with excellent results. What is, however, of more importance in the present connexion is the fact that those cases complaining of a coincident dysmenorrhœa were relieved of this symptom by the injection. I have since had the opportunity of demonstrating my technique to Prof. Young, and he agrees that, theoretically at least, it is preferable to Blos's original method.

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WHOOPING-COUGH

VALUE OF A SPECIFIC VACCINE IN TREATMENT

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FEW therapeutic measures can have given rise to more conflicting reports than the vaccine treatment of whooping-cough. Widely varying doses of whooping-cough bacilli, alone or in combination with other organisms, were used by the early investigators and the results, as might be expected, were equally varied.

In prophylaxis the reported results are excellent and the preventive value of a pertussis vaccine would seem proven. A protective vaccine to have any success must be prepared from the hæmolytic smooth form of the bacillus. Madsen,[1] using a vaccine of this nature, has obtained either protection or attenuation in recent epidemics of whooping-cough on the Faroe Islands. On the other hand, Krueger [2] believes that mechanical disruption of the bacillary body is necessary in order to avoid possible denaturation. In this way an endo-antigen is obtained and has been successfully used by Munns and Aldrich [3] in prophylaxis. It is doubtful whether the results obtained with pertussis antigen are any better than those achieved with the intact bacillus.

Success in prophylaxis has caused a revival of interest and has stimulated further investigations into the value of the newer vaccines or antigens in treatment. Stallings and Nicholls [4] treated 232 patients in the catarrhal and paroxysmal stage of whooping-cough with undenatured pertussis antigen. Abatement of symptoms appeared to follow, but the experiment was inadequately controlled. It is generally agreed that, if success is to follow vaccine therapy, the initial injections must be given early in the disease, large doses must be injected, and smooth colonies must be used in the preparation of a vaccine. Although such a vaccine has been enthusiastically advocated, the few adequately controlled experiments which have been carried out do not show that it is of any value in the treatment of whooping-cough.

PRESENT INVESTIGATIONS

It should be emphasised that we were not concerned with prevention. An attempt was here made to assess the value of a pertussis vaccine in the treatment of early cases of whooping-cough. Certain limitations are immediately imposed on such an experiment in hospital practice. It is the general experience that only in severe epidemics are whooping-cough cases admitted to hospital in the early catarrhal stage of the disease. This is probably due to the fact that, during marked prevalence, every cough is regarded with suspicion. In less severe epidemics, on the other hand, suspicion is not aroused until the cough has become paroxysmal or until a whoop develops. During the period of this investigation the epidemic was of moderate severity and, in consequence, early cases were limited to those already in the paroxysmal stage of the disease.

The investigation was conducted along the following lines: (1) Cases of whooping-cough, in the paroxysmal or early whooping stage, numbering 60, were graded according to severity on admission. (2) All the cases received routine treatment such as fresh air and simple drugs when indicated. (3) Half of them received, in addition, a specific pertussis vaccine. (4) In a certain number of cases leucocyte counts were done on admission and in early convalescence.

Classification of severity.—This is avowedly unsatisfactory in whooping-cough. Nevertheless, some classification is necessary for purposes of comparison and the following simple one was used:—

1. Total spasms in 24 hours did not exceed 10. Character of spasms mild—cyanosis never seen.
2. Total spasms in 24 hours exceeded 10 but not 20. Spasms of moderate severity—cyanosis occasionally seen.
3. Total spasms in 24 hours exceeded 20. Severe spasms with cyanosis the rule—convulsions occasionally.

All the cases in this series fell into the first or second group of this classification on admission. No case with a severe respiratory complication such as broncho-pneumonia was included.

Vaccine administration.—The vaccine was prepared from recently cultivated smooth strains of *Hæmophilus pertussis* and put up so that 1 c.cm. contained 10,000 million organisms. Bacilli used in making the vaccine were of proven virulence on guinea-pig injection, and when used for active immunisation of rabbits could protect them against fatal doses of a virulent culture of the same organism. Alternate cases of similar age and apparent clinical severity were given a routine course of this suspension subcutaneously. A course consisted of 0·2, 0·5, 1, 1·5, 2, and 2·5 c.cm. at intervals of 2–3 days. It was always possible to complete a course within 14 days of admission.

Reactions after vaccination.—Local reactions consisting of erythema and induration were common but transient. General reactions were rare. Three children had a sharp rise of temperature on the evening of injection, but by the next day the temperature had fallen to normal. A clinical impression was gained that children occasionally experienced an increase in frequency and severity of their spasms during the course of injections. The discussion of the significance of this finding we will leave for the moment.

VALUE OF VACCINE THERAPY

Children of approximately the same age and at the same stage of disease were alternately placed in the vaccine or control series and in this way two groups of cases were obtained. Table I. has been compiled to show the result of this classification. It will be seen in section A of this Table that, as far as age and stage of disease is concerned, the distribution is almost identical. It was hoped that the two

groups would be also identical as far as severity on admission was concerned. Reference to section B of the Table will show that this was not achieved. The distribution is less favourable for the vaccine series as the percentage within the Group 2 classification of severity is greater than that for the controls. This is readily explained by the fact that classification

TABLE I

Showing Percentage Distribution of Cases: (A) *according to Age and Stage of Disease:* (B) *according to Severity on Admission.*

Age.	A						B		
	Controls.			Vaccine.					
	Paroxysmal.	Whooping.	Total.	Paroxysmal.	Whooping.	Total.	Severity grouping.	Controls.	Vaccine.
0–½ yr.	10·0	6·7	16·7	6·7	6·7	13·4	..	..	..
½–2 yrs.	13·3	20·0	33·3	13·3	20·0	33·3	1	70·0	50·0
2–5 ,,	20·0	16·7	36·7	13·3	26·7	40·0	2	30·0	50·0
5–10 ,,	0	13·3	13·3	6·7	6·6	13·3	..	..	..
—	43·3	56·7	100·0	40·0	60·0	100·0	..	100·0	100·0
	100·0			100·0					
	N = 30							N = 30	

was attempted on the actual day of admission, in order that there should be no delay in the administration of vaccine. Early classification of severity in such a variable disease as whooping-cough has obvious disadvantages, and in this case has resulted in a disparity for which allowance must be made in any comparison of results between the two series. Allowance can be made in this way. If it can be assumed that the vaccine-treated cases, distributed according to severity on admission, would experience the same increases in severity after admission as the control series, then the total number of vaccine cases who might be expected to get worse would be 15·23. The actual number was 17 (Table II.). In like manner comparisons can be made between the number of vaccine cases who might be expected to cease whooping at a particular period of the disease and the number who did in fact cease at that period. Reference to Table II. will show that the vaccine cases behaved exactly as might be expected, except in the first four weeks of the disease. Here it is significant to note that approximately five fewer vaccine cases ceased to whoop at the end of two weeks, but that five more than were expected had ceased whooping at the end of four weeks.

It seems reasonable to assume, from the figures given in Table II., that the only demonstrable effect of the vaccine was a tendency to increase the severity of the spasms and to prolong the whoop beyond the 14-day period during which vaccine was being injected. This effect is in agreement with the clinical impression obtained during this investigation and has been previously recorded by Howell [5] in an investigation at this hospital. It need not necessarily be interpreted as a result of vaccine per se and might be attributed to a psychological effect. Information on this point could be gained in a future investigation by injecting the control series with small quantities of sterile water.

EFFECT OF VACCINE ON BLOOD COUNT

In conclusion an attempt was made to determine whether the injection of pertussis vaccine had any effect on the leucocyte response in whooping-cough. Of 23 children, who formed the subject of this investigation, 12 had received vaccine and the remaining 11 acted as controls. A leucocyte count was done on admission and repeated 14 days later—i.e., at the usual termination of a vaccine course. It was found that both groups showed leucocytosis and lymphocytosis on admission, but that 14 days later the count had returned to normal irrespective of whether vaccine had been given or not. Thus it was impossible to demonstrate, from these counts, any leucocyte change which could be attributed to the injection of vaccine.

CONCLUSIONS

The position with regard to vaccine treatment, as judged by this investigation, would seem to be clear. The injection in the paroxysmal stage of large doses of a pertussis vaccine prepared in accordance with modern methods and beliefs is shown neither to curtail the duration of the disease nor to ameliorate the symptoms. Indeed the only effect obtained was an undesirable one, although not serious. It is noteworthy that no case in the vaccine or control series was fatal. This, in face of the not inconsiderable mortality which prevailed for the general run of cases in the epidemic, appears to be a potent argument for the early hospitalisation of whooping-cough.

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TABLE II

SHOWING (1) INCREASES IN SEVERITY, (2) DURATION OF WHOOP, IN CONTROL AND VACCINE SERIES

Severity grouping.	Control series.						Vaccine series.									
	Cases	Increase in severity and per cent.	Duration of whoop.				Cases	Increase in severity.		Duration of whoop.						
			2 weeks.	4 weeks.	6 weeks.	8 weeks.				2 weeks.		4 weeks.		6 weeks.		8 weeks.	
								Act.	Exp.	Act.	Exp.	Act.	Exp.	Act.	Exp.	Act.	Exp.
1	21	12 (57·1)	11 (52·4)	9 (42·8)	1 (4·8)	0 (0·0)	15	12	8·6	5	7·9	8	6·4	2	0·7	0	0
2	9	4 (44·4)	2 (22·2)	4 (44·5)	2 (22·2)	1 (11·1)	15	5	6·6	2	3·3	10	6·7	2	3·3	1	1·7
	30	16 (53·3)	13 (43·4)	13 (43·4)	3 (10·0)	1 (3·2)	30	17	15·2	7	11·2	18	13·1	4	4·0	1	1·7

Act. = actual. Exp. = expected.