2. INTERSTITIAL LUNG DISEASE

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LECTURE OUTLINE

- Definition
- Clinical presentation and evaluation
- Radiographic features
- Classification
- Treatment
- Prognosis

PULMONARY INTERSITIUM

- This is the space interposed between the air space epithelium (from the main bronchi to the alveoli, the vascular endothelium and the pleural mesothelium

- The remnant of the **splanchnopleuric mesenchymal bed** into which the airway tubes and blood vessels have grown during lung morphogenesis

- The **gas exchange unit**
  - Capillary endothelium
  - Alveolar epithelium
  - Interstitial space

COMPONENTS OF THE ALVEOLAR/INTERSTITIAL SPACE

- Fibroblasts
- Myofibroblasts
- Pericytes
- Smooth muscle cells
- Undifferentiated mesenchymal cels
- Immune cells
- Matrix
- Basement membrane
- Endothelium

DEFINITION

- Few cells in the interstitium of the normal lung (pauci-cellular)
- Injury to the basement membrane shared by epithelium and endothelium
- Increased alveolar permeability and spillage of serum contents into the alveolar space and recruitment of fibroblasts
- Collagen deposition
- Also injury to small airways → respiratory bronchioles, alveolar ducts and terminal bronchioles

PATHOGENESIS

- UNKNOWN
- Some understanding of the mechanism of injury

- Initiating injuries are likely multiple:
  - Inhaled
  - Sensitization to allergens
  - Circulatory e.g. drugs like nitrofurantoin, amiodarone,

- With continued injury, ‘repair’ process continues with additional fibro-proliferation that is unchecked.

- There is an imbalance between injury and reparative processes.

IDIOPATHIC INTERSITIAL LUNG DISEASE (ILD) EPIDEMIOLOGY

- 81 in 100,000 prevalence in men
  - Mostly due to occupational exposure in men to noxious substances
- 67 in 100, 000 in women

- 32.5 in 100,0000 incidence in men
- 26 in 100,000 in women

- 200 in 100,000 incidence in age > 75
- 30 – 40% of all ILD → IPF

- Due to increasing numbers of cytotoxic drugs, increased detection of occupational lung diseases, and increasing life expectancy as well as better imaging and diagnostic testing e.g. **high resolution CT scan**, the incidence of these diseases is expected to rise.

CLINICAL CLASSIFICATION - ETIOLOGICAL

- Connective tissue diseases → RA, SLE, Scleroderma
- Drug induced → Nitrofurantoin, Amiodarone, Cytotoxic agents, Cocaine
- Radiation
- Primary unclassified → Sarcoidosis
- Occupational → Organic dusts - hypersensitivity pneumonitis; inorganic dusts - silicosis
- Idiopathic disorders → IPF, NSIF

EVALUATION OF ILD

- **Extensive history**
  - Longstanding cough (often)
  - Dyspnea → progressive
  - Weight loss

- Age, gender, underlying comorbidities, drugs, smoking, occupational history, hobbies, pets, Family history
  - **Idiopathic pulmonary fibrosis (IPF)** is a disease of the aged (> 60 years)
  - **Lymphangioleiomyomatosis (LAM)** → young females in their reproductive age are at a higher risk
  - **Respiratory bronchiolitis, Desquamative Interstitial Pneumonitis (DIP)** → largely diseases of smokers

- **Physical examination**
  - Wasting
  - Fever
  - Clubbing
  - Tachypnoea
  - Crackles
  - Cyanosis
  - Pulmonary HN and cor pulmonale

LABORATORY INVESTIGATIONS

- Extensive: Depends on presentation and likely etiology

VIGNETTE

- JKT is an **80 year old** male **diabetic and hypertensive** for the last 24 years maintained on Mixtard 20/10, Metformin 850 mg 8 hourly and Losartan 50 mg daily.

- He had presented 4 months ago with a history of cough and progressive dyspnea for **3 years**

- Cough brought on exertion, mostly dry, occasionally productive of clear, mucoid sputum, no hemoptysis

- He’d experienced progressive decline in exercise tolerance

CONT.

- He reported profuse night sweats often around 2:00 to 3:00am
- He however had not lost weight and had normal appetite.
- Lately he had been experiencing erratic glucose control and had therefore had his insulin dose increased.
- On CXR →
  - Peripheral, lower zone reticular opacification; that are symmetric, generalized & intersitital (opacification is in the form of lines) → extensive fibrosis
  - Honey comb pattern & small lungs
  - Prominent hilum (enlarged pulmonary vessels → pulmonary HTN)

CONT

- The CXR was reported as a chronic interstitial pneumonitis, pulmonary TB should be excluded
- An echocardiogram done previously showed normal biventricular function
- Renal function was normal
- Sputum collected was muco-salivary and negative for AFB
- The ESR was **24 mm/hr**

ON EXAMINATION

- O/E, he was comfortable at rest
- The GE was notable for **grade 3 finger clubbing**
- $SP0_2$ was 97% at rest but dropped to 92 after climbing one flight of stairs or + 20 m on the flat.
- Chest examination was notable for **reduced lung expansion** and fine end inspiratory bi-basal crackles.

INVESTIGATIONS

- Lung function tests
  - Spirometry
    - Preserved FEV_1
      - **FEV_1:FVC ratio is usually either hyper-normal or preserved in Interstitial Lung disease**
- High resolution CT scan (HRCT)
  - Confirms → symmetric, honey comb fibrosis
  - Traction bronchiectasis – dilated airways in the peripheral 2/3 of the lung fields
  - Relative sparing of apices
- Lung biopsy
  - Interlobular septal thickening
  - Traction bronchiectasis and bronchiolectasis
  - Fibroblastic foci
  - Temporal and spatial heterogeneity

FURTHER INFORMATION

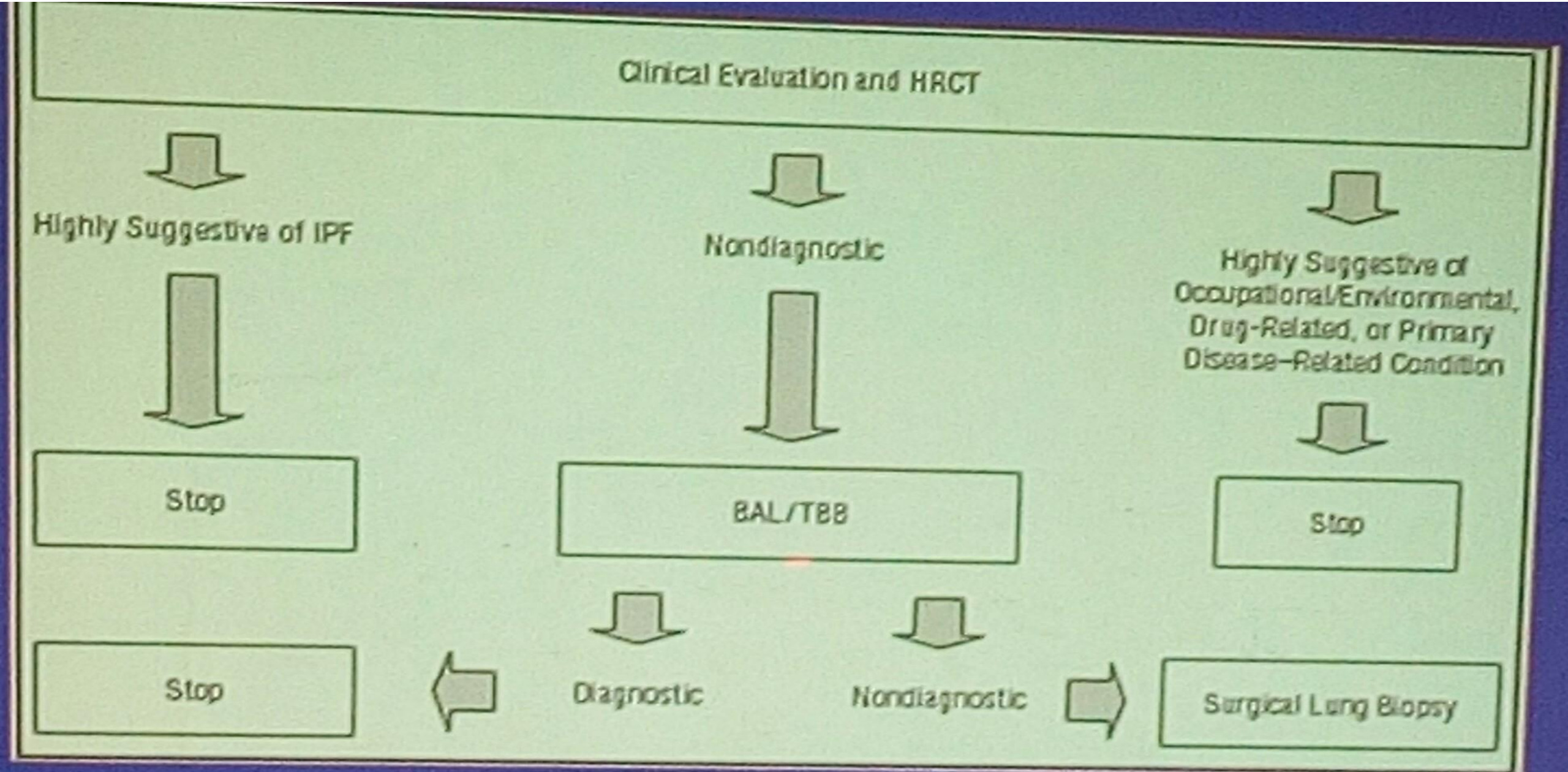
- Risk factors
  - Drug exposure
  - Occupational exposure
  - Systemic disease
  - Smoking history

IDIOPATHIC INTERSITIAL PNEUMONIA CLASSIFICATION: ATS/ERS 2000

- Idiopathic interstitial pneumonias (IIPs)
  - Idiopathic Pulmonary Fibrosis (IPF – UIP)

  - IIP other than IPF
    - Desquamative Interstitial Pneumonia (DIP)
    - Respiratory bronchiolitis interstitial lung disease (RB – ILD)
    - Acute Interstitial Pneumonia (AIP)
    - Cryptogenic organizing pneumonia (COP – OP)
    - Non-specific Interstitial pneumonia (NSIP)
    - Lymphoid Interstitial Pneumonia (LIP)
      - Associated with HIV

DIAGNOSTIC APPROACH TO THE PATIENT WITH SUSPECTED IIP



TREATMENT

	THERAPY	PROGNOSIS
IPF-UIP	CORTICOSTEROIDS, AZATHIOPRINE, NAC, LUNG TRANSPLANTATION	Median survival 2.5 – 3.5 years
NSIP	CORTICOSTEROIDS, AZATHIPRINE	Recovery, stable disease, release
RB-ILD & DIP	SMOKING CESSATION CURATIVE	Good
AIP	RESPIRATORY SUPPORT, CORTICOSTEROIDS	50% mortality

ASTHMA

BY: DR. MECHA

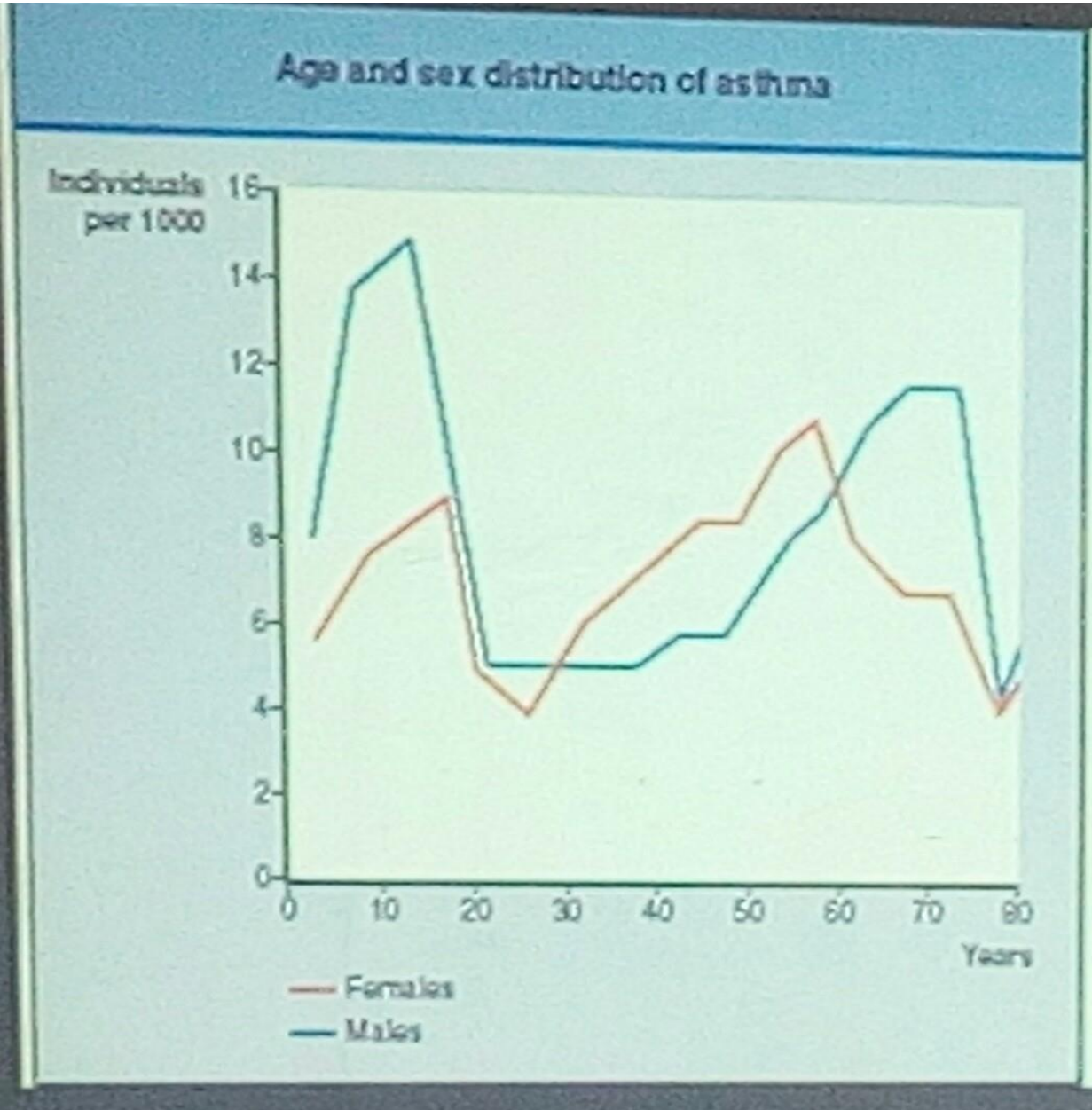
DATE: 13/9/2016

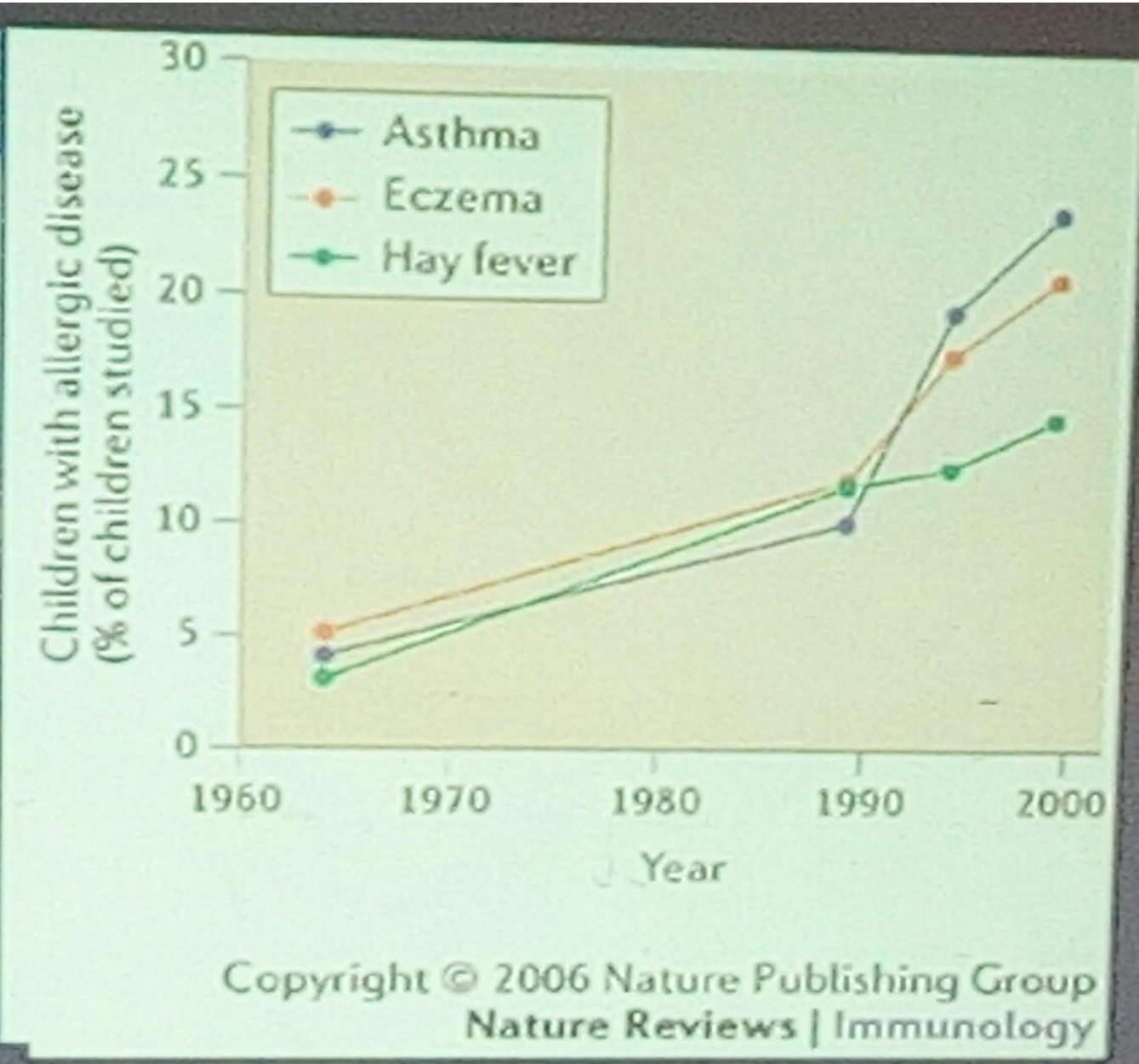
DEFINITION

- Asthma is a chronic inflammatory disease of the airways characterized by airway hyper-responsiveness (AHR) to various triggers resulting in wide-spread airway narrowing and airflow limitation

- Clinically, asthma presents as an episodic cough, wheeze and SOB which recovers spontaneously or with treatment.

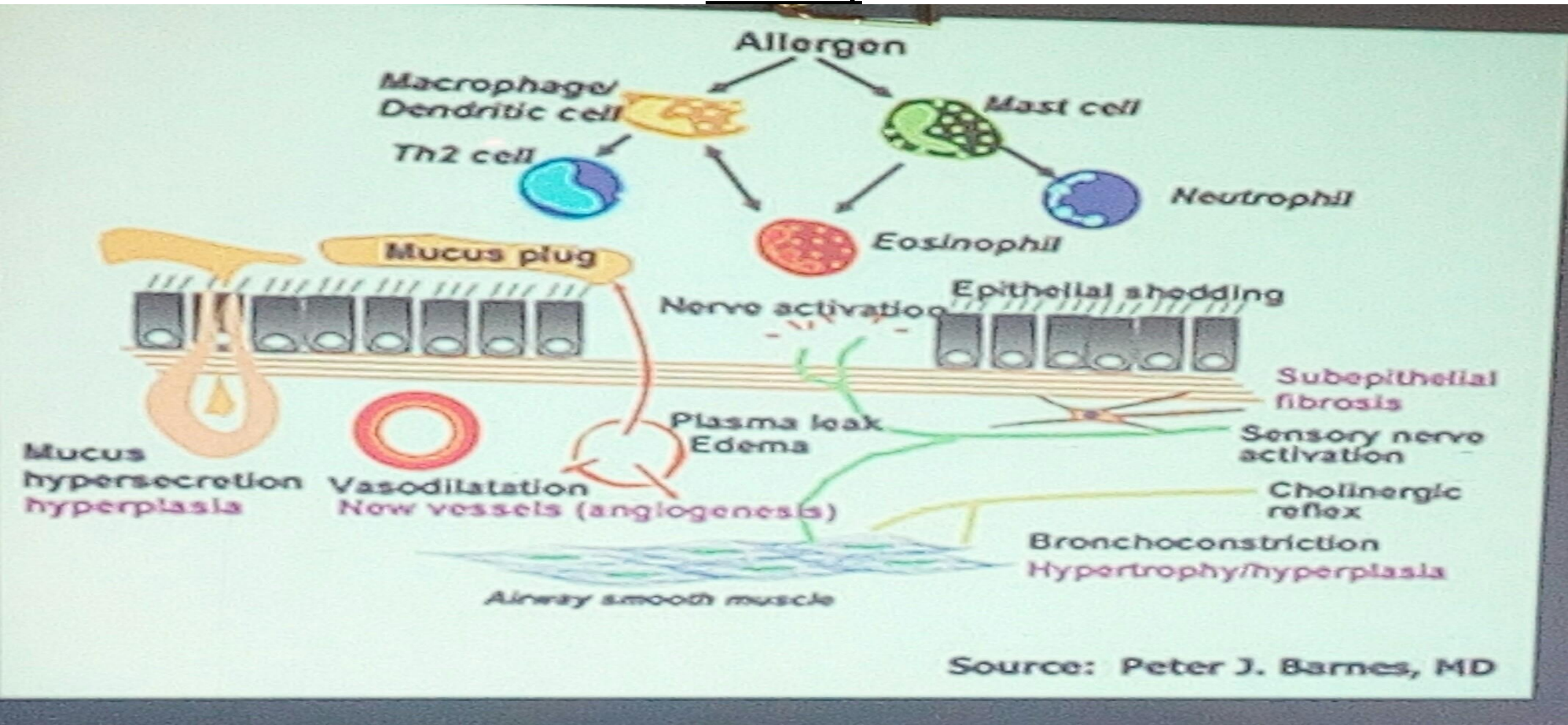
EPIDEMIOLOGY



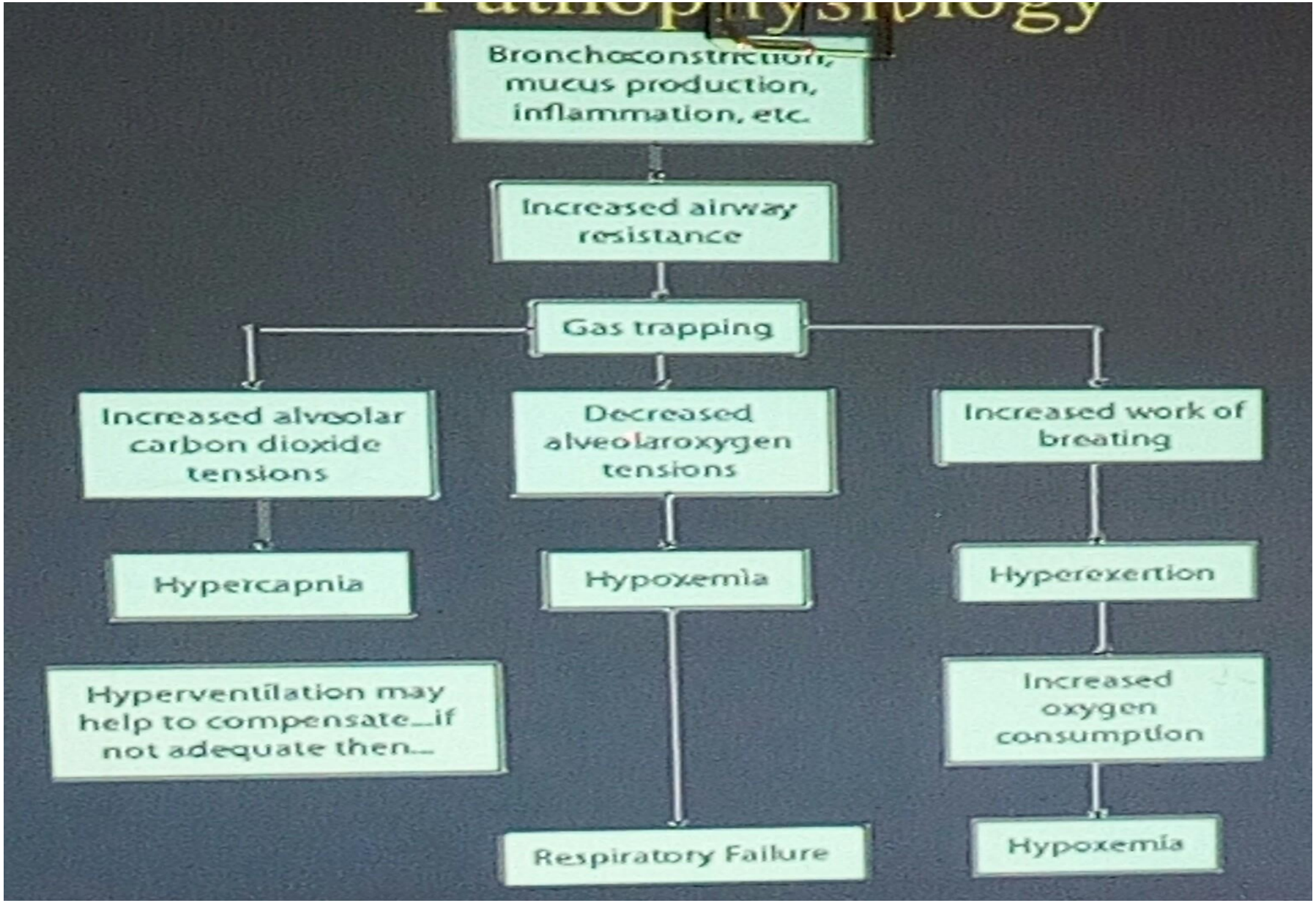


PATHOGENESIS:

There is an interaction between genetics and the environment (trigger factors)



PATHOPHYSIOLOGY



CLINICAL PRESENTATION - HISTORY

- Recurrent symptoms
  - Wheeze, chest tightness, SOB, cough

- Symptom variability
  - Vary over time and from one episode to the next
  - Tend to be nocturnal/or worse at night

- Associated symptoms of atopy
  - Allergic rhinitis or conjunctivitis or eczema

- Ask the patient for any specific trigger factors.

FACTORS THAT MAY EXARCERBATE ASTHMA (TRIGGER FACTORS)

Factor	Comment
Smoking	Active and passive
Infections	Especially rhinoviruses, respiratory syncytial virus, influenza virus
Exercise	Especially on cold dry days
Changes in the weather	Thunderstorms
Pollution	Ozone and sulfur dioxide
Allergens	Pet allergens, house dust and house dust mite, cockroach allergens, pollens
Drugs	Aspirin, nonsteroidal anti-inflammatory agents, β-blockers (oral and ophthalmic)
Occupational factors	Dusty work places, 'cold rooms'

DIFFERENTIAL DIAGNOSIS OF ASTHMA

Productive cough everyday, h/o smoking	Chronic bronchitis
Progressive SOB with exercise, h/o smoking	COPD
Chronic, productive cough, purulent sputum	Bronchiectasis
Exertional dyspnoea, chest pain, orthopnoea,	Angina, heart disease
Sensation of breathlessness without accompanying respiratory symptoms	Hyperventilation

Exclude tuberculosis in a patient who has had cough for more than 3 weeks

LUNG FUNCTION TESTS – PEAK EXPIRATORY FLOW RATE (PEFR)

Lung function test- Peak expiratory flow rate (PEFR)

- fastest flow rate that can be sustained for 10 milliseconds at the start of a maximal expiration after full inspiration
- Normal values depend on age, sex and height (300-700L/min)
- Cheap
- Result expressed as % of predicted

PEFR (%)= Observed PEFR/Predicted PEFRx100

OTHER TESTS

- LUNG FUNCTION TESTS - SPIROMETRY

CLASSIFICATION

- Etiological
  - Atopic/allergic/extrinsic
  - Intrinsic
  - Exercise-induced
  - Occupational

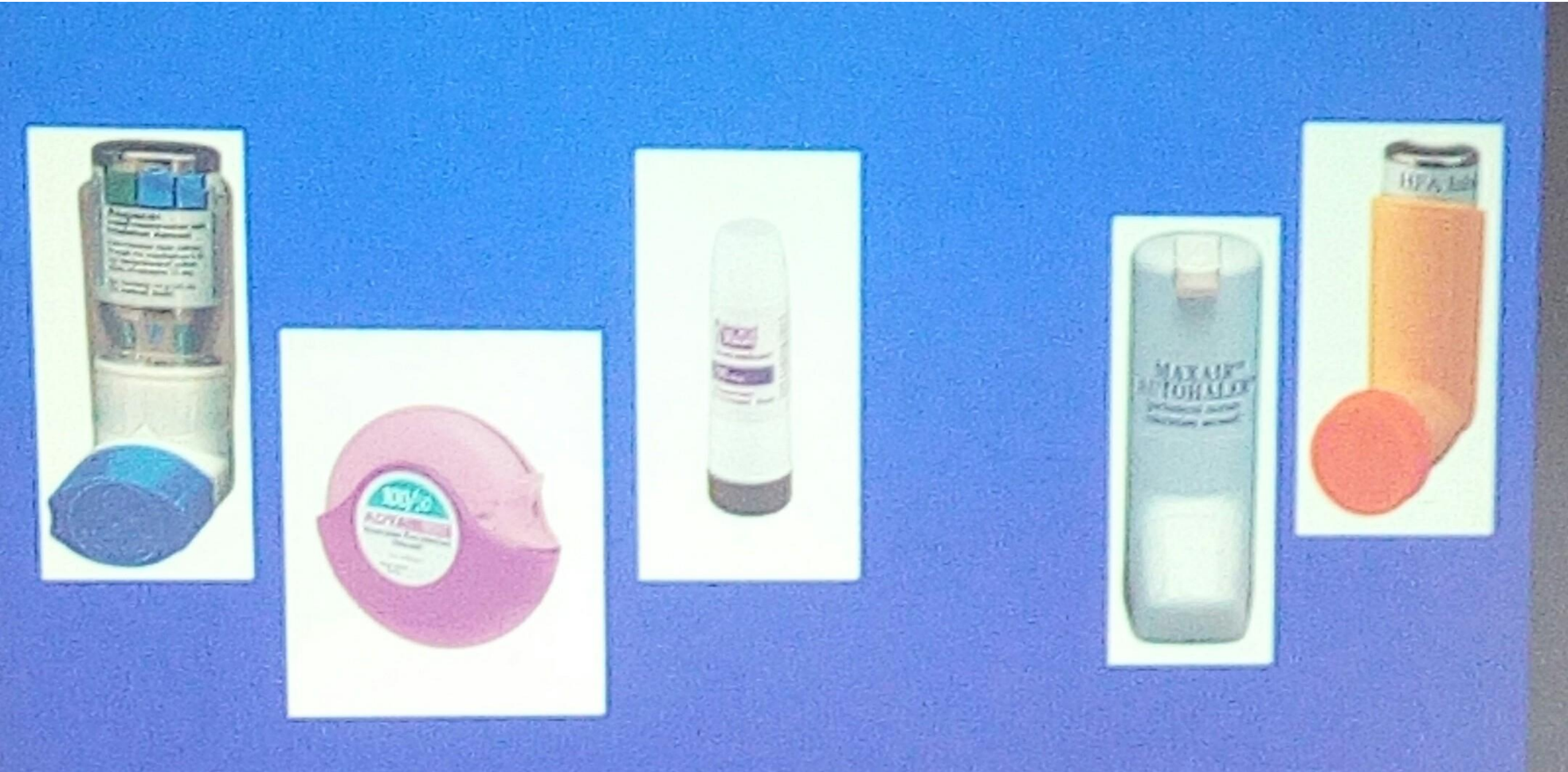
- Severity (based on symptoms and PEFR)
  - Acute asthma attack (mild → moderate → severe)
  - Chronic asthma
    - Intermittent
    - Persistent: Mild → moderate → severe

PRINCIPLES OF MANAGEMNET

- Non-pharmacological
  - Allergen avoidance
  - Patient education

- Pharmacological
  - The mainstay treatment → inhaler therapy depending on severity of the disease

INHALERS



PHARMAOCLOGIC AGENTS COMMONLY USED IN ASTHMA MANAGEMENT

Class	Examples	Action
Short acting β_2-agonists	Salbutamol, terbutaline	Rapid relieve of bronchospasm
Long-acting β_2-agonists	Salmeterol, formoterol	Relieve bronchospasm, control symptoms
Leukotriene modifiers	Montelukast, zileuton	Control symtoms, minimally anti-inflammatory
Steroids	Inhaled: beclomethasone, budesonide, flunisolide, mometasone, ciclesonide Oral: Prednisone	Potent anti-inflammatory, controllers
Anticholinergic	Ipratripium	Relieve bronchospasm

CONCLUSION

- Asthma is one of the most commonest chronic respiratory disorders
- The pathogenesis of asthma is multi-factorial involving genetic susceptibility and environmental factors
- Patient education, avoidance of triggers and proper use of pharmacologic therapies will achieve disease control in a majority of patients.

TYPED BY EFFIE NAILA