SEROLOGICAL EVIDENCE OF INFECTION WITH RESPIRATORY VIRUSES IN 1954-5

BY

P. J. WORMALD, M.D.

L. M. DOWSETT, M.D.

AND

J. H. C. WALKER, M.B., D.P.H.

From the Public Health Laboratory Service, Cambridge,
Norwich, and Luton

During routine diagnostic examination at the Public Health Laboratory, Cambridge, of sera from patients with acute upper respiratory infections, commonly designated " ? virus pneumonia," it was noticed that when results were plotted month by month they gave a clear index of the activity of various agents. In this report are described serological findings in patients who became ill during 1954 and 1955.

Materials and Methods

The majority of sera from Cambridge, of which 80% came from the Chest Clinic, were single specimens taken during the convalescent phase; those from Luton and Dunstable, of which nearly all came from the Chest Clinic, consisted of two specimens, one taken in convalescence and the other two to four weeks later. All sera were tested for complement fixation with influenza A and B soluble antigens, Q fever antigen, and psittacosis-LGV antigen; and for agglutination with streptococcus MG. Standard methods were used, similar to those employed at the Central Public Health Laboratory, Colindale, whence all the antigens were obtained except for the Q fever antigen; this was supplied by Dr. M. G. P. Stoker. All tests were done by one of us (P. J. W.) except for sera from 78 patients in Luton and Dunstable between January and November, 1954, which were carried out at Colindale.

Results

Aetiology, Month by Month, of Cases of "Virus" or Atypical Pneumonia

In the Chart and in Table I are analysed the results from 504 patients with clinical or radiological evidence of pneumonia. Diagnostic criteria have been taken as follows: in paired sera a fourfold or greater rise in titre; in convalescent sera a titre of 32 or above for influenza A or B, 80 or above for psittacosis-LGV, and 40 or above for streptococcus MG. No titres above 8 for Q fever were found except in one patient from Luton, whose serum remained steady at 32 in three convalescent and late specimens over a period of four months.

Patients in or near Cambridge (280).—A very sharp peak occurred in significant streptococcus MG titres in November and December, 1954, a wave of influenza B from December, 1954, to February, 1955, a small wave of influenza A from March to May, 1955, and an occasional psittacosis group infection. This was commoner in 1955 than in 1954. Large numbers of sera from patients with uncomplicated influenza during the epidemic period are, of course, excluded from these figures. No serological evidence of influenza A or B was detected in the winter of 1953-4, or in the winter of 1955 up to the end of the year.

Patients in Luton and Dunstable (224).—The distribution and prevalence of each entity is similar to that seen in

Cambridge, with the notable exception of the numbers with significant streptococcus MG titres in November and December, 1954, of which there were only 3 as against 42.

The 336 Patients (67%) With Negative Virus Serology.—Among the cases in Cambridge recorded as having negative serological findings, the four months in which numbers were greatly in excess of the average coincide precisely

Results of serological investigation of 504 cases of " ? virus pneumonia." ■ = Cambridge. □ = Luton and Dunstable. One square represents one case.

TABLE I.—Serological Investigation of 504 Cases of " ? Virus Pneumonia" with Onset During 1954-5

	Total No.	Total Pos.	Strep. MG.	Influenza		Q Fever	Psitt. LGV
				A	B		
Cambridge	280	111 (40)	78 (28)	5 (2)	17 (6)	—	11 (4)
Luton-Dunstable	224	57 (25)	20 (9)	5 (2)	17 (8)	1	14 (6)
Total	504	168 (33)	98 (19)	10 (2)	34 (7)	1	25 (5)

Figures in parentheses are percentages of totals.

with the peak of streptococcus MG activity and the wave of influenza B. This and the low-titre serological evidence (less than 40 and 32 respectively) in these four months suggest that at least some of the increase was due to these two agents. Similarly, the increase in Luton and Dunstable from December, 1954, to February, 1955, may be due to influenza B infections with serological titres of less than 32. Hence, apart from an unexplained increase in numbers from Luton and Dunstable in February to April, 1954, and irregular differences probably due to the small numbers, there is no fluctuation in incidence month by month other than the suggestion of a seasonal rhythm. Probably most of these cases fall into the non-specific aspiration and bacterial groups (Scadding, 1952).

Streptococcus MG Agglutinins in the Sera of Patients with Influenza in Norwich

As part of the M.R.C. influenza "spotting" scheme, paired sera from cases of clinical influenza, taken week by week from six different practices, were tested between December, 1954, and March, 1955. In mid-January the residue from a small batch was examined out of curiosity

for streptococcus MG agglutination. As several sera showed significant titres, all the pairs received subsequently were also tested. The results (Table II) show that sera from 22 of the 54 persons already had significantly high MG titres at the beginning of the influenzal attack, and that these did not increase during the course of illness. Inquiries were subsequently made from 51 of these persons. Only three of the MG positives and four of the MG negatives had any kind of history of upper respiratory infection during the previous six months, and none of pneumonia. Since there was thus no apparent clinical explanation for the MG agglutinins, 18 of the MG-positive persons and 13 of those from Cambridge who had had pneumonia were bled again 8 to 14 months later. In 28 out of the 31 the MG agglutinins had disappeared or greatly diminished (Table III), indicating that they had been formed from a relatively recent stimulus.

TABLE II.—54 Patients in Norwich with Clinical Influenza in January-March, 1955, from whom Paired Sera were Tested

Month of Onset	Streptococcus MG Titres	
	Negative or Less than 40	40 or Above
January	14	14 (50%)
February	11	6 (35%)
March	7	2 (22%)

All streptococcus MG titres remained stationary in paired sera except for 2 patients in whom they fell.

One patient in this series (not included in the table) developed symptoms of atypical pneumonia and the MG titre rose from negative to 80, and was negative again in a late specimen (9 months).

18 of these patients in January and 5 in February had influenza B.

TABLE III.—Disappearance of Streptococcus MG Agglutinins in Late Sera

"Virus" Pneumonia—Cambridge 13 Persons			Unspecified Stimulus—Norwich 18 Persons	
	Convalescent Sera	Late Sera (9-14 Months)	Early Sera	Late Sera (8-10 Months)
Titres	160 (3 persons)	80 (1); neg. (2)	160 (1 person)	20 (1)
	80 (5 ")	20 (1); neg. (4)	80 (5 persons)	40 (1); 20 (2); neg. (2)
	40 (5 ")	80 (1); 20 (1); neg. (3)	40 (12 ")	20 (5); 10 (1); neg. (6)

There appears to be a consistent reduction in the proportion of persons with significant MG agglutinins from January to March, 1955 (Table II). Among the January group 18 had influenza B, but there is no difference in the proportion of MG positives between them and the remaining 10 who were not serologically diagnosed influenza, and thus no suggestion that those who had developed MG antibodies were either more or less susceptible to an attack of influenza B.

These figures, therefore, indicate a very high prevalence of an agent stimulating MG agglutinins towards the end of 1954 (about the same time as the peak of MG activity in Cambridge), but with no clinical effect whatever in the group of persons examined.

Discussion

From the Chart and Table I it will be seen that if allowance is made for the epidemic of "streptococcus MG" pneumonia in Cambridge, and for 20% of the Cambridge sera having come from sources other than the Chest Clinic, the total numbers tested from Cambridge and from Luton and Dunstable are proportional to the populations from which the two sets of cases were drawn (approximately 100,000 and 130,000 respectively). If these are compared, the epidemic activity of influenza A and B is seen to be almost identical in the two places, and psittacosis group infections, though having no epidemic tendency, are also practically identical, even to showing a considerable increase in each locality in 1955. The contrast between the marked "streptococcus MG" activity in Cambridge in November and December, 1954, and its absence in Luton and Dunstable therefore appears all the sharper.

Although streptococcus MG agglutination is an empirical test, it is probable that these agglutinins are stimulated only as a result of infection with the agent or group of agents causing "primary atypical" or "virus" pneumonia (Stuart-Harris, 1953; Wilson and Miles, 1955). It is thought that many persons infected with this entity suffer from mild respiratory illness with no pneumonia, but though rates of 10 per 1,000 per annum have been recorded among Service personnel, and much higher rates in epidemics in small institutional populations, there are no reliable attack rates for civilian populations in general (American Public Health Association, 1955). Primary atypical pneumonia was thought to have reached a really high prevalence in the United States in 1940, and to have decreased strikingly in subsequent years (International Symposium, 1954). In England a report by the Virus Reference Laboratory (1953) for a two-years period in 1949-51 based on sera from patients in various parts of the country gave an overall figure of 38 (16%) of 241 cases diagnosed on streptococcus MG agglutination.

The evidence recorded above reveals in Cambridge a sharp epidemic prevalence in November and December, 1954, the same time as the school outbreak described by Wood (1956). The results of examinations on sera from numerous patients with acute respiratory infection or pneumonia in several other parts of East Anglia suggest that the prevalence covered a wide area. Figures from Norwich suggest, in addition, a very high infection rate with minimal clinical effects, at least among a quite widely dispersed group of people in one city.

The serological results from Luton and Dunstable among a series of cases clinically comparable to those in Cambridge do not support these findings, and neither do the figures of Shaw and Fry (1955), in which only 3 out of 70 cases occurring between October, 1954, and April, 1955, in a London suburb gave positive streptococcus MG tests. This epidemic prevalence was clearly less widespread than the activity of influenza virus B in the same winter.

Summary and Conclusion

Between January, 1954, and December, 1955, serological examination of 504 patients with pneumonia in Cambridge and in Luton and Dunstable gave a suggestive diagnosis in 168 cases (33%), comprising streptococcus MG 98 (19%), influenza A 10 (2%), influenza B 34 (7%), psittacosis-LGV 25 (5%), and Q fever 1 (possibly a previous infection). The epidemic waves which are concealed in such overall figures become apparent only when they are set out on a chronological basis.

In the winter of 1954-5 an agent of "primary atypical" pneumonia inducing streptococcus MG agglutinins developed a really high epidemic prevalence in Cambridge, Norwich, and possibly other parts of East Anglia, but not in Luton and Dunstable.

Our thanks are due to many clinicians for their helpful interest and for giving much valuable time, especially Drs. L. Capper and E. M. Cheffins, of the Chest Clinic, Cambridge; Drs. T. B. Anderson and A. S. Playfair, also of Cambridge; Drs. G. Barradell-Smith and P. Kissack, F. J. Bennett and F. C. Rutter, R. C. L. Brittain, E. F. Claridge, N. J. Pratt, and R. H. Scott, of Norwich; and Drs. Brian Shaw and M. A. Erooga, of the Chest Clinic, Luton. We are also indebted to Dr. F. O. MacCallum for his interest and advice.

REFERENCES

- American Public Health Association (1955). *Control of Communicable Diseases in Man*, p. 133. New York.
- International Symposium (1954). *The Dynamics of Virus and Rickettsial Infection*, p. 211. New York.
- Scadding, J. G. (1952). In *Diseases of the Chest*, edited by Sir Geoffrey Marshall and K. M. A. Perry, 1, 60. London.
- Shaw, A. B., and Fry, J. (1955). *British Medical Journal*, 2, 1580.
- Stuart-Harris, C. H. (1953). *Influenza and other Virus Infections of the Respiratory Tract*, p. 157. London.
- Virus Reference Laboratory (1953). *Lancet*, 1, 85.
- Wilson, G. S., and Miles, A. A. (1955). *Topley and Wilson's Principles of Bacteriology and Immunity*, 4th ed., p. 2100. London.
- Wood, P. (1956). *British Medical Journal*, 1, 711.