

The Incidence and Aetiology of Respiratory Tract Infections in General Practice – with Emphasis on *Mycoplasma pneumoniae*

Summary: The incidence of respiratory tract infections in patients seeking medical advice at a community care centre (Dalby) during 1973 and 1974 was studied. About every third patient seen at this primary health station presented with signs of such infections. In the age groups <10, 10–19, 20–39, 40–59 and ≥60 years, respiratory tract infections accounted for 65, 45, 32, 18 and 9% of the total number of diagnoses made during 1974. The aetiology of acute respiratory tract infections in a series of patients seen at this health station was studied. The series included randomly selected cases, but excluded children under seven years of age and patients presenting with signs of acute otitis media and tonsillitis. Attempts to establish the aetiology were made on the basis of the history, the clinical examination, and cultures for beta-haemolytic streptococci and *Mycoplasma pneumoniae*, complement fixation tests for influenza A and B, para-influenza 1, 2, and 3, adeno, cytomegalovirus and respiratory syncytial virus, and *Chlamydia psittaci*. Paul-Bunnell test and tests for cold agglutinins were also performed. With this test battery, an aetiological diagnosis was obtained in only 33% of the 101 patients studied. The findings suggest an infection with *M. pneumoniae* in 16%, with beta-haemolytic streptococci in 9%, and with viruses (adeno and para-influenza) in 7% of the patients. The present communication highlights the role of *M. pneumoniae* in upper respiratory infections, as few data have appeared on such infections in patients seen in general practice. The difficulty of establishing the aetiology of respiratory tract infections and the consequent treatment dilemma is discussed.

Introduction

Symptoms of respiratory tract infection are one of the most common reasons for a patient to seek a consultation with his physician. The causative agents of respiratory tract infections are known to vary with the season, climate, age of the population, and with the epidemiological environment. Therefore the relative importance of the various agents involved varies widely. It is well known that viruses are the cause of the majority of these infections. More than 150 different viruses have so far been shown to cause infections of the respiratory tract (17). There are only minor differences between the clinical signs and symptoms of the infections caused by various viruses. This is also true of respiratory tract infections caused by bacteria, including those caused by beta haemolytic streptococci (4, 5). It is therefore difficult to establish the aetiology on the basis of the clinical picture in any of these infections.

Mycoplasma pneumoniae is known as an important aetiological agent in pneumonia (11) but its relative importance in upper respiratory tract infection is still uncertain. In

Zusammenfassung: Häufigkeit und Ätiologie von Atemwegsinfektionen in der Allgemeinpraxis unter besonderer Berücksichtigung von *Mycoplasma pneumoniae*. Bei Patienten des Community Care Centers (Dalby) wurde in den Jahren 1973 und 1974 die Häufigkeit von Atemwegsinfektionen untersucht. Bei ungefähr jedem dritten der Patienten, die zu dieser Gesundheits-Hauptberatungsstelle kamen, lagen Symptome einer solchen Infektion vor. In den Altersgruppen <10, 10–19, 20–39, 40–59 und ≥60 machten Atemwegsinfektionen 65, 45, 32, 18 bzw. 9% der Diagnosen aus, die 1974 insgesamt gestellt wurden. Die Ätiologie akuter Atemwegsinfektionen wurde bei einer Reihe von Patienten dieser Beratungsstelle untersucht. Die Patienten wurden willkürlich ausgewählt, jedoch waren Kinder unter 7 Jahren sowie Patienten mit Symptomen einer akuten Otitis media oder Tonsillitis von der Prüfung ausgeschlossen. Die Feststellung der Ätiologie stützte sich auf Krankengeschichte, klinische Untersuchung sowie Kulturen auf β-hämolytische Streptokokken und *Mycoplasma pneumoniae*, Komplementbindungstests auf den Influenzavirus A und B, den Parainfluenzavirus 1, 2 und 3, Adenovirus, Zytomegalievirus und RS-Virus sowie auf *Chlamydia psittaci*. Ferner wurden der Paul-Bunnell-Test und der Test auf Kälteagglutinine durchgeführt. Mit dieser Testreihe wurde nur bei 32% der 101 untersuchten Patienten eine ätiologische Diagnose erzielt. Wie aus den Befunden hervorging, war die Infektion bei 16% auf *M. pneumoniae* zurückzuführen, bei 9% auf β-hämolytische Streptokokken und bei 7% auf Viren (Adenovirus und Parainfluenzaviren). Der vorliegende Bericht macht deutlich, welche Rolle *M. pneumoniae* bei Infektionen der oberen Atemwege spielt, da bisher wenig Angaben über diese Art von Infektionen bei Patienten von Allgemeinpraktikern vorliegen. In dem Bericht werden die Schwierigkeit, die Ätiologie von Atemwegsinfektionen festzustellen, und die sich daraus ergebenden Therapieprobleme diskutiert.

non-epidemic periods infections with this organism are known to be endemic. Epidemics seem to occur every fourth to fifth year (22). Infections are seen in all ages but are more common in older children. The incubation period is usually three weeks or more. The contagiousness is relatively low and spread of the infection seems to occur after prolonged and close contact, for example within families (12). A number of extra-respiratory tract manifestations have been described, including manifestations in the central nervous system (2, 28), the skin and the mucous membranes, and in parenchymatous organs such as the liver and the pancreas (26). It is rare for infections with *M. pneumoniae* to be fatal.

The present study reports the results of a survey of the incidence and aetiology of respiratory tract infections in patients who were seen at a Community Care Centre. In this survey particular attention was given to the role *M. pneu-*

Dr. P.-A. Mårdh, Institute of Medical Microbiology, University of Lund, Sölvegatan 23, S-22 362 Lund, Sweden.

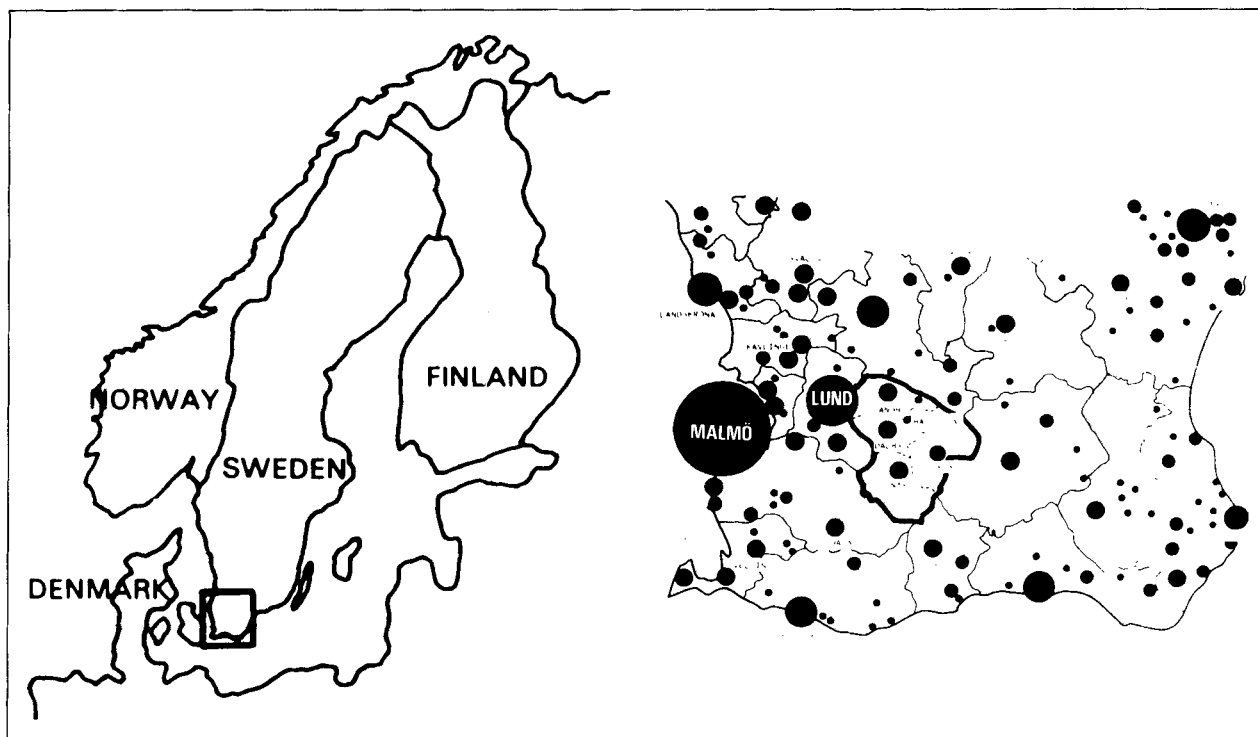


Figure 1: Map of Scandinavia (left). The square indicates the province of Skåne, the southern part of which is shown on the map to the right. It shows the Dalby Community Care District (thick, black border) (15,000 inhabitants), the towns of Lund (70,000 inhabitants) and Malmö (265,000 inhabitants).

moniae may play in upper respiratory tract infections. The value of the clinical examination and of microbiological tests in the establishment of the aetiology of respiratory tract infections is considered.

Materials and Methods

Incidence studies

One of the objectives of the Community Care Sciences Centre at Dalby, Sweden, is to perform research in general practice. It is a primary health station serving an area with a mixed rural and urban population of about 15,000 inhabitants. These inhabitants visit the Centre about 10,000 times each year. About 40% of the population is engaged in agriculture, and the remainder work at manufacturing, construction, in trade, or are in the public service. The village of Dalby is situated about ten kilometers from Lund, which is a university town with about 70,000 inhabitants. Dalby lies 24 kilometers from Malmö with its 265,000 inhabitants. Many of those living in the Dalby district are employed in these two towns (Figure 1).

Incidence of respiratory tract infections

The incidence of respiratory tract infections was determined in those seeking advice at the Dalby Community Care Centre during 1973 and 1974. The diagnoses which were made at the centre were coded according to the World Health Organization International Statistical Classification of Diseases, Injuries and Causes of Death.

Aetiological Studies

Clinical material

One hundred and thirteen patients with signs and symptoms of acute respiratory infection selected at random were studied. The age and sex distribution are shown in Figure 2. These patients

sought medical advice at the Division of Community Care Sciences, Dalby, or at a primary health station (ÖVC) in Lund, Sweden. The study was performed during August and September, 1975. Patients under the age of seven were excluded as it was not practical to draw blood from these young patients at a busy health clinic and it was not justified in view of the diagnosis of the children's condition. Patients with acute otitis media or obvious signs of acute tonsillitis were also excluded. All patients in the study paid their first visit to a doctor for the condition under study and had not taken any antibiotics prior to the visit.

The patients were asked to describe their symptoms (Table 8) and to note the day of their onset. A clinical examination was performed and the results recorded. A blood sample was drawn and the patients were instructed to return after two weeks for a second blood specimen to be collected. One hundred and one patients out of 113 returned. A control group was formed of 101 patients who presented to the Centre with symptoms other than those related to the respiratory tract. This control group was matched by sex and age to the patients with respiratory tract infections. One serum sample was drawn from these patients for serological tests.

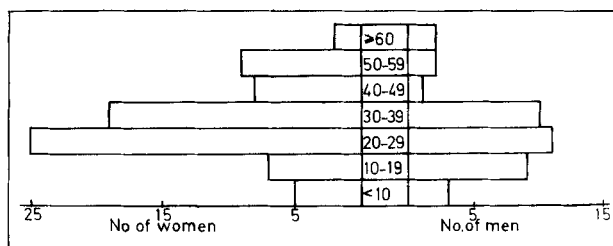
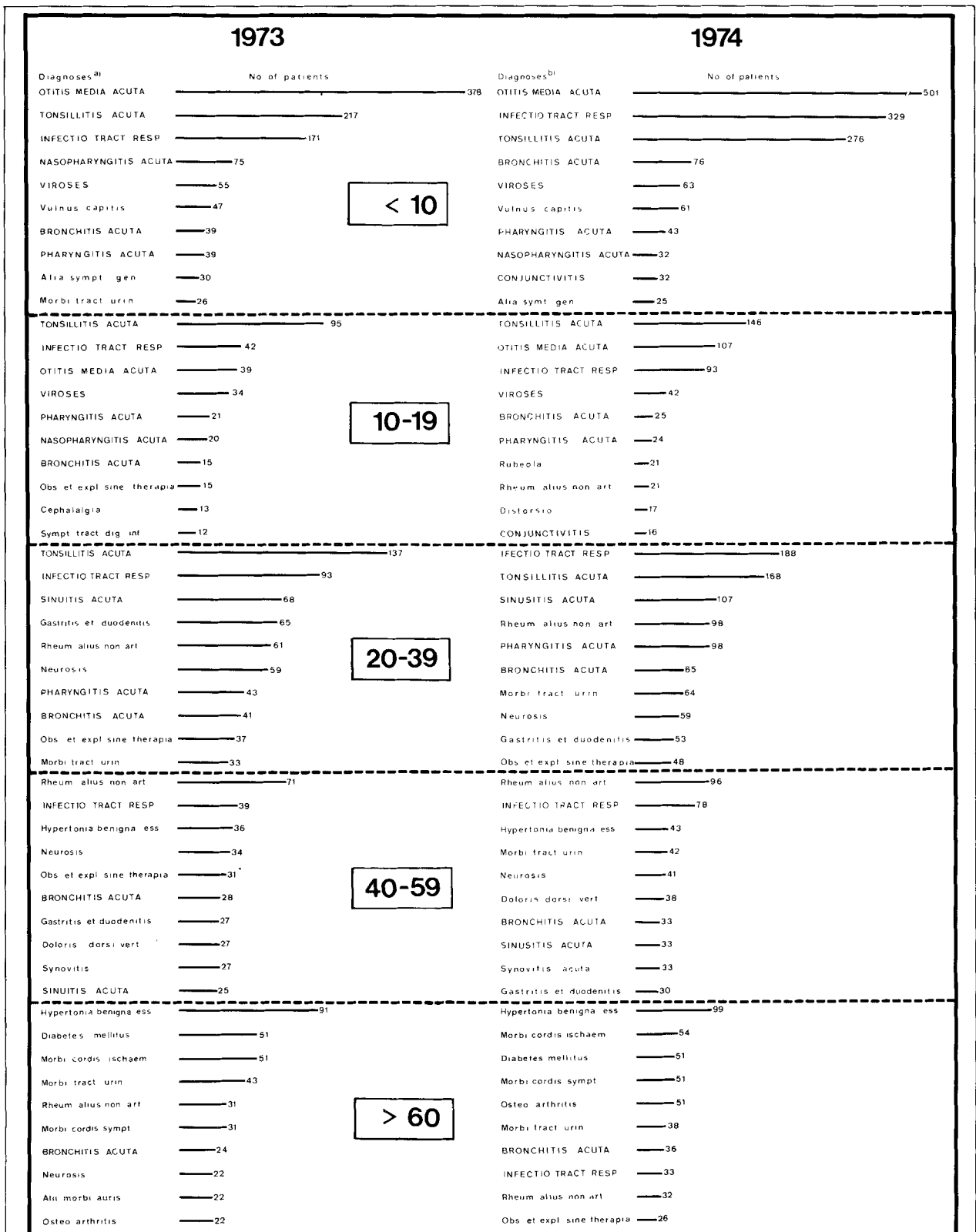


Figure 2: The figure shows the age and sex distribution of the investigated patients with respiratory tract infection.



(a) The total number of diagnoses made in 1973 was 6,689. In the five age groups studied, the corresponding figures were 1,662, 746, 1,923, 1,144, and 1,214, respectively.
 (b) The total number of diagnoses made in 1974 was 8,117. In the five age groups studied, the corresponding figures were 2,095, 1,036, 2,333, 1,314, and 1,339, respectively.

Figure 3: The ten most common diagnoses made in each of 5 age groups seeking advice at the Dalby Community Care Centre during 1973 (left) and 1974 (right).

Culture techniques

Beta-haemolytic streptococci. In all the patients with signs and symptoms of respiratory tract infection a culture was taken from the oropharynx. This was obtained with a cotton-tipped swab and inoculated directly onto a blood agar plate which contained 4% horse and 4% sheep blood. Isolated streptococci were grouped according to a method described by Christensen *et al* (8).

Mycoplasmas. Cultures for mycoplasmas were made from the last 59 patients in the respiratory infection group. The specimens were collected with a cotton-tipped swab from the oro-pharynx and inoculated directly onto three different solid media. Medium "A" consisted of seven parts of heart infusion agar (Difco), two parts of unheated horse serum (v/v), one part of a 25% (w/v) aqueous fresh yeast extract, and 0.002% (w/v) desoxyribonucleic acid (Sigma). Penicillin G (1000 IU/ml) and thallium acetate (final concentration 1:40,000) were used as bacterial inhibitors. Medium "B" consisted of the same basic ingredients, but was supplemented with 0.5 mg 2-mercaptoethanol (Sigma) per ml. Medium "C" also had the same basic composition, but to this medium was added 0.5 mg of L-cysteine hydrochloride (Merck) per ml. The agar plates were incubated at 37°C in a humid atmosphere of 90% N₂ and 10% CO₂. The plates were examined for the presence of colonies at regular intervals by the aid of a stereo-microscope (x120). The plates were discarded after four weeks, if no colonies had been observed. The isolated strains of mycoplasma were identified as to species by growth-inhibition tests using antiserum impregnated paper discs (32).

Serological techniques

Sera were stored at -20°C until tested. Complement fixation (CF) tests were performed by a micro-titration technique using disposable plates with the following antigens:

Mycoplasma pneumoniae. The *M. pneumoniae* antigen was a chloroform-methanol extract (19) of organisms detached from the glass after growth in Roux bottles (21). This antigen was kindly supplied by Dr. K. Lind, Statens Seruminstitut, Copenhagen.

Viruses. The sera were tested against influenza A and B, para-influenza 1, 2, and 3, as well as against cytomegalovirus (CMV). The antigens were obtained from Statens Bakteriologiska Laboratorium, Solna, Sweden. The sera were also tested against an adenovirus antigen prepared in our own laboratory, and the sera of persons above the age of 60 were tested against a respiratory syncytial (RS) virus antigen (Flow Labs., Ltd.).

Chlamydia. The sera were tested against a *Chlamydia psittaci* antigen (Wellcome) for group-specific antibodies to chlamydia.

Cold agglutinins

The sera were assayed for cold agglutinins with a 0.2% solution of group 0 erythrocytes from adults. Duplicate serum dilutions were made in saline to which was added a 10% erythrocyte suspension. The readings were made macroscopically after overnight incubation at 4°C.

Paul-Bunnell test

The Paul-Bunnell test was performed according to the method described by Davidsohn (9).

Results

Incidence of respiratory tract infections in patients seen at Dalby Community Care Centre during 1973 and 1974

The ten most frequent diagnoses in various age groups of the patients seeking medical attention at the Dalby Community Care Centre during 1973 and 1974 are shown in Figure 3. Respiratory tract infections accounted for about 30% of all the diagnoses made during these two years. Acute otitis media, acute tonsillitis, "respiratory tract infection", acute na-

so-pharyngitis, virosis, acute bronchitis, acute pharyngitis and conjunctivitis, were represented among the ten most frequent diagnoses. In 1974, respiratory tract infections accounted for about 65% of all the diagnoses in the children under ten years of age. The corresponding percentage in the age groups 10-19, 20-39, 40-59 and ≥60 years was 45, 32, 18, and 9%.

Isolation of beta-haemolytic streptococci

Beta-haemolytic streptococci were recovered from the oropharynx of ten of the 101 patients studied. Eight of these were group A and two were group G streptococci, while no group C streptococci were found. As indicated, the series did not include patients presenting clinical signs of acute tonsillitis.

Isolation of mycoplasmas

M. pneumoniae was recovered from seven patients when the cysteine hydrochloride containing medium (medium "C") was used. The organism was only recovered in one instance when medium "A", and in two when medium "B" was used. This difference between the three media tested was not observed for other species of mycoplasma (Table 1).

Complement fixation tests

Viruses. The numbers of cases who had a significant change in the titre of CF antibodies to para-influenza 2 and 3 and to

Table 1: Isolation of mycoplasmas from the oro-pharynx of 59 patients with signs of non-pneumonic respiratory tract infection by the use of 3 different culture media

Medium*	Organism isolated		
	<i>M. pneumoniae</i>	<i>M. hominis</i>	<i>M. salivarium</i> and/or <i>M. orale</i>
Basic	1	1	6
Basic + 2-mercaptoethanol	2	1	7
Basic + L-cysteine hydrochloride	7	1	8

*See text

Table 2: CF antibodies (titre ≥ 1:10) to some viruses in 101 randomly selected patients with respiratory tract infection* and 101 controls

Virus	Patients	Controls
Influenza A	70	79
B	56	63
Para-influenza 1	21	17
2	61	67
3	84	76
Adeno	73	68
CMV	49	51

*Children below the age of 7 and patients with acute otitis media and acute tonsillitis were excluded

Table 3: CF antibody titres against influenza A and B in 101 randomly selected patients with respiratory tract infection* and 101 controls (reciprocal of serum dilutions)

Antigen	Group	CF antibody titre			
		≤ 5	10	20	40
Influenza A	Patients	31	60	10	
	Controls	22	51	24	4
Influenza B	Patients	45	43	11	2
	Controls	38	45	15	3

* See footnote Table 2

Table 4: CF antibody titres against para-influenza 1, 2 and 3 in 101 randomly selected patients with respiratory tract infection* and 101 controls (reciprocal of serum dilutions)

Antigen	Group	CF antibody titre				
		≤ 5	10	20	40	80
Para-influenza 1	Patients	80	19	1	1	
	Controls	84	14	3		
Para-influenza 2	Patients	40	42	17	1	1
	Controls	34	50	17		
Para-influenza 3	Patients	17	49	31	4	
	Controls	25	56	15	5	

* See footnote Table 2

Table 5: CF antibody titres against adenovirus and cytomegalovirus (CMV) in 101 randomly selected patients with respiratory tract infection* and 101 controls (reciprocal of serum dilutions)

Antigen	Group	CF antibody titre			
		≤ 5	10	20	40
Adeno-Virus	Patients	28	36	24	13
	Controls	33	36	26	6
CMV	Patients	52	30	18	3
	Controls	50	30	18	3

* See footnote Table 2

Table 6: CF antibody titres against *M. pneumoniae* in 101 randomly selected patients with respiratory tract infection* and 101 controls (reciprocal of serum dilutions)

Group	CF antibody titre						
	≤ 5	10	20	40	80	160	> 160
Patients	70	11	10	4	2	1	3
Controls	78	8	8	4	1	0	2

* See footnote Table 2

adenovirus were four, one, and two respectively. No significant change was observed in the titres to the other viruses. The numbers of patients and control subjects who had stationary titres (titre ≥ 1:10) of CF antibodies to the different

viruses are shown in Table 2. There was no significant difference in the incidence of these antibodies to any of the viruses between the two groups. The titres to influenza A and B in the two groups are shown in Table 3 and those of para-influenza 1, 2, and 3 in Table 4. The titres of CF antibodies to the other viruses tested, i. e. adeno and CMV, are shown in Table 5. There is no difference in the distribution of the titres to any of the viruses between the controls and the patients presenting with a respiratory infection (Tables 3, 4 and 5).

Chlamydia. There was no significant change in the titres of CF antibodies to the chlamydia antigen used in any of the patients, but one of the controls had a high titre, i. e. 1:80, which was stationary.

Mycoplasma pneumoniae. CF antibodies to *M. pneumoniae* (≥ 1:10) were found in 31% of the patients and in 23% of the controls. The distribution of the titres in these two groups, which did not disclose any significant difference, is shown in Table 6. In 7 of the patients, a significant change in the titre was observed (Table 7). The results of the cultures for *M. pneumoniae* are also included in Table 7.

Cold agglutinins

Cold agglutinins (≥ 1:16) were found in 20% of the patients but in none of the controls. In the two patients who had a significant change in the titre of cold agglutinins there was also such a change in the titre of CF antibodies to *M. pneumoniae* (Table 7).

Paul-Bunnell test

In none of the patients or the controls were antibodies found indicating infectious mononucleosis.

Signs and symptoms

The signs and symptoms of the patients are shown in Table 8. The patients are divided into the various diagnostic categories, e. g. *M. pneumoniae*, beta-haemolytic streptococci, para-influenza (2 and 3) and adenovirus. The majority of the patients (67%) did not have a definite aetiological diagnosis.

Table 7: Results of CF tests and cultures for *M. pneumoniae* and cold agglutinins (CA) in 16 patients

	CF antibody titre			Culture	CA (≥ 1:16)
	Significant rise	High, but stationary (≥ 1:80)	Negative (≤ 1:10)		
2				pos	2
2				neg	0
3				ND*	1
		3		neg	1
		1		ND	1
			5	pos	1
Total 7	4		5		6

*ND = not done

Table 8: Symptoms and signs in 101 randomly selected patients with respiratory tract infection*

Symptom or sign	<i>M. pneumoniae</i> (N = 16)	β -haemolytic streptococci** (N = 10)	Para-influenza (2 + 3) (N = 5)	Adeno-virus (N = 2)	No aetiologic diagnosis (N = 68)
Temperature $\geq 38^{\circ}\text{C}$	14	7	8	1	23
Cough	11	2	3	2	52
Expectoration	7	2	2	2	30
Coryza	8	4	3	2	49
Sore throat	9	9	4	1	46
Headache	8	6	4		42
Muscle pains	9	3	4		27
Hoarseness	5	2		1	26
Earache	2	1	1		20
Diarrhoea, vomiting	2				4
Conjunctivitis					2
Exanthema	0	1			1
(Naso)pharyngitis	9	8	4	1	34
Bronchitis	3			1	9
Upper respiratory tract infection	4	2	1		25

*Children below 7 years of age and patients with acute otitis media and acute tonsillitis were excluded

**Group A streptococci were demonstrated in 8 patients, and group G streptococci in 2

Discussion

Respiratory tract infections quantitatively constitute one of the greatest problems in general practice. In the Dalby material about every third patient presented with symptoms and signs of such an infection.

The comparatively low frequency of infections associated with group A streptococci in this series must be because patients with definite signs of acute tonsillitis were excluded. It has been estimated that viruses account for 95% of all cases of acute pharyngitis. Of the remaining 5%, 95% are due to beta-haemolytic streptococci group A; group C and G streptococci are implicated in only a few cases. In the present study, group G streptococci were found in two cases. The diagnosis of acute pharyngitis had been recorded in all but two of the patients from whom, subsequently, beta-haemolytic streptococci were isolated. Sore throat, fever and headache were the three most frequent symptoms in these patients (Table 8).

It is known that viruses are the major causative agents of respiratory tract infections. The test battery used in this study was apparently not particularly suitable to establish the presence of such an infection, since a seroconversion was found in only 7% of the patients. Rhino and corona viruses which are the most common aetiological agents of respiratory tract infections cannot be routinely diagnosed by serological means as there are no commercially available antigens. Antibodies, at a titre of $\geq 1:10$, to all the viruses tested occurred in almost the same proportion in the patients and controls, and the titres had the same distribution. This certainly stresses the fact that it is necessary to examine both acute and convalescent sera.

Incidence figures for antibodies to *M. pneumoniae* in larger populations are available from studies in central laboratories in Denmark (22), Switzerland (20), the United King-

dom (29), the United States of America (13), and the Netherlands (16). The reported incidence of CF antibodies to *M. pneumoniae* in persons without known respiratory tract infection has been between 5 and 20%. In our control group the corresponding figure was 21%.

The present study was performed during the late months of an exceptionally hot summer. There was no *M. pneumoniae* epidemic during the period of our study. This statement is based on the low number of positive serological tests for *M. pneumoniae* that was seen in our laboratory during this period. The laboratory serves an area with about half a million inhabitants in the south of Sweden, including Dalby and Lund.

Most studies of *M. pneumoniae* infections outside hospitals have been obtained from studies conducted in closed communities, such as military units, university campuses (7, 10) and in families (12). It has been suggested that *M. pneumoniae* more often causes upper respiratory tract infections than pneumonia, but figures supporting this assumption are few. The reported incidence of *M. pneumoniae* in some selected series of patients with upper respiratory tract infections are shown in Table 9.

Incidence figures of *M. pneumoniae* infections in randomly selected patients in general practice have not to our knowledge been reported. We found evidence of a *M. pneumoniae* infection in 16 patients; a significant rise in titre of CF antibodies was found in seven, while four had high, but stationary, titres. The epidemiological data and the history strongly suggested an infection with *M. pneumoniae* in these four patients. Cold agglutinins were found in two of them. In five patients there was no serological evidence of a *M. pneumoniae* infection, but the organism was recovered from the oro-pharynx.

CF, indirect haemagglutination (IHA) and immunofluorescence (IF) tests have been used to detect serum antibodies

Table 9: Incidence of infections with *Mycoplasma pneumoniae* in some selected series of patients with non-pneumonic respiratory tract infections

Senior author, literature number and year of publication	Group studied	Diagnosis	No. of patients	Evidence of <i>M. pneumoniae</i>		Technique used*
				(n)	(%)	
Chanock (6) (1961)	Marine recruits	Febrile resp. illness	144	40	28	IF
		Afebrile resp. illness	131	11	8	IF
Grayston (15) (1965)	Miscellaneous groups of patients	Bronchitis	125	7	6	I
		Upper resp. inf.	123	8	7	I
Evans (19) (1967)	University students	Bronchitis	53	4	8	CF, IF, I
		Acute upper resp. tract inf.	125	1	0.8	CF, IF, I
		Pharyngitis – tonsillitis	92	4	4	CF, IF, I
Hers (16) (1967)	Selected groups of civilians (studied between 1961 and 1966)	Bronchitis	242	143	59	CF, IFS
		Laryngo-pharyngitis	40	12	30	CF, IFS
		Rhinitis	20	6	30	CF, IFS
Glezen (14) (1967)	Patients in pediatric practice	Pharyngitis	715	22	3	I
Biberfeld (3) (1968)	Hospitalized patients	Bronchitis	28	3	11	CF, I
		Upper resp. tract inf.	228	1	0.4	I

* I = *M. pneumoniae* isolation; CF = sera tested for complement fixation antibodies; IF = sera tested for immunofluorescent antibodies; IFS = *M. pneumoniae* demonstrated in clinical specimens by immunofluorescent technique

to *M. pneumoniae*. In patients with upper respiratory tract infections, the CF test has been found to detect more cases of *M. pneumoniae* infection than the IHA and the IF tests (23).

The frequency with which *M. pneumoniae* has been isolated from patients with serological evidence of infection with this organism has been low in most studies. Body fluids contain mycoplasmacidal substances that might influence the recovery rate (27). The composition of the culture media in general use may not be optimal for the isolation of *M. pneumoniae* from clinical specimens, although they may support the growth of "laboratory strains" of *M. pneumoniae*. In the present study we found that the addition of a reducing substance, i. e. cysteine hydrochloride, gave a higher recovery rate, but this observation needs further evaluation. Cysteine hydrochloride has been used earlier in culture media for ureaplasmas (30). It should be noted that the isolation rate of more rapidly growing mycoplasma species, e. g. *M. hominis*, *M. orale*, and *M. salivarium*, was not influenced by the presence of this substance. It is notable that *M. pneumoniae* was isolated from five patients who did not have any sero-

logical evidence of such an infection, which indicates the role of culture studies in attempts to establish upper respiratory tract infections with this organism.

Cold agglutinins are known to occur in 50 to 75% of patients with signs of pneumonia and with a significant change in the titre of CF antibodies to *M. pneumoniae*. In our series of patients with non-pneumonic respiratory tract infections, cold agglutinins were found in three of those seven with such a titre change. It has been recently demonstrated that cold agglutinins may also occur in CMV infections of the respiratory tract (24), but we did not find any evidence of such an infection in our cold agglutinin positive cases.

The present study seems to indicate that *M. pneumoniae* infections are not uncommon in patients presenting with symptoms of upper respiratory tract infection. This type of infection was the most common diagnosis made in our series. But it must be stressed that children below the age of seven and cases of acute tonsillitis and acute otitis media were excluded.

The physician often obtains little guidance from the history, and the clinical examination of the patient does not often al-

Table 10: Antibiotic treatment given to the patients studied

	<i>M. pneumoniae</i> (N = 16)	β -haemolytic streptococci (N = 10)	Para-influenza (2 + 3) (N = 5)	Adeno-virus (N = 2)	No aetiological diagnosis (N = 68)
Penicillin	4	7	1	1	16
Ampicillin	1				2
Doxycycline	1	1			9
Erythromycin	3				6
No antibiotics	7	2	4	1	35

low the physician to establish the aetiology of a respiratory tract infection. The signs and symptoms in the present series of patients with either a streptococcal, viral or *M. pneumoniae* infection showed certain common characteristics, but the clinical picture was not sufficiently distinct to make a definite diagnosis without the laboratory tests (Table 8). The information the physician obtains from the microbiological laboratory often arrives too late to be of help in the treatment of the individual case. The physician therefore usually has to decide whether or not to treat a respiratory tract infection without the knowledge of the aetiology of the patient's condition. A retrospective study of the treatment which had been given to our patients clearly indicates the difficulties involved (Table 10). The liberal prescription of penicillin to patients presenting with signs of pharyngo-ton-sillitis may seem justified in relation to the difficulty of basing the diagnosis of an infection with beta-haemolytic streptococci group A on clinical grounds (1, 4), and when it is known that early institution of penicillin reduces the incidence of complications, such as acute glomerulonephritis (18). Such a therapy may also be of epidemiological significance.

The duration of fever and cough in cases of pneumonia caused by *M. pneumoniae* may be reduced by the use of tetracyclines or erythromycin. Whether such treatment of upper respiratory tract infections caused by this organism is of any benefit is not known, and it could not be determined from our study. *M. pneumoniae* is susceptible to these antibiotics *in vitro* (25), but they have been shown to persist *in vivo* despite their usage (31).

Literature

1. Axelsson, A., Ekedahl, C., Hallen, O.: Acute pharyngeal infection, aetiological and diagnostic viewpoints. *Läkartidningen* 71 (1974) 3923-3926.
2. Biberfeld, G.: Antibodies to brain and other tissues in cases of *Mycoplasma pneumoniae* infection. *Clin. exp. Immunol.* 8 (1971) 319-333.
3. Biberfeld, G., Stenbeck, J., Johnsson, T.: *Mycoplasma pneumoniae* infection in hospitalized patients with acute respiratory illness. *Acta path. microbiol. scand.* 74 (1968) 287-300.
4. Breese, B. B., Disney, F. H., Rochester, N. Y.: The accuracy of diagnosis of beta streptococcal infections on clinical grounds. *J. Pediatrics* 44 (1954) 670-673.
5. Cars, O., Forsum, U.: Aspects of the diagnosis of throat infections with beta haemolytic streptococci group A. *Läkartidningen* 72 (1975) 3219-3220.
6. Chanock, R. M., Mufson, M. A., Bloom, H. H., James, W. D., Fox, H. H., Kingston, J. R.: Eaton agent pneumonia. *J. Amer. med. Ass.* 175 (1961) 213-220.
7. Chanock, R. M., Fox, H. H., James, W. D., Gutekunst, R. R., White, R. J., Senterfit, L. B.: Epidemiology of *Mycoplasma pneumoniae* infection in military recruits. *Ann. N. Y. Acad. Sci.* 143 (1967) 484-496.
8. Christensen, P., Kahlmeter, G., Jonsson, S., Kronvall, G.: New method for the serological grouping of streptococci with specific antibodies adsorbed to protein A-containing staphylococci. *Infect. Immunol.* 7 (1973) 881-885.
9. Davidsohn, I., Lee, C. L.: Serologic diagnosis of infectious mononucleosis. *Amer. J. clin. Path.* 41 (1964) 115-125.
10. Evans, A. S., Allen, V., Suelmann, S.: *Mycoplasma pneumo-*

- niae* infections in University of Wisconsin students. *Amer. Rev. resp. Dis.* 96 (1967) 237-244.
11. Foy, H. M., Grayston, J. T.: Pneumonia, *Mycoplasma pneumoniae*. In: Communicable and infectious diseases (Ed.: F. H. Top, P. F. Wehrle), p. 480. C. V. Mosby Company, St. Louis 1972.
12. Foy, H. M., Grayston, J. T., Kenny, G. E., Alexander, E. R., McMahan, R.: Epidemiology of *Mycoplasma pneumoniae* infection in families. *J. Amer. med. Ass.* 197 (1966) 859-866.
13. Foy, H. M., Kenny, G. E., McMahan, R., Mansy, A. M., Grayston, J. T.: *Mycoplasma pneumoniae* pneumonia in an urban area. Five years of surveillance. *J. Amer. med. Ass.* 214 (1970) 1666-1672.
14. Glezen, P. W., Clyde, Jr. W. A., Senior, R. J., Sheaffer, C. I., Denny, F. W.: Group A streptococci, mycoplasmas and viruses associated with acute pharyngitis. *J. Amer. med. Ass.* 202 (1967) 455-460.
15. Grayston, J. T., Alexander, E. R., Kenny, G. E., Clarke, E. R., Fremont, J. C., MacColl, W. A.: *Mycoplasma pneumoniae* infections. *J. Amer. med. Ass.* 191 (1965) 97-102.
16. Hers, J. F. Ph., Masurel, N.: Infection with *Mycoplasma pneumoniae* in civilians in the Netherlands. *Ann. N. Y. Acad. Sci.* 143 (1967) 447-460.
17. Hobson, D.: Acute respiratory virus infections. *Brit. Med. J.* (1972/2) 229-231.
18. Holm, S. E., Ekedahl, C., Bengtson, U.: Prevention of acute glomerulonephritis with early treatment of tonsillitis with penicillin. *Scand. J. infect. Dis.* 5 (1973) 115-122.
19. Kenny, G. E., Grayston, J. T.: Eaton pleuropneumonia-like organism (*Mycoplasma pneumoniae*) complement-fixing antigen: Extraction with organic solvents. *J. Immunol.* 95 (1965) 19-25.
20. Krech, von U., Paccaud, M.: Vergleichende Untersuchungen über die Häufigkeit von *Mycoplasma-pneumoniae*-Infektion in Genf und St. Gallen. *Path. et Microbiol. (Basel)* 30 (1967) 1037-1040.
21. Lind, K.: An indirect haemagglutination test for serum antibodies against *Mycoplasma pneumoniae* using formalinized, tanned sheep erythrocytes. *Acta path. microbiol. scand.* 73 (1968) 459-472.
22. Lind, K.: Incidence of *Mycoplasma pneumoniae* infection in Denmark from 1958 to 1969. *Acta path. microbiol. scand. Sect. B* 79 (1971) 239-247.
23. Lind, K.: Personal communication.
24. Lind, K., Spencer, E. S., Andersen, H. K.: Cold agglutinin production and cytomegalovirus infection. *Scand. J. infect. Dis.* 6 (1974) 109-112.
25. Mårdh, P.-A.: Human respiratory tract infections with mycoplasmas and their *in vitro* susceptibility to tetracyclines and some other antibiotics. *Chemotherapy* 21 Suppl. 1 (1975) 47-57.
26. Mårdh, P.-A., Skude, G., Åkerman, M., Ursing, B.: *Mycoplasma pneumoniae* infection: A cause of acute pancreatitis and non-specific, reactive hepatitis in man and experimentally infected animals. p. 403-410. INSERM, Paris 1974.
27. Mårdh, P.-A., Taylor-Robinson, D.: New approaches to the isolation of mycoplasmas. *Med. microbiol. Immunol.* 158 (1973) 259-266.
28. Mårdh, P.-A., Ursing, B., Lind, K.: Persistent cerebellar symptoms after infection with *Mycoplasma pneumoniae*. *Scand. J. infect. Dis.* 7 (1975) 157-160.
29. Noah, N. D.: *Mycoplasma pneumoniae* infection in the United Kingdom-1967-73. *Brit. med. J.* (1974/II) 544-546.
30. Shepard, M. C., Lunceford, C. D., Ford, D. K., Purcell, R. H., Taylor-Robinson, D., Razin, S., Black, F. T.: *Ureaplasma urealyticum* gen. nov., sp. nov.: proposed nomenclature for the human T (T-strain) mycoplasmas. *Int. J. syst. Bact.* 24 (1974) 160-171.
31. Smith, C. B., Friedewald, W. T., Chanock, R. M.: Shedding of *Mycoplasma pneumoniae* after tetracycline and erythromycin therapy. *New Engl. J. Med.* 276 (1967) 1172-1175.
32. Stundbridge, E., Hayflick, L.: Growth inhibition test for identification of *Mycoplasma* species utilizing dried antiserum-impregnated paper discs. *J. Bact.* 93 (1967) 1392-1396.

Résumé: L'incidence des infections respiratoires chez les patients fréquentant la polyclinique de Dalby en 1973 et 1974 a fait l'objet d'une étude. Environ un patient sur trois examinés présentait des signes d'infection respiratoire. Dans les groupes d'âges de moins de 10 ans, de 10-19 ans, de 20-39 ans, et 40-59 ans et de plus de 60 ans, les pourcentages respectifs d'infection respiratoire diagnostiquée en 1974 étaient de 65, 45, 32, 18 et 9%. L'étiologie des infections respiratoires aiguës dans un groupe de malades examinés à Dalby a fait l'objet d'une étude. Ce groupe comportait des cas choisis au hasard, à l'exclusion d'enfants de moins de 7 ans et de patients présentant des signes d'otite moyenne aiguë et d'amygdalite. L'étiologie a été recherchée sur base de l'anamnèse; de l'examen clinique et des cultures visant à la mise en évidence de streptocoques bêta hémolytiques et de *M. pneumoniae*; d'épreuves de fixation du complément pour la recherche des influenza A et B, des parainfluenzas 1, 2 et 3, des adénovirus, cytomégalovirus et du virus respiratoire syncytial, ainsi que de *Chlamydia psittaci*. Les épreuves de Paul-Bunnell et des agglutinines froides ont également été réalisées. Cette batterie de tests a permis d'obtenir un diagnostic étiologique dans 32% seulement des 101 patients de l'étude. Ces constatations permettent de croire à une infection à *M. pneumoniae* dans 16% des cas, à streptocoques bêta-hémolytiques dans 9% et à virus (adénovirus et para-influenza) dans 7%. L'auteur souligne le rôle de *M. pneumoniae* dans les infections des voies respiratoires supérieures; rares sont les données publiées sur ce type d'infections chez les patients examinés en pratique générale. L'auteur discute encore de la difficulté d'établir l'étiologie des infections respiratoires et du dilemme thérapeutique qui en résulte.

Samenvatting: De frequentie van luchtweginfecties bij patiënten die voor een consult kwamen in het gemeenschaps gezondheidscentrum (Dalby) gedurende 1973 en 1974 werd onderzocht. Ongeveer iedere derde patiënt die in dit eerstelijns gezondheidscentrum werd gezien vertoonde symptomen van een dergelijke infectie. In de leeftijdsgroepen ≤ 10 , 10-19, 20-39, 40-59 en ≥ 60 jaar vertegenwoordigden luchtweginfecties 65, 45, 32, 18 en 9% van het totaal aantal gedurende 1974 gestelde diagnoses. De etiologie van acute luchtweginfecties bij een serie patiënten die in dit gezondheidscentrum werden gezien, werd onderzocht. De serie omvatte aselect gekozen gevallen, uitgesloten waren echter kinderen jonger dan 7 jaar en patiënten die symptomen van acute otitis of tonsillitis vertoonden. Er werd getracht de etiologie vast te stellen op basis van de anamnese, het lichamelijk onderzoek en kweken op beta haemolytische streptococci en *M. pneumoniae*, complement bindingsreacties voor influenza A en B, parainfluenza 1, 2 en 3, adeno-, cytomegalovirus en respiratoir syncytium vormend virus en *Chlamydia psittaci*. De Paul-Bunnell test op koude agglutinenen werd ook verricht. Met deze testbatterij werd een etiologische diagnose gesteld in slechts 32% van de 101 bestudeerde patiënten. De uitslagen laten in 16% een infectie met *M. pneumoniae* zien, in 9% met beta-haemolytische streptococci en in 7% met virussen (adeno-, en para-influenza). Deze communicatie benadrukt de rol van *M. pneumoniae* in hogere luchtweginfecties, waar tot nu toe weinig gegevens zijn gepubliceerd over dergelijke infecties bij patiënten in de huisartsenpraktijk. De moeilijkheden rond het vaststellen van de etiologie van luchtweginfecties en het daaruit voorkomende behandelingsdilemma wordt besproken.

Resumen: Se estudió la incidencia de infecciones respiratorias en pacientes que visitaban al médico en un centro asistencial (Dalby) durante 1973 y 1974. Uno de cada tres pacientes de los examinados en aquel centro sanitario presentaba signos de la mencionada patología. En estos grupos de edades: <10, 10-19, 20-29, 40-59 y ≥ 60 años, las infecciones del tracto respiratorio representaron el 65%, 45%, 32%, 18% y el 9% respectivamente del número total de diagnósticos realizados durante el año 1974. Se estudió la etiología de las infecciones agudas del árbol respiratorio en una serie de pacientes examinados en este centro sanitario. La serie incluyó casos seleccionados al azar, excluyendo niños menores de 7 años de edad así como pacientes que presentaban síntomas de otitis media aguda y amigdalitis. Se intentó establecer la etiología basándose en la historia del proceso, el examen clínico y el examen bacteriológico con cultivo para determinar la presencia del estreptococo beta-hemolítico y el *M. pneumoniae*, además de las pruebas de fijación de complemento para los virus influenza A y B, parainfluenza 1, 2 y 3, adenovirus, citomegalovirus, respiratorio sincitial y el *Chlamydia psittaci*. También se realizaron las pruebas de Paul-Bunnell y la de crioprecipitación para aglutininas. Con esta batería de pruebas, solamente se obtuvo un diagnóstico etiológico en el 32% de los 101 pacientes estudiados. Los hallazgos sugieren una infección por el *M. pneumoniae* en el 16% de los casos, por el estreptococo beta-hemolítico en el 9% y debida a virus (adenovirus y para-influenza) en el 7% de los pacientes. La presente comunicación resalta el papel del *M. pneumoniae* en las infecciones del tracto respiratorio superior ya que han aparecido pocos datos sobre tales infecciones en pacientes observados en la práctica diaria. Se discute la dificultad para determinar la etiología de las infecciones del tracto respiratorio y el dilema de establecer un tratamiento adecuado.

Riassunto: È stata studiata la frequenza di infezioni dell'apparato respiratorio in pazienti che hanno richiesto una visita medica al Centro di Dalby negli anni 1973-74. Circa un terzo dei pazienti presentatisi a questo Centro Sanitario di screening presentavano segni di tali infezioni. Nei gruppi di età inferiori a 10 anni, tra 10-19, 20-39, 40-59 e superiori, o pari, a 60 anni, le infezioni dell'apparato respiratorio corrispondevano al 65, 45, 32, 18 e 9% del numero totale di diagnosi dell'anno 1974. È stata anche studiata la eziologia delle infezioni acute dell'apparato respiratorio in un gruppo di pazienti osservati in questo Centro. Questi gruppi comprendevano soggetti selezionati a caso, con l'esclusione di bambini al di sotto di 7 anni e di pazienti che presentavano segni di otite media acuta e tonsillite. Si tentò di stabilire l'eziologia sulla base della anamnesi, dell'esame obiettivo e degli esami culturali per lo Streptococco Beta-emolitico e per il *M. pneumoniae*, nonché mediante tests di fissazione del complemento per influenza A e B, para influenza 1, 2 e 3, adenovirus, citomegalovirus, virus respiratorio sinciziale e *Chlamydia psittaci*. Furono anche praticati test di Paul-Bunnell e agglutinine de freddo. Utilizzando questa batteria di tests una diagnosi eziologica fu ottenuta solo nel 32% dei 101 pazienti studiati e i dati ottenuti indicano un'infezione con *M. pneumoniae* nel 16%, con lo streptococco beta-emoico nel 9% e con virus (adeno e para influenza) nel 7%. La presente comunicazione sottolinea il ruolo del *M. pneumoniae* nelle infezioni dell'apparato respiratorio superiore, poichè pochi dati sono disponibili su queste infezioni nei pazienti osservati nella pratica generica. Viene anche discussa la difficoltà di stabilire l'eziologia delle infezioni dell'apparato respiratorio e i conseguenti dubbi sul trattamento.