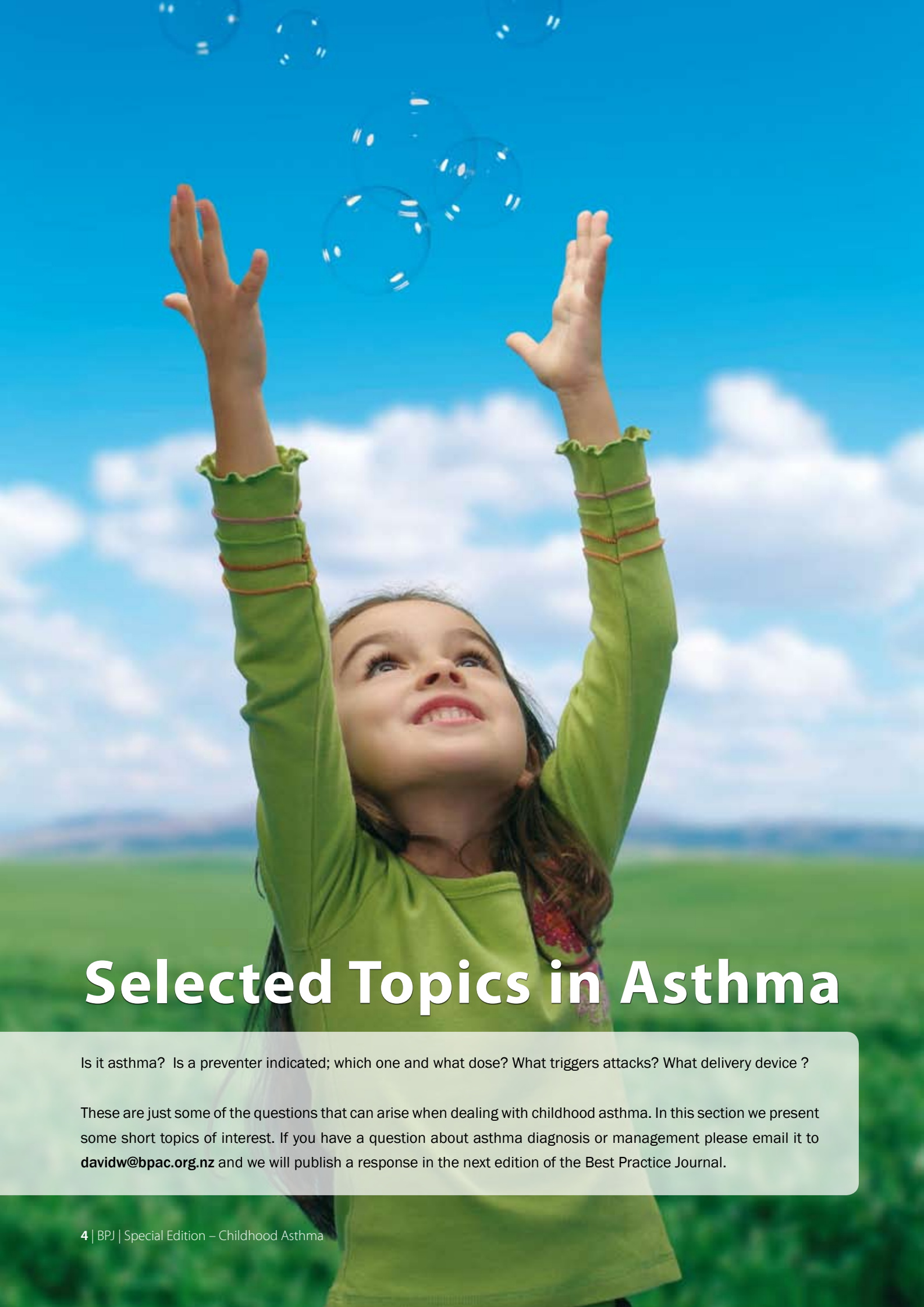

Selected Topics in Asthma

Is it asthma? Is a preventer indicated; which one and what dose? What triggers attacks? What delivery device ?

These are just some of the questions that can arise when dealing with childhood asthma. In this section we present some short topics of interest. If you have a question about asthma diagnosis or management please email it to **davidw@bpac.org.nz** and we will publish a response in the next edition of the Best Practice Journal.

Intermittent or persistent asthma and the role of preventers

It is important to obtain the historical pattern of asthma symptoms to determine if asthma is persistent or intermittent and the need for regular preventer treatment. If the pattern of symptoms is uncertain, consider the use of a symptom diary or organise frequent reviews until the pattern becomes clear.

Intermittent asthma

Infrequent intermittent asthma

About 75% of children with asthma have infrequent intermittent asthma[2] in which children have isolated episodes of asthma lasting from 1–2 days up to 1–2 weeks. Characteristics of infrequent intermittent asthma are:

- triggered by URTI or environmental allergen
- episodes more than 6–8 weeks apart
- asymptomatic in the interval periods

Although the severity of episodes varies, most are relatively mild but they still account for a significant number of hospital admissions.

Regular preventive therapy is not usually recommended for infrequent intermittent asthma. Management involves recognition and treatment of symptoms, reducing the risk of infections and minimising exposure to triggers. Complete avoidance of exposure to cigarette smoke is also important.

ICS may be overprescribed in this group in the misconception that they reduce the number of exacerbations due to viral infections and have beneficial effects on lung function and asthma disease progression. There is no evidence to support maintenance ICS for the prevention and management of mild episodic viral induced wheeze.[12]

Frequent intermittent asthma

About 20% of children with asthma have frequent intermittent asthma (more than two exacerbations per month and minimal symptoms between episodes) and may benefit from regular preventer therapy, usually low dose ICS. The preventer may only be required during the winter months.

Persistent asthma

About 5 – 10% of children with asthma have persistent asthma where symptoms occur on most days and often include; sleep disturbance due to cough or wheeze, early morning chest tightness, exercise intolerance and spontaneous wheeze.

Acute asthma episodes, as in intermittent asthma, may also be superimposed on this persistent pattern. Severity ranges from mild (daytime symptoms several times per week) to severe (continual daytime symptoms).

Regular preventive treatment is indicated for persistent asthma (usually starting with a low dose ICS) and titrated to effect, with add on therapy as required.

Which inhaled corticosteroid?

The inhaled corticosteroid preparations available in New Zealand are listed in Table 2 (see page 16). Clinically they are all equally effective at equivalent doses.

Note: 200 mcg of fluticasone is equivalent to 400 mcg of budesonide or beclomethasone.

Choice might be governed by the type of inhaler device available or intolerance to the propellant. For example:

- Switching from beclomethasone (Beclazone) to budesonide (Pulmicort) if the child is able to efficiently use a breath activated inhaler
- Switching to fluticasone (Flixotide) if a CFC-free preparation is preferred
- Child personal preference (e.g. what their friend has)

Safety of inhaled corticosteroids

In children, doses of ICS greater than 200 mcg/day fluticasone or 400 mcg/day beclomethasone may be associated with systemic side-effects including growth failure and adrenal suppression. Children receiving such doses should preferably be seen by a paediatrician and their asthma management plan should include advice about steroid replacement during severe illness.[2]

Common Asthma Triggers

Cigarette smoke

Cigarette smoke and its constituent chemicals that are absorbed into the environment (e.g., into furniture, clothes and cars) are irritants and can cause asthma and/or worsen symptoms.

Currently, one in ten children in New Zealand is exposed to second-hand smoke in their home.[13] It is uncertain exactly how many infants are exposed to cigarette smoke in-utero, however exposure to tobacco smoke during key developmental stages, in-utero and a few months post-birth, greatly increases the risk of developing asthma and allergy.[14]

Among teenagers who smoked, there is evidence to show that their risk of developing asthma increased four-fold if they smoked regularly. Furthermore, the risk of developing asthma doubled if their mothers had also smoked while pregnant with them.[15]

Repeated exposure to the irritants in cigarette smoke causes hyperplasia of mucous glands, leading to increased production of mucous that accumulates in airways. Chronic inflammation of smaller airways may also occur in developing lungs, narrowing the airways and leading to decreased lung capacity. The effects contribute to asthma symptoms and other respiratory illnesses.[16]

All carers of asthmatic children should be asked whether they smoke and provided with support to quit. They should also be provided with effective ways to protect their children from the harmful effects of cigarette smoke exposure, for example, suggest smoking outside or changing clothes before picking up young children.

Allergens

Allergens can include house dust mites, pets, pollen, moulds and in rare cases, foods. If the allergen is not clear from the history consider skin sensitivity testing.

Colds and Flu

Many children have intermittent asthma in which symptoms are only triggered by a viral infection. These children do not generally benefit from regular preventer treatment, and the focus is on management of exacerbations and minimising exposure to triggers, including active or passive exposure to tobacco smoke.[17]

Physical factors

Physical factors such as exercise, cold air and mould associated with damp housing can provoke asthma symptoms. Portable, unflued gas heaters are the only source of heating in many New Zealand homes. These heaters release a significant amount of water into the home environment. Asthma symptoms induced by environmental or seasonal changes often require increased dose of preventer or reliever medicine as appropriate.

- Smoking and exposure to tobacco smoke contributes to the risk of developing asthma, exacerbates asthma symptoms and increases the risk of virus triggered asthma attacks
- People who smoke and are in close proximity to children (e.g., parents in the home) should be advised of the many adverse effects of smoking on children, including increased wheezing in infancy. Smokers should be offered advice and support to stop smoking and provide smoke free homes and cars.

What is the place of mast cell stabilisers, sodium cromoglycate and nedocromil?

Sodium cromoglycate inhibits the immediate and late response to allergen challenge and is potentially useful if used before allergen exposure in susceptible children.

It may be useful as initial preventer treatment for children with intermittent asthma or mild persistent asthma, especially if there are reasons that an ICS cannot be used.

- Onset is slow but an effect is usually seen after one to two weeks. A four week trial is recommended before considering other treatments
- There is no additional benefit from adding sodium cromoglycate to an established regimen of ICS or oral corticosteroid
- It can be used in addition to or instead of a SABA to prevent exercise induced asthma
- No clear benefits have been shown in children aged under five years
- Side effects are minimal
- Powder for inhalation (Intal Spincaps) and aerosol (Vicrom) are partly subsidised

Nedocromil is chemically different to corticosteroids and cromoglycate. It inhibits asthmatic reactions to allergens and exercise, and has a similar protective effect as cromoglycate against these stimuli, but is longer acting.

Nedocromil appears to have a place in the treatment of asthmatic cough due to a direct effect on sensory nerves. Any reduction in cough usually occurs within the first two to three days.

Long acting beta-2 agonists (LABA) in treatment of asthma

There are currently two long acting beta agonists (LABAs) available in New Zealand; eformoterol (Oxis, Foradil) and salmeterol (Serevent).

Role of LABAs

The addition of a LABA may improve lung function and reduce exacerbations in children who are still symptomatic despite regular preventer treatment with an ICS.

For children on a standard dose of ICS (100 mcg/day fluticasone or 200 mcg/day beclomethesone) a LABA can be added as an alternative to increasing the ICS dose. Improved symptom control may be seen also when LABA are added to higher doses of ICS (200 mcg/day fluticasone or 400 mcg/day beclomethesone).

Research from the UK, and anecdotal experience from New Zealand, indicate that children are often prescribed higher doses of ICS instead of the addition of a LABA. The addition of a LABA should be considered before increasing the dose of ICS above 200 mcg/day fluticasone.

In children who are already on high dose ICS (200 mcg/day fluticasone or greater) a dose reduction may be considered after the LABA is added.

How to use LABAs

LABAs are not preventers, but are sometimes referred to as symptom controllers. They need to be used concurrently with an ICS.

LABAs are not licensed for use in children aged under four years (salmeterol) and under six years (eformoterol) but may be an option as add on therapy on the advice of a paediatrician.

Good patient education is required when prescribing a LABA with the main emphasis on advising continued use of the ICS. Many people who are switched to a LABA perceive that the ICS preventer is no longer required and either don't pick up repeats at their pharmacy or become less compliant. Children and their caregivers should be advised about the importance of continuing the use of their ICS, even if the dose is reduced.

There is some concern that regular LABA use may reduce the bronchodilatory response to SABA. When a LABA is added careful review of symptom control is required to assess whether there is any change in response to SABA. Children using LABA may need more doses of SABA to relieve bronchoconstriction than those not using LABA and should be told about this. They should be reminded that their new inhaler is not a reliever and to have their reliever available to use if they have symptoms.

It is recommended a short acting beta agonist (SABA) is prescribed with any LABA preparation.

Combination LABA/ICS preparations

Available preparations are salmeterol with fluticasone (Seretide) and eformoterol with budesonide (Symbicort and Vannair). These preparations may be useful if it is considered that the patient would benefit from a combined inhaler.

Eformoterol may be used as a reliever when used in the combination ICS product but salmeterol cannot as its onset of action is too slow (15 – 20 minutes).

Role of nebulisers in childhood asthma

Nebulisers have a limited role in childhood asthma. MDI with a spacer is as effective as a nebuliser, quicker to use, more portable and usually more acceptable to the child and caregiver.

Indications for nebuliser use in children include;

- When the asthma is so severe that the child cannot move the spacer valve
- When the child is sensitive to the aerosol propellant
- When the child does not tolerate/refuses delivery by a spacer

The nebuliser should only be used if it delivers adequate flow. If it takes longer than five minutes to deliver 2.5 mL of solution, the airflow is inadequate for correct nebulisation. Nebulisers should be serviced at least annually.

Optimal use of spacers

- Use a spacer with a mask for children under two years and a spacer without mask as soon as the child can breathe consistently using the spacer mouthpiece
- The size of the spacer is relatively unimportant but small volume spacers are more convenient
- Shake the inhaler before each puff
- Deliver one puff in to the spacer at a time.
- Allow the child to breath normally through the spacer for six breaths after each puff
- Replace spacers every six months if they are used regularly
- Wash the spacer once per week using dishwashing liquid. Allow to air dry.
- A new spacer or one that has not been used for several months requires priming before use. A spacer can be primed by washing as above or by firing ten puffs of reliever into the spacer.

Paracetamol and the link with asthma

No reason to stop using paracetamol in children for pain and fever.

A recent New Zealand study published in the Lancet found that the use of paracetamol for fever in the first year of life was associated with increased risk of asthma, rhinoconjunctivitis or eczema at age 6 – 7 years.

Background

The prevalence of asthma has been increasing for over 50 years but the reasons for this are not understood. During this period the use of paracetamol has also increased. Earlier studies have shown a link between paracetamol use and asthma. The latest study reports some findings from Phase Three of ISAAC which is an ongoing, multicentre, international study, looking at asthma and allergies in children.

Parents of children aged 6 – 7 years were asked about their child's use of paracetamol in the previous 12 months and about the use of paracetamol use for fever in the child's first year of life. Parents were asked about symptoms of wheeze (as an indication of asthma), symptoms of itchy eyes and nose, and symptoms of itchy skin rash. Other variables such as country of residence, age, gender, parental smoking and diet were considered.

Key Study findings

- Paracetamol use in the first year of life was associated with an increased risk of asthma symptoms ("wheezing or whistling in the chest") when aged 6 – 7 years (OR 1.46; 95%CI 1.36 – 1.56)
- There was an association between asthma symptoms in the previous 12 months and reported use of paracetamol in the previous 12 months. The paracetamol use was classified as medium (at least once per year) and high (at least once per month).
- Medium and high current users of paracetamol were more likely to have "severe" asthma than never users.

In conclusion the authors suggest that use of paracetamol may be a risk factor for the development of asthma and other allergic conditions. However, an observational study like this can identify signals for further investigation but not establish causality. Some possible confounders and sources of bias identified by the authors and other commentators are;

- Recall bias; accuracy of reporting of paracetamol use and symptoms by parents
- Problems with translations and interpretations of questionnaires in different countries
- Children with the reported symptoms may have been more likely to be given paracetamol
- The symptom of wheeze has many other causes other than asthma in this age group

Conclusion

A causal link between the use of paracetamol and the development of asthma has not been shown but further research in to the long term effects of paracetamol is justified. Paracetamol is still indicated for the treatment of pain and fever but as with any medicine, it should only be used when indicated. Antipyretic drugs should not be given routinely to children if they are otherwise well but either paracetamol or ibuprofen may used if the child is distressed or unwell. Ibuprofen may cause more adverse effects than paracetamol and can aggravate or provoke asthma symptoms in some children.

For more information

Beasley R. Association between paracetamol use in infancy and childhood, and risk of asthma, rhinoconjunctivitis, and eczema in children aged 6–7 years: analysis from Phase Three of the ISAAC programme. Lancet 2008; 372:1039-1048

Paracetamol associated with asthma symptoms

http://www.medsafe.govt.nz/hot/alerts/ParacetamolAsthma.asp

References and bibliography

1. Management of Asthma in Children Aged 1 – 15 Years. Paediatric Society of New Zealand, 2005.
   Available from: http://www.nzgg.org.nz Keyword:asthma
2. British Thoracic Society; Scottish Intercollegiate Guidelines Network. British Guideline on the Management of Asthma, May 2008.
   Available from http://www.sign.ac.uk Keyword:asthma
   (Accessed September 2008)
3. AMH. Asthma Management Handbook. National Asthma Council of Australia, 2006.
   Available from: http://www.nationalasthma.org.au/cms/index.php
   (Accessed September 2008)
4. ISAAC Steering Committee. Worldwide Variation in Prevalence of Symptoms of Asthma, Allergic Rhinoconjunctivitis and Atopic Eczema: ISAAC. Lancet. 1998;351:1225-7.
5. Asher M, Barry D, Clayton T, Crane J, D'Souza W, Ellwood P, et al. The Burden of Symptoms of Asthma, Allergic Rhinoconjunctivitis and Atopic Eczema in Children and Adolescents in Six New Zealand Centres: ISAAC Phase One. NZ Med J. 2001;114:114-20.
6. Asher MI, Stewart AW, Clayton T, Crane J, Ellwood P, Mackay R, et al. Has the prevalence and severity of symptoms of asthma changed among children in New Zealand? ISAAC Phase Three. NZ Med J. 2008;121:52-63.
7. Pattemore PK, Ellison-Loschmann L, Asher MI, Barry DM, Clayton TO, Crane J, et al. Asthma prevalence in European, Māori, and Pacific children in New Zealand: ISAAC study. Pediatric Pulmonology. 2004;37(5):433-42.
8. BPAC. Asthma and chronic cough in Māori children. Best Practice Journal May 2008;13:20-4.
   Available from http://www.bpac.org.nz Keyword:cough
9. Chang AB et al. Cough in children: definitions and clinical evaluation. Position statement of the Thoracic Society of Australia and New Zealand. MJA 2006; 184:398-403.
10. Van Asperen PP, Mellis CM, Sly PD. The role of corticosteroids in the management of childhood asthma. MJA 2002;176:169-74.
11. Masoli M, Weatherall M, Holt S, Beasley R. Systematic review of the dose response relation of inhaled fluticasone propionate. Arch Dis Child 2004;89:902-7.
12. Mckean M, Ducharme F. Inhaled steroids for episodic viral wheeze of childhood. Cochrane Database of Systematic Reviews (Online). 2000(2):CD001107.
13. Ministry of Health (2007). Portrait of Health, Ministry of Health: Wellington.
   Available from http://www.moh.govt.nz Search:portrait
14. Early Exposure to Tobacco Smoke. Karolinska Institutet (July 2008)
   Available from http://ki.se Select English and Keyword:Tobacco
15. Gilliland, FD, Islam T, Berhane, K, Gauderman, WJ, McConnell, R, Avol, E, and Peters, JM. Regular smoking and asthma incidence in adolescents. American Journal of Respiratory and Critical Care Medicine Vol 174. pp. 1094-100, (2006).
16. Clearing the Air: Asthma and Indoor Air Exposures (2000)
   Committee on the Assessment of Asthma and Indoor Air, Division of Health Promotion and Disease Prevention, Institute of Medicine. National Academies Press, 2000.
   Available from http://www.nap.edu Keyword:asthma
17. Pattemore P. Intermittent Asthma in Children. NZ Fam Physician 2008;35(3):207-10,