Eur Respir J
1992, 5, 418–423

High prevalence of asthma in patients with bronchiectasis in Hong Kong

M.S.M. Ip, S-Y. So, W-K. Lam, L. Yam, E. Liong

High prevalence of asthma in patients with bronchiectasis in Hong Kong. M.S.M. Ip, S-Y. So, W-K. Lam, L. Yam, E. Liong.

ABSTRACT: Eighty five Chinese patients with diffuse or localized bronchiectasis (non-cystic fibrosis) were studied regarding the prevalence of asthma.

Twenty three of the 85 had concomitant asthma, diagnosed by history and reversibility on lung function testing either spontaneously or after bronchodilator. None fulfilled the diagnostic criteria of allergic bronchopulmonary aspergillosis (ABPA). Asthma preceded the onset of bronchiectasis in 13 patients and developed after long duration of bronchiectasis in seven, while the temporal onset could not be differentiated in three patients. Patients with both asthma and bronchiectasis had inferior spirometric values, higher prevalence of bronchial hyperresponsiveness to methacholine, higher prevalence of skin atopy, elevated serum immunoglobulin E (IgE), and more sputum eosinophilia, compared with their non-asthmatic counterparts.

Possible mechanisms by which asthma and bronchiectasis predispose to each other include asthmatic obstruction contributing to development of bronchiectasis, and sensitization of airways with increased lability due to microbial colonization of the ectatic bronchial tree.

Eur Respir J., 1992, 5, 418–423.

Dept of Medicine
University of Hong Kong
Queen Mary Hospital
Hong Kong.

Correspondence: M. Ip
Dept of Medicine
University of Hong Kong
Queen Mary Hospital
Hong Kong.

Keywords:
Asthma
bronchiectasis.

Received: November 22, 1990
Accepted after revision November 23, 1991.

Known causes of bronchiectasis include cystic fibrosis, post-infection, ciliary dysfunction, hypogammaglobulinaemia and allergic bronchopulmonary aspergillosis (ABPA). Many cases, ranging from 24–78% in different series, were idiopathic [1]. Bronchial asthma (non-ABPA) has been cited in textbooks as a cause of bronchiectasis [2, 3], although a review of the literature reveals that studies on the association between bronchiectasis and asthma have been scanty. We therefore studed 85 patients with proven bronchiectasis, with particular reference to co-existent asthma, and the interrelationship between the two conditions.

Subjects and methods

Eighty five subjects, *i.e.* approximately 90% of those attending the Bronchiectasis Clinic of the Department of Medicine, University of Hong Kong, were studied between 1987 and 1989. The diagnosis of bronchiectasis was based on: 1) clinical symptoms of chronic or intermittent sputum production and/or haemoptysis; and 2) radiological evidence of bronchiectasis on one or more of the following investigations: chest radiography (CXR), bronchogram (BG), computerized tomography of the thorax (CT).

The criteria for radiological diagnosis of bronchiectasis were as follows:

CXR - only presence of cystic spaces was accepted as definite evidence of bronchiectasis. Other changes such as crowding and loss of definition of vascular markings, bronchial wall thickening, patchy or confluent pulmonary shadows [4] were thought to be more subject to variability of interpretation and were, therefore, not used as definitive criteria. If changes were localized to one lobe on CXR, further investigations with BG or CT were performed to define the extent. If changes involved more than one lobe on CXR, this was taken as diffuse disease and further radiological investigations were only done as clinical condition required.

BG - loss of normal peripheral tapering of bronchi with abrupt squared-off ends, irregular bronchial outline with bulbous ends, expanding bronchi with balloon-like appearance, and luminal filling defects [5].

CT - air-fluid levels in distended bronchi, linear array or cluster of cysts or dilated bronchi in the periphery of the lung, and bronchial wall thickening [6].

The distribution of patients diagnosed by the various radiographic methods were as follows: CXR only - 35; BG - 26; CT - 24.

Aetiological factors that were actively elicited from history, physical examination and laboratory investigations included previous infections (measles, whooping cough, pneumonia, tuberculosis), panhypogammaglobulinaemia, immunoglobulin subclass deficiency, allergic bronchopulmonary aspergillosis,

autoimmune diseases and alpha$_1$-antitrypsin deficiency. Cystic fibrosis is a genetic disease affecting predominantly Caucasians and, therefore, sweat tests have not been performed in this group of Chinese patients. Ciliary dyskinetic syndromes were only screened in cases with suggestive features such as dextrocardia or male infertility.

Questionnaire

Specific information on the following points was obtained at patient interview and review of records:

- symptoms of asthma: episodic cough, dyspnoea and wheezing;
- age at onset of symptoms or diagnosis of asthma and bronchiectasis;
- family history of asthma;
- allergic diathesis;
- smoking habit;
- current medication.

Lung function tests

Tests were performed in the stable clinical state with no recent (past four weeks) acute respiratory exacerbation. The Gould 5000IV computerized pulmonary function system was used. Spirometric measurements included forced expiratory volume in one second (FEV_1), forced vital capacity (FVC) and maximal mid-expiratory flow rate (FEF_{50}). If FEV_1/FVC ratio was less than predicted, hexaprenaline, a β_2-agonist, 1 mg, was given by nebulization and the test repeated 15 min later. The data of DA COSTA [7] were used as reference for normal values.

In subjects whose baseline FEV_1 was ≥50% predicted, methacholine (MCh) inhalation test was done using the Wright's nebulizer method [8]. Bronchial hyperreactivity (BHR) was defined as a provocative concentration producing a 20% fall in FEV_1 (PC_{20}) of ≤8 mg·ml^{-1}.

Diagnosis of asthma

Symptoms of episodic cough, dyspnoea and wheezing and either: 1) documented increase in FEV_1 of >15% after inhaled β_2-agonist during the acute episode or the stable state; or 2) spontaneous diurnal variation in peak expiratory flow rate (PEFR) >20% on home monitoring with mini-Wright's peak flow meter.

Skin test

Skin test was performed using the prick method with 10 commercial extracts (Bencard, UK): *D. farinae, D. pteronyssinus,* grass pollen, *Cladosporium herbarum,* cat fur, dog fur, Penicillia, *Pullaria pullulans, A. fumigatus, A. niger.* The test was positive if a 2 mm wheal was obtained in the presence of a negative saline control.

Tests for allergic bronchopulmonary aspergillosis (ABPA)

Immediate skin reaction to *Aspergillus fumigatus* and *A. niger* was elicited by prick test. A venous blood sample was tested for precipitating antibody to *Aspergillus* spp. using the double diffusion method with a commercial antigen preparation derived from mycelial phase cultures of *A. fumigatus, A. niger,* and *A. flavus* (Meridian Diagnostics Incorp., USA). A sputum sample was cultured for *Aspergillus* spp. Total serum immunoglobulin E (IgE) was measured using enzyme-linked radio-immunoassay. Specific IgE was not done. Peripheral blood eosinophilia was noted. Radiological evidence of central bronchiectasis was sought.

Sputum assessment

A sputum specimen was obtained in the stable clinical state. Macroscopic appearance of sputum was classified as mucoid, mucopurulent or purulent.

Sputum leucocyte count was performed on a Wright's stain smear of the macroscopic specimen above and examined for polymorphs (PMN) and eosinophils (Eos). Specimens with predominance of epithelial cells were discarded as contaminated with oropharyngeal secretions. An average count of five fields at magnification ×400 was taken and graded into three groups: 0–20, >20–50, >50 PMN·field^{-1}. Eosinophils were counted in 20 fields at ×400 magnification and expressed as % of leucocytes per field.

Average daily sputum volume was assessed by patients' own estimate from a scaled sputum container and categorized as follows: 0–20, >20–50, >50 ml·day^{-1}.

Analysis of data

Mean and standard deviation values were calculated for various parameters. Mann-Whitney U-test was used to compare the two groups with and without asthma for continuous variables, whilst Fisher's exact test was used for enumeration data.

Results

Eighty five patients with bronchiectasis were studied, demographic features of whom are shown in table 1.

There was a continuum of bronchodilator response in FEV_1 in the symptomatically stable state, and a general trend of increased bronchial hyperreactivity to methacholine and allergic features in those with greater bronchodilator reversibility (table 2).

Table 1. – Clinical features of 85 patients with bronchiectasis

Age yrs	49 (17–75)*
Male/female n	33/52
Smoking habit n	
Current smokers	3
Ex-smokers	15
Nonsmokers	67
Disease extent n	
Localized (1 lobe)	13
Diffuse (2 or more lobes)	72
Aetiology of bronchiectasis n	
Measles	3
Pneumonia	2
Tuberculosis	3
Kartagener's syndrome	2
Unknown	75
Other medical conditions n	
Rhinitis/sinusitis	44
Asthma	23
Pulmonary emphysema	2
Systemic lupus erythematosis	1
Rheumatoid arthritis	1

*: mean (range); n: number of patients.

Table 2. – Distribution of bronchodilator response and other features of airway lability and atopy in 85 patients.

	BDR % baseline FEV_1				
	0–5	>5–10	>10–15	>15–20	>20
Patients n	42	12	12	7	12
BHR n +ve/done	6/29	4/9	8/9	1/2	3/4
Asthma % of group	7	15	36	57	77
+ve skin atopy % of group	24	31	36	29	38
Blood eos $\times 10^9 \cdot l^{-1}$*	0.20 ±0.36	0.30 ±0.33	0.12 ±0.14	0.12 ±0.15	0.33 ±0.19
Serum IgE $IU \cdot ml^{-1}$*	62 ±108	40 ±45	360 ±639	37 ±38	227 ±412

BDR: bronchodilator response; FEV_1: forced expiratory volume in one second; BHR: bronchial hyperreactivity to methacholine; eos: eosinophil; n: number of patients. *mean±SD.

Twenty three of the 85 patients fulfilled our diagnostic criteria of asthma, giving a prevalence rate of 27% in this study population. Two of the 23 asthmatics had nocturnal symptoms but no bronchodilator response in daytime spirometry, and home monitoring of peak expiratory flow rate (PEFR) confirmed a spontaneous diurnal variation of 50 and 35%, respectively, in these two patients. There were four subjects who had >15% increase in FEV_1 after bronchodilator, but no suggestive symptoms and no diurnal variation in PEFR, and were therefore not labelled as asthmatics.

There was no significant difference in age and sex distribution, duration of bronchiectasis, smoking habit, incidence of localized *versus* diffuse disease, and number of infective episodes in the past year between those with and without asthma. Eleven of the 23 asthmatic subjects were on inhaled steroids and none was on oral steroids.

None of the asthmatic subjects had evidence of ABPA. *Aspergillus fumigatus* and/or *A. niger* skin tests were positive in 6 of the 23 subjects, but all were negative for aspergillin antibody. Skin atopy to *Aspergillus spp.* was also found in non-asthmatic bronchiectatic subjects. There were no radiological features of central bronchiectasis. Sputum culture yielded *A. fumigatus* in one patient with both asthma and bronchiectasis and *A. niger* in one patient with only bronchiectasis.

Retrospective analysis of the clinical course showed that in addition to the 23 subjects with current asthma, two subjects had symptoms of asthma in childhood but had gone into remission. The age of onset of asthma ranged from early childhood to 56 yrs. More than 50% (13 out of 23) of the asthmatic subjects had well-documented symptoms and lung function confirmation of asthma preceding that of onset of symptoms of bronchiectasis by a range of 5 to >30 yrs. In seven patients, there was a long-standing history of bronchiectasis before occurrence of episodes of intermittent dyspnoea and wheezing. In three patients, it was not possible to dissect the temporal onset of the two conditions retrospectively. Those with asthma had significantly lower spirometric values, with a greater degree of airflow obstruction compared with their non-asthmatic counterparts (table 3). MCh bronchial challenge was performed in 53 subjects. Twenty nine did not undergo challenge because of poor lung function and three did not consent to the procedure. Twenty two of the 53 subjects who underwent bronchial challenge had a PC_{20} of MCh ≤8 $mg \cdot ml^{-1}$, and 12 of the 22 were asthmatic. Of the 23 asthmatic subjects, 12 underwent bronchial challenge and all were hyperreactive.

Table 3. – Lung function data in stable state in patients with and without asthma

	Asthma	No asthma
Patients n	23	62
FEV_1 l	1.20±0.55*	1.69±0.83
FEV_1 % pred	54±22	73±30
FEV_1/FVC %	54±11#	71±16
FEF_{50} $l \cdot s^{-1}$	0.73±0.63#	1.89±1.43
Bronchodilator response % of baseline FEV_1	20±15++	6±10
Bronchodilator response % of predicted FEV_1	8.8±5.1++	2.9±4.3
Bronchodilator response ml	197±112++	61±82
Bronchial challenge		
PC_{20} ≤8 $mg \cdot ml^{-1}$ MCh n (%)	12 (52)+	10 (16)
PC_{20} >8 $mg \cdot ml^{-1}$ MCh n (%)	0 (0)++	32 (52)
Challenge not done n (%)	11 (48)	20 (32)

Lung function data are given as mean±SD. +: p<0.01; *: p<0.05; #: p<0.001; ++: p0.0001; n (%): number of patients (percentage of group); FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; FEF_{50}: maximal mid-expiratory flow; PC_{20}: provocative concentration producing a 20% fall in FEV_1.

Of the markers of allergic disposition, the asthmatic group had more skin atopy, elevated serum IgE (>100 IU·ml^{-1}), peripheral blood eosinophils and sputum eosinophils (table 4.)

Table 4. – Markers of allergic disposition in patients with and without asthma

	Asthma	No asthma
Patients n	23	62
Skin atopy n	11*	14
Aspergillin skin atopy n	6	8
Aspergillin precipitin n	0	0
Elevated IgE n	9*	8
IgE† IU·100 ml^{-1}	544±1316	51±64
Blood eosinophils† $10^9 \cdot l^{-1}$	0.27±0.27*	0.20±0.32
Family history of asthma n	5	5
Allergic rash n	4	13
Sputum eosinophils detected n	10#	4
Sputum eosinophils† % of leucocytes	13±31#	1±2

n: number of patients; †: mean±SD; *: $p<0.05$; #: $p<0.001$. IgE: immunoglobulin E.

Sputum sample for assessment was available in 62 of 85 patients. The remaining subjects had either no sputum in the stable state or the specimens were not true sputum on microscopic analysis and were, therefore, rejected. Sputum characteristics of daily output, macroscopic appearance, and polymorph count were similar in the two groups. Eosinophils were detected in the sputum of 14 subjects, ranging from 2–95%, mean 18%, median 5%. Ten of these 14 patients were asthmatic.

Discussion

The association between bronchial asthma and bronchiectasis was well-documented in allergic bronchopulmonary aspergillosis (ABPA) [9]. Besides this entity, there have been only a few studies examining the relationship between these two conditions. The Dutch authors first postulated that asthma and allergic diathesis may have a role in the pathogenesis of bronchiectasis [10]. BAHOUS *et al.* [11] found that 11 of 50 (22%) bronchiectatic subjects had asthma, five of whom possibly had ABPA. VARPELA *et al.* [12] noted asthma in 11 of 48 subjects with bronchiectasis, and none of them had evidence of ABPA. PANG *et al.* [13] reported that only one of 36 patients with bronchiectasis had asthma. In the series of patients with chronic bronchial sepsis studied by COLE [14] wheezing was a very common symptom, occurring in 83% of 412 subjects, although no definite reference to asthma was made. The occurrence of bronchiectasis among patients with asthma has also been infrequently reported. In the 1960s and 1970s the condition of mucoid impaction of bronchi was described [15]. A majority of these patients had asthma, and untreated mucoid impaction could result in bronchiectasis. Some of these cases were probably ABPA [15]. Cystic distal bronchiectasis has been detected in 12 of 57 asthmatic children undergoing bronchography [16]. In a prospective follow up of 72 children with non-IgE mediated asthma, OSTERGAARD [17] noted that 5 (7%) developed severe bronchiectasis. Most recently, a study on the use of CT scanning in evaluation of ABPA unexpectedly found changes of bronchiectasis in three of eight patients with non-ABPA asthma [18].

Recent epidemiological studies on the prevalence of asthma in Hong Kong demonstrate a point prevalence of 8% in children [19], and a cumulative prevalence of about 7% in those aged over 15 yrs [20]. Hence, a prevalence rate of 27% in this group of bronchiectatic patients is considered high. The possibility of sample bias due to higher rate of follow-up at a specialist clinic when patients have two disease cannot be excluded, although there has been no particular selection of patients for the study other than the diagnosis of bronchiectasis.

The establishment of two separate diagnoses may be difficult because symptoms of cough, sputum, dyspnoea and wheezing can occur in either asthma or bronchiectasis alone. The diagnosis of bronchiectasis in asthmatic subjects was supported by radiological evidence on BG or CT in 20, and definite cystic changes on CXR in three. Diagnosis of asthma is more complicated if there is significant baseline airflow obstruction. The contention exists as to the differentiation of asthma and other chronic obstructive airways disease based on a relative FEV_1 response in the setting of pre-existent obstruction [21]. Improvement of airways obstruction after inhaled bronchodilator has been reported in bronchiectasis [22], and was present in varying degrees in many subjects in our series. The diagnosis of asthma in our subjects was unlikely to be "artefactual" for several reasons. In 13 patients asthma was well-documented on lung function tests before onset of symptoms leading to diagnosis of bronchiectasis. The mean absolute increase in FEV_1 after bronchodilator, and also the bronchodilator response expressed as a percentage of predicted FEV_1, suggested as the parameter least dependent on baseline lung function [23], were significantly higher than in the non-asthmatic group, suggesting that the improvement was real and not only relative. The finding of BHR to MCh in all 12 asthmatic subjects who underwent bronchial challenge was also supportive of the diagnosis. However, it must be emphasized that presence of BHR in bronchiectasis should be interpreted within the clinical context. Nonspecific BHR has been found in bronchiectasis without clinical asthma, both in our series of patients [24] and other reports [11, 13]. Finally, sputum eosinophilia in the asthmatic group was another feature in favour of the diagnosis [25].

Analysis of the pattern of bronchodilator response shows that there was a spectrum of reversibility of airflow obstruction in bronchiectasis. There was also suggestion of an increased disposition to airway lability and atopy in those with greater bronchodilator

response. It therefore appears that, by our definitive criteria of asthma, we have delineated the segment of patients whose airway lability was much increased. It has been reported that bronchial infection and treatment with antibiotics may affect lung function in bronchiectasis acutely, although results have been conflicting [26, 27]. In this study of patients in the clinically stable state, those with asthma did not have more severe infection as reflected in sputum volume, purulence, polymorph count and frequency of infective episodes in the past year. This would suggest that airways lability was not directly related to the severity of infection. However, baseline spirometric vales were significantly worse in those with asthma, suggesting that asthma was an important factor in lung function impairment in bronchiectasis.

Airways obstruction in asthma with mucus plugging and decreased mucociliary clearance theoretically predisposes to persistent infection and bronchiectasis. In our patients with both conditions, at least half of them had asthma preceding bronchiectasis and, in these, bronchial asthma could well have been a contributing factor to the development of bronchiectasis. It is not known if prompt vigorous treatment of asthma could have prevented the occurrence of bronchiectasis.

Alternatively, instead of being the consequence of obstruction in asthma, bronchiectasis may be the predisposing cause of asthma. Ectatic airways are often colonized by bacteria or fungi. Bacteria have not been shown to induce asthma, although bacterial product mediated mechanism could provoke BHR [28]. Organisms other than Aspergillus have been incriminated in allergic bronchopulmonary syndromes [29], suggesting that various fungi and bacteria can potentially cause asthma. Recently, it was reported that *Trichophyton dermatitis* could also lead to asthma [30]. The structural deformity of airways, impaired tracheobronchial clearance either primary or secondary to bacterial damage, and increased epithelial permeability may all facilitate colonization of microorganisms and penetration of microbial antigens or other inhaled antigens, and predispose to development of asthma.

Our findings suggest that there is an association between asthma and bronchiectasis and one condition may predispose to the development of the other. Further studies on the mechanisms involved will contribute to the understanding of the pathogenesis of these two diseases of the bronchial tree. In the clinical context, it is important to recognize the two components and to treat appropriately.

Acknowledgement: The authors thank K.M. Lo and K.M. Tse for technical assistance, and K. Law for typing the manuscript.

References

1. Barker AF, Bardana EJ. – Bronchiectasis: update of an orphan disease. *Am Rev Respir Dis*, 1988; 137: 969–978.
2. Murray JF. – Bronchiectasis and broncholithiasis. *In*: Harrison's principles of internal medicine. E. Brunwald *et al.* eds, McGraw Hill Book Co., Hamburg, 1987; pp. 1082–1085.
3. Swartz MN. – Bronchiectasis. *In*: Pulmonary diseases and disorders, 2nd edn. A.P. Fishman ed., McGraw-Hill Book Co., New York, 1988; pp. 1553–1581.
4. Reid LM. – Reduction in bronchial subdivision in bronchiectasis. *Thorax*, 1950; 5: 233–247.
5. Gudbjerg CE. – Roentgenologic diagnosis of bronchiectasis. An analysis of 112 cases. *Acta Radiologica*, 1955; 43: 209–214.
6. Naidich DP, McCauley DI, Khouri NF, Stitik FP, Siegelman SS. – Computed tomography of bronchiectasis. *J Comput Assist Tomogr*, 1982; 6: 437–444.
7. Da Costa JL. – Pulmonary function studies in healthy Chinese adults in Singapore. *Am Rev Respir Dis*, 1971; 104: 128–131.
8. Cockcroft DW, Killian DN, Mellon JJA, Hargreave FE. – Bronchial reactivity to inhaled histamine: a method and clinical survey. *Clin Allergy*, 1977; 7: 235–243.
9. Rosenberg M, Patterson R, Mintzser R, Cooper BJ, Roberts M, Harris K. – Clinical and immunologic criteria for the diagnosis of allergic bronchopulmonary aspergillosis. *Ann Inter Med*, 1977; 86: 405–414.
10. Israels A, Warringa R, Lowenberg A. – Bronchiectasis. *In*: Bronchitis I. N.G.M. Orie, H.J. Sluiter eds, Royal Vangorcum, Assen, 1954; pp. 171–180.
11. Bahous J, Cartier A, Pineau L, Bernard C, Ghezzo H, Martin RR, Malo JL. – Pulmonary function tests and airway responsiveness to methacholine in chronic bronchiectasis of the adult. *Bull Eur Physiopathol Respir*, 1984; 20: 375–380.
12. Varpela E, Laitinen LA, Keakinen H, Konhala D. – Asthma, allergy and bronchial hyperreactivity to histamine in patients with bronchiectasis. *Clin Allergy*, 1978; 8: 273–280.
13. Pang J, Chan HS, Sung JY. – Prevalence of asthma, atopy and bronchial hyperreactivity in bronchiectasis: a controlled study. *Thorax*, 1989; 44: 948–951.
14. Cole PJ. – Host microbial interaction in chronic respiratory disease. *In*: Recent advances in infection 3. D. Reeves, A. Geddes eds, Edinburgh, 1989; pp. 141–151.
15. Katzenstein AL, Liebow AA, Friedman PJ. – Bronchocentric granulomatosis, mucoid impaction, and hypersensitivity reactions to fungi. *Am Rev Respir Dis*, 1975; 111: 497–537.
16. Robinson AE, Campbell JB. – Bronchography in childhood asthma. *Am J Radiol*, 1972; 116: 559–566.
17. Ostergaard PA. – A prospective study on non-IgE mediated asthma in children. *Acta Paediatr Scand*, 1988; 77: 112–117.
18. Neeld DA, Goodman LR, Gurney JW, Greenberger PA, Fink JN. – Computerized tomography in the evaluation of allergic bronchopulmonary aspergillosis. *Am Rev Respir Dis*, 1990; 142: 1200–1205.
19. Hedley AJ, Tam A, Lam TH, Wong CK. – Is air pollution a causative factor in respiratory symptoms and asthma in the children of Hong Kong? Proceedings of the 11th Asia Pacific Congress on Diseases of Chest, Bankok, 1989; 357.
20. Catarivas M, Munro C, Lam C, Cho SK. – The prevalence of asthma and related respiratory symptoms in general practice - preliminary results from Hong Kong, Part II. *Hong Kong Practitioner*, 1991; 1410–1421.
21. Editorial. – Assessment of airflow obstruction. Lancet, 1986; ii: 1255–1256.
22. Nogrady SG, Evans WV, Davies BH. – Reversibility

of airways obstruction in bronchiectasis. *Thorax*, 1978; 33: 635–637.
23. Weir DC, Sherwood Burge P. – Measures of reversibility in response to bronchodilators in chronic airflow obstruction: relation to airway calibre. *Thorax*, 1991; 46: 43–45.
24. Ip M, Lam WK, So SY, Liong E, Chan CY, Tse KM. – Analysis of factors associated with bronchial hyperresponsiveness to methacholine in bronchiectasis. *Lung*, 1991; 169: 43–51.
25. Sanerkin NG, Evans DMD. – The sputum in bronchial asthma: pathognomonic patterns. *J Path Bact*, 1965; 89: 535–541.
26. Cole PJ, Roberts DE, Davies SF, Knight PK. – A simple oral antimicrobial regimen effective in severe chronic bronchial suppuration associated with culturable *Haemophilus influenzae*. *J Antimicrob Chemother*, 1983; 11: 109–113.
27. Hill SL, Morrison HM, Burnett D, Stockley RA. – Short-term response of patients with bronchiectasis to treatment with amoxycillin given in standard or high doses orally or by inhalation. *Thorax*, 1986; 41: 559–565.
28. Norn S, Stahl Skov P, Jensen C *et al.* – Lectin-mediated reactions: a new mechanism in bronchial hyperresponsiveness. *In*: Bronchial hyperresponsiveness: normal and abnormal control, assessment and therapy. J.A. Nadel, R. Pauwels, P.D. Snashall eds, Blackwell Scientific Publications, New York, 1987; pp. 331–336.
29. Ricketti AJ, Greenberger PA, Mintzer RA, Patterson R. – Allergic bronchopulmonary aspergillosis. *Chest*, 1984; 86: 773–778.
30. Ward GW, Karlsson G, Rose G, Platts-Mills TAE. – Trichophyton asthma: sensitisation of bronchi and upper airways to dermatophyte antigen. *Lancet*, 1989; i: 859–862.