

Progress Report on Pertussis Immunization*

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SINCE the latter part of 1932, a study of whooping cough has been in progress in Grand Rapids. The work has been outlined and certain bacteriological findings have been summarized in previous reports.^{1, 2, 3} In this paper, we are reporting our findings to date in connection with our investigation of the value of *B. pertussis* vaccine in the prevention of whooping cough.

Most notable of the reports on the use of *B. pertussis* vaccine as a prophylactic measure are those of Madsen and of Sauer. In an epidemic in the Faroe Islands in 1929 Madsen⁴ reported that of 1,832 vaccinated children, 458, or 25 per cent, did not contract whooping cough; of 446 non-vaccinated children, 8, or less than 2 per cent, failed to become infected. He considered these results favorable and thought they rested on the use of young strains of *B. pertussis*, a total dose of 22,000 million bacteria and the completion of vaccination shortly before the onset of the epidemic.

Sauer⁵ concluded from his series that if injections were completed at

least 3 months before actual exposure to the disease, a total dose of 70,000 to 80,000 million organisms conferred immunity against whooping cough.

Our own study has not been carried on for a sufficient time nor do our results embrace sufficient numbers to warrant final conclusions. However, we believe they do contain sufficient interest to justify a progress report.

GENERAL PLAN

The vaccine used has been described.³ Briefly, it is a once-washed 10,000 million per c.c. suspension of *B. pertussis*, Phase I of Leslie and Gardner,⁶ grown on Bordet-Gengou medium enriched with 15 per cent sheep's blood. The organisms are killed with merthiolate 1:10,000 or phenol 0.5 per cent allowed to act at cold room temperature for a week or more.

The optimum dosage by no means has been determined. Sauer used more than 3 times as large a total dose of vaccine as Madsen—perhaps the most important difference between the procedures of these two authors. The fact that Sauer reports such excellent protection results calls attention to the need for considering the question of total amount of injected antigen. In most of our vaccine treated individuals we have used a total quantity of vaccine close to that suggested by Sauer.

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Actually we are following our test group in two series—one including those children who have had a total of 6.0 to 7.5 c.c. of vaccine—most of them having had 7.0 c.c.; the other all those who have had less than 6.0 c.c. but have had at least 2 injections and a total of no less than 1.5 c.c.

The present scheme of injection which provides for a total of 7.0 c.c. is as follows:

Dose No.	Subcutaneous Injection at Site of	Quantity	
		Right c.c.	Left c.c.
1	Biceps		1.0
2	Triceps	1.5	
3	Triceps		1.5
4	Deltoid	1.5	1.5

The muscles are specified merely in an effort to systematize clinic procedure and to avoid giving 2 doses in the same site.

The study is directed toward the preschool child and vaccine is used therefore in presumably nonimmune children in the age group of 8 months to 5 years, with emphasis on 1 and 2 year old children.

The test group comprises the vaccine injected children. The control group is made up of children of the same age group and chosen at relatively the same time as the test children but who have not received vaccine injections. A special effort is made to leave untreated children in the families containing vaccine injected individuals.

The forms for keeping records include a vaccine inoculation blank, home visit slip and exposure record, case history form and permanent file card for recording all information on each child in the study. The follow-up information on exposure to whooping cough and subsequent cases is obtained through the Bureau of Public Health Nursing of the City Health Department by nurses' visits at 3 to 4 months intervals. Information is also gained by

checking laboratory records of cough plate findings which are filed alphabetically according to patients. When there is a record of a questionable cough, a case history is obtained on the child and also one on the source of exposure together with a record of exposure details.

DEFINITION OF TERMS

Before recording the results it is necessary to define the terms used. The difficulties of describing accurately the type of exposure, the severity of a case of whooping cough, and, indeed, of drawing a satisfactory line between what is and what is not a case of whooping cough, cannot entirely be overcome. We have drawn up rather arbitrary standards, realizing that they are not entirely adequate.

We have classified exposures as definite, indefinite, and unknown. A definite exposure may be in the family or it may be a household exposure outside the family—that is, an intimate indoor exposure to a child with whooping cough during the first 3 weeks after onset of first symptoms. Indefinite exposures include the wide variety of reported contacts which do not classify under definite exposures. An unknown exposure describes the exposure of a child who contracts whooping cough but for whom there is no record of any exposure to the disease.

To indicate the severity of the disease we have used the terms severe, typical, light and very light. A case is severe if paroxysms are unusually frequent and violent, if the duration of disease is more than 6 weeks, if loss of weight is marked, or if complications such as bronchopneumonia occur. Typical cases include those with the characteristic whoop and an uncomplicated disease duration of 4 to 6 weeks. A light case is one in which the duration is less than 4 weeks with only occasional whooping or vomiting

TABLE I
OUTLINE SUMMARY OF STUDY

<i>Groups in Study</i>	<i>Test Group Vaccine Dosage</i>			<i>Control Group</i>	<i>Totals</i>
	<i>6.0-7.5 c.c.</i>	<i>1.5-5.5 c.c.</i>	<i>Total</i>		
Number in group	552	160	712	880	1,592
No record of case or exposure	503	149	652	796	1,448
Exposures: all kinds	49	11	60	84	144
Whooping cough contracted	3	1	4	63	67
Not contracted	46	10	56	21	77
Discontinued from study for various reasons; no follow-up records					80

and no obvious interference with nutrition. A case is considered very light if there is no whooping and no vomiting but a cough which lasts for more than 1 week in conjunction with a history of definite exposure or positive cough plate findings. A cough of less than a week's duration is not considered whooping cough.

THE FINDINGS TO DATE

The number of children in the study up to August 20, 1935, is 1,592—not including 80 discontinued for various reasons, largely because they could not be located after change of address. In Table I the division into test and control groups is indicated and the results

of exposure to whooping cough outlined.

A more detailed record of exposures and subsequent cases is given in Table II.

In considering the definite exposures recorded in the whole test group, if we add the 2 instances in which whooping cough occurred with unknown exposure, then there would be 29 definite exposures followed by 4 cases of whooping cough, that is, the subsequent cases are 13.7 per cent of the definite exposures. Following the same scheme in the control group, 45 cases followed 50 definite exposures—or the cases are 90 per cent of the definite exposures. Considering all types of exposure, there

TABLE II
EXPOSURES TO WHOOPING COUGH AND RESULTING CASES IN TEST AND CONTROL GROUPS

<i>Type of Exposures</i>	<i>Test Group Vaccine Dosage</i>					
	<i>6.0-7.5 c.c.</i>		<i>1.5-5.5 c.c.</i>		<i>Control Group</i>	
	<i>Exposures</i>	<i>Cases</i>	<i>Exposures</i>	<i>Cases</i>	<i>Exposures</i>	<i>Cases</i>
Definite						
In family	14	0	2	1	32	29
Other household	7	1	4	0	7	5
Indefinite	26	0	5	0	34	18
No record of exposure but contracted whooping cough	2	2	0	0	11	11
Totals	49	3	11	1	84	63
Total exposures	60				84	
Total cases	4				63	

were in the test group 4 cases, or 6.6 per cent of 60 exposures; in the control group there were 63 cases, or 75 per cent of the 84 exposures.

While expressing these figures in terms of percentages, we call attention to the danger of giving them too much weight in the face of the relatively small number of whooping cough cases.

An interesting point is the occurrence of 11 cases of whooping cough in the control group without known exposure compared with 2 in the test group. One is tempted to consider the possibility that there have been more instances than recorded of exposure in the test group not followed by whooping cough.

A comparison of the severity of disease in the test and control groups is made in Table III.

The number of cases is not large but it may be of significance that all 4 cases which occurred in the test group were either very light or light, while of the 63 cases in the control group, 10, or about 15 per cent, were correspondingly light.

A question which has received some comment in the literature, and which was referred to in our introductory remarks, is the length of time required for immunity to develop, if *B. pertussis* vaccine actually does protect. In Table IV the exposures and cases are classified in relation to the interval between the completion of vaccine injections and the exposure to whooping cough or the onset of disease.

Of the 4 cases in the test group, 1 occurred between 1 and 2 months, 1 at 5 to 8 months, and 2 at 9 to 12 months after completion of the vaccine injections. The 58 exposures not followed by whooping cough are well divided among the different periods. The data do not justify any conclusion. From certain of our experimental data not yet published we know that the opsonins as well as agglutinins usually appear during the course of vaccine

TABLE III
WHOOPING COUGH CASES
SEVERITY OF DISEASE IN TEST AND
CONTROL GROUPS

Group	Number of Cases				Totals
	Severe	Typical	Light	Very Light	
Test group					
Dosage					
7.0-7.5 c.c.	0	0	2	1	
3.75 c.c.	0	0	0	1	
Total					4
Control group	11	42	7	3	63
Totals	11	42	9	5	67

TABLE IV
EXPOSURES TO WHOOPING COUGH AND SUBSEQUENT CASES IN RELATION TO TIME
SINCE THE LAST DOSE OF VACCINE

Result of Exposure to Whooping Cough	Number of Exposures						Totals
	Months Since Last Injection					Total	
	1-2	3-4	5-8	9-12	13-18		
Followed by cases:							
Definite exposures	1	0	1	0	0	2	4
Unknown exposures	0	0	0	2	0	2	
Not followed by cases:							
Definite exposures	3	3	7	11	4	28	58
Indefinite exposures	9	3	3	9	6	30	
Totals	13	6	11	22	10	62*	

* These 62 exposures are for 60 individuals; in all other tables, the exposures have indicated individuals.

injections and reach a relatively high level soon after the 4th and frequently after the 3rd injection. However, we are unable to correlate these circulating antibodies with protection.

SUMMARY AND CONCLUSIONS

A progress report has been made on a pertussis immunization study in Grand Rapids, Mich.

The series to date includes 1,592 children—712 in the test group, and 880 in the control group. In the whole series there have been 67 cases of whooping cough, of which 63 occurred among controls.

The data presented suggest that an active immunity has followed the injection of *B. pertussis* vaccine under the conditions described. However, before a proper evaluation can be made of the data or definite conclusions drawn, it will be necessary to increase the number in our study and to await the accumulation of follow-up data over a longer period.

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