

# Continued High Incidence of Diphtheria in a Well-Immunized Community

By W. J. MURPHY, M.D., M.P.H., V. HAMILTON MALEY, M.D.,  
and LILLIAN DICK, B.S., R.N.

THE incidence of diphtheria in the United States has steadily declined during the past few decades. Morbidity and mortality have decreased in each of the various geographic areas, but not to a similar extent (1, 2). The most abrupt drop has occurred in the Northeast, which prior to 1920 reported the highest rates in the country. In contrast, the most leisurely decline was observed in the South. At present, the rates reported from several of the southeastern States, including Georgia, are among the highest in the Nation.

Although evidence indicates that the abrupt drop in diphtheria morbidity during the past 25 years is related to the widespread use of active immunization, it is generally agreed that other factors have contributed to the decline. It is probable, too, that current variations in incidence in different areas may be due, in part, to factors unrelated to artificial immunization.

In an area of north Georgia comprising 10 counties with a combined population in 1950

of 156,175, the average annual morbidity rate for 1949-53 was 26.2 per 100,000 population as compared with a rate of 7.6 for the State. At the center of that area is Hall County, which reported an average annual rate of 47.8 during the same period. This report deals primarily with the diphtheria experience of Hall County.

Hall County, Ga., is located in the Piedmont Plateau of the foothills of the Appalachian Mountains and had a population of 40,113 in 1950, approximately 10 percent of which was Negro. Gainesville, the principal city, had a population of 11,936. On the whole, the county is prosperous and ranks in median family income among the upper 15 percent of Georgia's 159 counties.

Medical, public health, and hospital facilities are considered adequate. Since 1921, Hall County has had an organized health department with full-time professional personnel. Gainesville has a modern hospital with 114 beds. In 1953, there were 27 practicing physicians in the county.

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*Dr. Murphy is director of the division of epidemiology, Georgia Department of Public Health, Atlanta, Ga. Dr. Maley is commissioner of health for Hall County, Ga. Miss Dick, on assignment to the Georgia Department of Health at the time of this study, is now public health nursing supervisor and coordinator, Public Health Service Outpatient Clinic, Washington, D. C.*

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## Diphtheria Incidence

From 1935 through 1953 no appreciable decline was observed in the diphtheria incidence in Hall County. This is shown in table 1 which compares the county's average annual morbidity and mortality rates with those for the State.

In view of the small Negro population in

**Table 1. Average annual morbidity and mortality rates per 100,000 population for Hall County and for Georgia, 1935-53**

Years	Georgia		Hall County	
	Mor- bidity	Mor- tality	Mor- bidity	Mor- tality
1935-39-----	35.3	3.9	31.0	3.0
1940-44-----	18.4	1.7	35.6	1.7
1945-49-----	14.1	1.2	66.7	2.6
1950-53-----	6.4	.4	28.8	2.4

Hall County, the white and Negro rates are not considered separately. Until recently, the reported incidence of diphtheria in the white population was considerably above that for the Negroes. The rate for the white population has declined more rapidly, however, and since 1952 it has been slightly below the rate for Negroes.

The age distribution of diphtheria in Hall County does not differ appreciably from that of the State. At present in Georgia approximately 85 percent of all cases are reported in children below the age of 15 years, the highest rate being observed in the group 5 to 9 years old.

During the 5-year period 1949-53, diphtheria occurred in all sections of the county with relative frequency. Of the 96 cases reported for the period, 28 occurred in Gainesville and 68 in the remainder of the county. The average annual rates per 100,000 population for the 2 areas were 46.9 and 48.2, respectively. No undue concentration of cases was apparent in any particular occupational group. In keeping with the seasonal rise in incidence observed throughout the State, 50 percent of the cases were reported in October and November.

#### Diagnostic Criteria

To evaluate the criteria of diagnosis, we reviewed the records of the 96 cases of diphtheria reported during 1949-53. Primary consideration was given to: (a) the occurrence of a febrile illness of several days' duration; (b) evidence of a localized infection as indicated by a membrane in the throat, laryngeal involvement, or both; and (c) laboratory studies. In approximately four-fifths of the cases the local

and constitutional symptoms and the laboratory findings were consistent with a diagnosis of diphtheria. Some patients were described as having a febrile illness, sore throat, and a positive culture, but they lacked a typical membrane. In the remaining cases, the diagnosis was based on clinical grounds, characteristically on the appearance of the membrane. Apparently, the diagnostic criteria in Hall County were comparable to those in other areas of the State.

#### Cultures

Since October 1948 all virulent diphtheria cultures received by the central laboratory of the Georgia Department of Public Health have been forwarded for typing to the Laboratory Branch of the Communicable Disease Center, Public Health Service. And since July 1950 virulent cultures received by the branch laboratories have also been forwarded for typing.

A total of 927 virulent cultures were submitted for typing from October 1948 through June 1954. This figure represents the number of persons from whom cultures were received, and it includes only actual cases and intimate contacts.

The different types of *Corynebacterium diphtheriae* found in the various areas of the State are shown in table 2. The classification method is the one used by Frobisher (3). Gravis strains predominated in north Georgia, particularly in Hall and adjacent counties, but comprised only a small proportion of the cultures received from central and south Georgia.

The area designated as north Georgia represents approximately the northern two-fifths of the State. It includes 59 counties, 9 of which are contiguous with Hall County.

Of the cultures received from Hall County, approximately one-third were obtained from clinical cases and the remainder from household contacts. In numerous instances, unfortunately, cultures from hospitalized patients were not forwarded for typing to the Georgia Department of Public Health. Of the 96 cases reported during 1949-53, cultures were received from 55, and, of these, 52 were gravis and 3 were mitis. In 13 additional instances, cultures were received from one or more members

**Table 2. Diphtheria cultures classified according to type, received from four areas of Georgia, October 1948–June 1954**

Area	Total cultures	Gravis		Mitis	Mini-mus	Indeterminate
		Number	Percent	Number	Number	Number
Total for State.....	927	393	42.3	413	105	16
Hall County.....	169	154	91.1	14	0	1
Adjacent counties.....	70	48	68.6	17	2	3
Other counties in north Georgia.....	372	165	44.4	177	22	8
Counties in central and south Georgia.....	316	26	8.2	205	81	4

of the immediate family but not from the patient. In 12 of these instances, cultures were gravis in character and 1 was indeterminate.

#### Immunization Status

The immunization status of 96 diphtheria patients (1949–53) was obtained from their clinical records. Patients recorded as having received one or more doses of an immunizing agent were separated into two groups: (a) those who had received at least 3 doses of an antigen, the last one within 3 years of the date of illness; and (b) all others who had received at least 1 dose. The first were considered to represent immunization failures while in the second group protection was classed as inadequate or lapsed.

Information as to prior immunization was available for all but 14 of the 96 cases. The findings are summarized below.

<i>Immunization</i>	<i>Number cases</i>
None.....	48
Inadequate or lapsed.....	27
Immunization failure.....	7
Unknown.....	14

Of the 27 patients for whom immunization was recorded as being inadequate or lapsed, 5 had received one dose and 3 had received 2 doses of alum-precipitated toxoid within 3 years of the date of illness. For the remaining 19, there was an interval of more than 3 years between the date of the last inoculation and the onset of illness.

The 34 patients in the inoculated group in-

cluded 12 preschool and 22 children of school age, 7 boys and 27 girls. This apparent sex difference may be of some significance since a similar preponderance of cases among girls in inoculated groups has been reported by other workers (4).

In the unimmunized group there were 36 preschool and 10 school-age children and 2 adults above age 30. Of these 48 patients, 25 were males and 23 females.

Four of the 96 diphtheria patients died. None of the four had received an immunizing agent.

#### Active Immunization

In April 1953, a study was made of the extent to which active immunization was being employed in Hall County. For that purpose, a 10-percent sample of recorded live births during 1948–51 was obtained by selecting every 10th name from an alphabetical list prepared by the Georgia Division of Vital Statistics. The names appearing in the sample were checked against the records of the Hall County Health Department. Those not appearing in the files were checked against the records of three pediatricians. The remaining names that failed to appear in the physicians' records were arranged alphabetically, and a 20-percent sample was obtained by selecting every fifth name. The homes of the selected children were visited. If there was a history of prior immunization, the name of the physician administering the inoculations was obtained and his office was visited. A child was included in the

inoculated group only if an immunization record was on file. Those who had moved from the county were considered unimmunized. Infants who had died prior to the study were not excluded from the tabulations.

The 10-percent sample of live births for the period, 1948-51, included 395 names. The records of the Hall County Health Department and those of three pediatricians showed that 239 had received one or more doses of a diphtheria antigen. In 192 instances, the inoculations had been given during the first year of life. Since a considerable period of time is required in administering multiple doses of an antigen, the date of the first inoculation was used.

For the most part, a combined diphtheria-tetanus-pertussis antigen had been administered, although during 1948 and 1949, the primary series sometimes consisted of 2 doses of alum-precipitated toxoid. Of the 239 infants for whom immunization records were on file, 184 had received at least 3 doses of a combined antigen; 37 had received 2 doses of an antigen, chiefly alum-precipitated toxoid, and 18 had received only 1 dose.

There remained 156 names which did not appear among the immunization records. As stated previously, a 20-percent sample was obtained, and the 31 children in the sample were visited. A history of prior immunization was obtained for 12 children and verified by a visit to the physician's office. Of this group, 9 had been inoculated during the first year of life. For 12 children, there was no history of prior immunization and 7 families had moved from the county.

The proportion of Hall County children born during 1948-51 who had received an immunizing agent during the first year of life was estimated as:

$$\frac{192 + (5 \times 9)}{395} = 60 \text{ percent.}$$

The estimates of 68.3 percent for the second and 74.4 percent for the third year of life were similarly prepared.

The inoculated group included only children with immunization records, and since infants who died were not excluded and those who had moved from the county were considered un-

immunized, the actual immunization rate probably exceeded the estimated figures.

By the age of 6 years, the proportion of inoculated children in Hall County approached 100 percent. Prior immunization against diphtheria is a requirement for entrance to school, and although the regulation is not rigidly enforced, comparatively few children fail to comply with it. It is also routine practice for representatives of the health department to visit the schools in the fall and to administer recall doses to those in the lower grades who have not received one within 3 years.

### Schick Tests

In December 1953, the children in 1 Negro and 2 white schools were Schick tested. The test group included 1,838 children ranging in age from 6 to 18 years. Both urban and rural areas were represented. Tests were made by injecting intradermally into the forearm 0.1 cc. of an appropriate dilution of a standard diphtheria toxin. Control tests were not employed. Readings were made on the sixth day and doubtful reactions were read as positive. Since the findings in each school group did not differ appreciably, they were considered together (table 3).

Even assuming some margin of error in connection with the technique employed, it is apparent that comparatively few school children in Hall County are Schick positive. This obviously implies an unusual immunization rate, either natural or artificial, or both.

In a number of previous surveys of school

**Table 3. Number and percent of positive Schick tests by age, Hall County, Ga., December 1953**

Age (years)	Number tests	Number positive	Percent positive
All ages	1,838	106	5.7
6-7	412	27	6.5
8-9	351	16	4.5
10-11	379	20	5.2
12-13	316	18	5.6
14-15	227	17	7.4
16-18	153	8	5.2

children in the South (5, 6), the proportion of Schick-negatives was also found to be high, even among those who had never received an immunizing agent. Similarly, in Schick surveys of young men entering the armed services (7, 8), the frequency of positives among men from the South has been lower than among those from most other areas of the country. In view of the findings in previous surveys, the results in Hall County are not surprising when considered in connection with the high diphtheria morbidity and the extent of artificial immunization.

### Discussion

The continued high incidence of diphtheria in Hall County is of interest in view of the general decline experienced throughout the Nation and in most areas of Georgia. Although it is conceivable that a variety of factors may have contributed to the Hall County experience, this study has been concerned primarily with the extent of active immunization, the prevailing strain of *Corynebacterium diphtheriae*, and the frequency with which clinical infections occurred among the immunized.

Hall County has had an organized health department for more than three decades and during most of that time immunization against diphtheria has been stressed by health officials and physicians alike. That the program has been reasonably successful in reaching a large proportion of the preschool population is indicated by the results obtained in checking a sample of live births against available immunization records. Although the estimates based on that sample cannot be readily compared with those reported from other areas in the past, immunization apparently has been used more extensively in Hall County than in numerous other localities (9-11), which have experienced a far lower incidence of diphtheria for a number of years. Obviously, the Hall County experience cannot be attributed solely to a lack of interest in active immunization. On the contrary, the incidence of diphtheria has continued at a high level despite a well-organized immunization program.

On the other hand, the evidence indicates that the use of a diphtheria antigen afforded

an appreciable degree of protection when recommended schedules were followed. In view of the proportion of children who had received an immunizing agent, 60 percent by the age 1 year and almost 100 percent by the age of 6 years, it is apparent that clinical infections were observed much less frequently among those who had received one or more inoculations. Moreover, of the infections observed in the inoculated group, the great majority occurred following inadequate dosage or after protection had been permitted to lapse.

It is possible that the high diphtheria incidence in Hall County may be associated with an unusually aggressive strain of *C. diphtheriae*. Since October 1948, when routine typing was begun, more than 90 percent of the cultures from that county and almost 70 percent of the cultures from neighboring counties have been gravis strains. The findings are in sharp contrast to the diphtheria flora usually encountered in other areas of the United States (12-14). Moreover, the serologic studies reported by Hermann and Parsons (15) indicate that the gravis strains isolated in north Georgia are closely related antigenically.

However, the clinical manifestations of the disease have not been unusual and case fatality rates have not been excessive, even among the unimmunized.

The association of a gravis strain with the continued high incidence of diphtheria in Hall County is not necessarily peculiar to that type of *C. diphtheriae*. Presumably, other types might be involved elsewhere in similar situations.

### Summary

From 1935 through 1953, the incidence of diphtheria in Hall County failed to decline in spite of a well-organized immunization program.

A study based on a sample of live births indicates that at least 60 percent of the infants born in the county receive an immunizing agent by the age of 1 year. By the age of 6 years, the figure approaches 100 percent.

A review of the diphtheria cases reported during the period 1949-53 indicates that active immunization afforded an appreciable degree

of protection. Of the cases observed among previously inoculated children, the great majority occurred following inadequate dosage or after protection had been permitted to lapse.

Since October 1948, more than 90 percent of the cultures received from Hall County have been gravis strains. In central and south Georgia gravis strains were encountered infrequently.

The clinical manifestations of the disease in Hall County have not been unusual.

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## Warns Against Hoxsey Treatment

An official public warning against use of the Hoxsey treatment for internal cancer was issued April 4, 1956, by the Food and Drug Administration.

The warning was based on the finding by the United States Court of Appeals for the Fifth Circuit that the treatment was worthless. Analysis of the contents of the liquids and pills issued by the Hoxsey clinics at Dallas, Tex., and Portage, Pa., showed no value in the cure of cancer and that they contained potassium iodide, a compound which has been indicated as one that may accelerate growth of some cancers. In addition, the Food and Drug Administration, despite a thorough study, stated it had not found a single verified cure of internal cancer effected by the Hoxsey treatment.

An injunction obtained October 26, 1953, prohibits the shipment of Hoxsey "medicines" in interstate commerce if the labeling represents, suggests, or implies that they are effective in the treatment of any type of internal cancer.