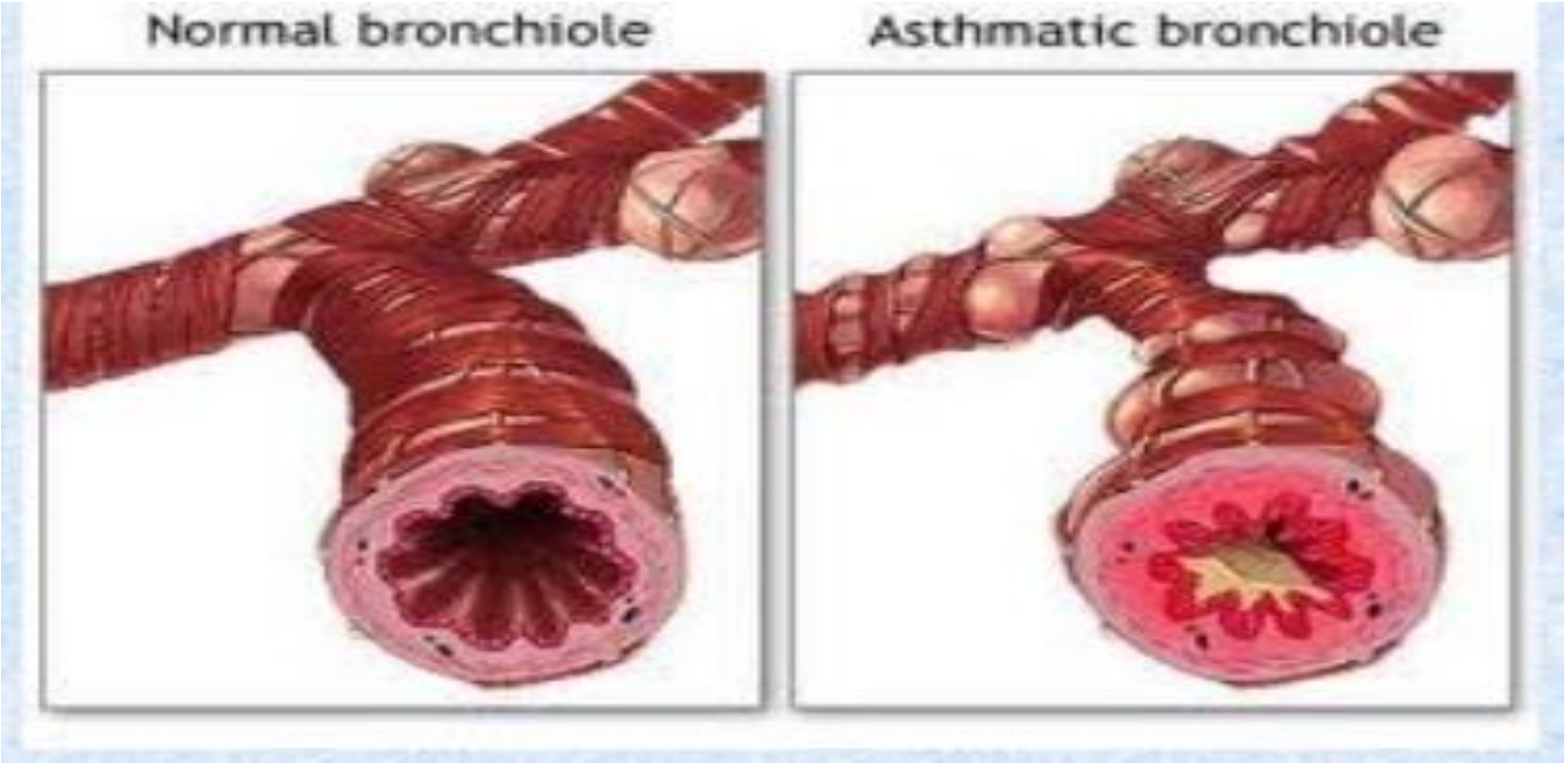
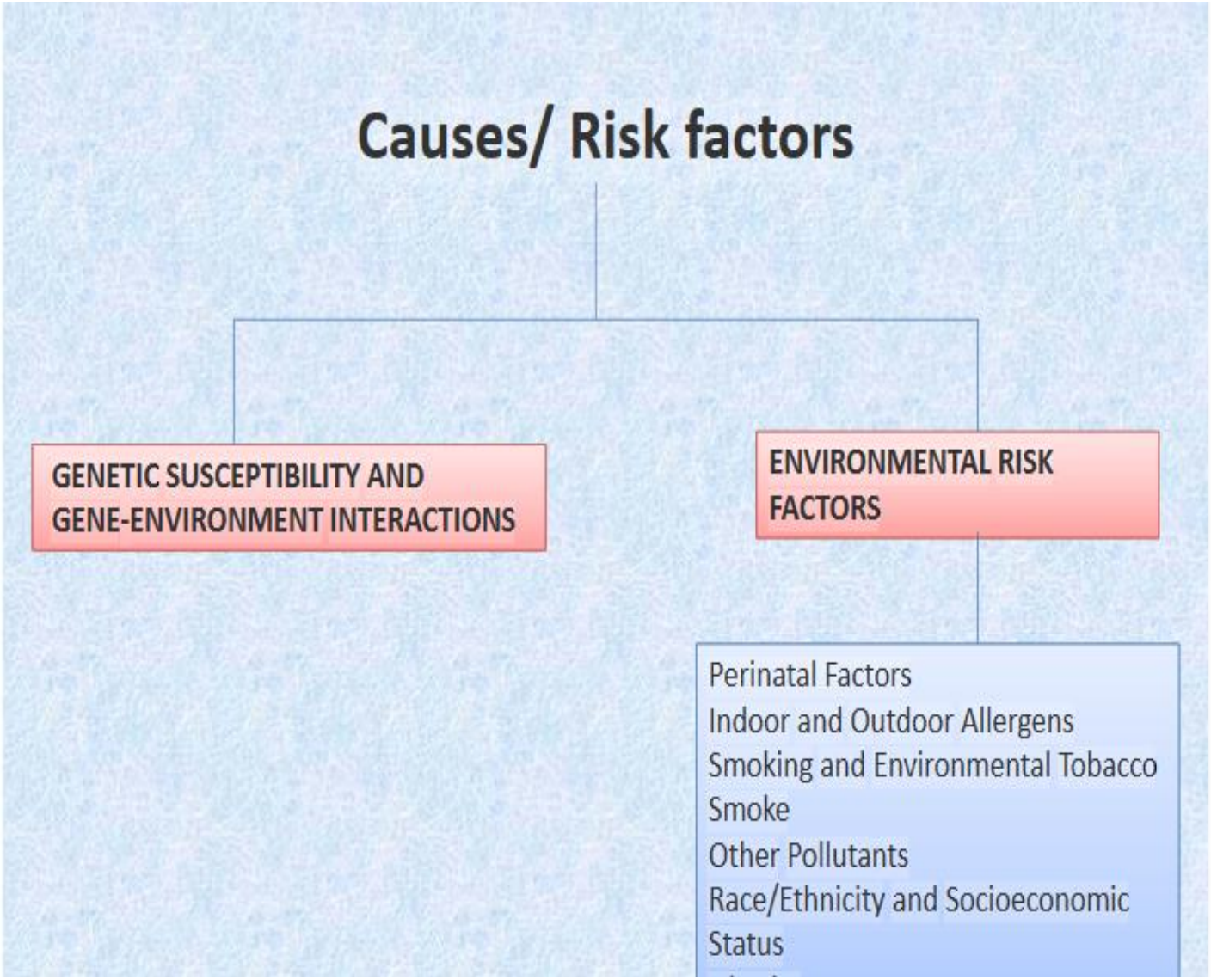
BRONCHIAL ASTHMA



Defenition -GINA

- Chronic inflammatory disorder of the airways
- Characterized by increased responsiveness of the tracheobronchial tree to a variety of stimuli
- Widespread spasmodic narrowing of the air passages which may be relieved spontaneously or on therapy.



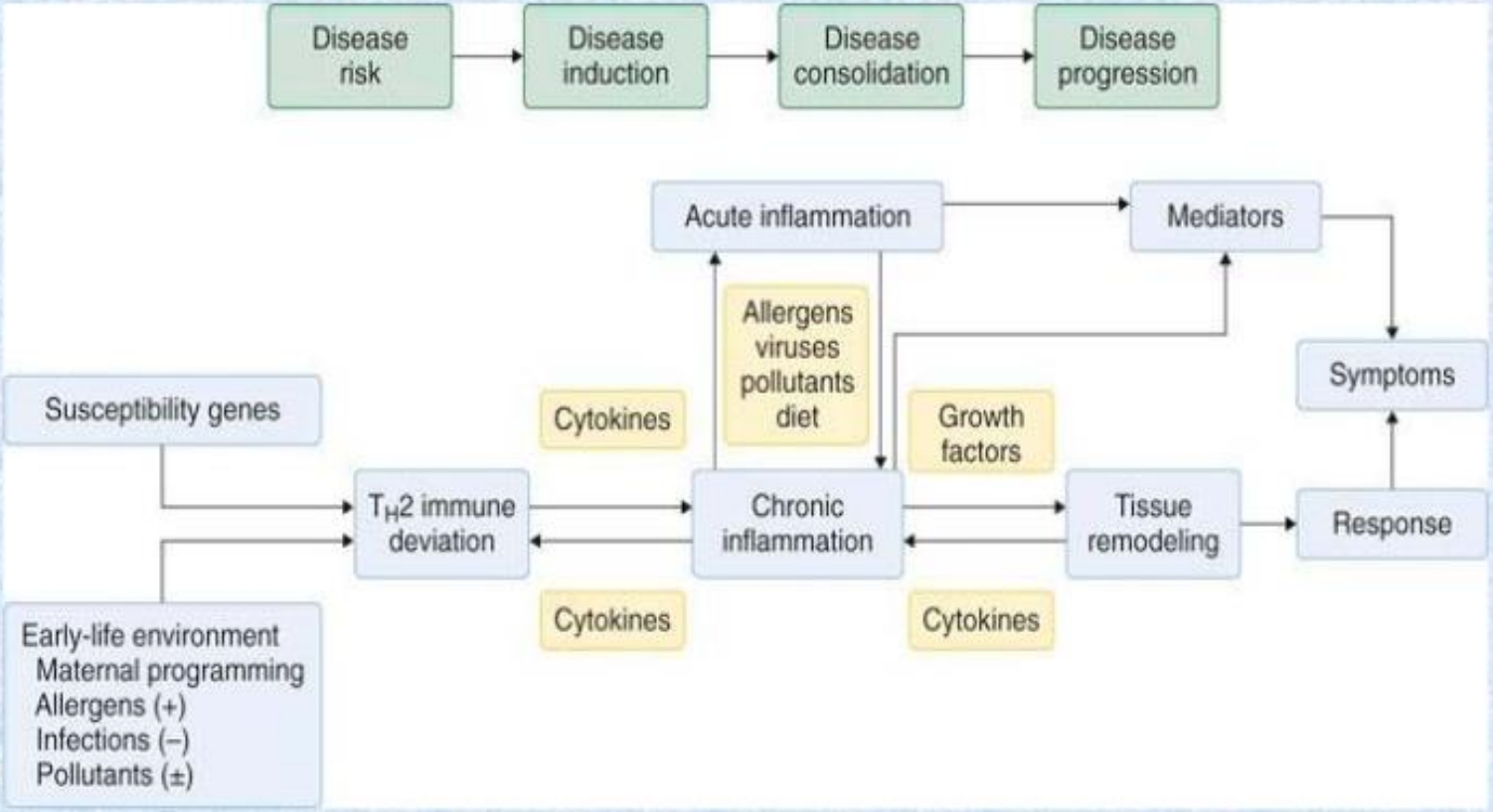
Obesity
Respiratory illness

CLASSIFICATION

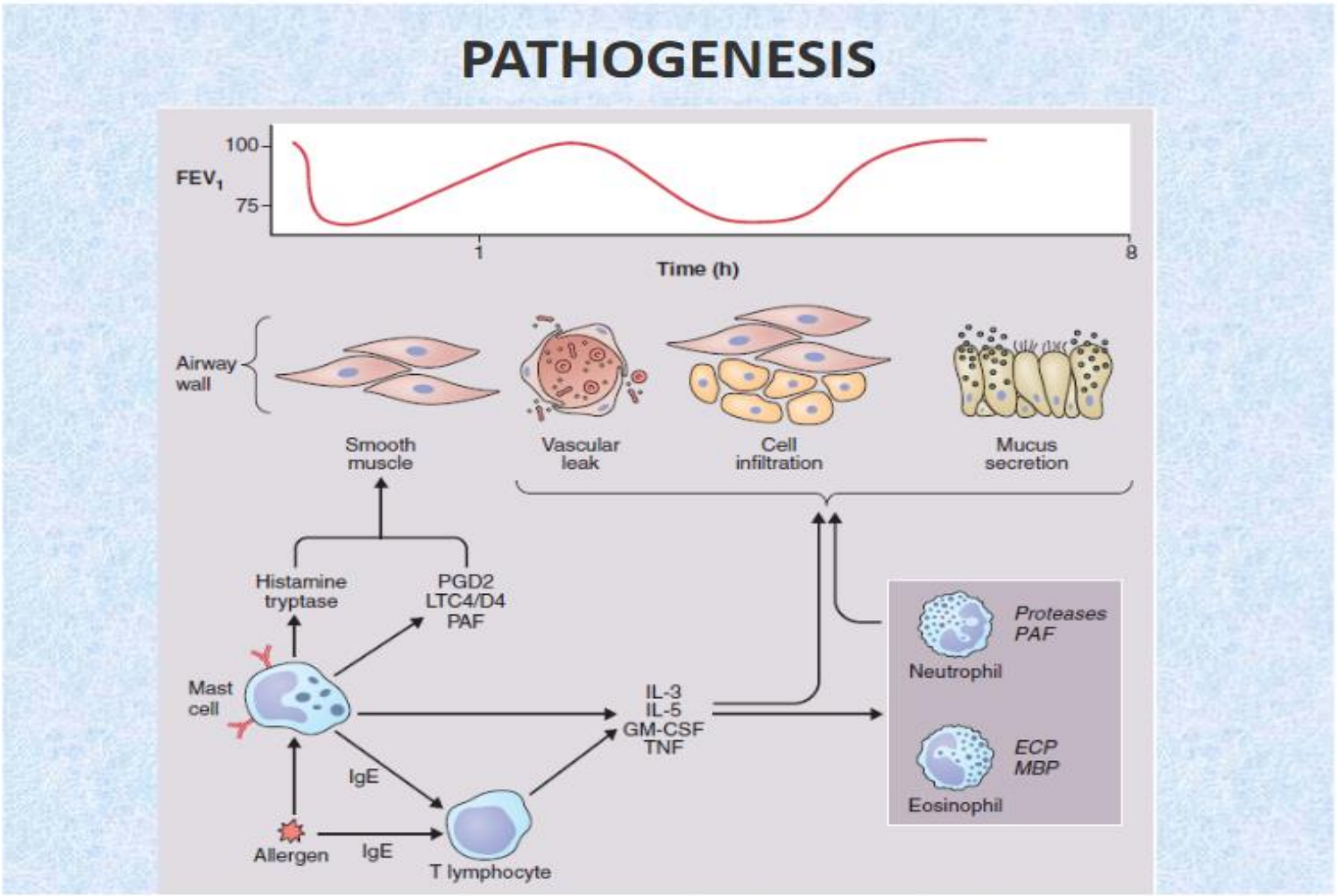
Based on the stimuli initiating bronchial asthma,broad etiologic types are described:

- Extrinsic(allergic, atopic) asthma
- Intrinsic(idiosyncratic,non-atopic) asthma
- Mixed type

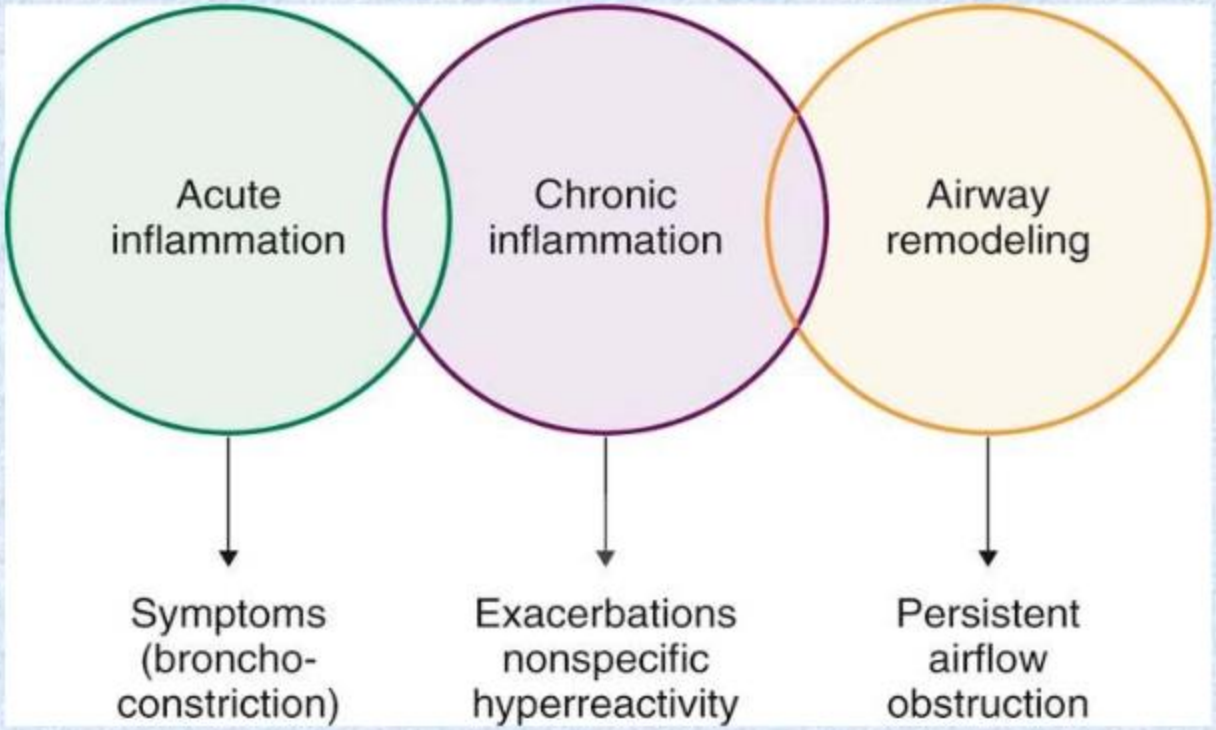
How Asthma develops.....



PATHOLOGICALLY-



ASTHMA - PATHOPHYSIOLOGY



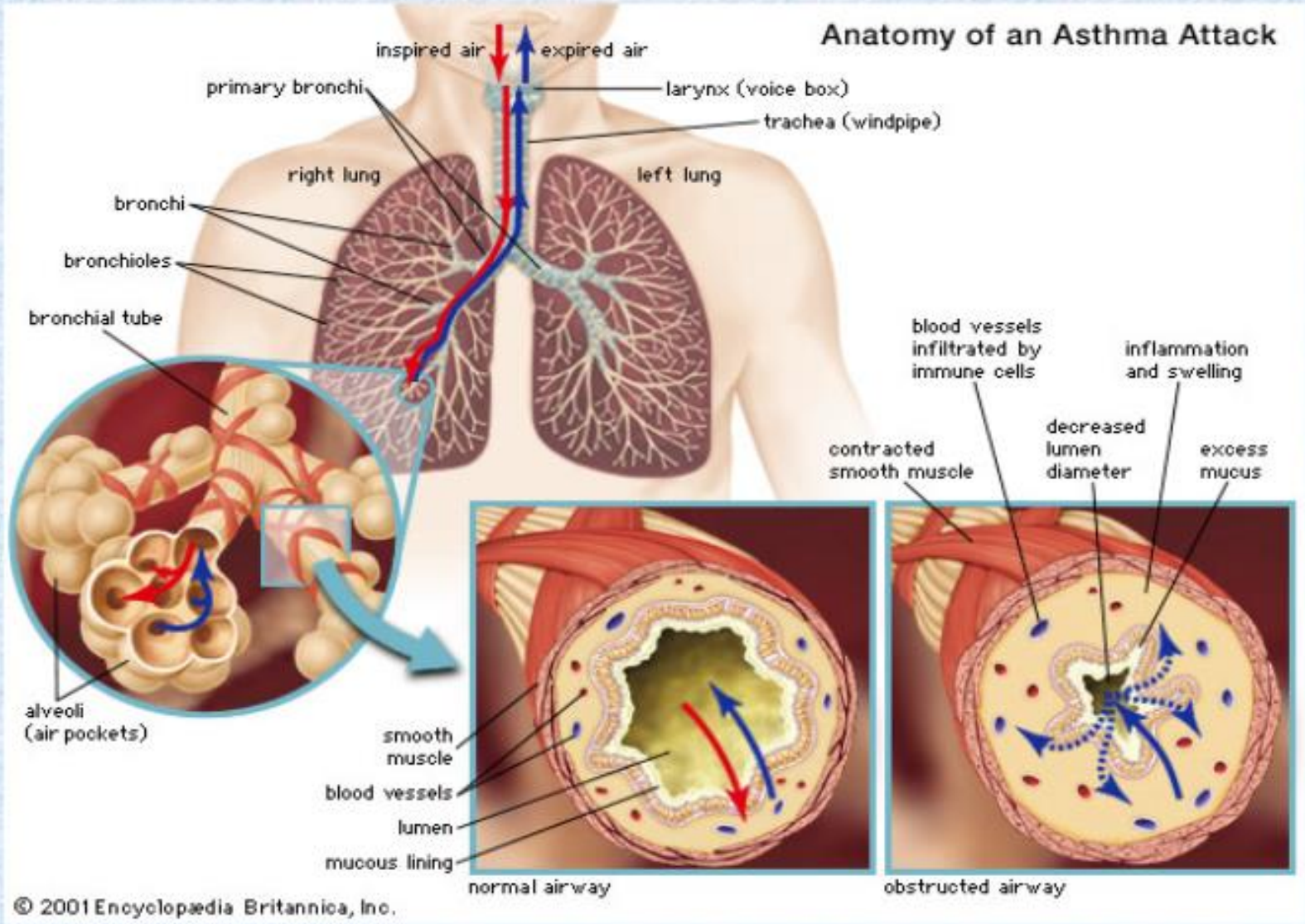
Genetic predisposition
Intrinsic vulnerability
Atopy/allergy

Inflammation underlies disease processes

Phenotype varies by individual and over time

Clinical symptoms also vary by individual and over time

PATHOLOGY


Anatomy of an Asthma Attack
inspired air
expired air
primary bronchi
larynx (voice box)
trachea (windpipe)
right lung
left lung
bronchi
bronchioles
bronchial tube
alveoli
(air pockets)
blood vessels
infiltrated by
immune cells
inflammation
and swelling
contracted
smooth muscle
decreased
lumen
diameter
excess
mucus
smooth
muscle
blood vessels
lumen
mucous lining
normal airway
obstructed airway
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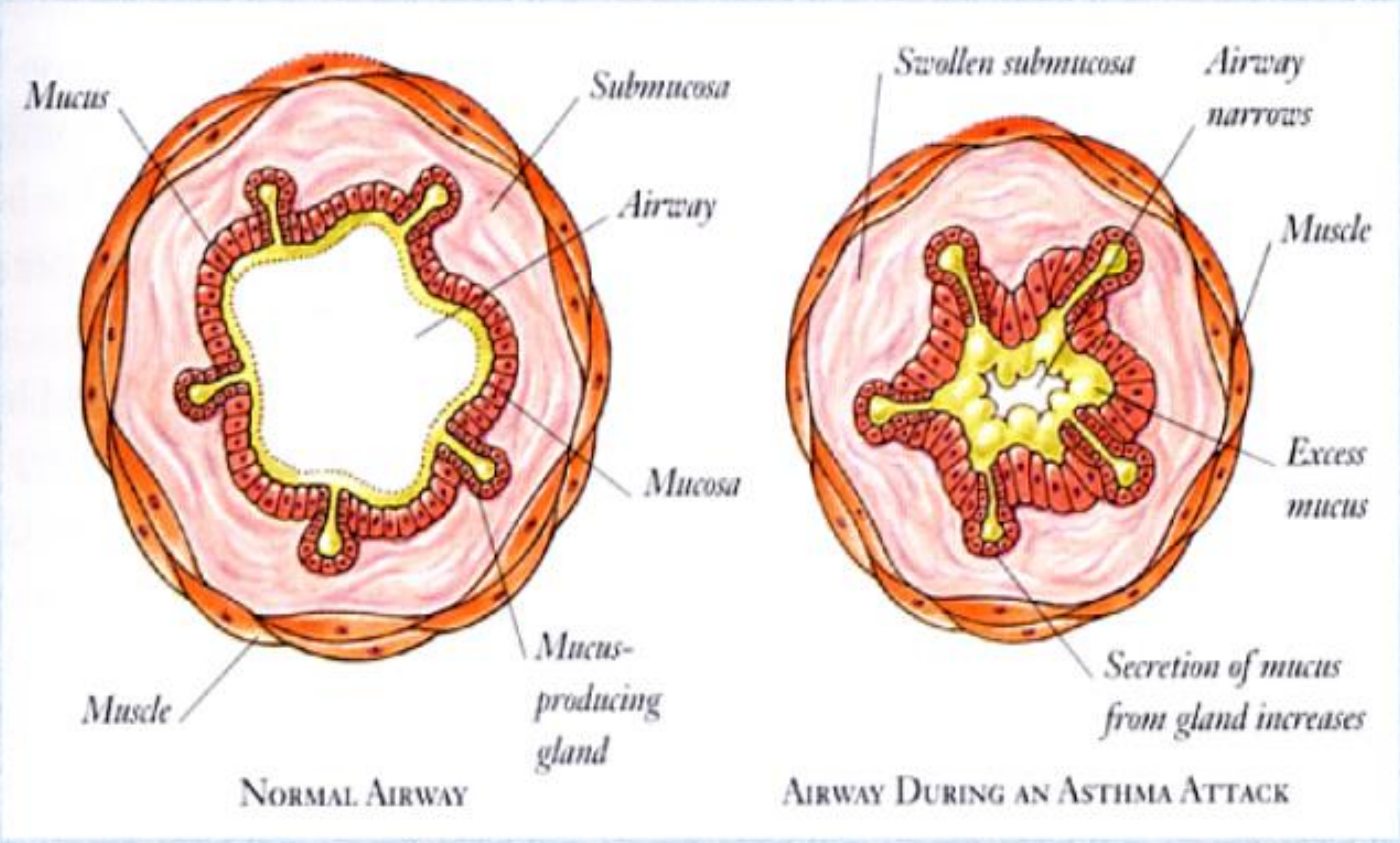
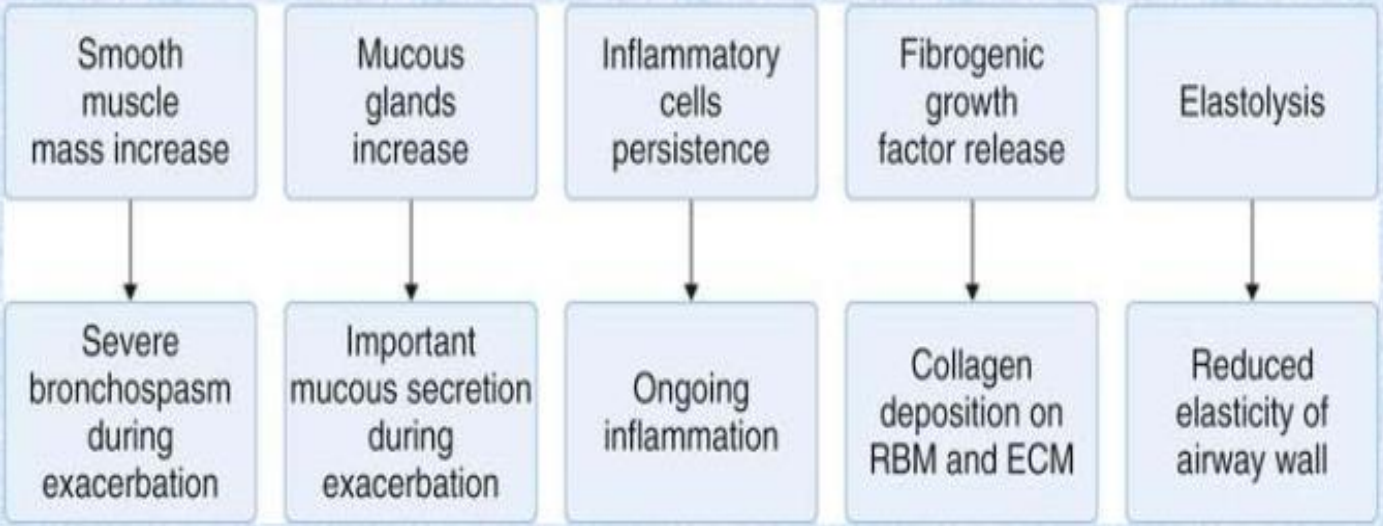
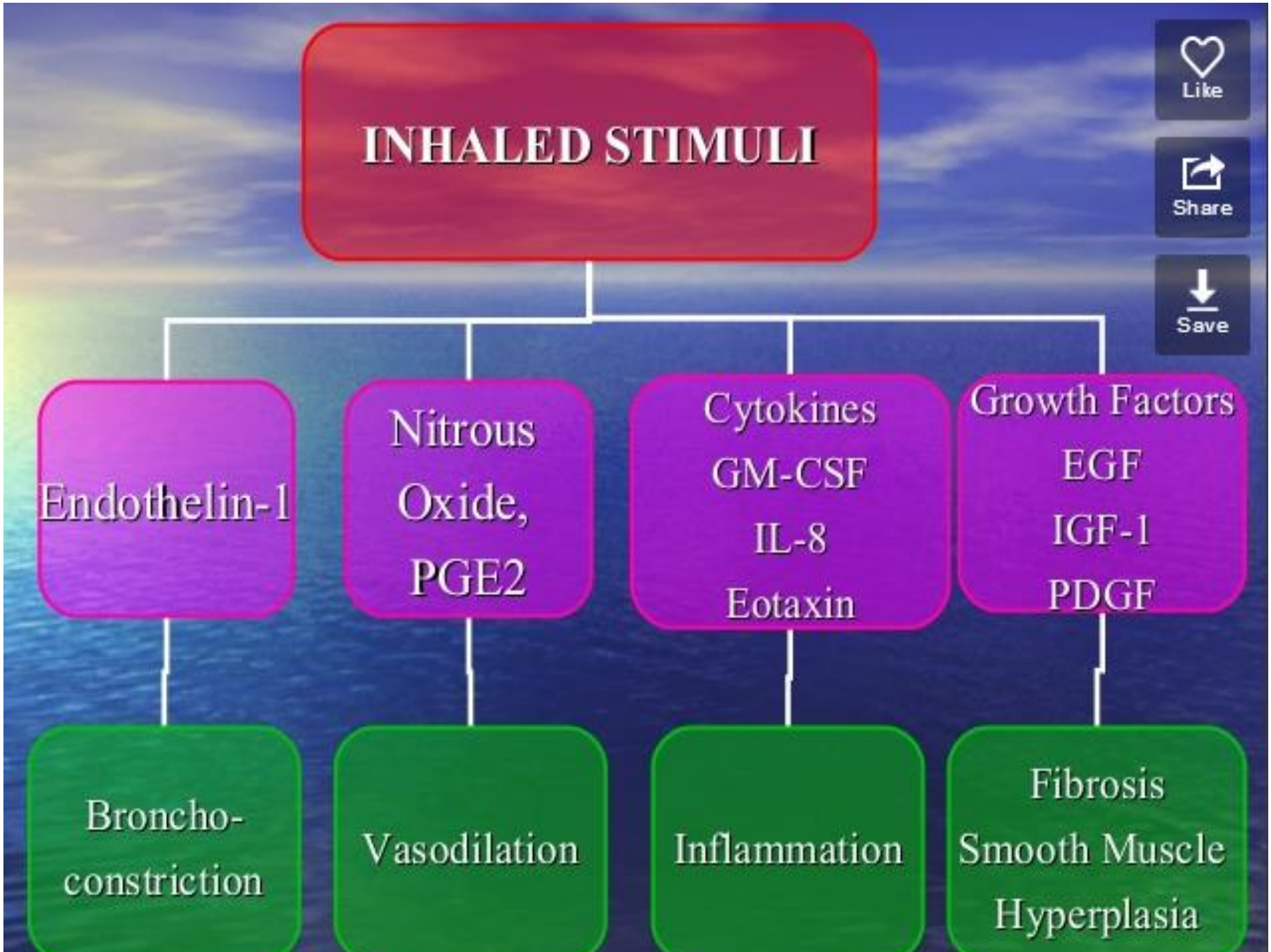
Asthma: Pathological changes



Pathology and consequences




INHALED STIMULI
Like
Share
Save
Endothelin-1
Nitrous Oxide, PGE2
Cytokines GM-CSF IL-8 Eotaxin
Growth Factors EGF IGF-1 PDGF
Broncho-constriction
Vasodilation
Inflammation
Fibrosis Smooth Muscle Hyperplasia

Asthma-Classic presentation

- Intermittent episodic, acute/subacute onset
- Breathlessness/chest tightness usually with wheeze
- Cough nocturnal or early morning.
- Diurnal and seasonal variation
- History of atopy, family history
- Polyphonic wheeze, prolonged expiration
- However, the examination can be normal.

Asthma-Types

- Chronic persistent
  - Intermittent
  - Mild persistent
  - Moderate persistent
  - Severe persistent
- Acute severe asthma

Stage 1-
Patient with intermittent asthma

Intermittent symptoms less than once per week,

Night symptoms less than 2 times per month

Normalcy between the episodes

FEV1 and PEF > 80%

Stage 2-*Mild persistent asthma*

Symptoms more than once per week, but less than once per day,

night symptoms more than 2 times a month.

FEV1 and PEF > 80%

Stage 3-*Moderate persistent asthma*

Symptoms daily,

Affects activity

Night symptoms more than once per week

FEV1 and PEF 60-80%

Stage 4- *Severe persistent asthma*

Continuous symptoms

Frequent exacerbations

Frequent night time attacks

Physical activity limited

FEV1, PEF < 60%

ACUTE SEVERE ASTHMA

- Severe breathlessness
- Heart rate > 110 /min
- Respiratory rate > 25/min
- Pulsus paradoxus
- PEFR < 50%

DIAGNOSIS OF BRONCHIAL ASTHMA

Compatible clinical history + either/ or

Spirometry

- Spirometry measurements (FEV_1, FVC, FEV_1/FVC)

1. More than 12%or more than 200ml improvement in FEV1/PFR

15 min following administration of 200mcg of inhaled salbutamol

Or following 2-4 week trial with oral corticosteroids- 30 to 40mg wysolone per day

INVESTIGATIONS

1. Chest X-ray
2. PFT- Obstructive lung disease, FEV1 following 2 puffs of beta agonists shows >= 12% increase
3. PEFR- serial recording may show overnight fall
4. Blood and sputum – eosinophilia
5. Serum IgE- increased in atopic asthma

MANAGEMENT

Principles of treatment:

- Avoidance of allergen
- Avoidance of precipitating factor
- Hyposensitization
- Drugs

CLASSIFICATION OF DRUGS:

- Bronchodilators-ß2 sympathomimetics : Salbutamol, Terbutaline,Salmetrol
- Methylxanthines : Theophylline, Aminophylline
- Anticholinergics : Ipratropium bromide,tiotropium bromide
- Leukotriene antagonists : Montelukast,

- Anti-inflammatory agents- Mast cell stabilisers : sodium cromoglycate, Nedocromil

- Corticosteroids: *Inhalational* -Beclomethasone, fluticasone , budesonide

Systemic -Hydrocortisone, Prednisolone

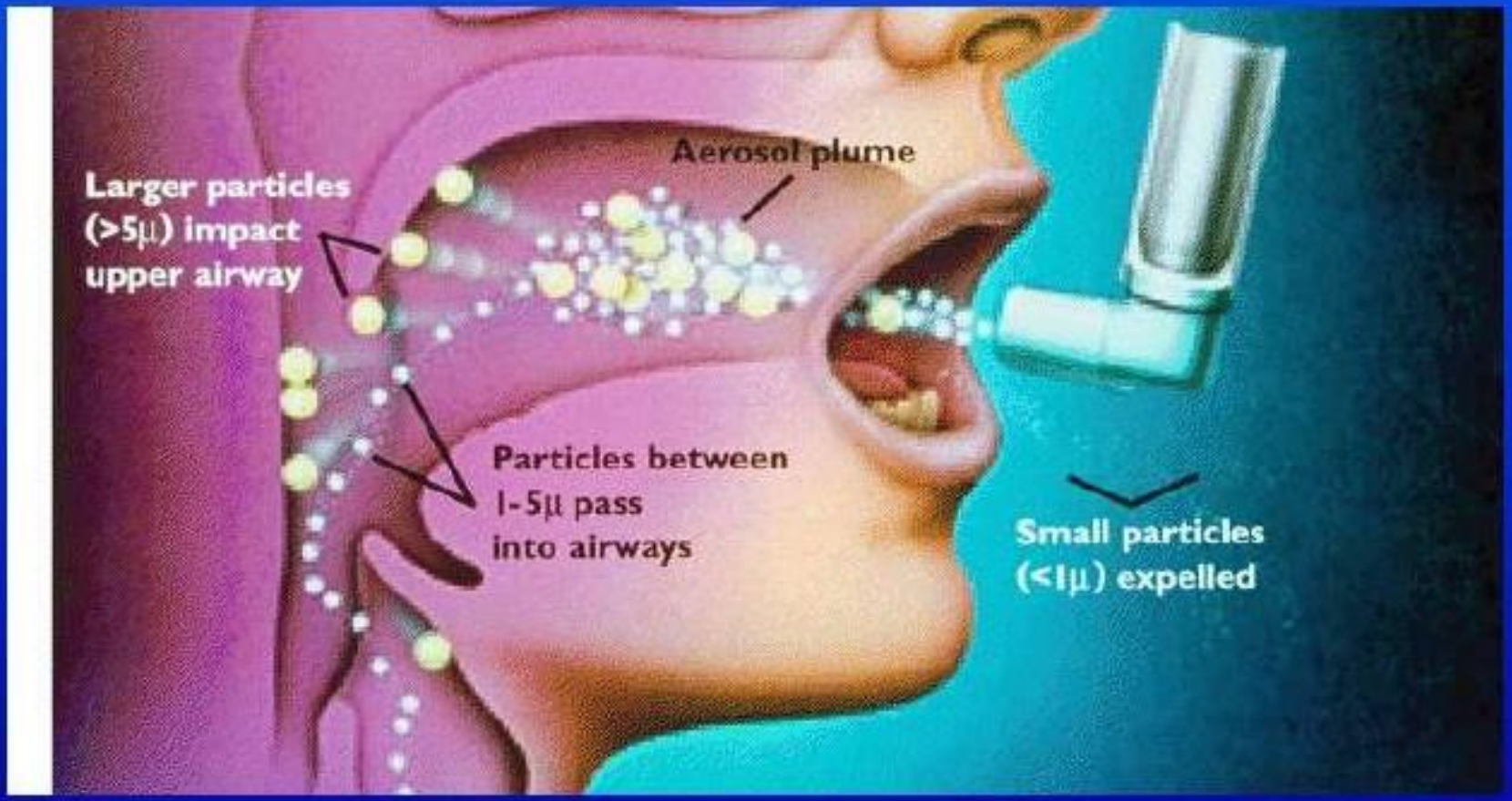
- Anti-IgE antibody : Omalizumab

- Lipo oxygenase inhibitor- Zileuton

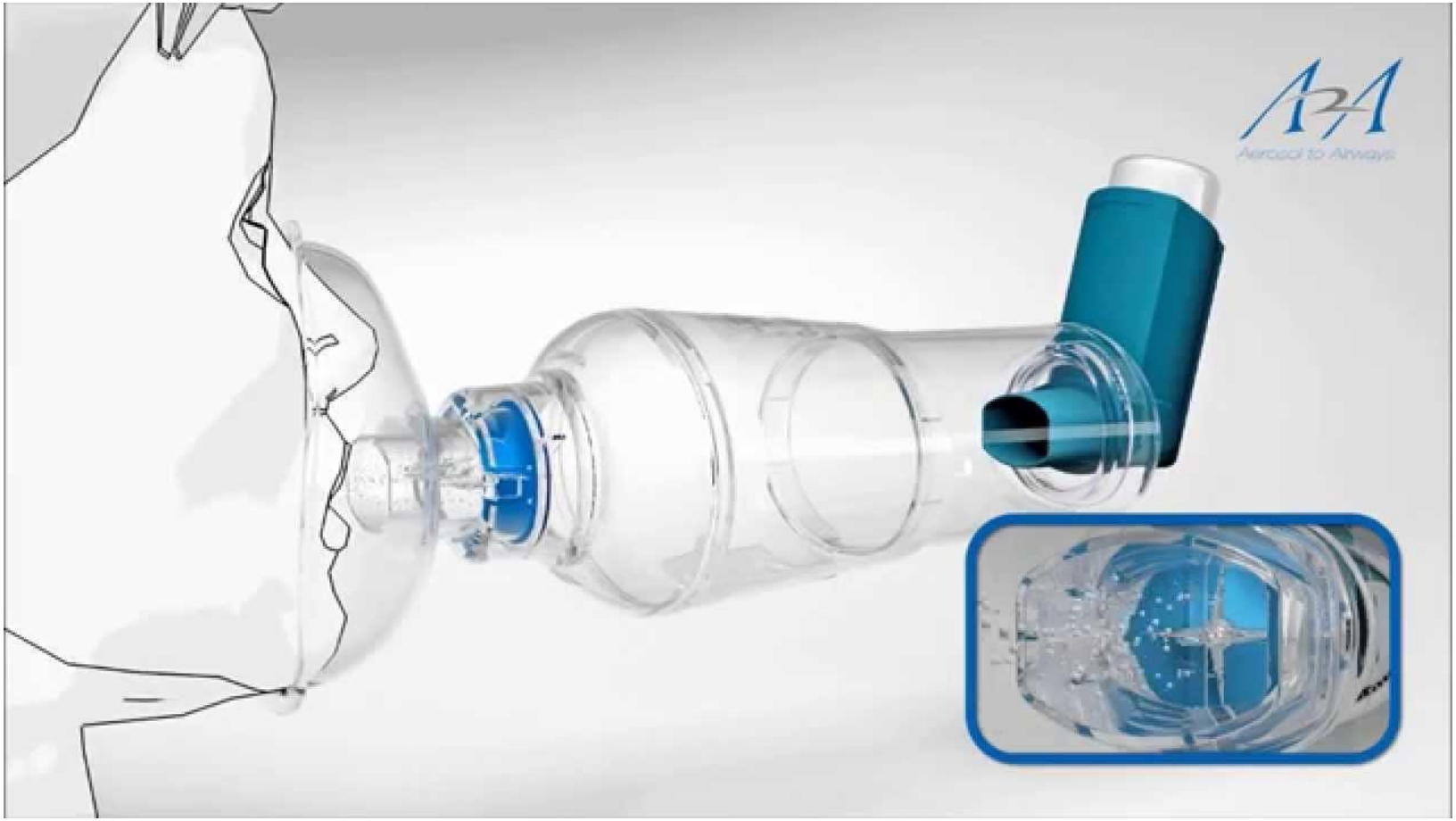
Modes of drug delivery

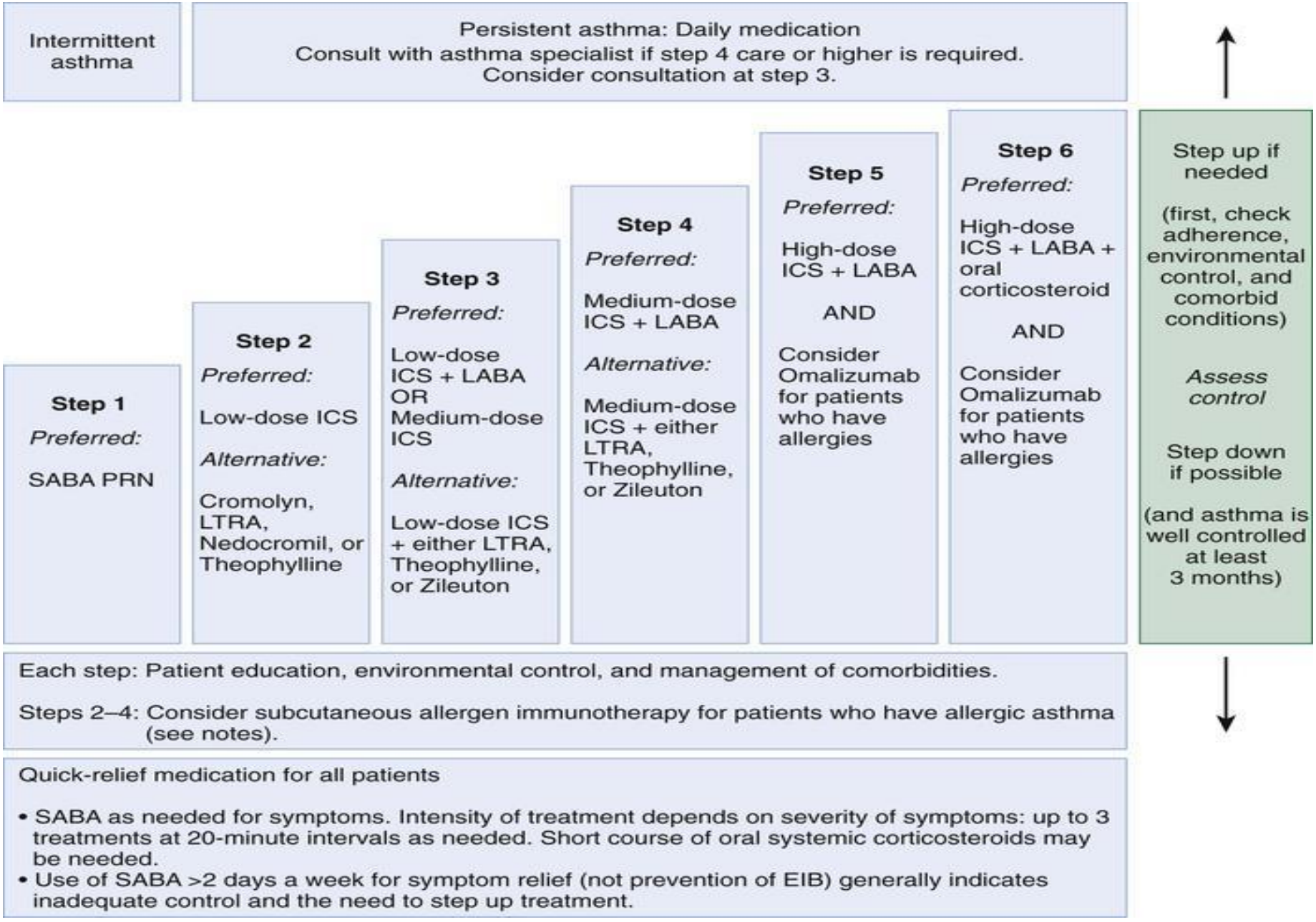
- MDI
- Dry powder Inhalers
- Nebulization
- Spacer

How MDI Technology Works



A spacer device enhances delivery by decreasing the velocity of the particles and reducing the number of l arge particles, allowing smaller particles of drug to be inhaled




Intermittent asthma
Persistent asthma: Daily medication
Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.
Step 1
Preferred:
SABA PRN
Step 2
Preferred:
Low-dose ICS
Alternative:
Cromolyn, LTRA, Nedocromil, or Theophylline
Step 3
Preferred:
Low-dose ICS + LABA OR Medium-dose ICS
Alternative:
Low-dose ICS + either LTRA, Theophylline, or Zileuton
Step 4
Preferred:
Medium-dose ICS + LABA
Alternative:
Medium-dose ICS + either LTRA, Theophylline, or Zileuton
Step 5
Preferred:
High-dose ICS + LABA
AND
Consider Omalizumab for patients who have allergies
Step 6
Preferred:
High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies
Step up if needed
(first, check adherence, environmental control, and comorbid conditions)
Assess control
Step down if possible
(and asthma is well controlled at least 3 months)
Each step: Patient education, environmental control, and management of comorbidities.
Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).
Quick-relief medication for all patients
• SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
• Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

Prevention of exacerbations

- Vaccination

EOSINOPHILS

- 1 to 6% of circulating white cells
- Show phagocytic activity
- Prominent orange granules – contain peroxidase capable of generating reactive oxygen species and proteins involved in intracellular killing of protozoa and helminths
- Phagocytose immune complexes
- Modulate type 1 hypersensitivity reaction

PULMONARY EOSINOPHILIA

Cough with wheeze

Lesions in lung producing chest radiographic abnormality

-No lesions

-Perihilar lesions

-Peripheral reticulo nodular lesions- suggesting interstitial affection

-May coalecse to form large areas of consolidation

- Central bronchiectasis

- Atelectasis

Blood eosinophilia

Absolute eosinophil count > 1500

Excellent response to glucocortico steroids

CLASSIFICATION

1. Extrinsic (cause known)

2. Intrinsic (Cause unknown)

EXTRINSIC CLASSIFICATION

CAUSE KNOWN

a. Helminths – Ascaris, Toxacara, Filaria

b. Drugs – Nitrofurantoin, PAS, Sulphasalazine, Imipramine

c. Fungi – Aspergillus fumigatus

INTRINSIC CLASSIFICATION

CAUSE UNKNOWN

a. Acute and chronic eosinophilic pneumonia

b. Churg – strauss Syndrome

c. Hyper-eosinophilic Syndromes

d. Polyarteritis nodosa

LOEFFLER'S SYNDROME

- Loeffler in 1932
- Passage of parasitic larvae through lung
- Allergic reaction

- Most common –
- Ascaris lumbricoids, Paragonimus Westermani and Ankiylostoma Braziliense

- “IgE mediated type 1 reaction
- Asthma” + Urticaria

- IgM – antigen complexes in lung resulting in pulmonary infiltrate – Type III reaction

PATHOLOGY

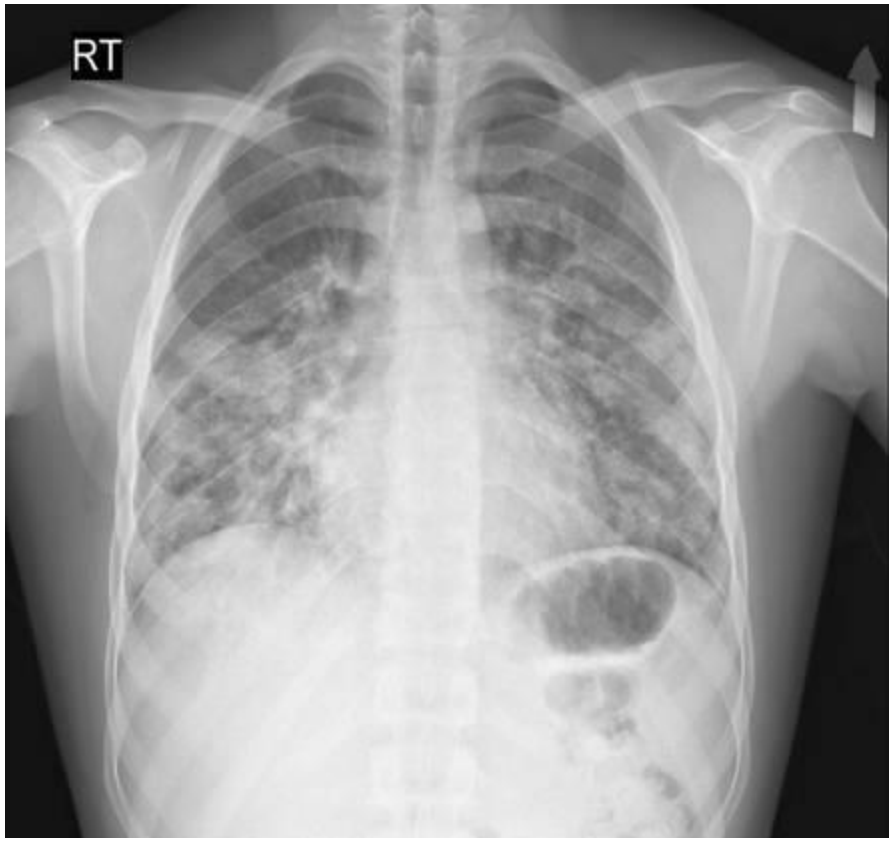
- Dilated bronchi and bronchioles filled with exudate containing eosinophils and neutrophils.
-
- Portion of nematode larvae may be present in some bronchi.
- Infiltration of pulmonary interstitium with eosinophils

CLINICAL FEATURES

- Asymptomatic
- Mild Fever, Cough, Rhinitis, Anorexia
- Sometimes wheezing and dyspnoea
- Urticaria +

INVESTIGATIONS

- **Sputum** – Eosinophils ± Larvae
- **X- Ray chest –**



- Transient
- Disappear in

10 – 12 days

(always within 1 month)

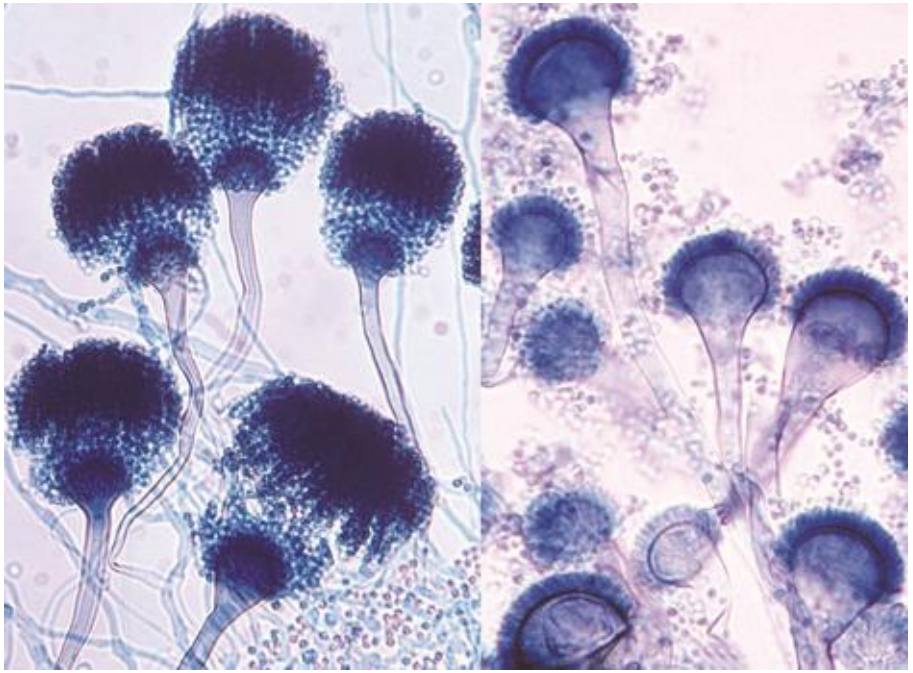
- Blood – Mild to moderate eosinophilia – AEC upto 5,000
- Stool for Ascaris ova (Development of Larvae to adult worm takes 6-8 weeks)
- Re-examine stool after 2 months

TREATMENT

- Spontaneous resolution common
- Short course steroids if acute symptoms
- De-worming when adult worms have developed (6 to 8 weeks)

ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS
(ASTHMATIC PULMONARY EOSINOPHILIA)

•**Highly aerobic in nature**
•They have **septate hyphae that form dichotomous branches (**lateral and/or apical branches the same width as the parent hyphae from



- World wide – commonest cause of pulmonary eosinophilia
- Aetiology – Type 1 Hypersensitivity reaction to Aspergillus fumigatus
- Positive skin prick test to Aspergillus antigen
- Steroids with Itraconazole or voriconazole

FEATURES

- Cough with wheeze

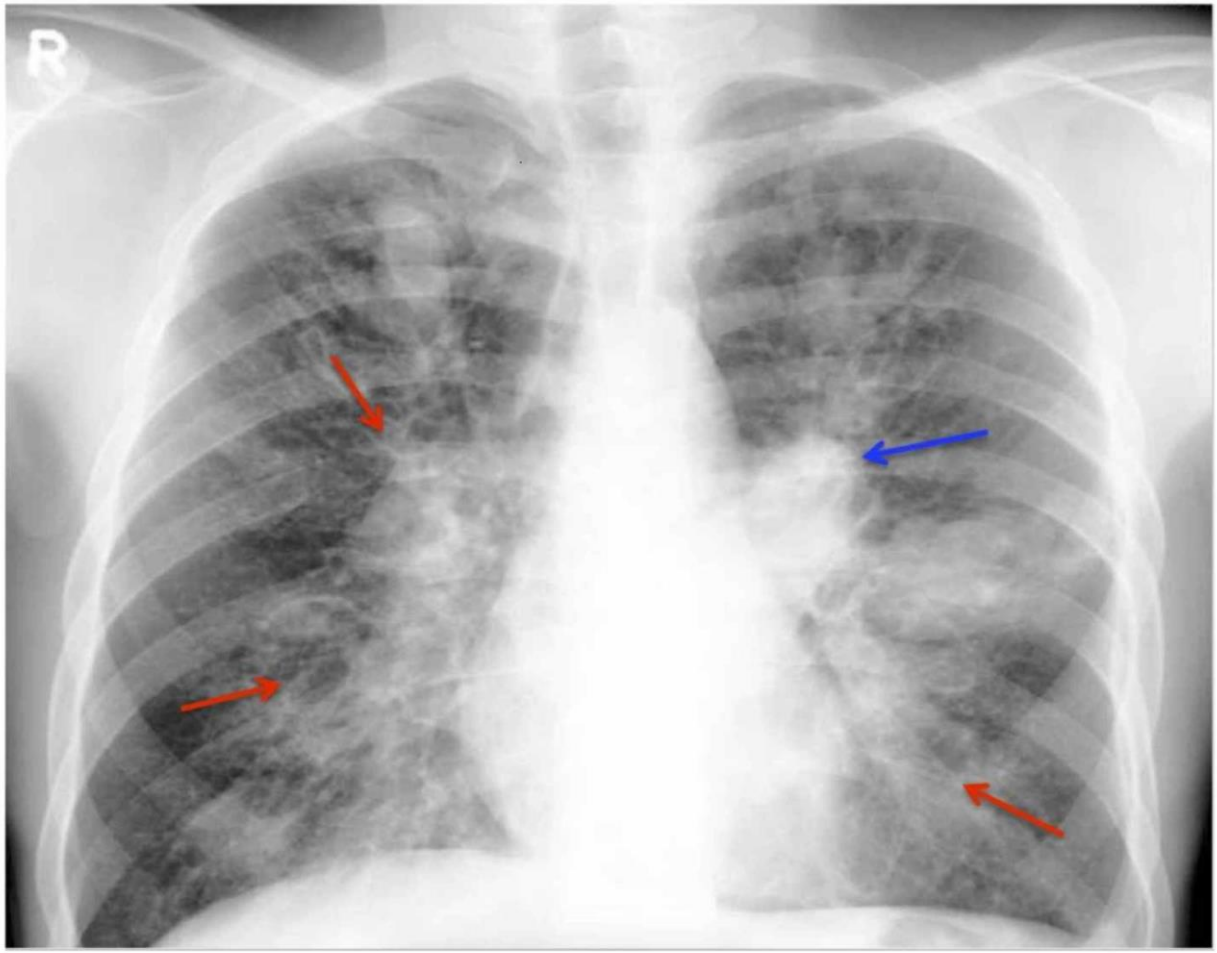
- Sputum – contains bronchial casts with eosinophils, desquamated epithelium and hyphae

- Serum IgE elevated – more during acute episodes
  IgM antibodies to aspergillus also may be ↑

- Recurrent episodes (lasting for weeks) → proximal bronchiectasis - confirm by HRCT

- Recurrent shadows on X- Ray chest

- Worsening in winter (aspergillus spore more abundant in air)



TROPICAL PULMONARY EOSINOPHILIA

TROPICAL PULMONARY EOSINOPHILIA

- Common in South Asia (Including India), South America, Africa

- Hypersensitivity reaction to filarial antigens – microfilaria trapped in Pulmonary capillaries and destroyed by allergic inflammation

- Acute presentation – Eosinophilic Pneumonia

- Chronic - Eosinophils + Histiocytes + Lymphocytes infiltration– organise to form nodular pattern

CLINICAL FEATURES

- 80% affected male
- Cough with sputum, Wheezing, Chest pain, Weight loss
- Symptoms for weeks / months, remission and relapse

INVESTIGATIONS

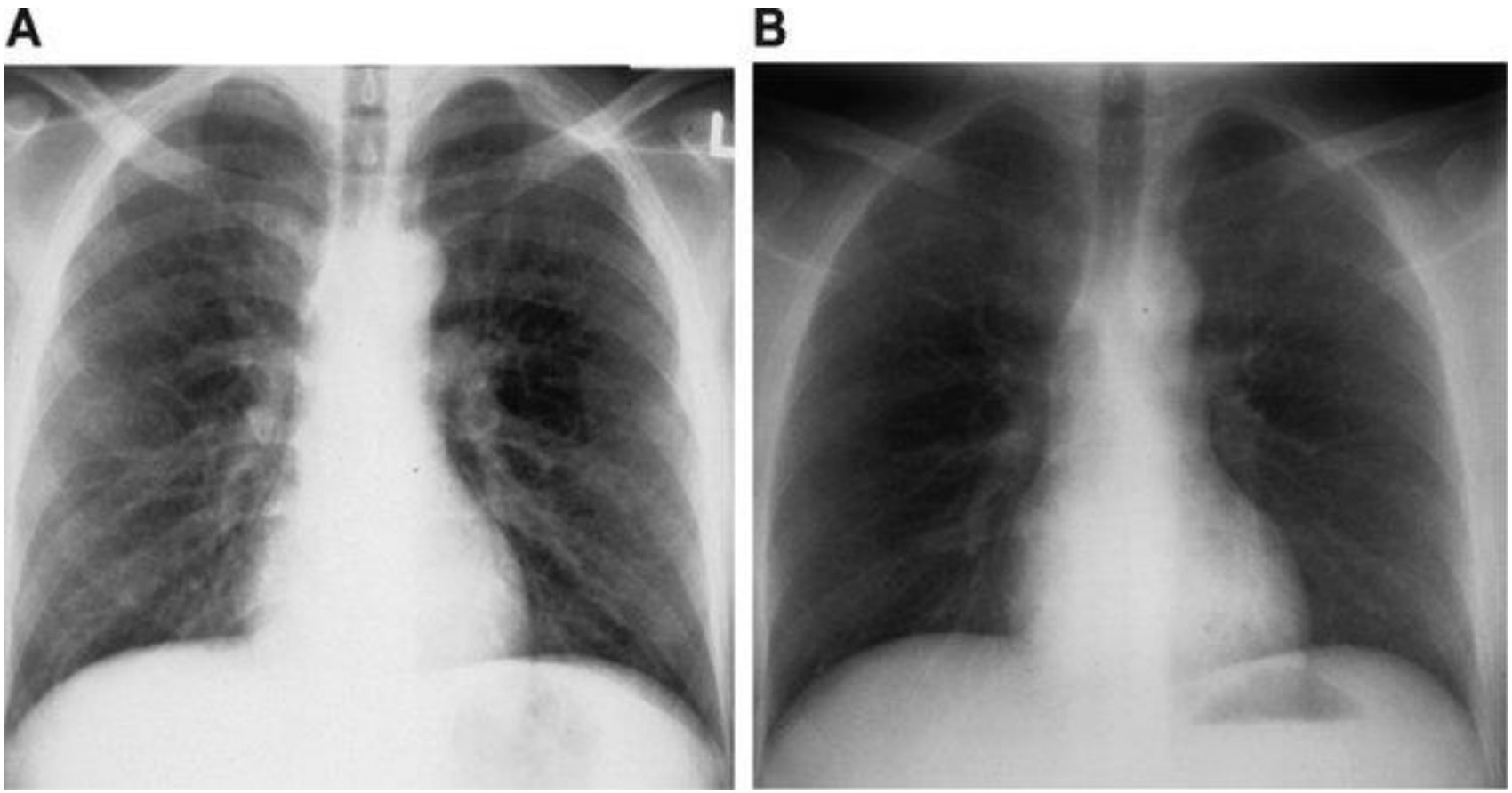
- Blood–Eosinophils can go upto 60,000

- Sputum and bronchoalveolar lavage fluid – eosinophils ↑

- IgE concentration–proportional to severity of eosinophilia - 3 fold high in relapsing disease compared to primary disease

X- RAY CHEST

- Occasionally – cavitation / pleural effusion



PULMONARY FUNCTION TEST

- Obstructive pattern early stage

- Untreated longstanding cases – restrictive pattern (Pulmonary Fibrosis)

TREATMENT

- DEC – 6 to 8 mg / Kg / day in 3 divided doses for 10 to 14 days – or even longer (upto 4 weeks)
- PFT show improvement if treatment started early
- Delay in starting treatment – irreversible pulmonary fibrosis

HYPEREOSINOPHILIC SYNDROME

HYPEREOSINOPHILIC SYNDROME

- Peripheral blood eosinophilia
- Eosinophilic infiltration of many organs
- Aetiology unknown

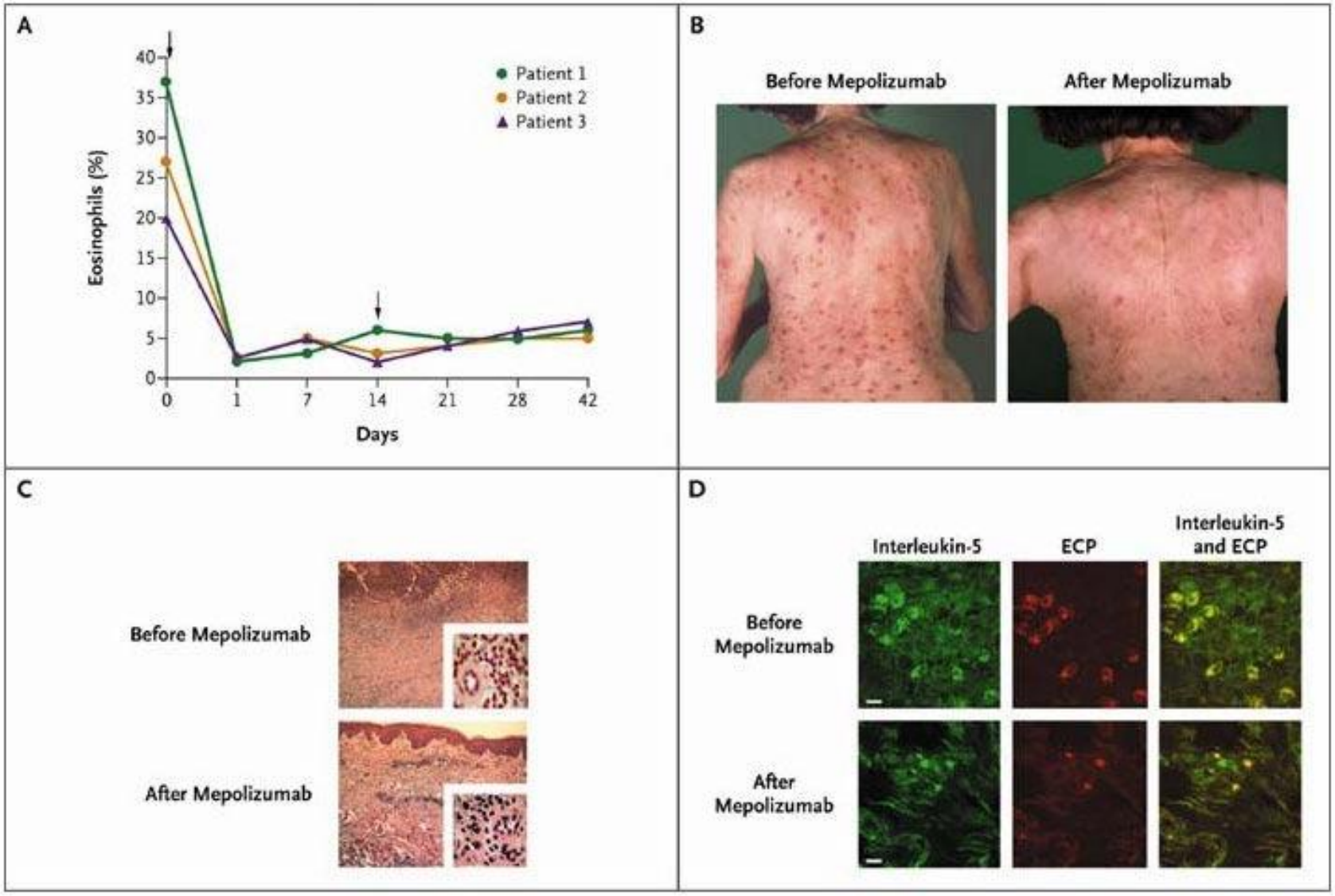
CRITERIA

- Persistent eosinophilia AEC of >1500 for > 6 months
- Signs and symptoms of organ involvement
- No evidence of other causes for eosinophilia like allergic, parasitic, vasculitic or neoplastic

CLINICAL FEATURES

- Onset 3rd / 4th decade
- Males > Female
- Features of eosinophilic pneumonia with Cough +
- CVS involvement
  - Endocardial fibrosis, Restrictive Cardiomyopathy, Valvular damage, Mural thrombosis

- Arterial and venous thrombosis described
- Splinted hemorrhage, infarction in organs
  (Kidney, Spleen, Cerebrum, Retina)
- Eosinophil infiltration of Kidneys, Skin, Joints, GIT, Muscles may be associated


A
Eosinophils (%)
40
35
30
25
20
15
10
5
0
0
1
7
14
21
28
42
Days
Patient 1
Patient 2
Patient 3
B
Before Mepolizumab
After Mepolizumab
C
Before Mepolizumab
After Mepolizumab
D
Interleukin-5
ECP
Interleukin-5 and ECP
Before Mepolizumab
After Mepolizumab

INVESTIGATION

- Peripheral eosinophilia may be profound
- Increased Eosinophils in Bone Marrow
- Bronchoalveolar lavage - ↑ Eosinophils

TREATMENT

Glucocorticoids

ACUTE EOSINOPHILIC PNEUMONIA

DIAGNOSTIC CRITERIA

- Acute febrile illness < 5 days duration
- Hypoxemic Respiratory Failure
- Diffuse alveolar / mixed alveolar and interstitial radiographic infiltrates
- Bronchoalveolar lavage > 25% eosinophils
- Absence of fungal / parasitic / other infections

CLINICAL FEATURES

- Myalgia
- Pleurisy common with mild Pleural effusion
- May need ventillatory support
- Diffuse inspiratory crepts usually without wheeze
- Prompt and complete response to steroids
- No relapse after discontinuing steroid

INVESTIGATIONS

- X- Ray chest -Infiltration dominantly in periphery
  - (Unlike chronic eosinophilic pneumonia)
- Peripheral blood eosinophilia usually absent
- PFT – Restrictive pattern with diffusion defect
- Lung biopsy – confirms the diagnosis of Eosinophilic Pneumonia

TREATMENT

- Glucocorticoid
- Ventillatory support if hypoxemic