A prospective study of bacterial flora in nasal cavity of patients with persistent allergic rhinitis*

M.B. Taylor[1], I.T. Tan[2], K.T. Chan[1], L. Shen[3], L. Shi[4], D.Y. Wang[2]

[1] Department of Microbiology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[2] Department of Otolaryngology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[3] Biostatistics Unit, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[4] Department of Otolaryngology, Qilu Hospital, Shandong University, China

Rhinology 50: 000-000, 2012
DOI: 10.4193/Rhino.10.140

***Received for publication:**
November 2, 2010
Accepted: December 23, 2010

Summary

It remains unanswered whether persistent allergic inflammation in nasal mucosa alters bacterial colonization and infection. The aim of this study was to investigate the bacterial flora in the nasal cavity of patients with persistent allergic rhinitis (PAR) and to correlate the bacteriological findings with presence of nasal symptoms, nasal eosinophil and neutrophil counts. A total of 255 subjects, aged between 6 – 74 years (mean 33.9 years) was randomly selected from a population-based rhinitis survey study in Singapore. All subjects went through a thorough medical history and nasal examinations. Serum specific IgE to a panel of common house dust mites, nasal cytological and microbiological examinations were performed. PAR was diagnosed in 107 patients and none of them had received previous regular therapy. There is a significant relationship between PAR and eosinophil grades, but not with neutrophil count. No statistically significant difference was found in quantitative and qualitative bacterial flora in nasal cavity between PAR patients and subjects with non-rhinitis or with non-allergic rhinitis. There is a significant inverse correlation between ongoing rhinorrhoea and quantitative bacterial load, and between signs of nasal mucosa (pale and edema) and the presence and type of bacterial pathogens. In conclusion, our study demonstrates that patients with untreated (or using PRN medicine) PAR do not result in a significant change in bacterial flora in their nasal cavity.

Key words: bacteria, flora, nasal cavity, persistent allergic rhinitis, prospective study

Introduction

The prevalence of atopic diseases such as allergic rhinitis has increased over the past decades, especially in developed countries. It is a common worldwide disease and is estimated to affect approximately 10 - 25% of the world's population [(1)]. The risk determinants for the increasing prevalence of allergic rhinitis remain unclear. During the past decade, there is a question of why atopic diseases are increasing in prevalence, which is inversely proportional to the prevalence of communicable diseases. This is due to the improvement of health care policy and hygiene standard, especially in developed countries. The so-called 'hygiene hypothesis' of allergy was first suggested by Strachan, who noted that the risk of developing allergies and asthma is inversely related to the number of children in the family [(2)]. This effect has since been confirmed using various markers of infectious burden such as number of older siblings [(3-5)], attendance at day care facilities [(6)], positive serology to orofaecal infections [(7,8)] and regular contact with farm animal before the age of 7 years [(9)]. These demonstrate the interplay between infection and development of allergic disorders.

Infectious and allergic rhinitis are the two commonest types of rhinitis. However, the association between bacterial infection and allergic inflammation has been a matter of controversy. Few retrospective and prospective series have shown allergic rhinitis to be closely related with and may be a causative factor in bacterial infection such as sinusitis [(10,11)]. In animal models, allergic inflammation had been shown to enhance bacterial infection [(12)]. However, there has not been any study in literature to date that looked closely into this aspect in the human

Corrected proof

population. It remains unanswered whether this persistent or intermittent mucosal inflammation in nasal mucosa predispose to bacterial growth and possible bacterial infection in the nasal environment.

In Singapore, the prevalence of rhinitis was found to be 13.1% from a population study [13]. Persistent allergic rhinitis (PAR) with IgE-mediated sensitization to house dust mites is almost exclusively the pattern of allergic rhinitis seen in our country, due to a typical tropical climate. These patients with persistent rhinitis are often symptomatic and suffer from a chronic condition of mucosal inflammation in the nose. The aim of this study is to investigate the bacterial flora in nasal cavity of these patients with allergic rhinitis and to correlate the bacteriological findings with the presence of nasal symptoms and nasal eosinophil count. This helps us understand the relationship of bacterial infection in allergic inflammation in the human nasal cavity.

Materials and methods

The target population in this study was a subset derived from the study population in a previous study published by the department [13]. In the earlier study, a total of 4,602 subjects aged 6 – 80 years (mean 33 years) was selected from Singapore housing areas by means of multistage, clustered, and age-proportionate stratified random sampling. One member of each household was randomly selected for the interview. The study population had a similar age distribution to the general population, but it was disproportionately stratified to have an equal proportion of Chinese, Malays, and Indians. All study subjects were investigated using an interviewer-administered questionnaire in their homes. The questionnaire was completed by either the subject or their proxy with little assistance of the field-interviewer. Approval to conduct this study was granted by the National Medical Research Council of Singapore and the institutional review board of the Medical Faculty of National University of Singapore.

Following this previous study, 920 subjects were randomly called to attend a rhinologic examination at the Otolaryngology outpatient clinic in the National University Hospital (NUH) of Singapore. There were 255 subjects, 130 males and 125 females, aged from 6 to 74 years (mean of 33.9 years), who agreed to participate in the study. All subjects went through the following examinations within a period of three months.

Four groups of patients were derived according to medical history, rhinological examinations and allergy testing [13]: 1) Allergic rhinitis: the occurrence of two or more symptoms (nasal obstruction, rhinorrhea, sneezing and itchy nose) on most days during the past year, and a positive serum sIgE to house dust mites (atopy) was confirmed, and thus persistent allergic rhinitis (PAR) was made; 2) Non-atopic rhinitis: subjects with rhinitis symptoms, but no evidence of allergic sensitization to common local allergens; 3) Non-rhinitis with atopy: subjects had no rhinitis symptoms, but a positive serum sIgE test; and 4) Non-rhinitis and non-atopy: subjects had neither rhinitis symptoms nor allergic sensitization (atopy).

Assessment of symptoms

The subjects were asked on symptoms of rhinitis, which included nasal obstruction, rhinorrhea, sneezing and nasal itching (for more than one hour on most days) during the last year [1,13,14]. In addition, ongoing nasal symptoms (during the last week) were specially recorded in order to compare with bacteriological cultural results. The use of any medications, especially antihistamines, oral or nasal steroids and antibiotics, during the past one-month was recorded. Asthma was recorded if subjects had a history of paroxysmal attacks of breathlessness commonly associated with a tightness of the chest and wheezing, and asthma was previously diagnosed by a physician.

Rhinological examinations

Routine rhinoscopic examinations were carried out on these subjects in the same consultation. Specific attention was paid to the anatomical situation in the nose (e.g., septal deviation and edema of the inferior turbinate), the color of the mucosa (e.g., pale mucosa), and the amount and aspect of the mucus [1]. All these assessments were performed based on subjective evaluation by the examiner. For subjects who have shown signs of sinus pathology (e.g., rhinosinusitis with or without nasal polyp), a thorough inspection of the nasal cavity was performed by a rigid nasal endoscope with the administration of local anesthesia and vasoconstriction.

Allergy testing

Three milliliter of peripheral blood was taken from each subject. Serum specific IgE (sIgE) to house dust mites including *Blomia tropicals (Blo t), Dermatophagoides pteronyssinus (Der p) and Dermatophagoides farinae (Der f)*, were measured by UniCAP system, using commercially available kits from Pharmacia Diagnostics (Fluoro-enzyme immunoassay, Phadia, Uppsala, Sweden). The detectable range was 0.35 - 100 IU/ml of serum sIgE. Atopy was made if sIgE is equal or higher than 0.35 IU/ml.

Nasal cytological examination

Nasal mucosa samples for cytological examination were collected by using the Rhino-probe (Rhino-probe, Synbiotics Corporation, San Diego, CA, USA) scraping method that had been previously described by Meltzer and Jalowayski [15]. Briefly, a disposable probe is placed into the nasal cavity 2 - 3 cm posteriorly. The cupped tip of the probe is gently pressed onto the mucosal surface of the medial aspect of the inferior turbinate. This maneuver is repeated two or three times before withdrawing the probe. Then, the contents of the cupped tip

Corrected proof

are spread over a labelled slide to make a monolayer of cells. The slide is then quickly placed in a jar containing 95% ethyl alcohol before it dries out. All slides are then stained using May-Grünwald-Giemsa and examined by a light microscopy. The nasal cytogram was graded at high power (oil immersion, x1000) as a mean of cells (eosinophils and neutrophils) per 10 high power fields, or qualitatively on a scale of 0 – 4 + as suggested previously [15]: 0: none; 1 +: a few scattered cells or 1 - 5 cells per high power field; 2 +: a moderate number of cells or 6 - 15 cells per high power field; 3 +: large clumps of cell or 16 - 20 cells per high power field; 4 +: large clumps of cells covering the entire field or > 20 cells per high power field.

Nasal cavity sampling and microbiological examinations

A single nasal swab was taken from both nasal vestibules for determination of possible methicillin-resistant *Staphylococcus aureus* (MRSA) carriage. Then, a single pernasal swab from the mucosa around the middle meatus of both sides was taken. These swabs were placed immediately in prepared Amies transport medium (Copan Italia, Italy) and transported immediately to the Department of Microbiology of the National University Singapore.

Each nasal swab was plated onto Methicillin Aztreonam Mannitol Salt Agar, a rapid screening medium for MRSA [16]. The pernasal swab was inoculated and plated out on two Blood Agar (BA) plates, and a single Chocolate Agar (CA) plate. One BA and the CA plate were incubated in a candle jar for 48 hours, and the second BA plate anaerobically for the same period. Bacteria were identified using standard laboratory techniques [16]. The results of bacterial cultures were coded for statistical analysis with the following parameters.

(a) Quanitative measurement

The quantitative measurement of bacterial growth was estimated into various categories according to the number of colonies and how many 'streaks' showed growth [17]:
Category 1: no growth; Category 2: +/- growth; Category 3: + growth; Category 4: ++ growth; and Category 5: +++ growth.

(b) Qualitative growth

Category 1 (low load) = no growth, +/-, + or ++ growth.
Category 2 (heavy growth) = +++ growth.

(c) and (d) Presence and type of potential pathogen

Category 1 = no growth, or presence of normal skin flora only (coagulase negative staphylococci and/or diphtheroids), or *Moraxella catarrhalis.* (No *Neisseria* spp were isolated in this study.)
Category 2 = presence of potential bacterial pathogens, which were further identified in 2 patterns:

- Growth of bacteria commonly associated with acute pyogenic infection: *Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae* and beta hemolytic *Streptococci*, singly or in combination.
- Growth of bacteria associated with chronic otorhinological infections: in this study, coliforms, *Stenotrophomonas maltophilia*, or anginosus group *Streptococcus*

Definition (c): 1 = no pathogen, 2 = any pathogen (acute or chronic)
Definition (d): 1 = no pathogen, 2 = acute pathogen, 3 = chronic pathogen.
No obligate anaerobic bacteria were isolated in this study.

Statistical analysis

All statistical tests were carried out using the SPSS software package for windows (release 10.0.5 – 27 November 1999; SPSS, Inc., Chicago, IL, USA). The Pearson chi-square and Fisher's exact tests were performed to evaluate the relationships between microbiological results and all parameters of diagnosis (e.g., PAR and asthma), current symptoms of rhinitis, signs of nasal mucosa, and cell counts (eosinophils and neutrophils). A p-value of less than 0.05 was considered to be statistically significant.

Results

The demographic characteristics, diagnosis and laboratory measurements of the study subjects are summarized in Table 1. Of the 255 subjects, 146 subjects had sensitisation to common local allergens (atopy). One hundred and forty-one subjects had persistent rhinitis and PAR was diagnosed in 107 patients. Asthma was reported in 34 patients. All PAR patients had history of rhinitis symptoms for more than 5 years and most of them had symptoms for more than 10 years. None of patients with PAR had received regular treatment (except on demand) with antihistamines or nasal steroids during the last month. Therefore, their PAR symptoms remained unchanged. Patients (n = 3) who received nasal steroids during the last month were excluded from the analysis.

The presence of current nasal symptoms (during the last week), i.e., itchy nose, sneezing, rhinorrhea, and nasal blockage were 43.5%, 54.1%, 40.4%, and 50.2% in PAR patients respectively. One hundred and eight subjects were found to have pale mucosa of inferior turbinate, and 69 of them (63.8%) were PAR. Edema of the inferior turbinate mucosa was found in 67 subjects and 53 of them (82%) were PAR. Four patients had purulent sinusitis and 4 patients had nasal polyposis. There was one patient who had both conditions, as confirmed by nasal endoscopic examination.

In subjects with symptoms of rhinitis, the incidence of positive serum sIgE to *Blo t, Der p and Der f* was 65%, 71% and 69 %, respectively. In subjects with no typical rhinitis symptoms, the incidence was 37%, 36%, and 34%, respectively. There is a good

Corrected proof

Table 1. Characteristics of the study subjects (n = 255) in different diagnostic groups.

Symptoms/Sign	Rhinitis		Non-Rhinitis	
	Atopic (PAR*)	Non-atopic	Atopic	Non-atopic
	n = 107 (%)	n = 34 (%)	n = 39 (%)	n = 75 (%)
Asthma	25 (23.4)	7 (20.6)	1 (2.6)	1 (1.3)
Ongoing nasal symptoms (during the last week)				
Itchy nose	84 (78.5)	22 (64.7)	1 (2.6)	4 (5.3)
Sneezing	97 (90.6)	31 (91.2)	6 (15.4)	4 (5.3)
Rhinorrhea	82 (76.6)	20 (58.8)	1 (2.6)	0
Blockage	97 (90.6)	27 (79.4)	3 (7.7)	1 (5.3)
Pale mucosa	69 (64.5)	11 (32.3)	15 (38.5)	13 (17.3)
Inf. tub. hypertrophy†	55 (51.4)	6 (17.6)	1 (2.6)	5 (6.7)
Eosinophilia (score ≥2)	32 (29.9)	4 (11.8)	6 (15.4)	0
Neutrophilia (score ≥2)	25 (23.4)	7 (20.6)	22(56.4)	6 (8.0)
Quantitative Bacterial load				
Category 1	15 (14.0)	4 (11.8)	1 (2.6)	3 (4.0)
Category 2	48 (44.9)	18 (52.9)	20 (51.3)	29(38.7)
Category 3	34 (31.8)	10 (29.4)	15 (38.5)	31 (41.3)
Category 4	10 (9.3)	2 (5.9)	2 (5.1)	11 (14.7)
Category 5	0	0	1 (2.6)	1 (5.3)
Qualitative Growth[a]				
Low	63 (58.9)	22 (64.7)	21 (53.8)	32 (42.7)
High	44 (41.1)	12 (35.3)	18 (46.2)	43 (57.3)
Present of Pathogen[b]	29 (27.1)	6 (17.6)	12 (30.8)	22 (29.3)
Pathogen type‡				
Acute	24 (22.4)	5 (14.7)	12 (30.8)	18 (24.0)
Chronic	5 (4.7)	1 (2.9)	0	4 (5.3)

* PAR: Persistent allergic rhinitis

†: Inferior turbinate hypertrophy

‡: See details in Table 2

a: Adjusted OR (PAR vs. all others): 0.718, 95% CI: 0.414 - 1.186

b: Adjusted OR (PAR vs. all other): 1.004, 95% CI: 0.574 - 1.757

coefficient correlation of atopy to the three named mite species (r = 0.980 for *Der p vs Der f*; r = 0.887 for *Der p vs Blo t;* r = 0.898 for *Der f vs Blo t)*.

There was no significant correlation between eosinophil and neutrophil counts in PAR patients. High eosinophil grades (equal or above 2) were found in 42 subjects, and 32 (76%) of them were PAR. There is only a significant relationship (r = 0.456, p < 0.001) between eosinophil grades and the number of patients with PAR. Neutrophilic cytogram (grade equal or above 2) were found in 60 patients, and 25 (41.6%) of them were PAR. There is no significant relationship (r = 0. 132, p > 0.05) between neutrophils grades and the number of PAR patients.

A negative culture result for MRSA was found in all patients from the nasal vestibule swab. No further bacterial analysis was possible from this site as a selective medium was deliberately employed used to screen for MRSA only. There were only 4 subjects with nasal polyps diagnosed by the rhinoscopic examina-

Corrected proof

Table 2. Number and type of pathogens (n=71) in different diagnostic groups.

Type of Pathogen	Rhinitis		Non-Rhinitis	
	Atopic (PAR*)	Non-atopic	Atopic	Non-atopic
	n = 107 (%)	n = 34 (%)	n = 39 (%)	n = 75 (%)
S. aureus (n = 49)	19 (17.8)	5 (14.7)	10 (25.6)	15 (20)
H. influenzae (n = 3)	1 (0.9)	0	2 (5.1)	0
S. aureus plus *H. influenzae* (n = 4)	3 (2.8)	0	0	1 (1.3)
S. pneumoniae (n = 3†)	2 (1.9)	0	0	1 (1.3)
Group C *Streptococcus* (n = 1)	0	0	0	1 (1.3)
Coliform (n = 8‡)	5 (4.6)	1 (2.9)	0	2 (2.6)
S. maltophilia (n = 3)	1 (0.9)	0	0	2 (2.6)

* PAR: Persistent allergic rhinitis

†: Plus a coliform in one patient; classified in "acute" category

‡: In one patient, with an anginosus group streptococcus

tion. One of them had no growth from the nasal swab, one had 2 + mixed bacterial growths and the remaining two had scanty skin flora. There were also 4 subjects with chronic rhinsinusitis (1 with concomitant nasal polyps). One patient had mixed skin flora from the nasal swab, while the other three had plausible pathogens from the nasal swabs (namely *Staphyloccocus aureus,* a coliform identified as *Citrobacter* sp. and an anginosus group *streptococcus*).

There were 7 subjects who received antibiotics therapy during the past 2 weeks prior to nasal examination and nasal swab and were excluded from the statistical analysis. There was one patient with no growth, 1 with scanty skin flora and 3 with scanty diphtheroids growth. The remaining 2 subjects had low bacterial growth from nasal swabs; one with 1 + diphtheroids and the other with 1 + mixed skin flora. These findings concluded that patients who received antibiotics therapy had either low or no bacterial growth from their nasal swabs.

There is no statistical difference for the results of bacterial culture (the quantitative bacterial load, qualitative bacterial growth, presence and type of pathogens) obtained from the meatal pernasal swab specimens between subjects with rhinitis (PAR and Non-allergic rhinitis) and Non-rhinitis (with and without atopy), and between PAR and any one of the three groups (Non-allergic rhinitis, Non-rhinitis with atopy, Non-rhinitis without atopy). There were 71 patients with pathogens cultured form the pernasal swab. Table 2 shows the different types of pathogens cultured form the micobiological examination, with the commonest being *S. aureus*. It is known that bacterial colonization of the nasopharynx can be affected by different seasons of the year. This is not an issue in our study as our country is a tropical country with no seasonal variation.

Comparison was also done between results of bacterial culture (the quantitative bacterial load, qualitative bacterial load, presence of pathogens and type of pathogens) obtained for the meatal pernasal swab specimens, and presence of current nasal symptoms (during the last week) and signs on nasal examination (Table 3). There is a statistically significant inverse correlation between ongoing rhinorrhea and quantitative bacterial load ($p = 0.029$), indicating less bacterial load in subjects with rhinorrhea. There is also a statistical inverse correlation between pale mucosa ($p = 0.007$) and presence ($p = 0.007$) and type of pathogens ($p = 0.009$), as well as between edema of inferior turbinate and the presence ($p = 0.002$) and type ($p = 0.009$) of pathogens (Table 4). Similarly, the above observation suggests the presence of less bacterial colonization in patients with edema of the inferior turbinate.

Discussion

The association between bacterial infection in the nose and allergic (atopy) rhinitis has not been well studied. With the hygiene hypothesis, Strachan postulated potential hazards for atopy with reduced infection secondary to better hygiene standard [2]. A recent study suggested an association of declining incidence of infections with rising prevalence of atopic diseases [18]. Allergic rhinitis has been considered to be an important factor in the development of infection like sinusitis. In large group studies, allergic inflammation also appears to be an important factor in

Corrected proof

Table 3. Comparison between results of bacterial culture (the quantitative bacterial load, qualitative bacterial load, presence of pathogens and type of pathogens), and presence of nasal symptoms (during the last week) and examinations in all study subjects (n = 255).

	Bacteria Load (Quantitative)	Bacterial Load (Qualitative)	Presence Of Pathogens	Type Of Pathogens
Ongoing nasal symptoms				
Nasal Itch	NS	NS	NS	NS
Sneezing	NS	NS	NS	NS
Rhinorrhea	0.029	NS	NS	NS
Nasal congestion	NS	NS	NS	NS
Nasal inspection				
Pale mucosa	NS	NS	0.007 (inverse)	0.009 (inverse)
Inferior turbinate hypertrophy	NS	NS	0.002 (inverse)	0.009 (inverse)
Asthma	NS	NS	NS	NS
Cytograms				
Eosinophils	NS	NS	NS	NS
Neutrophils	NS	NS	NS	NS

Table 4. Comparison between results of nasal inspection and presence and type of pathogens in all study subjects (n = 255).

Results of nasal inspection		Presence of Pathogens			Type of Pathogens			
		No	Yes	p-value	No growth	Acute	Chronic	p-value
Pale Mucosa	Normal	94	49		94	40	9	
	Pale	88	20	0.007	88	19	1	0.009
Inferior Turbinate	Normal	123	60		123	52	8	
	hypertrophy	58	9	0.002	58	7	2	0.009

acute and chronic sinusitis [19,20]. In this study, all PAR patients have not received a regular treatment (neither antihistamines nor nasal steroids), which is a common situation as reported in our previous population-based epidemiological study [13]. Thus, it provides an opportunity for studying qualitative and quantitative bacterial flora in nasal cavity of untreated patients with PAR.

It has been proposed that allergic rhinitis is also caused or augmented by local nasal infections. Nasal mucosal inflammation caused by allergic rhinitis can obstruct sinus drainage and enhance bacterial proliferation. A study published by Blair et al., [12] was able to show such association in a mouse model. Using mice instilled with bacteria, it was shown that allergic responses augmented bacterial infection in mice. However, to our knowledge, there is no similar study in a human population, which takes a closer look at the nasal bacterial flora in patients with allergic rhinitis. The presence of allergic rhinitis may similarly predispose to bacterial infection in the human nasal environment. It is shown in the Table 1 that the incidence of high bacterial flora is 41.1% for PAR subjects and 49.3% for non-PAR subjects (all others) (OR = 0.718, 95% CI 0.434 to 1.186). Their difference is - 8.2% (95% CI - 20.5% to 4.1%). Even though our sample size is not enough for detecting the difference (580 subjects per group is required to detect a difference of 41.1% vs. 49.3% with 80% power), it is enough for us to claim a non-inferiority if the non-inferiority range is set up as OR less than 1.2, or the difference less than 5%.

In comparison between basal symptoms and bacterial culture results, there was only an inverse correlation between ongoing rhinorrhea and the quantitative bacterial load. This observation could be explained with common understanding of the pathophysiology of IgE-mediated allergic inflammation. In allergic rhinitis, local release of inflammatory and chemical mediators from inflammatory cells (e.g., mast cells and eosinophils) act both directly and indirectly on the nasal vasculature, the mucus-secreting cells and glands, result in transudation and increase mucus secretion. With more rhinorrhea, nasal fluid may help in removing and washing away possible local nasal pathogens. This results in reduced bacteria load in the nasal mucosa. Secondly, activated eosinophils are able to phagocy-

Corrected proof

tose particles, such as bacteria, but their main killing mechanism is the release of toxic granule proteins and production of oxygen free radicals [21,22], the latter also effective against a range of bacterial pathogens.

There are known common features of allergic rhinitis, which include pale nasal mucosa and hypertrophy (oedema) of turbinates. Interestingly, it was shown in our study that with features of pale nasal mucosa and hypertrophied turbinates, there was a significantly smaller number of nasal pathogens present in this group of patients who have suffered PAR for more than 5 years. It suggests that the presence of chronic local inflammatory process in allergic rhinitis does not predispose to bacterial overgrowth, and indeed may even have a suppressive effect on bacterial numbers. This is an important finding, which will help in our management of patients with allergic rhinitis. Antibiotics are still prescribed by some physicians for treatment of allergic rhinitis. From our previous population study, it was found that 12% of our patients with persistent allergic rhinitis had been prescribed antibiotics empirically for treating or preventing bacterial infection [13]. Some physicians use antibiotics for their anti-inflammatory properties rather than their anti-infective properties. However, they should weigh the moderate benefits of antibiotic treatment against the potential for adverse effects, as it is likely to encourage the emergence and persistence of resistant strains of bacteria in these patients. Therefore, the use of antibiotics should be discouraged for the treatment of allergic rhinitis.

There is an increasing number of reports of community acquired MRSA infections in certain regions [23]. However, the present study revealed no evidence for MRSA carriage at the anterior nares site in Singapore. Sensitivity testing of bacteria from the middle meatal site was not carried out. In this report, the overall carriage rate for S. aureus at the middle meatal site (53/255 = 20%) is comparable to the literature report of 39% in healthy subjects [24]. Our data showed no difference of the number of S. aureus isolates between PAR patients and non-rhinitis controls. It was reported that colonization of the middle meatus with S. aureus is significantly more frequent in patients with nasal polyps (63.6%) compared to those with chronic rhinosinusitis (27.3%, $p < 0.05$), and is related to the prevalence of IgE antibodies to classical enterotoxins (27.8% vs 5.9%)[25]. However, our study is not able to address this issue since the number of patients with nasal polyps is small (n = 4) and S. aureus is not found in all of them. It is possible that there is a spectrum between ineffective and over-exuberant local immune response to bacterial pathogens, with infection and nasal allergic symptoms the consequences at the extremes. Further research is indicated for this purpose.

In conclusion, this prospective study has brought more light to our understanding of the pathogenesis and mechanisms for allergic rhinitis. Our study demonstrated that presence of chronic nasal mucosal inflammatory in patients with persistent allergic rhinitis does not predispose to bacterial overgrowth. On the contrary, with ongoing rhinorrhea, it may even have a suppressive effect on bacterial load. Thus the use of antibiotics for allergic rhinitis is not likely to be of any benefit and should be discouraged. The challenge in the future is to understand the complex interplay between allergy and infection. This will have important implications for the development of new therapeutic strategies and prevention of allergic diseases.

Acknowledgements

This study is supported by a grant (NMRC/0292/1998) from the National Medical Research Council (NMRC) of Singapore. We wish to thank Angela J. Waanders for her contributions in survey management of this project, and Drs Pengchi Zhang, Zhili Huang, Rui Yang for their kind assistance in this study.

References

1. Bousquet J, Van Cauwenberge P, Khaltaev N; Aria Workshop Group; World Health Organization. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol. 2001; 108 (Suppl5): S147-334.
2. Strachan DP. Hay fever, hygiene, and household size. BMJ. 1989; 299: 1259-60
3. Von Mutius E, Martinez FD, Fritsch C, et al. Skin test reactivity and number of siblings. BMJ. 1994; 308: 692-695.
4. Jarvis D, Chinn S, Luczynska C, et al. The association of family size with atopy and atopic disease. Clin Exp Allergy. 1997; 27: 240-245.
5. Bodner C, Godden D, Seaton A. Family size, childhood infections and atopic diseases. Thorax. 1998; 53: 28-32.
6. Krämer U, Heinrich J, Wijst M, et al. Age of entry to day nursery and allergy in later childhood. Lancet. 1998; 352: 450-454.
7. Matricardi PM, Rosmini F, Ferrigno L, et al. Cross-sectional retrospective study of prevalence of atopy among Italian military students with antibodies against hepatitis A virus. BMJ. 1997; 314: 999-1003.
8. Matricardi PM, Rosmini F, Riondino S, et al. Exposure to foodborne microbes versus airborne viruses in relation to atopy and allergic asthma: epidemiological study. BMJ. 2000; 320: 412-417.
9. Radon K, Windstetter D, Eckart J, et al. Farming exposure in childhood, exposure to markers of infections and the development of atopy in rural subjects. Clin Exp Allergy. 2004: 34: 1178-1183.
10. Spector SL. The role of allergy in sinusitis in adults. J Allergy Clin Immunol 1992; 90: 518-520.
11. Shapiro GG, Virant FS, Furukawa CT, Pierson WE, Bierman CW. Immunologic defects in patients with refractory sinusitis. Pediatrics. 1991; 87: 311-316.
12. Blair C, Nelson M, Thompson K, Boonlayangoor S, Haney L, Gabr U, Baroody FM, Naclerio RM. Allergic inflammation enhance bacterial sinusitis in mice. J Allergy Clin Immunol. 2001; 108: 424-429.
13. DY Wang, M Niti, JD Smith, KH Yeoh, TP Ng. Rhinitis: do diagnostic criteria affect the prevalence and treatment? Allergy. 2002: 57: 150–154.
14. Bousquet, J, Khaltaev, N, Cruz, AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008; 63 (Suppl 86): S1-160.
15. Meltzer EO, Jalowayski AA. Nasal cytology in clinical practice. Am Rhinol. 1998; 2: 47-54.

Corrected proof

16. Perry PL, Coombs GW, Boehm JD, Pearman JW. A rapid (20 h) solid screening medium for detecting methicillin-resistant Staphylococcus aureus. J Hosp Infect. 1998; 40: 67-72.
17. Medical Bacteriology: A Practical Approach, Hawkey PM and Lewis DA (eds), IRL Press 1989.
18. Resch A, Schlipkoter U, Crispin A, et al. Atopic disease and its determinants – a focus on the potential role of childhood infection. Clin Exp Allergy. 2004; 34: 1184-1191.
19. Savolainen S. Allergy in patients with acute maxillary sinusitis. Allergy. 1989; 44: 116-122
20. Rachelefsky GS, Siegel SC, Katz RM, Spector SL, Rohy AS. Chronic sinusitis in children (abstract). J Allergy Clin Immunol. 1991; 87: 219
21. Wolthers OD. Eosinophil granule proteins in the assessment of airway inflammation in pediatric bronchial asthma. Pediatr Allergy Immunol. 2003; 14: 248-254.
22. Kingham PJ, McLean WG, Walsh MT, Fryer AD, Gleich GJ, Costello RW. Effects of eosinophils on nerve cell morphology and development: the role of reactive oxygen species and p38 MAP kinase. Am J Physiol Lung Cell Mol Physiol. 2003; 285: L915-924.
23. Frazee BW, Lynn J, Charlebois ED, et al. High prevalence of methicillin-resistant Staphylococcus aureus in emergency department skin and soft tissue infections. Ann Emerg Med. 2005; 45: 311-320.
24. Araujo E, Palombini BC, Cantarelli V, Pereira A, Mariante A. Microbiology of middle meatus in chronic rhinosinusitis. Am J Rhinol. 2003; 17: 9-15.
25. Van Zele T, Gevaert P, Watelet JB, Claeys G, Holtappels G, Claeys C, van Cauwenberge P, Bachert C. Staphylococcus aureus colonization and IgE antibody formation to enterotoxins is increased in nasal polyposis. J Allergy Clin Immunol. 2004; 114: 981-983.

De Yun Wang, MD PhD
Department of Otolaryngology
Yong Loo Lin School of Medicine
National University of Singapore
10 Lower Kent Ridge Crescent
Singapore 119260

Tel: +65-67725373
Fax: +65-67753820
E-mail: entwdy@nus.edu.sg

Corrected proof