Treatment of COPD & Asthma

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COPD and Asthma Drugs

- Short-acting bronchodilators
  - Albuterol
  - Ipratropium
- Long-acting bronchodilators
  - Salmeterol, Formoterol
  - Tiotropium
- Steroids

β2 Agonists

- Activate adenylate cyclase → ↑cAMP
- Relax bronchiole smooth muscle
- Short acting: Albuterol
  - Nebulizer or inhaler
  - Use during acute attacks (prn)
- Long acting: Salmeterol, Formoterol
  - Not used as monotherapy for asthma (always with ICS)
- Systemic side effects (rare)
  - Tremor, arrhythmia

Muscarinic Antagonists

- Vagal nerve → Ach → Bronchoconstriction
- MA drugs block M receptors smooth muscle
- Prevents bronchoconstriction

Muscarinic Antagonists

- Short acting: Ipratropium
- Long acting: Tiotropium

Steroids

- Inhaled: Beclomethasone, Fluticasone, Budesonide
- Oral: Prednisone
- IV: Methylprednisolone (Solumedrol)

Steroids

- Inhibit synthesis of cytokines
- Bind to glucocorticoid receptor (GR)
- Many, many immunosuppressive effects
- ↓ expression many interleukins, IFN-γ, TNF-α, GM-CSF
- Inactivation NF-KB
  - Transcription factor
  - Induces production of TNF-α

Steroids

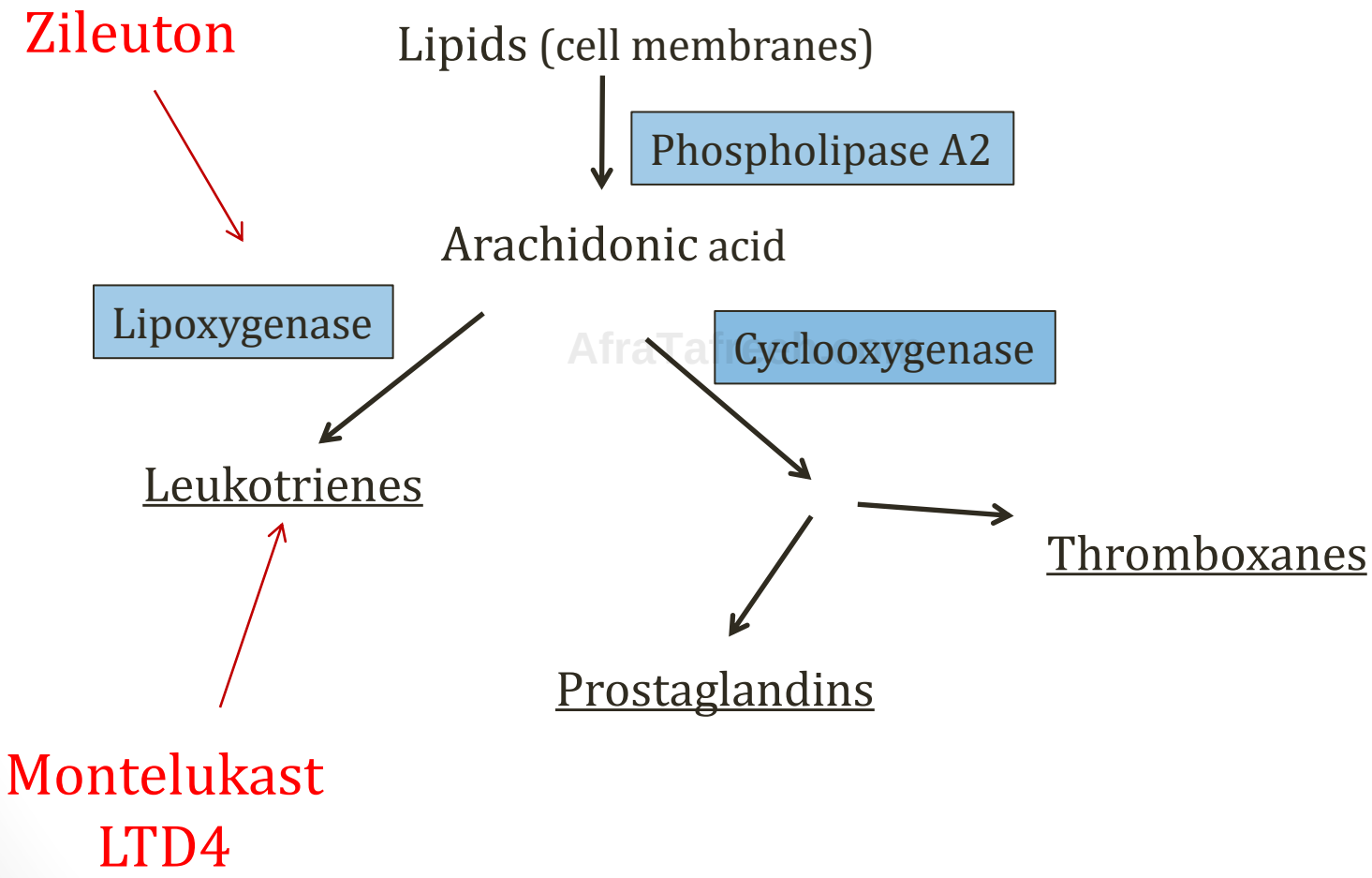
- Common side effect is oral candidiasis ("thrush")
- Patients instructed to rinse after inhalation

Image courtesy of James Heilman, MD

Special Asthma Drugs

- Leukotriene receptor antagonists (PO)
  - Montelukast (Singulair)
  - Useful in aspirin sensitive asthma
- Zileuton (PO)
  - 5-lipoxygenase inhibitors
  - Blocks conversion of arachidonic acid to leukotrienes

Eicosanoids



Special Asthma Drugs

- Omalizumab (SQ injection)
  - IgG monoclonal antibody
  - Inhibits IgE binding to IgE receptor on mast cells & basophils
- Cromolyn (inhaler/nebulizer)
  - Inhibits mast cell degranulation
  - Blocks release of histamine, leukotrienes

Theophylline

- Methylxanthines
- Multiple, complex mechanisms
- Bronchodilation
  - Likely through inhibition PDE
  - Less hydrolysis (breakdown) cAMP
  - ↑cAMP
- Also down-regulates inflammatory cell functions

Theophylline

- Narrow therapeutic index
- Levels must be monitored
- Dose must be titrated
- Goal is a peak serum concentration 10 to20mg/L

Theophylline

- Metabolized by P450
- Many drug-drug interactions
- Common culprits:
  - Cimetidine
  - Ciprofloxacin
  - Erythromycin
  - Clarithromycin
  - Verapamil

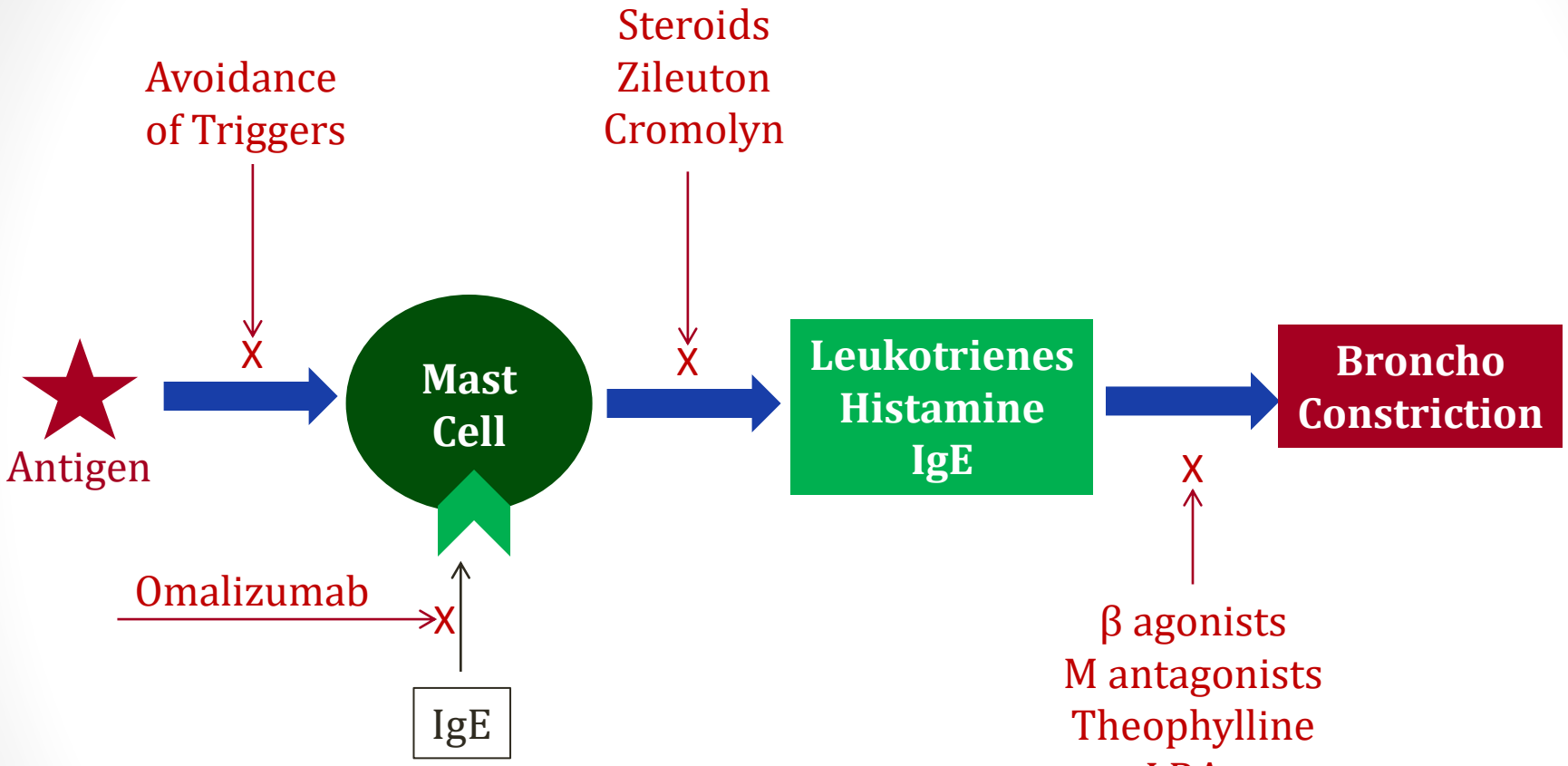
Theophylline

- GI toxicity
  - Nausea, vomiting
- Neurotoxicity
  - Seizures
- Overdose scenario: Nausea, vomiting, seizures

Theophylline

- Cardiotoxicity
  - Blocks adenosine receptors
  - Increased heart rate
  - Arrhythmias (atrial tachycardia, atrial flutter)
  - Cause of death in overdose/poisoning
- Key clinical scenario
  - Patient on theophylline for asthma/COPD
  - SVT
  - Adenosine fails to slow heart rate

Asthma

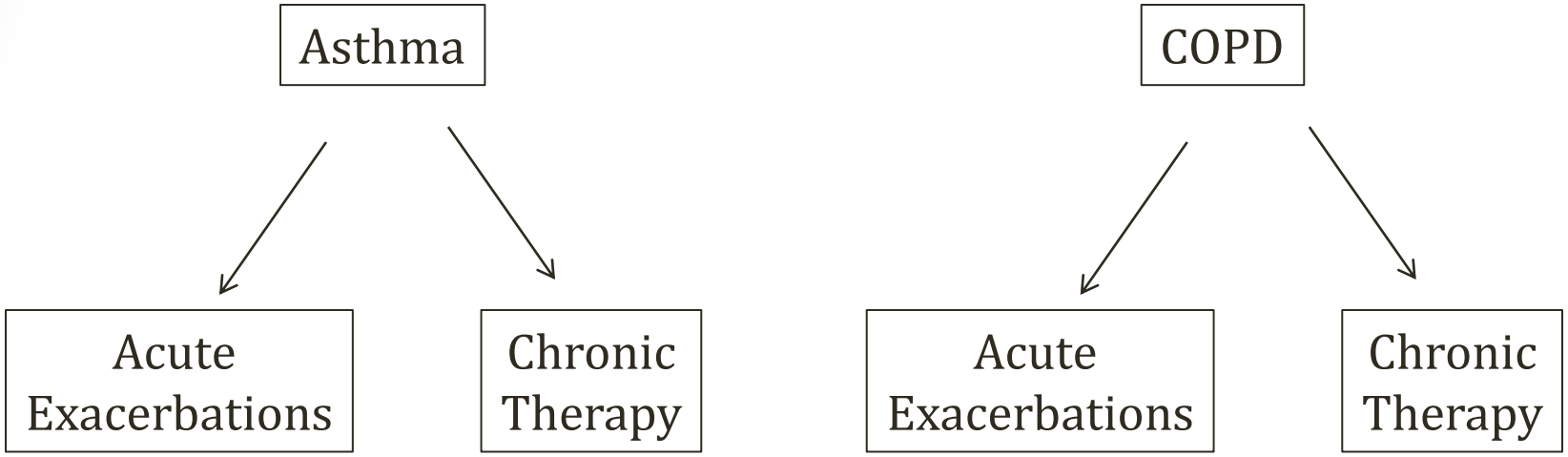


Special COPD Drugs

- Theophylline
- Roflumilast (PO)
  - Phosphodiesterase-4 (PDE-4) inhibitor
  - Decreases inflammation
  - May relax airway smooth muscle

Roflumilast is a phosphodiesterase-4 inhibitor

Treatment Asthma & COPD



COPD: Acute Exacerbations

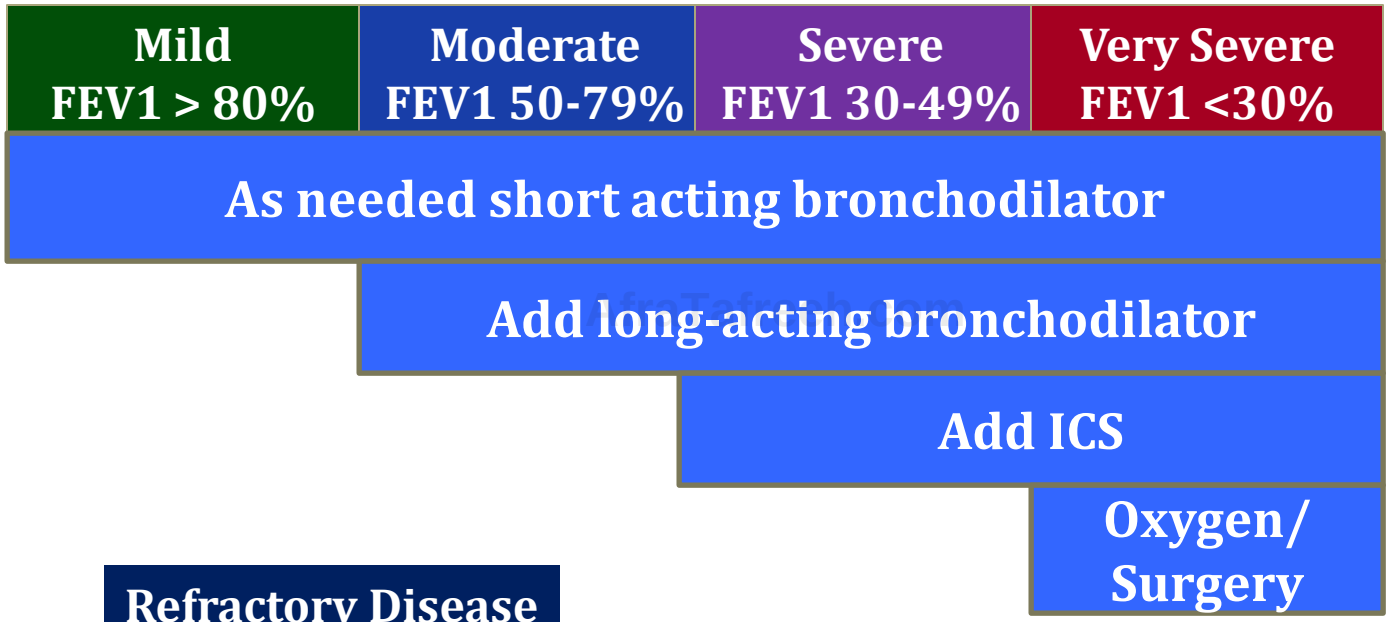
- Oxygen
- Nebulized albuterol +/- ipratropium (Combivent)
- IV or oral corticosteroids
  - Prednisone 60mg daily
  - Methylprednisolone 80mg IV q8hrs
- Antibiotics (severe, hospitalized patients)
  - Fluoroquinolones
  - Amoxicillin/clavulanate

GOLD Criteria

Global Initiative for Chronic Obstructive Lung Disease

Stage	Symptoms	FEV1
Gold 1	Mild	FEV1 >80%
Gold 2	Moderate	FEV1 50-79%
Gold 3	Severe	FEV1 30-49%
Gold 4	Very Severe	FEV1 <30%

COPD: Chronic Therapy



Refractory Disease
Theophylline
Roflumilast

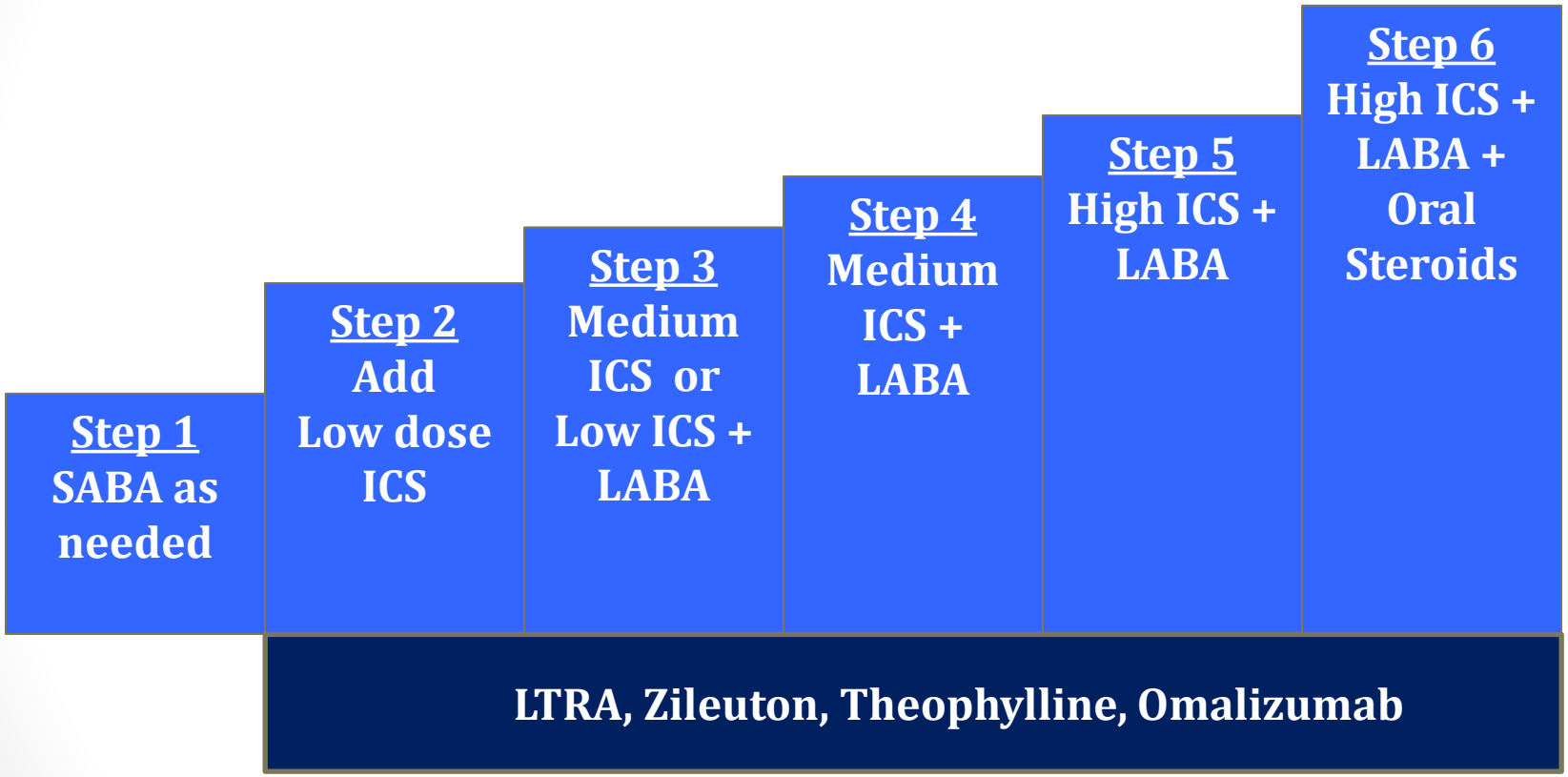
COPD: Chronic Therapy

- Oxygen
  - Associated with increased survival
  - PaO2 < 55mmHG or O2 sat <88%
- Pulmonary rehabilitation
  - Improves exercise capacity, quality of life
  - Decrease dyspnea
- Vaccinations
- Smoking cessation

Asthma: Acute Exacerbations

- Oxygen
- Nebulized albuterol
- IV or oral corticosteroids
  - Prednisone 60mg daily
  - Methylprednisolone 80mg IV q8hrs
- Rarely used:
  - Ipratropium
  - IV Magnesium sulfate

Asthma: Chronic Therapy



Surgical Treatment

- For advanced “end-staged” COPD
- Lung volume reduction surgery/Bullectomy
  - Remove diseased lung tissue
  - Allow healthy lung tissue more room to expand
- Lung transplant