

# Acute respiratory symptoms in adults in general practice

Ching-Ye Hong, Raymond TP Lin<sup>a</sup>, Elaine SL Tan<sup>b</sup>, Phui-Nah Chong<sup>b</sup>, Yvette SL Tan<sup>b</sup>, Yii-Jen Lew<sup>b</sup> and Liat-Hui Loo<sup>a</sup>

Hong C-Y, Lin RTP, Tan ESL, Chong P-N, Tan YSL, Lew Y-J and Loo L-H. Acute respiratory symptoms in adults in general practice. *Family Practice* 2004; **21**: 317–323.

**Background.** Community studies have shown that ~30% of patients with acute respiratory tract symptoms have no identifiable infective aetiology. This may not be applicable in general practice.

**Objective.** The purpose of this study was to determine the infective aetiology in patients who presented to primary care doctors with acute respiratory symptoms.

**Methods.** A prospective study was carried out in all nine primary care clinics belonging to the National Healthcare Group Polyclinics (NHGPs) in Singapore. The subjects comprised 594 consecutive patients (318 males, 276 females) aged  $\geq 21$  years who presented with complaints of any one of cough, nasal or throat symptoms of  $< 7$  days duration. Data collection was through interview using structured questionnaire, physical examination, throat swabs for bacterial culture and nasal swabs for virus identification by immunofluorescence (IF) and polymerase chain reaction (PCR). Additional PCR was performed on a subsample of 100 patients. Patients were followed-up until resolution of symptoms.

**Results.** The aetiological diagnosis by infective agent is as follows: 150 patients (25.2%) had virus infections, of which 90.7% (136/150) were by rhinovirus. Fourteen patients (2.4%) had bacterial infections, of which 10 were due to group G streptococcus. Group A streptococcus was not detected. Nineteen patients with new pathogens were identified by further PCR. These included parainfluenza 4, human coronavirus OC43, adenovirus, enterovirus and *Chlamydia pneumoniae*. No pathogen could be identified in 49% of patients. There were no differences in clinical presentation and socio-demographic variables between patients who had viral infections and those in whom no pathogen could be identified.

**Conclusion.** In about half of patients who presented at NHGPs, no pathogens could be identified even after PCR. A non-infective aetiology could be considered in these patients.

**Keywords.** Immunofluorescence, polymerase chain reaction (PCR), rhinovirus, upper respiratory tract infection (URTI).

## Introduction

Upper respiratory tract symptoms such as cough, runny nose and sore throat are the most common acute presentations encountered in general practice. The majority of these have been attributed by both patients and doctors

to infections of the upper respiratory tract (URTI). Viruses have been shown to be the main aetiological agents. In the absence of influenza epidemics, rhinoviruses account for ~30–50% of all respiratory illnesses annually.<sup>1</sup> Other viruses commonly isolated in adults with respiratory symptoms are parainfluenza, coronavirus, respiratory syncytial virus (RSV) and adenovirus.

Most of these studies were conducted in the community, such as the Cleveland Family Study<sup>2</sup> and the Tecumseh Study,<sup>3</sup> or among specific groups within a community, such as college students<sup>4</sup> or young military personnel.<sup>5</sup>

Illness and the experience of symptoms in the community are not the same as illness as presented to the GP. It is well known that physicians see only a small fraction of the health problems experienced by the population at large. In the Tecumseh Study, physician consultations were associated with only 25.4% of all

---

Received 25 February 2003; Revised 1 September 2003; Accepted 7 January 2004.

Special Projects Department, Research and Data Management Division, Health Promotion Board, <sup>a</sup>Microbiology Laboratory, KK Women's and Children's Hospital, and <sup>b</sup>National Healthcare Group Polyclinics, Singapore. Correspondence to Dr Ching-Ye Hong, Special Projects Department, Research and Data Management Division, Health Promotion Board, 3 Second Hospital Avenue, Singapore 168937; E-mail: hong\_ching\_ye@hpb.gov.sg

respiratory illnesses.<sup>6</sup> This suggested that the decision to consult GPs is not based solely on symptom complex or severity, especially for mild and self-limiting conditions such as URTI. Triggers ranging from self-perception to socio-economic factors can influence a person's decision to legitimize his sick role. Yet, in spite of this, recommendations for treatment of URTI in many clinical guidelines are based on results of community studies.

It would be helpful for GPs to know if the aetiological patterns of patients presenting to them with complaints of acute respiratory symptoms are the same as those of the subjects in community studies. To our knowledge, there is a paucity of such studies conducted in general practices. Lieberman *et al.* conducted a practice-based study on 122 patients in three general practices in Israel. They used increase in antibody titre in paired sera for identification of an infective cause, and reported a viral pathogen in 25%, bacterial in 30% and more than one pathogen in 22% of patients.<sup>7</sup>

With the advent of new laboratory methods such as immunofluorescence (IF) and polymerase chain reaction (PCR), it has been possible to improve the rate of virus identification. The main objective of our study was therefore to determine the aetiological cause in patients who presented with acute respiratory symptoms in nine primary care clinics in Singapore, using bacterial culture, IF and PCR. We also aimed to study the differences in clinical presentation between patients with different aetiological causes.

## Methods

### *Subjects*

We conducted this prospective study in all nine clinics belonging to the National Healthcare Group Polyclinics (NHGPs) in the Republic of Singapore. These clinics are one-stop primary care health centres, which provide subsidised services ranging from preventive health care to acute and chronic medical care. We recruited patients sequentially from each clinic, having first determined the order in a random fashion. The proportion of patients to be recruited from each clinic was based on the proportion of patients seen for URTI during the same period in the past year. Approval to conduct the study was obtained from the National Healthcare Group Ethics Committee.

The study population included 594 consecutive patients (318 males, 276 females) who presented with complaints of respiratory tract symptoms from February to April 2002. Inclusion criteria were all patients who were Singaporean residents, aged  $\geq 21$  years, who complained of any one of the following: cough, nasal (sneezing, runny nose, blocked nose) or throat (sore throat, throat clearing, phlegm in throat) symptoms of  $< 7$  days duration. Fever was not used as a criterion for patient selection as, in

doing so, we may inadvertently have excluded patients with infective aetiology who did not have fever. Patients were excluded if they had history of chronic respiratory problems such as allergic rhinitis, chronic sinusitis, asthma or chronic obstructive pulmonary disease, were currently on treatment for tuberculosis, or were immunocompromised in any way. Other exclusion criteria included long-term antibiotic use (such as for treatment of acne), or recent antibiotic use in the previous 2 weeks, recent travel or hospitalization, being pregnant or currently breast-feeding.

Out of a total of 821 eligible patients, 595 gave signed informed consent to participate in the study. One patient who did not complete the study (no microbiological analysis done) was excluded. This gave a response rate of 72.4%. There were more male respondents (80.9%) compared with females (69.4%). However, there were no differences between respondents and non-respondents with respect to age or ethnic distribution.

### *Data collection*

We collected data by several means, namely interview using a structured questionnaire, clinical examination using a standard recording form, throat swab for bacterial culture and nasal swab for virus identification. Patients were followed-up by phone interviews until resolution of symptoms.

Sections in the questionnaire included questions on general health status, past URTI experience and, for the present episode, the severity of each symptom from a list of 23 symptoms. All interviews and biological sample collection were conducted by the authors and qualified state-registered nurses who had been trained in the procedure. Resident doctors in each of the clinics, who had been briefed on the study protocol, conducted the physical examination and recorded the findings in structured recording forms. Prior to the study proper, we conducted a pilot study to test the questionnaire, the logistics, and the acceptability to patients of the sample collection methods.

We followed-up each patient 1 week later by a telephone call. For patients who have not recovered by the first week, second and subsequent phone calls were made until resolution of all symptoms.

### *Bacterial culture*

All bacterial culture and virus identification were performed at the laboratory of one of the authors (RTPL).

Throat swabs were collected in Amies transport medium (Copan, Italy) and sent to the laboratory on the same day. The swabs were plated on Columbia sheep blood agar and CDC anaerobic blood agar. The blood agar was incubated aerobically at 35°C in CO<sub>2</sub> and the anaerobic agar was incubated anaerobically at 35°C, both for 48 h. The aerobic plate was read at 18–24 h, and both aerobic and anaerobic plates at 48 h. The potential pathogens looked for were  $\beta$ -haemolytic streptococci

of Lancefield groups A, C and G; and predominant heavy growth of *Streptococcus pneumoniae*, *Haemophilus influenzae* or *Moraxella catarrhalis*. Identification of bacteria was by standard methods.<sup>8</sup>

#### *IF microscopy for respiratory viruses*

We used flexible wire swabs (Copan, Italy) to obtain specimens from patients' nasopharynx and they were transported in the virus transport medium. Upon arrival in the laboratory, the flexible wires were cut and put into plastic disposable tubes (Falcon, USA) containing 1 ml of phosphate-buffered saline (PBS) each (Oxoid, UK). The tubes were capped and vortexed for 1 min to produce a cell suspension. The specimens were processed for IF according to the manufacturer's instructions. Screened positive samples were tested again using the individual monoclonal antibodies (Light Diagnostics, Chemicon, USA) for influenza A, influenza B, parainfluenza 1, parainfluenza 2, parainfluenza 3 viruses, RSV and adenovirus.

#### *Nucleic acid detection*

The detection of rhinovirus RNA was performed on the cell suspension obtained from that used for IF described above. Viral RNA was extracted using the QIAamp Viral RNA mini kit (QIAGEN, Germany). The rhinovirus RNA was then amplified using the OneStep RT-PCR kit (QIAGEN, Germany). The entire reverse transcription and amplification was performed on a GeneAmp 2400 thermal cycler (Applied Biosystems, USA). The amplification products were digested using *BglII* (New England Biolabs, USA) at 37 °C for 2 h. The amplified products and digested products were run side by side on 2% agarose gels, stained with ethidium bromide and photographed. Samples which showed both 380 and 190 bp bands were considered positive for rhinovirus.<sup>9</sup>

In addition, 100 samples were examined for other pathogens, namely influenza A, B and C viruses, parainfluenza 1, 2, 3 and 4 viruses, adenovirus, RSV, human coronaviruses OC43, 229E, enterovirus, *M.pneumoniae* and *C.pneumoniae*, by PCR. From each batch of 20 samples processed for IF and rhinovirus PCR, five samples were selected arbitrarily for additional PCR, until 100 samples were reached. The same extract from the rhinovirus PCR test was used. Genomic RNA was amplified using the OneStep RT-PCR kit (QIAGEN, Germany) and genomic DNA was amplified using the Taq Core PCR kit (QIAGEN, Germany) following the manufacturers' instructions. The primers used for amplification were taken from various authors.<sup>10-14</sup> Four separate multiplex amplification runs were performed for each sample. Reverse transcriptions and amplifications were performed on a GeneAmp 2400 thermal cycler (Applied Biosystems, USA). The amplified products were run on 2% agarose gels, stained with ethidium bromide and photographed. The amplification product lengths were confirmed with the references cited.<sup>8,10-13</sup>

Samples which showed the presence of the corresponding amplification product were taken to be positive for the respective pathogen.

#### *Data management and analysis*

All data were checked for accuracy of entry and analysed using the Statistical Package for Social Sciences (SPSS) for Windows software version 11.0. Frequency tabulations were done for descriptive data. Student's *t*-tests were used for comparison of differences between means, and Mann-Whitney *U*-tests for differences between medians. Chi-square tests were used for comparison of differences in proportions. Odds ratios and 95% confidence intervals were calculated. For the analysis of the subgroup of patients on whom additional PCR was done, comparing patients with viral infections with those in whom no pathogen was isolated, patients with bacterial infections (*Streptococcus* and *C. pneumoniae*) were excluded.

## Results

#### *Descriptive profile of patients*

The mean age was 45.4 years (SD ± 14.9), and median 45.0 years (range 21-88). Ethnic distribution was: Chinese 69.1%, Malay 17.5%, Indian 11.1% and others 2.2%. Of the patient population, 69.8% were non-smokers, 20.7% current smokers and 9.4% ex-smokers.

The general health status of the patients was good, with 68% reporting excellent or good for 'general well-being in the past 3 months'. A high level of stress in the past 2 weeks was reported by 13.7% of patients; 90.3% of patients had at least one episode of 'flu' in the past 12 months, with 17.4% with at least five episodes.

#### *Present 'flu' episode*

For this present episode, the median duration of illness was 8.0 days (range 2-33). Of the patients, 62.3% had a total of ≥10 symptoms. Of these, cough was the most common (88.0%); 70.2% of patients complained of sore throat, 66.6% of runny nose and 59.4% had body aches. Fever was a complaint in 39.1% of patients.

On examination, 25.4% of patients had temperature of >37 °C, 71.1% were noted to have injected throat, 7.2% enlarged tonsils and 6.0% had enlarged cervical lymph nodes.

#### *Aetiological diagnosis*

Table 1 describes the pathogens isolated using IF and PCR for viral identification, and culture for bacterial isolation. About a quarter of patients (25.2%) had viral infections, and only 2.4% had bacterial infections. Of these, three patients had mixed infection with both rhinovirus and streptococcus group G. In patients with virus infections, rhinoviruses were the overwhelming majority (136/150, 90.7%). Streptococcus group A and

TABLE 1 Aetiological agents in 594 patients with acute respiratory symptoms

Pathogen	n (%)
<b>Viral agents</b>	
Rhinovirus	133 (22.4)
Influenza A	5 (0.8)
Parainfluenza 1	1 (0.2)
Parainfluenza 2	2 (0.3)
Parainfluenza 3	2 (0.3)
Respiratory syncytial virus (RSV)	4 (0.7)
<b>Bacterial agents</b>	
Streptococcus group C	2 (0.3)
Streptococcus group G	7 (1.2)
<i>Moxarella catarrhalis</i>	1 (0.2)
<i>Haemophilus influenzae</i>	1 (0.2)
<b>Mixed infection</b>	
Rhinovirus and streptococcus group G	3 (0.5)
<b>Normal flora</b>	
	433 (72.9)
<b>Total</b>	<b>594 (100.0)</b>

*S. pneumoniae* were not isolated from any patient. Of note is the finding that no pathogens were isolated in 72.9% of all patients.

The outcome of additional PCR on 100 selected patients is as presented in Table 2. New pathogens identified were parainfluenza 4, human coronavirus OC43, adenovirus, enterovirus and *C. pneumoniae*. This resulted in an additional 19 patients (19%) in whom a pathogen could be identified. In 49.0% of patients, no pathogens were identified.

Table 3 shows a comparison of patients with virus infection and those in whom no pathogen was isolated, in the 100 patients in whom additional PCR was performed. There were no differences between patients who had a viral infection, compared with those with no infection, with respect to demographic and social variables, as well as clinical presentation; the exception was that there were fewer male patients with virus infections (males 41.3%, females 63.6%,  $P = 0.04$ ).

## Discussion

To our knowledge, this is the first practice-based study on the aetiological diagnosis of a large group of patients presenting with URTI in primary care clinics in Asia, using IF and PCR as identification methods. We found that an infective aetiology was present in only 51% of patients. Of these, 47% were viral infections, and 4% were bacterial or mixed bacterial and viral infections. The proportion of patients in whom no infective cause could be found was higher than that found in community studies. In the Tecumseh Study, this was 23%,<sup>6</sup> even without newer methods of virus isolation. In a study among university students, with the use of IF, PCR and serology, no pathogen could be identified in 30% of subjects.<sup>4</sup>

TABLE 2 Further analysis of 100 samples by additional PCR

Pathogen	IF, rhinovirus PCR and bacterial culture n (%)	Further PCR n (%)	All methods combined n (%)
<b>Virus agents</b>			
Rhinovirus	20 (20.0)	–	17 (17.0)
Influenza A	5 (5.0)	5 (5.0)	5 (5.0)
Parainfluenza 1	1 (1.0)	1 (1.0)	1 (1.0)
Parainfluenza 2	2 (2.0)	2 (2.0)	2 (2.0)
Parainfluenza 3	2 (2.0)	3 (3.0)	3 (3.0)
Parainfluenza 4	–	4 (4.0)	2 (2.0)
RSV	4 (4.0)	3 (3.0)	4 (4.0)
Human coronavirus OC43	–	7 (7.0)	6 (6.0)
Adenovirus	–	1 (1.0)	1 (1.0)
Enterovirus	–	4 (4.0)	4 (4.0)
<b>Bacterial agents</b>			
<i>Chlamydia pneumoniae</i>	–	2 (2.0)	1 (1.0)
<b>Mixed infection</b>			
Streptococcus group G and rhinovirus	1 (1.0)	–	–
Streptococcus group G, rhinovirus and parainfluenza 4	–	–	1 (1.0)
<i>C. pneumoniae</i> and rhinovirus	–	–	1 (1.0)
Parainfluenza 4 and rhinovirus	–	–	1 (1.0)
Human coronavirus OC43 and rhinovirus	–	–	1 (1.0)
Parainfluenza 4 and <i>C. pneumoniae</i>	–	1 (1.0)	1 (1.0)
No pathogen detected	65 (65.0)	67 (67.0)	49 (49.0)

We examined the following factors in the study methodology that might have contributed to the high proportion of patients in whom no pathogen could be detected. First, the adequacy of sample collection. All samples were collected by the authors, or by qualified staff nurses who had been trained in the technique by the authors. Although nasopharyngeal aspirates were used in some studies,<sup>4</sup> we chose nasopharyngeal swabs for two reasons. Nasopharyngeal aspiration is the optimal sampling method with respect to viral culture, but there were not enough studies on aspirate versus swab for IF and PCR, and most sampling studies have been conducted in children. In our pilot study in adults in a clinic setting, we found in fact that aspirates gave a poor yield of cells for virus identification, whereas swabs yielded sufficient cells for IF. By extension, swabs should then be satisfactory, if not better, for PCR. In the main study, we noted that adequate cells were seen in almost all samples after processing the specimens for IF.

TABLE 3 Patient characteristics and clinical presentation by viral aetiology

Variable	Virus <i>n</i> = 47 <i>n</i> (%)	No pathogen <i>n</i> = 49 <i>n</i> (%)	<i>P</i> -value	Odds ratio (95% CI)
<b>Socio-demographic</b>				
Age (years)				
Mean (SD)	46.0 (15.3)	47.2 (16.3)	0.72	
Median (range)	45.0 (21–79)	47.0 (22–85)	0.65	
Gender				
Male	26 (41.3)	37 (58.7)	0.04	0.40 (0.17–0.96)
Ethnic group				
Chinese	30 (46.9)	34 (51.3)	0.47	0.73 (0.31–1.72)
Smoking history				
Non smoker	32 (50.0)	32 (50.0)	1.00	
Ex-smoker	6 (50.0)	6 (50.0)		1.00 (0.29–3.43)
Current smoker	9 (45.0)	11 (55.0)	0.92	0.82 (0.30–2.24)
<b>General health status</b>				
General well-being past 3 months				
Fair/poor	17 (58.6)	12 (41.4)	0.21	1.75 (0.72–4.22)
Stress level past 2 weeks				
High	4 (30.8)	9 (69.2)	0.16	0.41 (0.12–1.45)
<b>Current URTI episode</b>				
Total duration of symptoms				
Mean (SD)	7.3 (3.6)	7.9 (3.9)	0.47	
Median (range)	6.0 (3–24)	7.0 (3–17)	0.60	
Total number of symptoms <10	26 (56.5)	20 (43.5)	0.10	2.02 (0.88–4.64)
Selected symptoms				
Cough Yes	43 (51.2)	41 (48.8)	0.25	2.10 (0.59–7.50)
Runny nose Yes	38 (53.5)	33 (46.5)	0.13	2.05 (0.80–5.23)
Sore throat Yes	31 (51.7)	29 (48.3)	0.41	1.43 (0.62–3.30)
Fever Yes	22 (48.9)	23 (51.1)	0.99	1.00 (0.45–2.22)
Physical examination				
Body temperature >37 °C	17 (57.6)	13 (43.3)	0.28	1.62 (0.68–3.88)
Injected throat Yes	35 (49.3)	36 (50.7)	0.77	1.15 (0.45–2.91)
Enlarged tonsils Yes	3 (42.9)	4 (57.1)	0.76	0.79 (0.17–3.71)
Enlarged cervical lymph nodes Yes	4 (66.7)	2 (33.3)	0.36	2.24 (0.39–12.85)

A second factor was the choice of pathogens looked for and the methods for their identification. The pathogens detected by respiratory virus IF (RSV, influenza A and B, parainfluenza 1–3, adenovirus) were the usual ones detected in clinical laboratories. For the pathogens covered by IF, the sensitivity and specificity are comparable with virus culture.<sup>15</sup>

Virus culture was not performed in this study due to budget constraints. Virus culture may increase the detection rate although, in general, the yield will not be significantly higher.<sup>15</sup> However, with appropriate cell lines, virus culture may pick up rhinoviruses and enteroviruses—two pathogens which are not detectable by routine IF. We addressed this limitation by performing PCR instead. PCR has been shown to be more sensitive than culture and IF.<sup>16</sup> It is possible that virus culture may also pick up hitherto uncharacterized viruses, but this is quite rare. An example would be the recent characterization of human metapneumoviruses.<sup>17</sup> With further PCR, we have covered most of the known viruses causing URTI, except for human metapneumoviruses.

Although detection by PCR is more sensitive than IF or virus isolation in tissue culture, more sensitive types of PCR approaches could possibly have increased the yield, e.g. nested PCR and real-time PCR. However, nested PCR is not amenable to a multiplex protocol so will be significantly more costly and time consuming. Nested PCR has also not been described for all the viruses examined in our study. Real-time PCR recently has become more important in diagnostic tests, and its application in future could yield more sensitive results.

In the identification of bacterial aetiology from culture, we looked for heavy predominant growth of likely pathogens. It was not possible to have strict aetiological proof from culture alone. We could only tie in symptoms plus heavy growth and point to a likely suspect. In doing so, we have adopted the method that is commonly in use for interpreting culture results clinically, such as for the identification of group A streptococcus infections.

With bacterial culture, our use of 48 h incubation and additional plates in anaerobic conditions would have enhanced the detection of group A streptococci

and unusual pathogens such as *Arcanobacterium haemolyticum*. However, we did not detect group A streptococci. This was a little surprising. It could have been missed if specimen collection was inadequate. Taking two or more throat swabs would increase the sensitivity of culture, but this was not practical. In addition, the increased yield by double sampling is limited (90–96% using one swab compared with 100% using two swabs).<sup>18</sup> We believe that the study does reflect the relative paucity of group A streptococci in our community. Low carriage of group A streptococci has also been shown in other communities.<sup>19</sup>

We did not use paired sera, as used by Lieberman *et al.*, due to logistic constraints. It is possible that additional cases may have been picked up by serology. However, the use of IF and PCR on acute phase specimens would be expected to detect the pathogens targeted. Moreover, the range of pathogens targeted by our protocol is wider than what is usually available by serology.

Finally, we would like to propose the possibility of non-infective aetiology in some of the patients who presented to us with complaints of upper respiratory symptoms. One possible non-infective cause is air pollution. Hajat *et al.* reported an adverse effect of air pollution on general practice consultations for upper respiratory symptoms.<sup>20</sup> Pollutants in the air, such as large particles and SO<sub>2</sub>, can cause irritation of the upper respiratory tract mucosa and acute symptoms of coughing and increase in mucous secretion. There could also be a reduction of resistance to infection, as nitrogen dioxide (NO<sub>2</sub>) and ozone (O<sub>3</sub>) have been shown to impair ciliary action and the function of macrophages in animal studies.<sup>21</sup> There was, however, no documentation of increased levels of air pollutants in Singapore at the time of the study.

In addition to irritant-induced symptoms, there is also a group of syndromes loosely termed 'non-allergic rhinitis', where symptoms have been attributed to reactivity to a variety of common physical and chemical stimuli, such as changes in air temperature or humidity, perfume, household cleaning products, etc.<sup>22</sup> These are poorly understood and have not been studied extensively. They may also contribute to the aetiology of patients with upper respiratory tract symptoms seen in GPs' surgeries.

Both irritant and non-allergic causes of upper respiratory symptoms may also explain the absence of pathogens isolated from some 30% of individuals in many community studies. However, ours was a practice-based study, and patients sought consultation for a variety of reasons, some of which may not be medical in nature.

One of the reasons which may cue a person to consult a GP is the threshold of tolerance for symptoms, which is different for different people. The need to legitimize the sick role is another factor to consider. This is especially so for daily-rated workers, who do not have the privilege of paid medical leave without medical certification, and, in countries such as Singapore, where workers cannot call in sick. There may also be some hidden

agenda in seeing the doctor, as some patients who may need a day or two off to fulfill certain social roles (one commonly encountered reason being to look after a child who is ill) are unable to obtain leave from work, or unwilling to use up their limited holiday leave for this purpose. There is therefore need to examine these reasons in further studies.

### Conclusions

In patients presenting with acute respiratory tract symptoms of <7 days duration at the NHGPs in Singapore, an infective aetiology could only be found in 51%. Of these, 45% of patients had viral infections, with rhinovirus being the most common virus.

In 49% of patients, no infective aetiology could be identified. This could be partly due to non-infective causes of respiratory tract symptoms such as air pollution. It could also be due to differences between the population at large in the community, and the self-selective nature of patients presenting at general practices. Further studies are required to elucidate reasons for encounter, in order to equip GPs with the knowledge to manage their patients better.

### Acknowledgements

The authors would like to thank Dr Shanta Emmanuel, Chief Executive Officer of National Healthcare Group Polyclinics, and Professor David Koh, Head, Department of Community, Occupational and Family Medicine, National University of Singapore, for their encouragement and support. We would also like to thank the staff nurses and members of all the National Healthcare Group Polyclinics for their help in field work and, last but not least, Ms Orchid Chua, for her invaluable assistance in administrative work, field work and data management. This study was made possible by grant support from the National Healthcare Group Research and Development Committee (Grant No. NHG-RPR/01003).

### References

- 1 Heikkinen T, Järvinen A. The common cold. *Lancet* 2003; **361**: 51–59.
- 2 Badger GF, Dingle JH, Feller AE *et al.* A study of illness in a group of Cleveland families. II. Incidence of the common respiratory diseases. *Am J Hyg* 1953; **58**: 31–40.
- 3 Monto AS, Cavallaro JJ. The Tecumseh study of respiratory illness. II. Patterns of occurrence of infection with respiratory pathogens, 1965–1969. *Am J Epidemiol* 1971; **94**: 280–289.
- 4 Mäkelä MJ, Puhakka T, Ruuskanen O *et al.* Viruses and bacteria in the etiology of the common cold. *J Clin Microbiol* 1998; **36**: 539–542.
- 5 Gray GC, Schulz RG, Gackstetter GD *et al.* Prospective study of respiratory infections at the U.S. Naval Academy. *Mil Med* 2001; **166**: 759–763.
- 6 Monto AS. Studies of the community and family: acute respiratory illness and infection. *Epidemiol Rev* 1994; **16**: 351–373.
- 7 Lieberman D, Shvartzman P, Lieberman D *et al.* Etiology of respiratory tract infection in adults in a general practice setting. *Eur J Clin Microbiol Infect Dis* 1998; **17**: 685–689.

- <sup>8</sup> Murray PR, Baron EJ, Pfaller MA, Tenover FA, Tenover RH. *Manual of Clinical Microbiology*, 7th edn. Washington (DC): ASM Press; 1999.
- <sup>9</sup> Papadopoulos NG, Hunter J, Sanderson G, Meyer J, Johnston SL. Rhinovirus identification by Bgl I digestion of picornavirus RT-PCR amplicons. *J Virol Methods* 1999; **80**: 179–185.
- <sup>10</sup> Claas ECJ, Sprenger MJW, Kleter GEM, van Beek R, Quint WGV, Masurel N. Type specific identification of influenza viruses A, B and C by the polymerase chain reaction. *J Virol Methods* 1992; **39**: 1–13.
- <sup>11</sup> Aguilar JC, Perez-Brena MP, Garcia N, Cruz ML, Erdman DD, Echevarria JE. Detection and identification of human parainfluenza viruses 1, 2, 3 and 4 in clinical samples of pediatric patients by multiplex reverse transcription PCR. *J Clin Microbiol* 2000; **38**: 1191–1195.
- <sup>12</sup> Pitkaranta A, Virolainen A, Jero J, Arruda E, Hayden FG. Detection of rhinovirus, respiratory syncytial virus and coronavirus infections in acute otitis media by reverse transcriptase polymerase chain reaction. *Pediatrics* 1998; **102**: 291–295.
- <sup>13</sup> Romero JR, Rotbart HA. PCR detection of the human enteroviruses. In: Persing DH, Smith TF, Tenover FC, White TJ (eds) *Diagnostic Molecular Microbiology: Principles and Applications*. Washington (DC): ASM Press; 1993: 401–406.
- <sup>14</sup> Grondahl B, Puppe W, Hoppe A, Kuhne I, Weigl JAI, Schmitt HJ. Rapid identification of nine microorganisms causing acute respiratory tract infections by single-tube multiplex reverse transcription PCR: feasibility study. *J Clin Microbiol* 1999; **37**: 1–7.
- <sup>15</sup> Landry ML, Ferguson D. SimulFluor respiratory viral screen for rapid detection of multiple respiratory viruses in clinical specimens by immunofluorescence staining. *Clin Microbiol* 2000; **38**: 708–711.
- <sup>16</sup> Liolios L, Jenny A, Spelman D, Kotsimbos T, Catton M, Welleling S. Comparison of a multiplex reverse transcription-PCR-enzyme hybridization assay with conventional viral culture and immunofluorescence techniques for the detection of seven viral respiratory pathogens. *J Clin Microbiol* 2001; **39**: 2779–2783.
- <sup>17</sup> van den Hoogen BG, de Jong JC, Groen J *et al*. A newly discovered human pneumovirus isolated from young children with respiratory tract disease. *Nature Med* 2001; **7**: 719–724.
- <sup>18</sup> Kurtz B, Murtz M, Roe M, Todd J. Importance of inoculum size and sampling effect in rapid antigen detection for diagnosis of *Streptococcus pyogenes* pharyngitis. *J Clin Microbiol* 2000; **38**: 279–281.
- <sup>19</sup> Haidan A, Talay SR, Rohde M, Sriprakash KS, Currie BJ, Chhatwal GS. Pharyngeal carriage of group C and group G streptococci and acute rheumatic fever in an Aboriginal population. *Lancet* 2000; **356**: 1167–1169.
- <sup>20</sup> Hajat S, Anderson HR, Atkinson RW, Haines A. Effects of air pollution on general practitioner consultations for upper respiratory diseases in London. *Occup Environ Med* 2002; **59**: 294–299.
- <sup>21</sup> Lipfert FW. A primer on physiological effects of air pollution and measurement of respiratory function. In: Lipfert FW. *Air Pollution and Community Health: A Critical Review and Data Sourcebook*. New York: van Nostrand Reinhold; 1995: 92–107.
- <sup>22</sup> Shusterman D. Review of the upper airway, including olfaction, as mediator of symptoms. *Environ Health Perspect* 2002; **110** Suppl 4: 649–653.