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Asthma

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Abstract*:* Asthma is the most common respiratory disorder in Canada. Despite significant improvement in the diagnosis and management of this disorder, the majority of Canadians with asthma remain poorly controlled. In most patients,however, control can be achieved through the use of avoidance measures and appropriate pharmacological interventions. Inhaled corticosteroids (ICSs) represent the standard of care for the majority of patients. Combination ICS/long-acting beta2-agonists (LABA) inhalers are preferred for most adults who fail to achieve control with ICS therapy. Allergen-specific immunotherapy represents a potentially disease- modifying therapy for many patients with asthma, but should only be prescribed by physicians with appropriate training in allergy. Regular monitoring of asthma control, adherence to therapy and inhaler technique are also essential components of asthma management. This article provides a review of current literature and guidelines for the appropriate diagnosis and management of asthma.

KEYWORDS:Pathology,Diagnosis,Treatment

I. INTRODUCTION

Asthma remains the most common chronic respiratorydisease in Canada, affecting approximately 10% of the population . Although asthma is often believed to bea disorder localized to the lungs, current evidence indi- cates that it may represent acomponent of systemic air- way disease involving the entire respiratory tract, and this is supported by the fact that asthma frequently coexists with other atopic disorders, particularly allergic rhinitis. Asthma Control (TRAC) in Canada study suggest that over 50% of Canadians with asthma have uncontrolled disease . Poor asthma control contributes to unnecessary morbidity, limitations to daily activities and impairments in overall quality of life.

This article provides an overview of diagnostic and therapeutic guideline recommendations from the Global Initiative for Asthma (GINA) and the Canadian Thoracic Society and as well as a review of current literature related to the path physiology, diagnosis, and appropriate treatment of asthma.

Definition

Asthma is defined as a chronic inflammatory disease ofthe airways. The chronic inflammation is associated with airway hyperresponsiveness (an exaggerated airway- narrowing response to triggers, such as allergens and exercise), that leadsto recurrent symptoms such as wheezing, dyspnea (shortness of breath), chest tightness and coughing. Symptom episodes are generally asso- ciated with widespread, but variable, airflow obstruction within the lungs that is usually reversible either sponta- neously or with appropriate asthma treatment [4].

PATHOPHYSIOLOGY

Asthma is associated with T helper cell type-2 (Th2) immune responses, which are typical of other atopic conditions. Various allergic (e.g., dust mites, cockroach residue, furred animals, moulds, pollens) and non-aller-gic (e.g., infections, tobacco smoke, cold air, exercise) triggers produce a cascade of immune-mediated events leading to chronic airway

inflammation. hyperreactivity Evidence suggests that there may be a genetic predis- position for the development of asthma.

A number ofchromosomal regions associated with asthma susceptibility have been identified, such as those related to the production of IgE antibodies, expression of airway hyperresponsiveness, and the production of inflamma- tory mediators. However, further study is required to determine specific genes involved in asthma as well as the gene-environment interactions that may lead to expression of the disease .

DIAGNOSIS

The diagnosis of asthma involves a thorough medical history, physical examination, and objective assessments of lung function (spirometry preferred) to confirm the diagnosis Bronchoprovocation challengetesting and assessing for markers of airway inflammation may also be helpful for diagnosing the disease, particularly when objective measurements of lung func- tion are normal despite the presence of asthmasymptoms.

MEDICAL HISTORY

The diagnosis of asthma should be suspected in patients with recurrent cough,wheeze, chest tightness and short- ness of breath. Symptoms that are variable, occurupon exposure to allergens or irritants, that worsen at night,and that respond to appropriate asthma therapy are strongly suggestive of asthma Alternative causes ofsuspected asthma symptoms should be excluded, such as chronic obstructive pulmonary disease (COPD), bron- chitis, chronic sinusitis, gastroesophageal reflux disease, recurrent respiratory infections, and heart disease.

A positive family history of asthma or other atopic diseases and/or a personal history of atopic disorders, particularly allergic rhinitis, can also be helpful in identi- fying patients with asthma. During the history, it is also important to examine for possible triggers of asthma symptoms, such as dust mites, cockroaches, animal dan- der, moulds, pollens, exercise, and exposure to tobacco smoke or cold air. Exposure to agents encountered in the work environment can also cause asthma. If work- related asthma is suspected, details of work exposuresand improvements in asthma symptoms during holidays should be explored.

DURING ASTHMA ATTACK THE FOLLOWING CHANGES TAKES PLACE

The muscles around the airways tighten up,narrowing the airway.Less air is able to flow through the airway.Inflammation of the airways increases, furthernarrowing the airway.More mucus is produced in the airways,undermining the flow of air even more.In some asthma attacks, the airways are blocked such that oxygen fails to enter the lungs. This also prevents oxygen from entering the blood stream and traveling to the body's vital organs. Asthma attacks of this type can be fatal, and the patient may require urgent hospitalization. At the same time carbon dioxide deposition in the lungs leads to carbon dioxide poisoning[5].

TYPES OFASTHMA

Child-Onset Asthma

Asthma that begins during childhood is called child- onset asthma. This type of asthma happens because a child becomes sensitized to common allergens in the environment - most likely due to genetic reasons. The child is atopic - a genetically determined state of hypersensitivity to environmental allergens.Allergens are any substances that the body will treat as a foreign body, triggering an immune response. These vary widely between individuals and often include animal proteins, fungi, pollen, house-dust mites and some kind of dust. The airway cells are sensitive to particular materials making an asthmatic response more likely ifthe child is exposed to a certain amount of an allergen.

ADULT-ONSET ASTHMA

This term is used when a person develops asthma after reaching 20 years of age. Adult- onset asthma affects women more than men, and it is also much less common than child- onset asthma.It can also be triggered by some allergic material or an allergy. It is estimated that up to perhaps 50% of adult- onset asthmas are linked to allergies. However, a substantial proportion of adult-onset asthma does not seem to be triggered by exposure to allergen(s); this is called non-allergic adult-onset asthma. This non-allergic type of adult onset asthma is also known as intrinsic asthma.

EXERCISE-INDUCED ASTHMA

Coughing, wheezing or feeling out of breath during or after exercise is called as exercise- induced asthma. Level of fitness also matters a lot. A person who is unfit and runs fast for ten minutes is going to be out of breath asthma.

As with other types of asthma, a person with exercise- induced asthma will experience difficulty in getting air inand out of the lungs because of inflammation of the bronchial tubes (airways) and extra mucus.

COUGH-INDUCED ASTHMA

Cough-induced asthma is one of the most difficult asthmas to diagnose. The doctor has to eliminate other possibilities, such as chronic bronchitis, post nasal drip due to hay fever, or sinus disease. In this case the coughing can occur alone, without other asthma-type symptoms being present. The coughing can happen at any time of dayor night. If it happens at night it can disrupt sleep.

OCCUPATIONAL ASTHMA

This type of asthma is triggered by something in the patient's place of work. Factors such as chemicals, vapors, gases, smoke, dust, fumes, or other particles can trigger asthma. It can also be caused by a virus (flu), molds, animal products, pollen, humidity and temperature. Another trigger may be stress.

NOCTURNAL ASTHMA

Nocturnal asthma occurs between midnight and 8 AM. It is triggered by allergens in the home such as dust and petdander or is caused by sinus conditions. Nocturnal or nighttime asthma may occur without any daytimesymptoms recognized by the patient. The patient mayhave wheezing or short breath when lying down and may not notice these symptoms until awoken by them in themiddle of the night - usually between 2 and 4 AM. Nocturnal asthma may occur only once in a while or frequently during the week. However, when there are no daytime symptoms to suggest asthma is an underlying cause of the nighttime cough, this type of asthma will bemore difficult to recognize - usually delaying propertherapy.

STEROID-RESISTANT ASTHMA(SEVERE ASTHMA)

While the majority of patients respond to regular inhaled glucocorticoid (steroid) therapy, some are steroid resistant. Airway inflammation and immune activation play an important role in chronic asthma. Current guidelines of asthma therapy have therefore focused on the use of anti-inflammatory therapy, particularly inhaled glucocorticoids (GCs). By reducing airway inflammation and immune activation, glucocorticoids are used to treat asthma. However, patients with steroid resistant asthma have higher levels of immune activation in their airways than do patients with steroid sensitive (SS) asthma.

CAUSES OF ASTHMA

Allergies

Common sources of indoor allergens include animal proteins (mostly cat and dog allergens), dust mites, cockroaches, and fungi. It is possible that the push towards energy-efficient homes has increased exposure to these causes of asthma. Allergic reactions triggered byantibodies in the blood often lead to the airwayinflammation that is associated with asthma.

TOBACCO SMOKE

Tobacco smoke has been linked to a higher risk of asthma as well as a higher risk of death due to asthma, wheezing, and respiratory infections. In addition, children of mothers who smoke - and other people exposed to second-hand smoke - have a higher risk of asthma prevalence. Adolescent smoking has also been associated with increases inasthma risk.

ENVIRONMENTAL FACTORS

Allergic reactions and asthma symptoms are often the result of indoor air pollution from mold or noxious fumes from household cleaners and paints. Other indoor environmental factors associated with asthma include nitrogen oxide from gas stoves. In fact, people who cook with gas are more likely to have symptoms such as wheezing, breathlessness, asthma attacks, and hay fever.Pollution, sulfur dioxide, nitrogen oxide, ozone, cold temperatures, and high humidity have all been shown to trigger asthma in some individuals.Weather changes have also been known to stimulate asthma attacks.

OBESITY

Overweight adults - those with a body mass index (BMI) between 25 and 30 - are 38% more likely to have asthma compared to adults who are not overweight. Obese adults- those with a BMI of 30 or greater - have twice the risk of asthma. According to some researchers, the risk may be greater for nonallergic asthma than allergic asthma.

STRESS

People who undergo stress have higher asthma rates. Part of this may be explained by increases in asthma-related behaviors such as smoking that are encouraged by stress. However, recent research has suggested that the immune system is modified by stress as well.

GENES

It is possible that some 100 genes are linked to asthma - Genes linked to asthma also play roles in managing theimmune system and inflammation. There have not, however, been consistent results from genetic studiesacross populations - so further investigations are requiredto figure out the complex interactions that cause asthma. Three-fifths of all asthma cases are hereditary. The Centers for Disease Control (USA) say that having aparent with asthma increases a person's risk by three tosix times.Genetics may also be interacting with environmental factors. For example, exposure to the bacterial product endotoxin and having the genetic trait CD14 (single nucleotide polymorphism (SNP) C-159T) have remaineda well-replicated example of a gene-environment interaction that is associated with asthma.

AIRWAY HYPERREACTIVITY

Researchers are not sure why airway hyperreactivity is another risk factor for asthma, but allergens or cold air may trigger hyperreactive airways to become inflamed. Some people do not develop asthma from airway hyperreactivity, but hyperreactivity still appears to increase the risk of asthma.

DIAGNOSING ASTHMA

Common symptoms and signs include:

Wheezing

Coughing

Breathingdifficulty

Tightness in the chest

Worsening symptoms at night

Worsening symptoms due to cold air.

PHYSICALEXAM

A physical examination will generally focus on the upper respiratory tract, chest, and skin. A doctor will use a stethoscope to listen for signs of asthma in your lungs as you breathe. Physicians will also check for a runny nose, swollen nasal passages, and nasal polyps. Skin will be examined for conditions such as eczema and hives, which have been linked to asthma.Physical symptoms are not always present in asthma sufferers, and it is possibleto have asthma without presenting any physical maladies during an examination

ASTHMA TESTS

Lung function tests, or pulmonary function tests, are the third component of an asthma diagnosis. Spirometry is a noninvasive test that requires taking deep breaths and forcefully exhaling into a hose connected to a machine called a spirometer. The spirometer then displays two key measurements:

Forced vital capacity (FVC) - the maximum amount of air one can inhale and exhale Forced expiratory volume (FEV-1) - the maximum amount of air exhaled in one second

The measurements are compared against standards developed for a person's age, and measurements below normal may indicate obstructed airways.It is common for a doctor to administer a bronchodilator drug to open air passages before retesting with the spirometer. If results improve after the drug, there is a higher likelihood of receiving an asthma diagnosis.Children younger than 5 years of age are difficult to test using spirometry, so asthma diagnoses will rely mostly on symptoms, medical histories, and other parts of the physical examination. It is common for doctors to prescribe asthma medicines for 4 to 6 weeks to see how ayoung child responds[9].

OTHERTESTS

A "Challenge Test" (or bronchoprovocation test) is when a physician administers an airway-constricting substance (or something as simple as cold air) to deliberately trigger airway obstruction and asthma symptoms. Similarly, a challenge test for exercise-induced asthma would consist of vigorous exercise to trigger symptoms. A spirometry test is then administered, and if measurements are still normal, an asthma diagnosis is unlikely.

TREATMENT

Asthma medications are generally considered to fall into two classes: bronchodilators, which stop asthma attacks after they've started and help in preventing the attacksand anti-inflammatories, which control the airway inflammation and prevent asthma attacks from starting.

BRONCHODILATORS

Bronchodilators provide relief during an asthma attack. They relax muscles in the air tubes, forcing them to openup and allowing the patient to breathe. Bronchodilators also may help to clear mucus from the lungs, allowing it to move more freely and be more easily coughed out.Some examples of bronchodilators include short-acting beta-agonists used to prevent exercise-induced asthma, anticholinergics used in addition to or as an alternative to short-acting beta-agonists and theophylline a long-actingdrug used to treat severe asthma.

ANTI-INFLAMMATORIES

Anti-inflammatories prevent asthma attacks by keeping air tubes open all of the time.They are designed to reduce swelling in the air tubes and decrease the amount of mucus. Cromolyn and nedocromil are two examplesof anti-inflammatory medicines.Corticosteroids are the most popular class of anti- inflammatories and are the drug ofchoice for persistentasthma. Other anti-inflammatories include mast cellstabilizers

SIDEEFFECTS

There is always a risk of side effects associated with taking medicine. These may include sore throat, nervousness, nausea, rapid heartbeat, loss of appetite, or staying awake. A doctor will modify the treatment plans if side effects become severe.

OVER-THE-COUNTER

Over-the-counter asthma drugs such as "Primatene Mist" and "Bronkaid" are widely available bronchodilators that provide short term relief. These medicines, however, do not control long-term asthma and should not be used every day to relieve asthma symptoms. Check with a physician before using over-the-counter medicines.

METERED-DOSEINHALERS

The most common device used to deliver medicine to thelungs of asthmatics is the metered-dose inhaler. Inhalers have two parts: 1) a canister consisting of a propellant, the medicine, and stabilizers, and 2) an actuator or mouthpiece consisting of a discharge nozzle and a dust cap. Inhalers are easily used by pressing down the top of the canister and inhaling the gas that is released. Usually the medicine administered by metered-dose inhalers is a bronchodilator, corticosteroid, or a mast cell stabilizer.

DRYPOWDERINHALERS

As an alternative to the aerosol-based metered-dose inhalers, dry powder inhalersdeliver medicine from a capsule in powder form. These devices require the device into the lungs and can be more complicated to usethan metered-dose inhalers.

NEBULIZER

Medication may also be administered using a nebulizer, providing a larger, continuous dose. Nebulizers vaporize a dose of medication in a saline solution into a steady streamof foggy vapor that is inhaled by the patient. Nebulizers are more common in hospital settings for patients who have difficulty using a metered-doseinhaler.

AsthmaSpacer

Asthma spacers are attachments that can be added to metered-dose inhalers. The spacer goes between the patient's mouth and the mouthpiece of the inhaler and it acts as a reservoir that briefly holds the medication. Spacers allow a patient to inhale the medicinewithout having to coordinate the breathing and mechanical actions needed to use an inhaler. Spacers also help patients deliver the medication directly to the lungs, avoiding medicine on the side of the mouth and the condition known as "thrush".

CONCLUSIONS:

Asthma is the most common respiratory disorder in Canada, and contributes to significant morbidity and mortality. A diagnosis of asthma should be suspected in patients with recurrent cough, wheeze, chest tightness and dyspnea, and should be confirmed using objective measures of lung function (spirometry preferred). Allergy testing is also recommended to identify possible triggers of asthmasymptoms.

In most patients, asthma control can be achieved through the use of avoidance measures and appropriate pharmacological interventions. ICSs represent the stan- dard of care for the majority of asthma patients. For those who fail to achieve control with low-to-moderate ICS doses, combination therapy with a LABA and ICS is the preferred treatment choice in most adults. LTRAs can also be used as add-on therapy if asthma is uncon- trolled despite the use of low-to-moderate dose ICStherapy, particularly in patients with concurrent allergic rhinitis. Anti-IgE therapy may be useful in select casesof difficult to control asthma. Allergen-specific immu- no therapy is a potentially disease-modifying therapy, but should only be prescribed by physicians with appropri- ate training in allergy. All patients with asthma should have regular follow-up visits during which criteria for asthma control, adherence to therapy and proper inhaler technique should be reviewed.

KEY TAKE-HOME MESSAGES

A clinical diagnosis of asthma should be suspected in patients with intermittentsymptoms of wheezing, coughing, chest tightness and breathlessness.Objective measurements of lung function, preferably using spirometry, areneeded to confirm the diagnosis.All asthma patients should be prescribed a rapid-act- ing bronchodilator to beused as needed for relief of acute symptoms.ICS therapy is the standard of care for most patients with asthma.

REFERENCES :

1. Public Health Agency of Canada: Life and breath: respiratory disease in Canada. Ottawa, Ontario; 2007, Available: http://www.phac-aspc.gc.ca/ publicat/2007/lbrdc-vsmrc/index- eng.php Accessed July 15, 2010.
2. Bourdin A, Gras D, Vachier I, Chanez P: Upper airway 1: Allergic rhinitis and asthma: united disease through epithelial cells. *Thorax* 2009, 64:999-1004.
3. FitzGerald JM, Boulet LP, McIvor RA, Zimmerman S, Chapman KR: Asthma control in Canada remains suboptimal: the Reality of Asthma Control (TRAC) study. *Can Respir J* 2006, 13:253-259.
4. Global Initiative for Asthma (GINA): Global strategy for asthma management and prevention. 2009, Available at: http://www.ginasthma.com Accessed July 15, 2010.
5. Lemanske RF, Busse WW: Asthma: Clinical expression and molecular mechanisms. *J Allergy Clin Immunol* 2010, 125:S95-102.
6. Lougheed MD, Lemière C, Dell SD, Ducharme FM, Fitzgerald JM, Leigh R, Licskai C, Rowe BH, Bowie D, Becker A, Boulet LP: Canadian Thoracic Society asthma management continuum: 2010 consensus summary for children six years of age and over, and adults. *Can Respir J* 2010,17:15-24.
7. Kaplan AG, Balter MS, Bell AD, Kim H, McIvor RA: Diagnosis of asthma in adults. *CMAJ* 2009, 181:E210-E220.
8. Kovesi T, Schuh S, Spier S, Bérubé D, Carr S, Watson W, McIvor RA: Achieving control of asthma in preschoolers. *CMAJ* 2010, 182:E172-E183.
9. Becker A, Lemière C, Bérubé D, Boulet LP, Ducharme FM, FitzGerald M, Kovesi T, Asthma Guidelines Working Group of the Canadian Network For Asthma Care: Summary of recommendations from the Canadian asthma consensus guidelines, 2003 and Canadian pediatric asthma consensus guidelines,2003
10. Crapo RO, Casaburi R, Coates AL, Enright PL, Hankinson JL, Irvin CG, MacIntyre NR, McKay RT, Wanger JS, Anderson SD, Cockcroft DW, Fish je Sterk PJ: Guidelines for methacholine and exercise challenge testing — 1999. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors July 1999. *Am J Respir Crit Care Med* 2000, 161:309-329.
11. Frew AJ: Allergen immunotherapy. *J Allergy Clin Immunol* 2010, 125:S306-313.
12. Abramson MJ, Puy RM, Weiner JM: Allergen immunotherapy for asthma. *Cochrane Database Syst Rev* 2003, 4:CD001186.
13. Calamita Z, Saconato H, Pela AB, Atallah AN: Efficacy of sublingual immunotherapy in asthma: systematic review of randomized clinical trials using the Cochrane Collaboration method. *Allergy* 2006, 61:1162-72.
14. Grembiale RD, Camporota L, Naty S, Tranfa CM, Djukanovic R, Marsico SA: Effects of specific immunotherapy in allergic rhinitic individuals with bronchial hyperresponsiveness. *Am J Respir Crit Care Med* 2000, 162:2048-2052.
15. Zielen S, Kardos P, Madonini E: Steroid-sparing effects with allergen- specific immunotherapy in children with asthma: A randomized controlled trial. *J Allergy Clin Immunol* 2010, 126:942-949.
16. Frew AJ: Allergen immunotherapy. *J Allergy Clin Immunol* 2010, 125:S306-313. Kaplan AG, Balter MS, Bell AD, Kim H, McIvor RA: Diagnosis of asthma in adults. *CMAJ* 2009, 181:E210-E220.
17. Kovesi T, Schuh S, Spier S, Bérubé D, Carr S,Watson W, McIvor RA: Achieving control of asthma in preschoolers. *CMAJ* 2010,182:E172 E18
18. Global Initiative for Asthma (GINA): Global strategy for asthma management and prevention.2009

19. Lemanske RF, Busse WW: Asthma: Clinicalexpression and molecular mechanisms. *J Allergy Clin Immunol* 2010, 125:S95-102

20. McFadden ER Jr. A century of asthma. *Am J Respir Crit Care Med*. 2004;170(3):215– 221

21. Wardlaw AJ, Brightling C, Green R, Woltmann G, Pavord I. Eosinophils in asthma andother allergic diseases. *Br Med Bull*. 2000;56(4):985–1003

22. Djukanovic R, Homeyard S, Gratziou C, et al. The effect of treatment with oral corticosteroids on asthma symptoms and airway inflammation. *Am J Respir Crit Care Med*. 1997;155(3):826– 832

23. ten Brinke A, Zwinderman AH, Sterk PJ, Rabe KF, Bel EH. "Refractory"eosinophilic airway inflammation in severe asthma: effect of parenteral corticosteroids. *Am J Respir Crit Care Med*.2004;170(6):601–605.

24. O'Byrne PM, Pedersen S, Lamm CJ, Tan WC, Busse WW. Severe exacerbations and decline in lung function in asthma. *Am J Respir Crit Care Med*. 2009;179(1):19–24.

25. Bousquet J, Bousquet PJ, Godard P, Daures JP. The public health implications of asthma. *Bull World Health Organ*. 2005;83(7):548–554.

26. Asthma UK. High cost of asthma in West Midlands. Available from:http:// www.asthma.org.uk/news_media/media_releases/high_cost_of_asthm_3.html. *Updated* 2009 Oct 22.

27. Howell JBL. Asthma: clinical descriptions and definitions. In: William W. Busse and Stephen T. Holgate, ed. Asthma and Rhinitis. Blackwell ScientificPublications. Boston, MA, 1995: Chapter 1.

28. National Asthma Education Program, Expert Panel Report. Executive Summary: Guidelines for the Diagnosis and Management of Asthma. National Heart, Lung, and Blood Institute, NIH. Bethesda,MD. June 1991.

29. Gergen PJ, Weiss, KB. Epidemiology of asthma. In: William W. Busse and Stephen T. Holgate, ed. Asthma and Rhinitis. Blackwell Scientific Publications. Boston, MA, 1995: Chapter 3.

30. Buist AS. Worldwide trends in asthma morbidity and mortality. Bull Int Tuberc Lung Dis 1991; 66:77-78.

31. Anderson HR. Is the prevalence of asthma changing? Arch Dis Child 1989;64:172-175.

32. Cookson JB. Prevalence rates of asthma in developing countries and their comparisons with those in Europe and North America. Chest 1987; 91:97S-103S.

33. Evans R, Mullally DI, Wilson RW, Gergen PJ, et al. National Trends in Morbidity and Mortality of Asthma in the US: Prevalence, hospitalization and death from asthma over two decades--1964-1984. Chest 1987; 91:65S-74S.

34. Haahtela T, Lindholm H, Björkstén F, Koskenvuo K, Laitinen LA. Prevalenceof asthma in Finnish young men. BMJ 1990;310:266-268.

35. Aberg N. Asthma and allergic rhinitis in Swedish conscripts. Clin Exp Allergy 1989;19:59-63.

36. Robertson CF, Heycock E, Bishop J, Nolan T, Olinsky A, Phelan PD. Prevalence of asthma in Melbourne schoolchildren: changes over 26 years. BMJ 1991; 302:1116-1118.

37. Peat JK, van den Berg RH, Green WF, Mellis CM, Leeder SR, Woolcock AJ. Changing prevalence of asthma in Australian children. BMJ 1994; 308:1591-1596.

38. Burney PGJ, Chinn S, Rona RJ. Has the prevalence of asthma increased in children? Evidence from the national study of health and growth 1973-86. BMJ 1990; 300:1306-1310.

39. Barry DM, Burr ML, Limb ES. Prevalence of asthma among 12 year old children in New Zealand and South Wales: a comparative survey. Thorax 1991; 46:405-409.

40. Burr ML, Limb ES, Andrae S, Barry DMJ, Nagel F. Childhood asthma in four countries: a comparative survey. Int J Epidemiol 1994; 23:341-347.

41. Sears MR. Worldwide trends in asthma mortality. Bull Int Union Tuberc Lung Dis 1991; 66:79-83.

42. Woolcock AJ. Worldwide trends in asthma morbidity and mortality: Explanation of trends. Bull Int Union Tuberc Lung Dis 1991; 66:85-89.

43. Jackson R, Sears MR, Beaglehole R, et al. International trends in asthma mortality: 1970-1985. Chest 1988; 94:914-918.