Bronchial asthma and treatment of acute severe asthma

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Definition

Chronic inflammatory disorder of airways that causes recurrent episodes of:

- Wheezing
- Breathlessness
- Chest tightness &
- Cough particularly at night and /or early morning

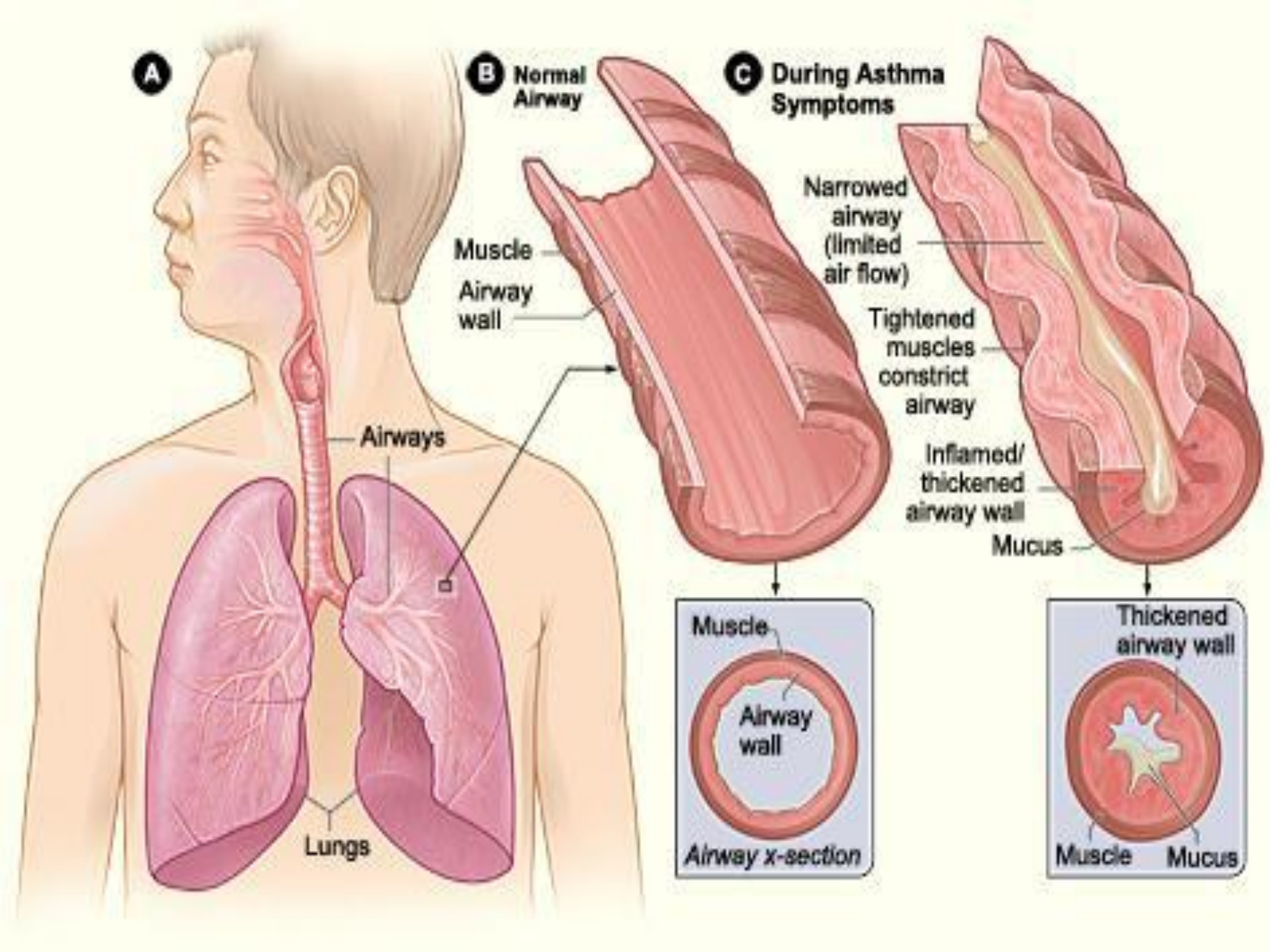
These symptoms are usually associated with wide spread but variable bronchoconstriction and air flow limitation that is at least partially reversible, either spontaneously or with treatment

It is thought that inflammation causes increase in airway responsiveness (bronchospasm) to a variety of stimuli

PATHOPHYSIOLOGY

Airway obstruction in asthma is caused by

- ❖ Edema and inflammation of mucous membrane lining the airways.
- ❖Excessive secretion of mucus, inflammatory cells and cellular debris.
- ❖Spasm of the smooth muscle of bronchi.


A
B Normal Airway
C During Asthma Symptoms
Muscle
Airway wall
Airways
Lungs
Narrowed airway (limited air flow)
Tightened muscles constrict airway
Inflamed/ thickened airway wall
Mucus
Muscle
Airway wall
Airway x-section
Thickened airway wall
Muscle
Mucus

- Atopic – IgE mediated and triggered by allergens
- Nonatopic – non IgE mediated and triggered by infections
- Mixed
- Exercise induced
- Aspirin induced

Early reaction

- Starts within 10 min of the exposure to allergen.
- Characterized by release of histamine, leukotrienes, prostaglandins, platelet activating factor and bradykinin from the mast cell bound IgE.
- Cause bronchoconstriction, mucosal edema and mucus secretion which manifests as airway obstruction.
- This phase is inhibited by B2- agonist drugs.

Late phase

- It develops 3-4 hrs later and peaks at 8-12 hrs

- The release of mast cells mediators is not prevented by premedication with B2-agonist.

- It is inhibited by premedication with steroids suggesting that airway narrowing is mainly due to an inflammatory reaction and mucosal edema.

TRIGGERS OF EPISODES OF ASTHMA

Viral infections:

Viral infections interfere with the integrity of the mucosal surfaces by opening up tight intraepithelial cell junction

Role of Exercise:

The loss of water from the respiratory tract induces mucosal hyperosmolarity , which stimulates mediator release from mast cells.

Weather change:

- Loss of heat and water from lower airways.
- Sudden release of airborne allergens in atmosphere resulting in Exacerbation of asthma.

Emotional factors:

Operated through the vagus nerve, initiates bronchial Smooth muscle

Role of food:

Allergy to food proteins.

Clinical features:

- Simple recurrent cough to severe wheezing.
- Acute asthma may usually begin with a cold, or bouts of spasmodic coughing .
- In early phase of the episode, the cough is nonproductive.
- Patient becomes dyspneic , with prolonged expiration and wheezing.
- Accessory muscles of respiration are excessively used .
- The child sweats profusely, may develop cyanosis and become apprehensive .restless and appear fatigued.
- In severe episodes the child may show air-hunger. The chest is hyper-resonant because of excessive air trapping.

As the obstruction becomes severe, the airflow decreases markedly.

- Wheezing which was earlier audible may disappear.

- Absence of wheezing in the presence of cyanosis and respiratory distress should not be considered as an evidence of clinical improvement.

- As the child improve, the airflow increases and wheezing may reappear. With remission, the wheeze disappears.

Diagnosis:

- The diagnosis of asthma is clinical in most cases, hence pulmonary function tests may not play significant role.

- The important parameters in spirometry include PEFR, FEV1, FVC and FEV25-75.

- FEV1 is commonly used parameter for documentation of severity of asthma.

- FEV25-75 is effort independent and is probably more sensitive indicator of airway obstruction.

- Abnormality in PEFR suggestive of asthma include:
  a) A diurnal variation of more than 20%.
  b) <80% of predicted
  c) Improvement of >20% after bronchodilator therapy.

Classification of Asthma According to Severity

Step 1 Intermittent

Symptoms:

Less than 1 time a week; asymptomatic and normal PEFR between attacks.

Night time symptoms

Less than 2 times a month.

Peak expiratory flow rate:

Less than 80% predicted, variability less than 20%

Step 2 Mild persistent

Symptoms

More than 1 time a week, but less than 1 time a day.

Night time symptoms

More than 2 times a month

Peak expiratory flow rate

More than 80% predicted, variability 20 -30%

Step 3 Moderate persistent

Symptoms

Daily use B2- agonist; daily attacks affect activity.

Night time symptoms

More than 1 times a week.

Peak expiratory flow rate

More than 60% and less than 80% predicted; variability more than 30%.

Step 4 Severe persistent

Symptoms

Continuous; limited physical activity

Night time symptoms

Frequent

Peak expiratory flow rate

Less than 60% predicted; variability more than30%

STEPWISE TREATMENT OF ASTHMA

Step 1 Intermittent

Long-term prevention

Inhaled short-acting B-agonist as required for symptomatic relief. If needed more than 3 times per week.

Step 2 Mild persistent

Long-term prevention

-Inhaled short-acting B-agonist as required+

-inhaled budesonide, fluticasone or beclomethasone(100-200 microgram) or
cromolyn sodium or
sustained release theophylline or
leukotriene modifiers.

Step 3 Moderate persistent

Long-term prevention

-Inhaled short-acting B-agonist as required +

-inhaled budesonide, fluticasone or ----
beclomethasone (100-200 microgram q 12 hr). If needed, salmeterol(50 microgram q 12-24 hr) and s

- sustained release theophylline.

Step 4 Severe persistent

Long-term prevention

-Inhaled short-acting B-agonist as required+

-inhaled budesonide, fluticasone or beclomethasone (200-400 microgram q 12-24 hr) + salmeterol or formoterol and

-sustained release theophylline +

- oral low dose prednisolone on alternate days (if symptoms not relieved with above treatment)

ACUTE SEVERE ASTHMA

Clinical Definition

- Severe asthma that fails to respond to inhaled β2 agonists, oral or IV steroids, and O2, and that requires admission to the hospital for treatment

Pathophysiology

- Primary pathophysiology
  - Airway inflammation & hyper-reactivity
  - Smooth muscle spasm
  - Mucosal edema & plugging

- Status asthmaticus
  - Reversible
  - Recurrent
  - Diffuse
  - Obstructive

Presentation

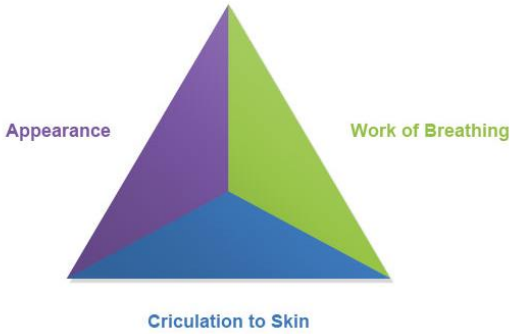
Varies by severity, asthmatic trigger, and patient age.

- Cough
- Wheezing
- Increased work of breathing.
- The noisy chest

Assessment

Initial Assessment (PAT)

- Colour
- Breathing
- Circulation



Primary assessment

- Airway
- Breathing
- Circulation
- Disability
- Exposure

ation)

Predict it

High risk factors for asthma severity and fatality

- Previous severe sudden deterioration,
- Past PICU admissions
- Previous respiratory failure
- Need for mechanical ventilation.

Presentation ‘Red-alerts’

Severe respiratory compromise:

- ‘Silent Chest’ with increased respiratory efforts usually precede respiratory failure.
- Agitation or dyspnea
- Altered consciousness
- Inability to speak >1-2 words at a time
- Central cyanosis
- Diaphoresis
- Inability to lie down
- Pulsus paradoxus >25 mmHg
- PaCO2 normalization or hypercapnia (ominous)
- Bradycardia
- Severe Hypoxia

Assessment of severity

- Becker Asthma score

Score	Respiratory rate (per min)	Wheezing	I/E ratio	Accessory muscle use
0	<30	None	1:1.5	None
1	30–40	Terminal expiration	1:2	1 site
2	41–50	Entire expiration	1:3	2 sites
3	>50	Inspiration and entire expiration	>1:3	3 sites or neck strap muscle use

- A score >4 is moderate status asthmaticus
- score 7 and above is severe and needs ICU admission

Assessment of severity

- Clinical Asthma score

Variables	Score		
	0	1	2
Cyanosis	None	In 21% O_2	In 40% O_2
or PaO_2, mm Hg	70–100 in 21% O_2	< 70 in 21% O_2	< 70 in 40% O_2
Inspiratory breath sounds	Normal	Unequal or absent	Decreased
Accessory muscles used	None	Moderate	Maximal
Expiratory wheezing	None	Moderate	Marked
Cerebral function	Normal	Depressed or agitated	Coma

*From Wood et al.[82] A score of ≥ 5 indicates impending respiratory failure; a score of ≥ 7 is consistent with respiratory failure.

- A score >4 is impending Resp failure
- Score 7 and above is Resp failure

Oxygen therapy

- 100% oxygen
- Oxygen saturation monitoring
- Other monitors

Cardiopulmonary Interactions

- Severe the attack, more negative intrapleural pressure
- Increased left ventricular afterload
- Increased transcapillary filtration of edema fluid into airspaces resulting in a high risk for pulmonary edema.
- Overhydration increases microvascular hydrostatic pressure and further worsens pulmonary edema.

Cardiopulmonary Interactions

- High right ventricular afterload due to
  - Hypoxic pulmonary vasoconstriction,
  - Acidosis
  - Increased lung volume.

Chest Radiography

Limited role but indicated in-

- First time wheezers
- Clinical evidence of parenchymal disease
- Those requiring admission to PICU.
- Suspected air leak or pneumonia
- When the underlying cause of wheezing is in doubt

Arterial blood gas

- In all children at baseline
- Subsequently as indicated
- Hypocarbia in early stage
- Normalization of CO_2 with persistent respiratory distress indicates impending respiratory failure.

- A $PaO_2 < 60$ mm Hg and a normal or increased $PaCO_2$ (>45 mm Hg) indicates the presence of respiratory failure

PICU Admission

- Comfortable environment
- IV access
- Maintain euvolemia
- Continuous cardio-respiratory monitoring
- Avoid sedation
- Monitor potassium
- Antibiotics, if indicated
- If ventilated -arterial and central venous

Fluid

- Restoration of euvolemia
- Isotonic fluid like normal saline or Ringer's lactate
- Fluid balance
- Avoid overhydration; Risk of pulm edema
- Serum potassium monitoring

Antibiotics

- Not routinely indicated
- Reserved for children with evidence of bacterial infection
  - High fever
  - Purulent secretions
  - Consolidation on X ray film or
  - Very high leucocyte counts

Pharmacologic Targets

- Improving oxygen delivery
- Relaxation of bronchial smooth muscles
  - B_2 receptors
  - M_1 receptors
- Attenuating underlying inflammation
- Instituting vigorous pulmonary toilet

Pharmacologic Therapies

- Oxygen
- β2 agonists
- Steroids
- Anticholinergics
- Magnesium Sulfate
- Aminophylline
- Ketamine
- Heliox

Inhaled β2 agonists

- The mainstay of therapy
- Inhaled, intravenous, subcutaneous, or oral routes
- Salbutamol and terbutaline have relative β2-selectivity.

- No difference in clinical response to treatment with racemic salbutamol vs lev-salbutamol in acute severe asthma in children

Intravenous β2-agonists

- Not to give routinely in acute exacerbations
  - Use in patients unresponsive to inhaled β2-agonists
  - Those in whom nebulization is not feasible
    - Intubated patients,
    - patients with poor air entry
  - IV Terbutaline
    - Loading 10 mcg/kg IV over 10 min, followed by continuous infusion at 0.1–10 mcg/kg/min.

Subcutaneous β2 agonist

- Primarily used for children with no IV access
- As a rapidly available adjunct to inhaled β2 agonist.
- Subcutaneous terbutaline 0.01 mg/kg/dose (max of 0.3 mg)
- May be repeated every 15–20 min for up to three doses.

Adverse effects of β2-agonists

- Cardiovascular system
  - Tachycardia
  - Increased QTc interval
  - Dysarrhythmia
  - Hypertension
  - Diastolic hypotension.

Corticosteroids

- First line of therapy
- Early during their hospital visit
- Parenteral: preferred for critically ill children.
- Oral: equal efficacy if it can be given
- Aerosolized: limited role in status asthmaticus
- Effect starts in 1–3 h and reach at max in 4–8 h.

Corticosteroids

- Mechanism:
  - Systemically reduce inflammation, decrease mucus production, and enhance the effects of B_2-agonists
  - Prevents the sustained inflammatory phase which occurs 6-8 hours after allergen exposure
- Dosing:
  - Hydrocortisone: 10 mg/kg followed by 5 mg/kg 6hrly
  - Methylprednisone: 0.5–1 mg/kg IV q 6h (2-4 mg/kg/day)
  - Dexamethasone: 0.15 mg/kg/dose 4-6 hrly
  - Prednisolone: 1-2 mg/kg/day
- Duration 5-7 days
- In status, steroids should be administered IV to assure adequate drug delivery in a timely manner

Corticosteroids: Side effects

- Short-term use of high-dose steroids
  - Hyperglycemia
  - Hypertension
  - Acute psychosis
- Prolonged steroid
  - Immunosuppression
  - Hypothalamic-pituitary-adrenal axis suppression,
  - Osteoporosis
  - Myopathy
  - Weakness

Anticholinergic Agents

Ipratroprium Bromide

- Mechanism:
  - Muscarinic agonist (anticholinergic)
  - M_1 receptor → decrease cGMP → decreases intracellular Ca^{2+}
- 125–500 mcg inhaled every 20 min for up to three doses.
- Subsequently every 4–6 h.
- Dry mouth, bitter taste, flushing, tachycardia, and dizziness.
- Caution: Sometimes unilateral pupillary dilation (local effect)

Magnesium Sulfate

- Mechanism:
  - Inhibits Ca^{2+} influx into cytosol → smooth muscle relaxant
  - Increases B_2 agonist affinity for its receptor, thereby potentiating its effect
  - Inhibits histamine release from mast cells
- 50 mg/kg IV over 20-30 min with max of 2 gm
- Repeat once or twice after 4–6 h.

Magnesium -Side effects

- Hypotension
- CNS depression,
- Muscle weakness
- Flushing

- Very high serum magnesium levels (usually >10–12 mg/dL).
  - Cardiac arrhythmia/ complete heart block,
  - Respiratory failure due to severe muscle weakness
  - Sudden cardiopulmonary arrest

- Treatment: IV Calcium Gluconate

Aminophylline

- Mechanism
  - Xanthine derivative
  - Decreases intracellular Ca^{2+}
  - Inhibits TNF-alpha and leukotriene synthesis
- Loading dose: 6 mg/kg over 20 min IV
- Continuous infusion: 0.6–1 mg/kg/min IV
- Limited role in children unresponsive to steroids, inhaled and IV β2 agonist, and O2 with status asthmaticus

Aminophylline Toxicity

- Nausea and vomiting
- Tachycardia
- Agitation

- Severe toxicity (high serum concentrations)
  - Cardiac arrhythmias,
  - Hypotension,
  - Seizures
  - Death

- Monitor drug level in blood:
  - Level q8hr after drug initiation and then every morning.
  - Therapeutic levels are 10 – 20 mcg/ml.

Mechanical Ventilation

Indications

- Poor response to initial therapy
- Severe hypoxia
- Rapid deterioration in mental state
- Rising PCO2
- Cardiopulmonary arrest

Intubation Tips

- Preoxygenate with 100% oxygen
- Anticipate hypotension
- Cuffed ET tube with the largest appropriate diameter
- Avoid histamine-producing agents like morphine or atracurium
- Ketamine: preferred induction agent due to its bronchodilatory action.
- Use atropine, Benzodiazepam and by a rapid-acting muscle relaxant (vecuronium).

Ventilation Principles

- Maintain adequate oxygenation,
- permissive hypercarbia with arterial pH of >7.2
- Adjust minute ventilation
- Slow ventilator rates
- Avoid air trapping:
- Prolonged expiratory phase, short inspiratory time
- Minimal PEEP (debatable)
- Attempt extubation as soon as possible.

Typical Ventilator Setting

- VT of 5–6 mL/kg,
- RR approximately half of the normal for age,
- I: E ratio of 1:3
- PEEP of 2–3 cm of H2O.

- In infants, pressure controlled ventilation: adjust PIP to achieve adequate ventilation;

Complications

- Hypotension
- Oxygen desaturation
- Pneumothorax/ subcutaneous emphysema,
- Cardiac arrest

- Suspect tension pneumothorax and treat promptly

Sedation, Analgesia and Muscle Relaxants

- Is sedation needed at all?
- Non ventilated in agitation ?? sedation

- Ketamine
- Fentanyl vs morphine
- Vecuronium vs atracurium

Ketamine

- Mechanism:
  - “Dissociative” anesthetic
  - Bronchodilates by intrinsic catecholamine release
  - Decreases airway resistance and maintains laryngeal tone & reflexes
- 0.5–1 mg/kg IV
- Continuous infusion 1-2 mg/kg/hr

Heliox

- Mechanism:
  - Low-density gas that increases laminar flow of oxygen and decreases turbulent flow.

- Adjunct therapy
- For children unresponsive to conventional therapy
- Children on high-pressure mechanical ventilatory support

- Dosing: 60%/40% or 80%/20% helium/O2
- No systemic side effects

Noninvasive Mechanical Ventilation

- An alternative to conventional mechanical ventilation in early phase
- While weaning off conventional ventilator

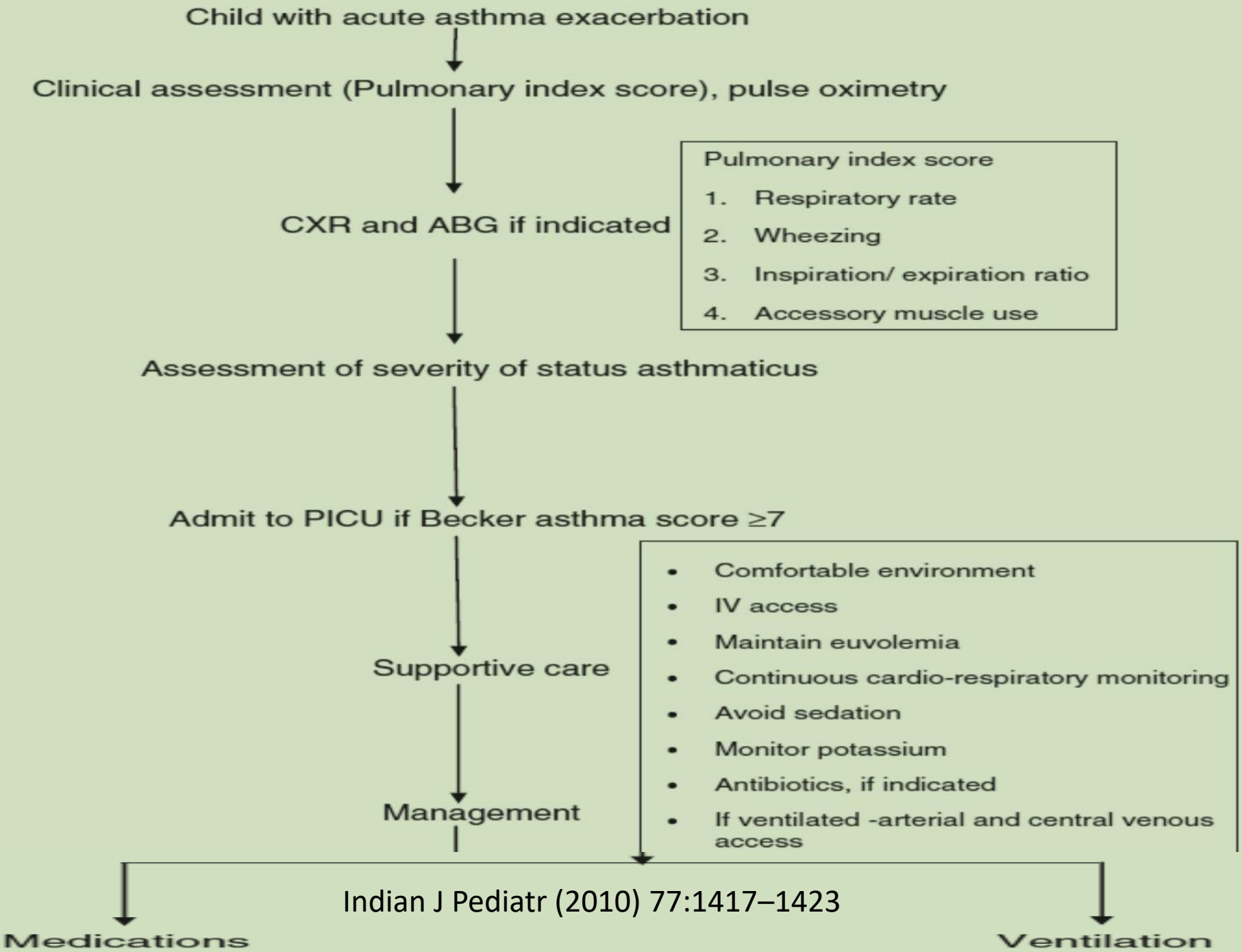
Chest Physiotherapy

- Useful in children with segmental or lobar atelectasis.
- In others no therapeutic benefit in the critically ill patient with status asthmaticus.

Leukotriene Modifiers

- Little data to suggest a role for leukotriene modifiers in acute asthma
- It is not part of standard management of status asthmaticus

SUMMARY



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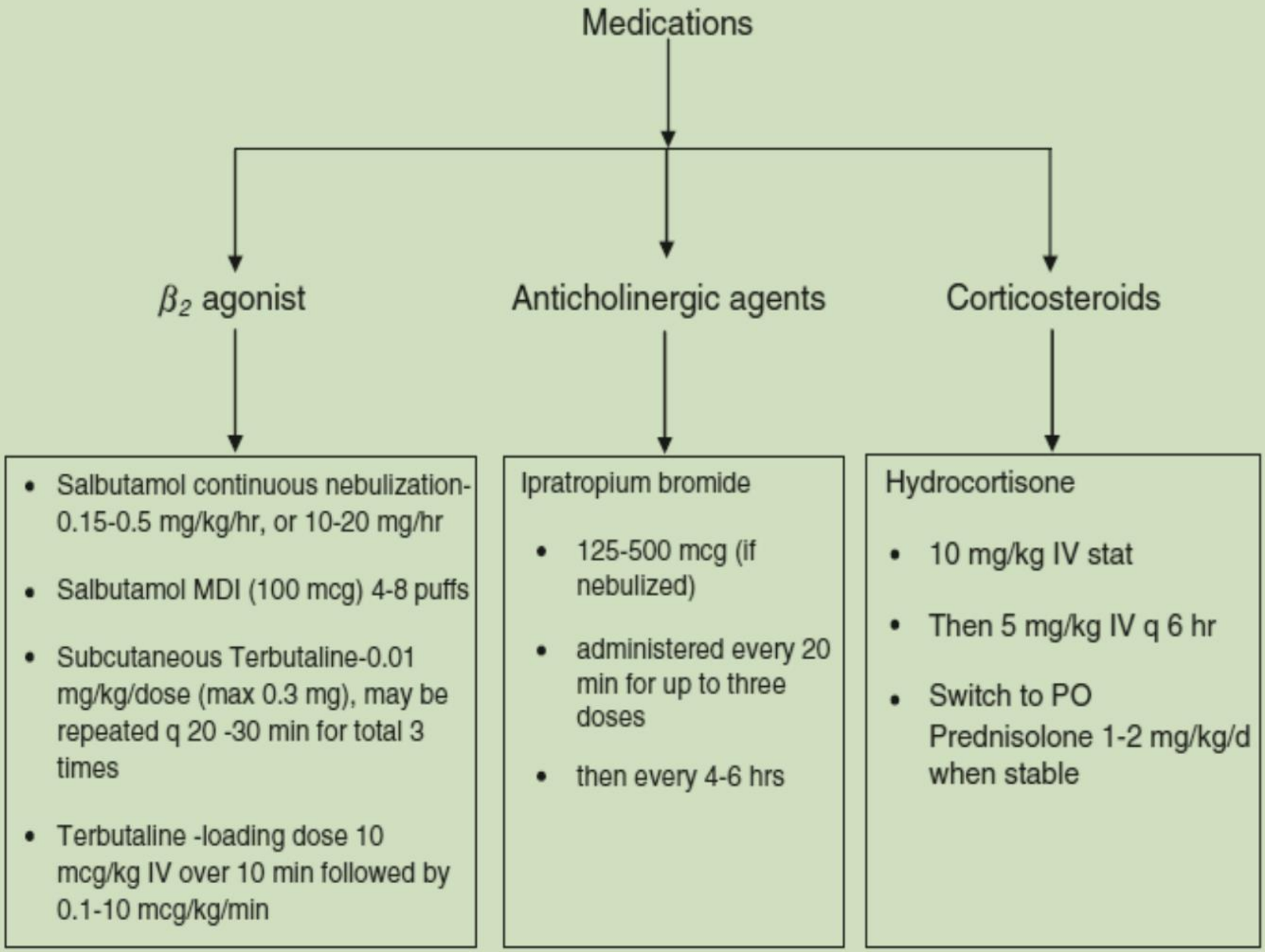

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Other medications

- Magnesium- 50 mg/kg/dose over 30 min or infusion at a rate of 10-20 mg/kg/hr, can repeat once or twice after 4-6 hrs
- Theophylline- loading dose of 5-7 mg/kg infused over 20 min followed by 0.5-0.9 mg/kg/hr
- Ketamine- 1 mg/kg/hr, titrated to effect
- Vecuronium- 0.1 mg/kg/hr, titrated to effect

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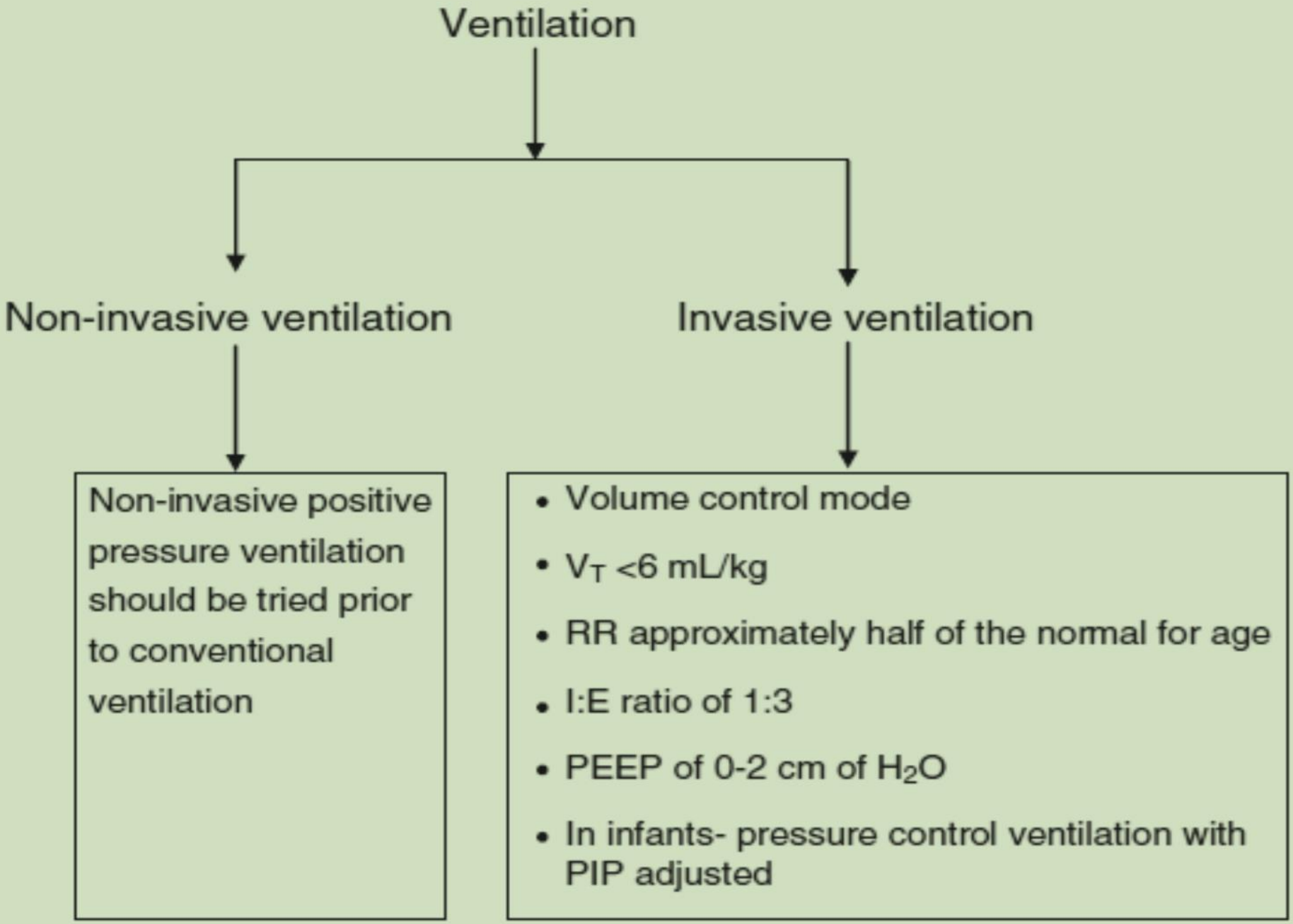

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