Treatment of Bronchial Asthma in Latin America*

Edgardo Carrasco, M.D., F.C.C.P.

The therapeutic approach to asthma can be systematized from a practical point of view, as follows: 1. symptomatic treatment of respiratory obstruction, a) acute, and b) chronic; 2. prophylactic treatment of asthma; 3. specific treatment (immunotherapy). The way the different therapeutic resources are applied differs from patient to patient and constitutes what could be defined as the therapeutic strategy of asthma.

The first consideration in the plan of treatment is to determine if the disease has an immunologic background, and if there is any occupational factor involved in its pathogenesis. This pre-treatment decision-making is important to help determine the type of treatment to be applied (Table I).

Symptomatic Treatment of Bronchial Asthma

We attempt to establish the frequency of asthmatic episodes, the grade of severity (slight, moderate, severe and status asthmaticus), and finally the pattern of their presentation throughout the day (nocturnal, morning dipping, labile or permanent). The objective is to use an adequate intensity of therapy so as to control the symptoms both day and night.

A diary for assessing frequency and severity of episodes, and the daily recording of peak expiratory flow measurements can be helpful. As noted in Table 2, these determinations receive a score in order to facilitate the use of the therapeutic resources.

Treatment of Acute Asthma

Adult asthmatic patients with a forced expiratory volume in one second ($FEV_1$) ≤1,000 ml or a peak expiratory flow (PEFR) of ≤150 L/min are considered to have acute obstruction. If they are also dyspneic, pale, sweating, using the accessory respiratory muscles and speaking a monosyllabic language, we consider their obstructive disease severe, an assessment that is further strengthened by the presence of tachycardia, cyanosis and pulsus paradoxus. If the $FEV_1$ is ≤700 ml and PEFR is ≤100 L/min, the patient should be hospitalized, and if the arterial $PaO_2$ falls below 60 mm Hg, we will consider admission to the intensive care unit. Depending upon the behavior of the arterial $PaO_2$, $PaCO_2$ and pH, respiratory failure may be seen in the asthmatic patient with progressive deterioration. Mechanical ventilation may become necessary.

Treatment of Severe Acute Asthma

Due to the intensity and severity of airway obstruction, the use of intravenous medication is mandatory, applying: a) anti-inflammatory measures (corticosteroids), b) bronchodilators (aminophylline, $\beta_2$ sympathomimetics), and c) hydration (5 percent glucose solution). Other measures include correction of hypoxia (oxygen), expectorants and support measures.

<table>
<thead>
<tr>
<th>Types of Asthma and Therapeutic Possibilities</th>
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<tbody>
<tr>
<td><strong>Extrinsic Asthma</strong></td>
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<tr>
<td>Atopic</td>
</tr>
<tr>
<td>ABPA</td>
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<tr>
<td><strong>Intrinsic Asthma</strong></td>
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<tr>
<td>Occupational Asthma</td>
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<tr>
<td>Exercise Asthma</td>
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</tbody>
</table>

ABPA: Allergic bronchopulmonary aspergillosis.
Table 3—Treatment of Acute Severe Asthma

**Venous corticosteroid:** Hydrocortisone succinate  
Initial bolus: 5 mg/kg bodyweight (≤ 300 mg in adults)  
Daily dose: 12 mg/kg bodyweight (≤ 700 mg in adults)  
24 hours dose: ≤ 1,000 mg in adults

**Venous Aminophylline**  
Initial bolus: 5 mg/kg bodyweight (≤ 300 mg in adults)  
Daily dose: 0.5 mg/kg bodyweight/hour (≤ 700-1,000 mg)  
Corrections: Minus 50% in card insufficiency, pneumonia, hepatic disease; minus 25% over 60 years

**Selective \( \beta \)-sympathomimetics:** Aerosol or intravenous terbutaline, salbutamol

**Hydration:** 5% Glucose solution: 2-3 L/day

**Correction of hypoxia:** Oxygen 28-35%

In severe asthma stage 3: mechanical ventilation

(kinesitherapy, mucolytics, physiotherapy, etc), as represented in Table 3. A special comment should be made regarding the use of bronchodilators (epinephrine, aminophylline and \( \beta \)-sympathomimetics) in the child under one year of age. Different publications\(^4\)\(^5\) have reported less effect from bronchodilators in infants as a result of the bronchial obstruction being due more to mucosal edema and mucous hypersecretion than bronchospasm. In spite of these initial reports of little benefit from the use of oral or aerosolized bronchodilator therapy in infants,\(^6\) new studies have shown clear benefit from administration of aminophylline and salbutamol.\(^7\)\(^8\)

Treatment of Acute Moderate Asthma

The symptomatic treatment of acute moderate asthma is done on the basis of a step-wise approach. In adults, we initially use epinephrine at 1:1,000 dilution (or terbutaline or salbutamol), 0.4-0.5 ml subcutaneous injection.

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Table 4—Medication Available in Latin America for Asthma Treatment

<table>
<thead>
<tr>
<th>Medication</th>
<th>Oral</th>
<th>Aerosol</th>
<th>Parenteral</th>
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<tbody>
<tr>
<td><strong>Prophylactic</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Disodium cromoglycate</strong></td>
<td>20 mg qid</td>
<td>2 mg qid</td>
<td>10 mg qid</td>
</tr>
<tr>
<td><strong>Ketotifen</strong></td>
<td>1 mg bid</td>
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</table>

**Bronchodilators**

- **\( \beta \)-Sympathomimetics**
  - Terbutaline: 0.075 mg/kg qid (5 mg qid)
  - Metaproterenol: 0.25-0.50 mg qid
  - Fenoterol: 2 puffs qid
  - Clembuterol: 0.5 mg/kg bid (200 µg bid)
  - Salbutamol: 0.10 mg/kg qid (200 µg bid)
  - Albuterol: 2 puffs qid
  - Bitolterol mesylate: 2 puffs tid (740 µg tid)

- **Methylxanthines**
  - Theophylline (anhydrous): 4-6 mg/kg qid
  - Theophylline sust. action: 5-7 mg/kg bid
  - Aminophylline: 5 mg/kg qid

- **Anticholinergic agents**
  - Ipratropium bromide: 2 puffs qid (40 µg qid)
  - Ipratropium + Fenoterol (0.02 mg + 0.05 mg): 2 puffs qid (40 µg + 100 µg)

- **Corticosteroids**
  - Systemic: Prednisone 1 mg/kg/day, Prednisolone 1 mg/kg/day, Methyl-prednisolone 0.5 mg/kg/day, Hydrocortisone succinate 2.5 mg/kg/day
  - Inhaled: Beclomethasone 1 mg bid
  - Betamethasone valerate 200 µg bid

- **Systemic**
  - Prednisone 1 mg/kg/day
  - Prednisolone 1 mg/kg/day
  - Methyl-prednisolone 0.5 mg/kg/day
  - Hydrocortisone succinate 2.5 mg/kg/day

- **Inhaled**
  - Beclomethasone 2 puffs qid (100 µg qid)
  - Betamethasone valerate 200 µg bid

- **Prophylactic**
  - Disodium cromoglycate 20 mg qid
  - Ketotifen 1 mg bid

**Note:** Children: 6 mg/kg (bolus) 0.7-1.3 mg/kg (maintenance)
ously, plus 250 mg of aminophylline intravenously. If the PEFR does not increase 15 percent or more with the above therapy, we continue to a second phase of treatment, in which hydrocortisone succinate (300 mg), aminophylline (250 mg) and 30 ml of 5 percent glucose solution is employed by the intravenous route. If with these measures and the additional use of a β₂ sympathomimetic aerosol the obstructive problem does not improve significantly in 30-60 minutes, the patient is considered to have severe acute asthma and the additional therapy mentioned above is employed. The initial doses recommended for children are: 0.01 ml/kg bodyweight for 1:1,000 epinephrine; 10 micrograms/kg bodyweight for salbutamol; 7 mg/kg bodyweight for aminophylline, and 5-7 mg/kg bodyweight for hydrocortisone.7,4

Treatment of Chronic Asthma

The wide therapeutic armamentarium available (Table 4), must be employed rationally, graduating its use in relation to the type, severity and pattern of the disease. With frequent episodes of bronchospasm it is important to consider a prophylactic strategy (Table 5).

Treatment of Slight Chronic Asthma

Only one bronchodilator drug will be recommended, either a β₂ selective agonist, or a long-acting theophylline, when the symptoms are concentrated at a particular time (nocturnal or morning dipping); or twice a day, when the symptoms, although slight, have a continuous distribution. In small children, we prefer oral administration, using either a rapid or sustained-released theophylline, or a β₂ selective agonist syrup.

Treatment of Moderate Chronic Asthma

We generally use a combination of a β₂ selective sympathomimetic (orally tid or 2 puffs of aerosol qid), and a sustained-release theophylline, administered every 8 to 12 hours, depending upon the initial serum theophylline value (optimal range 10-20 μg/ml).

If this initial approach does not control the disease, we add an inhaled corticosteroid (2 puffs qid). Following a widely recommended “scator” procedure,” if we still fail to control the disease, we use a short course of oral corticosteroids, at an initial dose of 1-2 mg/kg bodyweight (average 60 mg for an adult), decreasing 5 mg every two days, to stop in 14 days. In patients, where we know the annual evolution of symptoms, the prophylactic use of cromolyn sodium (1 capsule of 20 mg qid), or a combination of a β₂ sympathomimetic and ipratropium aerosol (2 puffs qid) should be considered. In patients with a clear extrinsic allergic etiology, it will be worthwhile to start a specific immunotherapy program with periodic injections.

Treatment of Severe Chronic Asthma

In general, we start with three drugs: (1) β₂ selective sympathomimetic, preferably by aerosol every 6 hours, (2) beclomethasone aerosol (alternatively: ipratropium associated with a β₂ agonist) and (3) oral theophylline (sustained release). There are combined forms of a selective β₂ agonist, fenoterol plus ipratropium bromide (Berodual or Beraclid), and salbutamol with beclomethasone (Vendide), which facilitate combined therapy. The oral theophylline is given every 8-12 hours, adjusting it based on age (more in children, less in patients over 60 years old), smoking habits (higher dose), and intercurrent diseases (less needed during pneumonia, cardiac failure, cor pulmonale, and liver disease).

If we fail in controlling the bronchial obstruction with the above, we proceed to the use of oral corticosteroids, associated with aerosolized beclomethasone. The use of oral corticosteroids will be limited to bring the acute exacerbation to a more stable stage.

If the severe symptoms reappear after eliminating the oral corticosteroid, the patient is considered corticosteroid-dependent, fortunately a rare condition. In this situation, alternate-day therapy is preferred to try to avoid adrenal suppression.

Prophylactic Treatment of Bronchial Asthma

Asthma is a disease characterized by asymptomatic periods of variable extension, over which are superimposed acute episodes. The prophylactic drugs available are: a) true preventive drugs, which act by blocking the liberation of mediators from the mast cells or the effect of them over the shock organ receptors or diminishing bronchial hyperreactivity. Drugs in this category include cromolyn sodium (capsules of 20 mg, aerosol of 1 and 5 mg per puff, and solution for nebulizers) and ketotifen, an oral product used as one capsule (1 mg) every 12 hours;¹⁰ b) indirect prophylactic drugs, such as any β₂ agonist drug in aerosol, or ipratropium aerosol, which acts by lowering the bronchial hyperreactivity. The proper and continuous use of these drugs in slight and moderate chronic asthma, during asymptomatic periods will help prevent acute recurrence.¹⁰

Table 5—Basis of Symptomatic Treatment of Chronic Asthma

<table>
<thead>
<tr>
<th>Characterize asthma</th>
<th>Type, severity, pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchodilators</td>
<td>β₂ selective agonist (oral, aerosol)</td>
</tr>
<tr>
<td></td>
<td>Theophylline oral (10-20 μg/ml)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Beclomethasone aerosol</td>
</tr>
<tr>
<td></td>
<td>Systemic short action with intermittent maintenance</td>
</tr>
<tr>
<td>Prophylaxis</td>
<td>Cromoglycate, Ketotifen, β₂ selective agonist aerosol, ipratropium aerosol</td>
</tr>
</tbody>
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SPECIFIC TREATMENT OF ASTHMA

Finally, in a reduced group of asthmatic patients, those in the atopic extrinsic allergic group (about 40-60 percent of the total), one could offer the specific treatment of immunotherapy. After an accurate etiologic study, based on history, prick cutaneous tests, and in doubtful cases RAST and bronchial provocation tests, we could decide to start immunotherapy, mainly in patients sensitized to pollens, house dust, dermatophagoids and molds. In general, in Latin America, "vaccines" for food allergens are not used; however, a small group of specialists still use bacterial vaccines, in spite of its doubtful benefit.

REFERENCES
11. Carrasco E, Galleguillos F, Bernath Z. The orally administered anti-allergic agent, ketotifen; efficacy in atopic and non-atopic bronchial asthma. Allergol et Immunopatho 1981; 9:335-42