

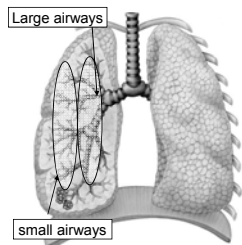
### Risk factors and Pathogenesis Of Asthma and COPD



www.cfindia.com

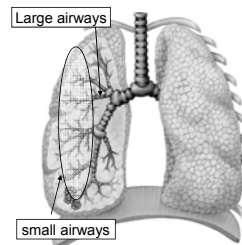
**Asthma and COPD are chronic inflammatory diseases of the airways**

### Asthma



- Airway Hyperresponsiveness
- Variable airway Inflammation and obstruction
- Characteristic symptoms  
Cough, Wheeze  
Breathlessness.
- Affects all the age groups.

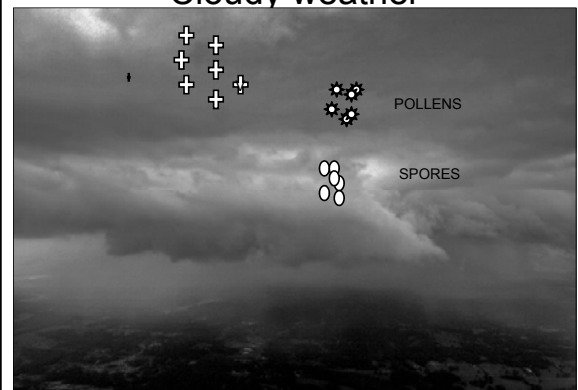
### COPD

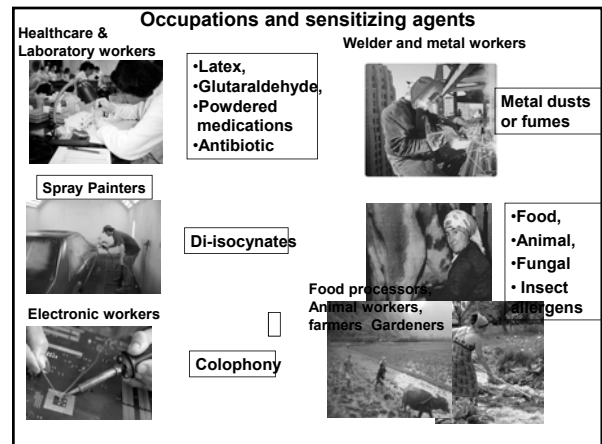
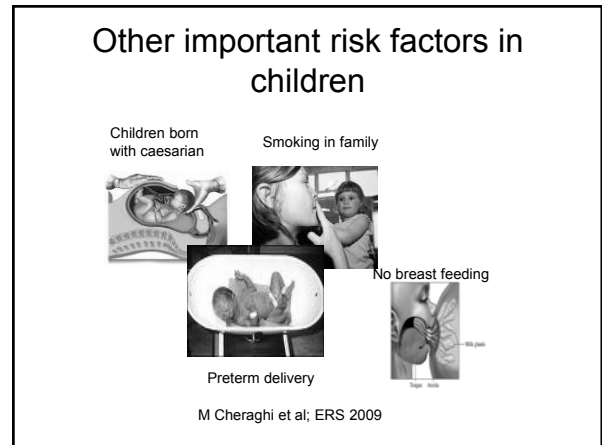
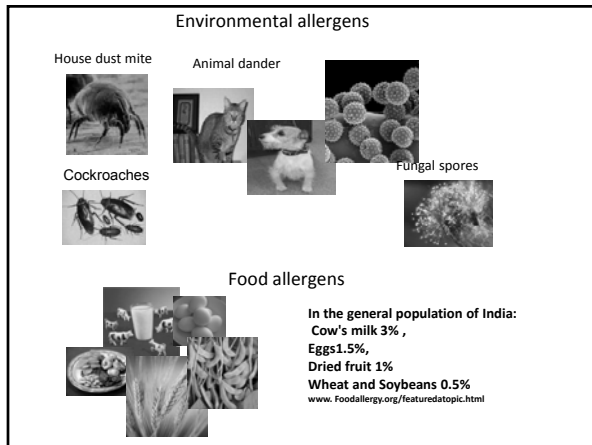
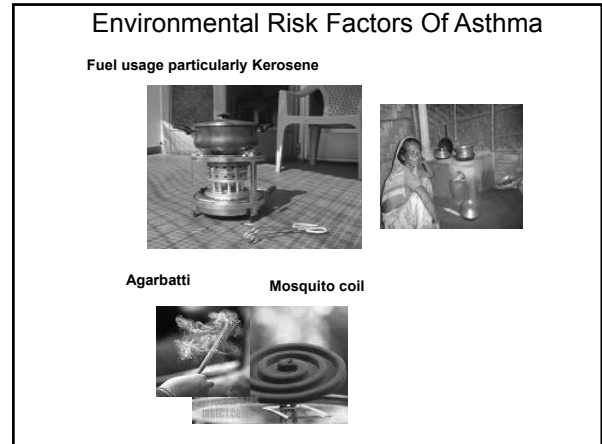
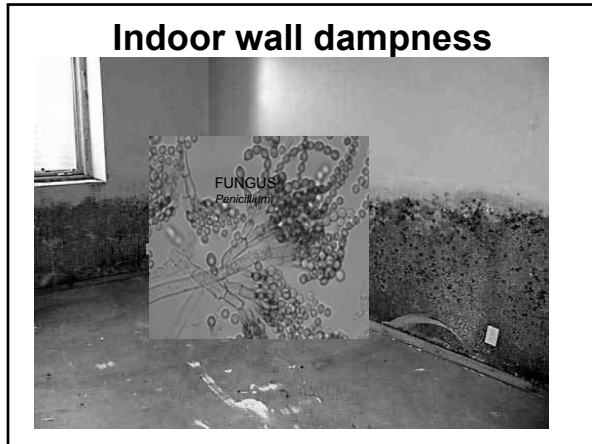


- Persistent Inflammation and obstruction
- Progressive
- Characteristic symptoms  
Cough with expectoration  
Breathlessness
- Generally affects subjects more than 40 years of age

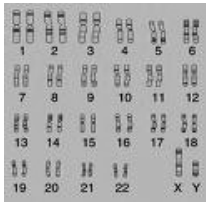
### ASTHMA RISK FACTORS

### Cloudy weather





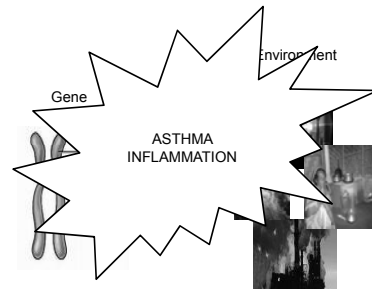
## GENETICS



Chromosomes 5, 6, 11, 14, and 12

Genes : IL-5, IL8, TNFR, CREB NFK-Beta, ADAM33 etc

## How does asthma develop?



## COPD RISK FACTORS

### 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

- $\alpha$ 1-antitrypsin deficiency
- TNF- $\alpha$  gene, Microase epoxide hydrolase gene, Aquaporin gene etc

## Asthma Inflammation

### Inflammatory armaments in asthma

**Mast cells**

**Eosinophils**

**CD4 TH2 Lymphocytes**

**Dendritic cells**

**Basophils**

IL-5, IL13, RANTES, EOTAXIN, TNF- $\alpha$  etc

Enzymes: Tryptase, chymase, elastase, MMPs etc

### Allergen induced Asthma Inflammation

Antigen presenting cell

Sensitization

Anti-IgE Antibody (Omalizumab)

Lymphoid cells

TH2

IL13

IL4

IL5

B cells

Eosinophils

Immunotherapy causes increase in IgG4 and decrease in IgE

Combination of beta-2 agonist and steroids abolish their formation

Wenzel SE et al: Lancet 2007

### Asthma Inflammation

**Mast cells**

**Enzymes**  
Heparin, Tryptase, Chymase, Histamine, Cyt/Chemo, IL5, IL4, TNF- $\alpha$

**Prostaglandins**

**Leukotrienes**

**Steroids**

**Reactive oxygen species**  
-OH, O $_2^-$  etc

**Cytotoxic proteins**  
Lipid mediators, ECP, MBP etc

**Inflammatory**  
IL3, IL2, IL4, IL5, etc

**•Inflammation**

**•Airway remodeling**

**•Steroid resistance**

**•Airway remodeling**

**•Inflammation**

**•Airway remodeling**

**•Eosinophil activation**

**•IgE**

### Neutrophil (rare)

**Low dose Macrolide antibiotics**

- Severe Asthma
- Difficult to treat
- Asthma/ Refractory to steroids
- Asthma developing into COPD

Curr Opin Allergy Clin Immunol. 2007;7(1):43-50.

### Broncho-hyperresponsiveness and airway Reversibility in Asthma

**NORMAL AIRWAYS**

**Asthmatic AIRWAYS**  
Airway Remodelling

Subepithelial Collagen deposition

Smooth Muscle Hyperplasia

- 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

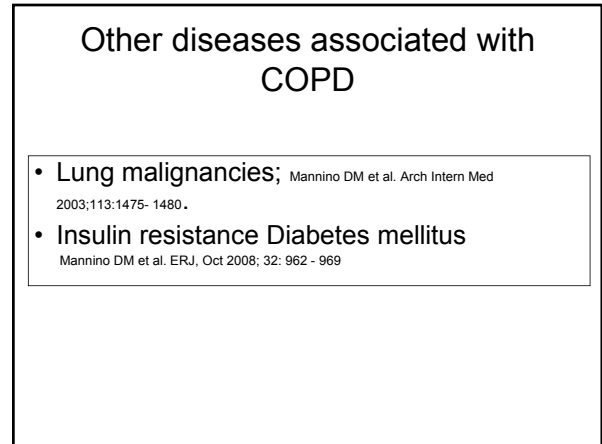
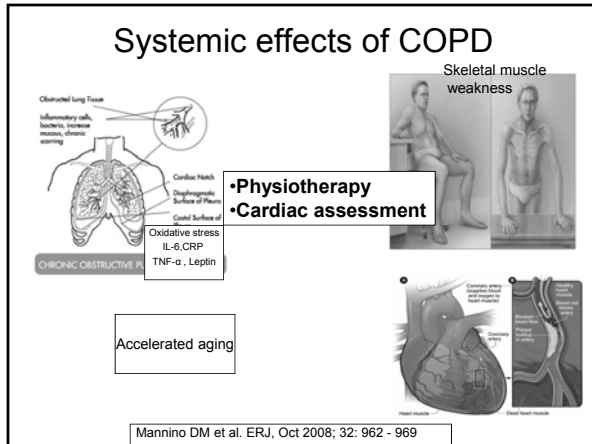
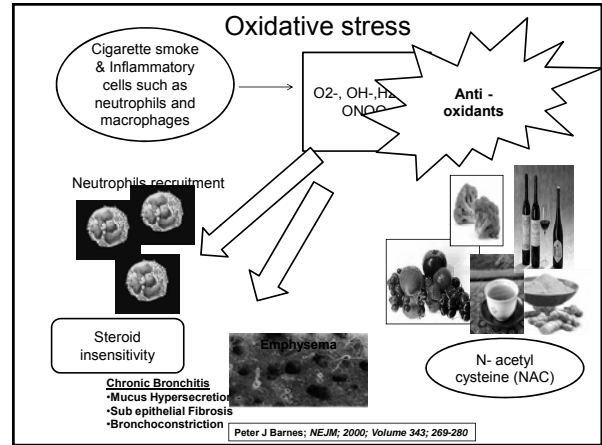
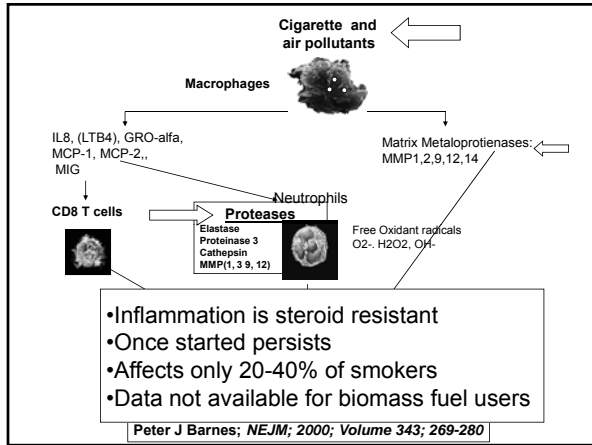
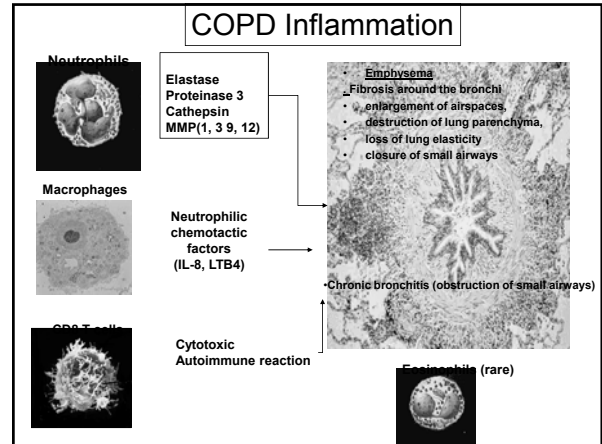
Bronchial Thermoplasty with the Alair System by Asthmax

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



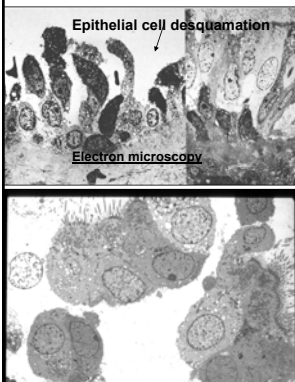
**Carry Home message**

<p><b>ASTHMA</b> Chronic inflammatory disease Inflammation highly sensitive to corticosteroids</p>	<p><b>COPD</b> Chronic inflammatory disease <u>Oxidative stress</u> Inflammation not sensitive to corticosteroids <u>Systemic inflammation</u></p>
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Thank You

Recent Advances in Asthma pathogenesis

**Bronchial-Epithelial cells**

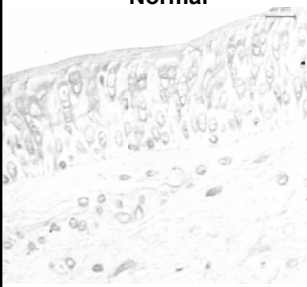



Epithelial cell desquamation  
Electron microscopy

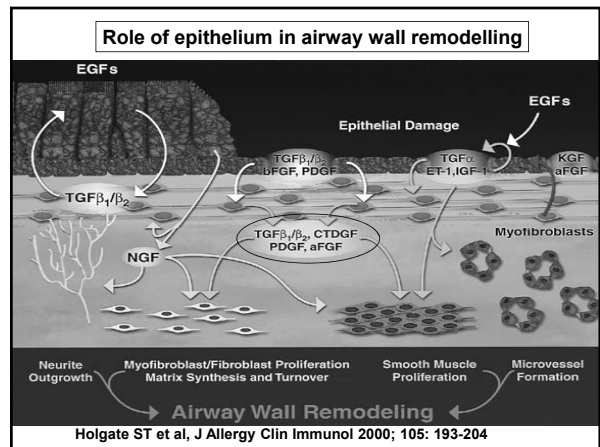
- Friable epithelial cells
- Constantly in a healing phase (similar to a chronic wound)

Detachment of epithelial cells

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

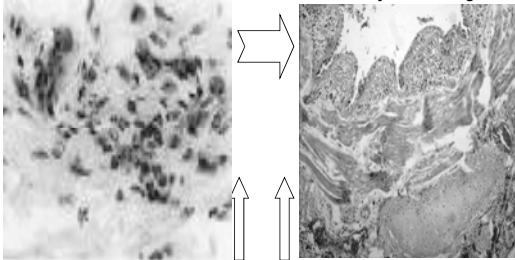
<p><b>Normal</b></p> 	<p><b>Asthmatic</b></p>  <p>IL8, IL5, RANTES, IL1, IL10, TNF<math>\alpha</math> (Immunohistochemical staining)</p>
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Epithelial cells as active players in asthmatic airway inflammation



**Theory Of Remodeling**  
**New Concept in Pathogenesis of asthma**

**Inflammation**      **Airway Remodeling**



Holgate ST et al, J Allergy Clin Immunol 2000; 105: 193-204

