

## **Psittacosis/ornithosis in Cambridgeshire 1975–1983**

BY J. NAGINGTON

*Public Health Laboratory, Level 6, Addenbrooke's Hospital, Hills Road,  
Cambridge CB2 2QW*

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### **SUMMARY**

In a population of approximately 300 000 there were 150 illnesses attributable to chlamydial infection from January 1975 to June 1983 and nearly all were presumed due to *Chlamydia psittaci*. Diagnosis was based on the complement-fixation (CF) test, the disadvantages of which are discussed, especially anamnestic responses.

There were 73 cases of pneumonia, 37 febrile respiratory infections, 35 miscellaneous conditions and five asymptomatic seropositive contacts.

The annual number of cases was lowest in 1976 (3) and increased to a maximum in 1980 (28) followed by a sustained high level. No seasonal variation was observed.

A presumptive bird source was present in only 17% and detailed consideration of cases in one rural practice suggests that the infection may possibly be more endemic than zoonotic.

### **INTRODUCTION**

The diagnosis of psittacosis/ornithosis infections by the CF test has indicated an increase in the number of cases in recent years. One local country practice with an interest in respiratory infections has drawn attention to the frequency of cases with no bird connexion. The question arises – do the CF titres in these cases reflect genuine *Chlamydia psittaci* infections or could they be anamnestic responses to other infections? Two to three per cent of a normal population in one U.S.A. study had CF titres of  $\geq 16$ , 20% of veterinarians and sexually active women in San Francisco had such titres (Schachter & Dawson, 1978) and the same percentage of Scandinavian blood donors have been reported to have CF antibody (Broholm *et al.* 1977). With such a frequency of antibody anamnestic responses need to be considered. If the local infections are genuine, do they represent only a local situation or are they representative of a regional or national pattern? In either instance can we determine the part played by avian contacts and is there need for a reappraisal of those cases in which an avian source cannot be implicated?

The following is an account of the experience of the Public Health Laboratory, Cambridge, England, in the eight and a half years from January 1975 to June 1983.

## MATERIALS AND METHODS

*CF tests*

The CF test used is the standard one based on Bradstreet & Taylor (1962) adapted to U-well microtitre trays which require mechanical shaking with a Dynatech microshaker. Overnight fixation at 4 °C is followed by 30 min at 37 °C then sensitized sheep erythrocytes are added and incubation continued for a further 30 min. The end-point is the highest serum dilution to give 50% haemolysis.

The chlamydial group-specific antigen is supplied by the Department of Microbiological Reagents, Central Public Health Laboratory, Colindale, and it is made from the organism of ovine epidemic abortion (OEA).

Sera from patients with respiratory infections are titrated at dilutions from 1 in 8 to 1 in 256 against the antigens of influenza A and B, *C. psittaci*, *Coxiella burnetii*, *Mycoplasma pneumoniae* and adenovirus.

*Sera*

The diagnostic serum samples were those submitted by the hospitals and general practitioners served by the laboratory.

Blood-donor sera were kindly provided from three individual donor sessions by the Regional Blood Transfusion Service, Cambridge.

## RESULTS

*CF antibody titres*

In the diagnosis of psittacosis/ornithosis 'at best, the current status of chlamydial diagnostic serology leaves much to be desired' (Schachter & Dawson, 1979). Since we were restricted to the CF test it was necessary to make our own assessment of the value to be attributed to our results.

During the study period 10381 sera were examined for chlamydial antibodies. The results showed that there were 506 patients with a serum antibody titre  $\geq 16$ .

(a) Thirty-four of these patients provided paired sera with a 4-fold or greater rise in chlamydial antibody titre. Only three had CF titres suggestive of current or recent infection with other agents, i.e. two influenza B (titres 32 and 64) and one *M. pneumoniae*, titre 2048 (Fig. 1).

A 4-fold rise in chlamydial antibody is therefore unlikely to be due to one of the common infections for which we have tested and in the absence of such a second antibody we have accepted a 4-fold rise as diagnostic for the purpose of this study.

(b) Among the first 240 patients who provided single samples with a titre of  $\geq 16$  or multiple samples in which the titre was constant there were 90 (37%) who had one or more other CF antibodies at titres we find indicative of recent or current infection, i.e.  $\geq 32$  for influenza A and B,  $\geq 64$  for adenovirus and  $\geq 128$  for *M. pneumoniae* and *C. burnetii* (Fig. 2).

This proportion of high CF titres to other agents associated with chlamydial CF titres of  $\geq 16$  indicates that the latter may be due to an anamnestic response and none can be taken unequivocally to signify recent chlamydial infection. It is of

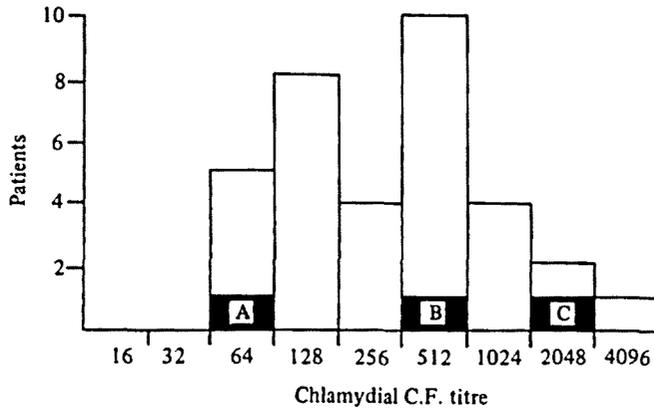


Fig. 1. Maximum CF titres in 34 patients with 4-fold or greater rise in chlamydial CF antibody titre. High CF titres to other agents are indicated by A (*M. pneumoniae* titre 2048), B (influenza B titre 64) and C (influenza B titre 32).

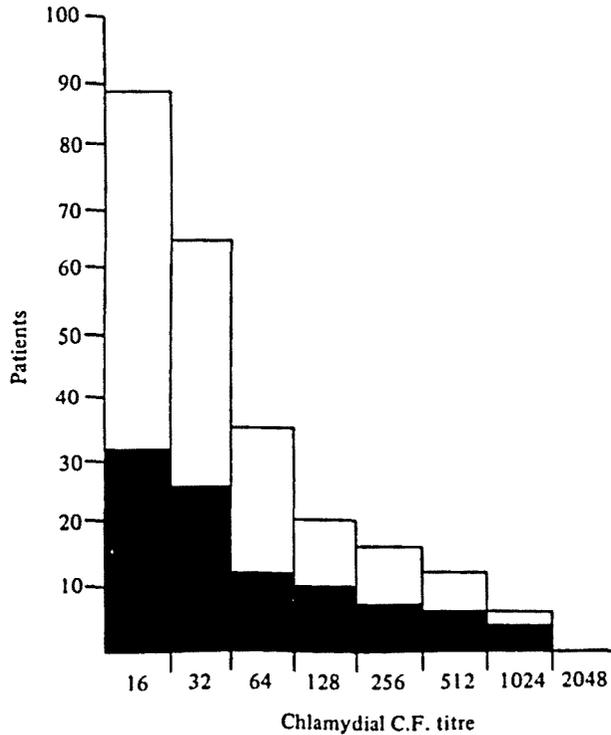


Fig. 2. High CF titres to other agents (shaded columns) among 240 patients with a single or repeated samples giving a chlamydial CF antibody titre of  $\geq 16$ .

course possible that associated high titres can themselves be due to a general increase in antibody production or to a chlamydial infection itself.

Thus we consider that there is serological evidence of recent chlamydial infection when a 4-fold rise or a single or constant titre of  $\geq 128$  without an associated antibody to one of the commoner respiratory infections is demonstrated.

Table 1. Comparison of results of Cambridge survey with those of England and Wales

Year	Sera tested	Cambridge survey				Total positives in England and Wales †
		Patients positive			Patients with titres 16-64 with or without associated titres	
		4-fold rise	> 128*	Total		
1975	647	8	9	17	30	176
1976	1003	0	3	3	22	167
1977	884	1	4	5	40	129
1978	1243	2	7	9	34	111
1979	1896	3	11	14	23	176
1980	996	6	22	28	54	373
1981	974	2	22	24	31	352
1982	1623	5	21	26	47	309
1983‡	1115	7	17	24	75	N/A
	10381	34	116	150	356	1793

\* No associated infection demonstrable.

† Figures supplied by Communicable Disease Surveillance Centre, unpublished. They are based on titres of  $\geq 256$  or 4-fold rise.

‡ January to June.

## RESULTS

### *Incidence of infections in Cambridgeshire and adjacent areas*

During the study period there were 150 patients with serological evidence of chlamydial infection by our criteria. These differ slightly from those of the Communicable Disease Surveillance Centre, Colindale, who use a titre of  $\geq 256$  or a 4-fold rise. When comparison is made between the Cambridge figures and those for England and Wales (Table 1) it can be seen that local events mirror the national trend despite the much smaller sample. In each instance the lowest incidence was in 1976-8, followed by a rise to a fairly constant higher level in 1980-2. The bulk of the increase is in single or repeated high titre samples and this conforms to the national trend in which 60% of the increase in reported cases in 1980 was based on single high titres (Palmer, 1981).

To what extent our sample of the local population is an indication of the total number of infections is hard to estimate. The population in the Cambridge Health Authority is currently 262800 and an approximation of the population served by this laboratory is probably about 300000, of which about half can be considered urban. Thus the rate of infection in the population served by the laboratory is 1 per 2000 over the eight and a half years of the study.

### *Incidence of infection in Practice A*

Practice A is a rural one on the Huntingdon/Cambridgeshire border and in June 1983 had 4292 patients. The practice conducts serological examination of patients with respiratory infections more thoroughly than most and is therefore likely to show the true incidence perhaps more than indicating a genuinely higher local incidence.

**Table 2. Patients in practice A 1982–1983**

No.	Sex	Age	Onset	Occupation	Possible source of infection
1	F	49	17 July 82	Cook/waitress café	—
2	M	48	13 Oct. 82	Lecturer in education	—
3	F	11	20 Dec. 82	Schoolgirl (A)	Household contacts
4	M	38	26 Dec. 82	Car salesman	
5	M	13	—	Schoolboy (A)	
6	M	13	2 Feb. 83	Schoolboy (A)	Exposed to poultry two months previously
7	F	37	21 Feb. 83	Schoolteacher (B)	Household contact of patient 6
8	F	45	1 Mar. 83	Secretary	—
9	M	55	10 Mar. 83	Accountant	—
10	F	51	25 Mar. 83	School canteen (C)	—
11	F	21	3 Apr. 83	Housewife	Household contacts and exotic birds in house
12	M	21	10 Apr. 83	Storeman	
13	M	15	5 May 83	Schoolboy (A)	—
14	F	13	13 June 83	Schoolgirl (A)	Looked after budgerigar previous week

All patients had pneumonia or lower respiratory tract infections, except number 5 who was asymptomatic.

\* A, B, C denote different schools. Children in school A all in separate classes, patient 13 in separate Upper School.

There were 18 symptomatic cases in the practice during the course of the study and this gives an approximate case rate of 1 per 240 over eight and a half years. This is almost ten times the rate in the local population as a whole.

In the seven years 1975–81 there were five clinically and serologically acceptable cases of psittacosis/ornithosis. In the year July 1982 to June 1983 inclusive there were 13 symptomatic cases and one asymptomatic family contact with serological evidence of infection (Table 2). Three of the 13 had good evidence for birds being the source of infection – a husband and wife who kept exotic birds in the house and a schoolgirl who looked after a neighbour’s budgerigar for the week before she became ill. No attempt was made to confirm infection in any of these birds.

The other 10 cases had no evidence of direct bird contact although a schoolboy had worked on a farm with a deep-litter poultry house 8 weeks before his illness.

The only common feature was an association with schools in six instances – three school children aged 11, 13 and 15 years (the asymptomatic family contact was also a schoolboy, aged 13 years), one teacher, one school-dinner lady and one lecturer in education. However, none of the children was in the same class as another case, the teacher was from a different school, the school dinner lady from a third school and the lecturer occasionally visited various schools. None of the schools had birds or other animals on the premises.

*Blood donors*

The incidence of chlamydial antibody in blood donors is sometimes used as a guide to the frequency of infections in the population. To see if different areas in our catchment population showed any variation, groups of donors from east and west rural areas were compared with Cambridge urban donors. There were none with CF titres > 64 and the 2-fold difference between the groups is not considered

Table 3. *Chlamydial CF titres of blood donor sera*

No. tested ...	West (St Neots)	Cambridge	East (Ely)	Total (%)
	100	100	88	288
<b>Titre</b>				
64	1	1	0	2 (0.7)
32	1	3	5	9 (3.1)
16	3	4	1	8 (2.7)
8	1	4	5	10 (3.5)
< 8	94	88	77	261 (90)
<b>Total with antibody</b>	<b>6 (6)</b>	<b>12 (12)</b>	<b>11 (12.5)</b>	<b>29 (10)</b>

Table 4. *Symptoms at presentation*

73 pneumonia	1 with cardiomyopathy and mitral stenosis; 1 with erythema nodosum; 1 with rash on arms
37 fever and cough	1 with heart murmur, 1 with erythema nodosum
34 miscellaneous	11 pyrexia of unknown origin 6 coryza 4 chronic cough 3 L.G.V. or inguinal lymphadenopathy 2 cardiomyopathy 2 erythema nodosum 1 erythema nodosum plus rash on arms 1 rash on arms 1 chest pain 1 fever, jaundice and haematuria 1 sore throat and myalgia
5 no symptoms	
1 no information	

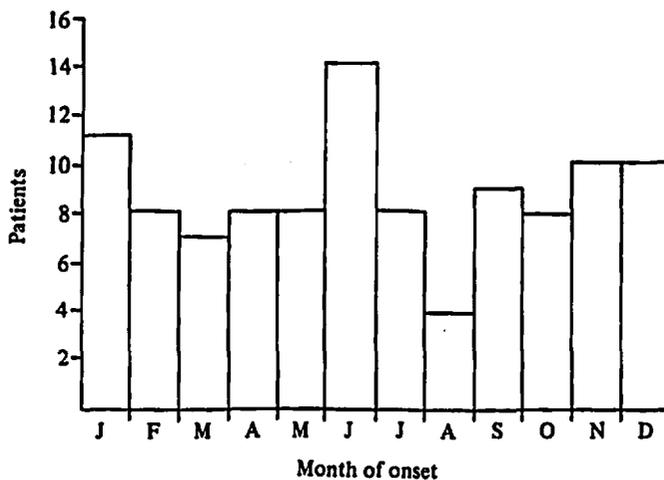


Fig. 3. Distribution of date of onset of the 105 cases for which the date was known (1975-1982).

Table 5. *Type of infection in positive patients*

	Pneumonia	Cough and fever	Others	Total
1975	8 (A <sub>4</sub> B <sub>1</sub> )	2 (A <sub>1</sub> )	7	17
1976	0	0	3	3
1977	2	2	1	5
1978	2	2	5 (B <sub>2</sub> )	9
1979	6 (A <sub>1</sub> )	5 (B <sub>1</sub> )	3	14
1980	16 (C <sub>2</sub> )	7	5 (B <sub>1</sub> )	28
1981	11	6 (C <sub>1</sub> )	7 (A <sub>1</sub> )	24
1982	13 (A <sub>1</sub> )	6 (A <sub>1</sub> )	7 (A <sub>2</sub> )	26
1983 (Jan.–June)	15 (A <sub>2</sub> B <sub>1</sub> D <sub>2</sub> )	7	2	24
	73	37	40	150

The codes in parentheses signify the association with birds (A, psittacine; B, poultry; C, ducks; D, exotic caged birds). The suffix is the number of cases associated with each group of birds.

Table 6. *Association of cases of C. psittaci infection with birds*

Symptom group	No. of patients	Psittacine	Poultry	Ducks	Cage birds	Total (%)
Pneumonia	73	9*	2	2	2	15 (20)
Cough and fever	37	2	1	1	0	4 (10.8)
Coryza	6	0	1	0	0	1 —
Others	34	4	2	0	0	6 (17.6)
Total	150	15	6	3	2	26 (17)

\* Three members of one family.

significant (Table 3). The west area is representative of the area of Practice A. These figures are lower than those of surveys in Sweden (20%) (Broholm *et al.* 1977), Finland (21.6%) (Janssen, 1960) and in Australia (22%) (Dane, 1955).

*Symptoms*

The number of patients diagnosed as chlamydial infections seemed high and it appeared relevant to see if the symptoms were compatible with *C. psittaci* infection. As can be seen from Table 4 there were 73/150 with unequivocal pneumonia and many of the 37 who presented with a fever and cough were likely to have had lower respiratory infections. Thus the cases were compatible with *C. psittaci* infection and only a few likely to have been *C. trachomatis* infections.

*Seasonal incidence*

The distribution of cases where the date of onset was known was practically constant throughout the year (Fig. 3). This contrasts with patients with titres of 16–64 who had a winter peak and summer trough, as might be anticipated from antibody levels subject to anamnestic variation in relation to other winter respiratory infections.

The annual number of cases with pneumonia, cough and fever rose conspicuously in 1979–80 whereas the number with other symptoms was less affected. (Table 5).

*Association with birds*

Birds were a possible source of infection in 26 of the 150 patients (Table 6) and psittacines were the most conspicuous. In Practice A there were 11 instances of infection in 1982/3 if each of the family clusters is regarded as one instance. There was an association with birds in only two of these 11 instances. This parallels the results with the group of 150.

## DISCUSSION

The object of this study was to try to discover the nature of the local situation with regard to chlamydial antibody responses in respiratory infections. It is apparent that the interpretation of results is made difficult by the background of CF antibody in about 10% of the population. This antibody can rise anamnesticly in individuals with non-chlamydial respiratory infections and probably in other infections. We have observed this in specific infections (Fig. 2) and by an increase in the frequency of low titres in the population during the winter months. Any serological study or laboratory diagnosis of a sick patient must take this factor into account.

The source of the background level of antibody in the population is unclear. *C. trachomatis* from genital infections may contribute (Schachter & Dawson, 1978) but we are short of data and the general impression is more that of a population exposed to endemic infection, chlamydial or bacterial. The source of antigenic overlap to produce anamnestic antibody rise is unclear. *Acinetobacter calcoaceticus* antibody has been demonstrated in psittacosis (Volkert & Matthieson, 1956; Brade & Brunner, 1979, 1980) and Ormsbee *et al.* (1978) found unconvincing evidence of a relationship with a strain of *Legionella pneumophila*.

We diagnosed acute chlamydial infection on the basis of a CF antibody rise or a single titre of  $\geq 128$ , unassociated with any other infection diagnosable by commonly available tests. This yielded 150 cases in eight and a half years and we were surprised by this high figure. It may be incorrect, from the factors already discussed and perhaps more rigid criteria should be applied. However, the criteria are reasonably representative of what is accepted in this country as diagnostic of psittacosis/ornithosis (Palmer, 1981). It has long been known that genuine infections may produce a minimal antibody response, so low that it could be missed; for example, McKendrick, Davies & Dutton (1973) had to ether-extract the antigen to demonstrate diagnostic levels of antibody and tetracycline can markedly reduce the antibody response (Schachter & Dawson, 1978). In view of the high rate of infection in Cambridgeshire generally and of the infection rate in a practice that actively seeks a diagnosis it would seem more than likely that our figures represent an underestimate of the infections occurring. If this is so for the rest of the country the underestimate would be considerable.

The clinical details of the 150 cases are so predominantly respiratory that it seems reasonable to consider them as due to *C. psittaci* and not to *C. trachomatis*, since the latter has only been associated with lower respiratory infections of neonates (Harrison *et al.* 1978), and immunosuppressed adults (Tack *et al.* 1980). They reflect the national incidence and lead to the inference that the national figures are also likely to be indicative of *C. psittaci* infections.

Two aspects of the current series of cases are especially interesting – the low incidence in 1976–8 with a rise to a higher level in 1980–2, and the lack of association with birds.

Several factors may have influenced the variation in the number of diagnoses. The introduction of diagnostic tests for Legionnaires' disease in 1978 led to an increased interest in the serological diagnosis of respiratory tract infections. The imposition of the Captive Birds Order, March 1976, designed to prevent importation of Newcastle Disease virus, required 35 days quarantine on all imported birds, including psittacines, and may possibly have reduced temporarily the number of *C. psittaci* excretors imported (the Ornithosis Order was rescinded in 1966 so this would not be relevant). Serological diagnosis by CF was improved in July 1977 when the human *C. psittaci* strain EPY 135 used for antigen preparation was replaced by the OEA strain.

In the winter of 1979–80 infections were first indentified in the duck-rearing industry in this country (Andrews, Major & Palmer, 1981; Palmer, Andrews & Major, 1981), although they have been known for 30 years in Europe (Strauss, 1967), where the infection is regarded as an occupational disease in the duck industry.

To what extent these factors may have contributed is conjectural. We may only be recording the normal fluctuations that occur in any infectious disease. Even so there does appear to be a real increase in the annual number of cases since 1979–80.

The association with birds in 17% of instances in the series is based on normal questioning procedures and provides only a rough guide, although it is similar to the national rate. In Practice A much more detailed investigation was used, the patients were questioned on several occasions by different individuals yet good evidence for birds being the source of infection was only discoverable in two episodes. The findings in this practice may reflect the epidemiology of psittacosis/ornithosis in the world outside.

So, although there is no doubt that psittacines and other birds are the direct cause of some infections, and this has long been established, we are left with the problem of the source of infection in about 80% of cases. Is the environment a continuous source of infection from dried bird excreta? If so this might explain the absence of any seasonal change in the incidence of cases. Is it time for a change in our attitude to the epidemiology of *C. psittaci*? Should we not consider the possibility that case-to-case transmission plays a greater role than we have attributed to it? In most instances it is virtually impossible to distinguish possible patient-to-patient infection from common source infection. There is convincing documentary evidence for the spread of *C. psittaci*, from coughing pneumonic patients to close contacts such as nursing staff (cited by Schachter & Dawson, 1978; Christie, 1980) and similar instances have been observed by Pether (personal communication) and Nagington & Hambling, 1982.

We have encountered six patients with predominantly coryzal symptoms and two pneumonia cases had acute coryza with rhinorrhoea for about a week before the pneumonia. One infected her sister, whom she met only during the coryzal stage. All the patients with respiratory infections had a cough and some had a chronic cough even before the onset. It is known that infectious droplets can be shed during convalescence and even long-term carriage has been recorded (Schachter & Dawson, 1978; Meyer & Eddie, 1951). Schoolchildren are likely not

only to be susceptible to infection but also to be impartial about their distribution of droplets by coughing. Perhaps there is sufficient infectivity in the early stages of infection for case-to-case transmission to be a more important mode of spread than is realized.

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