

CLINICAL PRACTICE

The management of asthma in children in Papua New Guinea

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SUMMARY

In the last decade advances in knowledge of the aetiology and pathogenesis of asthma, and the availability of metered-dose inhalers and nebulisers, has led to a change in emphasis in both the preventive and curative aspects of the management of children with asthma. Metered-dose inhalers are available in Papua New Guinea, and can be used successfully, with spacing devices, even in children less than 2 years of age. Inhaled beta-sympathomimetics, now widely available and relatively inexpensive, may be all that is required for the majority of children with infrequent episodic asthma. For those with frequent episodic and chronic asthma, preventive therapy with inhaled steroids is available and should be given wherever practicable. In the management of acute severe asthma inhaled beta-sympathomimetics should be combined with a short course of oral or parenteral steroids (covered with isoniazid in areas where tuberculosis is prevalent). Whilst asthma classically presents with wheeze, medical personnel should be aware of its other presentations. It is possible, and should be the aim, to achieve a very high level of control for the majority of asthmatic children using currently available therapy.

Background

“Asthma is a disease characterised by airway inflammation, airway hyperresponsiveness to a variety of stimuli, and the presence of airway obstruction that is reversible either spontaneously or as the result of treatment” (1).

Whilst asthma is, fortunately, a rare cause of death in Papua New Guinean children, it is a significant cause of morbidity. Asthma accounted for 2-3% (approximately 70) of admissions to the children's wards, 2% (approximately 1300) of Children's Outpatients Department (COPD) attendances and 6-8% (approximately 700) of admissions to the COPD observation ward of Port Moresby General Hospital (PMGH) in 1992-1993 (2). The prevalence of asthma in Papua New Guinean children is not known but with changing patterns of lifestyle it is reasonable to predict that it will increase. Current estimates from western countries are that between 13% and 23% of school-age children are affected by asthma (3).

In Papua New Guinea the standard management of asthma in children and adults has been based for many years on oral treatment with salbutamol and aminophylline tablets, with intravenous aminophylline for those patients sick enough to be admitted. The advent of nebulised beta-sympathomimetics – first orciprenaline and then salbutamol – made the management of patients with moderate and severe asthma presenting to those hospitals and major health centres with nebulising equipment much more efficient, and reduced the need for inpatient management. Whilst the Health Department encouraged the use of nebulised beta-agonists, the costs of the nebulisers, and the relative fragility of the manual nebulising pumps, masks and chambers, made widespread availability and use theoretical rather than practical. Metered-dose inhalers (MDIs) of beta-agonists have been available at pharmacies and intermittently as C category prescription items for some years, but were previously expensive, and were limited to use in adults and older children.

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Within the last decade or so there have been advances in the understanding of the processes involved in the development and manifestations of asthma, in both children and adults, which have led to a change in emphasis towards prevention as well as treatment of acute attacks, and towards improved symptomatic control for those with persistent or chronic asthma. These advances include a much better understanding of the causes of wheezing in early childhood (4) and of the major importance of the inflammatory process in the initiation and continuation of symptoms (3).

There appears to be a genetically determined susceptibility to asthma. Various environmental factors, the most important of which in young children are viral infections, cigarette smoke and some allergens, act as inducers of bronchial hyperreactivity. Once induction has occurred, asthma is precipitated by a number of triggers. In infants and young children these triggers are mainly nonallergic (infections, cigarette smoke and other irritants, exercise, changes in air temperature and humidity, coughing, laughing and strong emotion) whilst in older children allergens become more important. The majority of children whose wheeze starts in early childhood will 'grow out of it' by late childhood. In those who still have asthma at this time – and in those whose asthma develops in late childhood – the condition is likely to persist into adulthood.

The inflammatory response is highly complex, involving early and late phases and the release of a bewildering array of inflammatory mediators (including leukotrienes, prostaglandins and interleukins) resulting in mucosal oedema, bronchial smooth muscle constriction and excess production of mucus.

Emphasis in the treatment of asthma has broadened from its previous focus on smooth muscle relaxant therapy to include therapeutic efforts both to prevent and to control the inflammatory response.

Recent guidelines for the management of children (and adults) based on this new knowledge and emphasis have been produced in a number of western countries (5-7). These

guidelines are extremely helpful but are not, for a variety of reasons, entirely applicable to Papua New Guinea and other similar countries. In this article an attempt is made to modify the recommendations for use in Papua New Guinea. In so doing a number of important points have been considered:

1. A significant number of frequently symptomatic children can and should be rendered relatively symptom-free with the use of relatively inexpensive medication.
2. Metered-dose inhalers can be used effectively in young children if they are used in conjunction with spacing devices.
3. Home-made devices are effective and can be made cheaply and easily.
4. Metered-dose inhalers with spacers are as effective, if not more effective, than nebulisers in children, even those less than 5 years of age (8).

Pharmacological management of asthma

1. Bronchodilators

a. *Beta-sympathomimetic agents*

These drugs provide the mainstay of symptomatic relief for patients with asthma. In Papua New Guinea salbutamol is the most widely prescribed and should be available in tablet form from all health institutions. Salbutamol nebulising solution should also be available at hospitals and health centres. The cost of MDI salbutamol has become much more reasonable. A standard inhaler – which should, if used correctly, last most patients about a month – currently retails at around 5 to 6 kina.

b. *Methylxanthines (aminophylline, theophylline)*

These drugs are no longer as widely used as previously. They produce their effects on the bronchial smooth muscle by inhibiting the breakdown and thus increasing the levels of cyclic AMP (adenosine monophosphate). Beta-sympathomimetic agents also act through increasing levels of cyclic AMP – by increasing its production.

Thus there is no advantage to be gained in giving aminophylline with adequate doses of beta-agonists, and the side-effects of aminophylline may be serious. Recent recommendations from the United Kingdom are that aminophylline should no longer be used in children at home (6). Aminophylline does, however, have other beneficial effects, and its use is still recommended in the management of patients with severe asthma which cannot be controlled by other standard methods (see below).

2. Antiinflammatory agents

- a. *Sodium cromoglycate*
- b. *Steroids*

Both sodium cromoglycate and steroids are used in the prevention of asthma. Orally and intravenously administered steroids also have an important role in the management of acute severe asthma.

3. Anticholinergic agents

- a. *Ipratropium bromide (Atrovent)*

This drug has a limited role in the modern management of severe asthma in children unresponsive to routine treatment, but it is not widely available in Papua New Guinea.

Methods of administration of drugs in asthma

It is now well established that administration of beta-sympathomimetic drugs by inhalation is both more effective and associated with less side-effects than oral administration. Also well established is the efficacy of inhaled steroid preparations and sodium cromoglycate (see below).

It has been considered previously that metered-dose inhalers should be used in adults and older children, but that children younger than 5 years are unable to use these devices effectively, and require beta-agonists to be

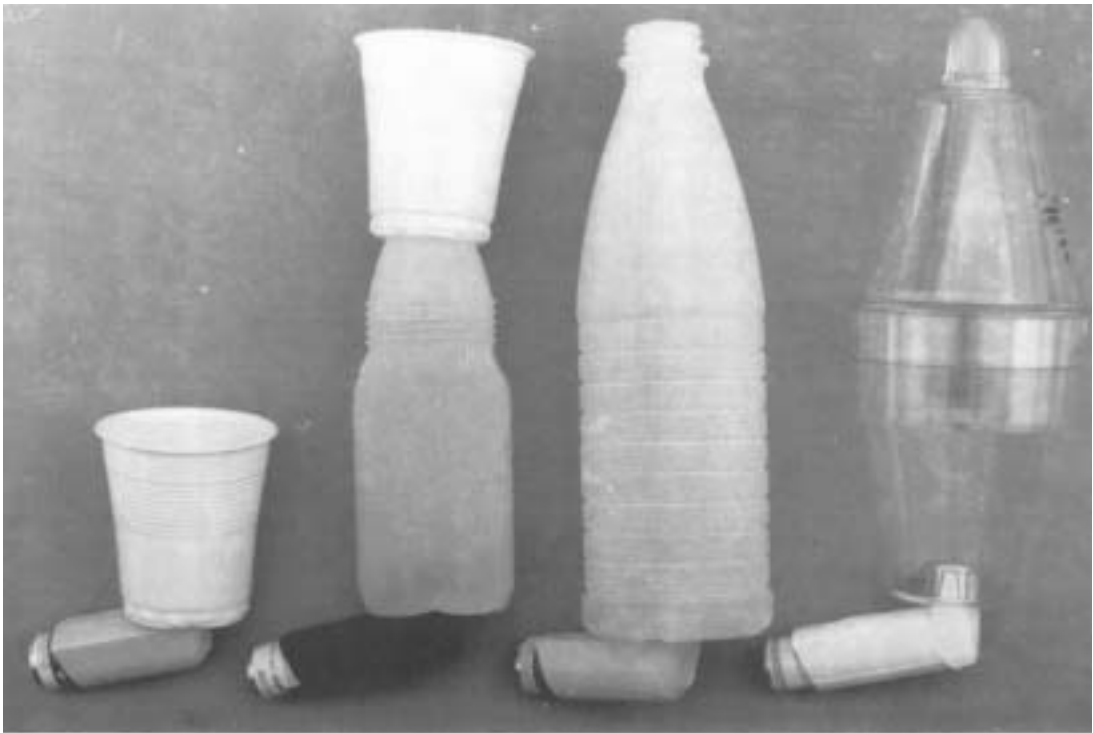


Figure 1. A commercial (Volumatic) and three home-made spacing devices for administration of metered-dose aerosol inhalations.

given through a nebulising device. The problem with nebulisers, however, is that they require a pump, a nebulising device, a mask, the beta-agonist preparation for the nebuliser and a diluent. (It is of practical note that the use of water as a diluent has been associated with increasing rather than decreasing the severity of bronchospasm in some patients and that, wherever possible, normal saline should be used.) Electrically driven pumps are very expensive and even the hand pumps have a significant cost. Fortunately, as noted above, it has now been clearly shown that metered-dose inhalers used in conjunction with an adequate spacing device are as effective if not more so than nebulisers in mild and moderate asthma. They may be equally effective in severe asthma; and whilst the nebuliser will still probably be preferred for such situations when it is available, the MDI and spacer should certainly be used when it is not.

The use of spacers results not only in the drug being administered effectively in a child unable to coordinate activating the inhaler with breathing in, but also in a reduction in the total dose of drug given, without a reduction in that delivered to the intrapulmonary airways (9).

A number of commercial spacers are available, all at some cost. Recommendations as to the volume of the spacer differ. The standard Volumatic 750 ml Spacer has a one-way valve to increase efficiency. Smaller 150 ml spacers are also available for younger children but may offer no great advantage. An effective spacer can be made very cheaply from a plastic 750 ml cordial bottle with an appropriately sized hole to fit the MDI. A plastic cup can be used either on its own as a combined spacer and mask, or as a mask on a larger spacer for children who are unable to cooperate in breathing through the bottle neck. These devices are shown, with the Volumatic Spacer, in Figure 1.

Classification of asthma

It is convenient to classify children with asthma into three groups (6):

- 1) Mild infrequent episodic (75%)
- 2) Frequent episodic (20%)
- 3) Persistent (chronic) (5%).

Children in group 1 have mild to moderate asthma attacks less than once a month, and are completely symptom-free in between episodes (apart from those whose attacks are precipitated by exercise).

Children in group 2 are normal or near normal in between attacks, but these attacks are usually moderate to severe, and occur more frequently than once a month.

The children in group 3 are symptomatic on most days or nights, and have frequent acute exacerbations at less than monthly intervals. If lung function can be measured it is usually abnormal.

There is inevitably some overlap between the groups, and some children may be worse at certain times than others.

Prevention of asthmatic attacks

1. General considerations: avoidance of inducers and triggering agents

Cigarette smoke, viral infections and allergens are the most important inducers of bronchial hyperreactivity in childhood. There is good evidence that parental smoking both during and after pregnancy predisposes the child to asthma. The harmful effects of cigarette smoking on babies and children need to be emphasized to individual parents and to the community at large. Whilst it is difficult to avoid viral infections in early childhood, the effects of allergens are markedly reduced if the child is fully breastfed. This is yet another reason for emphasizing the importance and benefits of breastfeeding and trying to combat the increasing use of artificial feeding in the country.

In older children environmental allergens assume more importance as triggers, and an attempt should be made to identify specific allergens in individual patients. The likely importance of allergy to the house dust mite has been recognized in the highlands of Papua New Guinea (10,11). Efforts to reduce exposure to house dust may therefore be important. Allergies to other insects such as cockroaches, to animals such as dogs and cats, to pollens, and to foodstuffs are all well recognized.

2. Preventive medication

Who should be treated?

For children with frequent episodic asthma (group 2) who are having episodes more than 3 times a week **and for those with chronic asthma, preventive medication is indicated.** For those in group 2 with attacks which, though less frequent, are seriously impairing the quality of life, preventive therapy should also be seriously considered.

What medication can be given?

Beta-agonists are not considered as preventive agents. Indeed there is some evidence that long-term continuous use of inhaled beta-agonists may result in impaired lung function.

These agents are used for control of acute symptoms in conjunction with preventive therapy.

There are basically two forms of preventive medication: inhaled sodium cromoglycate (Intal) and inhaled corticosteroids.

- a. **Sodium cromoglycate** has a number of actions among which is the prevention of the release of inflammatory mediators from mast cells. Originally it was packaged as a powder for inhalation, but is now available also as a metered-dose inhaler. It is certainly effective in many patients (though it must be given for 2-3 weeks before benefit can be expected) and is virtually free of side-effects. It is, however, currently prohibitively expensive in Papua New Guinea (40-50 kina for one inhaler). The starting dose is 10 mg (2 puffs of Intal Forte) three times a day but this can be reduced to 10 mg twice a day when control is achieved.
- b. The most important action of inhaled **corticosteroids** is in suppressing and modifying the inflammatory response in the respiratory tract. Three preparations are available: budesonide, beclomethasone and the most recently introduced (and expensive) fluticasone. Beclomethasone

(Becotide) is readily available in pharmacies throughout Papua New Guinea. Whilst not listed in the current Health Department Medical Stores Catalogue, it is available on special order and should become a category C item in the near future. It is available in three strengths: Becotide Junior (50 micrograms per puff, retail price about 10 kina); Becotide 100 (100 micrograms per puff, 24-25 kina); and Becloforte (250 micrograms per puff, 30-31 kina). It is normally given twice daily, in the lowest dose that will provide satisfactory control. High doses, more than 400 micrograms daily, may be associated with side-effects, of which growth retardation is of most concern in children, but there is no doubt whatsoever that judiciously and appropriately used inhaled steroids may transform the lives of those severely affected by asthma. Initial therapy should be between 50 and 200 micrograms twice daily. If control is not achieved quickly, higher doses of 400-800 micrograms twice a day can be given, and the doses subsequently reduced to the lowest that will provide reasonable control.

Management of acute severe asthma in children

An acute severe attack of asthma may occur in a child who has recently been healthy, or in a child already on treatment for frequent episodic or chronic asthma (5).

Indications of severe asthma in children are:

Too breathless to talk
 Too breathless to feed
 Respiratory rate greater than 50/min
 Pulse rate greater than 140/min.

Indications of life-threatening asthma are:

Cyanosis
 A silent chest or poor respiratory effort
 Fatigue or exhaustion
 Agitation or reduced level of consciousness.

It should be noted that because of poor respiratory effort a child with severe asthma may not appear to be in respiratory distress.

Immediate management

1. Give **high-flow oxygen** via a face mask if available or by nasal cannula if not (it is possible that putting in a nasal cannula may cause agitation and deterioration).
2. Give **nebulised salbutamol** as soon as possible (5 mg to older children, 2.5 mg to those less than 1 year or 9 kg). If no nebuliser is available use a **metered-dose inhaler and a spacer** as described above. Give one puff every few seconds until improvement occurs – up to a maximum of 20 puffs (5).
3. Give either **prednisolone** 2 mg/kg orally daily or **intravenous hydrocortisone** 100 mg every 6 hours.

IF THERE IS IMPROVEMENT

4. Give **nebulised salbutamol** 0.15 mg/kg (or by MDI and spacer if no nebuliser) every 1 to 4 hours as required.
5. Continue **prednisolone** for 4 to 5 days and then stop. In areas where tuberculosis is common it is advisable to cover this steroid treatment with daily isoniazid (INAH) at standard doses.

IF THERE IS NO IMPROVEMENT OR IF THERE ARE LIFE-THREATENING FEATURES

6. Give **nebulised salbutamol** 0.15 mg/kg (or by MDI and spacer if no nebuliser) **every half hour** if necessary.
7. Give **intravenous aminophylline** 5 mg/kg over 20 minutes followed either by an infusion of 1 mg/kg per hour or 5 mg/kg every 6 hours infused over one hour. If the child has been taking oral aminophylline it is safest to maintain the 1 mg/kg/hour infusion. Use 4.3% dextrose in 0.18% normal saline as the maintenance fluid.

These suggested guidelines for the management of children with asthma are summarized in Table 1.

Note 1. Insertion of an intravenous line, whilst desirable in severely ill children, may be difficult and may cause deterioration in the

child's condition. Administration of beta-agonists is the most important aspect of management, and steroids can be given orally. An intravenous line can be established, if necessary for intravenous medication and for maintenance of hydration, after the inhaled beta-agonist has been given.

Note 2. If inhaled beta-agonists are not available it is worth remembering that in severe asthma subcutaneous adrenaline in a dose of 0.01 ml/kg of 1 in 1000 was formerly recommended treatment, and is certainly highly effective.

Other considerations in childhood asthma

1. Presentation of asthma: nocturnal cough

Asthma classically presents as episodes of dyspnoea and wheezing. It is, however, important to realize that asthma may present as a chronic cough. Characteristically the cough is worse in the early hours of the morning, often waking the child and the family. In these children it is always worth testing lung function if possible (see below). Should the tests indicate the likelihood of asthma, the child should be given a trial of inhaled steroids and beta-agonists over two to three weeks, with retesting. In the likely event of improvement, the child can continue treatment as suggested for frequent episodic or chronic asthma. If testing is not possible, a trial of inhaled steroids and beta-agonists is always worthwhile.

2. Use of long-acting bronchodilators

Beta-sympathomimetic. In the last few years salmeterol has been marketed as a twice daily as opposed to a 3-4 times daily MDI. It may be of help for those particularly troubled by early morning symptoms, but it is at present very expensive (around 75 kina per inhaler) and its superiority over standard beta-agonist preparations for routine management of asthma symptoms is still disputed.

Theophylline and aminophylline. Sustained release preparations are available (Theodor and Nuelin SR). They are given twice daily but are considerably more expensive than

standard preparations (costing around 10-15 kina per 100). Like salmeterol they may be helpful in those with troublesome early morning symptoms. As with the standard preparations, there is a wide variation in individual metabolism of the drugs and ideally they should be used with drug-level monitoring, currently impracticable in Papua New Guinea. In spite of these drawbacks, however, they may be useful in individual patients.

3. Testing and monitoring lung function

Lung function tests are not essential for the diagnosis and monitoring of most children with asthma. Indeed it is recognized that

older children and teenagers may sometimes 'manufacture' the results to suit themselves! There is, however, no doubt that they can be very useful and should be more widely used in Papua New Guinea.

The simplest test is the peak flow rate, measured by a simple **peak flow meter**. The best of three attempts is recorded and results are correlated with the child's height.

The **Vitalograph** measures forced expiratory volume in one second (FEV1) and vital capacity (VC). In children with normal airways function *FEV1/VC should be greater than 85%*. The Vitalograph is

TABLE 1

SUMMARY OF SUGGESTED MANAGEMENT OF CHILDREN WITH ASTHMA

Infrequent episodic asthma (75%)

- Beta-sympathomimetics by metered-dose inhaler (MDI) with spacer, or nebuliser

If severe attack:

- Oxygen if available
- Frequent beta-sympathomimetic by nebuliser or MDI with spacer (every 1-4 hours as necessary – half-hourly in extreme cases)
- Short-course steroids, with isoniazid (INAH) cover if indicated
- Intravenous aminophylline in those not responding

Frequent episodic asthma (20%) and chronic asthma (5%)

- Regular inhaled steroids by MDI with spacer: lowest dose to give good control
- Beta-sympathomimetics by MDI with spacer, or nebuliser as required

If deterioration in control:

- Increase dose of inhaled steroids by MDI with spacer

If severe acute attack or exacerbation:

- Oxygen if available
- Frequent beta-sympathomimetic by nebuliser or MDI with spacer (every 1-4 hours as necessary – half-hourly in extreme cases)
- Short-course steroids, with isoniazid (INAH) cover if indicated
- Intravenous aminophylline in those not responding

relatively easy to use, but requires the correct recording paper.

4. Exercise-induced asthma

Exercise is a well-recognized trigger for asthma in children as in adults. Beta-sympathomimetics taken by MDI before the exercise may prevent the asthmatic symptoms.

5. “All that wheezes is not asthma”

This well-known dictum applies as much to children as to adults (Table 2). In neonates wheezing may be caused by anatomical abnormalities of the respiratory and vascular systems such as vascular rings. **Gastrooesophageal reflux** may cause persistent respiratory tract symptoms, including cough and wheeze in neonates and infants, and chlamydial infection may

present in similar fashion. As in other countries, **bronchiolitis**, usually caused by respiratory syncytial virus (RSV), is probably the most common cause of wheezing in infancy. Infection is seasonal, and is accompanied by fever and signs of upper respiratory as well as lower respiratory tract involvement. Neither bronchodilators nor steroids have been shown to be of significant benefit in children with confirmed bronchiolitis, and the former may cause deterioration in oxygen saturation in children with severe symptoms (12). Whilst recurrent RSV infection and bronchiolitis can occur, such a history should raise the possibility of asthma; then the use of bronchodilators and steroids is warranted and likely to be effective. The old adage that children under the age of 18 months do not have bronchial smooth muscle has been shown to be false.

TABLE 2

CAUSES OF WHEEZING IN CHILDREN

Neonate	Anatomical obstruction to airway Gastrooesophageal reflux Infections, e.g. chlamydia
Infant	Bronchiolitis Chlamydial and other infections Asthma Anatomical obstruction to airway Gastrooesophageal reflux
Young child	Asthma Inhaled foreign body Obstruction to airways by mediastinal nodes Bronchiectasis Infection, e.g. mycoplasma
Older child	Asthma Obstruction to airways by mediastinal nodes Bronchiectasis Infection, e.g. mycoplasma

In young children and toddlers, recent onset of cough and/or wheezing should raise the possibility of **inhaled foreign body**. Comparison of chest X-rays taken in inspiration and expiration may reveal air trapping in the expiratory film.

Wheezing may be caused by obstruction to the larger as well as to the small airways, and the possibility of **airway compression by lymph nodes**, most often caused by tuberculosis, should be kept in mind.

Bronchiectasis is unfortunately common in older children – often as a sequel to tuberculosis. Regular physiotherapy (easy to prescribe, very difficult to do) and antibiotics form the mainstay of treatment; but a number of affected children benefit from the use of bronchodilators.

Conclusion

The means are available to improve the management of many Papua New Guinean children with asthma. Whilst treatment with oral salbutamol and aminophylline is readily available and certainly beneficial for many patients, it is less than optimal. We should be moving to a much greater use of inhaled medication and preventive therapy.

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