Asthma and COPD are chronic inflammatory diseases of the airways.

**Asthma**
- Variable airway inflammation and obstruction
- Large airways obstruction
- Characteristic symptoms: Cough, Wheeze, Breathlessness.
- Affects all the age groups.

**COPD**
- Persistent inflammation and obstruction
- Progressive
- Characteristic symptoms: Cough with expectoration, Breathlessness
- Generally affects subjects more than 40 years of age

**Asthma Risk Factors**
- Cloudy weather
- Pollens
- Spores
Indoor wall dampness

Environmental Risk Factors Of Asthma
Fuel usage particularly Kerosene

Agarbatti  Mosquito coil

Environmental allergens
House dust mite  Animal dander  Cockroaches  Fungal spores

Food allergens
In the general population of India:
Cow’s milk 3%,  Eggs 1.5%,  Dried fruit 1%  Wheat and Soybeans 0.5%
www.foodallergy.org/featuredatopic.html

Other important risk factors in children
Children born with caesarian  Smoking in family  Preterm delivery  No breast feeding
M Cheraghi et al; ERS 2009

Indian Express, 21 Sept. 2008
Paracetamol use in babies increases asthma risk: global study

Occupations and sensitizing agents
Healthcare & Laboratory workers
- Latex, - Glutaraldehyde, - Powdered medications - Antibiotic

Spray Painters
- Di-isocynates

Electronic workers
- Colophony

Welder and metal workers
- Metal dusts or fumes

Food processors, Animal workers, farmers, Gardeners
- Food, - Animal, - Fungal - Insect allergens
GENETICS

Chromosomes 5, 6, 11, 14, and 12
Genes: IL-5, IL8, TNFR,
CREB NF-kB, ADAM33 etc

How does asthma develop?

Environmental Risk Factors Of COPD

Other Risk Factors
- Air pollution
- Occupational exposure
- Latent Viral infection (adenovirus)
- Infection in early life
- Nutritional compromise
- Low birth weight
- Asthma (20%)

GENETICS
- α1-antitrypsin deficiency
- TNF-α gene, Microlase
- epoxide hydrolase gene,
- Aquaporin gene etc

COPD RISK FACTORS

Asthma Inflammation
Inflammatory armaments in asthma

Mast cells

Eosinophils

Dendritic cells

Enzymes

Heparin, Trypsin, Chymase, Histamine, Cytokines, etc.

IL-4, IL-5, IL-13, RANTES, EOTAXIN, TNF alpha, etc.

Lymphoid cells

Mast cells

Eosinophils

IgE antibody

Sensitization

Allergen induced Asthma inflammation

Antigen presenting cell

Anti-IgE Antibody

(Omalizumab)

Immunotherapy causes increase in IgG4 and decrease IgE

Combination of beta-2 agonist and steroids abolish their formation


Asthma inflammation

Mast cells

Enzymes

Heparin, Trypsin, Chymase, Histamine, Cytokines, etc.

IL-4, IL-5, IL-13, RANTES, EOTAXIN, TNF alpha, etc.

Inflammation

Airway remodeling

Steroid resistance

Steroids

Low dose Macrolide antibiotics

• Neutrophil (rare)

• Severe Asthma

• Difficult to treat

• Asthma developing into COPD


Broncho-hyperresponsiveness and airway reversibility in Asthma

NORMAL AIRWAYS

Asthmatic AIRWAYS

Airway Remodeling

• The moment the airways are irritated whole of the airway muscle mass get contracted. This forms basis of broncho-hyperresponsiveness.

• The moment this contracted muscle is relaxed especially with beta-2 agonist the whole of the airway muscle mass get relaxed. This forms basis of reversibility test

Bronchial thermoplasty Targeting Hyperplastic smooth muscles

Airway smooth muscle, almost have no capacity for regeneration

Within the next coming years, a profile of the potential role of this therapy in human asthma should be developed fully.

Eur Respir J 2004; 24:659-663
COPD Inflammation

- Neutrophils
- Macrophages
- Neutrophilic elastase
- Proteinase 3
- Cathepsin
- MMP (1, 3, 9, 12)

- Emphysema
- Fibrosis around the bronchi
- Enlargement of airspaces
- Destruction of lung parenchyma
- Loss of lung elasticity
- Closure of small airways

CD8 T cells

- Chemotactic factors (IL-8, LTB4)
- Cytotoxic autoimmune reaction
- Eosinophils (rare)

- Chronic bronchitis (obstruction of small airways)

IL8, (LTB4), GRO-alfa, MCP-1, MCP-2, MIG, N- acetyl cysteine (NAC)

- Matrix metaloproteinases: MMP1, 2, 9, 12, 14
- Neutrophils recruitment
- Anti-oxidants

- Neutrophils and macrophages
- Oxidative stress
- Cigarette smoke
- Inflammatory cells
- N2-, OH-, H2O2, ONOO-

- Neutrophilic chemotactic factors (IL-8, LTB4)
- Chronic bronchitis
- Sub epithelial Fibrosis
- Bronchoconstriction

- Chronic bronchitis
- Mucus Hypersecretion
- Sub epithelial Fibrosis
- Bronchoconstriction

- N-acetyl cysteine (NAC)
- Steroid insensitivity

- COPD Inflammation

- Other diseases associated with COPD
  - Insulin resistance Diabetes mellitus; Mannino DM et al. ERJ, Oct 2008; 32: 962 - 969
Recent Advances in Asthma pathogenesis

- **ASTHMA**
  - Chronic inflammatory disease
  - Inflammation highly sensitive to corticosteroids

- **COPD**
  - Chronic inflammatory disease
  - Oxidative stress
  - Inflammation not sensitive to corticosteroids
  - Systemic inflammation

**Carry Home message**

**Thank You**

**Bronchial-Epithelial cells**

- Friable epithelial cells
- Constantly in a healing phase (similar to a chronic wound)

**Epithelial cells as cellular sources of various inflammatory mediators and pro-inflammatory cytokines**

- Normal
- Asthmatic

- IL8, IL5, RANTES, IL1, IL10, TNFα (Immunohistochemical staining)

- Epithelial cells as active players in asthmatic airway inflammation

**Role of epithelium in airway wall remodelling**

Inflammation → Airway Remodeling


Oxidative Stress in COPD

Peter J Barnes; NEJM; 2000; Volume 343; 269-280

Emphysema