THESIS FOR DEGREE OF M.D.

W H O O P I N G C O U G H.

"A Laboratory and Clinical Investigation
with special reference to the value of Vaccine Therapy".

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JOHN PAUL JONES PATON M.B., Ch.B.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

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1. Introduction.

Whooping Cough, or Pertussis is a zymotic disease, occurring chiefly in temperate climates. Persons of all ages are susceptible, but it is essentially a disease of infants and young children, clinical cases of Whooping Cough being comparatively uncommon after the age of 9 - 10 years. In Glasgow, where the work for this investigation was carried out, it occurs in epidemics every two years and usually reaches a peak in Spring.

Pertussis, a term first used by Sydenham, has been given various names which refer either to the paroxysmal attack of coughing or to the peculiar crowing sound produced on inspiration after such an attack. The commonest synonym is Whooping Cough; in England the disease is also known as Chin-Cough, in Scotland as Kink-Cough or Kink-Hoast; in France as La Coqueluche, and in Germany Keuch-husten.

Although recognised in Europe, and in Britain, from early times, Whooping Cough does not appear to have been described by the ancient Greeks or Romans, nor by Arabian authors. A physician, Willis [quoted by Watt (1) (1813)], who practised in Oxford and London and who died in 1675, speaks of Chin-Cough as being of common occurrence. He recorded that it was an epidemic disease occurring chiefly in Spring and Autumn, children being most commonly attacked, and that it was apt to run its course in spite of every mode of treatment.

Writing in 1813, Watt (1) stated that "in Glasgow the greatest number of deaths by Chin-Cough during the last 30 years was in 1809 when they amounted to 259 or something more than 11½ per cent. of the whole deaths of the year". In 1935 in the Glasgow Burgh (2) there were 166 deaths from Scarlet Fever and Diphtheria combined, whilst in the same year the number of deaths from Whooping Cough numbered 271.

At the present time there are 2,000 to 6,000 deaths from Whooping Cough annually in England and Wales (3), whilst Sauer (4) (1933) quotes a recent United States Public

Health Series report which "shows that about 95 per cent. of our 6,000 or more annual Whooping Cough deaths occur before the third year of life. About 2 per cent. of all infected children succumb, but the mortality for infected infants is about 15 per cent. Because of its greater prevalence, Whooping Cough causes as many deaths as does Diphtheria, or as many as do Scarlet Fever and Measles combined". In 1932 169,283 cases of Whooping Cough were reported in the United States (5) (excluding Utah) of whom 4,508 died. These figures indicate as has been frequently remarked in the medical press of recent years, the need for a more intensive study of Whooping Cough, particularly with regard to improvement in early diagnosis, treatment and prevention.

The salient points in the laboratory diagnosis of Whooping Cough are briefly the following:-

In 1906 Bacillus Pertussis was first described by Bordet and Gengou (6) as the causal organism of Whooping Cough. They (7) also found (1907) that the serum of patients convalescing from the disease had the property of deviating complement when Bacillus Pertussis was used as antigen. Leucocytosis in Whooping Cough had been previously described by Frölich (8) (1897), while later investigators found that a relative lymphocytosis was the outstanding feature of the haematological picture. The bacteriological diagnosis of Whooping Cough by the "cough plate method" was introduced by Chievitz and Meyer (9) in 1916, and has since been used extensively in Denmark and other countries with considerable success in the early diagnosis of the infection. In 1931 Leslie and Gardner (10), dealing with the antigenic structure of the organism, clarified the confusion on the subject by describing four antigenic phases of Bacillus Pertussis. Phase 1 is the most toxic and the best antigen for vaccines; with Phase 11 it corresponds to the "smooth" state, whilst Phases 111 and 1V correspond to the "rough" state of other organisms.

An intradermal test for the diagnosis of Whooping Cough has been used by several investigators with varying results. Siebler and Okrent (11) (1934) came to the conclusion that children with a previous history of Whooping Cough usually gave negative skin tests, the converse also being true - that children with no previous history of Whooping Cough usually gave a positive skin reaction. The vaccine used by these investigators was one prepared in a similar manner to that used by Sauer (4) (1933). On the other hand Paterson, Bailey and Waller (12) (1935) also using Sauer's vaccine, found that children with a previous history of Whooping Cough usually gave a positive skin reaction, whilst children with no previous history of Whooping Cough gave a negative skin reaction. In a subsequent letter in the same year, Paterson (13) (1935) stated that the results obtained varied with the batch of vaccine used.

There is a considerable literature on the use of pertussis vaccine as a therapeutic and prophylactic measure in Whooping Cough.

Favourable results from the use of Pertussis vaccines in the treatment of Whooping Cough were reported by various workers amongst whom were Freeman (14) (1909), Nicolle and Connor (15) (1913), Herrman and Bell (16) (1924), Bloom (17) (1925), Pierret (18) (1932) and Cockshut (19) (1933). Unfavourable results were obtained by Von Sholly, Blum and Smith (20) (1917), Paterson and Smellie (21) (1922), Howell (22) (1930), Thompson (23) (1930) and Begg and Coveney (24) (1936). With the exception of Bloom (1925) who used a vaccine prepared from Bacillus Pertussis and Bacillus Influenzae the other investigators used a vaccine prepared only from Bacillus Pertussis.

It would appear from a review of the literature that some workers have obtained negative or equivocal results while others report encouraging results; the majority of the latter are almost unanimous in saying that vaccino-therapy is of greatest value in the earliest stages of the

disease. It seems that very large doses of the vaccine can be tolerated without untoward effect and that the vaccine should be prepared from freshly grown organisms to ensure antigenic efficacy.

On theoretical grounds, in view of the common occurrence of respiratory complications, a mixed vaccine composed of Bacillus Pertussis and the organismsusually associated with bronchopneumonia could be employed in the treatment of Whooping Cough, but unfortunately in practice the use of vaccines in the treatment of pneumonia has been very disappointing.

Madsen (25) (1933), Sauer (26) (1933), Frawley (27) (1934) and Sauer (28) (1937) all report good results from the prophylactic use of pure Pertussis Vaccine and Sauer maintains that the degree of protection afforded is improved by the use of large doses.

Present Investigation.

The record which follows is based on a series of cases investigated in Belvidere Hospital over a period of three years, 1934 - 1937, where after a short experience of work in Whooping Cough wards it became apparent that Pertussis in conjunction with its complications was probably the most fatal of all the zymotic diseases commonly affecting children. This is well illustated in the figures shown in Tables I, III and IV in the appendix.

In the present investigation (see page 59) Bronchopneumonia, Bronchitis, Enteritis and Convulsions were found to be the commonest fatal complications, particularly in the earlier age groups.

From the therapeutic aspect the long list of drugs advocated indicates how unsatisfactory is the position. Consequently it was decided to investigate Whooping Cough from as many aspects as possible, special attention being directed to (a) the diagnosis by specific tests and (b) the effect of specific vaccine therapy.

The inquiry involved investigation of 458 cases in all, which for the sake of simplicity will be divided into various groups described under their appropriate headings. The work was commenced in Belvidere Hospital in November, 1934 and finished in September, 1937 whilst I was a resident medical officer there.

Diagnosis.

Clinical Diagnosis.

The early clinical diagnosis of Whooping Cough is notoriously difficult, and at best can only be a surmise; amongst the 257 cases of Whooping Cough under survey very few were admitted in the Catarrhal stage. Of the features commonly found in the Catarrhal stage, which may last 4 - 21 days, the following are worthy of note.

In a high percentage of cases a history of exposure to Pertussis of children who have not been previously infected will be found, often the onset of the disease is insidious, but the occurrence of listlessness, pyrexia and a short sharp cough associated with injected fauces, coryza and respiratory catarrh are all pointers to the possibility of Pertussis being present. The paroxysmal cough which is occasionally followed by vomiting, usually worst at nights, belongs properly to the paroxysmal stage, but in severe cases of Pertussis the disease may commence with the paroxysmal cough, and in young children convulsions may be one of the early symptoms. Obviously, therefore, there is a great need for a reliable method of early diagnosis. No doubt there are many cases of mild or abortive Whooping Cough which cannot be diagnosed clinically. In the later stages diagnosis is usually easy, although patients with bronchitis, bronchopneumonia or other respiratory conditions leading to enlargement of the hilum glands of the lung may have a spasmodic cough not unlike Whooping Cough.

Laboratory Diagnosis.

The Laboratory Diagnosis of Whooping Cough involves a consideration of tests specific and non-specific in nature.

By Specific Tests are meant tests for the isolation of Bacillus Pertussis or the demonstration of specific antibodies to this organism. Their value and reliability rest on the assumption that the Whooping Cough Bacillus is the causal organism of the disease. The arguments for and against this view are stated below:-

(1) Recent investigations have shown that the organism is present in expectorated droplets in a high proportion of early cases.

(2) It has been found that there is one specific serological type of the Bacillus Pertussis.

(3) Specific antibodies to the Bacillus Pertussis have been found to develop in the blood of infected patients and rarely in non-affected children.

(4) Experimental work on young boys has shown that the disease can be produced by a culture of Bacillus Pertussis and that a filter passing virus plays no part in the aetiology of Pertussis. (H. Macdonald and E. J. Macdonald (29) 1933).

The Virus aetiology of Pertussis gained support from the researches of the following workers:-

(1) Rich (30) (1932), stated on the basis of experimental work on chimpanzees that filtered tracheal secretions obtained from children suffering from Pertussis was capable of producing a condition resembling Whooping Cough, but also that Pertussis Bacilli were capable of producing the disease and that the virus was not proved to be distinct from the virus of the common cold. As further confirmatory evidence they pointed out the occurrence of pulmonary intranuclear inclusion bodies, mononuclear infiltration of the bronchial walls and interstitial pneumonia.

(2) Stocks and Karn (31) (1932) suggested that from a epidemiological point of view measles, probably a virus disease, bore some resemblance to Whooping Cough.

Despite the conflicting views the tissue changes render the special diagnostic tests of value, no matter whether the disease is of virus or bacillary origin or a

combination of both.

Specific Tests.

Isolation of the Organism.

Since the Cough Plate method of diagnosis was first used by Chievitz and Meyer (9) in 1916 a large number of workers have utilised this method. More recent investigations [(Sauer and Hambrecht (32) (1930), Kristensen (33) (1933) and Sauer (34) (1935)] indicate that, provided a suitable Bordet Gengou medium is used with a good technique the Haemophilus Pertussis can be obtained from a high percentage of patients in the early stages of the disease; thereafter the percentage of positive results rapidly falls and by the end of the fourth week, after the onset of the paroxysmal stage, the incidence of the organism is very low.

In the present investigation, Cough Plates were taken from 167 patients suffering from Whooping Cough, with and without complications. The greater number of cases were in the paroxysmal stage.

The isolation of the organism proved to be difficult and cough plates from 147 patients showed no growth of Haemophilus Pertussis. In plates from the remaining 20 cases difficulty was experienced in obtaining a pure growth of the specific organism, for agglutination purposes, mainly as a result of profuse growth of Pfeiffer's Bacillus. The following suggested reasons may explain these unsatisfactory results :-

(1) A possible over or under exposure of the cough plate.

(2) The majority of the cases examined were in the late stages of the disease.

(3) As explained above, pertussis colonies were difficult to isolate on account of the growth of other organisms.

(4) The Bordet media used contained only 25 per cent. of blood and it is possible that this blood content is on the low side.

In an attempt to inhibit the growth of organisms other than the Haemophilic group, penicillin was employed,

drops of a broth filtrate of the mould penicillium notatum being poured on to the surface of the plate before exposure to the patient. This procedure successfully inhibited the Gram positive organisms, but seemed to favour particularly the Bacillus Influenzae group. *

Demonstration of Antibodies.

In 1907, Bordet and Gengou (35) first demonstrated that the serum of patients recovered from Pertussis had the power of deviating complement when the Whooping Cough Bacillus was used as an antigen. Friedlander and Wagner (36) (1914) showed that the test became positive in the early stages of the disease in a high proportion of cases while Madsen (37) (1925) stated that the specific antibodies in Pertussis only attained a maximum in the fifth to seventh week of the disease, after which there was a gradual decline.

Prophylactic inoculation of non-immune children with successive doses of pure pertussis vaccine has been shown to produce positive complement fixation tests about twenty days after the first injection of vaccine: after this the level of antibody gradually fell Huenekens (38) (1917), Kristensen and Larsen (39) (1926) . The latter investigations show that when pure pertussis vaccine was used as a therapeutic measure in the early stages of the disease immune-body developed in excess of the natural rate of production.

Macdonald,H. and Macdonald,E.J. (29) (1933), administered 8 c.cm. of Sauer's Vaccine in three successive doses to two

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* A culture of Penicillium notatum is seeded heavily on to ordinary broth in a flat bottle which is incubated lying on its side with a loose cotton wool plug to allow free access of oxygen. Incubate for 6 - 7 days at 22 C. or 10 days at room temperature. Filter, add a little phenol red and sufficient acid to bring the colour to yellow. On exposure the filtrate tends to become alkaline and more acid should be added to maintain the yellow colour.

susceptible children. Five months after the last injection these immunized boys did not develop the disease when inoculated with living pertussis bacilli. Two months later both showed positive complement fixation reactions possibly a response to the introduction of living bacilli.

It would appear that the complement fixation reaction first becomes positive about 2 - 3 weeks after the onset of Whooping Cough although in exceptional cases it probably becomes positive earlier, and gradually reaches its peak about the fifth to seventh week, thereafter there is a gradual decline in the amount of antibody.

After prophylactic inoculation of children with Pertussis Vaccine the peak of the antibody curve appears about the third week after the first injection : thereafter there is a gradual decline in the amount of antibody in the blood.

When Pertussis vaccine is used as a therapeutic agent early in the disease it apparently stimulates the formation of antibodies in excess of the natural rate of production, and this would seem to suggest the need for early vaccine treatment.

Results of Complement Fixation Tests.

The complement fixation test was done on 165 cases in all, of whom 114 were patients suffering from Whooping Cough with or without complications, admitted to the wards of Belvidere Hospital during the epidemic of Whooping Cough in Glasgow in the Winter and Spring of 1934-35. 51 children convalescent from bronchopneumonia during the following winter were used as controls.

The results will be considered in four separate groups:-

(1) Cases not treated therapeutically with B.pertussis vaccine.

(2) Cases treated with what was believed to be a smooth strain of the organism. (43 cases).

(3) Cases treated with a known rough strain. (13 cases).

(In each of the preceding groups special analysis will be made of cases with negative reactions in an attempt to find out the causes of the negative tests).

(4) A control group of 49 children aged 0 - 6 years convalescing from bronchopneumonia.

Table I indicates how the readings were recorded. In the analysis of results doubtful positive reactions were recorded as negative.

TABLE I.

Complement Fixation Tests.

M.H.D. of complement	2	3	5	Serum Control 2	Result
Haemolysis	c.	c.	c.	c.	Negative -ve
"	m. tr.	c.	c.	c.	Doubtful positive D
"	tr.	a.c.	c.	c.	Weak positive ±
"	0	tr.	c.	c.	Positive +
"	0	0	c.	c.	Positive ++
"	0	0	tr.	c.	Positive +++

M.H.D. = minimum haemolytic dose: 0 = no haemolysis:
tr. = trace of haemolysis: m. tr. = marked trace:
a.c. = almost complete: c. = complete haemolysis.

Group I. Non-vaccine Treated.

There were 58 patients in this group of whom 44 or 75.8 per cent. gave positive complement fixation tests.

The average duration of infection from the onset of the illness until the blood had been withdrawn was 42.54 days, the duration varying from 5 days to 101 days. Patients from whom blood had been withdrawn on or before the twenty-first day of illness numbered 21, of whom 15 or 71.42 per cent. gave positive complement fixation reactions. The duration of illness from the onset until blood was withdrawn in the remaining six cases with negative complement fixation tests was respectively 6, 9, 18, 19 and 21 days. The exact date of onset of Whooping Cough is difficult to determine with certainty, consequently these figures must be accepted with caution. There were 37 patients who had blood taken off after the third week of illness, and of these 29

or 78.4 per cent. gave positive complement fixation tests. In the 7 cases where bronchopneumonia was present when blood was withdrawn 5 gave positive complement fixation reactions. An analysis of the reactions according to age-groups in these 58 cases suggests that the antibody response is less active in the younger children, so that the negative tests are most likely to occur in the younger age-groups (see Tables 2 and 3).

TABLE 2.

Variation of Complement Fixation Reaction with Age.

Age in Years	Number of cases	Negative	
		Number	Per Cent.
--2	15	5	33.3
- 5	34	9	26.4
5 -	9	0	0

TABLE 3.

Variation of Complement Fixation Reaction with Age.

Age in Years	Total number of cases.	Negative			Positive				
		Number		Total	Number				Total.
		-	D		±	+	++	+++	
- 1	8	2	0	2	3	2	1	0	6
- 2	7	0	3	3	1	1	2	0	4
- 3	10	1	1	2	2	2	3	1	8
- 4	12	1	1	2	4	3	1	2	10
- 5	12	4	1	5	4	1	2	0	7
5 -	9	0	0	0	2	3	4	0	9
	58	8	6	14	16	12	13	3	44

Anticomplementary Sera.

Of the 58 cases, 20 had anticomplementary sera of whom 17 gave satisfactory clearing and positive reactions, usually by repeating the test with the serum re-inactivated by heating for one quarter hour at 58° C. instead of 56° C.

Relation of Severity of Whooping Cough to Complement Fixation Reaction and Age.

An analysis of the complement fixation reactions according to the severity of the illness in these 58 cases suggests that the antibody response is not so active in children in whom the severity of the illness appears to be milder (Table 5); the severity of the illness being assessed on the highest number of coughs occurring daily prior to the blood being taken.

TABLE 4.

Criteria of Severity of Illness.

(1) Mild - 0 - 200 coughs per day

(2) Moderate - 200 - 400 coughs per day

(3) Severe - 400 and over coughs per day.

The proportion of negative reactions to positive in the types mild, moderate and severe in the 58 cases are as follows :-

TABLE 5.

Variation of Complement Fixation Reaction with Severity.

Mild	-	Number of Negatives	8	28.55% negative
		" " Positives	20	
Moderate	-	" " Negatives	4	25% negative
		" " Positives	12	
Severe	-	" " Negatives	2	14.28% negative
		" " Positives	12	

It is possible that the explanation of the 2 cases with negative fixation tests occurring in the severe type is that the Whooping Cough took a severe form because the antibody response was poor in these cases, although 1 case had less than the optimal amounts of antigen and serum whilst the other had only been ill for 21 days. Both sera showed true negative complement fixation reactions. The former was aged 2 10/12 years, the latter aged 4 10/12 years. (Chr. Rob. and John B.)

TABLE 6.

Age in Years	Number of cases	Severity of Whooping Cough: Cases with Pos. Comp.Fix.Tests. No. of mild	No. of mod.	No. of severe	Cases with Neg. Comp.Fix.Tests. No. of mild	No. of mod.	No. of severe	Cases with Neg Comp.Fix.Tests No.	%
0-2	15	7	1	2	5	-	-	5	33.3
2-5	34	9	7	9	3	4	2	9	26.4
5-	9	4	4	1	-	-	-	-	-
		20	12	12	8	4	2		

Neg. Comp. Fix. Tests = Negative Complement Fixation Tests.
Pos. Comp. Fix. Tests = Positive Complement Fixation Tests.
Mod. = Moderate.

Dealing with the severity of the illness in relation to the age group, it is interesting to note the tendency for the severity of the disease to be in inverse ratio to the age but proportional to the antibody response. (Tables 2, 3, 5 and 6). For example, of the 15 cases in the 0 - 2 age group 12 out of 15 cases or 80 per cent. were mild compared to the 16 out of 43 or 37.2 per cent. in the two and over age group and of the mild cases 5 out of 12 or 41.66 per cent. showed negative complement fixation reactions in the 0 - 2 age group while in the two and over age group 3 out of 16 or 18.75 per cent. showed negative reactions. Although Whooping Cough appears to be less severe in young children, especially those under 1 year, it should be borne in mind that what appeared to be a mild degree of Whooping Cough in a young child would probably assume a more severe form in an older child. Therefore, in assessing the real severity of Whooping Cough, a patient's age, size and power of reaction should be taken into account.

When the 14 cases with the negative complement fixation reactions were further analysed various factors possibly responsible for a negative reaction were elicited. These are as follows:-

(1) Extreme youth; 4 cases were less than a year old when

blood was withdrawn.

(2) A short duration of illness before the blood was withdrawn; 6 cases had blood withdrawn 3 weeks or less from the onset of the disease.

(3) Anticomplementary sera; 3 cases were labelled as having negative complement fixation tests because their sera were anticomplementary.

(4) A severe form of Whooping Cough; 2 cases had severe Whooping Cough when the blood was withdrawn.

(5) The presence of acute complications; 2 cases had bronchopneumonia when the blood was withdrawn.

(6) In addition, in 6 cases, less than what was later regarded as the optimal amounts of antigen of serum, or both was used, while 6 of the 14 cases were recorded as "doubtful positives".

It is of interest to note that 9 of the 14 cases were observed to whoop during their stay in hospital. Of the cases which were not observed to whoop, 3 were one year or less in age, their days of illness when the blood was withdrawn respectively being 10, 19 and 22 days, the remaining 2 were in their thirty seventh and thirtieth day of illness on admission, and 1 of them was definitely stated to have whooped before admission. It may be noted in the previous analyses that various factors may have influenced the negative results.

The Complement Fixation Test in Atypical Cases of Whooping Cough.

Of the 44 cases with positive complement fixation tests in Group 1, 12 cases were not observed to whoop prior to blood being taken.

10 of these cases whooped neither before nor after the blood for the complement fixation test had been withdrawn; 4 of these cases had been ill 21 days or less whilst 3 had been ill 6 weeks or more. 3 cases were less than one year old, their days of illness respectively being 21 days, 24 and 58 days when blood for the test was taken. As will be shown later (page 69) (Charts A. B. C. D.) whooping occurs less frequently in

the early stages and in the late paroxysmal stages. This observation was also noted in young infants. The remaining 2 of the 12 cases only whooped after blood for the test had been taken, hence the complement fixation test may be of value in confirming the diagnosis in early and late, as well as atypical cases, of Whooping Cough.

Group 2: Vaccine Treated - Of 43 cases treated with the smooth form of pertussis vaccine 36 or 83.7 per cent. gave positive complement fixation reactions. The average duration of the illness from the onset until the blood was withdrawn was 55.8 days the duration varying from 13 days to 174 days. The average amount of vaccine given to an individual patient up to the time when the blood was withdrawn was 14.75 c.cm. of a vaccine containing 4,000 million "smooth" whooping cough bacilli per c.cm. the dosage varying from between 2 c.cm. and 73 c.cm. In this group there were only 4 cases from whom blood had been withdrawn on or before the twenty-first day of illness. Each of these 4 cases gave positive complement fixation reactions. Of the 39 cases who had blood taken off after the third week of illness 32 gave positive complement fixation reactions. (82.05 per cent.).

Again as in Group 1 it is interesting to note the number of cases with negative complement fixation reactions in the various age-groups. (Tables 7 and 8).

TABLE 7.

Variation of Complement Fixation Reaction with Age.

Age in Years	Number of Cases	Negative	
		Number	Per Cent.
- 2	22	5	22.7
- 5	16	2	12.5
5 -	5	0	0

TABLE 8.

Variation of Complement Fixation Reaction with Age.

Age in Years	Number of Cases	Negative			Positive				Total
		-ve	D	Total	±	+	++	+++	
- 1	15	2	2	4	2	6	2	1	11
- 2	7	1	0	1	1	3	2	0	6
- 3	9	1	0	1	0	2	5	1	8
- 4	3	0	0	0	0	0	2	1	3
- 5	4	1	0	1	0	0	3	0	3
5 -	5	0	0	0	0	2	3	0	5
	43	5	2	7	3	13	17	3	36

On comparison of the results on Table 3 with those on Table 8 it was found that a larger number of cases gave greater degrees of positivity in the smooth vaccine treated group. (Table 3, 8, 9). Although the average duration of illness (55.8 days) was longer in the smooth vaccine treated group than in the group untreated by vaccine (42.54 days) yet the age distribution of the cases suggests the likelihood of good immunological responses occurring in the latter group as approximately two thirds of the cases were over the age of two years whereas in the former group roughly half of the cases were over the age of two years.

TABLE 9.

Variation in the Complement Fixation Reaction in the Non-Vaccine and Smooth Vaccine Treated Groups.

	Group 1 Non-Vaccine Treated Group						Group 2 Smooth Vaccine Treated Group					
	Neg. Comp. Fix. Reaction		Pos. Comp. Fix. Reaction				Neg. Comp. Fix. Reaction		Pos. Comp. Fix. Reaction			
	-	D	±	+	++	+++	-	D	±	+	++	+++
No.	8	6	16	12	13	3	5	2	3	13	17	3
%	13.8	10.3	27.6	20.7	22.4	5.2	11.6	4.6	7.0	30.2	39.5	7.0

Total number of cases = 58
- 2 age group = 15 cases
2 - age group = 43 cases
Average duration of illness = 42.54 days

Total number of cases = 43
- 2 age group = 22 cases
2 - age group = 21 cases
Average duration of illness = 55.8 days

Anticomplementary Sera.

Of the 43 cases in Group 2, 11 had anticomplementary sera of whom 8 gave satisfactory clearing and positive reactions usually by repeating the test with the serum reinactivated by heating for one quarter hour at 58° C. instead of 56° C.

Relation of Severity of Whooping Cough to Complement Fixation Reaction and Age.

As in Group 1 an analysis of the 43 cases again suggests a tendency for the illness to be less severe in young children in whom the antibody response is poorer.

Mild $\frac{\text{Number of Negative C.F.T.}}{\text{Number of Positive C.F.T.}} = \frac{5}{17} = 22.72\%$ Negative

Moderate $\frac{\text{Number of Negative C.F.T.}}{\text{Number of Positive C.F.T.}} = \frac{1}{11} = 8.33\%$ Negative

Severe $\frac{\text{Number of Negative C.F.T.}}{\text{Number of Positive C.F.T.}} = \frac{1}{8} = 11.11\%$ Negative

The one case with the severe type of illness and negative complement fixation reaction was J. L. aged 7 months; he was in his 74th day of illness when blood was withdrawn, the serum was not anticomplementary and the optimal amounts of antigen and sera were used. This patient had received 2 cc. of a vaccine containing 8,000 to 10,000 million organisms per c.cm. the complications present when the blood was withdrawn were Bronchitis, Rhinitis and Conjunctivitis. There is a suggestion in this case that the disease was severe because of the lack of antibody response in a young infant.

The case with the negative complement fixation reaction in the "moderate" type was E. M. aged 1 10/12 years who had been ill for 89 days when blood was taken for the test. The only negativing factor was Bronchopneumonia which was present when the blood was withdrawn. She had received 8 cc. of a vaccine containing 8,000 - 10,000 million organisms per c.cm. prior to withdrawal of the blood.

TABLE 10.

Relationship of Severity to Age and Immunological Response in the Smooth Vaccine Treated Group.

		Severity of Whooping Cough							
		Cases with Positive Comp. Tests			Cases with Negative Comp. Tests			Negative Comp. Fixation Tests	
Age in Years	Number of Cases	No. of mild	No. of mod.	No. of sev.	No. of mild	No. of mod.	No. of sev.	Number	Per Cent.
- 2	22	9	4	4	3	1	1	5	22.7
- 5	16	6	6	2	2	0	0	2	12.5
5 -	5	2	1	2	0	0	0	0	0
		17	11	8	5	1	1		

No. = Number, Mod. = Moderate, Comp. Fix. Tests = Complement Fixation Tests, Sev. = Severe.

Compared to Group 1 (page 13, Table 6) there appears to be a tendency for an increase in the severity of the disease and in the amount of antibody formed especially in the younger age groups in Group 2 (Table 10 and Table 11)

TABLE 11.

Relation of Severity to Age Groups in Smooth Vaccine Treated Group and Group Untreated by Vaccine.

	Age Group	Number of Cases	Number of mild cases	Percentage of mild cases.
Group 1	(- 2	15	12	80 per cent.
	(2 -	43	16	37 per cent.
Group 2	(- 2	22	12	54.5 per cent.
	(2 -	21	10	47.61 per cent.

For example in Group 2 of the 22 cases in the - 2 age group, 12 or 54.5 per cent. were mild compared to 10 out of 21 or 47.61 per cent. in the 2 - age group whereas in Group 1 the corresponding figures for the mild cases in the - 2 group and 2 - age group are respectively 12 out of 15 cases or 80 per cent. mild and 16 out of 43 cases or 37 per cent. mild (Table 11).

Of the mild cases 3 out of 12 or 25 per cent. showed negative complement fixation reaction in the - 2 group while in the 2 - age group 2 out of 10 cases or 20 per cent. showed

negative reactions (Table 10). In Group 1, on the other hand, the corresponding figures for the - 2 age group and the 2 - age group are respectively 5 out of 12 cases or 41.66 per cent. negative and 3 out of 16 cases or 18.75 per cent. negative (page 13 Table 6).

An analysis of the 7 cases with negative complement fixation tests reveals similar factors to those acting in Group 1, and again the result of each complement fixation test may have been influenced by one or more factors.

(1) Extreme youth: 4 children were less than a year old when the blood was withdrawn.

(2) Anticomplementary sera: the sera were anticomplementary in three cases, each result being labelled negative.

(3) A severe form of Whooping Cough: 1 case had severe Whooping Cough when the blood was withdrawn.

(4) The presence of acute complications: 1 case had bronchopneumonia when the blood was withdrawn, although two cases with bronchopneumonia gave positive complement fixation reactions.

(5) In 2 cases less than the optimum amounts of antigen or sera or both were used, and there were 2 doubtful positives amongst the 7 cases recorded as having negative complement fixation reactions.

Group III. Rough Vaccine Treated :- Rough vaccine is a vaccine prepared from Pertussis colonies subcultured repeatedly on a blood-free medium, so giving rise to "rough colonies". The organisms correspond to phases III and IV of the Pertussis Bacillus described by Leslie and Gardner. The rough vaccine possesses little or no antigenic efficacy. There were 13 patients in this group of whom 10 or 76.92 per cent. gave positive complement fixation tests. The average duration of illness from the onset until the blood had been withdrawn was 56 days, the duration varying from 34 to 72 days. An analysis of the results according to age groups in the 13 cases would appear to indicate that negative reactions are commoner in the 2 - 5 age groups; this is probably due

to the small number of cases under consideration which is the reason for not analysing the cases further along the same lines as Group 1 and 2.

TABLE 12.

Variations of Complement Fixation Reaction with Age.

		Negative	
Age in Years	Number of Cases	Number	Per Cent.
- 2 years	7	1	14.2
- 5 years	5	2	40
5 -	1	0	0

It will be noticed that 76.92 per cent. (10 out of 13 cases) display positive complement fixation reactions compared to 75.8 per cent. (44 out of 59 cases) in Group 1, and 83.7 per cent (36 out of 43 cases) in Group 2. The average duration of infection in Groups 1, 2 and 3 was respectively 42.54 days varying from 5 to 101 days, 55.8 days varying from 13 days to 174 days and 56 days varying from 34 to 72 days. The number of positives in Group 1 and 3 are strikingly similar even although 21 patients had blood withdrawn before the 21st day of illness in Group 1. Groups 1 and 3 are thus acting as controls for each other and for Group 2. The results would appear to support the contention that immune bodies are not appreciably increased by the use of rough strain Pertussis vaccine.

Change in the Complement Fixation Reaction during the Progress of the Disease.

The cases which show changes in the complement fixation reactions may again be divided into 3 groups according to the treatment adopted, viz., Non-vaccine treated, Rough Vaccine treated and Smooth Vaccine treated:-

TABLE 13.

Changes in Complement Fixation Test.

(1) Non-vaccine Treated.

Name	Age	Day of illness when blood taken	Severity of Whooping Cough in interval before blood was taken	Result of C.F.T.
(a) B. M. female	3½ yrs.	11	Severe	- Negative
		38	Severe	D Doubtful Positive
		71	Moderate (became mild)	+ Positive
(b) M. N. female	7 months	6	Mild	- Negative
		20	Mild (Mild through out)	± Weak Positive
(c) J. E. male	4 yrs.	45	Mild	± Weak Positive
		73	Mild	+ Positive
(d) R. A. male	4½ yrs.	14	Severe	± Weak Positive
		33	Severe (became mild)	+++ Positive
(e) S. P. female	3 11/12 yrs.	66	Moderate	D Doubtful Positive
		95	Mild	D Doubtful Positive
(f) J. B. male	3 3/12 yrs.	101	Severe	± Weak Positive
		134	Mild	± Weak Positive

It is of interest to note that in two cases (Cases a and b) in the foregoing table the complement fixation tests which were at first negative became positive when repeated after an interval of several days. In another two cases (Cases c and d) there was an increase in the positivity of the test. Thus four of the six cases showed an increase in the amount of antibody as the disease progressed. In the

last two cases (Cases e and f) there was no change in the positivity of the test a finding which is expected as it is feasible that demonstrable serum immunity tends to fade with time.

TABLE 14.

Changes in Complement Fixation Test.

(11) Rough Vaccine Treated.

Name	Age	Day of illness when blood was taken.	Severity of Whooping Cough in Interval before blood was taken	Result of C.F.T.	Amount of Vaccine given in interval before blood was taken 8,000 million organisms per cc.
(a) J. M. male	5 yrs	32	Mild	-ve	2.5 cc.
		54	Mild	+++	8.5 cc.
(b) M. G. female	3/12 yrs.	15	Mild	-ve	0.5 cc.
		37	Mild	±	4.5 cc.
(c) C. G. female	6/12 yrs.	43	Mild	-ve	2.5 cc.
		66	Mild	++	6.5 cc.
(d) A. McM. male	4 10/12 yrs.	18	Mild	-ve	0 cc.
		38	Moderate (becoming mild later)	D	4 cc.
(e) H. McA. female	4 yrs.	39	Moderate	D	0 cc.
		59	Mild	++	2 cc.

In the rough vaccine treated group four cases (Cases a, b, c, e) which at first showed negative reactions later gave positive reactions. The remaining case (Case d) showed an increase in the positivity.

TABLE 15.

Changes in Complement Fixation Test.

111. Smooth Vaccine Treated.

Name	Age	Day of illness when blood was taken.	Severity of Whooping Cough in interval before blood was taken	Result of C.F.T.	Amount of Vaccine given in interval before blood was taken.
(1) J. M. male	5/12 yrs.	53	Mild	-	7 cc. Old Glaxo
		99	(More) Mild	+	None in addition
(2) V. W. female	2 5/12 yrs.	9	Mild	-	2 cc. Danish
		33	Mild	+	13.5 cc. Danish
(3) E. McF. female	11/12 yrs	80	Mild	-	20 cc. New Glaxo
		149	Stopped coughing	+	22 cc. " "
(4) G. P. male	6 yrs.	26	Severe	D	2 cc. Old Glaxo
		43	Mild	++	4 cc. " "
(5) M. D. female	3 10/12 yrs.	19	Mild	+	0 cc.
		51	(Very) Mild	++	19 cc. Old Glaxo
(6) H. G. female	6 yrs.	100	Moderate	±	None
		125	(More) Moderate	++	53 cc. Old Glaxo
(7) C. McC. male	2 9/12 yrs.	93	Mild	±	No vaccine
		125	Mild	++	5 cc. Old Glaxo
(8) A. H. female	6 1/12 yrs.	17	Mild	±	No vaccine
		49	Mild	+++	13 cc. Old Glaxo
(9) A. McC. female	2 4/12 yrs	150	Moderate	D	7 cc. Danish
		174	Mild	+++	8.5 cc. Danish
(10) J. L. male	7/12 yrs	21	Moderate	±	8 cc. Danish
		69	Mild	+++	12 cc. "
(11) A. R. female	9/12 yrs.	31	Mild	±	1 cc. Danish
		86	Mild	+	13 cc. "

(12) J. G. female	8/12 yrs.	17 70	Mild Mild	± −	No vaccine 5 cc. Old Glaxo
(13) D. F. male	4 yrs.	28 59	Moderate Moderate	+ −	6 cc. Danish 16 cc. "
(14) S. P. female	7 yrs	13 28	Moderate Mild	+ −	1 cc. Danish 13 cc. Danish

In the Smooth Vaccine treated group (14 cases), 3 cases, nos. 1, 2 and 3, which were originally negative became positive on examination later.

8 cases, nos. 4 to 11 inclusive, showed an increase in the positivity of the test, whilst the remaining 3 cases, nos. 12, 13 and 14, showed ~~an~~ a decrease. In 12 and 13 no negativing factors for the test are apparent, but in case 14 less than the optimum amount of serum was used.

In this small series of cases it is extremely difficult to prove any relationship between the severity of the Whooping Cough and the degree of positivity of the test, but it would appear that the amount of antibody in the blood increases during the course of the disease.

Group IV (Control Series). This consisted of 51 cases convalescing from bronchopneumonia all under 6 years of age; 37 of these children aged 3 months to 5 years were convalescing from bronchopneumonia and did not give a history of previous Whooping Cough: 36 of them had negative complement fixation reactions, and one gave a "doubtful positive" reaction.

14 children aged from 11 months to 6 years gave a history of previous Whooping Cough; 7 of these gave negative and 2 positive complement fixation reactions. One of the 7 cases with negative tests was a child aged 11 months, he was said to have been born with Whooping Cough! The remaining 5 cases were all said to have had Whooping Cough two or more years previously, and two of them who gave positive complement fixation reactions were respectively R. B.,

a girl aged 4 years, who gave a weak positive reaction (±) and was said to have had Whooping Cough one year previously and a girl, M. H., aged 2 years and 11 months, who gave a "doubtful positive" (D) reaction; she was said to have suffered from Whooping Cough 6½ months previously.

The remaining group of 3 children aged 8 months, one year, and one year and two months respectively, who had all been exposed to Whooping Cough at birth, did not develop clinical signs of the disease. Two of the three children gave negative complement fixation reactions, and the one aged 6 months gave a doubtful positive reaction.

The figures obtained from this control group of cases would therefore appear to confirm the view that the complement fixation reaction is specific and may be demonstrated over a considerable period.

SUMMARY.

(1) The complement fixation test was of value in confirming the clinical diagnosis of Whooping Cough. In atypical cases the test by itself established the diagnosis of Pertussis by conversion from a negative to a positive reaction or vice-versa during the course of the illness.

(2) The majority of patients in the series was admitted in the later stages of the infection; there is evidence in the numbers admitted in the first three weeks of the disease that the complement fixation test becomes positive early in the infection in a high proportion of cases.

(3) Negative results were most commonly obtained in very young children probably as a result of deficient powers of reaction. Other probable causes of a negative reaction were short duration of the disease, very severe infection or presence of complications, and anticomplementary sera. The use of less than the optimal amounts of antigen, sera, or both also tended to give negative reactions.

(4) The disease appeared to be milder in young children, but in assessing the severity of the disease the size and power of response of the patient must be taken into account.

(5) The mild cases showed a higher percentage of negative complement fixation reactions, but many of the cases who had a mild infection were in the younger age group.

(6) A larger number of cases showed greater degrees of positivity in the smooth vaccine group in whom the severity of the disease appeared to be increased especially in the younger age groups.

(7) Specific serum immunity may persist for about a year after the onset of the disease.

Agglutinins in Whooping Cough.

The presence of agglutinins in the blood in Pertussis was not investigated but the following is a resumé of the more important work dealing with this aspect.

In 1907 Bordet and Gengou (7) studying agglutination and complement deviation in Pertussis found that the serum of patients suffering from Whooping Cough, or convalescing from the disease was inconstant in agglutinating power: sometimes it was present in a marked degree, but at other times it was non-existent. They said that "la méthode de la fixation de l'alexine donne toujours des résultats positifs très accentués. Il y a donc dissociation des deux propriétés". The agglutination test in Pertussis has been tried by other workers with equally unsatisfactory results. [Shiga, Imai and Eguchi (40), 1913, Wollstein (41), 1909, Povitzky and Worth (42), 1916.] In 1931 Leslie and Gardner (10) found that each phase of the organism is usually agglutinated by the corresponding phase serum.

"The Intradermal Test".

Some of the more recent work dealing with this test has been discussed on page 3; McArdle (43) (1935) and O'Brien (44) (1937) using Sauer's vaccine confirmed earlier work carried out by Paterson which he had later felt constrained to modify. Thompson (45) (1938) using Pertussis endotoxin as antigen found that the intradermal test was positive in approximately 85 per cent. of children with a past history of Whooping Cough.

He also obtained positive reactions in 30 per cent. of individuals with no previous history of the disease.

The results (46) of some of the skin tests controlled by complement fixation tests done for the purposes of this investigation were published in 1937. These show that 69.7 per cent. of 43 patients with Whooping Cough gave positive intradermal tests, and 86.1 per cent. of 37 patients with no previous history of Whooping Cough gave positive intradermal tests. Westwater (47) (1937) obtained results similar to those quoted in this last paragraph.

The object of the skin test was to investigate its possible value in the diagnosis of Whooping Cough, using the complement fixation test as a control. The blood for the complement fixation reaction was withdrawn in each case before the skin test was done except in the group of cases treated by smooth vaccines.

The cases fall into 3 groups :

Group A was composed of 43 patients untreated by vaccines, most of whom were under 5 years of age, the oldest being aged 9 years.

Group B consisted of 42 patients all of whom had been treated with a vaccine prepared from a smooth strain of Pertussis organisms. The average dose used was 14.97 cc., the minimum 1 cc. The majority of the patients were under 5 years of age, the oldest being aged 6 years and 2 months.

Groups A and B consisted of patients who had been admitted to the wards with a diagnosis of Whooping Cough, with or without complications.

Group C. This group consisted of 49 patients convalescing from Bronchopneumonia aged up to 6 years. 37 of these patients with no history of Whooping Cough were 5 years of age or under; 9 cases aged up to 6 years were said to have had Whooping Cough 6½ months or more previously. The remaining 3 children aged 8 months, 1 year, and 1 year and 2 months had all been exposed to Whooping Cough but did not develop the disease.

Group C has thus been used as a control to Groups A

and B of this series as well as acting as control material for the complement fixation test.

Results of the Intradermal Test.

Group A (Untreated by Vaccines).

Of the 43 cases Sauer's vaccine was used for the skin test in 25, St. Mary's vaccine in 14, Glaxo vaccine in 3 and Kreuger's vaccine in 1 case. Positive complement fixation reactions were obtained in 31 cases of whom 21 gave positive skin tests. Of the 12 cases with negative complement fixation reactions 9 gave positive skin tests. Altogether 30 of the 43 cases (69.7 per cent.) gave positive intradermal tests.

Group B (Smooth Vaccine Treated).

Of the 42 cases St. Mary's vaccine was used for the skin test in 15, Sauer's vaccine in 14, Glaxo vaccine in 10 and Kreuger's vaccine in 3 cases.

30 cases had blood withdrawn for the complement fixation test before the skin test was done, and in the remaining 12 cases the skin test was done after the blood was taken. Out of the 42 cases, 36 gave positive complement fixation reactions and of these 36 cases 25 gave positive skin tests. Of the 6 cases with negative complement fixation reactions, 5 gave positive skin tests. Altogether 30 of the 42 cases (71.43 per cent.) gave positive skin reactions.

Group C (Control Group).

The antigens used for the skin tests in this group were Sauer's vaccine and Glaxo vaccine containing the constituents of 8,000 million Whooping Cough bacilli per cc. Each case was tested at the same time with the 2 vaccines.

Of the 37 cases with no previous history of Whooping Cough, 36 gave negative complement fixation reactions and 1 case gave a "doubtful positive" reaction. In the skin tests 31 cases of the 36 were positive (86.1 per cent.) with both Sauer's and Glaxo vaccine. Of the remaining 5 cases, 3 gave negative skin tests with both antigens, 1 gave a negative skin test with the Sauer antigen, and a positive skin test with the Glaxo antigen, whilst the other gave a positive skin test

with Sauer's vaccine and a negative skin test with the Glaxo vaccine. The case with the doubtful positive complement fixation reaction gave a positive skin test with both the Sauer and the Glaxo vaccine. Of the 9 cases with a previous history of Whooping Cough 7 gave negative complement fixation reactions of whom 5 showed positive and 2 negative skin tests. 2 cases showed positive and doubtful positive complement fixation reactions, the skin tests being positive and negative respectively.

There were 3 children with a history of exposure to Whooping Cough of whom 2 gave negative complement fixation reactions, the skin tests being positive and negative respectively. The remaining case gave a doubtful positive complement fixation reaction and a positive skin test.

Repeat Skin Tests .

In several instances the skin test was done more than once on the same case. These cases have been divided into two groups according to the method of treatment. Group I consisted of patients whose treatment did not vary. Group II was composed of cases who had skin tests done before and after treatment with vaccine.

Group I may be further subdivided into the following sub-groups :-

(a) Non-vaccine Group Repeat Skin Tests.

(b) Smooth Vaccine Group Repeat Skin Tests.

(c) Rough Vaccine Group Repeat Skin Tests.

Group II may be subdivided into the two following sub-groups :-

(a) Original test in the non-vaccine treated group, and repeat tests after Smooth Vaccine treatment.

(b) Original test in the non-vaccine treated group, and repeat tests after treatment with Rough Vaccine.

The repeat tests were examined for the following variations :-

(1) Remained positive.
(2) Remained negative.
(3) Change from a negative to a positive reaction.
(4) Change from a positive to a negative reaction.
(5) Other variations.

Results of Repeat Skin Tests :-

Group I :- Repeat Skin Tests on cases whose treatment was unchanged

I (a) Non Vaccine Treated Group.

TABLE 16.

Remained Positive	Remained Negative	Change from a Negative to a Positive Reaction	Change from a Positive to a Negative Reaction	Other Variations	Total Cases
4	2	6	0	0	
33.33%	16.66%	50%	-	-	12

I (b) Smooth Vaccine Treated.

TABLE 17.

Remained Positive	Remained Negative	Change from a Negative to a Positive Reaction	Change from a Positive to a Negative Reaction	Other Variations	Total Cases
3	2	3	1	-	
33.33%	22.22%	33.33%	11.11%	-	9

I (c) Rough Vaccine Treated.

TABLE 18.

Remained Positive	Remained Negative	Change from a Negative to a Positive Reaction	Change from a Positive to a Negative Reaction	Other Variations	Total Cases
-	1	-	1	-	2

Group II Repeat Skin Tests :- Original in the non-vaccine treated group and repeat tests in the vaccine treated group.

II (a) Original test whilst untreated with vaccine and repeat test after treatment with smooth vaccine

TABLE 19.

Remained Positive	Remained Negative	Change from a Negative to a Positive Reaction	Change from a Positive to a Negative Reaction	Other Variations	Total Cases
5	2	2	1	2	
41.66%	16.66%	16.66%	8.33%	16.66%	12

II (b) Original test before treatment with rough vaccine and repeat tests after treatment

TABLE 20.

Remained Positive	Remained Negative	Change from a Negative to a Positive Reaction	Change from a Positive to a Negative Reaction	Other Variations	Total Cases
3	1	1	-	-	5

Results of all the Repeat Skin Tests.

TABLE 21.

Remained Positive	Remained Negative	Change from a Negative to a Positive Reaction	Change from a Positive to a Negative Reaction	Other Variations	Total Cases
15	8	12	3	2	40
37.5%	20%	30%	7.5%	5%	

From these tables it is seen that the method of treatment has little effect on the dermal response.

SUMMARY.

The intradermal test failed to give specific results. A high percentage of cases with Whooping Cough gave positive reactions but so also did a group of control patients with no history of previous Whooping Cough. There was no correlation between the intradermal test and the complement fixation reaction.

Non Specific Tests.

(1) Blood Picture. Leucocytosis was first described by Frölich (1897) while later investigators found that the lymphocytes were increased absolutely and relatively. Churchill (48) (1906) thought that the lymphocytosis was commonest in the early or catarrhal stage of the disease. Sauer and Hambrecht (49) (1931) confirmed the presence of leucocytosis and lymphocytosis in Whooping Cough, but found that the change was greatest at the height of the paroxysmal stage: at the beginning and end of the illness there was often a leucopenia. They also noted a terminal decrease in the lymphocyte count.

Begg and Coveney (50) (1935) found that in Whooping Cough leucocytosis was constantly present. Lymphocytosis was less constant, and this was particularly so in children under six months of age. The blood changes were at a maximum early in the disease and rapidly subsided after the whoop became established.

(2) Sedimentation Rate. Bell and Gold (51) (1936) found that a spasmodic cough, a blood picture of lymphocytosis in association with leucocytosis and a retarded, normal, or subnormal sedimentation rate was of value in the diagnosis of atypical cases but that the absence of positive findings did not invalidate a diagnosis of Pertussis.

SYMPTOMATOLOGY.

This chapter is based upon work carried out in wards in Belvidere Hospital devoted to cases of Whooping Cough with or without complications admitted during the epidemic in Glasgow in the Winter and Spring of 1934 - 35.

Clinical Findings.

TABLE 22.

Disposition of Cases .

Number of Cases discharged well.	Number of Deaths.	Irregular Dismissals.	Transfers due to cross-infection.	Total number of cases.
179	66	4	8	257

257 cases of Whooping Cough with or without complications were considered. Of these 179 patients were dismissed directly from hospital, and of the remaining 78 cases death accounted for 66, 4 left hospital against the wishes of the Medical Officer and of these 2 had bronchopneumonia, one had bronchitis and one had cervical adenitis. Cases transferred on account of cross-infections accounted for 8 patients: 7 developed Scarlet Fever and the remaining case pulmonary tuberculosis with tuberculous cervical adenitis.

Of the 257 cases admitted to hospital there were 8

deaths within 24 hours of admission. The average duration of stay in hospital of the 178 patients dismissed well was 46.59 days.

TABLE 23.

Average Duration of Stay in Hospital of Patients Dismissed Well.

	0-1 yrs.	-2 yrs.	-3 yrs.	-4 yrs.	-5 yrs.	5 - yrs.	Total
Cases	54	54	29	23	11	7	178
Days	50.9	49.15	47.12	44.35	34.82	34.43	46.59

TABLE 24.

Effect of Treatment on Length of Stay in Hospital.

Age Group	Non-Vaccine Treated		Smooth Vaccine Treated		Rough Vaccine Treated.	
	Average Number of Days in Hospital	Number of Patients	Average Number of Days in Hospital	Number of Patients	Average Number of Days in Hospital	Number of Patients
0-1	46.96	25	56.625	24	43.40	5
- 2	40.705	34	56.80	15	83.60	5
- 3	53.2	15	40.75	12	40.00	2
- 4	48.615	13	37.00	7	42.33	3
- 5	32.166	6	34.00	3	44.00	2
5 -	40.00	2	32.20	5		
	44.8	95	48.81	66	54.64	17

Caution must be exercised in drawing conclusions from a small series of cases but it would appear from a consideration of the above figures that the younger patients remained longer in hospital than did the older ones.

Age and Sex Incidence of Whooping Cough and Mortality Rate.

TABLE 25.

Table to Illustrate Incidence and Mortality Rate of 257 Cases of Whooping Cough.

	0 - 1 yrs.		- 2 yrs.		- 3 yrs.		- 4 yrs.		- 5 yrs.		5 - yrs.		Total.	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Cases	40	60	37	34	16	22	11	15	7	6	8	1	119	138
Deaths	20	26	9	5	2	1	0	2	0	0	1	0	32	34
Percentage Mortality													26.89	24.63

The above table would suggest that the incidence of the disease is higher amongst females and young children and that there are more fatalities amongst the younger age groups. Also in this series there would appear to be a higher mortality rate amongst the young male patients, a finding contrary to that usually expressed, but this is probably the result of the small series examined.

It is of interest to note that amongst the 157 patients untreated by vaccines there were 53 deaths, a mortality rate of 33.76 per cent. 8 of these deaths however occurred within 24 hours of admission. There were 11 deaths amongst the 78 patients treated with the smooth vaccine, a mortality rate of 14.6 per cent. 2 of the 22 patients treated with rough vaccine died, giving a mortality rate of 9.09 per cent. In the latter two groups there were no deaths within 24 hours of admission.

The 257 cases will first be considered from various aspects so that a general idea of the disease may be obtained. The analyses take the form of an enquiry into the various aspects of the disease

(A) prior to admission

(B) on admission

(C) developing after admission to Hospital.

(A) Conditions obtaining prior to admission.

(1) Average Duration of Illness.

The average duration of the infection in 255 cases prior to admission, was 22.112 days, there being 2 cases in whom the duration of illness could not be ascertained. This figure suggests that cases reach hospital late on in the disease when the paroxysmal stage has developed, and this may be explained by the fact that Hospital beds for Whooping Cough in Glasgow are intended for those cases which develop acute complications, especially pulmonary complications which usually arise in the latter stages of the disease, and partly because of the difficulty of early clinical diagnosis. The figure given should probably be higher as Whooping Cough is

a disease in which the exact date of onset is extremely difficult to fix.

The table given below gives the average duration of illness of patients in the various age groups :-

TABLE 26.

Duration of Illness.

Age Groups	Number of patients.	Average Duration of illness
0 - 1	99	19.9 days
- 2	71	23.3 "
- 3	38	23.9 "
- 4	25	25.9 "
- 5	13	21.3 "
5 -	9	30.3 "

It would appear from the above figures that patients are sent into Hospital approximately on the 19th to the 25th day after the onset of the disease plus a time interval when the disease has passed unnoticed in the early stages, and the children in the 0 - 1 group are sent into Hospital earlier possibly because of the alarming complications of the disease such as convulsions.

(II) The Effect of Overcrowding.

As Whooping Cough admissions to Belvidere Hospital are largely drawn from the poorer classes an analysis of housing conditions has been done. See table below :-

TABLE 27.

Apartments - 429. Adults - 589. Children - 648.
Persons per Apartment - 2.8
Adults per Apartment - 1.3
Children per Apartment- 1.5

A child has been taken as a person under 10 years of age, being counted as 0.5 persons.

It would appear from these figures that overcrowding was present and that dissemination of the disease would be rapid and widespread not only because of overcrowding, but also because of the tenement system of housing which obtains in Glasgow. These same factors would also tend to produce a widespread latent immunity since in Glasgow there is a

biennial epidemic incidence of the disease. It would be justifiable therefore to suppose that a large percentage of children would be immune after an epidemic with the exception of those children of one year and under. The possibility of some inherited immunity must be considered, however, in the very young children.

Some interesting facts emerge from the analysis of symptoms present prior to admission. As these symptoms were obtained from parents too much reliance should not be placed on them, as even under close medical supervision certain symptoms are often extremely difficult to observe.

(III) Incidence of Coughing.

In the analysis of the occurrence of coughing in the various age groups, the term coughing has been used in preference to the term spasmodic coughing which is often difficult to make clear to uneducated parents.

TABLE 28.

Incidence of Coughing.

Age Groups	Number of Children	% of children with coughing.
0 - 1	100	100
- 2	71	100
- 3	38	100
- 4	26	100
- 5	13	100
5 -	9	100

The above figures show that coughing is always present in children with Whooping Cough.

(IV) Incidence of Feverishness.

Feverishness is a term which in a medical sense indicates pyrexia and its concomitants such as sweating, dryness of throat and mouth, thirst, flushing of the face, restlessness, but by the lay person may be used to indicate any one of these symptoms.

TABLE 29.

Incidence of Feverishness.

Age Incidence	Number of patients	% of patients showing feverishness.
0 - 1	100	15
- 2	71	19.71
- 3	38	21.62
- 4	26	15.38
- 5	13	23.07
5 -	9	22.22

These results would appear to indicate that "feverishness" is less common in the 0 - 1 group. This is probably false as an infant under one year runs a greater danger of being ill without people becoming aware, especially when the child is teething and the mother is busy.

(V) Incidence of Vomiting.

Vomiting is a symptom about which there can be little doubt as to its occurrence.

TABLE 30.

Incidence of Vomiting.

Age Group	Number of Patients.	Percentage Incidence.
0 - 1	100	58
- 2	71	42.25
- 3	38	54.05
- 4	26	38.46
- 5	13	53.84
5 -	9	66.66

It would appear that vomiting is a fairly common symptom in Whooping Cough.

(VI) TABLE 31.

Incidence of Whooping.

Age Group	Number of patients.	Percentage Incidence.
0 - 1	100	62
- 2	71	81.69
- 3	38	83.78
- 4	26	76.92
- 5	13	84.61
5 -	9	88.88

It is surprising to find the incidence of whooping

so high especially in the 0 - 1 group, the figures are based upon the observations of untrained observers whose findings must be interpreted with caution.

(VII) TABLE 32.

Incidence of Convulsions.

Age Group	Number of patients	Percentage Incidence.
0 - 1	100	7
- 2	71	5.63
- 3	38	0
- 4	26	0
- 5	13	0
5 -	9	0

The incidence of convulsions in the ' - 2' age group is more marked than in any of the other groups.

(VIII) TABLE 33.

Incidence of Enteritis.

Age Group	Number of patients	Percentage Incidence.
0 - 1	100	10
- 2	71	1.4
- 3	38	2.7
- 4	26	0
- 5	13	0
5 -	9	0

Enteritis occurs mainly in young age groups, especially in children under one year.

TABLE 34.

Recapitulation of Signs and Symptoms prior to admission to Hospital.

Age Group	Number of Patients	Cough	Fever	Vomiting	Whooping	Convul-sions	Enteritis
0 - 1	100	100%	15%	58%	62%	7%	10%
- 2	71	100%	19.71%	42.25%	81.69%	5.63%	1.4%
- 3	38	100%	21.62%	54.05%	83.78%	-	2.70%
- 4	26	100%	15.38%	38.46%	76.92%	-	-
- 5	13	100%	23.07%	53.84%	84.61%	-	-
5 -	9	100%	22.22%	66.66%	88.88%	-	-
	257						

SUMMARY.

The most noteworthy features of the conditions obtaining prior to admission in this series of 257 cases are as follows :-

(1) The greater number of cases were in the younger age groups, 235 out of 257 cases (91.44 per cent.) being 4 years of age or under.

(2) The average duration of illness before admission was approximately three weeks.

(3) Cough was present in every case.

(4) Fever, vomiting and whooping were evenly distributed throughout the various age groups.

(5) Convulsions and Enteritis were only found in the younger age groups.

(B) Conditions Present on Admission to Hospital.

(1 and 2). Respiratory Conditions present on Admission.

The differentiation of bronchitis from broncho-pneumonia is often difficult especially as the one may often precede the other. The criteria of pneumonia in this investigation were a high temperature, increase of pulse and respiration rate, some variation from normal of the percussion note and where the respiratory murmur was tubular or broncho-vesicular with crepitations and râles. In some instances it was found that percussion was unimpaired even in definite cases of pneumonia. These findings in conjunction with the toxaemia and distressed appearance of the patient have been the standards by which a diagnosis of pneumonia was made.

Bronchitis was diagnosed when the temperature level was not markedly elevated nor the pulse and respiration rates markedly increased, where the patient did not appear markedly toxic or distressed, where impairment of percussion note could not be elicited and where the respiratory murmur showed slight prolongation of the expiratory phase and was accompanied by rhonchi or râles.

TABLE 35.

(1 and 2) Incidence of Respiratory Complications.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number with Pneumonia	54	36	17	11	5	5	128
Percentage Incidence	54	50.7	44.7	42.3	38.5	55.5	49.9
Number with Bronchitis	27	21	14	10	7	2	81
Percentage Incidence	27	29.6	36.8	38.5	53.8	22.2	31.5

In Glasgow as hospital beds for cases of Whooping Cough are intended for complicated cases it is not surprising to find that out of the 257 cases admitted, 209 or 81.3 per cent. of cases had bronchitis or pneumonia, the former accounted for 81 or 31.5 per cent. and the latter for 128 or 49.9 per cent. Bronchitis and pneumonia appear to be equally common in the various age groups.

(3) Malnutrition.

TABLE 36.

Incidence of Malnutrition.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number with Malnutrition	27	23	5	7	6	3	71
Percentage Incidence	27	32.4	13.2	26.9	46.2	33.3	27.6

Of the 257 cases, 71 or 27.6 per cent. showed signs of malnutrition, and this was found to occur with almost similar frequency in all the age groups except for the - 3 age group where the incidence was low, only 13.2 per cent. or 5 out of 38 cases being affected. It is not surprising to find that this condition was common since Whooping Cough by itself may cause excessive vomiting in addition to favouring the occurrence of other conditions which predispose to wasting, e.g. respiratory infections, enteritis and otitis

media.

(4) Enteritis

TABLE 37.

Incidence of Enteritis.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number with Enteritis	42	8	4	0	0	0	54
Percentage Incidence	42	11.3	10.5	0	0	0	21.0

Enteritis is common in young children suffering from Whooping Cough. 54 of the 257 cases (21 per cent.) were suffering from this condition on admission. These 54 cases were all in the younger age groups, and this complication was found in 42 out of 100 cases in the 0 - 1 age group, 8 or 11.3 per cent. of 71 cases in the - 2 age group, and 4 or 10.5 per cent. of 38 cases in the - 3 age group. The stools in these cases were green in colour, liquid and frequent.

(5) Fraenal Ulcer.

TABLE 38

Incidence of Fraenal Ulcer.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number with Fraenal Ulcer	10	13	9	5	1	2	40
Percentage Incidence	10	18.3	23.7	19.2	7.7	22.2	15.6

This condition was present in 40 (15.6 per cent.) of 257 cases. Fraenal ulcer is said to be produced by the uncontrollable protrusion of the tongue during a paroxysm, causing injury to the fraenum of the tongue by the lower incisor teeth. In 4 cases in this series the ulcer was found to be remote from the fraenum. These ulcers, fraenal or parafraenal, are of necessity only present in those children

possessing lower incisor teeth and often the first indication of pressure is a small tear or abrasion; occasionally at the beginning of the paroxysmal stage a small greyish area of epithelium was observed with no actual ulceration, this later developed into an ulcer when the paroxysms became more severe. These ulcers usually heal up satisfactorily during convalescence.

(6) Congestion of Fauces and Tonsillitis.

TABLE 39.

Incidence of Tonsillitis.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number with Tonsillitis	8	11	11	6	1	3	40
Percentage of Incidence	8	15.5	28.9	23	7.7	33.3	15.6

Congestion of the fauces was present in every case whilst the tonsils were found to be enlarged and congested in 40 or 15.6 per cent. of the 257 cases. The presence of congestion of the fauces is not surprising in view of the persistent coughing and expectoration of sputum in these cases.

(7) Rhinitis.

TABLE 40.

Incidence of Rhinitis.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number with Rhinitis	12	15	5	3	2	0	37
Percentage Incidence	12	21.1	13.2	11.5	15.4	0	14.4

37 or 14.4 per cent. of the 257 cases exhibited signs of rhinitis and with the exception of the 5 - age group the incidence appears roughly to be fairly evenly

distributed. The discharge in practically all of these cases was of the serous type; several resembled nasal diphtheria and were examined bacteriologically but always with negative result. It is possible that this condition was a further symptom of the inflammatory state of the upper air passages.

(8) Conjunctivitis.

TABLE 41.

Incidence of Conjunctivitis.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number with Conjunctivitis	8	2	2	2	1	0	15
Percentage Incidence	8	2.8	5.3	7.7	7.7	0	5.8

The presence of a seropurulent or purulent discharge from the eyes was taken as evidence of conjunctivitis. The condition was of isolated occurrence and was present in 15 (or 5.8 per cent.) of the 257 cases.

(9) Convulsions.

TABLE 42.

Incidence of Convulsions.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of Cases	100	71	38	26	13	9	257
Number with Convulsions	2	4	2	1	0	0	9
Percentage Incidence	2	5.6	5.3	3.8	0	0	3.5

Convulsions may be single or multiple; they are usually generalized and they appear to mark the onset of some complication. They are not infrequently associated with the collapse of an area of lung tissue, and have also been attributed to cerebral haemorrhage, meningeal haemorrhage and thrombosis of the brain sinuses. In many instances

it is possible that they may be due to the toxins of the disease. In the present series convulsions occurred mostly in younger children; there were 9 (or 3.5 per cent.) of the 257 children with signs of convulsions.

(10) Otorrhoea.

TABLE 43.

Incidence of Otitis Media.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number with Otitis Media	3	3	0	2	0	0	8
Percentage Incidence	3	4.2	0	7.7	0	0	3.1

8 or 3.1 per cent. of the cases showed signs of otorrhoea on admission. This complication is probably associated with the inflamed state of the upper air passages.

(11) Cardiac Complications in non-fatal cases.

TABLE 44.

Incidence of Cardiac Lesions.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number with Cardiac Lesions	2	2	0	0	0	0	4
Percentage Incidence	2	2.8	0	0	0	0	1.5

On examination on admission 4 of the 257 cases showed signs of cardiac collapse. 2 of these had just experienced a severe paroxysm of coughing and on physical examination there was evidence of dilatation of the heart. 24 hours later enlargement of the heart could not be found clinically. This condition may be explained by the recurring attacks of paroxysmal coughing which must entail a great strain being imposed on the heart of the already toxic patient.

(12) Haemorrhages.

TABLE 45.

Incidence of Haemorrhages.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number with Haemorrhages	0	1	0	0	0	1	2
Percentage Incidence	0	1.4	0	0	0	11.1	0.77

Only 2 cases in this group displayed evidence of haemorrhage, one in the 5 - age group had a nasal epistaxis and the other in the - 2 age group had a subconjunctival haemorrhage of the right eye. These haemorrhages are probably another indication of passive congestion.

(13) Prolapse of the Rectum.

TABLE 46.

Incidence of Prolapse Rectum.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of Cases	100	71	38	26	13	9	257
Number with Prolapse Rectum	1	0	1	0	0	0	2
Percentage Incidence	1	0	2.6	0	0	0	0.77

Two cases had prolapse of the rectum on admission, one in the 0 - 1 age group and the other in the - 3 age group. It is surprising that this condition is not found more frequently in view of the greatly increased intra-abdominal pressure induced by the paroxysmal coughing.

(14) Miscellaneous Conditions.

TABLE 47.

Incidence of Miscellaneous Conditions.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of Cases	100	71	38	26	13	9	257
Number with Miscellaneous conditions	29	18	7	10	8	3	75
Percentage Incidence	29	25.4	18.4	35.5	61.5	33.3	29.1

By these are meant intercurrent conditions, the majority of which could have arisen apart from the patient having had Whooping Cough.

The miscellaneous complications number 58, of which 49 were lesions of the skin and mucous membranes. 14 cases showed clinical signs of rickets.

The remaining complications do not fall into any distinctive group and for the sake of simplicity will be enumerated under their various headings and age groups.

TABLE 48.

Miscellaneous Conditions.

Age Group in Years	0 - 1	- 2	- 3	- 4	- 5	5 -
Umbilical Hernia	2					
Hydrocoele of Tunica Vaginalis	1					
Abscess of Neck	1			1		
Fracture of Digital Phalanx		1				
Acute Miliary Tuberculosis		1				
Cervical Adenitis			1			
Coliform Bacilluria				1		
	4	2	1	2	0	0

TABLE 49

Conditions Observed on the Day of Admission to Hospital.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of Cases	100	71	38	26	13	9	257
Number with Pneumonia	54	36	17	11	5	5	128
Percentage Incidence	54	50.7	44.7	42.3	38.5	55.5	49.9
Number with Bronchitis	27	21	14	10	7	2	81
Percentage Incidence	27	29.6	36.8	38.5	53.8	22.2	31.5
Number with Malnutrition	27	23	5	7	6	3	71
Percentage Incidence	27	32.4	13.2	26.9	46.2	33.3	27.6
Number with Enteritis	42	8	4	0	0	0	54
Percentage Incidence	42	11.3	10.5	0	0	0	21.0
Number with Fraenal Ulcer	10	13	9	5	1	2	40
Percentage Incidence	10	18.3	23.7	19.2	7.7	22.2	15.6
Number with Tonsilitis	8	11	11	6	1	3	40
Percentage Incidence	8	15.5	28.9	23	7.7	33.3	15.6
Number with Rhinitis	12	15	5	3	2	0	37
Percentage Incidence	12	21.1	13.2	11.5	15.4	0	14.4
Number with Conjunctivitis	8	2	2	2	1	0	15
Percentage Incidence	8	2.8	5.3	7.7	7.7	0	5.8
Number with Convulsions	2	4	2	1	0	0	9
Percentage Incidence	2	5.6	5.3	3.8	0	0	3.5
Number with Otitis Media	3	3	0	2	0	0	8
Percentage Incidence	3	4.2	0	7.7	0	0	3.1
Number with Cardiac Lesions	2	2	0	0	0	0	4
Percentage Incidence	2	2.8	0	0	0	0	1.5
Number with Haemorrhages	0	1	0	0	0	1	2
Percentage Incidence	0	1.4	0	0	0	11.1	0.77
Number with Prolapse Rectum	1	0	1	0	0	0	2
Percentage Incidence	1	0	2.6	0	0	0	0.77
Number with Miscellaneous conditions	29	18	7	10	8	3	75
Percentage Incidence	29	25.4	18.4	38.5	61.5	33.3	29.1

SUMMARY.

In the 257 cases presented an analysis of the various conditions present on admission reveals that serious complications were present in a large proportion of cases.

First in order of frequency were respiratory complications which were present in 209 or 81.4 per cent. of the series; next in order came malnutrition and enteritis which were present respectively in 71 or 27.6 per cent. and 54 or 21 per cent. of the 257 cases. Convulsions were ninth in order of frequency and account for 9 or 3.5 per cent. of the series.

In the next section the preceding complications will be considered when they developed after admission. The possible causation of those various conditions has already been discussed in the foregoing pages and therefore no attempt will be made to further elaborate.

(C) Conditions manifested after Admission.

Table 63 shows the numbers of cases which on admission were free from the complications listed on that table. Table 64 displays the incidence of these conditions on, and developing after, admission. The following paragraphs compare these figures with those of the complications present on admission (Table 49). In Tables 50 to 62 inclusive uncomplicated is used to signify cases free from the conditions on admission listed in these tables.

(1) Respiratory Complications.

TABLE 50

Incidence of Respiratory Complications.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	46	35	21	15	8	4	129
Number with Pneumonia	9	1	2	1	1	0	14
Percentage Incidence	19.7	2.85	9.52	6.7	12.5	0	10.85
Number of uncomplicated cases	73	50	24	16	6	7	176
Number with Bronchitis	15	4	2	3	1	0	25
Percentage Incidence	20.5	8.0	8.3	18.7	16.6	0	14.2

(a) Pneumonia occurred in 14 cases (10.8 per cent. of 129 cases) which compares very favourably with the figure of 49.9 per cent. present on admission. From Table 64 it is seen that the total incidence of pneumonia was 142 out of 257 cases (55.3 per cent.).

(b) Bronchitis was found to develop in 25 out of 176 cases (14.2 per cent.). This again indicates the value of hospitalisation as the incidence of this condition on admission was 81 out of 257 cases (31.5 per cent.). Bronchitis, therefore, follows close on pneumonia as a complication, the total figures being 106 out of 257 cases (41.2 per cent.).

(2) Malnutrition.

TABLE 51

Incidence of Malnutrition.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	73	48	33	19	7	6	186
Number with Malnutrition	6	0	1	0	0	1	8
Percentage Incidence.	8.2	0	3	0	0	16.5	4.3

During the stay in hospital 8 cases, 4.3 per cent., of the 186 cases non-debilitated on admission, showed signs of wasting. This figure compares very favourably with that found on admission which was 71 cases or 27.6 per cent. of the 257 cases. Here again this proves to be a common complication, a total of 79 out of 257 cases (30.7 per cent.) being observed.

(3) Enteritis.

TABLE 52

Incidence of Enteritis.

Age groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	58	63	34	26	13	9	203
Number with Enteritis	27	7	2	1	1	0	38
Percentage Incidence	46.5	11.11	5.9	3.8	7.7	0	18.7

Of the 203 cases, 38 or 18.7 per cent. developed enteritis after admission to hospital as compared with 54 or 21 per cent. who had the condition on admission. The total incidence is 92 out of 257, 35.8 per cent., and the condition would appear to be more common amongst the younger age groups. It is seen that the incidence of this complication is about equal in home and hospitalised cases and is probably the result of auto-infection.

(4) Fraenal Ulcer.

TABLE 53.

Incidence of Fraenal Ulcer.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	90	58	29	21	12	7	217
Number with Fraenal Ulcer	0	0	0	0	0	0	0
Percentage Incidence	0	0	0	0	0	0	0

None of the cases developed fraenal ulcer after admission to hospital which is to be expected as the majority of the cases were in the paroxysmal stage of the disease on admission.

(5) Tonsillitis and Congestion of Fauces.

TABLE 54.

Incidence of Tonsillitis.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	92	60	27	20	12	6	217
Number with Tonsillitis	1	0	0	3	0	1	5
Percentage Incidence	1	0	0	15	0	16.6	2.3

Congestion of the fauces was present in all the cases. The tonsils were enlarged and congested in 2.3 per cent. of cases as compared with 15.6 per cent. present on

admission, giving a total incidence of 17.5 per cent.

(6) Rhinitis.

TABLE 55.

Incidence of Rhinitis.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	88	56	33	23	11	9	220
Number with Rhinitis	17	11	2	7	0	0	37
Percentage Incidence	19.31	19.6	6	30	0	0	10.6

Rhinitis developed in 37 out of 220 cases (10.6 per cent.) which is slightly less than the figure of 14.4 per cent. present on admission. 74 cases developed the condition out of the total series, giving a percentage incidence of 28.8.

(7) Conjunctivitis.

TABLE 56.

Incidence of Conjunctivitis.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	92	69	36	24	12	9	242
Number with Conjunctivitis	10	7	1	2	1	1	22
Percentage Incidence	10.9	10.1	2.8	8.3	8.3	11.1	9.25

Conjunctivitis developed in 9.25 per cent. of cases as compared with 5.8 per cent. present on admission, a total incidence of 14.4 per cent.

(8) Convulsions.

TABLE 57.

Incidence of Convulsions.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	98	67	36	25	13	9	248
Number with Convulsions	15	3	2	0	1	0	21
Percentage Incidence	15.3	4.5	5.5	0	7.7	0	8.4

Convulsions developed in 8.4 per cent. of cases compared with 3.5 per cent. present on admission, a total of 11.7 per cent. The majority of these convulsions occurred in the younger age groups.

(9) Otorrhoea.

TABLE 58.

Incidence of Otitis Media.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	97	68	38	24	13	9	249
Number with Otitis Media	9	12	3	0	0	2	26
Percentage Incidence	9.3	17.5	7.9	0	0	22.2	14.8

Otorrhoea was present in 14.8 per cent of cases compared with 3.1 per cent. present on admission, the total incidence being 13.2 per cent. The relatively high incidence of this condition is doubtless associated with the congested nasopharynx present in all these cases.

(10) Cardiac Lesions. (Not associated with death occurring immediately afterwards.)

TABLE 59.

Incidence of Cardiac Lesions.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	98	69	38	26	13	9	253
Number with Cardiac Lesions	5	1	0	1	1	1	9
Percentage Incidence	5.1	1.4	0	3.8	7.7	11.1	3.5

Of the 5 cases who displayed cardiac complications in the 0 - 1 group, 3 were designated cardiac collapse; in these cases dilatation of the heart had not been determined. The remaining 2 cases were respectively cardiac collapse with temporary dilatation of the heart, and pericarditis. The 3 cases in the 'under 2', 'under 3' and '5 and over' age groups were cases of cardiac collapse with temporary dilatation of the heart, whilst the remaining case in the 'under 5' age group was one of cardiac collapse with no clinical indication of dilatation. All the cases of cardiac collapse, with or without clinical dilatation of the heart, described here and previously on page 44 occurred after severe paroxysms of coughing. The total incidence of cardiac complications was 5.0 per cent.

(11) Haemorrhages.

TABLE 60.

Incidence of Haemorrhages.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	100	70	38	26	13	8	255
Number with Haemorrhages	0	1	0	1	1	1	4
Percentage Incidence	0	1.4	0	3.8	7.7	12.5	1.6

Nasal epistaxis occurred in 3 cases, 1 from each of the following age groups: 'under 4', 'under 5', '5 and over'. 1 case with petechial haemorrhages into the skin occurred in the 'under 2' age group. The incidence was therefore 1.6 per cent. and the total incidence was 2.3 per cent.

(12) Prolapse of Rectum.

None of the cases developed prolapse of the rectum after admission.

(13) Miscellaneous Complications.

TABLE 61.

Incidence of Miscellaneous Conditions.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	71	53	31	16	5	6	182
Number of Miscellaneous Conditions.	24	12	10	8	2	3	59
Percentage Incidence	33.8	22.6	3.2	50	40	50	32.4

These number 59 of which 34 were lesions of the skin or mucous membranes. The remaining complications are tabulated under the various headings and age groups in the following table.

TABLE 62.

Miscellaneous Complications.

	0 - 1	- 2	- 3	- 4	- 5	5 -
Tetany	1					
Abscess of Sacral Region	1					
Abscess of Cheek	1		1			
Empyema	3			1		
Orbital Cellulitis	1	2				
Pulmonary Tuberculosis		2		1		
Alveolar Abscess		1				
Bronchiectasis			1			1
Scarlatina			3		1	
Abscess of Thigh			1			
Facial Palsy			1			
Double Ethmoiditis			1			
Double Orbital Cellulitis			1			
	7	5	9	2	1	1

TABLE 63.

Conditions Developing after Admission to Hospital.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number of uncomplicated cases	46	35	21	15	8	4	129
Number with Pneumonia	9	1	2	1	1	0	14
Percentage Incidence	19.7	2.85	9.52	6.7	12.5	0	10.85
Number of uncomplicated cases	73	50	24	16	6	7	176
Number with Bronchitis	15	4	2	3	1	0	25
Percentage Incidence	20.5	8.0	8.3	18.7	16.6	0	14.2
Number of uncomplicated cases	73	48	33	19	7	6	186
Number with Malnutrition	6	0	1	0	0	1	8
Percentage Incidence	8.2	0	3	0	0	16.5	4.3
Number of uncomplicated cases	58	63	34	26	13	9	203
Number with Enteritis	27	7	2	1	1	0	38
Percentage Incidence	46.5	11.11	5.9	3.8	7.7	0	18.7
Number of uncomplicated cases	90	58	29	21	12	7	217
Number with Fraenal Ulcer	0	0	0	0	0	0	0
Percentage Incidence	0	0	0	0	0	0	0
Number of uncomplicated cases	92	60	27	20	12	6	217
Number with Tonsillitis	1	0	0	3	0	1	5
Percentage Incidence	1	0	0	15	0	16.6	2.3
Number of uncomplicated cases	88	56	33	23	11	9	220
Number with Rhinitis.	17	11	2	7	0	0	37
Percentage Incidence	19.31	19.6	6	30	0	0	10.6
Number of uncomplicated cases	92	69	36	24	12	9	242
Number with Conjunctivitis	10	7	1	2	1	1	22
Percentage Incidence	10.9	10.1	2.8	8.3	8.3	11.1	9.25
Number of uncomplicated cases	98	67	36	25	13	9	248
Number with Convulsions	15	3	2	0	1	0	21
Percentage Incidence	15.3	4.5	5.5	0	7.7	0	8.4
Number of uncomplicated cases	97	68	38	24	13	9	249
Number with Otitis Media	9	12	3	0	0	2	26
Percentage Incidence	9.3	17.5	7.9	0	0	22.2	14.8

Number of uncomplicated cases	98	69	38	26	13	9	253
Number with Cardiac Lesions	5	1	0	1	1	1	9
Percentage Incidence	5.1	1.4	0	3.8	7.7	11.1	3.5
Number of uncomplicated cases	100	70	38	26	13	8	255
Number with Haemorrhages	0	1	0	1	1	1	4
Percentage Incidence	0	1.4	0	3.8	7.7	12.5	1.6
Number of uncomplicated cases	99	71	37	26	13	9	255
Number with Prolapse Rectum	0	0	0	0	0	0	0
Percentage Incidence	0	0	0	0	0	0	0
Number of uncomplicated cases	71	53	31	16	5	6	182
Number of Miscellaneous Conditions	24	12	10	8	2	3	59
Percentage Incidence	33.8	22.6	3.2	50	40	50	32.4

Uncomplicated in this table is used to signify cases free from the conditions on admission listed in this table.

TABLE 64.

Total Incidence of the Conditions Observed on and After Admission.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Total number of cases in series	100	71	38	26	13	9	257
Number with Pneumonia	63	37	19	12	6	5	142
Percentage Incidence	63	52.1	50	46.1	46.2	55.5	55.3
Number with Bronchitis	42	25	16	13	8	2	106
Percentage Incidence	42	35.2	42.1	50	61.5	22.2	41.2
Number with Malnutrition	33	23	6	7	6	4	79
Percentage Incidence	33	32.4	15.8	26.9	46.2	44.4	30.7
Number with Enteritis	69	15	6	1	1	0	92
Percentage Incidence	69	21.1	15.8	3.8	7.7	0	35.8
Number with Fraenal Ulcer	10	13	9	5	1	2	40
Percentage Incidence	10	18.3	23.7	19.3	7.7	22.2	15.6
Number with Tonsillitis	9	11	11	9	1	4	45
Percentage Incidence	9	15.5	28.9	34.5	7.7	44.4	17.5

Number with Rhinitis	29	26	7	10	2	0	74
Percentage Incidence	29	36.6	18.5	28.4	15.4	0	28.8
Number with Conjunctivitis	18	9	3	4	2	1	37
Percentage Incidence	18	12.6	7.9	15.4	15.4	11.1	14.4
Number with Convulsions	17	7	4	1	1	0	30
Percentage Incidence	17	9.8	10.6	3.8	7.7	0	11.7
Number with Otitis Media	12	15	3	2	0	2	34
Percentage Incidence	12	21.5	7.9	7.7	0	22.2	13.2
Number with Cardiac Lesions	7	3	0	1	1	1	13
Percentage Incidence	7	4.2	0	3.8	7.7	11.1	5
Number with Haemorrhages	0	2	0	1	1	2	6
Percentage Incidence	0	2.8	0	3.8	7.7	22.2	2.27
Number with Prolapse Rectum	1	0	1	0	0	0	2
Percentage Incidence	1	0	2.6	0	0	0	0.77
Number of Miscellaneous Conditions	53	30	17	18	10	6	134
Percentage Incidence	53	42.3	44.7	69.3	76.9	66.6	52

SUMMARY.

(1) An analysis of the conditions developing after admission has been carried out, and their total incidence given.

(2) The analysis shows that hospitalisation is advantageous in the paroxysmal stage of Whooping Cough as fewer complications developed in the majority of cases so treated.

(3) Serious complications were found to develop in a considerable number of the cases after admission.

The total incidence of the more important of these is given below.

(a) Pneumonia. This condition was present in 142 out of 257 cases (55.3 per cent.)

(b) Bronchitis. 106 cases out of 257 (41.2 per cent.) showed this condition.

(c) Enteritis. 35.8 per cent. of the series, 92 out of 257 cases suffered from this serious complication.

(d) Malnutrition. 79 out of 257 cases (30.7 per cent.) developed wasting and this is probably dependent to some extent on the vomiting and enteritis.

(e) Convulsions. 30 out of 257 cases (11.7 per cent.) showed this complication.

With the exception of Enteritis and Convulsions which were more common amongst the younger age groups, the other complications were found to be fairly evenly distributed throughout the age groups. From the foregoing figures it will be seen that despite the efficient treatment obtainable in hospital the more serious complications still tend to develop although less frequently.

A Study of the 66 Fatal Cases.

As has been described previously (page 40 et seq), 209 patients were admitted to hospital showing respiratory complications, 54 with enteritis and 9 with convulsions. Those are the more dangerous of the complications of Whooping Cough and an attempt will be made to assess their relative importance as causes of fatality.

TABLE 65.

Relative Incidence of Probable Causes of Death.

	Age Groups.						
	0 - 1	- 2	- 3	- 4	- 5	5 -	Total number of deaths.
Total Number of Deaths	46	14	3	2	0	1	66
Pneumonia present in	44	12	3	1	0	1	61
Bronchitis present in	2	0	0	0	0	0	2
Enteritis present in	32	5	0	0	0	0	37
Convulsions present in	13	7	2	0	0	0	22
Pulmonary Tuberculosis present in	0	2	0	0	0	0	2

This table indicates that several complications might be present in one case. Pneumonia was the most frequent complication, being present in 61 out of 66 fatal cases.

Although Enteritis in Whooping Cough would more properly come under contributory causes of death as it is

almost invariably a secondary manifestation of broncho-pneumonia, yet it is of such severity in many cases as to be classed an immediate cause of death. It was present in 37 of the 66 fatal cases.

Convulsions were present in 22 of the 66 fatal cases, but bronchitis and pulmonary tuberculosis were relatively infrequent, being present respectively in two of the fatal cases.

TABLE 66.

The Incidence of Other Complications in the 66 Fatal Cases.

	Age Groups						
	0 - 1	- 2	- 3	- 4	- 5	5 -	Totals
Number of Patients in age group	100	71	38	26	13	9	257
Number of Deaths in age group	46	14	3	2	0	1	66
Malnutrition present in	21	8	0	2	0	1	32
Otitis Media present in	4	2	0	0	0	0	6
Rickets present in	2	1	0	0	0	0	3
Tetany present in	1	0	0	0	0	0	1
Empyema present in	3	0	0	0	0	0	3
Cervical Adenitis present in	1	0	1	1	0	0	3
Bronchiectasis present in	0	0	1	0	0	1	2

The above table shows that Malnutrition appears to be a fairly frequent contributory cause of death, whereas otitis media, rickets, tetany and cervical adenitis appear to be relatively infrequent. Empyema was present in 3 and bronchiectasis in 2 cases.

VACCINES IN THE TREATMENT OF WHOOPING COUGH.

Much has been written on the use of Pertussis vaccine as a therapeutic measure in the treatment of Whooping Cough. A resumé of the more important recent literature is to be found in the introduction, This would appear to suggest that although some workers have obtained negative or equivocal results others report greater success. The majority of the

latter workers are almost unanimous in saying that vaccines are of greatest value in the early stages of the disease. It seems that very large doses of Pertussis vaccine can be tolerated without untoward effect and that the vaccine should be prepared from phase 1 of the organism to ensure antigenic efficacy. The majority of workers have used pure Pertussis vaccine.

Scheme followed in use of Vaccine.

All the cases were treated under conditions which were as comparable as possible. A standard diet was adopted and similar drugs were used for all patients as far as possible with the exception of chloral hydrate which was used only in cases with convulsions. A record, as accurate as possible, was kept of the coughs, whoops, vomiting, cyanosis and convulsions in each case as an index of the severity of the disease.

Clinical examinations were carried out on each patient daily as far as possible. Later when the epidemic was at its height this was found to be impracticable and examinations were made on each patient every third day.

Vaccine Treatment.

In order to evaluate the possible beneficial effect of vaccines in treatment the 257 cases were subdivided into 3 groups :

(a) 78 cases were treated with smooth vaccines which had been prepared from freshly grown strongly antigenic smooth strain organisms. (Phases I and II Leslie and Gardner).

(b) 22 cases were treated with rough vaccine prepared from old stock laboratory cultures. (Phase IV Leslie and Gardner).

(c) 157 cases which did not receive any vaccine treatment.

Group (a) is thus controlled by group (b), both of which are in turn controlled by group (c).

With regard to the general medical treatment, all cases were put on a simple expectorant mixture.

Prescription A.

Pot. Cit.	℥iv
Tinct. Ipecac.	℥i
Syrup Tolu.	℥ij
Syrup Simplex	℥ii
Aqua ad.	℥iv

Sig. ℥ii ex acua 4 times daily for children over 2 years; ℥i for children under 2 years.

It was felt that such a mixture might have a beneficial effect in aiding the patients to get rid of the thick viscid sputum, Potassium Citrate being added to aid elimination by the kidneys: drugs of an anti-spasmodic and sedative nature were not used in a routine manner.

A second prescription, Prescription B, was used when resolution of bronchopneumonia or bronchitis was delayed.

viz:	Pot. Iod.	℥i
	Tinct. Ipecac.	℥ii
	Syrup Tolu.	℥ii
	Syrup Simplex	℥ii
	Aqua ad.	℥vi

A similar system of dosage was employed as with prescription A. Children under 2 years received half the dose.

TECHNIQUE OF VACCINE THERAPY.

(1) Choice of Case.

The cases in which vaccination with pure Pertussis vaccine was carried out were unselected, every case being treated regardless of the stage of the disease, with the following exceptions.

Children who were judged to be acutely ill from the complications of Whooping Cough or from intercurrent disease, and children who were apparently moribund.

The choice of a vaccine composed solely of Haemophilus Pertussis was made for the following reasons:

(1) Large doses of Whooping Cough vaccines composed of H. Pertussis alone may be given without the constitutional and local upset so common with other vaccines.

(2) It was thought that an attempt should be made to attack solely the specific infection.

(3) Whooping Cough is a disease which usually runs a long course, and it was thought that if the length and severity of the disease was dependent on the fact that immunity took a long time to develop then the giving of smooth vaccine parenterally might accelerate the amount and rate of

acquisition of specific immunity.

TYPES OF VACCINE.

The vaccines used were composed of whole B. Pertussis micro-organisms in suspension, or their chemically dissolved constituents.

(1) Vaccines composed of whole organisms in suspension.

(a) Whooping Cough vaccine (Prophylactic A) containing 4,000 million whole organisms per c.cm. prepared by the inoculation department, St. Mary's Hospital (issued by Parke Davis & Co.). This vaccine consists of whole organisms in suspension in normal saline to which 0.05 per cent. of phenol had been added. The medium on which the organisms were grown was said to be glycerol potato blood agar, horse blood being used.

(b) Madsen's vaccine containing 8,000 million B. Pertussis organisms per c.cm. in suspension in normal saline to which 0.05 per cent. phenol had been added. The media stated to be used was one composed of glycerol potato blood agar, the blood used being horse blood. This vaccine was prepared by the State Serum Institute, Denmark, and is marketed in this country by British Drug Houses.

(c) Whooping Cough dissolved vaccine containing the dissolved constituents of 4,000 million or 8,000 million to 10,000 million B. Pertussis organisms per c.cm. The organisms were stated to be grown on Bordet Gengou media using horse blood. This vaccine is prepared and marketed by the Glaxo Laboratories Ltd.

(d) Rough strain vaccine containing 8,000 million whole B. Pertussis organisms per c.cm. prepared from old stock laboratory cultures by Dr. Robert Cruickshank, lately Bacteriologist to the Royal Infirmary, Glasgow.

With the exception of the rough strain vaccine all these vaccines were stated to have been prepared from freshly isolated strains of the organism so that the antigenic efficacy of the vaccines seemed assured.

Dosage of Smooth Vaccine.

When the vaccines were first used small doses were tried as it was thought advisable to proceed cautiously. Therefore the initial dose of vaccine was often as low as 400 million organisms, whilst later in accordance with the practice of recent workers [Cockshut (19) (1933), Sauer (28) (1937)] a single dose of 32,000 million organisms was frequently used and even larger single doses were employed in exceptional circumstances. The total amount of vaccine given in each case was dependent, not only upon considerations of caution, but also on the progress of the illness and the development of other contra-indications; this has given rise to an apparently systemless method of dosage. A somewhat decreased dosage was used for children under the age of 1 year, an effort being made to give the optimum dose, bearing in mind that an amount of vaccine above that capable of producing the maximal antibody response is valueless. The vaccines were usually injected at intervals of 2 - 7 days. It was found that when large amounts of vaccine were administered subcutaneously in the subdeltoid regions a raised indurated area usually developed at the site of the injection with some inflammatory reaction. This area was variable in size and was usually roughly proportional to the amount of vaccine injected and occasionally took several days to disappear. The local reaction was most marked in from 16 to 24 hours after injection. When large doses of vaccine were thought to be necessary the intramuscular route was chosen, injection being made into the external aspect of the thigh, with little local disturbance. It was also thought that the antibody response to intramuscular injection might be quicker. Ill effects consisted of local pain and stiffness which usually passed off in a few days. The route of administration had no effect on the general reaction which was never severe.

The Value of Vaccine Therapy.

Dosage of Vaccine.

Each individual case was treated according to its anticipated requirements, and no attempt was made to adopt a standardised dosage. The concentrations of the vaccines used varied and an arbitrary unit of 4,000 million organisms per c.cm. was adopted.

The results of treatment by vaccines were judged solely on cases who completed successfully their course of injections. Cases transferred or dismissed irregularly and deaths are thus excluded. This leaves for consideration 179 cases of which 96 were untreated by vaccines, 66 which received smooth vaccines and 17 which had the rough vaccine.

TABLE 67.

Disposition of Cases.

	Non-Vaccine Treated Group	Smooth Vaccine Treated Group	Rough Vaccine Treated Group	Total
Irregular Dismissals.	4	0	0	4
Transfers	5	0	3	8
Number of Cases Dismissed as well	96	66	17	179
Deaths	52	12	2	66
Number of Cases Admitted	157	78	22	257

Group 1. Smooth Vaccine Treated.

There were 66 cases in this group. The average dose per case was 18.593 c.cm. of smooth vaccine. The minimum dose was 1.c.cm. and the maximum 73 c.cm.

The vaccines used were prepared by three firms, viz:

(1) Glaxo Vaccine (23 cases).

(2) St. Mary's Hospital Vaccine (19 cases).

(3) Danish Vaccine (24 cases).

TABLE 68.

Average, Minimum and Maximum Doses of Smooth Vaccine given in the Various Age Groups.

Number of Patients	Age Groups	Average Amount of Vaccine	Minimum Dose of Vaccine	Maximum Dose of Vaccine
24	0 - 1 yrs	17.0 c.cm.	1 c.cm.	44.0 c.cm.
15	- 2 yrs	16.32 c.cm.	6 c.cm.	36.0 c.cm.
12	- 3 yrs	21.54 c.cm.	5 c.cm.	44.0 c.cm.
7	- 4 yrs	17.55 c.cm.	6.2 c.cm.	32.0 c.cm.
3	- 5 yrs	12.33 c.cm.	5.3 c.cm.	19.7 c.cm.
5	5 - yrs	22.04 c.cm.	5.2 c.cm.	73 c.cm
66		18.593 c.cm.		

Group 2. Rough Vaccine Treated, 17 Cases.

There were 17 cases in this group and the average case dosage was 11.11 c.cm., the minimum 2 c.cm. and the maximum 20 c.cm.

TABLE 69.

Average, Maximum and Minimum Doses of Rough Vaccine given in the Various Age Groups.

Number of Patients	Age Groups	Average Amount of Vaccine	Minimum Dose of Vaccine	Maximum Dose of Vaccine
5	0 - 1 yrs	9.4 c.cm.	2 c.cm.	15 c.cm.
5	- 2 yrs	14.4 c.cm.	8 c.cm.	20 c.cm.
2	- 3 yrs	11.5 c.cm	6 c.cm.	17 c.cm.
3	- 4 yrs	5.33 c.cm.	2 c.cm.	10 c.cm.
2	- 5 yrs	15.5 c.cm.	12 c.cm.	19 c.cm.
0	5 - yrs			
17		11.11 c.cm.		

Group 3. Cases not Treated by Vaccines.

There were 96 cases in this group, the majority of whom were younger children, see Tables 70 and 71.

TABLE 70.

Distribution of Cases in Non-Vaccine Treated Group.

Age Groups	Number of Patients.
0 - 1	25
- 2	34
- 3	15
- 4	13
- 5	6
5 -	3
	96 Total.

TABLE 71.

Age Distribution of the Patients in the Non-Vaccine Treated Group.

In Whole Group.

Number of Patients	Age Group	Deaths		Transfers	Irregular Dismissals	Regular Dismissals.
		Number	Per Cent.			
59	0 - 1 yrs.	33	55.9	0	1	25
49	- 2 "	13	26.53	1	1	34
24	- 3 "	3	12.50	4	2	15
15	- 4 "	2	13.33	0	0	13
7	- 5 "	1	14.28	0	0	6
3	5 - "	0	0	0	0	3
157		52	33.12	5	4	96

Record of Results.

Observations of the temperature, pulse and respirations were taken every four hours and charted until such time as they had fallen within the limits of normal, and then morning and evening records only were taken. When vaccines had been given, the height of the temperature, pulse rate and respiration rate were recorded every 2 hours for the first 24 hours after the injections had been given. The various symptoms, signs, complications and intercurrent diseases which developed were noted. Efforts were made to assess the severity of the disease; and the success of this depended entirely upon the enthusiasm and conscientiousness of the nursing staff who noted the various criteria throughout the 24 hours from day to day whilst the patient was in hospital. The results were charted in the following form for each patient every day:-

Name; Age; Date of Admission; Day of Illness on Admission;

Date	Number of Paroxysms	Average Number of Coughs per paroxysm	Total Number of Coughs per day	Total Number of Whoops per day	Incidence of Cyanosis	Incidence of Convulsions

A paroxysm was taken to be a series of involuntary coughs following each other in close succession and ending in (1) a pause, (2) whooping, (3) vomiting, (4) convulsions and occasionally cardiac collapse. From these observations graphs have been constructed to illustrate the course of the disease, see page 69 et seq.

Results.

Changes in Severity in the Smooth Vaccine Treated and Non-Vaccine Treated Cases.

(1) Smooth Vaccine Treated.

65 cases treated with smooth vaccines (not 66) will be considered as in one case the date of onset of the disease could not be fixed with any degree of certainty. In the control group there were 59 cases, here again the duration of the Whooping Cough could not accurately be determined in 37 cases.

TABLE 72.

Distribution of Cases and Severity on Admission or Prior to Administration of Vaccine.

124 cases (65 treated 59 controls).

Age Groups	Mild		Moderate		Severe		Totals			
	Tr	Ct	Tr	Ct	Tr	Ct	Tr		Ct	
							No.	%	No.	%
0 - 1	19	10	3	3	2	2	24	36.9	15	25.42
- 2	8	16	5	9	1	0	14	21.5	25	42.4
- 3	9	3	1	5	1	2	11	16.9	10	16.9
3 -	12	5	3	3	1	1	16	24.6	9	15.2
Totals	48	34	12	20	5	5	65		59	
Per Cent.	73.8	52.3	18.5	30.8	7.7	7.7		100		100

Tr = Cases treated with 'smooth vaccine'.
Ct = Cases untreated with vaccine.
No. = Number
% = Per cent.

From a perusal of Table 72 it is seen that the largest number of cases were mild, and that there were more mild cases in the treated than in the control group.

TABLE 73.

Total Duration of Disease.

Total Duration of Cough	Treated Group Cases relieved		Control Group Cases relieved		Duration of Whoop	Treated		Controls	
	No.	Percentage	No.	Percentage		No.	Percentage	No.	Percentage
0 - 3 wks	0	0	17	28.8	0 - 2 wks.	4	7.8	12	34.3
- 5 "	10	15.4	14	23.7	- 4 "	12	23.5	7	20.0
- 7 "	20	30.8	22	37.3	- 6 "	13	25.5	12	34.3
- 9 "	19	29.2	5	8.5	- 8 "	15	29.4	3	8.6
- 11"	5	7.7	1	1.7	8 - "	7	13.7	1	2.9
11 - "	11	16.5	0						
Totals	65		59			51		35	

Wks = Weeks

This table indicates that 14 untreated cases did not whoop at any time and 24 of the control groups were similarly free. The figures would appear to indicate that the duration of the disease was prolonged by the administration of vaccine in spite of the fact that there were more mild cases amongst the treated group.

Rough Vaccine Treated Group.

TABLE 74.

Distribution of Cases according to Severity.

on Admission.

Age Groups	Mild.
0 - 1	5
- 2	5
- 3	2
3 -	5
Totals	17

The 17 cases were all of the mild variety.

TABLE 75.

Total Length of Disease including Period of Symptoms present before admission to Hospital.

Total Duration of Cough	Number of cases relieved	Total Duration of Whoop	Number of cases relieved
0 - 3 weeks	0	0 - 2 weeks	0
- 5 weeks	2	- 4 weeks	1
- 7 weeks	2	- 6 weeks	0
- 9 weeks	8	- 8 weeks	7
- 11 weeks	0	8 - weeks	4
11 - weeks	5		
Totals	17		12

This small group of 17 cases would appear to suggest that there may be a prolongation of the paroxysmal coughing and whooping phases similar to the findings obtained in the smooth vaccine treated group.

Analyses of the Graphs of Coughs and Whoops.

The coughs and whoops were noted daily and charted. The resultant curves were sorted out into what were considered representative types. See charts A, B and C (on page 69 et seq.).

CHART A.

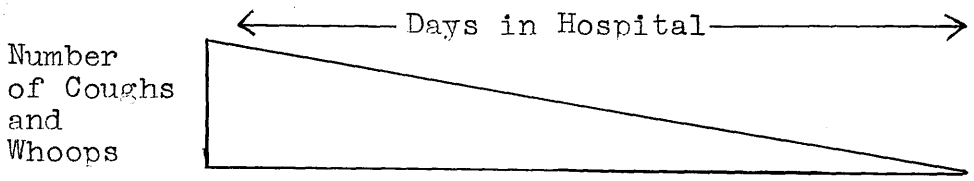

Chart A:- This shows a gradual diminution in the number of coughs and whoops

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CHART B.

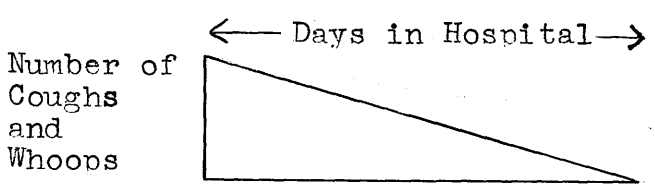


Chart B:- Where the fall in the number of coughs and whoops was not so gradual as in Chart A.

CHART C.

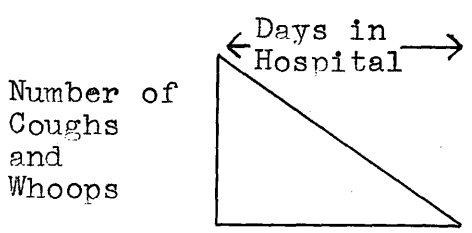


Chart C:- A rapid fall in the number of coughs and whoops took place.

The following table illustrates the incidence of these various curves.

TABLE 76.

		Curve A	Curve B	Curve C
Non-Vaccine Treated Cases	149	55.4%	26.2%	18.4%
Smooth " " "	78	65.5%	20.7%	13.8%
Rough " " "	22	83.3%	8.3%	8.3%
Total	249			

This table excludes 8 deaths occurring within 24 hours of admission in the non-vaccine treated group.

From these figures it is seen that the Curves A, B and C occurred in that order in decreasing frequency irrespective of the method of treatment adopted.

FREDERICK Moore. 3½ years.

February. 15 16 14 18 19 20 21 22 23 24 25 26 24 28 1 2 3 4 5 6 4 8 9 10 11 12 13 14 15 16 14 18 19

60 64 69 44 49 84 89

120 900

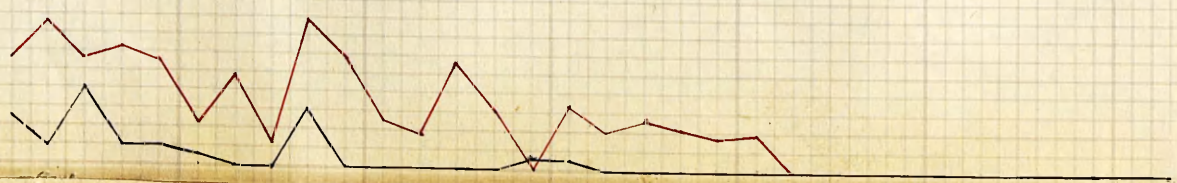
100 750

80 600

60 450

40 300

20 150



Discharged 18th March 1935.

CHART A

—— = Number of Coughs per Day.

—— = Number of Whoops per Day.

JOHN ROBERTSON aged 3 years admitted 14..2..35

14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

120 900

100 750

80 600

60 450

40 300

20 150

CHART B

—— = Number of Coughs per Day

—— = Number of Whoops per Day

JANET MORRISON aged 3½ years admitted 29.4.35.

29 30 31 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22.

15 19 24 29 34 39

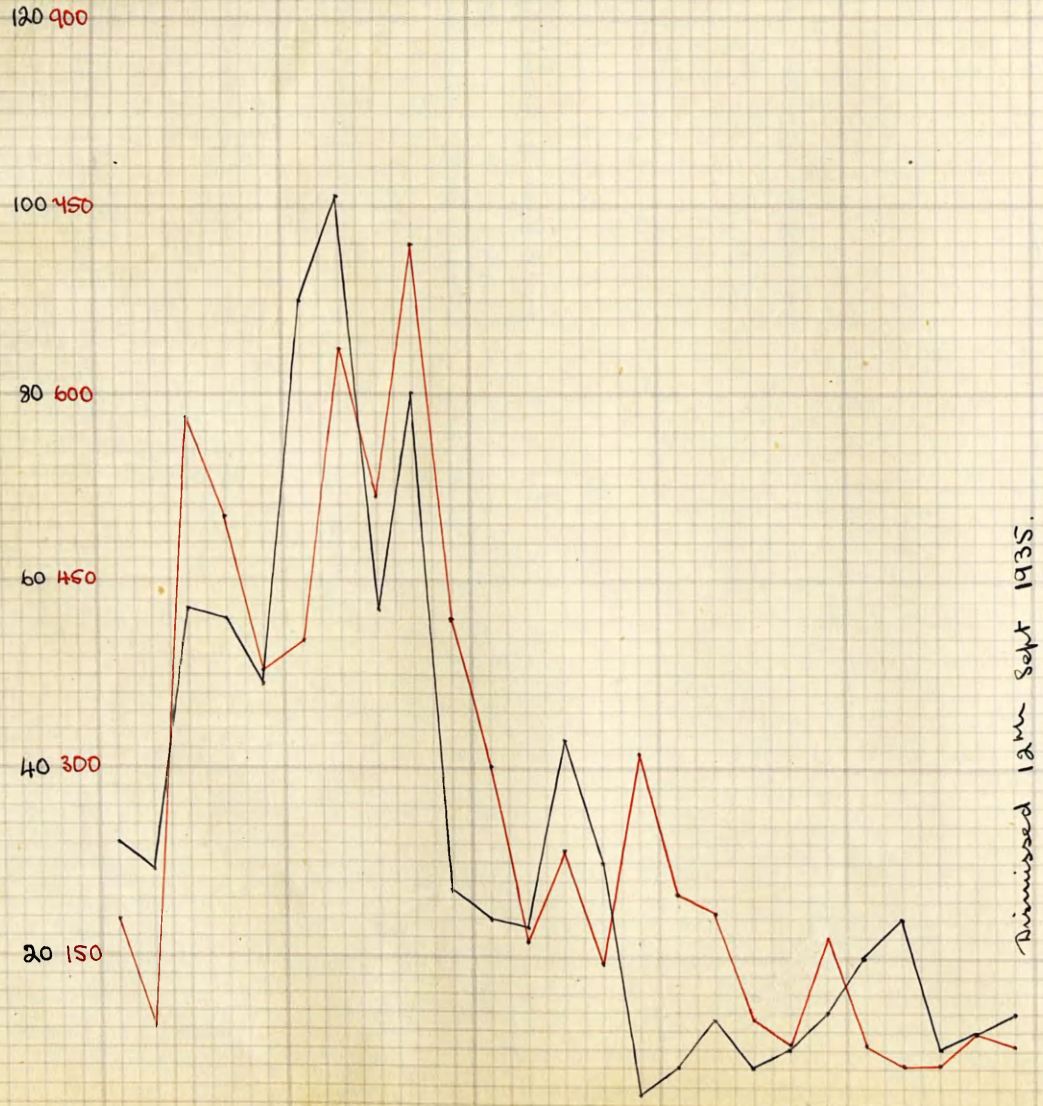


CHART C

—— = Number of Coughs per Day

—— = Number of Whoops per Day

AGNES BAIRD aged 2 years admitted 5.5.35.

5 6 4 8 9 10 11 12 13 14 15 16 14 18 19 20 21 22 23 24 25 26 24 28 29 30 31 1 2 3 4 5 6 4 8 9 10 11 12 13 14 15 16 14 18 19 20 21 22 23 24 25 26

9 13 18 23 28 33 38 43 48 53 58 63

4000 Million B Pertussis (Baugh Strain)

8000 Million B Pertussis (Baugh Strain)

8000 Million B Pertussis (Baugh Strain)

8000 Million B Pertussis (Baugh Strain)

8000 Million B Pertussis (Baugh Strain)

16000 Million B Pertussis (Baugh Strain)

16000 Million B Pertussis (Baugh Strain)

8000 Million B Pertussis (Baugh Strain)

CHART D

—— = Number of Coughs per Day

—— = Number of Whoops per Day

120 900

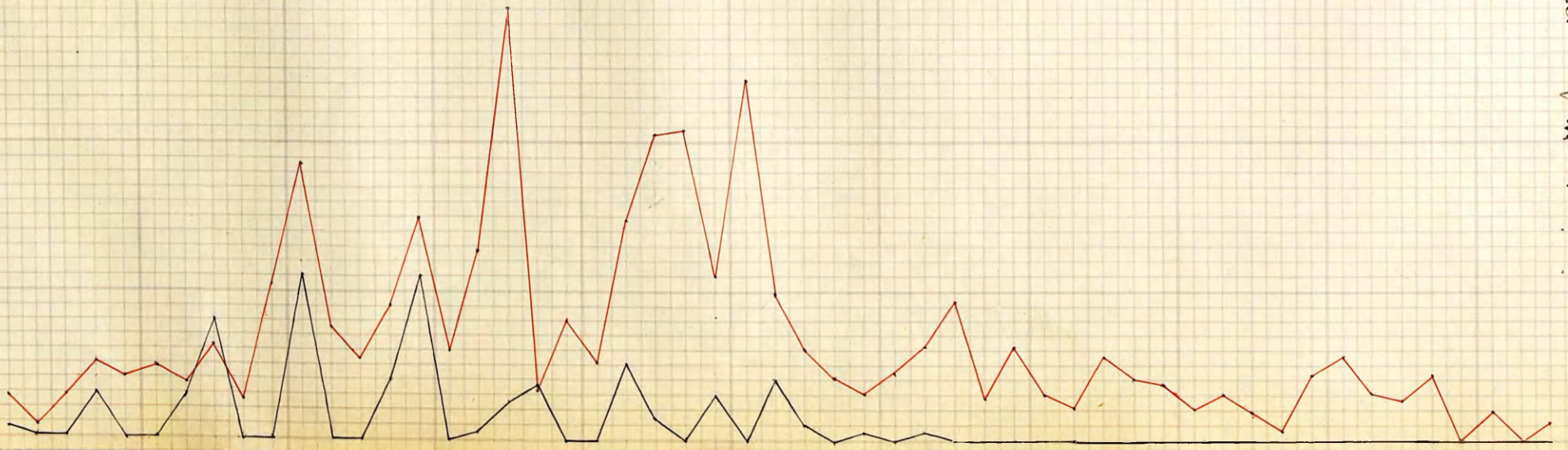
100 750

80 600

60 450

40 300

20 150



Dismissed 28th June 1935.

It would appear that the non-vaccine treated group contains a larger number of cases which show a more rapid diminution of the coughs and whoops than do the vaccine treated group. This finding suggests that Pertussis vaccines are of little value as a therapeutic measure, in fact in some instances (see chart No. D) the administration of vaccine appeared to increase the number of paroxysms. Little difference was noted in the effects of the rough and smooth vaccines, although there is a suggestion that the rough vaccine is of even less use than the smooth.

SUMMARY.

(1) A series of 141 patients suffering from Whooping Cough have been examined with a view to determining the value of vaccines in treatment. 65 cases were treated with smooth vaccines, 17 with rough vaccines and 59 cases which did not receive vaccines acted as a control group.

(2) Although there were more mild cases in the smooth vaccine-treated than in the control group, the duration of the disease appeared to be prolonged in the former.

(3) The severity of the disease appeared to be aggravated as a direct result of injection of the vaccine in the smooth vaccine treated group.

(4) The small number of cases in the rough vaccine-treated group forbade any decisive conclusions from being drawn although there was a suggestion that the findings were similar to those obtained in the smooth vaccine-treated group.

(5) The analysis of the Graphs illustrating the duration and severity of the disease confirm the view that vaccines are of little value as a therapeutic measure.

PROPHYLAXIS.

Sauer (52) 1933 states that complete protection is given by the prophylactic inoculation of children with doses of 2 - 3 c.c. of pure pertussis vaccine at weekly intervals, 7 - 8 c.c. in all being given (1 c.c. containing 10,000 million whole organisms.

Madsen (25) 1933 reported that in an epidemic of Whooping Cough occurring in the Faroe Islands a total dose of 22,000 million whole micro-organisms per person inoculated conferred protection on a large proportion of the cases, whilst the vaccinated cases who developed the disease ran a mild course.

Frawley (27) 1934 reports good results using 8 c.c. of active undenatured Haemophilus pertussis antigen.

Sauer (28) 1937 using 10 c.c. of his vaccine for children over 2 years reports further good results.

Material Used in Present Investigation.

This consisted of 104 cases in the 'up to 5' age group with no previous history of Pertussis and convalescent from pneumonia who had been admitted to the Wards between December, 1936 and July, 1937 when an epidemic of Whooping Cough was present in Glasgow. Of the 104 cases given prophylactic inoculations of pure Pertussis vaccine 83 returned for examination. The remaining 21 cases could not be traced.

Dosage.

The total dose of vaccine varied from 7 c.cm. to 8 c.cm. with the exception of 1 patient who received 4 c.cm. [1c.cm. = 8,000 million organisms or their equivalent chemically dissolved.] The vaccines used were Madsen's Danish Vaccine composed of whole organisms or Glaxo Vaccine composed of Pertussis micro-organisms chemically dissolved. The total dose was given in 3 divided doses at weekly intervals of 1, 3 and 4 c.cms. subcutaneously in the subdeltoid region for the smaller doses and into the external aspect of the thigh for the larger doses. 31 cases were exposed to Whooping

Cough and of these 12 received 7 c.cm and 19, 8 c.cm. of vaccine. Glaxo vaccine was given to 16 cases and Danish vaccine to 14 cases. One received Glaxo and Danish vaccine mixed.

Exposure.

Of the 83 cases 31 gave a history of subsequent exposure as will be seen in the accompanying table.

TABLE 77.

Exposure in Home	Exposure in Hospital	Exposure in Adjacent House	Exposure more Doubtful.	Total
Cases 10	1	13	7	31

The 31 cases exposed to infection were all in the - 3 age group with the exception of 5 patients aged 5 8/12, 5 years, 6 years, 7 years and 5 years respectively. Of these 5 cases, 1 was exposed in the home, 3 in neighbours' houses and the remaining 1 to an infected playmate.

Results.

(1) Hospital and Home Exposures.

There were 11 patients in this group each of whom had been intimately exposed to one or more cases of Whooping Cough. The single case which had been exposed to infection in hospital developed Whooping Cough in a mild form. Unfortunately, the total number of patients exposed to the infection at the same time was not elicited but there were certainly several who developed the disease.

Of the remaining 10 cases exposed in the home, 2 were said by the parents to have developed the disease in a mild form whilst one parent thought her child had developed Whooping Cough but could give no opinion as to the severity.

Co-Exposures (Brothers and Sisters of the Immunised Children).

There were 14 supposedly susceptible children exposed to the disease prior to or simultaneously with 8 of the previously artificially immunised children exposed at home. Of these 8 immunised cases, 1 developed Pertussis in a mild form whilst another developed a doubtful attack,

leaving 6 who escaped the infection. Of the 14 unprotected children only 2 escaped infection.

(2) Cases Resulting from Less Intimate Exposure.

There were 20 artificially immunised children in this group but none of them developed Whooping Cough. The susceptible brothers and sisters of the above children numbered 25 and again none developed the disease.

Conclusions.

The results from this small series would suggest that the prophylactic inoculation of children is of some value but would only appear to be justifiable where intimate exposure is likely.

VACCINATION OF WHOOPING COUGH CONTACTS WITH PERTUSSIS VACCINE.

46 contact cases were treated with vaccines. These children were known to have been in intimate contact with certified cases of the disease. 6 of the 46 cases did not return after they had been given the first dose of vaccine. The 40 remaining cases varied in age from 6 months to 7 years, 7 cases being in the - 2 age group, 16 in the 2 - 5 age group and 17 in the 5 and over age group.

Time of exposure.

The duration of exposure of these 40 cases was three weeks or less. 26 cases only were observed throughout and completed the course of injections, the remaining 14 cases having failed to complete the course.

Vaccine used.

The vaccine used was Danish vaccine consisting of 8,000 to 10,000 million organisms per c.cm. The initial dose varied from 0.5 c.cm. to 1 c.cm., and later doses varied from 1 to 2 c.cm. The vaccines were injected subcutaneously into the deltoid region.

The average total dose administered to the 26 cases

was 5.35 c.cm., the minimum total dose given being 2 c.cm. and the maximum 10 c.cm.

Results.

Only the 26 cases who were observed throughout will be considered.

6 patients showed no signs of Whooping Cough when first seen nor did they develop any signs of the disease during the course of injections. 3 cases, however, developed mild symptoms suggestive of Whooping Cough which lasted for an average period of 8 days. 8 other cases had a slightly more severe attack with an average duration of 20 days. The remaining 9 cases suffered from an attack of the disease which was not apparently mitigated; the average duration being 45 days.

TABLE 78.

Contacts Treated with Vaccine.

Severity

Mild		Moderate		Unmodified		Severe	
Number of cases	Duration of symptoms in days	Number of cases	Duration of symptoms in days	Number of cases	Duration of symptoms in days	Number of cases	Duration of symptoms in days
1	19	1	15	1	48	1	46
1	3	1	18	1	65		
1	3	1	18	1	47		
		1	21	1	36		
		1	21	1	59		
		1	24	1	33		
		1	20	1	32		
		1	21	1	37		
3		8		8		1	

Total number of unprotected cases = 20
" " " protected cases = 6
" " " cases = 26

SUMMARY

These results would appear to indicate that Pertussis vaccines are of value in (1) preventing, (2) mitigating the severity of the infection and (3) shortening the duration of the disease should it develop.

The significance of the results is impaired, however, by the fact that the series investigated was small and uncontrolled.

PROGNOSIS.

In this section an attempt is made to evaluate the factors which influence prognosis in hospital cases by a study of this series of 257 patients.

(1) Age Incidence and Mortality.

From the figures in the accompanying table it would appear that Whooping Cough is more frequent amongst the younger age groups, and that the mortality is highest in infants (0 - 1 year).

TABLE 79.

Age Incidence and Mortality.

Age Groups	0 - 1	- 2	- 3	- 4	- 5	5 -	Total
Number of cases	100	71	38	26	13	9	257
Number of deaths	46	14	3	2	0	1	66
Mortality Per Cent.	46%	19.7%	7.9%	7.7%	0%	11.1%	26%

Of the 257 patients 209 or 81.32 per cent. were under and 48 or 18.68 per cent. over the age of 3 years, the oldest being aged 9 years, the mortality rate being 30.14 per cent. and 6.25 per cent. respectively.

TABLE 80.

Age and Sex Incidence and Mortality.

	0 - 1		- 2		- 3		- 4		- 5		5 -		Total	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Cases	40	60	37	34	16	22	11	15	7	6	8	1	119	138
Deaths	20	26	9	5	2	1	0	2	0	0	1	0	32	34
Mortality Rate Per Cent.													26.9	24.53

M = Male F = Female

The above table shows that in this series there were more female patients attacked by the disease than males, and that the death rate of the males (26.9 per cent.) was slightly higher than that of the females (24.53 per cent.).

The mortality rate of 26.9 per cent. (Table 80) is probably unduly high as the patients dealt with all belonged to the hospital class. The mortality rate of 46 per cent. in the children of one year or under emphasises the importance of age in prognosis as described on page 58 et seq. Malnutrition was present in 32 of the 66 fatal cases, otitis media in 6 cases, rickets in 3, tetany in 1, empyema in 3, cervical adenitis in 3 and bronchiectasis in 2 cases.

As previously described, see page 58, it would appear that pneumonia, convulsions and enteritis are the most common of the probable immediate causes of death as pneumonia was present in 61 of the 66 deaths, convulsions were confined to 22 of the 63 fatal cases all under 3 years of age, and enteritis in 37 of the 60 fatal cases all under 2 years of age.

Severity of Whooping Cough.

The severity of Whooping Cough is extremely difficult to assess as practically the only symptom common to all ages is the spasmodic cough. Whooping is frequently absent in young children, whereas convulsions are more common. The incidence of the classical symptoms is extremely variable and to assess accurately the severity of illness it is necessary to consider the age, physique and probable power of response of the individual patient. The cases in the younger age group may appear to be mild on primary examination, but this apparent slight severity is probably the result of a poor power of response to the infection and it is in this group that the mortality is highest (pp. 25 and 58). It was found in practice that the most reliable index of severity was the frequency of the spasmodic cough.

Delayed Effects of Whooping Cough.

Although no attempt was made to follow up cases after dismissal from hospital, it is probable that chronic bronchitis, post-pneumonic fibrosis and bronchiectasis are common sequelae. This assumption is based on the morbid histology of the lungs in fatal pneumonic cases (page 78) and the high incidence of bronchitis and pneumonia in the

present series (page 56).

Pulmonary tuberculosis is said to be an occasional sequel of Whooping Cough, and this was borne out in the present series where 4 cases developed the complication.

SUMMARY.

(1) An attempt has been made to analyse the various factors in the Prognosis of Whooping Cough.

(2) Whooping Cough was commoner amongst the younger age groups.

(3) The mortality rate was higher in the younger age groups.

(4) There was no apparent relationship between the Sex and Mortality Rate.

(5) Bronchopneumonia, Enteritis, Malnutrition, Convulsions and Bronchitis were the most important factors influencing the prognosis.

(6) The younger children whose power of response is poor suffer most severely.

MORBID ANATOMY AND HISTOLOGY OF THE LUNGS IN WHOOPING COUGH.

All cases admitted were complicated by some condition other than Whooping Cough.

Cases 257. Deaths 66. Autopsy on 26.

Of the 257 cases the complications owing to which the patients were admitted were Bronchopneumonia, Bronchitis, Convulsions and Enteritis in younger children.

Of the 26 autopsies 20 died as a direct result of Bronchitis and Bronchopneumonia (Cases 1 - 20).

E. McK.	1	Convulsions (Case 21)	
E. M.	1	Myocardial failure (Case 22)	
M. B.	1	Enteritis (Case 23)	
W. W.)	2	Pulmonary Tuberculosis	(Case 24)
P. W.)			(Case 25)
H. K.	1	Acute Miliary "	(Case 26)

It will be noted that all the cases on which an autopsy was conducted had involvement of the respiratory system.

Cases 21 - 23 inclusive were cases in which bronchopneumonia had developed although this was not taken to be the precipitating cause of death.

Cases 1 - 26 when examined at autopsy showed the following affections of the pulmonary tract:-

23 cases of Bronchopneumonia (Cases 1 - 23) .

3 cases of Pulmonary Tuberculosis (Cases 24 - 26).

Lung sections from 22 cases were examined histologically and all stages of the disease were exemplified from those in which the changes were little more than those of bronchitis (Cases 7 and 21) to those in which the inflammation was widespread. Case No. 12 had to be omitted on account of damage to the specimens.

Cases of Bronchopneumonia.

In the 22 cases of bronchopneumonia examined histologically all stages of the disease were exemplified from those in which the histological changes were little more than those of bronchitis (Cases 7 and 21) to cases in which the

inflammation was widespread in the lung substance.

Especial attention must be directed to those cases in which the bronchopneumonia was the actual factor leading to a fatal termination.

Considerable difficulty has been experienced in classifying the series. Obviously the best classification would be to arrange them according to the duration of the bronchopneumonia. This, however, was impossible as in most instances the child was sent to Hospital because it already had bronchopneumonia and frequently no reliable history could be obtained from the parents as to the onset of the complication.

Another classification would have been to arrange the cases according to the period at which bronchopneumonia occurred in the course of Whooping Cough. This again was impossible for the same reason as given in the preceding paragraph.

A third method was to arrange the cases according to the age of the patient. Although the least satisfactory of the three methods indicated, this was the one which had to be adopted.

In all the cases of bronchopneumonia examined the wall of the bronchioles was inflamed as shown by cellular infiltration and dilation of blood vessels. The cells were mostly mononucleated; in 8 out of 20 cases there were in addition a certain number of polymorphonuclear leucocytes.

In the lumen of the bronchioles no exudate was present in cases 7, 9 and 23. These cases showed the earliest changes, and the condition in the lung was confined to the interstitial tissues of the organ.

In the remainder of the cases the contents of the bronchiole were those commonly found, namely descuamated epithelial cells, polymorphonuclear, mononucleated including "catarrhal" cells and in 3 cases a few red blood corpuscles.

In 17 of the cases of bronchopneumonia, infiltration by mononucleated cells of the interstitial tissues of

the pulmonary substance had occurred and in many of the cases this was the chief histological feature. Of the remaining 4 cases, in 3 the pneumonia was of the "septic" type (Cases 14, 17, 18) and in 1 (Case 20) it was of the "caseous" type.

This infiltration of the alveolar walls is one of the chief characteristics in the morbid histology of bronchopneumonia and has been emphasised especially by A. R. Macgregor, (53) 1929. The exudate within the pulmonary alveoli varied in its composition: in cases 3, 8, 9 and 10 it consisted of mononuclear cells, including "catarrhal" cells and polymorphonuclear leucocytes; in cases 5, 6 and 18 of "catarrhal" cells only; in case 11, of "catarrhal" cells and polymorphonuclears; in case 15 "catarrhal" cells, red blood corpuscles and polymorphonuclear leucocytes; in cases 16 and 20, polymorphonuclear leucocytes; in case 19 mononucleated cells and oedematous fluid; in case 22, mononucleated cells and a few polymorphonuclear leucocytes. In case 6 the exudate was undergoing caseous (non-tuberculous) change while in cases 13 and 14 septic foci (commencing abscesses) occurred.

Some authors, [e.g. A. R. Rich (30) 1932, Feyrter (54) 1927, Sauer and Hambrecht (55) 1929] have claimed that in cases of Whooping Cough developing bronchopneumonia the histology of the lungs presents certain specific features, and especially have they emphasised the mononuclear character of the cellular exudate in the walls of the bronchus and bronchioles and in the interalveolar septa. They have claimed further that these features are a strong indication that Whooping Cough is caused by a virus.

Whether the infecting agent in Whooping Cough is a virus or not, so far as the morbid histology is concerned the air passages and pulmonary substance show no changes other than those met with in primary bronchopneumonia.

Sections of the lungs of four representative cases (Cases 5, 6, 7 and 23) were submitted to Dr. A. R. Macgregor for her observation on this point. After studying the preparations, Dr. Macgregor confirmed the above statement. In

a personal communication on the subject she states:

"I do not think it can be said that there is anything really distinctive about them, which would not be found in other bronchopneumonias. Nor are all the cases quite similar in respect of outstanding histological changes. For example, in Case 7, and in Case 5, especially in the former, the really striking feature is the interstitial infiltration of the bronchial walls by inflammatory cells; whereas in Case 6 there is much more copious exudation into the alveoli and bronchi and much less interstitial infiltration. It seems to me that Case 6 shows a histological picture which might be found in any case of confluent bronchopneumonia. The picture in Case 5 I have seen many times in presumably "primary" bronchopneumonia in which the patches remain discrete, and sometimes in bronchopneumonia following measles. Case 7 I take to be an earlier stage of the same lesion, with alveolar exudation only just beginning; and Case 23 still earlier with hardly any exudation. The very profuse infiltration of bronchial walls which Cases 5 and 7 show, I have come to associate with cases from which Pfeiffer's bacillus can be isolated, usually accompanied by other micro-organisms such as pneumococcus. Whether these are influenza cases or true primary bronchopneumonia (as they often seem to be) I should not like to say; but anyway I an sure that this type of histological change occurs quite apart from Whooping Cough. It seems to me that a histological picture would have to be very distinctive indeed to justify a claim that it can be produced only by one specific micro-organism or virus; and I do not think the changes in these cases are nearly distinctive enough for that".

Another statement frequently found in the literature dealing with the histology of Whooping Cough is that the columnar epithelium lining the trachea and bronchial tree has not infrequently undergone metaplastic change into squamous epithelium. Here again the authors imply, if not definitely

suggest, that the process involved is characteristic of Whooping Cough.

The examination of the present series does not support the statement that epithelial metaplasia is common. In only two cases (5 and 8) was the epithelium flattened; in another case (4) the histological picture indicated that a metaplastic process of this nature had begun.

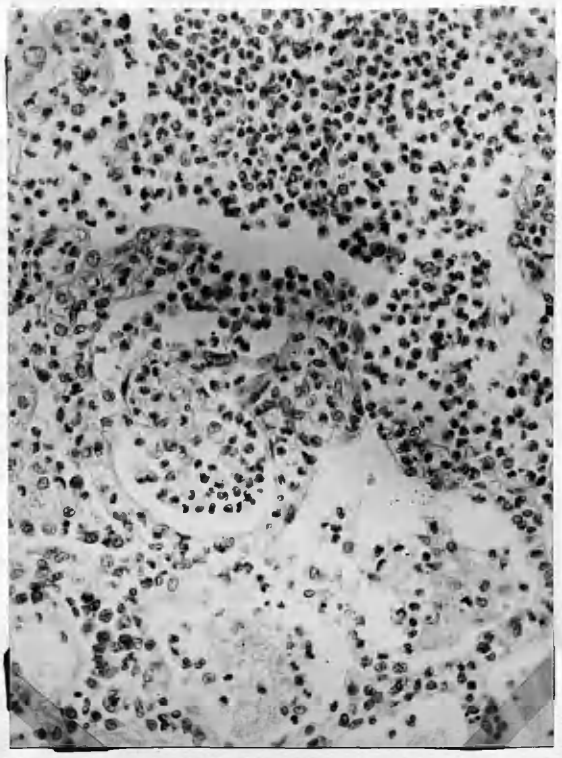
It must be remembered that by whatever cause bronchioles become partially occluded, the epithelium in the distal parts tends to become flattened and this change is best and most commonly met with in cases of bronchiectasis. Again, chronic irritation such as purulent sputum in contact with the columnar epithelium may cause a similar metaplastic change.

In the cases of epithelial metaplasia in this series, all had undergone a prolonged course. The histology of Case 5 showed that inflammation had produced profound changes in the walls of the bronchioles concerned. In Case 8 changes were found which showed that a chronic inflammatory process had been present. These two cases are exactly the type in which metaplasia of bronchial epithelium is not unexpected.

SUMMARY

The outstanding feature of the histological changes in the lungs was an interstitial infiltration by mononucleated cells. No evidence other than the interstitial reaction was found that might suggest the virus aetiology of Pertussis.

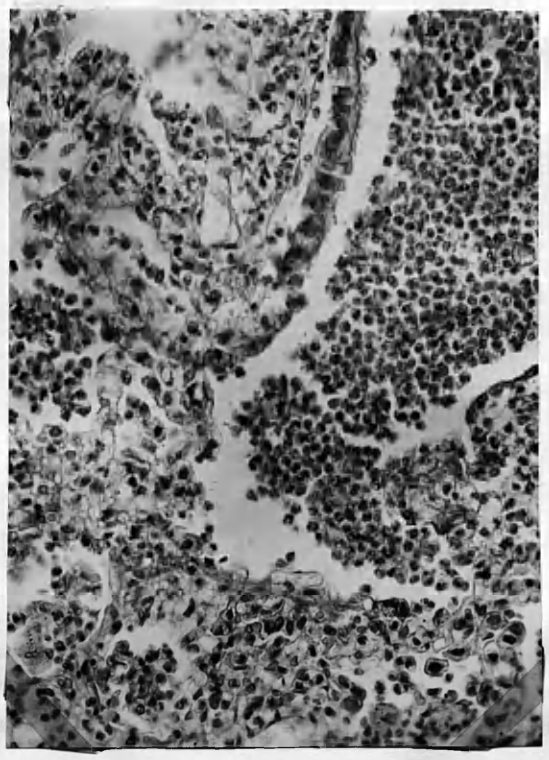
Case No. 1. N. McL. male. aet 1 year.



Section of Lung. Above, the exudate is composed for the most part of cells in various stages of disintegration; below, it is more fibrinous in character and haemorrhage has occurred into the alveoli.

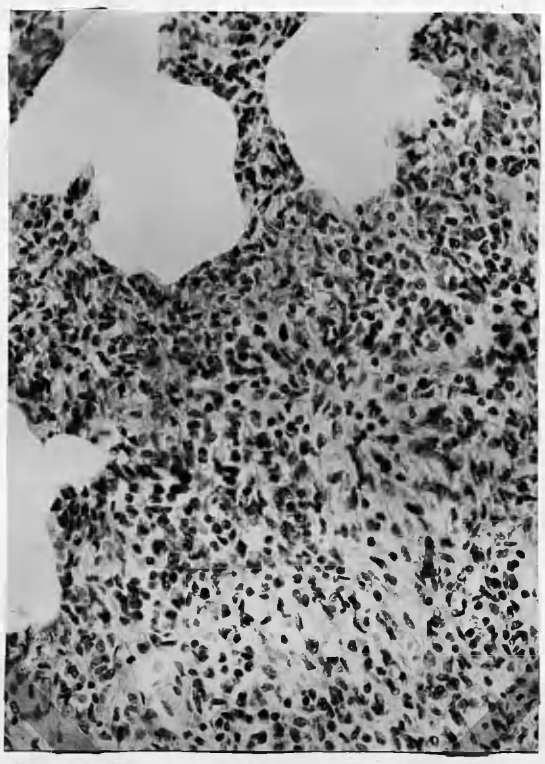
Preparation cut in paraffin and stained by haematin and eosin.

Case No. 2. M. O. aet. 14 months.



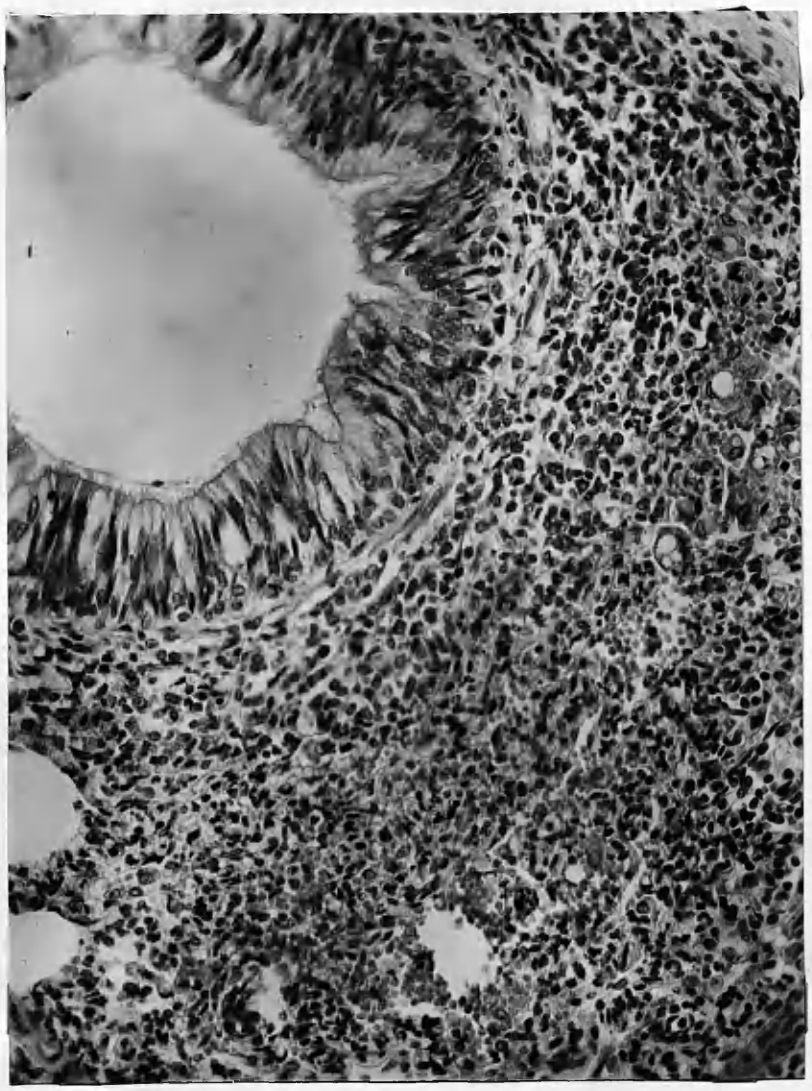
Section of Lung. The alveoli are filled with a cellular exudate; most of the cells are large and mononucleated in type. Exudate has also occurred into the wall of the bronchus and to some extent into the alveolar walls. Preparation cut in paraffin and stained by haematin and eosin.

Case No. 7. C. D. female. aet 6 months.



Section of Lung. Low power - Below and to the right, is a sharply delimited area in which the alveoli have been practically completely obliterated. From here, the infiltration consisting almost entirely of mononucleated cells, extends into the adjacent alveolar walls causing them to be much thickened. The capillaries have been compressed. Preparation cut in paraffin and stained by haematin and eosin.

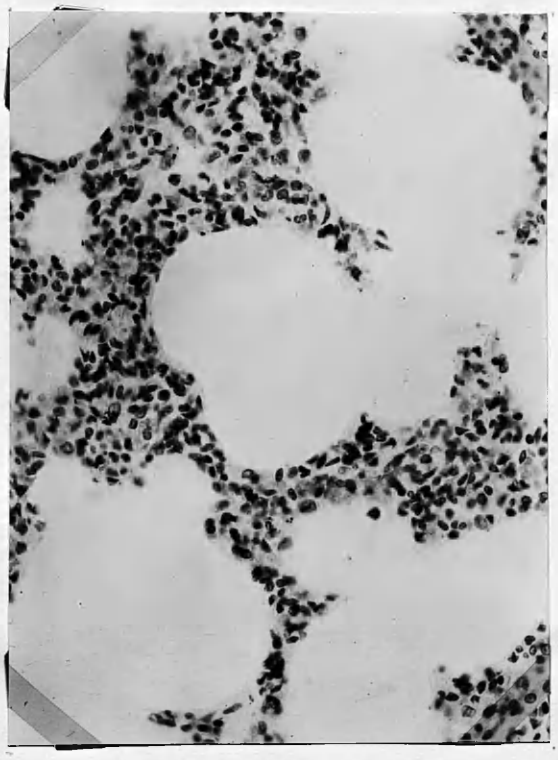
Case No. 7. C. D. female. aet 6 months.



Section of Lung. High power - The lumen of the bronchus is free and its columnar lining is intact. The bronchial wall is densely infiltrated by mononucleated cells. The exudate extends into the walls of the adjacent alveoli: they are so greatly thickened that the alveolar lumina are obliterated.

Preparation cut in paraffin and stained by haematin and eosin.

Case No. 23. M. B. female. aet 9 months.



Section of Lung. The alveolar walls are much thickened by a cellular exudate consisting of round and elongated mononucleated cells; the capillaries are compressed. The alveolar lumen contains no exudate.

The histological picture is typical of the interstitial type of pneumonia.

Preparation cut in paraffin and stained by haematin and eosin.

SUMMARY.

An investigation has been carried out on 458 cases involving the isolation of specific organisms by the cough plate method, examination of the blood serum for the complement fixation reaction and testing the patients for a specific skin response.

The clinical side of the work encompassed the consideration of conditions present prior to admission, conditions developing during the stay in hospital and also an analysis of the fatal cases.

Pertussis vaccines were used and an attempt made to evaluate their worth.

Prophylaxis of non-immune children and the vaccination of whooping cough contacts were investigated.

A special study of the morbid histology of the lungs was undertaken and an attempt made to correlate the clinical and pathological findings.

CONCLUSIONS

A series of 257 cases of Whooping Cough have been considered.

The majority of the cases were admitted in the paroxysmal stage and consequently the diagnosis was easily made as the classical signs and symptoms were almost constantly present.

Laboratory methods of diagnosis were carried out and it was found that the most satisfactory was the complement fixation reaction, whilst the intradermal tests proved quite valueless.

The cases treated came from the more densely populated parts of the city and this may partially explain the high incidence of respiratory complications. The other common complications were present in a considerable number of cases and were of importance in influencing the prognosis.

In order not to modify the effect of the Vaccine treatment, drugs were exhibited as infrequently as possible.

It was found that therapeutically vaccines were valueless in the later stages of the disease but there was some slight suggestion that they might prove of value in the earlier stages. It is felt that vaccines may prove of use prophylactically.

The prognosis was found to depend chiefly on the age and physique of the patient governed to a great extent by the presence of the severe complications such as the respiratory, alimentary and those resulting from toxaemia.

Histologically the findings were those of bronchopneumonia with no indication that might suggest a virus infection although a marked feature was the interstitial infiltration of the lungs by mononucleated cells.

I desire to acknowledge my indebtedness to Dr. A. S. M. Macgregor, Medical Officer of Health for the City of Glasgow and to Dr. Thomas Archibald, Superintendent of Belvidere Fever Hospital for permission to make use of the clinical material and for their advice and encouragement.

The complement-fixation tests and the examination of the Cough Plates were carried out in the Bacteriological Department of the Royal Infirmary, Glasgow under the supervision of Dr. Robert Cruickshank, lately Bacteriologist to the Royal Infirmary. The morbid histology was investigated at Stobhill Hospital, Glasgow under the supervision of Dr. F. E. Reynolds, Pathologist to the City of Glasgow Corporation Hospitals. Their assistance and kindly encouragement is gratefully acknowledged.

I am also indebted to Dr. W. G. Barnard, Pathologist to the London County Council, Archway Hospital, London for the micro-photographs shown in the text.

X - BIBLIOGRAPHY.

1. Watt, R., (1813) Treatise on the History, Nature and Treatment of Chincough, 22. Published by John Smith and Son, Glasgow; and Longman, Hurst, Rees, Orme and Brown, London.

1. - (1813) Ibid. 25.

2. Registrar General for Scotland., (1935) Eighty-first Annual Report, 79.

3. Registrar General for Great Britain excluding Ireland., (1929 - 1932 inclusive) Annual Returns.

4. Sauer, L. W. (1933) J. Amer. med. Ass. 101, 1451, footnote 4.

5. League of Nations Annual Epidemiological Report (1932), 29.

6. Bordet, J., and Gengou, O. (1906) Ann. Inst. Pasteur, 20, 731.

7. - - (1907) Ibid, 21, 721.

8. Frölich, J. (1897) Jb. Kinderheilk. 44, 53.

9. Chievitz, T., and Meyer, A. H. (1916) Ann. Inst. Pasteur, 29, 503.

10. Leslie, P. H., and Gardner, A. D. (1931) J. Hyg., Camb. 31, 423.

11. Siebler, S. K., and Okrent, S. (1934) J. Pediat. 4, 188.

4. Sauer, L. W. (1933) J. Amer. med. Ass. 101, 1449.

12. Paterson, D., Bailey, R. H., and Waller, R. G. (1935) Lancet, 2, 363.

13. - (1935) Ibid, 2, 1207.

14. Freeman, J. (1909) Brit. Med. J. 2, 1064.

15. Nicolle, C., and Connor, A. (1913) C. R. Acad. Sci., Paris, 156, 1849.

16. Hermann, C., and Bell, T. (1924) Arch. Pediat., 41, 13.

17. Bloom, C. J. (1925) Arch. Pediat., 42, 485.

18. Pierret, R. (1931 - 1932) Proc. Roy. Soc. Med., 1329.

19. Cockshut, R. W. (1933) Brit. med. J. 2, 819.

20. von Sholly, A. I., Blum, J., and Smith, L. (1917) J. Amer. med. Ass. 68, 1451.

21. Paterson, D., and Smellie, J. M. (1922) Brit. med. J. 1, 713.

22. Howell, N. G. (1930) The London County Council., Med. Officer of Health's Rep., 1V, part 111, 136.

23. Thompson, A. R. (1930) The London County Council., Med. Officer of Health's Rep., lV, part 111, 129.

24. Begg, N. D., and Coveney, M. F. (1936) Lancet, 1, 82.

25. Madsen, Th. (1933) J. Amer. med. Ass. 101, 188.

26. Sauer, L. W. (1933) J. Amer. med. Ass. 100, 239.

27. Frawley, J. M. (1934) J. Amer. med. Ass. 103, 960.

28. Sauer, L. W. (1937) J. Amer. med. Ass. 109, 488.

29. Macdonald, H., and Macdonald, E. J. (1933) J. infect. Dis. 53, 328.

30. Rich, A. R. (1932) Bull. Johns Hopk. Hosp. 51, 357.

31. Stocks, P., and Karn, M. N. (1932) J. Hyg., Camb. 32, 581.

9. Chievitz, T., and Meyer, A. H. (1916) Ann. Inst. Pasteur, 29, 503.

32. Sauer, L. W., and Hambrecht, L. (1930) J. Amer. med. Ass. 95, 263.

33. Kristensen, B. (1933) J. Amer. med. Ass. 101, 204.

34. Sauer, L. W., (1935) New Eng. J. Med. 213, 1061.

35. Bordet, J., and Gengou, O. (1907) Ann. Inst. Pasteur, 21, 721.

36. Friedlander, A., and Wagner, E. A. (1914) Amer. J. Dis. Child. 8, 134.

37. Madsen, T. (1925) Boston med. Surg. J. 192, 50.

38. Huenekens, E. J. (1917) Amer. J. Path. 14, 283.

39. Kristensen, M., and Larsen, S. A. (1926) C. R. Soc. Biol., Paris. 95, 1110.

29. Macdonald, H. and Macdonald, E. J. (1933) J. infect. Dis. 53, 328.

7. Bordet, J., and Gengou, O. (1907) Ann. Inst. Pasteur. 20, 731.

40. Shiga, K., Imai, N., and Eguchi, C. (1913) Cbl. Bakt., 1 abt., 69, 104.

41. Wollstein, M. (1909) J. exp. Med. 11, 41.

42. Povitsky, O. R., and Worth, E. (1916) Arch. intern. Med. 17, 279.

10. Leslie, P. H., and Gardner, A. D. (1931) J. Hyg., Camb. 31, 423.

43. McArdle, B. (1935) Lancet. 2, 454.

44. O'Brien, B. (1937) Ibid. 1, 131.

45. Thompson, A. R. (1938) J. Hyg., Camb. 38, 104.

46. Paton, J. P. J. (1937) Lancet. 1, 132.

47. Westwater, J. S. (1937) Ibid. 1, 290.

48. Churchill, F. S. (1906) J. Amer. med. Ass. 46, 1506.

49. Sauer, L. W., and Hambrecht, L. (1931) Amer. J. Dis. Child. 41, 1327.

50. Begg, N. D., and Coveney, M. F. (1935) Lancet 2,1113.

51. Bell, H. O., and Gold, A. E. (1936) Amer. J. Dis. Child. 52, 25.

19. Cockshut, R. W. (1933) Brit. med. J. 2, 819.

28. Sauer, L. W. (1937) J. Amer. med. Ass. 109, 488.

52. Sauer, L. W. (1933) J. Amer. med. Ass. 100, 239.

25. Madsen, T. (1933) J. Amer. med. Ass. 101, 188.

27. Frawley, J. M. (1934) J. Amer. med. Ass. 103, 960.

28. Sauer, L. W. (1937) J. Amer. med. Ass. 109, 488.

30. Rich, A. R. (1932) Bull. Johns Hopk. Hosp. 51, 346.

53. McNeil, C., Macgregor, A. R., and Alexander, W. A. (1929) Arch. Dis. Childh. 4, Nos. 19 - 23, 12.

54. Feyrter, F. (1927) Z. Path. 35, 213.

55. Sauer, L. W., and Hambrecht, L. (1929) Arch. Path. 8, 944.

A P P E N D I X

THESIS FOR DEGREE OF M.D.

W H O O P I N G C O U G H.

"A Laboratory and Clinical Investigation

with special reference to the value of Vaccine Therapy".

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JOHN PAUL JONES PATON M.B., Ch.B.

Index to Appendix.

1. Isolation of Bacillus Pertussis by the Cough Plate Method.

(1) The success of this procedure depends upon

(a) The use of appropriate medium carefully prepared and plated.

(b) The proper exposure of the plates which involves the close co-operation of the nursing staff.

(c) Careful examination of the plates after incubation

(2) The Medium.

Preparation of Bordet Gengou Medium.

Clean and pare potatoes and cut into thin slices.

Add 250 grams slices to 500 cc. tap water and 9 grams NaCl.

Boil till potato slices fall to pieces.

Make up water lost in boiling.

Filter through linen.

Adjust reaction to pH 7.0.

To 1,500 cc. tap water add 60 grams B.D.H. agar powder (to give final 3%).

Dissolve.

Add 500 cc. of the potato extract 20 cc. glycerine and 1% Proteose peptone 'DIFCO' - B. and T.

Distribute in flasks.

Autoclave. (Free steam for 1 hour and run up to 5 lbs). Store till required.

Melt in Steamer for 1 hour, then invert several times.

Place in water bath at 55°C. for 5 minutes until agar has dropped to approximately 70°C.

Stand defibrinated horse blood in 55°C. bath for 2 - 3 minutes to take chill off.

Add 1 part of blood to 2 parts glycerine-potato agar.

Mix thoroughly and pour plates.

NOTE. Plates should not be dried in the incubator but are stored in the cold room and may be used up to 2 weeks after preparation.

(3) The Exposure of the Plate.

Two plates of the Bordet Gengou medium should be used as one plate of a pair may be positive and the other negative. The plates are held 3 - 4 inches in front of the patient's mouth, and exposed during a paroxysm of natural or induced coughing. For infants under one year a long exposure is required (20 - 30 coughs), for older children a short exposure (6 - 10 coughs) is necessary.

(4) The Identification of the Organism.

The plates are incubated and examined on the second and third days. Typical colonies, which are minute raised pearly or mercury-drop in appearance, may sometimes be recognised on the second, more often on the third day, and are picked off on to slopes or plates of Bordet Gengou medium. A Gram-stained film shows small ovoid Gram-negative bacilli of uniform size and often a characteristic thumb print distribution. The subculture is tested for slide-agglutination after 24 - 48 hours, and later is tested to titre for its agglutinability.

2. Technique of the Complement-Fixation Test.

The antigen used in the majority of the Complement-Fixation tests was the St. Mary's Hospital prophylactic A vaccine issued by Parke, Davis and Co. in a concentration of 4,000 million whole B.pertussis per c.cm. This vaccine is stated to be prepared from smooth strains of B.pertussis. It was found that a dilution of 1 : 5 of this antigen had practically no anticomplementary effect.

In the test proper 0.25 c.cm. of the diluted antigen was added to each of the 4 test-tubes. To each of these, and to a fifth serum control tube containing 0.25 c.cm. of normal saline, the patient's serum was added in amounts which varied from 0.05 c.cm. in the first series of cases to 0.2 c.cm. of serum from the later batches of sera, this latter amount of serum having been considered to be the optimum amount for the test. The complement dose of fresh guinea-pig's serum was estimated for 0.5 c.cm. of sensitised sheep cells (3 per cent.) and 2, 3, 5 and 7 doses of complement were added to tubes

1, 2, 3 and 4 and two doses to the fifth serum control tube. In the later complement-fixation tests the fourth test-tube, containing 7 doses of complement was omitted. The test-tubes and their contents were incubated for 1¼ hours at 37°C. after which 0.25 c.cm. of sensitised sheep cells (3 per cent.) was added, incubation being carried out for a further hour at 37°C. In each batch of complement-fixation tests, serum and antigen controls were put up, and a positive human or rabbit serum was included in the tests.

In order to test the antigenic efficacy of the various vaccines a rabbit was given intravenous injections of the St. Mary's vaccine and complement-fixation tests were done in the usual way, using St. Mary's vaccine, Madsen's Danish vaccine and Sauer's vaccine. All the vaccines fixed complement satisfactorily, best results being given with the Sauer's vaccine.

3. Technique of the Intradermal Test.

The following vaccines were used for the skin test:

(1) Sauer's pertussis vaccine containing 10,000 million organisms per c.cm.

(2) Whooping-cough dissolved vaccine containing the dissolved constituents of 4,000 million or 8,000 million organisms per c.cm., prepared by the Glaxo Laboratories Ltd.

(3) Whooping-cough vaccine (prophylactic A) containing 4,000 million organisms per c.cm., prepared by the Inoculation Department, St. Mary's Hospital (issued by Parke, Davis and Co.).

(4) Kreuger's bacterial antigen prepared by mechanical disruption of masses of B. pertussis, 1 c.cm. of the endenatured antigen being roughly equivalent to 10 billion bacilli.

All of these vaccines consist of whooping-cough bacilli alone, either in the intact state (e.g. Sauer's and St. Mary's vaccine), mechanically disrupted (e.g. Kreuger's vaccine), or chemically dissolved (e.g. Glaxo vaccine). None of the vaccines used were in a dilution lower than 4,000 million organisms per c.cm.

In each case 0.1 c.cm. of the vaccine was injected

intradermally on the flexor aspect of the forearm, the proper antigen control being used for each different type of vaccine, except in one case where Kreuger's vaccine was used without a control. The readings were taken when the reaction were at their height, usually 18 hours after the test had been done. Later readings were also taken, but these were invariably found to be less intense than the 18-hour readings.

A skin reaction was considered positive when the area of redness was 1 cm. or more in its longest diameter, the control test being negative. There is usually an area of induration which may or may not be more than 1 cm. across in each skin test if it is positive: this indurated area when present is both visible and palpable.

4. Preparation for Injection of Vaccines.

Surgical cleanliness was obtained by scrubbing the hands with soap under running hot water and they were then dipped in succession into Dettol, and then saline, drying being affected by means of a sterile towel.

Syringes and Needles.

The syringes used are as described below:-

(A) This syringe consisted of a long thin glass barrel reinforced by steel guards at the inflow and outflow and graduated in 1/100ths of a c.cm. The plunger and ferrule were of steel. The needles used were dental needles and consisted of a stylar portion with a soft metal head. The needle was inserted into the metal container consisting of two parts which were then screwed together making a water tight junction. The advantage of this type of needle was that the needle portion could be discarded and replaced by another sharp needle portion very quickly.

(B) An ordinary 10 cc. record syringe, care being taken to use sharp and thin needles.

The needles and syringes were sterilised by boiling for 20 minutes prior to use, and thereafter placed in normal saline.

Vaccine Bottles.

The vaccine containers consisted of rubber cap

bottles containing from 2 cc. to 25 cc. of vaccine. If wax were present on the cap it was passed through a spirit flame and when cooled rubbed with a swab soaked in surgical spirit. The cap was then rubbed with a sterile swab moistened in sterile saline and then dried, the cap then being pierced with the needle and the requisite amount of vaccine removed.

Preparation of Skin.

The skin over the site chosen for injection was swabbed with surgical spirit and after drying the part was painted over with sub-tincture of iodine.

TABLE I

Glasgow, 1931-35; Whooping Cough - Number of Cases intimated; Number removed to Hospital; and Number of Deaths registered.

Year	Number of Cases intimated	Cases intimated per Million of Population.	Number of Cases removed to Hospital	Number of Deaths	Deaths per Million of Population
1931	9,219	8,470	890	464	426
1932	4,666	4,260	337	128	117
1933	6,441	5,838	557	227	206
1934	5,936	5,321	494	176	158
1935	7,773	6,918	705	277	247

Public Health Department,
GLASGOW:
10th February, 1938.

TABLE II

Glasgow, 1931-35: Whooping Cough - Number of Cases intimated in each Month.

Month	1931	1932	1933	1934	1935
January	2,020	188	1,457	260	1,989
February	1,711	229	1,099	257	1,346
March	1,639	191	1,032	347	1,434
April	1,273	313	935	479	907
May	809	273	777	558	1,056
June	565	257	411	484	408
July	102	75	80	117	100
August	424	437	238	736	222
September	200	301	96	386	120
October	180	521	80	502	60
November	161	919	134	843	57
December	135	962	102	967	74
Total	9,219	4,666	6,441	5,936	7,773

Public Health Department, GLASGOW:
10th February, 1938.

TABLE III

Glasgow, 1931-35: Whooping Cough - Deaths registered, according to Age and Sex.

Age	1931	1932	1933	1934	1935
Males:					
-1 year	117	25	55	34	65
-2 years	69	21	38	30	46
-5 "	32	13	9	17	18
-10 "	1	-	1	1	2
-15 "	-	-	-	-	-
15- "	-	-	1	-	-
	219	59	104	82	131
Females:					
-1 year	110	22	62	35	68
-2 years	85	25	41	32	51
-5 "	46	21	20	26	21
-10 "	4	1	-	1	6
-15 "	-	-	-	-	-
15- "	-	-	-	-	-
	245	69	123	94	146
Both Sexes:					
-1 year	227	47	117	69	133
-2 years	154	46	79	62	97
-5 "	78	34	29	43	39
-10 "	5	1	1	2	8
-15 "	-	-	-	-	-
15- "	-	-	1	-	-
	464	128	227	176	277

10th February, 1938.

TABLE IV

Glasgow, 1931-35: Whooping Cough - Number of Cases dismissed from Fever Hospitals; Number of Deaths among these; and Case Mortality per cent.

Age	1931			1932			1933			1934			1935			1931-35 (combined)		
	Cases	Deaths	Case Mortality %	Cases	Deaths	Case Mortality %	Cases	Deaths	Case Mortality %	Cases	Deaths	Case Mortality %	Cases	Deaths	Case Mortality %	Cases	Deaths	Case Mortality %
Males:																		
-1 year	122	59	48	18	7	39	70	33	47	43	20	55	117	54	46	370	173	47
-2 years	116	46	40	42	17	41	75	20	27	52	18	35	115	33	29	400	134	33
-3 "	78	15	19	14	5	36	45	5	11	27	4	15	53	6	11	217	35	16
-4 "	50	8	16	14	2	14	26	1	4	14	5	36	47	4	9	151	20	13
-5 "	32	4	12	5	-	-	33	2	6	14	3	21	32	2	6	116	11	9
-10 "	37	1	3	6	-	-	28	1	4	16	1	6	36	2	6	123	5	4
-15 "	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-
15- "	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	436	133	31	99	31	31	277	62	22	166	51	31	400	101	25	1,378	378	27
Females:																		
-1 year	114	50	44	28	10	36	91	40	43	38	17	45	115	45	39	386	162	42
-2 years	134	58	43	36	11	31	102	34	33	40	16	40	118	35	30	430	154	36
-3 "	74	15	20	33	9	27	55	5	9	29	6	21	77	11	14	268	46	17
-4 "	65	8	12	10	3	30	47	5	11	29	7	24	54	3	6	205	26	13
-5 "	32	4	12	11	1	9	28	1	4	11	2	18	26	4	15	108	12	11
-10 "	54	3	6	21	1	5	29	-	-	19	1	5	41	4	10	164	9	5
-15 "	-	-	-	-	-	-	1	-	-	-	-	-	1	-	-	2	-	-
15- "	2	-	-	-	-	-	3	-	-	2	-	-	1	-	-	8	-	-
	475	138	29	139	35	25	356	85	24	168	49	29	433	102	24	1,569	409	26

Age	1931			1932			1933			1934			1935			1931-35 (combined)		
	Cases	Deaths	Case Mort-ality	Cases	Deaths	Case Mort-ality	Cases	Deaths	Case Mort-ality	Cases	Deaths	Case Mort-ality	Cases	Deaths	Case Mort-ality	Cases	Deaths	Case Mort-ality
			%			%			%			%			%			%
Both Sexes																		
-1 year	236	109	46	46	17	37	161	73	45	81	37	45	232	99	43	756	335	44
-2 years	250	104	42	78	28	36	177	54	31	92	34	37	233	68	29	830	288	35
-3 "	152	30	20	47	14	30	100	10	10	56	10	18	130	17	13	485	81	17
-4 "	115	16	14	24	5	21	73	6	8	43	12	28	101	7	7	356	46	13
-5 "	64	8	12	16	1	6	61	3	5	25	5	20	58	6	10	224	23	10
-10 "	91	4	4	27	1	4	57	1	2	35	2	6	77	6	8	287	14	5
-15 "	1	-	-	-	-	-	1	-	-	-	-	-	1	-	-	3	-	-
15- "	2	-	-	-	-	-	3	-	-	2	-	-	1	-	-	8	-	-
	911	271	30	238	66	28	633	147	23	334	100	30	833	203	24	2,949	787	27

Public Health Department,
GLASGOW:
10th February, 1938.
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6. CLINICAL AND PATHOLOGICAL NOTES ON 26 FATAL CASES.

Case No. 1.

Name. N. McL. Male. Aet 1 year.

General Conditions.

The child lived in a 1 apartment house along with 2 adults and other 3 children. There was no history of the patient having had any previous infectious disease. He had not been vaccinated.

Clinical Course.

On 16th April, 1935 the patient became ill with a spasmodic cough; on the 22nd April he was first heard to whoop.

On 4th May in the afternoon the child was admitted to hospital. The temperature was 100.8 F., pulse rate 152 and respiration rate 60.

He was a moderately well nourished boy who had a cough of the spasmodic type; this was followed by whooping. The face was puffy; a mild conjunctivitis and a serous rhinitis were present.

The tongue was lightly coated; there was a small ulcer on the fraenum; the faucial structures were congested; the stools were normal; examination of the abdomen was negative. The appetite was fairly good.

There was no definite impairment of percussion note over the chest. The respiratory murmur over both lungs was harsh vesicular and occasional fine râles were heard. The sputum was tenacious and mucoid in character. The superficial area of cardiac dullness was not increased and the heart sounds were pure and of good tone. The pulse was of good volume.

Progress.

Throughout the illness the face remained puffy.

On 10th May, the patient began to pass green-coloured stools and this occurred intermittently up to the date of death.

From 10th May a slight degree of progressive wasting was noticed. The pulse rate was now over 160 and its volume

poor. The superficial area of cardiac dullness was not increased but the heart sounds were of poor quality.

On 11th May the child was obviously very ill. The percussion note over the base of the right lung was impaired; the breath sounds were broncho-vesicular in type and accompanied by fine râles. The temperature had risen to 101.8 F.

On 17th May similar signs were elicited over the base of the left lung. The temperature had been of the irregularly intermittent type.

On 20th May, twitching of the face and arms occurred.

On 21st May the patient died.

Report of Autopsy.

Post-mortem performed 27 hours after death.

The body was that of a moderately well nourished child.

The mucous membrane of the trachea and bronchi were injected; the tracheo-bronchial lymphatic glands were enlarged. The lower $\frac{3}{4}$ of the left lung and the lower lobe of the right lung were consolidated and multiple small abscess cavities were present in its substance.

The heart was not enlarged; the cusps showed no deviation from the normal and the valves were competent.

The liver which was not enlarged was brownish in colour with dark red arborescent mottling.

The bowel was thin and atrophic. The mesenteric glands were enlarged.

Microscopical Examination.

Larynx and Trachea.

No change in the type of epithelium had occurred. The columnar epithelial cells retained their cilia. In the region of the vocal cords, the subepithelial connective tissue was densely infiltrated by smaller and larger mono-nucleated cells.

Lungs.

In the solid portions of the lungs the consolidation was not uniform in character nor were these portions sharply

demarcated. The alveoli were filled with an exudate which in places was composed largely of cells in various stages of disintegration.

In other places the exudate was fibrinous; again, small areas occurred in which haemorrhage had taken place into the alveolar space. For the most part throughout the solid areas the interalveolar capillaries were dilated; many of the smaller bronchi were lined by epithelium which was distinctly flat in type resembling cuboidal cells. There was infiltration of the bronchi and bronchioles with mononuclear and polymorphonuclear cells but this was not a marked feature.

Mediastinal Glands.

Proliferation of the lymphoid elements had occurred. The blood vessels were engorged and the lymph sinuses especially towards the periphery were dilated.

Heart.

In frozen sections treated by Scharlach R. no fat was present in the cardiac muscle fibres.

Liver.

The parenchymal cells were swollen and were encroaching on the lumen of the blood sinusoids. Throughout the lobule but particularly throughout the inner zone larger and smaller globules occurred throughout the liver cells.

In sections stained for fat a moderate amount was demonstrated in the inner zones of the lobules.

Spleen.

The blood sinuses were dilated and congested.

Kidney.

No changes had occurred in the glomeruli; there was a small amount of swelling of the cells lining the convoluted tubules and their cytoplasm showed increased granularity.

Commentary.

The case was an example of confluent bronchopneumonia, the exudate having occurred into the alveolar spaces. Interstitial changes were present, but these were not very marked.

Case No. 2.

Name. M. O. Female. Aet. 14 months.

General Conditions.

The patient came from a 1 apartment house and the family consisted of 2 parents and their 4 children.

There was no history of any previous infectious disease.

Clinical Course.

On 26th June, 1935 the patient was heard to whoop by her parents.

On 5th July, in the evening, the patient was admitted to Hospital. The temperature was 97.4 F., pulse rate 176 and respiration rate 38.

The child was well nourished but was listless. She had a barrel shaped chest with prominent costal cartilages. She had a nasal discharge, serous in character; the tongue was coated; the tonsils were enlarged and congested; the fauces were congested; a spasmodic cough and whoop was present.

The child was cutting teeth. Examination of the abdomen was negative. The heart was within normal limits, the sounds were pure and of moderately good quality; the pulse was of quite good volume and its rhythm was regular. The percussion note at the right pulmonary base was slightly impaired and there was bronchial breathing with occasional fine râles. The sputum was mucopurulent and tenacious. The child had green diarrhoea, and this condition persisted until death.

On 6th July, the temperature had risen to 99.8 F, the pulse rate was 160 beats per minute and the respiration rate 58.

On 9th July the appetite, which hitherto had been good, became poor and remained so until death. No vomiting occurred during the patient's stay in hospital.

Bacteriological examination of the urine revealed numerous B.coli and a few pus cells.

On 5th July the patient developed twitchings of the

face; these continued intermittently for 3 days.

By 16th July the patient had become very emaciated and pallid; listlessness persisted and the fever was of the remittent type. The pulse rate varied between 160 - 170 but the rhythm continued to be regular; the volume had been poor for some days. The respiration rate was usually about 160 or over. The urine was now clear.

On 15th July the physical signs of pneumonia were still present at the right base and the left base was now involved.

On 19th July death occurred.

The patient was heard to whoop once on 6th, twice on 10th and twice on 11th July; spasmodic coughing was present throughout the illness but was not followed by vomiting.

Report of Autopsy.

The body was emaciated. The chest was barrel shaped and the costal cartilages were enlarged.

Chest.

The pericardial sac contained some excess of fluid. The heart muscle was pale in colour and although the organ appeared to be large for a child of that age, the valves were competent; there was no apparent abnormality of the cusps. The thymus gland appeared to be large considering the age of the child. Near the hilum of the right lung at the posterior aspect of the middle lobe a few organised pleural adhesions were found. The lower and middle lobes of the right lung and the lower lobe of the left lung were consolidated. On section of these lobes small greyish areas were visible scattered throughout each lobe. The tracheo-bronchial glands were enlarged. Mucopurulent material was expressed from the cut ends of the bronchi. The larynx and trachea were congested.

Abdomen.

The liver was not enlarged and appeared somewhat pale. The spleen was not enlarged but was dark in colour. The kidneys were pale in colour.

Microscopical Examination.

Larynx and Trachea.

The larynx and that portion of the trachea immediately adjacent were lined by squamous epithelium. Below, the trachea was lined by columnar epithelium; the cilia persisted in the preparations. The interstitial tissue between the acini of some of the groups of mucus secreting glands were densely infiltrated by mononucleated cells.

Lungs.

Sections taken from the consolidated portions of the lung showed areas in which the alveoli were almost completely filled by large mononucleated cells together with a certain number of polymorphonuclear leucocytes. There was also collapse of alveoli furthest from the bronchioles. In other areas the exudate into the alveoli was not so copious and consisted almost entirely of large mononucleated cells: the cytoplasm of these was granular and vacuolated and they had ingested red blood cells and particles of debris. In those portions of the lung which did not show massive consolidation the walls of the bronchioles were thickened and infiltrated by cells; in the pulmonary substance especially in those portions related to bronchioles a cellular exudate had occurred into the alveolar walls, causing them to be greatly thickened. There was a tendency, however, for the exudate to occur in the alveolar spaces.

Lymphatic Glands.

Tracheal Lymphatic Gland.

The blood vessels were dilated and in one portion there was a small haemorrhage. The lymph sinuses were much dilated and in their lumen were numerous large mononucleated cells.

Liver.

The parenchymal cells were much vacuolated; the vacuoles in many of the cells being large.

Spleen.

The blood sinuses were much congested and in places considerable endothelial hyperplasia had occurred into the

lumen.

Kidney.

The cells lining the convoluted tubules were swollen and their cytoplasm was coarsely granular.

Commentary.

The extent of the squamous epithelium in the larynx was not pathological due to metaplasia but was an anatomical variation. The case was an example of bronchopneumonia in the lower lobes of both lungs with secondary collapse and alveolar catarrh producing an appearance of lobar consolidation. In other portions of the lung the typical cellular infiltration of the bronchial wall with extension into the alveolar wall had occurred. The extreme vacuolation of the liver was due to fatty change.

Case No. 3.

Name S.C. Female Aet 8 weeks.

Clinical Course.

On 17th July, the patient became ill with spasmodic coughing followed by vomiting; on this day she was heard to whoop. She had not been vaccinated and had had no previous infectious disease. On 22nd July, the patient was sent to Hospital as a case of Whooping Cough with pulmonary congestion.

On admission the child was well nourished but listless and the face was puffy. The temperature was 98, pulse 160 and respirations 60. The tongue was clean but the fauces were congested. There was no impairment of the percussion note over the lungs but over both bases the respiratory murmur was bronchial in character and numerous fine râles were heard. Spasmodic coughing was present, the sputum was scanty in amount and of a tenacious, muco-purulent character. Examination of the abdomen was negative but the stools were green in colour.

The heart sounds were pure and of moderately good quality; volume of the pulse was good.

On 23rd July, the child's appetite was good but the spasmodic cough caused her to vomit.

On 24th July, a patchy consolidation with bronchial breathing and numerous fine râles had developed at the bases of both lungs; the temperature was remittent; the pulse was about 160 and of poor volume; respiration rate remained about 60. Vomiting had ceased. On 25th July, the child developed a serous conjunctivitis. On 28th July, the patient died.

During the whole time in Hospital the stools were green in colour and during the last few days before death the appetite had been poor and the baby had become progressively emaciated.

Autopsy.

The body was poorly nourished and dehydrated.

The thymus was within the normal limits for size.

No excess of fluid was found in any of the serous sacs. The cardiac muscle was pale; the valves were competent but the mitral cusps were bright red in colour.

The mucous membrane lining the larynx and trachea was injected. In the middle and lower lobes of the right lung and in the lower lobe of the left lung in relation to small bronchi were patches of consolidation and purulent material could be expressed from the cut ends of the smaller bronchi; general pulmonary oedema was present.

The tracheo-bronchial lymphatic glands were enlarged and a certain degree of enlargement was present in the abdominal lymphatic glands.

The liver, spleen and kidneys were dark in colour.

Microscopical Examination.

Mitral Cusp.

In areas of one surface of the cusp the lining endothelium was thickened and, in part, had been lost; at a short distance deep to this the fibres of the cusp itself were swollen and stained deeply with eosin.

Larynx and Trachea.

No metaplastic change had occurred in the epithelium lining these upper air passages.

Lungs.

Comparatively large areas of lung substance had collapsed these being in relation to neighbouring bronchioles. Elsewhere and especially extending from the collapsed areas the alveolar walls were widened owing to a cellular exudate. In the collapsed portions the capillaries were dilated and many of the smaller bronchioles showed to a marked degree narrowing of the lumen; but the columnar lining cells still persisted: they contained a muco-cellular secretion. Areas of polymorphonuclear leucocytes were present and here the lung tissue was breaking down (early abscess formation). In parts more distal to the collapsed areas emphysema was present and a cellular exudate was seen around the bronchioles.

Mediastinal Lymphatic Gland.

The lymph sinuses were dilated and contained numerous large rounded cells. The blood capillaries were also dilated.

Liver.

The hepatic parenchymal cells were much swollen and had largely obliterated the blood sinusoids; their cytoplasm was coarsely granular but vacuolation had not occurred.

Spleen.

The blood sinuses were dilated and there was consequent diminution in the size of the Malpighian bodies. In the sinuses were many cells containing blood pigment.

Kidney.

The venae rectae were congested and the cells lining the convoluted tubules were swollen and their cytoplasm was coarsely granular.

Commentary.

The explanation of the bright red colour of the mitral cusps presented some difficulty. Possibly it was due to a commencing endocarditis; this view was supported by the localised areas of infection (commencing abscesses) in the lungs. On microscopical examination the absence of the thin layer of blood clot could be accounted for by it having become detached during subsequent manipulation. Although an interstitial pneumonia was present, the most noteworthy feature in this case was the collapse of the lung substance. This may have been due to the rapidly progressing debility which occurred in the patient, a baby only 8 weeks old. Again, the plugging by mucoid secretion of the bronchi related to the collapsed portion of the lung although not a marked feature, may have been a contributing factor.

Death occurred from a combination of enteritis and bronchopneumonia.

Case No. 4.

Name D.M. Male. Aet 4 months.

General Conditions.

The patient lived in a one apartment house along with two adults and four other children.

Clinical History.

On 15th December, 1935, the patient became ill with a spasmodic cough. The temperature was 98.6 F. the pulse rate 160 and the respiration rate 44. There was no history of any previous infectious disease.

On 23rd January, 1935, the patient was admitted to Hospital. The child was pale, listless and emaciated; he had a spasmodic cough but no whoop. The face was puffy; a chronic bilateral blepharitis of the upper eyelids was present; the tongue was moist and clean; the faucial structures were injected; there was no fraenal ulcer of the tongue. Abdominal examination revealed no abnormality.

The percussion note over the chest was not impaired. The respiratory murmur at both pulmonary bases posteriorly was bronchial in character and was accompanied by numerous fine râles. The size of the heart was within the normal limits and the sounds were pure but of poor quality. The volume of the pulse was poor. The urine did not show any abnormal constituents.

Progress.

On 24th January, it was noticed that the child was passing green coloured stools; these continued for a week but returned on 12th February and persisted until death.

During the first few days after admission to hospital the temperature varied from subnormal to 100 F. and the pulse and respirations increased, the latter being about 60; the rises in temperature appeared to be associated with the frequency in the passage of green stools.

On 29th January, the temperature, pulse and respiration rate subsided to normal and thereafter no increase occurred.

Throughout the time in Hospital the condition of the chest as ascertained by physical examination remained the same. During the last 2 weeks of life emaciation was progressive and marked.

On 14th February, the patient died.

Report of Autopsy.

Performed 14th February, 1935, 5 hours after death.

The body was very emaciated.

The heart was small and the cardiac muscle was brownish in colour; there was no abnormality of the valves or cusps.

The lungs showed small patches of consolidation; these were not in relation to the bronchi. The tracheo-bronchial glands were not enlarged and the thymus was normal for the child's age and size. The bowel wall was thin and atrophic.

The kidneys, liver and spleen were not enlarged but were deeply congested.

Microscopical Examination.

Lungs.

Sections were taken from three representative portions of lung. In each instance the cells lining the bronchioles were for the most part columnar in type; in a few cases the bronchioles had to a large extent collapsed and in these the lining was tending to be flattened in type; much of it was undergoing necrobiotic change and the lumen which remained was largely filled by desquamated epithelial cells. In this series of sections there were patches in which the alveoli were filled by an exudate consisting of smaller and larger mononucleated cells together with a fair number of polymorphonuclear leucocytes. In other portions small areas of collapse were present. In other portions again the alveolar walls were greatly thickened by a fluid and cellular exudate; considerable emphysema existed.

In sections from another portion of the lung, collapse

was complete and in consequence the bronchioles were numerous and approximated to each other.

In the third series of sections considerable interstitial exudate had occurred in patches; in this portion of the lung emphysema was a marked character. The walls of the bronchioles were thickened owing to an exudate, the cells of which were mononucleated and the alveoli in the immediate neighbourhood contained a cellular exudate.

Kidney.

The cells lining the convoluted tubules were swollen and almost completely filled the lumen; their cytoplasm was coarsely granular.

Spleen.

Great proliferation of the endothelial elements had occurred. Only a small amount of blood was present in the blood sinuses.

Mediastinal Lymphatic Gland.

The architecture of the gland was maintained but the lymph sinuses were dilated and contained numerous large round mononucleated cells.

Brain.

Sections from the cerebral hemisphere, pons and medulla showed no changes of pathological importance.

Case No. 5.

Name. M. T. Female. Aet 4 months.

Clinical Course.

On 1st February, the child began to suffer from spasms of coughing followed by vomiting; there was no history of any previous infectious disease. She lived in a one apartment house with her father and mother.

On 28th February, she began to whoop. On 20th March she was sent to hospital as a case of Whooping Cough and bronchopneumonia.

When admitted in the evening, the temperature was 100.4 F., pulse rate 160 and respiration rate 60. She was pale, listless, poorly nourished and was obviously seriously ill. The tongue was furred and the fauces congested. Nowhere over the lungs was the percussion note impaired but the respiratory murmur was bronchial and accompanied by numerous fine râles. The cardiac sounds were pure but of poor tone.

23rd March - Since admission the appetite had been fairly good, the patient had slept well but had been troubled by a spasmodic cough which now was followed by vomiting although hitherto this had not occurred.

On 1st April, the stools were green in colour.

4th April - the temperature, pulse and respirations were beginning to return to normal but physical signs of bronchitis were present.

13th April - the tongue had been clean for the past few days and by this date the inflammation of the fauces had disappeared. Further, the stools had become normal in colour.

29th April - the child developed diarrhoea, the stools again being green in colour. She started again to vomit; on 14th May the patient died.

The stools had remained frequent and green in colour. During the past fortnight the child had become marasmic and dehydrated.

Autopsy.

The body was greatly emaciated; the chest was barrel-shaped. The heart was not enlarged and the cardiac muscle was dark in colour. No lesion was present in the valves or their cusps.

The whole of the right lung and the lower lobe of the left lung presented areas of consolidation; in many instances the areas were definitely related to smaller bronchi.

The lymphatic glands at the roots of the lungs were enlarged.

The liver, spleen and kidneys were congested.

The wall of the intestine was thin and atrophic.

Microscopical Examination.

Larynx and Trachea.

The mucous membrane covering these portions of the upper air passages was lined by flattened epithelium; no keratinisation had occurred. The subepithelial layers of connective tissue were distinctly infiltrated by small round mononucleated cells.

Lungs.

The lining of some of the bronchioles was distinctly columnar; in others it was cuboidal in type while in others again it was so flattened as to approach the squamous type. In a few of the bronchioles the lining had completely desquamated. The walls of many of these bronchioles in which the lining epithelium had become cuboidal were much thickened by fibrous tissue and they were rather sparsely infiltrated by mononucleated cells.

Areas of lung occurred which were entirely solid owing to the alveoli having been completely filled by a cellular exudate which consisted mostly of larger and smaller mononucleated cells; round these areas the walls of the alveoli were diffusely and irregularly thickened by cellular exudate, but on the other hand the alveolar walls in numerous instances were thin, stretched and had broken through. Here and there towards the periphery of the consolidated portions

collections of small round mononucleated cells were seen.

In a few instances the alveoli in the solid areas were small and lined by cuboidal epithelium. In the peripheral portions the consolidated patches were seen to be around bronchioles.

Heart Muscle.

The cross striation was not well seen; many of the muscle fibres had small granules within them but no fat was present.

Liver.

The parenchymal cells were swollen encroaching upon the blood sinusoids. Within the cytoplasm were numerous small dark granules. Hardly any vacuoles occurred.

Spleen.

The walls of the blood sinuses showed an increase in their cellular elements; many of the cells were elongated. The cells lining the sinuses were large and a considerable amount of proliferation into the lumen had occurred; Malpighian bodies were numerous.

Kidneys.

No changes which were of pathological significance could be seen in the constituents of the cortex.

Commentary.

The metaplasia of the columnar epithelium into that of a cuboidal and flattened type which had occurred in the air passages indicated a chronic inflammatory condition. This coincided with the clinical history, the child having suffered from bronchitis or bronchopneumonia of a greater or lesser severity for about 3½ months.

In this case the bronchopneumonia was fairly well limited to patches of lung associated with the bronchioles and a cellular exudate into the alveolar spaces was a marked feature. The histological picture of the lungs was far more that of a patchy alveolar pneumonia as opposed to an interstitial pneumonia. The progressive emaciation which was a marked feature in the case was due not only to the continued

pulmonary condition but also to the enteritis as indicated by green diarrhoea. Hence, death was due to the action of the toxaemia induced by the enteritis on a body already markedly debilitated by the effects of Whooping Cough and broncho-pneumonia.

Case No. 6.

Name. J. McC. Female. Aet 6 months.

General Conditions.

The patient lived in a 1 apartment house in which she resided with her parents and four other children. There was no history of any previous infectious disease.

Clinical Course.

On 27th January, 1935 the patient developed feverishness and spasmodic coughing; the latter was followed by vomiting.

On 1st February the patient was admitted to hospital. The temperature then was 101.2 F., pulse rate 160 beats per minute and respiration rate over 60.

She was well nourished, pale, listless, with a spasmodic cough but no whoop.

The tongue was coated and the faucial structures were congested. There was no impairment of the percussion note over the chest but over both pulmonary bases posteriorly the respiratory murmur was bronchovesicular with a few fine râles. The sputum was mucoid and tenacious in character.

The heart was within normal limits; the sounds were pure but of poor tone; the volume of the pulse was poor.

Examination of the nervous system and abdomen revealed no abnormality; the stools were normal in appearance.

Progress.

On 4th February there were areas posteriorly over both pulmonary bases where the percussion note was impaired; the respiratory murmur over the upper lobes of both lungs was bronchial in character and accompanied by occasional fine râles, whilst over the lower lobes of both lungs and middle lobe of the right lung the respiratory murmur was broncho-vesicular with numerous fine râles and occasional crepitations.

On 13th February the child had frequent vomiting and this persisted daily up to the time of death. The symptoms and signs of bronchopneumonia still persisted whilst in addition marked emaciation and dehydration was observed.

On 18th February the patient was very pale and dyspnoeic and the signs of bronchopneumonia were still present. Cardiac collapse occurred at 10.30 p.m. but after the administration by injection of a $\frac{1}{4}$ c.c. of Pituitrin subcutaneously the patient's colour and pulse improved.

On 21st February the patient was in a state of collapse. There was dullness on percussion over both pulmonary bases posteriorly and here the respiratory murmur was bronchovesicular with numerous crepitations and fine râles; over the remainder of the chest the respiratory murmur was bronchial with occasional fine râles. The patient died at 11.55 p.m.

Report of Autopsy.

The body was that of an emaciated child; dehydration of the tissueswas marked. There was post-mortem staining of the flanks. No excess of fluid was present in any of the serous cavities.

The heart was not enlarged; the cardiac muscle was congested; no abnormality of the valves or their cusps were found.

On section of the lungs solid areas, in close relation to the bronchi were found in the lower lobes on both sides and in the middle lobe of the right lung. Mucopurulent material could be expressed from the cut ends of the smaller bronchi. The tracheobronchial glands were enlarged; they were firm and dark purple in colour.

The liver, kidneys and spleen were not enlarged but were deeply congested; the bladder was normal in appearance. The wall of the bowel was thin and atrophic.

Microscopical Examination.

Trachea.

The columnar ciliated epithelium persisted.

Lungs.

Large areas of lung substance were completely consolidated, the alveoli being filled with a cellular exudate; in many instances the cells had undergone necrosis

- and were disintegrated forming a granular mass. Haemorrhage into the alveoli had not occurred but the interalveolar walls were much thickened and the capillaries were dilated. Hyperplasia of the cellular elements within the alveolar walls had not occurred, the thickening was due mostly to oedema. In places, partial collapse had occurred, in other portions again, there was little exudate into the alveoli, a certain amount of emphysema was present and there was thickening of the alveolar walls due to increase in their cellular constituents. The bronchioles were lined by columnar epithelium.

Liver.

Large globules occurred in the parenchymal cells of the outer zone of the lobule, the liver cells were swollen and encroached on the blood sinusoids.

Spleen.

The blood sinuses were congested and contained numerous mononucleated cells.

Commentary.

The case was one in which bronchopneumonia developed in the course of Whooping Cough. The pulmonary condition persisted during the whole of the 3 weeks the patient was in Hospital and towards the end the patches of bronchopneumonia became confluent with areas of collapse. This accounted for the dullness on percussion noticed shortly before death. The progressive weakness due to the occurrence of green diarrhoea undoubtedly contributed to the persistence and course of the pulmonary condition.

Case No. 7.

Name C. D. Female. Aet 6 months.

The patient came from a two-roomed house and the family consisted of the two parents and their two children, including the patient. There was no history of any previous infectious disease.

Clinical Course.

On 4th April, 1935 the child developed Whooping Cough, and paroxysms of coughing were followed by vomiting.

On 29th April, in the evening, she was admitted to Hospital. The temperature was 98 F., pulse rate 158 and respiration rate 52.

The patient was a moderately well nourished child; she had a spasmodic cough and was pale and listless; the conjunctivae were injected. The tongue was coated and the fauces congested; the only abnormality revealed by examination of the circulatory system was the rapid pulse rate; examination of the abdomen was negative.

There was no impairment of the percussion note over the lungs but the respiratory murmur at the bases was harsh vesicular with occasional fine râles.

The sputum was muco-purulent in character and the stools were normal. Her appetite was good but vomiting occurred after each paroxysm of coughing.

On 1st May, the temperature rose to 103.8 F. On examination the pulse was of poor volume and difficult to count, the rate being about 160 beats per minute; the respiration rate was 60. She had definite signs of broncho-pneumonia and, further, had convulsions.

Report of Autopsy.

The body was that of a well nourished child.

The cardiac muscle was pale in colour; the valves were competent and showed no pathological changes.

The thymus gland was large for a child of this age but there was no general enlargement of lymphatic glands throughout the body.

No areas of consolidation were present in the lungs but gentle pressure caused frothy mucoid material to exude from the cut ends of the bronchioles.

The lymphatic glands at the roots of the lungs were not enlarged.

The liver was pale; the spleen was firm, congested but not enlarged; the kidneys were pale in colour.

The wall of the intestine was not unduly thin.

The cranium and its contents showed no pathological changes.

Microscopical Examination.

Larynx.

The epithelial lining had been lost; this was undoubtedly a post-mortem occurrence as the deeper tissues of the wall showed no pathological changes.

Trachea.

The epithelial layer was intact and consisted of columnar cells.

Lungs.

The lumen of the smaller bronchi contained little secretion and their epithelial lining was intact and consisted of columnar cells. A copious exudate in which were numerous mononucleated cells had occurred into the walls of the bronchioles together with a certain number of polymorphonuclear leucocytes. Around the bronchioles the areas of infiltration were quite sharply delimited but spread had occurred into the walls of the alveoli which were much thickened: the capillaries were dilated around the bronchioles and in the alveolar walls.

The alveolar spaces contained no exudate. Emphysema was present to some extent.

Heart.

In sections prepared to demonstrate fat, no globules were found in the cardiac muscle fibres.

Thymus Gland.

This showed no departure from the histological

structure normal in a child of the patient's age.

Liver.

In some areas the hepatic parenchymal cells were swollen encroaching upon the blood sinusoids whereas in other areas the sinusoids were dilated. Towards the periphery of the lobules the parenchymal cells contained a large amount of fat in the form of larger and smaller globules.

Spleen.

The blood sinuses were much congested and contained a large number of nucleated cells. Owing to the dilatation of the blood spaces the Malpighian bodies were apparently reduced in size.

Kidney.

The capillaries forming the glomerular tufts were in many cases rather congested. The cells lining the convoluted tubules were swollen and had nearly occluded the lumen; their cytoplasm was coarsely granular. The venae rectae in the medulla were congested.

Commentary.

The case was an example of early bronchopneumonia and death occurred during the active phase of Whooping Cough. Microscopical preparations of the lungs demonstrated the condition of those organs to be typically that of an interstitial inflammation around the bronchioles with spread into the adjacent alveolar walls. The entire absence of any exudate in the alveolar spaces was a particularly noteworthy feature. The convulsions, fatty changes in the peripheral zones of the hepatic lobules, and the cloudy swelling of the convoluted tubules of the kidney were expressions of toxaemia.

Case No. 8.

Name. C.S. Female Aet 7 months.

General Conditions.

The patient lived in a one apartment house along with 5 adults and 3 other children. There was no history of previous infectious disease.

Clinical History.

On 2nd April, 1935 the patient became ill with a paroxysmal cough followed by vomiting.

On 7th April the patient was first heard to whoop. On this date it was noticed that the child was passing green stools.

On 9th April at 2.45 p.m. the patient was admitted to hospital. The temperature was 97.6 F., pulse rate 148, respirations 48 per minute.

The baby was fairly bright and moderately well nourished; she had a slight spasmodic cough and nasal discharge, serous in type. The tongue was moist and clean; the faucial structures were congested; the tonsils were not enlarged; the child was teething; no fraenal ulcer was present. Examination of the abdomen was negative but the child was still passing green stools. Percussion note over the chest was not impaired; the respiratory murmur at the bases posteriorly was bronchovesicular and accompanied by fine râles and rhonchi; no sputum was obtained.

The heart was not enlarged, the rhythm was regular and the sounds were pure and of good tone; the pulse was of moderately good volume.

Progress.

Spasmodic coughing continued throughout the illness but it was not severe; on various occasions, however, the patient became cyanosed after an attack.

After 22nd April the signs of bronchopneumonia gradually diminished but on 5th May were again noted, the lower lobes of both lungs being involved; this condition persisted during the remainder of the illness.

The temperature was of an irregular remittent type. The pulse rate was about 160 and its volume at times was good but at other times poor. The respirations varied from 44 to 60 approximating more to the latter figure.

Throughout the patient's time in hospital the heart remained within the normal limits of size, the sounds were pure and until shortly before death were of moderately good tone.

On 8th May the patient died.

Commentary.

A case which started primarily as a Whooping Cough developed catarrh of the larger bronchi extending upwards to larynx, pharynx, nose and throat. This was followed by a low grade bronchopneumonia; in addition, the child had green diarrhoea and this led to dehydration of the tissues, and was a factor in producing the emaciation.

Report of Autopsy.

The body was greatly emaciated and the tissues were dehydrated.

The cardiac muscle was pale in colour; the valves were competent and their cusps showed no abnormality.

The mucous membrane lining the larynx and trachea was somewhat injected.

The lower lobe of the left lung and the middle and lower lobes of the right lung presented small areas of consolidation, many of which were in relation to smaller bronchi. Purulent secretion exuded from the cut ends of the bronchioles.

The lymphatic glands at the roots of the lungs were enlarged.

The liver and the kidneys were pale. The spleen was larger than the average size; it was dark and congested.

The wall of the intestine was thin and atrophic.

Microscopical Examination.

Larynx and Trachea.

No change in the normal columnar cells lining the

upper air passages had occurred nor did the subepithelial tissue show any cellular infiltration. In certain parts the blood vessels were considerably congested and those of the lymphatic glands in relation to the trachea showed a similar change. The lymph sinuses of these organs were not much dilated but hyperplasia of the lymphoid elements had occurred.

Lungs.

The lining of some of the larger bronchioles had become distinctly flattened in type. The pleura was thickened and presented infiltration by small round cells. In the lower lobes small areas were present in which lung tissue was breaking down (early abscess formation). In these lobes the lung tissue around the abscesses showed a certain degree of collapse. The alveoli were filled with a cellular exudate, the cells being polymorphonuclear leucocytes and large mononucleated cells. In portions in which the cellular exudate was not so great the pulmonary capillaries and smaller blood vessels were much congested. In certain portions the change was not so advanced there being many more alveoli without exudate in their lumen but here partial collapse had occurred. These pneumonic areas were related to bronchioles.

Heart.

No fatty droplets were present in the cardiac muscle fibres.

Liver.

The parenchymal cells were swollen encroaching upon the blood sinusoids, their cytoplasm contained numerous fine dark granules. In the peripheral zones of the lobules a small amount of fat was present.

Spleen.

The spleen was congested and considerable endothelial proliferation had occurred into the blood sinuses.

Kidney.

The cells lining the convoluted tubules were swollen

and their cytoplasm was coarsely granular.

Commentary.

The case was one of Whooping Cough complicated by bronchopneumonia and enteritis. The pneumonic condition cleared up to a large extent but a recrudescence occurred. In the final stages of the disease abscess formation in the lungs was beginning, and the organs showed under the microscope, patches in which the changes were ~~there~~ those associated with bronchopneumonia but in addition, areas resembling lobar pneumonia (in that the alveoli were filled by a copious cellular exudate most of the cells being polymorphonuclear leucocytes) were also present; it was in these latter areas that early abscesses were found and the change was probably to be associated with them. The congestion of the pulmonary blood vessels and that in the tracheal lymphatic glands was mostly active whereas in the other organs it was probably largely passive due to the gradual cardiac failure. A noteworthy structural feature of the case was the metaplasia of columnar cells into those of a more flattened type which had occurred in the smaller bronchi and bronchioles.

Case No. 9.

Name. J.W. Male Aet 8 months.

General Conditions.

The patient came from a one apartment house in which he resided with his parents and four other children. There was no history of any previous infectious disease.

Clinical History.

On 16th January, 1935 the patient developed a spasmodic cough which was followed by vomiting.

On 21st January he was admitted to Hospital. On admission the temperature was 99 F, the pulse rate was 136 beats per minute and the respiration rate 32.

The patient was a pale, moderately bright, well nourished child; spasmodic coughing and whooping followed by vomiting was present and persisted throughout the illness. He had a simple serous rhinitis which continued until death occurred. The tongue was lightly coated, the faucial structures were congested and there was a small ulcer on the fraenum of the tongue. Abdominal examination revealed no abnormality but persistent vomiting and intermittent attacks of enteritis were present during the illness. The percussion note was impaired over the base of the left lung posteriorly; bronchovesicular breathing was present with crepitations and fine râles. The heart was within normal limits, the sounds were pure and of moderately good tone; the volume of the pulse was fairly good.

Progress.

On 26th January, the temperature, pulse rate, and respiration rate, all became more elevated than before and there was dullness at the bases of both lungs posteriorly with bronchovesicular breathing, crepitations, and fine râles. The patient became listless on 28th January and his appetite which hitherto had been fairly good became poor. Exacerbation of the enteritis and clinical signs of dehydration

were also present. A simple conjunctivitis and incontinence of urine and faeces developed.

On 29th January the heart did not show any signs of dilatation but the sounds, although pure, were of poor quality.

On 1st February the baby collapsed; there was marked cyanosis and no pulse was palpable at the wrist. Death occurred at 1.10 p.m.

Report of Autopsy.

Performed on 1st February, 1935, 2½ hours after death.

The body was that of an emaciated child; dehydration of the tissues was marked. The pericardial fluid was slightly in excess. The right auricle and ventricle, and the left auricle were distended and filled with dark clotted blood; all the valves were competent and the cusps normal; the heart muscle was dark in colour.

Both lungs were partially collapsed and, on section, small solid areas were seen scattered throughout either lung, these areas being confluent at the bases of both lower lobes. Mucopurulent material exuded from the cut ends of the larger bronchioles. The tracheobronchial lymphatic glands were enlarged and plum coloured.

The liver showed areas of dark mottling. The spleen was not enlarged but was dark in colour. The kidneys were dark in colour. The alimentary tract showed no changes of primary pathological importance.

The bony vault of the skull was soft and thin and was tightly adherent to the underlying dura mater. The cerebrospinal fluid was clear and under slightly increased pressure, but there was no abnormality of the constituents; the brain was congested.

Microscopical Examination.

Lung. (upper lobe).

Throughout the sections were small consolidated areas related to bronchioles. The bronchiole walls were thickened owing to exudate; the cells in them were mostly mononucleated.

The alveolar walls were thickened and infiltrated by mononucleated cells and the alveoli in the neighbourhood of the bronchioles were filled with an exudate which was largely cellular in character. Small portions of lung had collapsed and a considerable amount of emphysema was present. The lining of the bronchioles was retained to a considerable extent and was columnar in type.

Leptomeninges.

In the pia-arachnoid meshes were numerous cells, these being mostly small mononucleated in type; a certain number of polymorphonucleated cells were present. This exudate was especially dense around the pial blood vessels. No excess of cells was present in the brain substance or in the perivascular sheaths of the cerebral blood vessels. Petechial haemorrhages had occurred from some of the smaller blood vessels in the brain substance.

Spleen.

The section showed congestion.

Kidneys.

The glomeruli were large, filling the first portion of the tubule. There was increase in their cellularity. The cells lining the convoluted tubules were somewhat swollen and their cytoplasm was coarsely granular.

In the portion of the lung examined the condition was typically that of a commencing bronchopneumonia.

The leptomeningitis was non-purulent in character and resembled the condition found in virus diseases affecting the leptomeninges.

Case No. 10.

Name. J.D. Male Aet 10 months.

General Conditions.

The patient lived in a 3 apartment house together with 3 adults and one other child. There was no history of any previous infectious disease.

Clinical History.

On 2nd May, 1935 the parents first heard the child whoop.

On 15th May, in the evening, he was sent to Hospital as a case of Whooping Cough and bronchopneumonia, the temperature then being 98 F, the pulse rate 108 and the respiration rate 36.

The patient was pale, listless and poorly nourished; he was obviously acutely and seriously ill. The tongue was coated and the faucial structures were congested but the tonsils were not enlarged; there was no fraenal ulcer. The appetite was poor and frequent vomiting occurred after the paroxysms of coughing. The stools were frequent and green in colour; this condition continued until death. Abdominal examination revealed neither tenderness nor rigidity.

Over both lungs the percussion note was impaired in patches; the respiratory murmur was bronchovesicular with occasional fine râles. No sputum was obtained.

On percussion the cardiac dullness was not increased. The sounds were of poor quality and tic-tac rhythm was present. The volume of the pulse was poor.

Progress.

During the four days in hospital the patient's condition showed no improvement; the fever was remittent in type; the pulse rate was 160 and the volume continued to be poor. The respiratory rate rose to about 55 per minute.

On 19th May early in the morning the patient had convulsions and shortly afterwards death occurred.

Clinical Commentary.

A case of Whooping Cough which initiated an acute bronchopneumonia as evidenced by the clinical signs, the temperature, pulse and respirations. Later an acute enteritis had developed. These conditions acting singly or in concert produced the acute toxaemia which led to the dehydration. The convulsions were the proximal cause of death and were a terminal expression of the toxaemia.

Report of Autopsy.

Performed 30 hours after death.

The body was that of a poorly nourished child; post-mortem lividity had developed in the abdominal wall.

The mucous membrane of the larynx and trachea was injected. The thymus gland was large for the child's age and size.

Scattered throughout both lungs were irregular solid areas, and the lower portions of both lower lobes appeared completely consolidated although portions taken from them did not sink in water. Mucopurulent material expressed from the cut ends of the smaller bronchi.

The mediastinal lymphatic glands were enlarged.

The cardiac muscle was pale in colour and the cavities of the heart were dilated; the aortic and mitral valves were slightly incompetent. The mitral and aortic cusps were injected, fine vegetations being present on the margins of the former opening. The liver and kidneys were not unduly congested. The spleen was not enlarged but it was firm and congested. The wall of the intestine was thin and atrophic, and the mesenteric lymphatic glands showed slight general enlargement.

Microscopical Examination.

Larynx and Trachea.

No change in the type of epithelium had occurred. The columnar epithelial cells retained their cilia.

Lungs.

In the smaller bronchi the lining epithelium was

columnar in type. Small and rather diffuse areas of consolidation occurred, a few of these were due to collapse but in most instances the change was a result of a cellular exudate in the alveolar spaces. The pneumonic patches were related to smaller bronchi, and where the condition was limited to the immediate surroundings of the bronchioles the blood vessels in the walls of the latter were engorged, and the tissues of the walls were infiltrated by mononucleated cells and by large numbers of polymorphonuclear leucocytes.

Heart.

In the wall of the left ventricle, in close proximity to the aortic valve, a small bundle of muscle fibres had undergone necrobiotic changes; the fibres had lost their bright red stain with eosin and many of them were fragmented.

In frozen sections treated with Scharlach R. no fat was demonstrated in the muscle fibres.

Thymus Gland.

The thymus gland showed no structural departure from the normal for a child of this age.

Liver.

The liver cells were swollen, their cytoplasm being coarsely granular, and throughout the lobules many of the parenchymal cells had larger and smaller vacuoles throughout their cytoplasm.

In sections prepared to demonstrate fat, a moderate amount was seen; it occurred in droplets in the hepatic parencymal cells throughout the lobule, but especially in the peripheral zone.

Spleen.

Great proliferation of the endothelial elements into the lumen of the blood sinuses had occurred. In small areas the latter were engorged.

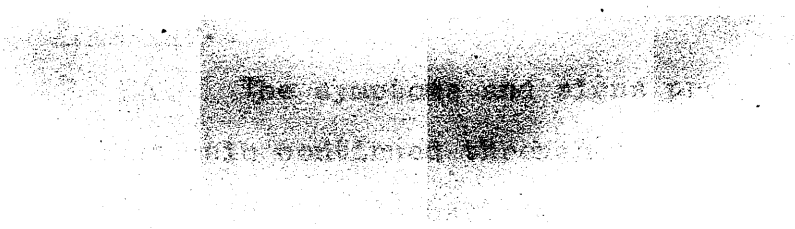
Kidney.

The cells lining the convoluted tubules were swollen and in many instances nearly completely occluded the lumen of the tube. The cytoplasm was coarsely

granular. No changes of pathological importance had occurred in the glomeruli.

Commentary.

The case was an example of bronchopneumonia and enteritis occurring during the course of Whooping Cough. The consolidated areas of lung were distinctly related to bronchioles, but the type of pneumonia was that associated with an exudate into the alveolar spaces rather than into the inter-alveolar walls. The explanation of the presence of 'vegetations' on the mitral cusps is not easy; these were recent in formation; there was nothing in the clinical course of the disease to indicate that the child had rheumatism. The child was marasmic, and it is a well authenticated fact that thrombosis is by no means rare in marasmic patients, but in these the clotting takes place within a blood vessel usually a vein, and it is generally regarded as due to alteration in the composition of the blood itself, and not to changes in the endothelium lining the wall of the blood vessel concerned. It is difficult to suppose that such a marasmic clot had occurredon a cardiac cusp. It would seem better not to attempt to give a definite opinion as to the factors leading to the formation of the small thrombi on the mitral cusps in this case, than to offer one which is contrary to clinical facts and pathological observations.



Case No. 11.

Name. W. F. Male Aet 11 months.

General Conditions.

The patient came from a two apartment house in which he lived with his father, mother and 2 other children. There was no history of any previous infectious disease.

Clinical Course.

On 16th June, 1935 the parents noticed that the child had started to cough and whoop. On 20th July, at 9.45 p.m. he was admitted to hospital as a case of Whooping Cough and bronchopneumonia, the temperature then being 101.6 F., the pulse 154 and the respirations 48.

He was a fairly bright moderately well nourished but pale child. There was a mucopurulent discharge from the right conjunctival sac, and a serous discharge from the nose. Examination of the mouth and throat induced coughing of the spasmodic type, but this was not followed by whooping.

The tongue was moist and clean, the faucial structures were congested and the tonsils enlarged. A small ulcer was present on the fraenum of the tongue. The stools were normal and abdominal examination revealed no abnormality.

The percussion note over both pulmonary bases posteriorly was impaired, the respiratory murmur being bronchovesicular in type and accompanied by numerous crepitations and fine râles. The sputum was mucopurulent. The superficial area of cardiac dullness was not increased; the heart sounds were pure and of moderately good quality.

Progress.

The symptoms and signs present on admission were in the main continued throughout the illness until death occurred on 20th August, at 11.30 p.m. with the exception of the following. The patient began to pass green stools on 1st August, and these persisted intermittently throughout the remainder of the illness. Until 14th August, the temperature had been of the low grade continued type; after that date it became higher and continued so until death.

The pulse rate continued much the same until 12th August when the volume became poor.

After the first week in hospital the respirations increased in frequency, and continued about 60 beats per minute.

On 15th August the mucopurulent discharge disappeared from both conjunctival sacs. On 18th August a small amount of thin pus containing small Gram-negative cocco-bacilli was obtained from each pleural cavity.

On 20th August the patient died.

Report of Autopsy.

The body was that of a poorly nourished child, the superficial fat being diminished in amount.

The pharynx, larynx and trachea were injected. Thin pus was smeared over the whole surface of the pleura on each side. In the left pleural cavity the exudate was greater in amount than on the right side and was more fibrinous in character, the pleura itself being thickened. Numerous fibrous adhesions had been formed between the layers of pleura posteriorly.

The lungs were consolidated, the consolidation being bronchopneumonic in type and small abscesses were present in the lower lobes of both lungs.

The cavities of the heart were not dilated; the valves were competent and the cusps normal.

The kidneys, liver and spleen were of average size and they were injected.

The wall of the intestine was thin and atrophied.

Bacteriology.

The pus from the pleural cavities showed small Gram-negative cocco-bacilli and a growth of these was obtained on blood agar.

Microscopical Examination.

Larynx and Trachea.

No metaplasia of the columnar epithelium had occurred. Here and there the tissue immediately below the mucous membrane was infiltrated by cells of the small mononuclear type.

Lungs.

On the surface of the lung there was a fibrino-purulent exudate. The pleura was thickened and its blood vessels much dilated. Some of the sections showed almost complete collapse of the lung substance; others demonstrated that the walls of the alveoli were much thickened and infiltrated by mononucleated cells. Throughout the section the blood vessels were dilated. The pneumonic areas were distinctly related to smaller bronchi, the walls of which were thickened and the lining epithelium had become flattened; in most instances the epithelium had retained the high columnar type.

Bronchial Lymphatic Gland.

The blood vessels and lymph sinuses were much dilated and a considerable amount of haemorrhage had occurred into the latter; they contained also large numbers of proliferated endothelial cells many of which contained red blood cells and blood pigment.

Liver.

In parts the liver cells were swollen, encroaching upon the blood sinusoids. In other parts this swelling of the parenchymal cells had not occurred and here the blood sinusoids were dilated. Numerous fat globules were present in the central and peripheral zones of the lobules; the middle zones showed very little fatty change.

Spleen.

The spleen was much congested.

Kidney.

The cells lining the convoluted tubules were swollen and their cytoplasm was coarsely granular; no changes were present in the glomeruli.

Commentary.

The case was an example of acute interstitial pneumonia with empyema and partial collapse of lung substance. The fact that no new blood vessels had grown from the pre-existing ones in the pleura into the exudate on its surface supported the clinical view that the empyema developed about the 15th August rather than a week prior to that date. The acute inflammation of the mediastinal lymphatic glands was more marked in this case than in those previously examined and was in keeping with the bacteriological findings that the pneumonia was due to an influenza-like bacillus and not to a pneumococcus. The marked fatty changes in the liver cells had probably been brought about partly by the absorption of toxins from the intestinal tract but also partly by the general toxaemia. The lesions described at autopsy as being small abscesses in the lungs were probably areas of acute gangrene in which liquefaction had occurred.

Case No. 12.

Name I.M. Female Aet 11 months.

General Conditions.

The patient lived in a 2 apartment house along with 4 adults and one other child. There was no history of previous infectious disease. The child had been vaccinated against small-pox.

Clinical Course.

On 28th March, 1935 the child became ill with a paroxysmal cough followed by vomiting. On 1st April, she was first heard to whoop.

On 21st April the patient was admitted to Hospital. The temperature was then 100.2 F., the pulse rate 148 and the respiration rate 24. During the morning she had an attack of convulsions.

She was a pale undernourished listless child; examination of the throat produced a spasmodic cough. The child was teething and had a purulent discharge from the eyes.

The tongue was furred; the faucial structures were congested and the tonsils were enlarged; there was no fraenal ulcer and the appetite was fair. Abdominal examination was negative. The percussion note at the left pulmonary base was slightly impaired, the respiratory murmur over the lungs was harsh and vesicular with occasional rhonchi and fine râles; the sputum was tenacious and mucopurulent in type.

The heart was within normal limits, the rhythm was regular and the sounds pure but of poor quality. The pulse was of moderately good volume.

Progress.

The state of nutrition became progressively worse, the child before death becoming emaciated and dehydrated. The child continued to be pale and listless throughout the illness. No whooping was observed, although spasmodic coughing was present during the time in hospital.

On 22nd April another convulsion occurred. On 26th April the tongue had become moist and clean but the

tonsils and fauces were still congested. A serous discharge from the nostrils had commenced.

During the illness the appetite varied sometimes being moderately good and at other times poor; the stools remained normal. On 30th April the child vomited but this was the only occasion.

On 29th April slight impairment of the percussion note at both pulmonary bases posteriorly was noted; the respiratory murmur over the lungs was bronchovesicular with rhonchi and fine râles; further at the bases occasional crepitations were audible. The fever was of the remittent type. The pulse rate was usually about 160 beats per minute. The heart showed no increase in the superficial area of dullness; its rhythm was regular and the sounds were pure but soft. The respiration rate was increased being usually about 60 beats per minute.

Report of Autopsy.

The body was that of a well nourished child.

The thymus gland was large for a child of this age but there was no general enlargement of the lymphatic glands throughout the body.

The heart muscle was pale; neither the valves nor their cusps presented any abnormality.

Areas of pneumonic consolidation were found in the lower lobes of both lungs. These areas were adjacent to the larger and smaller bronchi.

The lymphatic glands at the roots of the lungs were enlarged.

The liver was pale; the spleen was congested and, on section, the Malpighian bodies were prominent being greyish in colour; the kidneys were congested.

The wall of the intestine was not atrophied.

Case No. 13.

Name. C.N. Female Aet 1 year.

General Conditions.

The patient came from a 2 apartment house in which she resided with her parents and six other children. There was no history of any previous infectious disease.

Clinical Course.

On 4th February, 1935 the patient became ill with spasmodic coughing which was followed by vomiting.

On 8th February, 1935, at 4.35 p.m. the patient was admitted to Hospital.

The temperature was 99.4, the pulse rate was over 160 beats per minute and the respiration rate was 44.

She was a pale poorly nourished child who was very dyspnoeic and in a collapsed condition. There was movement of the alae nasi. The tongue was coated, the faucial structures were congested and there was a fraenal ulcer. Abdominal examination revealed no abnormality. On examination of the chest there was impairment of the percussion note at both pulmonary bases with bronchovesicular breathing, crepitations and fine râles. The heart was within normal limits, the sounds were pure but of poor quality with tic-tac rhythm.

Examination of the nervous system and of the genito-urinary system revealed no abnormality.

Progress.

On 8th February, at 6 p.m. generalised muscular twitchings were observed. On 9th February, the patient was in a moribund condition and death occurred at 8.30 p.m.

Report of Autopsy.

The body was that of a poorly nourished child with post-mortem lividity of the flanks.

Within the pericardium there was a considerable amount of clear fluid.

The heart was not enlarged and there was no

abnormality of the valves or cusps; the cardiac muscle was dark in colour.

The lower lobes of both lungs were consolidated owing to the coalescence of small scattered areas in close relation to the smaller bronchi. The thymus gland was large for the child's age and size. The spleen, liver and kidneys were not enlarged; they were dark in colour. The bowel showed no changes of primary pathological importance.

The central nervous system was not examined.

Microscopical Examination.

Lungs.

Sections taken from the lower lobes showed large areas of consolidation, the alveoli being filled with polyhedral cells and red blood corpuscles. The capillaries and smaller blood vessels were much dilated and haemorrhages had occurred into the lung substance. Areas of collapse were present. In other sections were areas in which necrosis of the lung was commencing and these portions contained large numbers of polymorphonuclear leucocytes. In the parts adjacent to the consolidated areas, the capillaries and smaller blood vessels were also much dilated, small haemorrhages having occurred into the alveoli; they contained a certain number of large rounded polyhedral cells together with a few polymorphonuclear leucocytes. In many instances the lining of the smaller bronchioles had been completely shed, in others some of it still persisted and was columnar in type. Sections taken from the upper lobes showed dilation of the capillaries in the alveolar walls; also there were diffuse areas in which the alveoli were filled with serous exudate and in which catarrhal cells and polymorphonuclear leucocytes were fairly numerous. The lining of the smaller bronchi was much better preserved than in the lower lobes.

Kidney.

The cells lining the convoluted tubules were much swollen and in many instances almost occluded the lumen. Their cytoplasm was coarsely granular.

Commentary.

The case was one of bronchopneumonia becoming confluent in the lower lobes with early pneumonic change in the upper lobes. The degree of vascular reaction with commencing breaking down of lung substance together with the dense infiltration of these areas by polymorphs indicated that the inflammation may have been in response to invasions by streptococci rather than pneumococci. The history that the illness lasted only a matter of 4 days before admission was probably incorrect as at that time the patient had a fraenal ulcer and the pneumonia was well established.

Case No. 14

Name. T.N. Male Aet 1 year.

General Conditions.

The patient came from a 2 apartment house in which he resided with his parents and two other children. He was unvaccinated and there was no history of any previous infectious disease.

Clinical Course.

On 9th January, 1935, the patient became feverish and developed a spasmodic cough followed by vomiting. His parents first heard him whoop on 14th January. On 1st February the patient was admitted to hospital and the temperature was then 100.4 F; pulse rate over 160 beats per minute and respiration rate over 60.

He was pale undernourished and was obviously acutely and seriously ill. Attacks of dyspnoea alternated with periods of apnoea with a heliotrope cyanosis of the face.

The tongue was moist and lightly coated and the faucial structures were congested.

The percussion note over both pulmonary bases was impaired; the respiratory murmur over the lungs was bronchovesicular with numerous fine râles and crepitations.

The heart was within normal limits. The sounds were pure but of poor quality and tic-tac rhythm was present; the volume of the pulse was poor.

Examination of the abdomen revealed no abnormality.

On 3rd February the patient died. During the two days in hospital his general condition had shown progressive deterioration.

Report of Autopsy.

The body was that of an undernourished child with post-mortem staining of the flanks.

Numerous firm adhesions were present between the pleural surfaces on both sides. There was no excess of

fluid in the pericardial and peritoneal sacs.

Small areas of consolidation were scattered throughout both lungs. Mucopurulent material exuded from the cut ends of the larger bronchioles. The cardiac muscle was dark in colour, the valves were competent and their cusps normal.

The liver, spleen and kidneys which were of normal size were deeply congested. The intestine was normal.

The cerebrospinal fluid was clear and was not excessive in amount. The blood vessels on the surface of the brain and those within its substance were congested.

Microscopical Examination.

Trachea.

In the sections examined the columnar epithelium was intact.

Lungs.

The walls of the bronchi were thickened owing to the dilation of the blood vessels and to serous exudate containing a considerable number of cells most of which were mononucleated in type. In some of the bronchioles the columnar epithelium was practically intact whereas in others it had been desquamated and the lumina were filled with dense cellular exudate derived from the deeper parts.

Considerable areas of lung showed complete consolidation, and there the bronchioles were full of exudate and the epithelial lining had been completely shed: small areas of collapse had also occurred: in these portions the alveoli were filled with a sero-cellular exudate. Most of the cells were mononucleated in type but there were a considerable number of polymorphonuclear leucocytes. Immediately under the pleura emphysema was marked.

Spleen.

The blood sinuses were much congested and considerable endothelial proliferation had occurred.

Kidney.

The cells lining the convoluted tubules were swollen and their cytoplasm was coarsely granular.

Commentary.

The numerous fine fibrous adhesions in both pleural cavities indicated that the patient had suffered from a chronic pulmonary condition such as bronchitis for some time before the onset of Whooping Cough.

In this case, therefore, the child would be especially apt to develop bronchopneumonia as a complication of pertussis. This condition of the lungs became widespread and when admitted to Hospital the general condition was too far advanced for treatment to be of any avail in averting a fatal termination.

Case No. 15.

Name. M.R. Female. Aet 1 year.

General Conditions.

The patient lived in a 2 apartment house along with 3 adults and one other child. There was no history of any previous infectious disease.

Clinical Course.

On 14th July, 1935 the child had an attack of 'convulsions' according to the parents' statement. She was first heard to whoop on 19th July.

On 1st August the child was sent in to hospital as a case of Whooping Cough and bronchitis. The temperature was 99.4, pulse over 160 and respirations 48 per minute.

She was a pale moderately well nourished baby with a spasmodic cough but no whoop. A left sided otitis media and a serous rhinitis were present.

The tongue was dry and coated; the faucial structures were congested but the tonsils were not enlarged; over the fraenum of the tongue there was a small patch of raised greyish epithelium whilst on the tip of the tongue a small patch of greyish epithelium was also present. The appetite was moderately good; abdominal examination revealed no abnormality.

A patchy impairment of the percussion note was present over the lungs; the respiratory murmur was bronchial in character and accompanied by fine râles. The superficial cardiac dullness was not increased; the sounds were pure but of poor tone; the volume of the pulse was poor.

Progress.

The patient's general condition became progressively worse. The fever was of the low grade, irregularly intermittent type until shortly before death when it rose sharply to 103 F., the pulse rate continued over 160, its volume remained poor. The respiration rate was in the region of 50.

By 6th August the pneumonic process had spread, the physical signs in the chest becoming more widespread and

pronounced. The appetite remained fairly good although vomiting occurred daily. The patient did not develop green stools. On 8th August the child died.

Report of Autopsy.

Performed 8th August, 1935, 12 hours after death.

The body was that of a well nourished child.

The mucosa of the trachea and larynx was injected. Patches of consolidation in relation to the bronchi were scattered throughout both lungs with the exception of the upper halves of the upper lobes on each side. The tracheo-bronchial glands were enlarged.

The heart was of normal size; the cardiac muscle was congested; the valves were competent but the cusps of the mitral and aortic valves were bright red in colour.

On section the liver was mottled in appearance. The spleen was not enlarged but it was congested. The kidneys were congested. The mesenteric glands were enlarged. The alimentary tract showed no lesions.

Microscopical Examination.

Larynx.

At a level immediately above that of the vocal cord, the sub-epithelial connective tissues were infiltrated by small round cells. No change in the type of lining epithelium was present.

Lungs.

In relation to the bronchioles patches of consolidation occurred, many of these being extensive. The consolidation was due to infiltration of the interalveolar walls by smaller and larger mononucleated cells, together with a certain number of polymorphonuclear leucocytes. The blood vessels both in the walls of the bronchioles and in those of the alveoli were much dilated. The thickening of the alveolar walls by exudate was so great that the alveolar spaces could not be recognised. The infiltration of the walls extended peripherally from the consolidated patches and

was present throughout the portions of lung examined. Away from the consolidated portions small areas were present in which partial collapse had occurred and in the upper portions of the superior lobes, where the condition was less advanced, a considerable amount of emphysema was present. The columnar epithelium lining the walls of the bronchioles was high columnar in type. The columnar epithelium lining the walls of the bronchioles had not been desquamated to any extent. In those bronchioles involved in the consolidated areas cells were present between the high columnar elements. Most of these were polymorpho-nuclear leucocytes but a few mononucleated cells were seen. The lumen was filled by cells of this type together with a certain amount of granular material; the appearance was strongly suggestive of cells passing from the solid portions of lungs outwards to the lumen of the bronchioles.

Heart.

In frozen sections treated with Scharlach R. no fat was demonstrated in the cardiac muscle fibres. Paraffin sections gave no histological explanation for the bright red colour of the aortic and mitral cusps.

Liver.

The parenchymal cells were swollen encroaching upon the blood sinusoids. Small fat droplets were fairly numerous throughout the liver lobule but especially in the peripheral zone.

Kidney.

The cells lining the convoluted tubules were swollen and their cytoplasm was coarsely granular.

Commentary.

The case was an example of bronchopneumonia. Exudate into the alveolar walls was very marked. Sections of the upper lobe demonstrated that the change had begun in the wall of the bronchus and spread outwards therefrom. Many of the patches had become confluent.

Case No. 16.

Name C. A. Female Aet 1 year 2 months.

General Conditions.

The patient lived in a one apartment house in which she resided with her father, mother and one other child. There was no history of any previous disease.

Clinical Course.

On 15th January, 1935 the patient became ill with spasmodic coughing followed by vomiting.

On 17th January, middle day, she was first heard to whoop by her parents.

On 31st January, the child was admitted to hospital. The pulse rate was more than 160 and the repiration rate over 60.

She was pale and under nourished and in a collapsed condition. The tongue was dry and lightly coated; the faucial structures were congested but the tonsils were not enlarged. Abdominal examination revealed no abnormality.

The percussion note was slightly impaired over both pulmonary bases and the respiration was bronchial in type and accompanied by numerous fine râles.

The heart was within normal limits but the sounds were inaudible. The volume of the pulse was poor.

Half an hour after admission the patient took convulsions and died almost immediately.

Report of Autopsy.

The body was that of a poorly nourished child.

There was no increase of fluid in any of the body cavities.

The cardiac muscle was dark in colour. The valves of the heart were competent and no lesions of the cusps were found.

Scattered throughout both lungs were patches of consolidation; mucopurulent material was expressed from the cut ends of the larger bronchioles.

The liver, spleen and kidneys were dark in colour.

The stomach and intestine showed no changes of primary pathological importance.

Microscopical Examination.

Lung.

Sections showing a consolidated patch.

In the consolidated portion the exudate was almost entirely cellular, the cells consisted of a certain number of cells polyhedral in type and large numbers of polymorphonuclear leucocytes.

The consolidated area was irregular in outline and in its immediate neighbourhood some of the alveoli were filled with an exudate which was largely serous in character.

In the more distal portions the process was most marked in the walls of the bronchioles and in the lung tissue immediately adjacent: here and there was a larger proportion of mononucleated cells than was present in that portion of lung where consolidation was complete. In the parts where the pneumonic areas had become confluent, areas occurred in which the cells were almost entirely polymorphonuclear in type. Throughout the sections the alveolar walls were more or less thickened owing partly to dilatation of the blood vessels and partly to an interstitial exudate composed of mononucleated cells.

In other portions the consolidation was not so extensive, there was a larger amount of serum but again polymorphonuclear leucocytes were frequent: in these portions considerable emphysema had occurred.

Tracheobronchial Lymphatic Gland.

Considerable hyperplasia of the lymphoid elements had occurred. The lymph sinuses were dilated, haemorrhages had occurred into them and there was considerable endothelial proliferation.

Commentary.

The case was one of bronchopneumonia developing during the course of Whooping Cough. The pulmonary condition became widespread throughout both lungs and at the end was

becoming confluent. Convulsions occurred and these were rapidly fatal.

Case No. 17.

Name A.O. Female Aet 1 5/12 years.

Clinical Course.

The patient was sent to Hospital on 6th April, 1935 with the diagnosis of Whooping Cough of eighteen days' duration.

On 6th April, when admitted, she was a fairly bright moderately well nourished but pale child. The tongue was furred and the patient had a fraenal ulcer; the fauces were congested. There was a mild generalised bronchitis with a small amount of purulent sputum. Examination of the heart revealed no abnormal features and the pulse was of quite good volume. Temperature was 99.2 F., pulse rate 132 and respiration rate 36.

During the day of admission it was noticed that the baby had spasmodic attacks of coughing but there was no whooping; green diarrhoea was present and the patient vomited on several occasions. Her appetite was fairly good and she slept quite well. No urine could be collected.

The diagnosis of Whooping Cough was accepted and the usual treatment adopted.

The condition remained much the same for the following week. On 14th April the left ear began to discharge, a mild conjunctivitis developed and the green coloured stools became more frequent. Her general condition continued to deteriorate; the body showed increasing dehydration and her appearance was characteristic of a toxic state.

On 16th April, the patient died; the duration of the illness was 28 days.

Autopsy.

The body was emaciated and dehydrated.

No excess of fluid was present in any of the body cavities.

The mucous membrane of the upper air passages was not inflamed; in the lungs muco-purulent secretion exuded from the cut bronchioles but no areas of consolidation

were seen. The bases of the lungs were oedematous.

The lymphatic glands in relation to the lower end of the trachea and to the bronchi were enlarged and tense but otherwise the lymphatic glands throughout the body showed no enlargement.

The heart muscle was pale in colour.

The liver was pale with darker mottlings; the spleen was not enlarged and was firm; the cortex of the kidneys was pale; the wall of the intestine was thin and semi-translucent. The other organs showed no changes of pathological significance.

Microscopical Examination.

Larynx and Upper Part of Trachea.

The columnar epithelium lining the upper part of the trachea was intact; the mucous glands in the sub-epithelial layers were actively secreting mucus. The deeper tissues showed no cellular infiltration.

Lungs.

Small diffuse patches of cellular infiltration were present; these were related to the smaller bronchioles. The infiltration consisted of mononucleated cells with a comparatively small number of polymorpho nuclears; it had occurred almost entirely into the tissues forming the wall of the bronchus and into the interstitium of the inter-alveolar walls.

The cellular infiltration of the interstitial tissues was widespread throughout the whole of the pulmonary substance examined but it was larger in amount in those parts closely related to the smaller bronchi.

The small areas of consolidation were due to the great increase in the thickness of the alveolar walls and not to an exudate into the lumen of the alveoli.

Heart.

In frozen sections stained by Scharlach R. small droplets of fat were demonstrated in many of the muscle fibres; they were situated at either pole of the nucleus.

Liver.

In frozen sections stained by Scharlach R. great fatty change was seen in the liver parenchymal cells and there was no differentiation in the amount of fat in any of the three zones. The fat was mostly in the form of a single large droplet filling the cell and in many instances the nucleus had been displaced to the periphery.

In preparations cut in paraffin and stained by haematoxylin and eosin, the histological picture corresponded to the above; the liver cells contained numerous vacuoles and many of them consisted of one large vacuole with the nucleus lying at the margin of the cell.

Kidney.

The Malpighian Bodies were swollen, many of them almost filling the space within Bowman's capsule; they showed increased cellularity. The cells of the convoluted tubules presented little if any changes.

Spleen.

The blood sinuses were dilated with consequent apparent diminution in the size of the Malpighian Bodies.

Commentary.

The case was a typical example of Whooping Cough complicated by the occurrence of green stools.

During the course of the disease she developed bronchopneumonia. The latter condition was not diagnosed during life since the classical signs - remittent temperature, dyspnoea, dullness on percussion, fine râles and crepitations - were absent; consequently the diagnosis of bronchitis only was made.

The absence of physical signs indicating bronchopneumonia were explained by the microscopical examination of the lungs. The expression of pulmonary inflammation was confined to the walls of the bronchi and its branches and to the inter-alveolar septa; practically no exudate had occurred into the alveolar spaces.

The extreme fatty change in the hepatic parenchyma and the fatty degeneration of many of the cardiac muscle

fibres were an expression of an acute and extreme toxaemia. This conformed to the clinical history; during the last three days or so of life the diarrhoea became progressively more pronounced and the patient showed progressive dehydration of the body. In this case the nature of the diarrhoea did not suggest that it was a manifestation of toxaemia; rather was it a condition which would give rise to absorption of bacterial toxins from the intestine. In this event, it was justifiable to expect that marked disturbance would occur in the liver, and it seemed probable that the great fatty change in this organ was due to this cause.

A second site from which toxic absorption occurred was the lungs. Bronchopneumonia not infrequently complicates Whooping Cough and is not directly related to the specific micro-organisms causing the primary condition; it is brought about by the invasion of the pulmonary tissues by the micro-organisms which are the common cause of bronchopneumonia in children and especially by Pneumococcus.

The fatty degeneration which had occurred in the cardiac muscle fibres was due probably to the combined toxins from the lung and the intestinal tract.

The enlargement of the mediastinal lymphatic glands can be adequately explained by toxic absorption from the inflammatory condition in the lungs.

It is of interest to note that in this case at all events the mediastinal lymphatic glands were not enlarged beyond that seen in many cases of bronchopneumonia unassociated with Whooping Cough. This is a fact against the explanation advanced by certain authors that the "whoop" is due to pressure on the recurrent laryngeal nerve either directly or indirectly through the vagus by the enlarged lymphatic glands in the mediastinum.

Case No. 18.

Name I.D. Female. Aet 1½ years.

Clinical Course.

The patient was admitted on 7th March, 1935 as a case of Whooping Cough with bronchopneumonia of ten days' duration.

When admitted the child was well nourished but listless; the tongue was coated; the tonsils were enlarged and there was general congestion of the faucial structures. The diagnosis of bronchopneumonia was confirmed. Examination of the heart revealed no abnormal features and the pulse rate was 168 and of moderately good volume. The child had spasmodic attacks of coughing but there was no whooping. A simple rhinitis was present. Temperature 100.8 F.; respiration rate 70.

At this time the child had green diarrhoea and after an attack of coughing she occasionally vomited. The latter ceased after eight days in Hospital.

Until 31st March, the patient's condition remained practically stationary: on that day the temperature began to subside and reached normal.

On 6th April, the chest presented clinical signs suggestive of a left side empyaema and exploration yielded pus; this was evacuated by aspiration. Films of the pus showed a Gram-positive diplococcus having the morphological characters of Pneumococcus. By this date the patient had lost a considerable amount of weight and the body was dehydrated to a marked extent, the green stools having persisted throughout.

The patient became quickly and progressively worse and died on 10th April.

The course of the disease, therefore, was 44 days.

Autopsy.

The body was that of an emaciated child.

The cardiac muscle was pale; no valvular lesions were found. A moderately large and encysted collection of pus was present in the left pleural cavity.

On section, throughout both lungs were small consolidated areas which were beginning to break down; purulent material exuded from the cut bronchioles.

The lymphatic glands at the roots of the lungs were enlarged.

The liver was pale with darker mottlings; the spleen was firm and dark in colour; the kidneys were congested; the wall of the intestine was thin and atrophic.

Commentary.

Bacteriology.

Films of the pus from the left sided empyaema showed Gram-positive lanceolate diplococci; these were most probably Pneumococci.

Microscopical Examination.

Liver.

Frozen sections stained by Scharlach R. demonstrated a considerable amount of fat throughout the lobules. In the central portions the fat was in the form of small discrete globules whereas, the hepatic cells towards the periphery contained large globules which in many cases were single filling the whole cytoplasmic area.

In sections cut in paraffin and stained by Haematin and Eosin, the cytoplasm of the liver cells at the periphery of the lobules was occupied by large vacuoles whereas, in the central portions the cytoplasm contained small vacuoles.

Lungs.

Portions of the left lung were taken from parts in immediate and more distal relationship to the localised empyema.

The pleura was much thickened by vascular fibrous tissue the histological picture being typically that of the later stages

of an organising pleurisy.

The pulmonary substance showed partial collapse this change being fairly generalised although it was more pronounced in certain areas. Change of the lining cells of the partially collapsed alveoli into the cuboidal type of epithelium was frequent. Areas of fibrosis had occurred in the lung; some of the new formed fibrous tissue being recent whereas some of it was of older standing, firmer and less vascular. In certain instances the new fibrous tissue had enclosed areas of lung substance which were much collapsed and showed to a marked degree cuboidal epithelium lining those alveoli which still remained.

Commencing abscess formation was frequent in some of the sections examined.

The walls of the smaller bronchi were thickened, densely infiltrated with cells and showed dilated blood vessels. Some of the larger bronchi were dilated, their walls being comparatively thin. The lining of the smaller bronchi consisted of columnar epithelium but some of the larger bronchi were lined by cuboidal epithelium.

Bronchial Lymphatic Gland.

The blood vessels and lymph sinuses were much dilated; the germinal centres were represented only by a rim of cells surrounding dilated lymph spaces.

In the lymph sinuses were many large mononucleated cells with vacuolated cytoplasm; some of these contained phagocytosed carbon pigment.

Spleen.

The Malpighian Bodies resembled very closely the germinal centres of the bronchial lymphatic gland; they consisted of a rim of lymphoid cells around dilated and apparently empty spaces.

A small amount of general fibrosis had occurred.

Kidney.

The cells of the convoluted tubules were swollen and their cytoplasm was coarsely granular.

Trachea.

The lining consisted of columnar epithelium. The subepithelial connective tissue was densely infiltrated by cells which for the most part were small, round and mononucleated in type. A certain amount of infiltration extended into the muscular tissue and at one place into the mucous glands lying in the wall of the trachea.

Commentary.

In this case the diagnosis of Whooping Cough was based on the fact that the child had spasmodic attacks of coughing terminating in vomiting.

The prominent clinical feature of the case was the bronchopneumonia which gave rise to an empyema. The intestinal derangement evidenced by the passing of green coloured stools was a minor factor in causing the fatal termination of the illness; clinically it would seem that the toxins finally responsible for the death of the patient were derived from the empyema since after this condition set in, the general condition of the patient rapidly deteriorated.

Although the presence of fluid in the left side of the chest was manifest only four days before death, the histological examination demonstrated an advanced stage of organisation. It is probable, therefore, that a serous exudate occurred into the pleural cavity soon after the commencement of the bronchopneumonia and later it was infected by the micro-organisms responsible for the pulmonary condition.

Empyema pus in the pleural cavity, may occur owing to rupture of a pulmonary abscess into the pleural cavity but in its acute form it occurs most commonly as a complication of acute pneumonia. In these cases, as the inflammatory process in the pulmonary substances approaches in its spread the surface of the lung, a non-purulent exudate occurs into the pleural

cavity as a result of 'irritation' of the serous membrane. This exudate, at first aseptic, becomes invaded by bacteria from the lung and later becomes purulent.

The partial collapse of the left lung in this case was due in part only to pressure of the pleural exudate. The latter was not massive enough to account for more than localised collapse whereas the condition was widespread throughout the pulmonary substance. Partial collapse as seen microscopically as in this case is common in children dying in an asthenic state and doubtless this was the factor operating in the present instance.

Case No. 19.

Name F.K. Male. Aet 1 6/12 years.

General Conditions.

The child lived in a 2 apartment house with her father, mother and one other child. On 14th April, 1935 the patient was first heard to whoop. There was no history of any previous infectious disease, but a history of convulsions was given.

Clinical History.

On 18th April he was sent into Hospital as a case of Whooping Cough and pneumonia. On admission the temperature was 101.2 F, the pulse rate was 160 and the respiration rate was 60. The child was pale but moderately well nourished; he had a dry eczema of the skin; there was no clinical evidence of rickets. The tongue was lightly coated; the faucial structures were congested. Examination of the abdomen revealed no abnormality; the appetite was fairly good; there was a mild degree of enteritis indicated by slightly green stools.

A serous nasal discharge was present and the conjunctivae were injected. Spasmodic coughing occurred daily throughout the illness but no whooping was heard. There was no definite impairment of percussion note over the lungs but at the pulmonary bases posteriorly, the respiratory murmur was broncho-vesicular with numerous fine râles.

The volume of the pulse was moderately good; the superficial area of cardiac dullness was not increased; the heart sounds were pure and of moderately good tone.

Progress.

The whole duration of the illness was 18 days of which only the last four were spent in hospital.

Whilst in hospital the fever was of the remittent type. The pulse varied between 130 and 160 and the respiration rate was 50 - 60. During the stay in hospital there was no amelioration of the patient's condition.

On 22nd May, 1935 the patient developed generalised convulsions and died 15 minutes later.

Report of Autopsy.

Post-mortem performed 22nd May, 1935, 13 hours after death.

The body was that of a well nourished child.

The thymus gland was large for a child of the patient's age and size.

The mucous membrane of the larynx and trachea was slightly injected. The lower lobes of both lungs were consolidated and a portion of this solid lung tissue sank in water. The tracheobronchial glands were enlarged.

The heart cavities were not dilated; the cardiac muscle was pale in colour but the heart valves were competent and the cusps normal.

The liver and kidneys were not enlarged and were pale in colour.

The spleen was enlarged; it was soft and somewhat friable.

The bowel appeared normal.

Report of Microscopical Examination.

Larynx.

The epithelium showed no change in type from the normal. The subepithelial connective tissue in that portion immediately below the vocal cord was infiltrated by small round cells.

Lungs.

The capillaries in the walls of the alveoli were much dilated and the walls infiltrated by round cells; this change was widespread in the portions of lung examined but was especially marked round the bronchioles.

The alveolar spaces still persisted and some of them near the bronchioles contained oedematous fluid; occasional cells were present in the lumen but for the most part the alveoli were empty.

Much of the epithelium lining the bronchioles was desquamating, and cells chiefly polymorphonuclear leucocytes were passing into the lumen.

Heart.

No fat was present in the cardiac muscle fibres.

Liver.

The liver cells were swollen and much vacuolated. In frozen sections treated with Scharlach R. a large amount of fat throughout the whole lobule was demonstrated; practically every liver cell had undergone fatty change.

Kidney.

The glomeruli were markedly cellular; the cells lining the convoluted tubules were swollen and their cytoplasm was coarsely granular.

Spleen.

Considerable proliferation of cells had occurred into the lumen of the blood sinuses; the organ was unduly congested.

Summary.

The case was an example of the interstitial type of pneumonia, the change being most advanced in the region of the bronchioles. Fatty change in the liver was pronounced and was due probably to the enteritis.

Case No. 20.

Name J.M. Female. Aet 5 years.

General Conditions.

The patient came from a one apartment home and the family consisted of her two parents and one other child. She had a previous history of measles and chicken pox.

Clinical Course.

On 18th March, 1935 the patient became ill; she had a paroxysmal cough followed by vomiting.

On 4th April, she was first heard to whoop.

On 18th April, at 10 p.m. she was admitted to Hospital. On admission the temperature was 98.6 F., the pulse rate 150 and the respiration rate 44.

The child was emaciated and neglected in appearance with clinical signs of rickets; she was listless, the lips were cracked and dry. The tongue was lightly coated and dry; the fauces were congested; there was a muco-serous discharge from the nostrils.

Abdominal examination was negative.

There was no definite impairment of the percussion note over the lungs but the respiratory murmur was broncho-vesicular with numerous fine râles.

By percussion, the heart was within normal limits; the sounds were pure but soft.

The urine contained a trace of albumen and the sputum was blood-stained.

The condition was diagnosed as malnutrition, Whooping Cough and bronchopneumonia.

On 20th April, the stools became loose and on the following day they were green.

On 22nd April the patient died. During the four days in hospital the child's appetite was fairly good and she slept quite well.

Autopsy.

The body was that of an emaciated child, the tissues being much dehydrated.

The heart muscle was somewhat pale in colour; the

valves were competent and the cusps were normal.

Patches of bronchopneumonia were present in the right middle lobe, in the lower half of the left upper lobe and in the left lower lobe; some of these areas felt distinctly hard and were pale in colour.

The lymphatic glands in relation to the roots of the lungs were enlarged.

The liver was pale with dark red mottlings; the spleen was not enlarged and was dark in colour; the kidneys were congested.

The bowel wall was thin and atrophic.

Microscopical Examination.

Lungs.

In portions the only abnormality noted in the lung tissue was a small degree of emphysema although in these parts there was some cellular infiltration of the walls of the smaller bronchi.

In other portions, however, there were areas in which the pulmonary alveoli were filled with a cellular exudate many of the cells being polymorphonuclear leucocytes. Adjacent to these were small areas in which the alveoli were filled with a serous exudate and again in other small neighbouring areas the alveolar walls were thickened owing to cellular infiltration.

The lining of the smaller bronchi was intact and composed of columnar epithelium.

Nowhere were the smaller blood vessels and capillaries dilated.

Larynx and Trachea.

Remote from the actual vocal cords, the air passage was lined by columnar epithelium, no metaplasia to a squamous type having occurred. Parts of the superficial tissues of the wall of the trachea showed a certain amount of round celled infiltration.

The lymphatic vessels in the wall of the trachea were dilated and contained mononucleated with occasional polymorphonucleated cells.

Liver.

The hepatic parenchymal cells were swollen and encroached on the blood sinusoids; their cytoplasm was coarsely granular and many of the liver cells contained an excess of finely granular brownish pigment.

Within the blood sinusoids were a large number of white blood corpuscles; most of these were mononucleated in type.

Spleen.

The walls of the blood sinuses were well marked and the endothelial lining approached a cuboidal type. In the lumen of the sinuses were many mononucleated cells and there was an excess of blood pigment. The Malpighian bodies were small.

Kidney.

The blood vessels, both of the medulla and cortex including the capillaries forming the glomerular tufts, were congested. The cells lining the convoluted tubules showed no change.

Commentary.

In this case, the chief feature in the lungs was the pneumonic patches in the left organ. Microscopically no marked and widespread interstitial pneumonia was found and the areas in the left lower lobe were of the nature of commencing abscesses. From the absence of pronounced vascular reaction around them, the early abscesses were undoubtedly terminal and due to infection by a micro-organism of 'low grade' virulence.

The dilated condition of the lymphatic vessels in the wall of the trachea was of especial interest as pointing to a possible source of infection of the lungs from the higher portions of the air passages. Particularly was this the case since a certain number of polymorphonuclear leucocytes were present within the lymphatic lumen. The presence of these, indicating a more acute process, may be associated with the terminal commencing pulmonary abscesses; the micro-organisms

responsible for these may have gained access to the pulmonary tissues from the upper respiratory passages by way of the intramural lymphatic vessels.

Both from the clinical and pathological aspects of the case, there was no doubt that the child died of inanition and this was due probably more to the condition of enteritis than to pneumonia.

Case No. 21.

Name. E. McK. Male Aet 1½ years.

General Conditions.

The patient lived in a two apartment house along with 4 adults and other 4 children. He had been vaccinated and there was a history of measles about 6 months prior to admission.

Clinical History.

On 19th January, 1935 the child became ill with feverishness and spasmodic coughing which was worse at night. He was first heard to whoop on 23rd January.

On 19th February, the patient was admitted to hospital, the temperature was 99 F., the pulse rate was 150 and the respiration rate was 50. He was a well nourished child and had severe spasmodic coughing with whooping. The face was puffy and listlessness was marked. The tongue was dry and coated; the faucial structures were congested but there was no ulcer of the fraenum. The appetite was fair, and the stools were normal in appearance. Abdominal examination revealed no abnormalities. There was no impairment of the percussion note over the chest; the respiratory murmur was bronchovesicular with numerous rhonchi and râles. The heart was within normal limits; the sounds were pure but of poor quality.

On 20th February, convulsions with concomitant cyanosis occurred at 5.30 a.m. and at 2.30 p.m.

On 21st February, at 10.30 p.m. the patient again developed convulsions; these were followed by collapse and he died at 2.30 a.m.

Report of Autopsy.

Autopsy performed on 22nd February, 1935, 11 hours after death.

The body was that of a well nourished child with post-mortem staining of the flanks.

No excess of fluid was present in any of the body cavities.

The right side of the heart was filled with dark

clotted blood; the valves were competent; there was slight injection of the cusps of the mitral valves but otherwise the cusps were normal; the cardiac muscle was deeply congested.

On section, the lungs presented small patches of consolidation scattered throughout their substance; the cut ends of the smaller bronchi exuded mucopurulent material. The tracheo-bronchial lymphatic glands were enlarged.

The liver, kidneys and spleen were not enlarged but were dark and congested.

The intestine was normal.

Microscopical Examination.

Trachea.

The columnar ciliated epithelium still persisted.

Lungs.

The walls of the larger bronchioles were greatly thickened, owing to intense cellular exudate which consisted of smaller and larger mononucleated cells, this exudate did not pass far into the surrounding pulmonary tissue but throughoutthe whole lung the capillaries and smaller blood vessels were congested. In places a serous exudate was present in the alveoli and there were portions in which emphysema was marked, the alveoli being dilated and their walls thin and ruptured. In another portion of the lung thickening of the alveolar walls was widespread and diffuse although here again much of it was due to great dilatation of the interalveolar capillaries and not to hyperplasia of the interstitial elements.

Tracheobronchial Lymphatic Glands.

To a large extent the general structural arrangement had been lost owing to the lymph sinuses being much dilated and containing a large number of mononucleated cells. The blood vessels within the node were greatly dilated and some small haemorrhages had occurred. The node therefore presented the usual changes associated with toxic absorption.

Liver.

The cells were swollen encroaching upon the blood sinusoids, their cytoplasm contained numerous small vacuoles.

Spleen.

The blood sinuses were dilated and contained large numbers of mononucleated cells. In the section numerous small rounded areas in which the cells were necrotic and becoming a homogeneous mass were seen, this change, however, was undoubtedly due to post-mortem disintegration.

Kidney.

The post-mortem changes were considerable.

Commentary.

The case was one in which the patient developed convulsions one month after the onset of Whooping Cough. He died from collapse following convulsions.

Throughout the body the organs were congested, this was passive in nature although a certain amount of interstitial pneumonia was present it was not a marked feature. The active changes in the lung were chiefly in the wall of the larger bronchioles.

Case No. 22.

Name E.M. Female. Aet 8 months.

General Conditions.

The patient lived in a two apartment house along with her father, mother and two other children. The patient was unvaccinated and there was no history of any previous infectious disease.

Clinical History.

The child developed spasmodic coughing on 10th January followed by vomiting. The child had not been heard to whoop.

On 4th February, at 1.30 p.m. the patient was admitted to Hospital. The temperature was 96 F, the pulse rate 160 and the respiration rate 56. The child was in a state of collapse; she was poorly nourished and had a spasmodic cough; the tongue was coated but there was no ulcer of the lingual fraenum; the faucial structures were congested and the tonsils were enlarged.

The percussion note at the bases of both lungs posteriorly was impaired; râles and crepitations were heard. The size of the heart was within normal limits; the sounds were pure but of poor quality; tic-tac rhythm was present. The volume of the pulse was poor.

Abdominal examination was negative.

A specimen of urine was not obtained.

Progress.

Immediate treatment for the collapse was instituted and this resulted in the temperature rising to 100 F and this was maintained. The pulse became 'running' and the respiration rate rose to about 80.

On 5th February, at 7.55 a.m. the patient died.

Report of Autopsy.

Performed on 5th February, 1935, 6 hours after death.

The body was that of a poorly nourished child.

There was no increase in the fluid of the body cavities.

On section of the lungs patches of consolidation in

relation to the bronchi were found and mucopurulent secretion was expressed from the cut ends of the bronchioles. The tracheo-bronchial glands were enlarged and the thymus was large for a child of the patient's age and size.

The heart muscle was dark in colour; the valves were competent and the cusps normal; some white thrombus was present in the right auricle.

The liver, on section, showed a dark arborescent mottling. The bowel presented no changes which were of primary pathological importance.

Commentary.

The case was one of Whooping Cough followed by bronchopneumonia. Death was due to myocardial failure.

Microscopical Examination.

Lungs.

The walls of the smaller bronchi were infiltrated by mononucleated cells together with a few polymorphonuclear leucocytes; the infiltration passed for a short distance into the walls of the adjacent alveoli. Small consolidated areas were present in which the alveoli were filled with a cellular exudate and in which a certain amount of collapse had occurred. The lining of the bronchioles persisted and was columnar in type.

Trachea.

The lining consisted of columnar cells. Around the mucous glands lying beneath the mucous membrane was a considerable amount of small round celled infiltration.

Spleen.

The spleen was congested. Considerable proliferation of the cellular elements had occurred.

Kidney.

The lining cells of the tubules showed a certain amount of swelling with increased granularity of the cytoplasm.

Commentary.

The patient was under observation in hospital for a matter of only 18 hours and it was difficult to assess the

parts played by the various pathological conditions present. The degree of pulmonary involvement seemed hardly sufficient to account for the fatal issue. On the other hand the thymus gland was large for a child of 8 months and this might be fairly taken to indicate a patient particularly susceptible to toxaemia.

The remarkable rapidity of the pulse rate together with the presence of white thrombus in the right auricle and the chronic congestion of the liver point to a condition of myocardial insufficiency.

It would seem probable on the whole that the case was one of Whooping Cough in which the heart was affected in a particular degree by the strain due to coughing. On this already taxed heart was thrown the additional strain of toxic absorption due to the patient developing bronchopneumonia.

These two factors caused a fatal myocardial failure.

Case No. 23.

Name M.B. Female. Aet 9 months.

The patient came from a two apartment house in which she resided with her two parents and two other children. There was no history of any previous infectious disease.

Clinical Course.

On the 21st March, 1935, the patient developed a cough. She was first heard to whoop by her parents on the 27th March, 1935.

The patient was admitted to Hospital on 3rd April, 1935 at 9 p.m. The temperature was 98.6 F., pulse rate 138 beats per minute, respiration rate 44.

The patient was moderately well nourished and the mental acuity was moderately bright. The child slept well on the night of admission, temperature 100.4 F., pulse rate 168 beats per minute and respiration rate 56 at 10 a.m. Whooping and spasmodic cough which was followed by vomiting was present. She had a serous rhinitis and a simple conjunctivitis which persisted throughout.

The tongue was coated, the faucial structures were congested and the tonsils enlarged. A small ulcer of the fraenum was present which disappeared on the 16th April. Abdominal examination revealed no abnormality. The appetite which was good on admission became poor on the 2nd May, 1935 and remained poor until death. "Green stools" were present on admission and persisted almost daily throughout the illness. On examination of the chest there was no impairment of the percussion note but the respiratory murmur was bronchial occasional fine râles being audible. These signs persisted throughout the illness. Just before death the temperature rose to 103.6 F. but previous to this the temperature was never higher than 100.4 F. nor lower than 97.2 F. The sputum was mucoid and tenacious in character. Just before death occurred on 10th May, 1935 the pulse rate reached 180 but prior to this had varied between 130 - 160, being of only moderately good volume. From 3rd April until about 3rd May the pulse

was of poor volume.

On admission the heart was found to be within normal limits and the sounds were pure but of moderately good tone. On 3rd May the heart sounds were of poor tone although no clinical signs of enlargement were present. Tic-tac rhythm was present.

On 3rd May, the child had become emaciated and on the 9th, the patient was very dehydrated.

From being a moderately bright and lively child on admission she appeared to be listless and apathetic on 6th May and continued to be so until death.

The patient slept well until just before death on 10th May. The tongue remained coated and the faucial structures were congested throughout the illness. The vomiting which was present on 4th April, 1935, the day of admission, occurred almost daily until 25th April when vomiting ceased. Vomiting recommenced on 6th May and was present daily until death. Whooping occurred daily throughout the illness.

Report of Autopsy.

The body was that of an emaciated child; the tissues were dehydrated.

The cardiac muscle was pale in colour but no anatomical abnormalities were found in the organ.

The lining mucous membrane of the larynx and trachea was injected.

On section the lung tissue in the neighbourhood of the antero-internal margins of both lungs showed small areas of consolidation; muco-purulent secretion exuded from the cut ends of the larger bronchioles.

The glands in relation to the roots of the lungs were enlarged, firm, and on section dark red in colour.

The liver was pale; the spleen was not enlarged but was dark in colour; the kidneys were pale.

The wall of the intestine was thin and atrophic. Two small intussusceptions were found to have occurred near

the middle of the ilium but these were easily reduced and there were no signs of any reaction; hence they were immediately ante-mortem in origin. The contents of the bowel were greenish in colour.

There was general enlargement of the mesenteric and retro-peritoneal lymphatic glands.

Microscopical Examination.

Larynx and Trachea.

No changes had occurred in the squamous or columnar epithelium of the larynx. In the trachea, some of the columnar epithelium had become definitely flattened in type.

Lungs.

The pleura was distinctly thickened by oedema. The peripheral portions of the walls of the bronchioles were densely infiltrated by small round and elongated cells. Areas of the pulmonary substance showed a similar cellular infiltration of the alveolar walls. This was so copious that the walls were greatly widened. In these patches the alveolar space contained practically no exudate. In certain portions, especially those in which the interalveolar infiltration had not occurred, the alveolar walls had broken down forming comparatively large air spaces.

Lymphatic Glands (Retroperitoneal.)

Hyperplasia of the lymphoid elements had occurred but the lymph sinuses were not dilated.

Heart.

Frozen sections treated with Scharlach R. and Osmic Acid did not show fat in the cardiac muscle cells.

Liver.

Except in the peripheral zone of the lobules the blood sinusoids were much narrowed, the hepatic parenchymal cells being closely approximated to each other; further, the cytoplasm had retained more of the haematoxylin stain than

was usual. The nuclei showed no departure from the normal structure nor was there greater vacuolation of the cytoplasmic portions of the cells.

Frozen sections treated by Scharlach R. and Osmic Acid had not demonstrated fat.

Kidney.

The glomeruli were filling up Bowman's capsule. The cells lining the convoluted tubules were for the most part occluding the lumen and their cytoplasm was coarsely granular.

Spleen.

The organ was somewhat congested and the splenic tissue was very cellular.

Commentary.

A certain amount of interstitial pneumonia in relation to bronchi was present. In this patient, however, the chief factor in bringing about a fatal termination was the long continued enteritis from which the patient suffered.

Case No. 24.

Name. W. W. Male Aet 2 years.

General Conditions.

The patient came from a one apartment house in which he resided along with his father, mother and one other child. There was a previous history of measles occurring nine months before and the patient had been vaccinated.

Clinical Course.

Towards the end of January, 4 weeks before admission, the patient became ill with listlessness, coughing and vomiting. He was heard to whoop by his parents 2 weeks after the first symptoms of his illness were observed.

On 23rd February, 1935 he was admitted to Hospital. The temperature was 97 F., pulse rate 160 beats per minute and respiration rate 50 per minute.

The patient was a pale, emaciated, listless child who slept well on the evening of admission; the appetite was poor. The temperature the next morning was 101.8 F., the pulse rate had risen to over 160 beats per minute and the respiration rate to 64 per minute; coughing was spasmodic but it was not followed by vomiting. The tongue was lightly coated; the faucial structures were congested; abdominal examination revealed no abnormality.

The percussion note was impaired at both pulmonary bases; the respiratory murmur which was bronchovesicular in type, was diminished and accompanied by numerous crepitations and fine râles. These signs persisted throughout the illness. The heart was within normal limits and the sounds were pure but of poor tone. The volume of the pulse was poor. The urine contained no abnormal constituents.

Progress.

On 25th February the patient looked acutely and seriously ill. The volume of the pulse was poor and the rate was still over 160 beats per minute. Head retraction and Kernig's sign were both present. When lumbar puncture was performed the fluid was under pressure and slightly turbid;

the protein was increased in amount; no micro-organisms were present; the cells were 254 per c.mm., lymphocytes predominating.

Throughout the stay in hospital the fever was of the remittent type, the pulse rate was never below 160 and the respiration rate varied between 50 and 86.

On 27th February, death occurred at 11.15 p.m.

Report of Autopsy.

Performed on 28th February, 1935, 14 hours after death.

The body was that of a marasmic child with post-mortem staining of the flanks.

The pericardial fluid was not increased in amount; the cardiac muscle was deeply congested; the valves were competent and their cusps normal.

At their bases both lungs were adherent to the visceral pleura.

On section, they were darkly congested and small greyish caseous nodules were visible in the left apex. Patches of consolidation in relation to the bronchii were found in either lung. Muco-purulent material was expressed from the cut ends of the smaller bronchi. The tracheo-bronchial lymphatic glands were markedly enlarged.

The liver, spleen and kidneys were not enlarged but were deeply congested. On section, the liver showed a nutmeg appearance and in the left kidney a caseous area was found near the hilum. The bowel was normal.

Small greyish nodules were found in the lepto-meninges and similar but larger nodules occurred in the substance of the brain. The lateral ventricles were dilated. The cerebrospinal fluid was increased in amount and was turbid.

Microscopical Examination.

Brain.

The leptomeninges of the brain were much thickened by fibrino-cellular exudate. The cells for the most part were small mononucleated in type. Areas of coagulation necrosis were present. The tubercles tubules in the brain substance

consisted of masses of necrosis surrounded by a narrow zone of cellular reaction. In one of the sections a 'tuberculoma' was continuous with the infected leptomeninges.

In sections of the upper cervical portion of the cervical spinal cord, the leptomeninges were densely infiltrated by small round cells. Further there were areas in which the exudate was fibrino-cellular and these showed commencing coagulation necrosis.

Commentary.

The case was an example of pulmonary tuberculosis occurring in a child aged 2 years. The meninges showed tuberculous infection and a number of tuberculous nodules had occurred in the substance of the brain. A tuberculous lesion was also present in the left kidney. It may well be that the bronchopneumonia in both lungs was actually tuberculous in nature. The question arises whether the condition from which the patient died had any relation to Whooping Cough.

Case No. 25.

Name. P. W. Female. Aet 11 months.

General Conditions.

The patient came from a 2 apartment house in which she resided with her father, mother and four other children. The patient was unvaccinated and there was no history of any previous infectious disease.

Clinical Course.

On 20th December, 1934 the patient became ill with spasmodic coughing which was followed by vomiting. Whooping was first heard by the parents on 25th December, 1934.

On the morning of 24th January, the patient was admitted to Hospital. The temperature was 99.8 F., pulse rate 160, respiration rate 60. The patient was a bright, well nourished child who did not appear acutely ill. Spasmodic coughing which was followed by whooping was present. There was a left otitis media. The tongue was moist and clean; the faucial structures were congested and the tonsils enlarged. Abdominal examination revealed no abnormality. The percussion note over the chest was not impaired but the respiratory murmur was harsh vesicular with occasional fine râles. The heart was within normal limits; the sounds were pure and of good tone.

Whooping and coughing were observed throughout the illness but these symptoms became less marked after broncho-pneumonia developed on 4th February.

On 30th January, the patient developed a simple serous rhinitis with injection of the conjunctivae.

The elevation of temperature present on admission subsided reaching normal on 26th January and remained so until the evening of 4th February when it rose to 99.8 F. On 5th February at 2 p.m. the temperature was elevated to 103 F. and thereafter the fever was of the irregularly remittent type. On this date the patient became ill and collapsed with poor colour and rapid pulse. There was slight impairment of the percussion note over the bases of

both lungs posteriorly with bronchovesicular breathing and occasional fine râles. The superficial area of cardiac dullness was slightly but definitely increased both to the right and to the left; the heart sounds were pure but of poor quality. On examination of a film from a catheter specimen of the urine Gram-negative bacilli and a few scanty pus cells were seen; the former were coliform bacilli. On 8th February there was dullness at both pulmonary bases posteriorly with bronchovesicular breathing, crepitations and fine râles. Enteritis, indicated by green stools, was present.

On 11th February, death occurred at 5.40 a.m.

Report of Autopsy.

Performed on 11th February, 1935, 8½ hours after death.

The body was that of a moderately well nourished child.

There was a slight increase of pericardial fluid.

The heart was not enlarged; the cardiac muscle was dark in colour.

There were a number of small, reddish vegetations on the cusps of the mitral valve; the other valves were competent and their cusps normal.

On section of the lungs, scattered patches of consolidation which were becoming confluent were observed in both lower lobes especially towards the bases; these areas of consolidation were in close relationship to the bronchi and mucopurulent material exuded from the severed ends of the larger bronchi.

The spleen was dark in colour and the liver presented dark mottling.

The kidneys were dark in colour and the lining of the urinary bladder was injected.

The cerebrospinal fluid was increased in amount but on examination it was found to be normal in composition. The brain was congested. Cultures from the lateral ventricles of the brain and from the spleen gave no growth of micro-organisms.

Microscopical Examination.

Lung.

In the section there were numerous small tubercles; the lesions were diffuse and were becoming confluent; necrosis was a marked feature and around the necrotic areas the alveoli were filled with an exudate consisting largely of mononucleated cells. Occasional multinucleated giant cells were present. The capillaries and smaller blood vessels were congested and there had been exuded into the alveoli a moderate amount of oedematous fluid. The smaller bronchioles had retained their columnar lining and the lumen was filled with fluid and mononucleated cells.

Mediastinal Lymphatic Glands.

These showed extensive caseation, in the glands examined very few lymphoid elements remained. The areas in which lymphoid tissue persisted showed numerous early tubercles.

Trachea.

The columnar ciliated epithelium persisted.

Liver.

The hepatic parenchymal cells were swollen and many of them contained larger or smaller vacuoles, these were present throughout the lobule; an occasional small early tubercle was present.

Kidney.

The cells of the convoluted tubules were swollen and almost completely filled the lumen. There was a large diffuse tuberculous focus in the medulla and nearby a similar but smaller one, the reaction round these being small mononucleated in type. Several multinucleated giant cells were present.

Spleen.

The spleen was congested and many large mononucleated cells occurred in the sinuses. No tubercle was present in the portions examined.

Commentary.

The case was one of tuberculous caseous broncho-

pneumonia and from the fact that the lesions were confined to the lower lobes it was probable that they were of very recent origin, the patient dying before dissemination into the upper lobes occurred. This view was supported by the histological features of the tubercles. Whenever infection took place, the tuberculous condition manifested itself to a marked degree only a week before death. Undoubtedly dissemination had been occurring prior to this as the lesions in the mediastinal lymphatic glands and kidney were undoubtedly older than one week; the final break down in the resistance of the body occurred then.

In this case it might be argued that the Whooping Cough was an important factor in predisposing the body to a general dissemination of tubercle from a focus which hitherto had been quiescent or only slowly progressive. The infection of the urinary tract by coliform bacilli was in association with tuberculosis of the kidney.

Case No. 26.

Name H.K. Female. Aet $2\frac{1}{2}$ years.

General Conditions.

The patient lived in a 2 apartment house with her parents and two other children.

Clinical Course.

On 27th December 1934, the child became ill with feverishness, cough and vomiting. Whooping was first noticed on 28th December 1934.

The patient was admitted to Hospital on the 11th January 1935. The temperature was then 99 F., the pulse rate 120 and the respiration rate 26.

She was a pale moderately well-nourished child who had moderately severe attacks of spasmodic coughing which were followed by whooping.

The tongue was moist and clean, the tonsils were enlarged and there was congestion of the fauces. There was a fraenal ulcer, the appetite was moderately good and abdominal examination revealed no abnormality.

The heart was within normal limits, the sounds were pure and of moderately good quality.

The percussion note over the lungs was unimpaired, the breath sounds were vesicular and no adventitia were audible.

The urine showed no abnormal constituents.

On 19th January there was a trace of albumen in the urine but this had cleared up by the 25th January.

On 20th February the patient ceased to whoop and on 3rd March she ceased coughing. She was dismissed well on 8th March 1935. During the stay in hospital there had been no signs of pulmonary involvement.

The patient was readmitted to Hospital on 9th April 1935.

The illness commenced on 10th April 1935 with cough and vomiting.

On admission the temperature was 100 F., pulse rate

110 and respiration rate 30. The temperature was irregularly intermittent throughout the illness.

She was a pale moderately well nourished child with a slight cough; the tonsils were enlarged and the fauces were injected; abdominal examination revealed no abnormality.

The heart was within normal limits, the sounds were pure and of moderately good quality.

The percussion note over the lungs was unimpaired; the breath sounds at the pulmonary bases posteriorly were bronchial with numerous fine râles.

On the 18th April the patient developed green diarrhoea and this persisted until death occurred.

On the 20th April the patient became semi-conscious, there was head retraction and slight nuchal rigidity; Kernig's sign was elicited on either side; the pupils were dilated and fixed. Lumbar puncture was performed under local anaesthesia.

The fluid was clear and under slightly increased pressure.

Examination of Cerebro-spinal fluid.

(1) Fluid clear.

(2) Pandy and Nonne-Apelt tests positive.

(3) Benedict's reagent was not reduced.

(4) The cells were increased in number (200 per cubic millimetre). The cells were of the mononucleated type.

The tubercle bacillus was not found on direct examination.

The fluid did not form a flocculent clot on standing.

The patient died on the 25th April.

Report of Autopsy.

The body was that of a poorly nourished child.

The thymus gland was not enlarged.

The size of the heart was within normal limits, the valves were competent and the cusps apparently normal. The cardiac muscle was congested.

There was oedema of both pulmonary bases, muco-purulent material could be expressed from the cut ends of the bronchi. There were no areas of obvious consolidation seen in relation to the bronchi. The tracheo-bronchial glands were enlarged.

The bowel wall was thin and atrophic but no other pathological lesions could be seen.

The liver was of normal size and pale in colour. Multiple small greyish pin-head tubercles were visible in the capsule and more superficial portions of the liver. The spleen was of normal size and was darkly congested. Multiple small greyish tubercles were visible in the capsule and throughout the substance of the spleen.

The kidneys were darkly congested.

Brain.

There was a greenish purulent infiltration of the meninges in the region of the mid-brain and pons.

Microscopical Examination.

Lungs.

Small tubercles were present showing the usual characters of recent formation.

Lymphatic Glands.

The tracheal and bronchial lymphatic glands contained numerous small tubercles. In some of the bronchial lymphatic glands these tubercles had become confluent.

Liver and Spleen.

Small tubercles were present.

Kidney.

No tubercles were present.

Leptomeninges from Base of Brain.

These contained a fibrinous exudate in which were large numbers of mononucleated cells and in which much diffuse necrosis had occurred.

Commentary.

The case was an example of acute miliary tuberculosis beginning shortly after an attack of Whooping Cough.

It was arguable whether or not the Whooping Cough predisposed in this case to general infection by B.tuberculosis.