The following seven papers from the Resident Staff of the Hospital for Sick Children, Toronto, were presented at a regular staff meeting at the hospital in 1940. Professor Alan Brown suggested their publication in the 'Archives of Disease in Childhood,' and the Editors gladly assented.

A LABORATORY INVESTIGATION OF PNEUMONIA AMONG INFANTS AND CHILDREN

BY

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The results of sputum examinations from 450 cases of pneumonia in infants and children covering a nine-month period from September 8, 1938, to June 8, 1939, were reported previously (Auger, 1939a). These results were characterized by numerous cases of empyema due to type I pneumococcus and many deaths. During the past pneumonia season from September 8, 1939, to April 18, 1940, a seven-month period, 450 cases have again been examined, but in these there was a low mortality rate and few cases of empyema. Evidently 1939-40 must be regarded as a mild season as compared with 1938-39, which constituted a severe season. In view of this apparent seasonal variation in pneumonia incidence and virulence a careful study and comparison has been made of the statistics for the two seasons from an etiological point of view. These results have been tabulated and interpreted graphically to show the most interesting and salient features.

The method used for examining and culturing sputum is unique. In most of the cases the sputum has been obtained from the nasopharynx. We believe that a nasopharyngitis always precedes pneumonia in children and that the best means of studying the bacteriology of an early case of pneumonia in a child is to study secretions from the nasopharynx. In cases of late pneumonia, whooping cough, or tuberculosis, laryngeal sputum is better suited to examination. The sputum is obtained by suction (Auger, 1939b) from the nasopharynx and a tentative report is made on examination of the direct smear. Sputum from the nasopharynx is ideal in this respect since it is relatively free from mouth organisms which are so easily confused with pneumococci. The sputum is then typed by the Neufeld method if pneumococci are present in the direct smear. The sputum is then cultured on a blood agar plate which is incubated in the presence of moist carbon dioxide (Auger, 1939c). The injection of mice is no longer considered necessary for the isolation of pneumococci in our laboratory.

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The pneumonia cases are all those reported to the laboratory with positive chest findings and checked in most instances by a positive roentgenogram and by a member of the attending staff. No distinction has been made between lobar- and broncho-pneumonia. The two conditions were never distinguishable on a basis of sputum examination. These cases have not been subdivided into primary or secondary pneumonia except in the mortality table, since the etiological cause at the onset of the pneumonia in children is of most interest and is likely to be the same whether the child has a congenital heart or a normal constitution. On the other hand, an underlying ailment may greatly influence the prognosis.

In fig. 1 is shown the monthly incidence of pneumonia cases and deaths for the past three years. The case incidence for all types of pneumonia is shown by

FIG. 1.—Graphic representation of monthly incidence of pneumonia cases and deaths for three pneumonia seasons. The upper line represents the number of cases and the lower line the deaths following primary pneumonia.

the upper line and the number of deaths following primary pneumonia by the lower line. The definition accepted of primary pneumonia is one in which the onset or progress is not influenced by any concurrent disease. The vertical coordinate gives the actual number of cases while the horizontal coordinate the first letter of the month.

In the first section are shown the statistics for 1937-38. These are incomplete, since the pneumonia study had just been begun: they are shown to emphasize the fact that a striking rise in case incidence without any corresponding rise in fatalities occurred in May. May is a spring month not usually associated with pneumonia.

In the second section are shown the curves for 1938-39 or the severe pneumonia season. Here it is seen that the case incidence forms a peak during the winter months of January, February, and March and again in May. The corresponding mortality curve roughly follows the case incidence curve, with a

crest during December, January, and February. It is interesting to note again that this curve falls away in May in spite of the corresponding sharp rise in case incidence.

In the third section are shown similar curves for 1939-40 or the mild season. Here the peak of case incidence is in October and November of 1939 and again in April, 1940. It is likely that the month of May will show a still higher case incidence, since there was an average of eight to twelve cases of pneumonia per day during the last two weeks before this paper was completed. It is most interesting to note that the curve of case incidence is a valley during the winter months of December, January, February, and March, or the reverse of the 1938-39 or severe pneumonia season. The mortality curve roughly follows the course of the incidence with its peak in November. However, it may be noted that the mortality curve significantly drops in April in spite of the rise in incidence. Evidently April and May can be severe months as to case incidence but are mild as to pneumonia virulence. From these curves it was judged that a severe pneumonia season among infants and children in Toronto is associated with a rise in case incidence during the winter months and a less severe or mild season with a low winter case incidence.

TABLE 1
SHOWING MORTALITY ACCORDING TO AGE FROM SEPT. 8, 1938,
TO JUNE 8, 1939, AND FROM SEPT. 8, 1939, TO APRIL 19, 1940

AGE	1938-1939		1939-1940	
	CASES	DIED (PER CENT.)	CASES	DIED (PER CENT.)
0-1 year	121	27.5	109	18.3
1-2 years	67	6.7	79	12.1
2 years	262	5.5	262	2.5
Total	450	10.5	450	7.1

In table 1 the mortality figures for the mild and severe pneumonia seasons are compared. These figures are based on statistics from 450 pneumonia cases among infants and children from September 8, 1938, to June 8, 1939, and September 8, 1939, to April 19, 1940. Only the deaths following primary pneumonia have been recorded. In about 80 per cent. of the deaths the lungs were examined culturally either at post mortem or by lung aspiration. When there was failure to obtain a post-mortem examination the case was judged to be a primary pneumonia on the basis of history and sputum examination. The cases have been classified according to age: up to one year, one to two years, and over two years. The mortality is seen to be highest for both seasons in infants under one year of age and is lowest in the over-two-years age group. A marked decrease in mortality is noted during the 1939-40 season. There is an exception in the one-to-two years age group, which possibly can be explained

on statistical variation, since there are many fewer cases. It should be pointed out that most of the pneumonia cases are in the over-two-years age group and it is here that the mortality and incidence of empyema are significant. The mortality was less than one half during the mild than in the severe season and a corresponding reduction in number of empyemas will later be shown.

Table 2 shows the incidence of the common pathogenic bacteria found in sputum from 450 cases of pneumonia from September 8, 1939, to April 19, 1940. These figures are remarkable in their similarity to the figures reported in a similar table for 1938-39. Practically all of these figures represent single specimens of sputum from the patient on admission to hospital. The cultures from lungs, blood cultures and pleural fluids agreed with the results of the sputum examinations in early pneumonia in about 90 per cent. of the cases.

TABLE 2
SHOWING INCIDENCE OF PATHOGENIC ORGANISMS IN PNEUMONIA
SPUTA FROM SEPTEMBER 8, 1939, UNTIL APRIL 19, 1940

AGE	NO. OF CASES	PNEUMO- COCCUS	MORE THAN ONE TYPE	MORE THAN ONE PATHOGEN	STREP. HAEM.	H. INFLU- ENZAE	STAPH. AUREUS	OTHERS
Under 2 years.	184	131	14	23	19	13	42	15
Over 2 years.	266	222	32	25	25	17	24	7
Total ..	450	353	46	48	44	30	66	22
Per cent.		78.4		10.7	9.8	6.7	12.4	4.9

Forty-six or 13 per cent. of the 353 sputa with pneumococci present contained two types, and in two instances three types, in the same sputum. This multiplicity of types may be very confusing in infants in whom the common virulent pathogens such as I, II, or V are uncommon. Two types of pneumococci in the same sputum usually indicate a severe case of pneumonia. Also included is a column for the cases with more than one pathogen in the same sputum, which amounted to 10.7 per cent. In many of these cases it is extremely difficult to know whether the pneumococci or the coincident pathogen or both is the cause of the pneumonia. Probably the pneumococci should receive preference in the initial stages, whereas the other pathogen should receive more consideration in the later stages of the pneumonia. This is particularly true for cases which are not responding to chemotherapy. In the other columns is recorded the incidence of other pathogenic bacteria when occurring in sufficient numbers to be recorded. The streptococcus haemolyticus has decreased from 22 per cent. for 1938-39 to 9 per cent. for the past winter. This striking reduction in the incidence of streptococcus haemolyticus in the sputum will be reflected in the empyema table. The column dealing with staphylococcus aureus has been transferred to table III. In the last column it is seen that only 4.9 per cent. of the pneumonia cases did not contain definite etiological bacteria in their sputa. Most of these were 'late' cases of pneumonia probably receiving some specific therapy at home.

TABLE 3

SHOWING INCIDENCE OF STAPHYLOCOCCUS AUREUS IN SPUTUM AND LUNGS AFTER DEATH ACCORDING TO AGE GROUP FROM SEPTEMBER 8, 1938, TO JUNE 8, 1939 AND SEPTEMBER 8, 1939, TO APRIL 19, 1940

AGE	1938-39		1939-40	
	INCIDENCE OF STAPH. AUR. IN SPUTUM	DEATHS WITH STAPH. AUR. IN LUNGS (PER CENT.)	INCIDENCE OF STAPH. AUR. IN SPUTUM	DEATHS WITH STAPH. AUR. IN LUNGS (PER CENT.)
Under 2 years ..	49	32.7	42	23.8
Over 2 years ..	22	9.0	24	0

Last year we reported a disproportion in the incidence of staphylococcus aureus in sputum of infants as compared with children over two years of age, and a correspondingly high incidence in the lungs of infants under one year of age at death. During the 1939-40 season a similar disproportion has been observed and table 3 was drawn up to direct further attention to this fact. Staphylococcus aureus in sputum from the nasopharynx was only recorded when it was judged to be in sufficient amount in the direct smear and blood agar plate to be a likely etiological factor. The lung cultures were obtained only from cases of primary pneumonia. In many of these lung cultures (about 50 per cent.) other pathogenic bacteria besides the staphylococcus were present. In the table it is seen that in 1938-39, 32 per cent. of infants under two years of age with staphylococcus aureus in their sputum died either partly or solely as a result of this infection. This high incidence was slightly lower for the 1939-40 season, namely 23 per cent. In the over-two-years age group there were fewer cases with staphylococcus in the sputum and also a proportionately smaller death rate; in fact, there were no deaths in the mild season of 1939-40 as a result of this organism. It would appear, then, that staphylococcus aureus in the nasopharyngeal sputum of infants is more serious than in older children. The greatest contribution modern chemotherapy can make to the problem of children's pneumonia is in the reduction of the high mortality in infancy, which is chiefly due not so much to the pneumococcus, as to staphylococcus aureus. The minor rôle of the pneumococcus in the mortality of infants was clearly shown in the table of mortality according to etiological agent in last year's report. Table 4 also suggests that a reduction in mortality due to staphylococcus aureus is partly associated with the mild pneumonia season of 1939-40.

Table 4 shows the incidence of the common or important types of pneumococci occurring singly in sputum for 1939-40. The usual preponderance of higher types of pneumococci in the under-two-years age group is well demonstrated. Attention should be paid to the incidence of type I. There were only forty-one cases or 13 per cent. of type I pneumococci and the corresponding figure for last season was 79 or 28 per cent. This reduction is reflected in the

correspondingly low incidence of type I empyema as shown in table 5. The other common types found in the sputum were VI, XIV, XIX and XXIII, and are similar in their percentage incidence to 1938-39

TABLE 4
INCIDENCE OF IMPORTANT TYPES OF PNEUMOCOCCI OCCURRING SINGLY
IN PNEUMONIA SPUTUM FROM SEPTEMBER 8, 1939, TO APRIL 19, 1940

CASES			TYPES								
			I	II	V	VI	XIV	XV	XIX	XXIII	UTP *
Under 1 year	..	117	4	0	0	16	8	7	14	9	18
Over 2 years	..	190	37	13	16	8	10	6	16	10	18
Total	..	307	41	13	16	24	18	13	30	19	36
Per cent.	..	..	13.3	4.2	5.2	7.8	5.9	4.2	9.8	6.2	11.7

* Untypable pneumococci which were bile soluble.

Table 5 shows the incidence of empyemas for the severe pneumonia season of September 8, 1938, to June 8, 1939, as compared with the mild season of September 8, 1939, to April 19, 1940, according to etiology and age group. These figures include all the cases of empyema in the wards in the intervals stated. The most interesting feature is the fact that there were over four times the number of empyemas during the severe than the mild season. It is next seen that empyemas due to type I pneumococcus and streptococcus haemolyticus show the most profound decrease in incidence during the mild season. It is also noticeable that these cases mostly occur in the over-two-years age group. Staphylococcal empyemas were the same for both seasons and were predominantly in the under-two-years age group. It could be argued that this reduction in empyema incidence is due to the fact that more children were

TABLE 5
SHOWING INCIDENCE OF EMPYEMAS FOR THE SEVERE AND MILD
PNEUMONIA SEASON ACCORDING TO ETIOLOGY AND AGE

	TOTAL		TYPE I		OTHER TYPES OF PNEUMO.		STAPH. AUR.		STREP. HAEM.		H. IN- FLUENZAE		MIXED ORGANISMS	
	S	M	S	M	S	M	S	M	S	M	S	M	S	M
Under 2 years.	10	7	0	1	2	0	5	5	0	1	1	0	2	0
Over 2 years.	44	5	28	3	4	1	1	1	9	0	1	0	2	0
Total	54	12	28	4	6	1	6	6	9	1	2	0	4	0

receiving chemotherapy (chiefly sulphapyridine) during the mild than the severe pneumonia seasons. It is undoubtedly true that more children in the hospital received sulphapyridine during the past winter, but 50 per cent. of cases of empyema include, for both pneumonia seasons, children admitted to the hospital with empyema who probably received inadequate treatment at home. It is hardly likely that the chemotherapy administered at home by the family physician would greatly influence or lower this 50 per cent. portion of the empyema incidence during the mild season.

Table 6 shows the results of specific serum treatment for cases of early type I pneumonia. It can be observed from table 5 that, for the two pneumonia seasons there were altogether 39 cases of pneumococcic empyema, of which 32 or 82 per cent. were due to type I. So that pneumonia in children due to type I pneumococcus is a serious problem and deserves special attention. We reported last year that in a small series of seventy-four early type I pneumonia cases 20 per cent. of the controls developed empyema, 16 per cent. following specific serum therapy and only 8 per cent. following sulphapyridine therapy. This year it was decided to eliminate the controls and concentrate on the lowering of the incidence of empyema. It was also decided to compare the efficacy of sulphapyridine and sulphapyridine plus serum therapy in the prevention of empyema. I am fully aware that it would have been better to have included a control group in light of what has been shown as to seasonal variation in pneumonia virulence. However, the series would have been too small to be of any use if the fifty-three cases had been divided into three groups. As it is, the number of cases in each group is about the same as last season but with the exception that there are no controls. So it was planned to divide the pneumonias into two groups, the first receiving sulphapyridine alone, and the second sulphapyridine plus type I specific anti-pneumococcal rabbit sera, which was given intravenously. The serum was obtained from the Connaught Laboratories, Toronto.

TABLE 6
SHOWING RESULTS OF EARLY TYPE I PNEUMONIA CASES TREATED
IN SERIES FROM SEPTEMBER 8, 1939, TO APRIL 19, 1940

	SULPHA- PYRIDINE	SULPHA. AND SERUM	TOTAL
No. of cases ..	27	26	53
Empyema	0	2	2
Percentage of empyema	0	7.7	3.8
Surgical drainage ..	0	2	2
Deaths	0	0	0

It is seen that the incidence of empyema, 3.8 per cent., is far below last year's incidence even for last year's sulphapyridine figure of 8 per cent. Undoubtedly this reduction could not be due solely to early specific therapy. Although the point cannot be proved, we are satisfied that this figure is a minimum and only a passage of years will decide. It is interesting to note that the two cases of

empyema were following serum plus sulphapyridine. It is admitted that these figures are too small to be conclusive.

Discussion

This investigation emphasizes the fact that before pneumonia statistics for any particular year or month can be assessed seasonal variation must be taken into account. This is particularly true for controlled serial investigations such as we have conducted in respect to specific treatment for cases of early type I pneumonia during the past two years. The investigation suggests that seasonal variation both from month to month and year to year in respect to pneumonia incidence and virulence can occur. These fluctuations in pneumonia virulence are most noticeable in the over-two-years age group in which the reduction in empyemas due to type I pneumococcus and streptococcus haemolyticus was most marked. The decrease in mortality was also most apparent in the over-two-years age group. Further investigation of the figures from the point of view of meteorology and the incidence of nasopharyngitis should prove interesting.

Summary

Laboratory investigation of pneumonia in infants and children indicates that the severe pneumonia season of 1938–39 was associated with a rise in case incidence during December, January, February, and March with a high mortality, whereas the mild pneumonia season of 1939–40 was associated with a decrease in incidence and a relatively low fatality rate during these months.

The reduction in mortality was particularly noticeable in the over-two-years age group, in which it was less than half during the mild as compared with the severe pneumonia season.

A study of the etiological bacteria in the sputum for the two pneumonia seasons showed that there was a striking reduction in incidence of type I pneumococcus and streptococcus haemolyticus, which was further borne out by a marked reduction in the incidence of empyemas due to these organisms during the mild season.

Staphylococcus in the sputum of infants under two years of age is of serious portent. The high mortality and incidence of empyema in this age group is relatively unaffected by seasonal variation.

It is concluded that seasonal variation in pneumonia incidence and virulence for childhood pneumonia can occur both from month to month and year to year. This interesting fact deserves more investigation.

REFERENCES

- Auger, W. J. (1939a). *J. Pediat.*, **15**, 646.
— (1939b). *Loc. cit.*, 640.
— (1939c). *Brit. J. exp. Path.*, **20**, 439.