen collection
Georgia: microtiter ox cell	1:40	Patient's age, sex, race, date of onset, county of residence, date of specimen collection
Iowa: screen with sheep red blood cell (RBC) slide agglutination; positives titered with Davidson differential, 2 percent sheep RBC, guinea pig kidney absorption	1:64	Patient's age, sex, race, date of onset, county of residence, date of specimen collection
South Carolina: monospot test ox cell hemolysin	1:40	Patient's age, sex, county of residence, date of specimen collection
Virginia: screen with sheep RBC agglutination; confirm with ox cell hemolysin	([1])	Patient's age, sex, race, occupation, county of residence, date of specimen collection
Wisconsin: microtiter guinea pig absorbed heterophile after screen with capillary sheep RBC test; microtiter ox cell hemolysis monospot test Epstein-Barr virus-immunofluorescent antigen	1:40	Patient's age, sex, county of residence, date specimen received

[1] Not measured.

Table 2. Number of specimens tested for infectious mononucleosis, by State and test results, April 1974–March 1976

State	Positive	Negative	Unknown	Total
Connecticut	2,250	7,368	105	9,723
Georgia [1]	606	2,297	30	2,933
Iowa	1,183	...	...	1,182
South Carolina	23	79	1	103
Virginia	1,368	1	2	1,371
Wisconsin	2,828	4,237	7	7,072
Total	8,258	13,982	145	22,385

[1] April 1974–August 1975 only.

Table 3. Infectious mononucleosis incidence rates, by State, April 1974–March 1976

State	Population (1970 census)	Number of tests positive	Crude annual incidence per 100,000
Connecticut	3,031,709	2,250	37.1
Georgia [1]	4,589,575	606	13.2
Iowa	2,825,041	1,183	20.9
South Carolina	2,590,516	23	0.4
Virginia	4,648,494	368	14.7
Wisconsin	4,417,731	2,828	32.0

[1] April 1974–August 1975 only.

positive tests were reported for both sexes in very young children (ages 0–4 years) as well as very old adults (85 years or older). Race was recorded for only 2,056 persons (24.9 percent) with positive results. As in other studies (7), cases in blacks were rare; in our study, 94.2 percent of the cases were in whites. This racial distribution pattern was similar for both sexes.

Discussion

This pilot study was conducted to gauge the feasibility of ongoing IM surveillance in the United States by using State laboratories as sources of information on cases. Although the results indicate that data generated from such sources can provide an approximation of certain broad epidemiologic parameters of IM occurrence, the system has major drawbacks.

First, since only a few States process a sufficient proportion of all expected IM case diagnostic material, a reasonably complete geographic coverage of case incidence cannot be achieved. In fact, it is expected that even fewer States will be doing the tests. For example, South Carolina's State laboratory stopped shortly after entering the study; until that time it had regularly processed sizable numbers of specimens. This projected falloff may result from the increased use of monospot tests and other simplified procedures for IM diagnosis directly in physicians' offices. In the absence of continuing central sources of case incidence data in a substantial number of States, surveillance would be difficult to maintain.

Second, the data available on individual IM cases vary widely from State to State, in terms of types of data and of the regularity and completeness with which data are recorded. In particular, information on date of specimen collection is only an approximation of date of case onset. Also, the likely occurrence of repeat specimens on individual persons is difficult to identify, which further impedes the data's usefulness.

Third, there is wide variation among State health departments in their laboratory procedures and criteria used for diagnosing IM. Obviously, this variation limits how precisely one can compare surveillance findings within States.

Fourth, even within States with relatively complete case ascertainment through State laboratory facilities (Connecticut and Wisconsin, for instance), it is likely that completeness of reporting varies greatly among intrastate divisions. The absence of case information on such important variables as race and socioeconomic status confounds this problem; in the absence of such data, one cannot be certain to what extent differences may reflect such variables and not just frequency of reporting.

Finally, the usefulness of surveil-

Table 4. Infectious mononucleosis incidence rates, by county, Connecticut, April 1974–March 1976

County	Population (1970 census)	Number of tests positive	Crude annual incidence per 100,000
Fairfield	792,814	327	20.6
Hartford	816,737	1,181	72.4
Litchfield	144,091	545	5.6
Middlesex	114,816	463	27.4
New Haven	744,948	348	23.4
New London	230,348	99	21.5
Tolland	103,440	25	12.1
Windham	84,515	256	92.3
Unknown	.....	5	...
State total	3,031,709	2,250	37.1

Table 5. Positive tests for infectious mononucleosis by age and sex, 6 States, April 1974–March 1976

Age group (years)	Male	Female	Unknown	Total
0– 4	50	34	0	84
5– 9	123	111	3	237
10–14	239	474	5	718
15–19	1,435	2,076	14	3,525
20–24	730	635	1	1,384
25–29	214	149	0	363
30–34	87	67	0	154
35–39	32	38	0	70
40–44	25	15	1	41
45–49	14	14	0	28
50–54	14	15	0	29
55–59	3	6	0	9
60–64	6	8	0	14
65–69	1	1	0	2
70–74	2	1	0	3
75–79	0	0	0	0
80–84	0	1	0	1
85 and over	3	4	1	8
Unknown	593	692	33	1,588
Total	3,571	4,359	283	8,258

Table 6. Positive tests for infectious mononucleosis by race and sex, 6 States, April 1974–March 1976

Race	Male	Female	Unknown	Total
White	896	1,038	2	1,936
Black	47	72	0	119
Other	1	0	0	1
Unknown	2,627	3,259	326	6,202
Total	3,571	4,359	328	8,258

lance for a disease such as IM, even if suitable data could be attained, is questionable. Previous studies have established quite clearly that the disease only rarely occurs in epidemic form (*10,11*), that many epidemics are spurious (*12*), and that IM usually follows predictable patterns defined largely by socioeconomic factors. In the absence of applicable immunization techniques, no public health control measures are currently available, and hence, surveillance can provide no direct service in measuring control effectiveness. Although continued epidemiologic studies of IM are needed, including basic studies of EBV infection more generally, it is unclear what useful role surveillance can play at present, unless reasonably complete case-reporting systems could be established.

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SYNOPSIS

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In a pilot study to explore the feasibility of surveillance of cases of infectious mononucleosis, data were collected on 8,258 positive specimens. These specimens had been submitted to six State laboratories—Connecticut, Georgia, Iowa, South Carolina, Virginia, and Wisconsin—during a 2-year period, April 1974–March 1976. Case reporting varied in completeness and geographic coverage. Data concerning case occurrence, by age, sex, and race of patients and month of specimen collection, confirmed previous observations regarding the descriptive epidemiology of the disease. The results indicated that the public health usefulness of extensive surveillance of infectious mononucleosis laboratory tests is limited.