The Association of Parenteral Injections with Poliomyelitis*

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THE appearance of a series of reports in the British medical literature during mid-1950,[1-5] all pointing to an association between the injection of certain vaccines and subsequent poliomyelitis, acutely disturbed health workers everywhere. The first question asked about these studies usually relates to the validity of the scientific findings; next, to how important this phenomenon is in the total poliomyelitis problem; and finally, to the damaging effect these observations might have on the well established immunization programs against several important communicable diseases. It will be recalled that all these studies showed a correlation between the site of injection and site of paralysis, limited sharply to the month before onset of poliomyelitis. Several of these investigators presented evidence to show that the severity of paralysis, at least in the inoculated limb, was greater following injections, and the suggestion was made that pertussis vaccine, either alone or in combination with other vaccines, was more frequently associated with this phenomenon than alum-precipitated diphtheria toxoid.

All except one of these studies dealt solely with poliomyelitis patients, so that an evaluation of the relative risk of acquiring poliomyelitis with or without preceding injection was not possible. Hill and Knowelden,[4] however, did compare their poliomyelitis patients with a group of matched control individuals. The sample was not large enough to settle the question but did "indicate that the group includes cases which would not have been diagnosed as poliomyelitis at all if there had been no previous and recent inoculation."

Obviously, further study of this relationship was needed and the present investigation was initiated at that time for the purpose of verifying the reports mentioned and extending the observations to include all types of injections and all age groups. In addition, an extensive control population was studied. Subsequently, the carefully documented report by Anderson and Skaar[6] appeared, confirming at all essential points the British findings and establishing the fact that the phenomenon existed in the United States and in another year, 1946, when the data upon which the report was based were collected. Although there has been considerable discussion as to the theoretical explanation and practical significance of these findings, there has appeared only one report[7] in sharp disagreement.

Another approach to the study of this association is the experimental one recently reported by Dean, Cohen, and Dalldorf.[8] Using mouse encephalomyeli-

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tis virus as the test agent given intracerebrally in mice, these investigators studied the course of subsequent paralysis in mice given different vaccines in the left front leg at varying intervals before and after the test virus was administered. Pertussis vaccine, either alone or in combination with other vaccines, yielded the most striking effects. The frequency of paralysis in the left front limb was seven times greater than expected. The mean interval between inoculation of virus and onset of paralysis was consistently shorter than in the control group given no supplementary injections. The effect was most marked when the virus and the vaccine were given simultaneously. Of especial interest in view of the findings to be reported here, the frequency of paralysis, irrespective of location, was no greater in the vaccine-treated than in the control group.

Method of Study

The only completely satisfactory method of evaluating the relative risk of acquiring poliomyelitis following an injection is to compare the poliomyelitis attack rate during a specified interval in a large injected population with the attack rate in a strictly comparable uninjected population of the same age, sex, geographic location, economic status, etc. Unfortunately, accurate and complete information on injections given to the population is not available in New York State. For that matter, data on diphtheria immunization, which are collected systematically by all local health departments in the state, were not found to be sufficiently complete for such an analysis, except in limited areas too small in population to furnish the necessary experience.

As a compromise, the following plan of study was developed, even though less desirable. Each case of poliomyelitis reported during the period June 1 through December 31, 1950, in upstate New York was to be visited and pertinent information obtained on a prepared form listing the age, sex, date of onset, distribution of maximum paralysis, and certain supplemental facts bearing on the diagnosis of poliomyelitis. Date of onset was considered to be the date on which the first obvious symptoms appeared, usually several days before paralysis developed. In addition, a record of all parenteral injections was obtained for the period two months prior to onset, specifying the type of material, the site, the date of injection, and whether the data had been checked with physician, school or hospital records. Exactly similar information was to be obtained by the same interviewer from each other member of the household and from the members of three additional control households located on either side and across the street from the home of the poliomyelitis patient. A two month interval was selected because according to published reports the association between injections and paralysis seemed to be strictly localized to the period one month before onset. It was therefore deemed unnecessary to extend the study backward for the collection of less reliable historical information. As will be seen later, limiting the study in this way was probably a mistake.

The informant in most instances was the mother of the household, and information was obtained on control individuals for the same two month period as used for the index case. The interviewers, except for the initial pilot study, were public health nurses or physiotherapists who were visiting the patient and family as part of the routine service program. The first 200 cases and associated controls were visited by medical students hired by the New York State Health Department during the summer period. Essentially all the visits were made within one month of the onset of poliomyelitis in the index case, and as a rule the data for a given patient, his

family, and the associated extra-household controls were obtained on the same day. Subsequently, detailed information was collected on muscle gradings performed during two periods—one to three months and six to eight months after onset. These were for the purpose of assessing more accurately the extent and severity of paralysis.

Every effort was made to avoid bias on the part of the interviewer and the informant with respect to the subject under investigation. It was for this reason that the control households were so rigidly specified, thus avoiding the possibility of deliberate or unintentional selection by the nurse. Investigators were urged to obtain the information on injections casually and indirectly during the course of inquiring about other unrelated matters. Perhaps one measurement of their success in this respect was the almost complete lack of public alarm created by the investigation. Considerable effort was made to verify the mother's statement through other sources of information.

RESULTS

Poliomyelitis was widespread in New York State during 1950, the third largest epidemic year on record. A total of 2,982 cases was reported from the state, exclusive of New York City. The disease did not differ clinically from that seen in recent years. Thus, there were 111 deaths, a case fatality rate of 3.8 per cent. Of the reported cases, 36 per cent were classified as nonparalytic and 26 per cent were over the age of 20 years, a distribution identical with that seen in the epidemic year 1949.

A total of 2,137 cases was included in the analysis presented here, with 6,055 household controls and 14,710 control individuals from the three adjacent households. These poliomyelitis cases represent essentially a random sample of the total group of 2,870 cases reported during the study period, with the exception that the case and control populations over 40 years of age were not tabulated. This was considered to be a justifiable deletion, since only 48 poliomyelitis patients above this age were interviewed, a number too small to warrant special analysis. The remainder of reported cases not included in the study were omitted, primarily because nursing services were not available in all counties for making the necessary home visits.

Comparison of Injections in Patients and Control Population

Table 1 presents the evidence collected on injections of immunizing substances in poliomyelitis patients and control individuals during the two months before onset. The material is tabulated by specific age groups and by whether the injections had been given during the first week, 8 to 31 days, or 1 to 2 months before onset. In instances where multiple injections had been received during this time period, the most recent injection was utilized for analysis. It is apparent that poliomyelitis patients gave histories of receiving immunizing injections during the two months prior to onset about twice as frequently as did the household and extra-household controls of comparable age. The number of individuals in any one age category may not be sufficient to demonstrate statistically significant differences, but the trend of the entire series is highly significant. Perhaps this is best summarized by the age-adjusted injection rates.

An unexpected observation was the persistence of this twofold difference during the second month. This disturbing finding is not in agreement with the conclusions reached by other investigators that the association between injections and poliomyelitis is restricted to the month prior to onset. Examination of the relationship by individual weeks throughout this period indicates that the twofold difference is present in

TABLE 1

Per cent of Poliomyelitis Cases and Controls, Household and Other, Immunized, by Age and Time Before Onset, New York State (Exclusive of New York City), 1950

Age, Years	Number Studied			Time Before Onset								
				Under 1 Week			8–31 Days			1–2 Months		
		Controls			Controls			Controls			Controls	
	Cases	Household	Other	Cases	Household	Other	Cases	Household	Other	Cases	Household	Other
Under 1	48	220	536	6.2	3.2	2.4	16.7	9.5	14.4	8.3	5.9	4.9
1	91	285	581	1.1	0.4	1.5	11.0	4.9	3.8	3.3	3.2	3.3
2	110	299	603	1.8	0.7	0.2	2.7	1.7	1.2	2.7	2.7	1.7
3	135	313	718	0.0	0.0	0.3	0.7	2.6	1.1	3.0	1.0	0.6
4	120	258	584	0.0	0.4	0.0	2.5	1.2	1.2	0.8	2.3	1.2
5	125	240	486	0.8	0.4	1.0	7.2	3.3	3.1	4.8	1.3	2.7
6	130	213	497	0.8	0.0	0.6	2.3	2.8	1.4	2.3	0.5	1.4
7	120	246	510	0.0	0.4	0.2	2.5	2.0	1.0	3.3	1.6	1.0
8	113	199	459	1.8	0.5	0.2	4.4	0.5	0.9	0.9	0.5	0.9
9	89	177	397	0.0	0.6	0.5	1.1	1.1	0.5	2.2	0.6	0.8
10–14	334	630	1,637	0.0	0.0	0.2	0.9	0.6	0.7	1.2	0.3	0.6
15–19	211	409	1,290	0.0	0.0	0.2	1.4	0.2	0.2	0.9	0.4	0.3
20–24	154	348	1,116	0.0	0.0	0.0	1.3	0.9	0.4	0.6	0.3	0.2
25–29	167	660	1,658	0.6	0.0	0.1	0.0	0.2	0.2	0.0	0.2	0.1
30–39	190	1,558	3,638	0.0	0.2	0.0	0.0	0.0	0.1	0.5	0.0	0.1
Total	2,137	6,055	14,710	0.51	0.30	0.30	2.53	1.35	1.21	1.82	0.91	0.81
Age-adjusted rates				0.51	0.26	0.34	2.53	1.48	1.26	1.82	0.97	0.98

each of the four weeks of the second month. There is no adequate explanation for this apparent discrepancy, although supplementary information bearing on the matter is presented later under the heading, "Discussion." Unfortunately, the investigation was so designed that data were collected only for the period two months before onset; hence, study of the persistence of this difference in the antecedent period was not possible.

Figure 1 illustrates this experience graphically for the full two month period. The peak periods of immunization under 1 year and at 5 years before entry into school, and the consistent excess of injections in poliomyelitis patients at each age, stand out sharply. Detailed study of the patients under 1 year of age showed that although most of them experienced onset after reaching 6 months of age, and the injections were concentrated in this age group, the excess of injections in cases was maintained throughout the first year.

Tabulation of the types of immunizing agents used indicated that 65 per cent of the injections given during the two month period to poliomyelitis patients were recorded as combined diphtheria-pertussis-tetanus vaccine. Twelve per cent represented smallpox vaccinations and the remainder consisted largely of combined diphtheria-tetanus toxoid. The distribution of types of vaccine given to the control populations was essentially the same, with 58 per cent listed as combined diphtheria-pertussis-tetanus toxoid. The data were not extensive enough to furnish significant analyses by individual type of vaccine. The same general relationships, however, were shown by smallpox vaccination as by diphtheria-pertussis-tetanus and diphtheria-tetanus vaccine injections. This was noted both with respect to the comparison of patient and control groups and to the correlation of site of paralysis with site of injection.

Similar information for injections of penicillin is presented in Table 2 with almost identical findings, except that

Figure 1

PER CENT OF POLIOMYELITIS PATIENTS AND CONTROL INDIVIDUALS, HOUSEHOLD AND OTHER, RECEIVING IMMUNIZING INJECTIONS WITHIN TWO MONTHS PRIOR TO ONSET, BY AGE

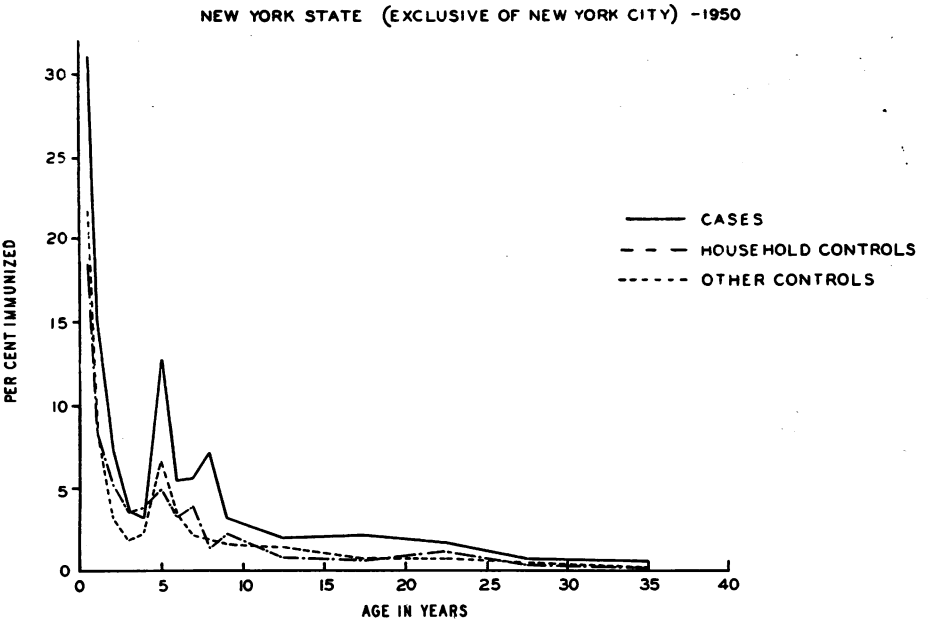


TABLE 2

Per cent of Poliomyelitis Cases and Controls, Household and Other, Receiving Penicillin Injections, by Age and Time Before Onset, New York State (Exclusive of New York City), 1950

Age, Years	Number Studied			Time Before Onset								
				Under 1 Week			8–31 Days			1–2 Months		
		Controls			Controls		Controls			Controls		
	Cases	Household	Other	Cases	Household	Other	Cases	Household	Other	Cases	Household	Other
Under 1	48	220	536	0.0	0.5	0.6	0.0	1.8	1.7	0.0	0.5	0.2
1	91	285	581	3.3	0.0	0.9	9.9	3.2	3.1	1.1	0.7	1.5
2	110	299	603	3.6	2.0	0.7	4.5	4.0	2.5	1.8	0.7	0.5
3	135	313	718	3.0	1.6	0.6	3.7	1.9	1.5	0.7	0.6	1.0
4	120	258	584	3.3	1.2	0.7	4.2	0.8	1.5	0.8	1.2	0.5
5	125	240	486	3.2	1.7	0.4	5.6	1.3	1.0	2.4	0.4	0.6
6	130	213	497	1.5	0.9	1.2	3.1	0.9	1.4	0.0	0.5	0.0
7	120	246	510	0.8	1.6	0.8	3.3	1.2	0.8	0.0	0.4	1.2
8	113	199	459	0.9	0.5	0.2	0.0	1.0	2.0	0.9	0.5	1.1
9	89	177	397	3.4	1.7	0.0	1.1	1.1	0.5	0.0	0.0	0.8
10–14	334	630	1,637	0.9	0.8	0.2	1.5	1.3	0.7	1.2	0.3	0.4
15–19	211	409	1,290	1.4	0.2	0.2	0.5	0.7	0.2	0.9	0.0	0.5
20–24	154	348	1,116	3.2	0.0	0.2	3.2	0.6	1.2	0.0	0.6	0.3
25–29	167	660	1,658	2.4	0.2	0.2	1.8	0.8	0.8	1.2	1.5	0.5
30–39	190	1,558	3,638	3.7	0.6	0.4	2.6	0.8	0.8	1.1	0.5	0.7
Total	2,137	6,055	14,710	2.29	0.78	0.41	2.71	1.32	1.14	0.94	0.51	0.61
Age-adjusted rates				2.29	0.84	0.44	2.71	1.29	1.04	0.94	0.54	0.61

these injections were less heavily concentrated in the early years of life. The same twofold difference in the per cent of poliomyelitis patients receiving injections as compared to controls is observed during each of the three time periods and at each age level. Figure 2 illustrates the data on injections of penicillin given during the entire two month period, exclusive of the first week before onset; the injections given during this week were excluded, since they might well have been administered because of the poliomyelitis illness and would therefore arbitrarily increase the injections in patients in a biased fashion.

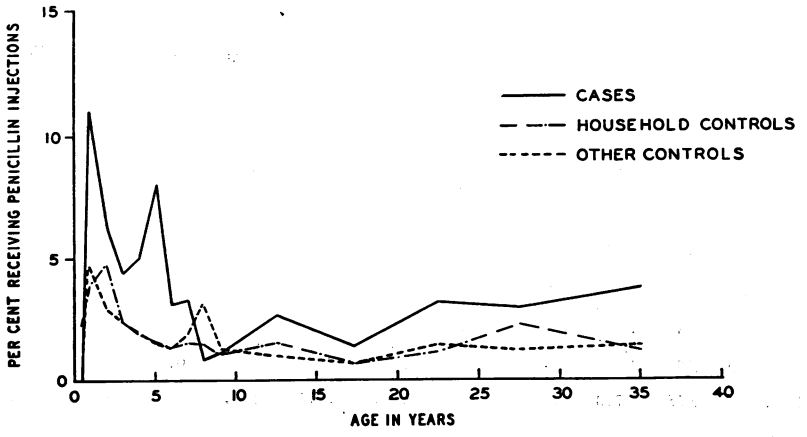
Table 3 and Figure 3 present similar evidence for other types of injections. Of the 79 such injections in poliomyelitis patients, 26 were novocain, 26 hormone and vitamin, 11 sedative, 14 venipuncture, and 2 gamma globulin. These same five categories include essentially all the injections given to persons in the control population (limited to those under 40 years). Since the latter group was considerably older than the poliomyelitis patients, injections of hormone were more common and made up 58 per cent of the total. Examination of this table shows that the same relationship noted for immunizing injections and penicillin injections exists here. It may be worth recording that 2 gamma globulin injections had been received during the two months before onset by the 929 patients under 7 years of age (0.21 per cent), while 18 (0.29 per cent) such injections were recorded for the 4,515 controls in this same age group during the same period.

By combining the material from the first three tables on an age-adjusted basis, it is seen that 12.9 per cent of the poliomyelitis cases had received some type of injection during the two months before onset, as compared to 6.1 per cent of the household associates and 6.1 per cent of the extra-household associates. Thus, even though it is assumed

Figure 2

PER CENT OF POLIOMYELITIS PATIENTS AND CONTROL INDIVIDUALS, HOUSEHOLD AND OTHER, RECEIVING PENICILLIN INJECTIONS WITHIN TWO MONTHS PRIOR TO ONSET,* BY AGE

NEW YORK STATE (EXCLUSIVE OF NEW YORK CITY) -1950



* Exclusive of first week before onset.

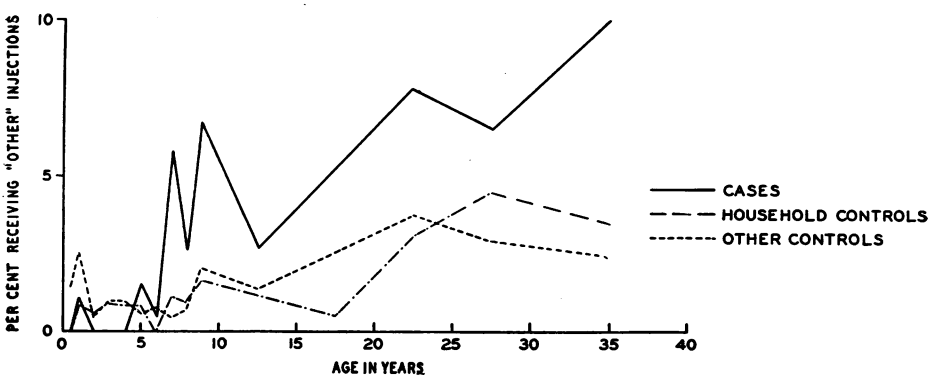
TABLE 3

Per cent of Poliomyelitis Cases and Controls, Household and Other, Receiving "Other Injections," by Age and Time Before Onset, New York State (Exclusive of New York City), 1950

Age, Years	Number Studied			Time Before Onset								
				Under 1 Week			8–31 Days			1–2 Months		
		Controls			Controls			Controls			Controls	
	Cases	Household	Other	Cases	Household	Other	Cases	Household	Other	Cases	Household	Other
Under 1	48	220	536	0.0	0.0	0.2	0.0	0.0	0.9	0.0	0.0	0.4
1	91	285	581	0.0	0.4	0.2	0.0	0.4	0.9	1.1	0.0	1.5
2	110	299	603	0.0	0.3	0.0	0.0	0.3	0.0	0.0	0.0	0.5
3	135	313	718	0.0	0.0	0.0	0.0	0.6	0.3	0.0	0.3	0.7
4	120	258	584	0.0	0.0	0.2	0.0	0.0	0.3	0.0	0.8	0.5
5	125	240	486	0.8	0.4	0.2	0.8	0.4	0.2	0.0	0.0	0.2
6	130	213	497	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.2
7	120	246	510	0.8	0.0	0.0	4.2	0.8	0.4	0.8	0.4	0.0
8	113	199	459	0.9	0.0	0.0	0.0	0.5	0.7	1.8	0.5	0.0
9	89	177	397	1.1	0.6	0.0	3.4	1.1	1.3	2.2	0.0	0.8
10–14	334	630	1,637	0.3	0.2	0.1	1.5	0.8	1.0	0.9	0.3	0.4
15–19	211	409	1,290	1.4	0.0	0.5	2.4	0.0	1.9	1.4	0.5	0.2
20–24	154	348	1,116	1.3	0.3	0.2	3.9	1.9	2.3	2.6	0.9	1.3
25–29	167	660	1,658	0.0	0.6	0.5	2.4	2.1	1.7	4.2	1.7	0.8
30–39	190	1,558	3,638	2.1	0.3	0.4	5.8	2.4	1.5	2.1	0.9	0.6
Total	2,137	6,055	14,710	0.61	0.25	0.26	1.92	1.16	1.21	1.22	0.61	0.59
Age-adjusted rates				0.61	0.21	0.19	1.92	0.85	1.03	1.22	0.49	0.45

Figure 3

PER CENT OF POLIOMYELITIS PATIENTS AND CONTROL INDIVIDUALS, HOUSEHOLD AND OTHER, RECEIVING "OTHER" INJECTIONS WITHIN TWO MONTHS PRIOR TO ONSET, BY AGE
NEW YORK STATE (EXCLUSIVE OF NEW YORK CITY) -1950



that an increased hazard of poliomyelitis exists following injections, this would apply at most to only 6 per cent of the reported cases of poliomyelitis. Table 4 has been added to show that the excess of injections in patients as compared to controls is still present when the analysis is limited to cases of paralytic poliomyelitis. In view of the well known variations in the sex ratio of reported poliomyelitis cases at different ages and the possibility that injection rates might

TABLE 4

Per cent of Paralytic Poliomyelitis Cases and Controls, Household and Other, Receiving Parenteral Injections Within Two Months Prior to Onset, by Age and Type of Injection, New York State (Exclusive of New York City), 1950

Age, Years	Number Studied			Per cent Immunized			Per cent Receiving Penicillin Injections *			Per cent Receiving Other Injections		
		Controls			Controls			Controls			Controls	
	Paralytic Cases	Household	Other	Paralytic Cases	Household	Other	Paralytic Cases	Household	Other	Paralytic Cases	Household	Other
Under 1	39	220	536	35.9	18.6	20.5	0.0	2.3	1.9	0.0	0.5	2.6
1	73	285	581	17.8	7.4	7.2	13.7	3.9	4.6	1.4	1.8	4.0
2	86	299	603	9.3	4.3	2.7	7.0	4.7	3.0	0.0	1.3	0.8
3	98	313	718	4.1	3.5	1.8	5.1	2.6	2.5	0.0	1.0	1.1
4	76	258	584	3.9	3.5	2.4	7.9	1.9	2.1	0.0	0.8	1.0
5	77	240	486	11.7	2.5	5.3	10.4	1.7	1.6	2.6	3.3	2.1
6	71	213	497	9.9	3.3	3.4	2.8	1.4	1.4	1.4	0.0	0.8
7	63	246	510	7.9	4.1	1.8	1.6	1.6	2.0	7.9	1.2	0.8
8	64	199	459	9.4	1.5	2.0	0.0	1.5	3.2	1.6	1.0	0.7
9	50	177	397	2.0	2.3	1.5	0.0	1.1	1.3	8.0	1.7	2.3
10–14	190	630	1,637	2.1	1.0	1.4	3.7	1.6	1.2	2.1	1.3	1.7
15–19	133	409	1,290	3.0	0.5	0.3	0.0	0.7	0.7	3.0	0.7	2.9
20–29	198	1,008	2,774	0.0	0.6	0.4	3.5	1.9	1.4	10.1	3.7	3.4
30–39	121	1,558	3,638	0.0	0.1	0.2	3.3	1.3	1.5	9.9	3.7	2.6
Total	1,339	6,055	14,710	5.8	2.3	2.1	4.2	1.8	1.7	4.0	2.3	2.3

* Exclusive of first week prior to onset.

vary by sex, the data in Tables 1, 2, and 3 were studied separately for males and females. No significant changes were revealed by this more refined analysis. In general, the females showed distinctly higher injection rates in the older age groups and particularly for "other" types of injections.

The relationship between injections and poliomyelitis described in this report may be translated into terms of poliomyelitis "attack rates" in injected and noninjected populations, if one accepts the premise that the injection rates in the large study control population represent a fair sample of the experience in upstate New York. By applying the age-specific injection rates by month in the study control group to the same age brackets in the upstate New York population, one may estimate the proportion of the population receiving a specific type of injection for each month under consideration.

Since similar information is available for the cases of poliomyelitis, one may estimate attack rates. This has been done in Table 5, which shows for all ages combined the attack rate in each month from July through November, for those injected within the preceding one month and for those not injected within the preceding one month. The attack rate during the month after injection is about twice that observed during a comparable period in individuals who had received no injection within this period.

If one calculates the attack rate during the two months after injection, a similar ratio is observed. This phenomenon occurs in each age group and among those receiving immunizing, penicillin, and "other" injections. The same twofold difference was observed when paralytic poliomyelitis alone was studied. Although the differences in rates between injected and noninjected populations are statistically significant, the numerical differences are small. This, of course, is a reflection of the low incidence of clinical poliomyelitis even in epidemic

TABLE 5

*Poliomyelitis Attack Rates * for Injected and Noninjected Populations, by Month of Onset and Type of Injection, Cases per 1,000 Population, New York State (Exclusive of New York City), 1950*

Month of Onset	All Injections	Immunizations	Penicillin †	Other Injections	No Injections
July	0.15	0.14	0.18	0.14	0.07
August	0.39	0.46	0.52	0.27	0.16
September	0.43	0.34	0.54	0.38	0.21
October	0.21	0.35	0.15	0.15	0.12
November	0.07	0.09	0.14	0.00	0.04

* Estimated from study for one month period.
† Exclusive of penicillin injections within one week prior to onset.

TABLE 6

Arm Involvement in Paralytic Poliomyelitis Cases with and Without History of Injections, by Site of Injection and Interval Between Injection and Onset, New York State (Exclusive of New York City), 1950*

		Site of Paralysis				
Site of Injection	Days Before Onset	Arm Only	Arm and Other	Total with Arm Involvement	Other	Per cent with Arm Involvement
Arm:	1– 7	1	1	2	8	20
	8–14	6	4	10	3	77
	15–21	4	1	5	4	56
	22–28	3	1	4	3	57
	29–42	2	2	4	11	27
	43–56	1	3	4	7	44
	Total	17	12	29	36	45
Leg;	—	5	15	20	71	22
No injection	—	113	276	389	787	34

* Immunizations and penicillin.

periods. The data on poliomyelitis attack rates must be accepted with distinct reservation because of certain puzzling factors in the material presented in Tables 1 through 4, upon which the estimates were based.

Correlation of Site of Injection with Site of Paralysis

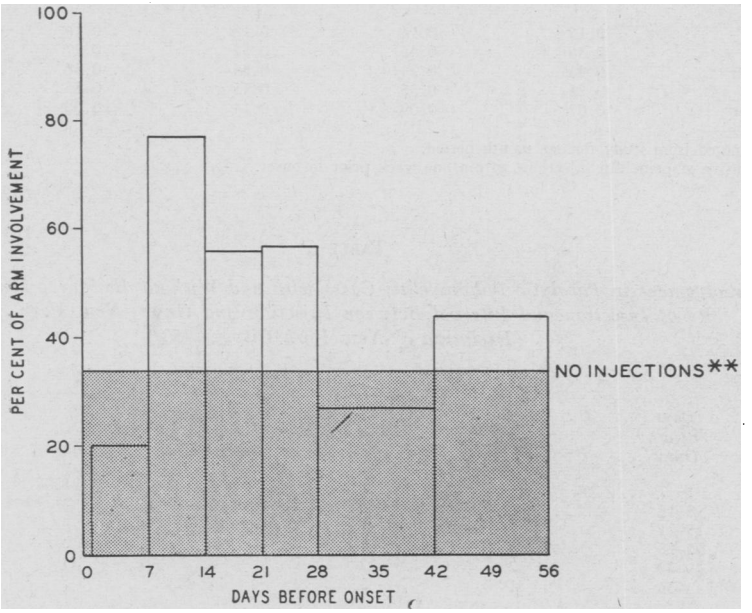
The data correlating site of injection with site of paralysis furnish perhaps the most convincing bit of evidence supporting the conclusion that there is an association between injections and poliomyelitis. This relationship has been observed by all who have studied the problem and is shown clearly in the present study for arm injections in Table 6 and Figure 4 and for leg injections in Table 7 and Figure 5. For the purpose of this analysis, immunizing and penicillin injections were combined. Actually, however, only 8 of the arm injections were penicillin and 14 of the leg injections immunizing; hence, the two tables do not present such a mixture as might be supposed.

There is a distinct excess of arm paralysis in those receiving arm injections during the period 7 to 28 days before onset. A similar but less marked excess is observed in leg paralysis following leg injections during this same period. Although not presented here because the numbers are too small to warrant illustration, the material on

Figure 4

PER CENT WITH ARM INVOLVEMENT AMONG PARALYTIC POLIOMYELITIS PATIENTS WITH ARM INJECTIONS* AND NO INJECTION BY DAYS BEFORE ONSET

NEW YORK STATE (EXCLUSIVE OF NEW YORK CITY) -1950



* Immunization and penicillin.

** This indicates per cent with arm involvement in paralytic poliomyelitis patients without prior injection.

TABLE 7

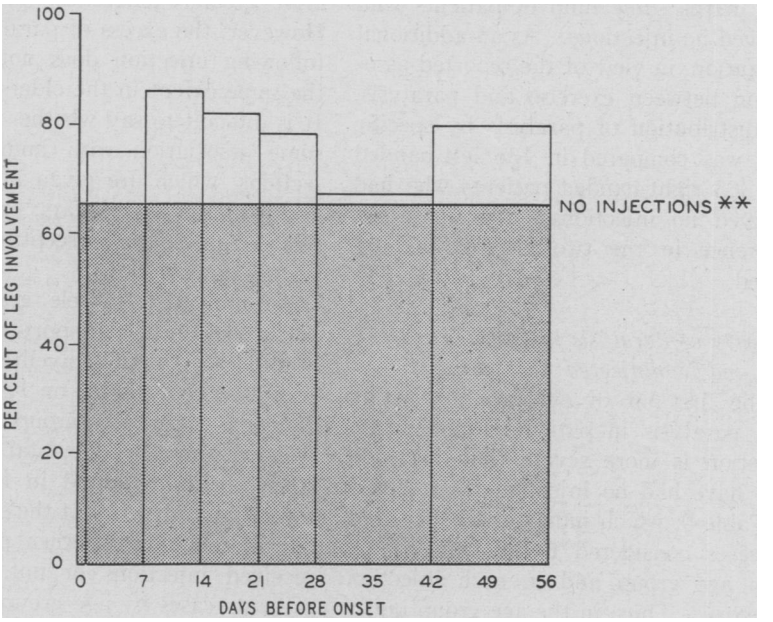
Leg Involvement in Paralytic Poliomyelitis Cases with and Without History of Injections, by Site of Injection, and Interval Between Injection and Onset, New York State (Exclusive of New York City), 1950*

Site of Injection	*Days Before Onset*	*Site of Paralysis: Leg Only*	*Leg and Other*	*Total with Leg Involvement*	*Other*	*Per cent with Leg Involvement*
Leg:	1– 7	9	12	21	7	75
	8–14	12	6	18	3	86
	15–21	6	3	9	2	82
	22–28	5	2	7	2	78
	29–42	4	4	8	4	67
	43–56	6	2	8	2	80
	Total	42	29	71	20	78
Arm:	—	19	19	38	27	58
No injection	—	418	369	787	389	66

* Immunizations and penicillin.

Figure 5

PER CENT WITH LEG INVOLVEMENT AMONG PARALYTIC POLIOMYELITIS PATIENTS WITH LEG INJECTIONS* AND NO INJECTION BY DAYS BEFORE ONSET
NEW YORK STATE (EXCLUSIVE OF NEW YORK CITY) - 1950



* Immunization and penicillin.
** This indicates per cent with leg involvement in paralytic poliomyelitis patients without prior injection.

other types of injections (most of them in the arm) demonstrates the same distribution. Thirteen, or 57 per cent, of 23 patients receiving such injections in the arm developed arm paralysis compared to only 219, or 39 per cent, of the 344 patients of comparable age who were not injected. In view of observed variations in the ratio of arm to leg paralysis at different ages, the data presented in Tables 6 and 7 were analyzed by specific age groups. This showed that the excess of paralysis in injected limbs was manifest in each age group studied.

Poliomyelitis following novocain injections deserves special comment. There was a total of 26 cases of poliomyelitis with history of such injections during the two months before onset, 19 of which were for dental work. Of this latter group, 4 had bulbar disease, 11 had other types of paralysis, and 4 were nonparalytic. Three of the bulbar cases were associated with injections during the period 8 to 14 days before onset and the fourth with an injection 2 days before onset. This is in sharp contrast to the observation that only 2 non-bulbar paralytic and one nonparalytic case were associated with injections during this two week period. One cannot, of course, exclude the possibility that the factor involved in this excessive amount of bulbar poliomyelitis was actually the dental extraction or other dental manipulation rather than the injection of novocain (extraction was performed in all except one instance).

Concerning the association between

paralysis of a specific limb and the site of injection, Table 8 furnishes further detail, again confirming previous observations. In each instance, paralysis is more frequent in the injected limb than in the same limb of patients who received no injections. As an additional precaution, in view of the reported association between exercise and paralysis, the distribution of paralysis by specific limb was compared in 136 left-handed and 303 right-handed patients who had received no injections. No significant difference in the two groups was observed.

Severity of Paralysis in Injected and Noninjected

The first bit of evidence suggesting that paralysis in patients following an injection is more severe than in those who have had no injection is presented in Table 9, which indicates the per cent of cases considered to be paralytic in each age group and in each injection category. Thus, in the age group under 1 year, 93.3 per cent of the cases occurring after immunizing injection were paralytic, as compared to 78.1 per cent of the group without injection. Similarly in the next age group, 1 to 4 years, an even greater difference was observed. However, the excess of paralytic disease following injection does not persist to the same extent in the older age groups. It is difficult to say whether this implies some association with immunizing injections, which are given almost exclusively in the early years, or whether it relates to a special susceptibility of this young age group.

As indicated, muscle gradings were performed on a large portion of the reported cases of poliomyelitis. Detailed reports were available on 1,004 of these. To some extent this group represents a selected sample of the total cases in the study, being weighted in favor of the severely paralyzed, but the selection had no reference to whether patients had received injections or not. Table 10 presents cases by age group, severity of

TABLE 8

Site of Paralysis in Poliomyelitis Cases, by Specific Site of Injection and Interval Between Injection and Onset, New York State (Exclusive of New York City), 1950*

Site of Injection	*Interval, Injection to Onset, in Days*	*Cases with Paralysis in Limb Injected*	*Cases with Paralysis in Other Sites Only*	*Per cent with Involvement of Injected Limb*		*Per cent of Noninjected Cases with Involvement of Same Limb*
				By Interval	*Total*	
Left arm:	1– 7	0	5	0	41	20
	8–28	9	6	60		
	29–56	4	8	33		
Right arm:	1– 7	2	2	50	56	14
	8–28	5	3	62		
	29–56	2	2	50		
Left leg:	1– 7	4	3	58	50	48
	8–28	3	4	43		
	29–56	3	3	50		
Right leg:	1– 7	2	1	67	67	43
	8–28	2	0	100		
	29–56	2	2	50		
Both legs:	1– 7	6	3	67	76	66
	8–28	19	4	83		
	29–56	6	3	67		

* Immunizations and penicillin.

TABLE 9

Paralytic and Nonparalytic Cases of Poliomyelitis, According to Injection History, and Age, New York State (Exclusive of New York City), 1950

Age, Years	Diagnosis	Total	Number of Cases Receiving				Per cent Paralytics Among Cases Receiving			
			Immunizations	Penicillin	Other Injections	No Injections	Immunizations	Penicillin	Other Injections	No Injections
Under 1	Paralytic	39	14	0	0	25	93.3	—	—	78.1
	Nonparalytic	8	1	0	0	7				
1– 4	Paralytic	333	28	27	1	277	93.3	93.1	—	73.7
	Nonparalytic	103	2	2	0	99				
5– 9	Paralytic	325	28	11	13	273	71.8	55.0	72.2	56.4
	Nonparalytic	236	11	9	5	211				
10–19	Paralytic	323	8	7	8	300	66.7	70.0	61.5	61.3
	Nonparalytic	201	4	3	5	189				
20–29	Paralytic	198	0	7	20	171	—	70.0	87.0	64.8
	Nonparalytic	102	3	3	3	93				
30–39	Paralytic	121	0	4	12	105	—	57.1	63.2	70.0
	Nonparalytic	56	1	3	7	45				
Total	Paralytic	1,339	78	56	54	1,151	78.0	73.7	73.0	64.1
	Nonparalytic	706	22	20	20	644				

TABLE 10

Severity of Paralysis in Poliomyelitis Patients with and Without History of Injections During the Two Months Before Onset, by Age Group, New York State (Exclusive of New York City), 1950*

Age, Years	History of Injections	Number					Per cent Distribution				
		Total	Severe	Moderate	Mild	Light-None	Severe	Moderate	Mild	Light-None	Total
Under 5	No injections	152	33	38	31	50	22	25	20	33	100
	Injections	35	9	9	12	5	26	26	34	14	100
5– 9	No injections	254	25	56	75	98	10	22	29	39	100
	Injections	29	4	5	6	14	14	17	21	48	100
10–19	No injections	259	27	38	79	115	10	15	31	44	100
	Injections	19	4	6	2	7	21	32	10	37	100
20–29	No injections	134	36	38	30	30	27	28	22	22	100
	Injections	28	4	10	6	8	14	36	21	29	100
30–39	No injections	86	20	26	15	25	23	30	17	29	100
	Injections	8	2	1	3	2	25	13	37	25	100
Total	No injections	885	141	196	230	318	16	22	26	36	100
	Injections	119	23	31	29	36	19	26	24	30	100

* Includes all types of injections.

involvement (based on gradings one to three months after onset), and whether injections had been given during the two months prior to onset. The results are not striking or completely consistent, but there is some trend toward greater severity of paralysis following injection. The extent of paralysis as determined by muscle gradings was summarized for each patient in a numerical fashion, utilizing a technique described elsewhere.[9]

DISCUSSION

Every reported investigation of the association between injections and poliomyelitis has demonstrated a definite positive correlation between site of paralysis and site of injection, an observation which is clearly confirmed by the present study. If this were the only factor involved, neither the medical profession nor the public would be unduly disturbed. The association might be compared to that existing between tonsillectomy and poliomyelitis, except that in the latter the increased hazard of bulbar poliomyelitis furnishes cogent reasons for concern. Certain details are missing in this study which would have served to define the relationship more accurately—for example, the exact types of materials injected (whether fluid or alum-precipitated vaccine, soluble or repository penicillin); route of injection (intracutaneous, subcutaneous, or intramuscular); and the sequence in the pattern of developing paralysis following injections. Unfortunately, the limitations of the study method made it impossible to obtain refined information along these lines.

The problem of major concern to health workers and to the public at large relates to whether the hazard of acquiring paralytic poliomyelitis is actually increased by injections given during a period when exposure to the virus is likely. The data presented in this study would tend to indicate that this hazard is doubled during the two months following an injection of immunizing material, penicillin, or a variety of other materials. The validity of this conclusion is challenged by the observation that the data also show an increased risk extending through the second month before onset. This is not in keeping with preconceived ideas on the subject, nor does it fit the recorded facts on the incubation period of poliomyelitis.

Naturally, the question has arisen, whether the interviewers or the informants were prone to obtain more complete information on injections in poliomyelitis patients than in the control population. Great efforts were made during the course of the study to avoid this source of bias. It would certainly seem likely that such a discrete and definite entity as a parenteral injection given during the two month period immediately preceding onset of the poliomyelitis would be engraved upon the memory of the mother equally well for all members of her family. One factor in the analysis seems to support this contention; namely, the close similarity at each age level in the per cent receiving various types of injections, among the household controls, as compared to the extra-household controls. If the mother of the poliomyelitis patient recalled more completely the injections given to the patient, it would seem that she might in turn recall injections among her other children more completely than did the mothers in adjacent households where poliomyelitis was not present.

One technique for evaluating this possibility of bias would have been to include on the investigation form miscellaneous unrelated questions concerning each household member, which, if bias existed, should have shown the same twofold difference between cases and controls. Unfortunately, such questions were not included. The only method readily available for verifying the reliability of these data was to cross-check the study cases and control individuals from certain areas against the immunization record files in health departments. In only two counties of the state, Erie and Westchester, were these records sufficiently complete to warrant this type of evaluation.

The results of this cross-checking (limited to patients and control individuals under 15 years of age) are presented in Table 11. It can be seen that, based on information obtained in the study survey, 7.2 per cent of the 180

TABLE 11

Immunizing Injections Given During Two Months Before Onset to Poliomyelitis Patients and Controls, As Determined by Study and Health Department Records, Erie and Westchester Counties, 1950*

Groups	Total in Study	Immunization Within 2 Months			
		Number		Per cent	
		Study Record	Health Department Record	Study Record	Health Department Record
Patients	180	13	4	7.2	2.2
Controls	809	38	13	4.7	1.6
Total	989	51	17	5.1	1.7

* Limited to patients and controls under 15 years of age.

patients had received an immunizing injection within the two months before onset, as compared to 4.7 per cent of the 809 control individuals, a ratio of 1.5 to 1. Through search of the health department files, with records entirely independent of this study, it was established that 2.2 per cent of the patients had received immunizing injections during the two months before onset, as compared to 1.6 per cent of the controls, an almost identical ratio of 1.4 to 1. These numbers are too small to provide a statistically significant answer to this question but they at least tend to confirm the validity of the comparison between patients and control individuals.

It is worth noting that in reviewing the immunization records on file in health departments for the 989 individuals studied, only 3 instances were uncovered where health department files recorded an immunization which had not been discovered through the study survey.

Even though one accepts the statement that the risk of acquiring poliomyelitis during the two months after an injection is doubled, this does not necessarily prove that the increased risk is caused by the injection. It has been suggested that attendance at an immunization clinic or a visit to the doctor's office, with attendant exposure to infection, might be the deciding factor instead of the injection itself. It must be admitted that all injections of penicillin were probably given because of some febrile illness. Thus, it is impossible to say whether the injection, *per se*, or the underlying illness was the factor involved in precipitating poliomyelitis.[10]

All these suggestions, however, tend to be refuted by the observation that the site of injection is correlated with the site of paralysis, an association that could hardly be explained by any of these factors. The data presented here do not help much in understanding the mechanism involved in this phenomenon. One cannot say whether this relates to the introduction of virus at the site of injection or to some nonspecific "trigger" mechanism furnished by the injected material which precipitates poliomyelitis illness or paralysis in a person already infected. Although the numbers of cases are small, it may be worth recording that in this study the median interval between immunizing injections in the arm and paralysis was 23 days, while for injections in the leg it was 30 days. No consistent difference in pattern was observed in different age groups.

Although the final evaluation of the hazard involved was not complete, the New York State Health Department felt it necessary to take some administrative action in June, 1951. It was recommended to all physicians in the

state that elective injections be avoided during the poliomyelitis season, except in infants under six months of age, at which age the danger of poliomyelitis is insignificant and the bulk of routine immunizations should be performed. It recommended further that if poliomyelitis became epidemic in a given area, these injections be discontinued in infants as well.

The medical profession and public were much disturbed by the issuance of these recommendations, since they were misread to imply that all types of injections be discontinued. Obviously, it was not intended that important therapeutic and prophylactic injections be interrupted because of the relatively small hazard of poliomyelitis. Even though one accepts the evidence pointing to a doubling of the poliomyelitis attack rate during the month following an injection, one could be accused merely of doubling the weight of a feather. Perhaps a better way of stating the situation would be to indicate that, based on data in Table 5, the likelihood of escaping poliomyelitis during the month following an injection was in September, the peak month, 999.6 per 1,000 injected individuals. This compares with the rate of 999.8 per 1,000 noninjected persons. Nevertheless, the increased hazard, though small, seemed sufficiently significant to warrant the recommendations issued.

A striking reduction in the quantity of diphtheria-pertussis-tetanus vaccine distributed by the State Health Department occurred immediately after this announcement. During the remaining portion of the poliomyelitis season, this reduction persisted but did not differ particularly from the customary summer decline in distribution noted consistently during the past decade.

SUMMARY

1. A study of the association between injections and poliomyelitis was conducted through the collection of data on injections from a group of 2,137 poliomyelitis patients, 6,055 members of the patients' households, and 14,710 other control individuals from adjacent households.

2. The per cent of patients with a history of immunizing injections, penicillin injections, or a miscellaneous group of other injections during the two months before onset was twice that seen during the same period in the control population of similar age.

3. The excess of injections among patients as compared to controls was present throughout the two month period.

4. A positive correlation between the site of paralysis and site of injection was demonstrated.

5. Paralysis in patients tended to be slightly more severe following injection than in those who had had no injections.

6. The study confirms the previous reports of an association between injections and poliomyelitis. The exact hazard in terms of increased risk of poliomyelitis after injections should be defined more accurately, and further evaluation of the practical importance of this phenomenon in public health practice is needed. However, the postponement of *elective* injections in areas where poliomyelitis is epidemic or during the poliomyelitis season in certain age groups seems justified for the time being, until these matters have been settled.

ACKNOWLEDGMENT—The authors wish to thank the many health officers, public health nurses, physiotherapists, and medical students who participated in the collection of the basic data, for the conscientious efforts they put into the study. Special thanks are due Wendell Ames, M.D., M.P.H., Deputy Commissioner of the Erie County Health Department, and William A. Holla, M.D., Commissioner of the Westchester County Health Department, for assistance in searching their files for immunization records of persons from these counties in the study population.

REFERENCES

1. Martin, J. K. Local Paralysis in Children After Injection. *Arch. Dis. Childhood* 25:1–14 (Mar.), 1950.
2. McCloskey, Bertram P. The Relation of Prophylactic Inoculations to the Onset of Poliomyelitis. *Lancet* 659–663 (Apr. 8), 1950.
3. Geffen, Dennis H. The Incidence of Paralysis Occurring in London Children Within Four Weeks After Immunization. *M. Officer* 83:137–140 (Apr. 8), 1950.
4. Hill, A. Bradford, and Knowelden, J. Inoculation and Poliomyelitis. *Brit. M. J.* 2:1–6 (July 1), 1950.
5. Banks, H. S., and Beale, A. J. Poliomyelitis and Immunization Against Whooping Cough and Diphtheria. *Brit. M. J.* 2:251–252 (July 29), 1950.

6. Anderson, Gaylord W., and Skaar, Audrey E. Poliomyelitis Occurring After Antigen Injections. *Pediatrics* 7:741–759 (June), 1951.
7. Goerke, L. S. The Precipitation of Clinical Poliomyelitis by Injections. *California Med.* 74:383–384 (May), 1951.
8. Dean, Donald J., Cohen, Sophia M., and Dalldorf, Gilbert. The Effect of Unrelated Vaccines on the Localization of Paralysis in Mouse Encephalomyelitis. *Proc. Soc. Exper. Biol. & Med.* 77:834–836, 1951.
9. Bahlke, Anne M., and Perkins, J. E. Treatment of Pre-paralytic Poliomyelitis with Gamma Globulin. *J.A.M.A.* 129:1146–1150 (Dec.), 1945.
10. Ingalls, T. H., and Aycock, W. L. Upper-Respiratory Infection as a Factor Influencing Susceptibility to Poliomyelitis. *New England J. Med.* 245:197–203 (Aug. 9), 1951.

Commission To Survey Health Needs

President Truman by executive order has created a 15 member Commission to study the nation's total health requirements. This Commission on Health Needs of the Nation has the responsibility of recommending within a year ways for meeting the health needs in both the immediate and distant future.

In announcing the Commission, the President declared that the present world crisis made it particularly important that "we should seek to limit the drain upon our strength through illness and death. . . . Many vital problems remain unanswered, such as insuring an adequate supply of physicians, dentists, nurses and allied personnel; developing local public health units throughout the nation; making more hospitals and hospital beds available where needed; stepping up the tempo of fundamental medical research; meeting the needs of the chronically ill and aged; and providing adequate diagnostic, rehabilitative, and other services to all income groups."

Paul B. Magnuson, M.D., former medical director of the Veterans Administration, has been appointed chairman of the Commission. He is the author of a proposed national health program based largely on local diagnostic clinics charging what the patient could afford. Under his plan treatment would be by private physicians, and losses incurred by the clinics met by contributions from federal, state, and local governments and private organizations. The other members of the Commission, as announced, of whom 4 are Fellows of the American Public Health Association, and representing a wide variety of consumer interests as well as medicine and medical education, are:

Dean A. Clark, M.D., general director, Massachusetts General Hospital, Boston
Joseph C. Hinsey, Ph.D., dean, Cornell University Medical College, New York City
Gunnar Gundersen, M.D.,* a trustee of the American Medical Association, La Crosse, Wis.
Russel V. Lee, M.D., associate clinical professor of medicine, Stanford University School of Medicine, San Francisco
Evarts A. Graham, M.D., surgeon, St. Louis
Marion W. Sheahan, R.N., director, National Committee for the Improvement of Nursing Services, New York City
Ernest G. Sloman, D.D.S., president-elect, American Association of Dental Schools, San Francisco
Walter P. Reuther, president, United Automobile Workers, C. I. O., Detroit
A. J. Hayes, president, International Association of Machinists, Washington
Clarence Poe, president and editor, *The Progressive Farmer,* Raleigh
Charles S. Johnson, president, Fisk University, Nashville
Lowell J. Reed, Ph.D., vice-president, Johns Hopkins University and Hospital, Baltimore
Chester I. Barnard, president, Rockefeller Foundation, New York City
Elizabeth S. Magee, general secretary, National Consumers League, Cleveland

* It is reported that Dr. Gundersen has withdrawn from the Commission.