DRUG INDUCED PULMONARY DISEASES

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DEFINITION

- Drug-induced pulmonary disease is lung disease caused by a bad reaction to a medication.

- Many types of lung injury can result from medications, and it is often impossible to predict who will develop lung disease resulting from a medication or drug.

- The clinical manifestations of Drug Induced Pulmonary diseases are difficult to find because of Non Specific Pathological changes.

- The diagnosis is based on exclusion of all other possible causes.

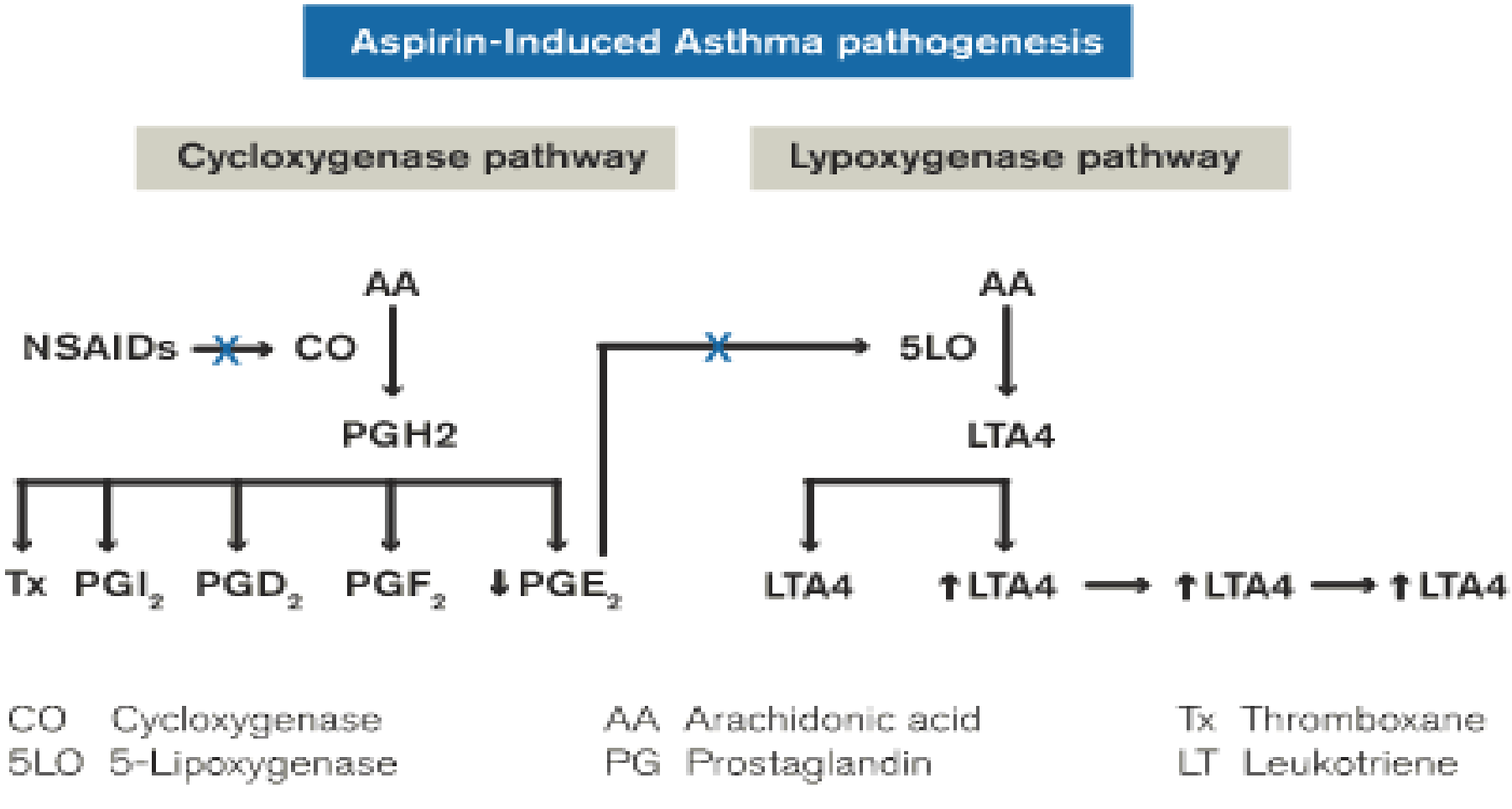
DRUGS THAT INDUCE BRONCHOSPASM

Anaphylaxis (IgE-Mediated)	
Penicillins	F[a]
Sulfonamides	F
Cephalosporins	F
Cimetidine	R
Tetracyclines	I

a=Relative frequency of reactions:
F = frequent;
I = infrequent;
R = rare.

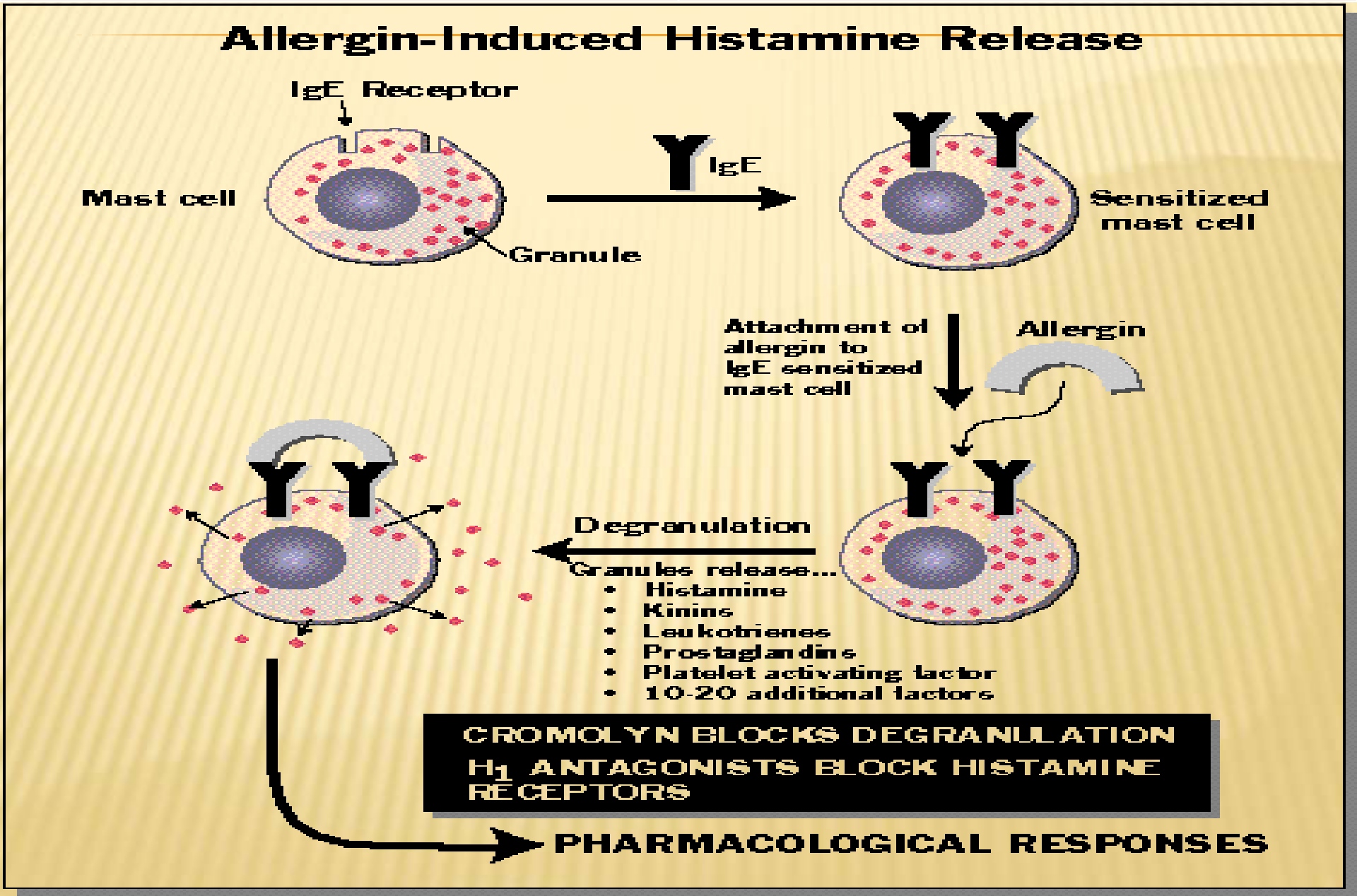
Cyclooxygenase Inhibition

Aspirin	F
Phenylbutazone	I
Acetaminophen	R



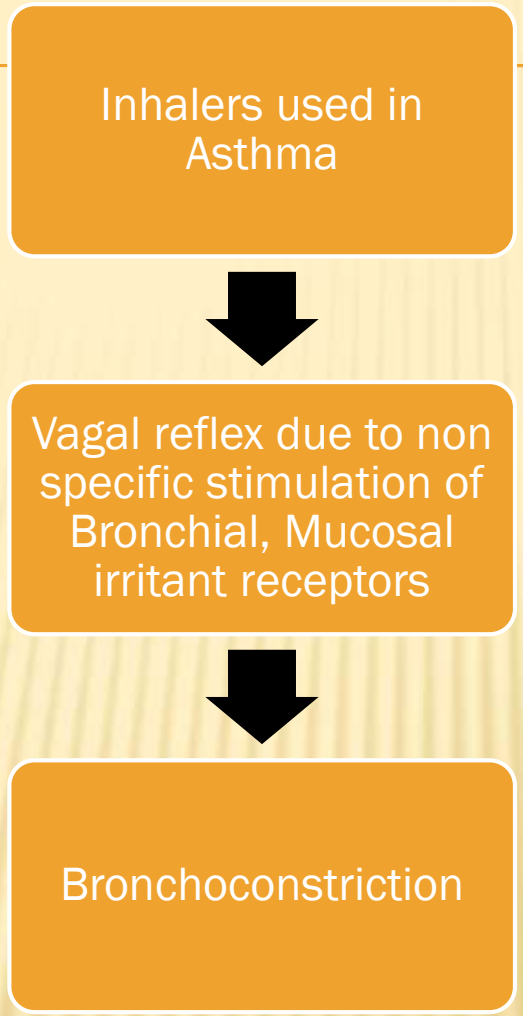
Anaphylactoid Mast-Cell Degranulation

Iodinated-radiocontrast media	F



Direct effect on Smooth Muscle	
Carbachol	
Pilocarpine	
Methacholine	
Inhibit Hydrolysis of Meditor	
Neostigmine	
Physostigmine	
Antagonism at beta receptors	
Propranalol	
Atenalol	

Reflex Bronchoconstriction :



To overcome this effect a combination of Sodium Chromoglicate and Isoprenaline should be given.

SULFITES :

Two mechanisms are involved

Sulfites
E.g. Potassium metabisulfite

Stimulation of afferent parasympathetic irritant receptors

Bronchoconstriction

IGe mediated Sulfite-sensitive anaphylactic reactions

Positive skin test due to reduced hydrolase enzyme

TREATMENT :

- Pretreatment with **Cromolyn, Anticholinergics, Vitamin B_{12}**

- **Vitamin B_{12} catalyses the oxidation of sulfite to sulfate.**

OTHER PRESERVATIVES

- EDTA : Potentiates bronchial responsiveness to Histamine mediated by calcium chelation of EDTA.
- Benzalkonium chloride : Mast cell degranulation and stimulation of irritant –C fibers in airways.
- Treatment : **Cromolyn**

PULMONARY OEDEMA

- Pulmonary oedema results from failure of Homeoststic mechanisms.

Etiology

- ↑ in the Hydrostatic pressure due to left ventricular failure.
- Disrupted osmotic and oncotic pressure in vasculature.
- Integrity of alveolar epithelium.
- Interstial lymph flow.

Signs and Symptoms :

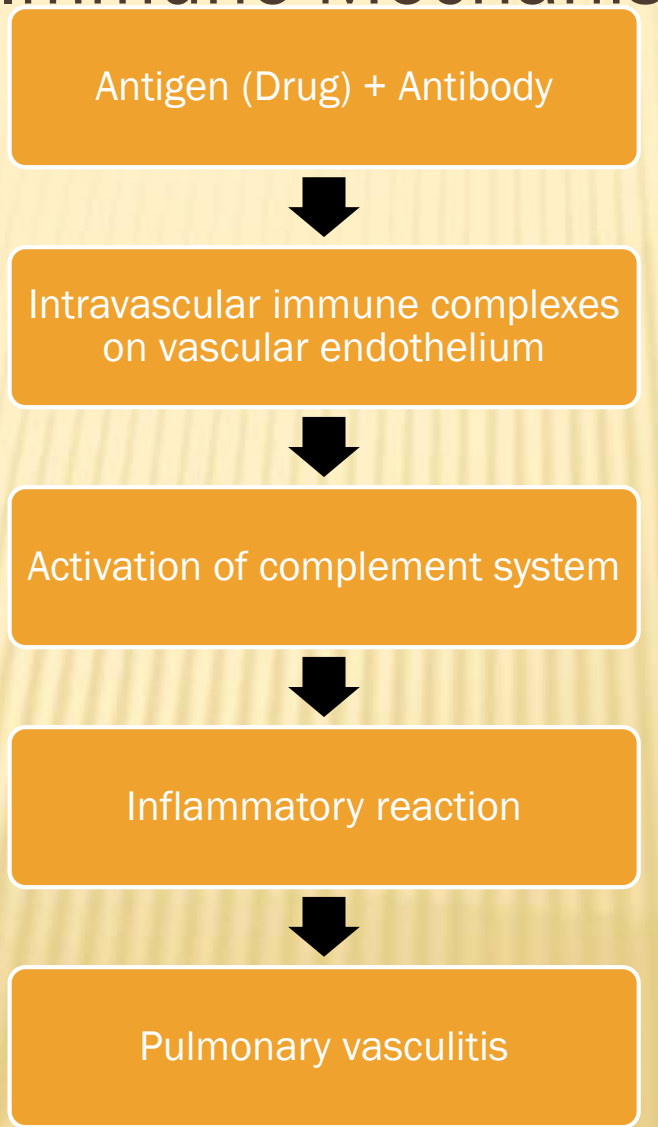
- Persistent cough
- Tachypnea
- Dyspnea
- Tachycardia
- Stiff lungs
- Hypoxemia

DRUGS

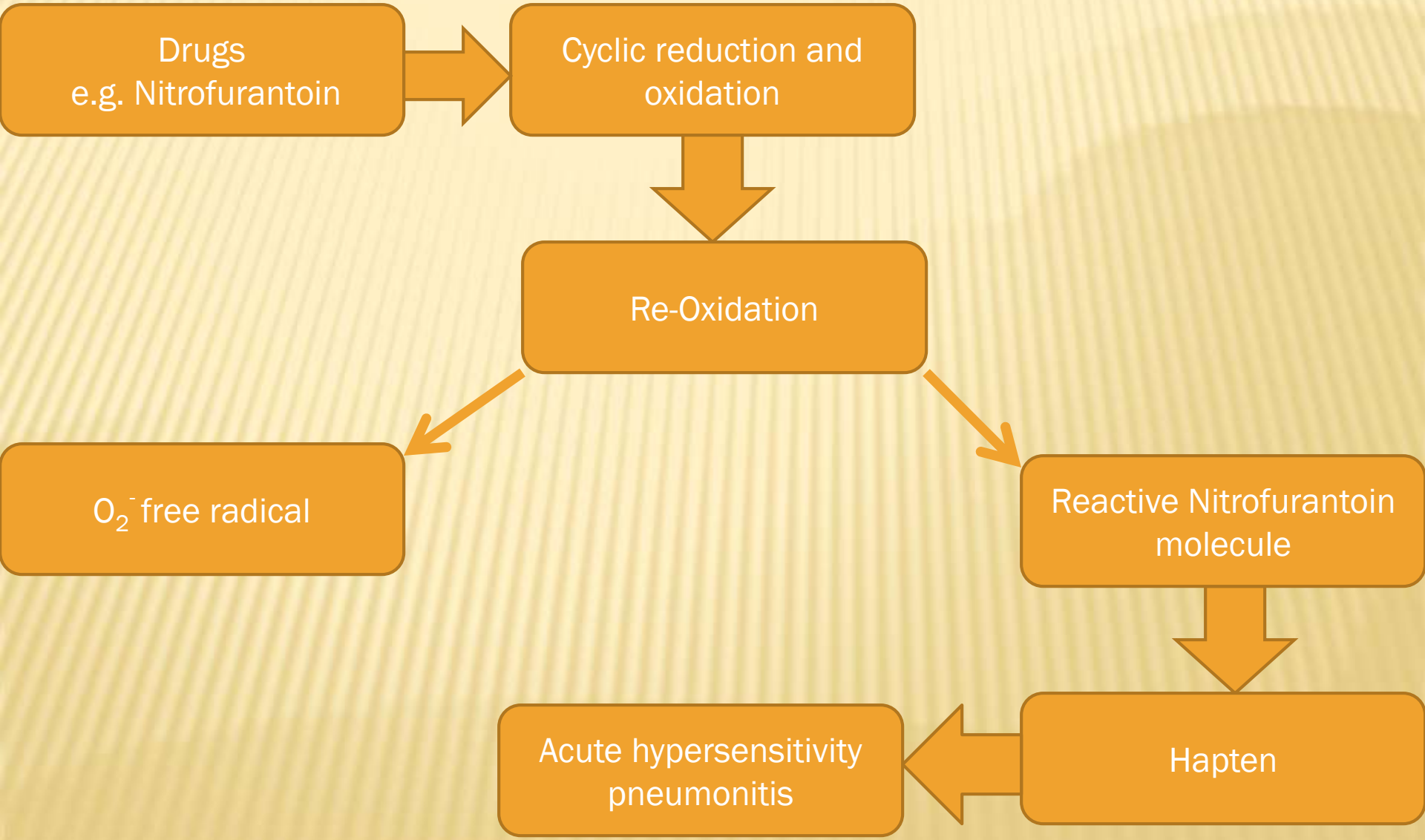
Naloxone,Codeine ⟶ Direct toxicity on alveolar capillary membrane.

PULMONARY VASCULITIS

- Results from a Immune Mechanism

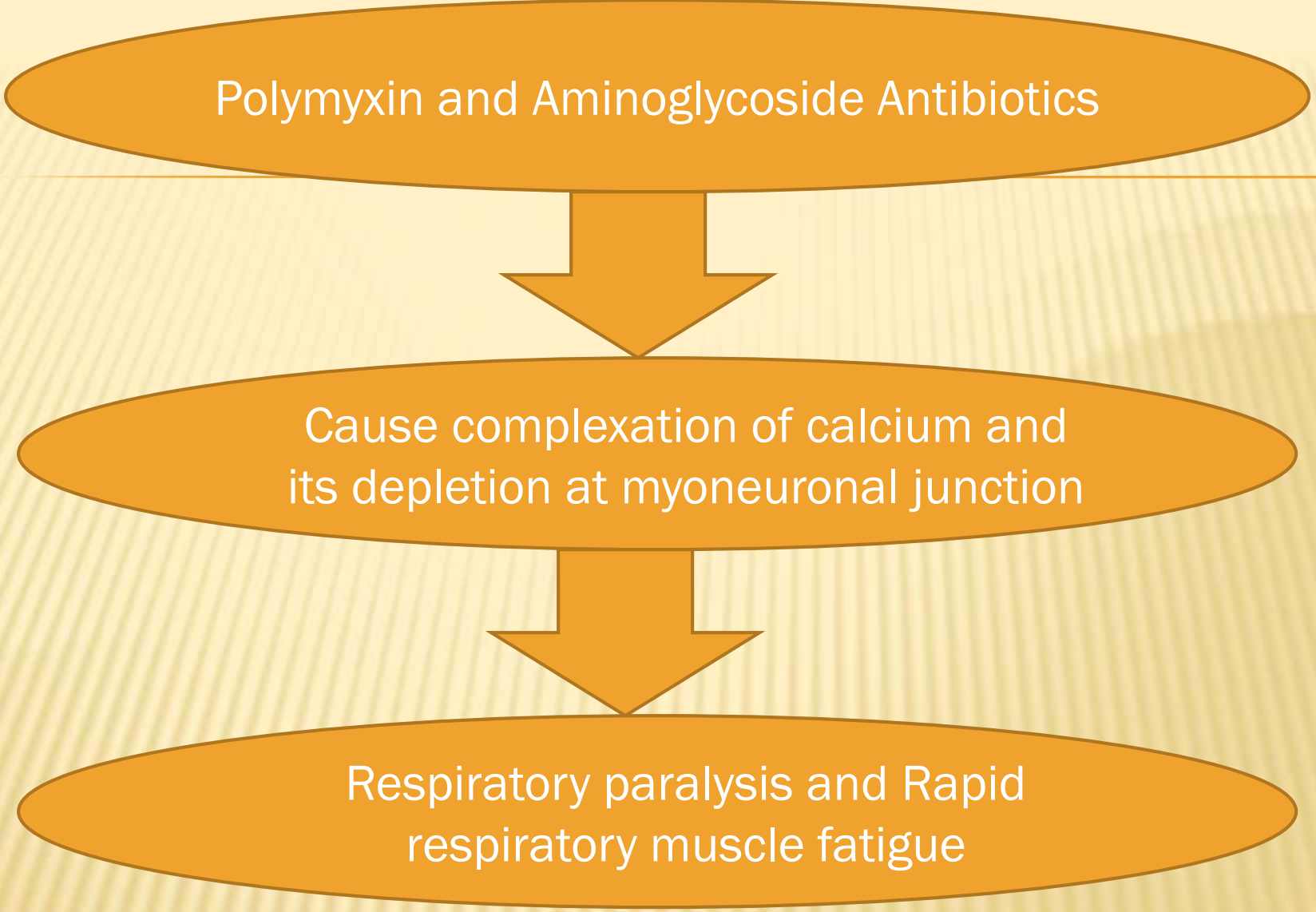


HYPERSENSITIVITY PNEUMONITIS



DRUG INDUCED APNEA

- Patients suffering with COPD, Alveolar hypoventilation, Chronic co_2 retention show exaggerated response to sedatives and narcotic analgesics.
- Class of drugs involved include
  - Benzodiazepines : e.g. midazolam
  - Aminoglycoside Antibiotics: e.g. Streptomycin, Gentamycin



IV Calcium chloride is given to reverse paralysis

INTERSTITIAL LUNG DISEASE

- Types of ILD :

a) Pulmonary Eosinophilia
b) Bronchiolitis Obliterans Organizing Pneumonia
c) Pulmonary Fibrosis
d) Diffuse alveolar damage
e) Oxidant Injury

- **Symptoms :**

  Non productive cough,

  Dyspnea,

  Low grade fever.

- **Management :**

✓ Withdrawal of Causative drug.

✓ Respiratory failure is treated with high dose of Methyl prednisolone.

✓ Respiratory distress treated with low dose of methyl prednisolone.

✓ Immunosupperesents

PULMONARY EOSINOPHILIA

- Pulmonary infiltrates with eosinophlia

- **Symptoms :**
  - ✓ Fever
  - ✓ Non productive cough
  - ✓ Bilateral pulmonary infiltrate
  - ✓ Lung biopsy revels perivasculitis with infiltration of eosinophils, macrophages and proteniaceous fluid in the alveoli.

BRONCHOLITIS OBLITERANS ORGANIZING PNEUMONIA

- It is the inflammation of the lungs characterized by alveolar fibrosis.
- **Symptoms :** Dyspnea, low grade fever, acute pleuretic chest pain.

Amphoterecin-B
Statins
Sulfasalazine
Amiodarone
Acebutalol

DIFFUSE ALVEOLAR HAEMORRHAFE AND DAMAGE

- Characterized by bleeding from capillaries leading to accumulation of RBCs in alveolar spaces.
- Pathogenesis :
- ✓ Hypersensitivity reactions.
- ✓ Direct toxicity.
- ✓ Coagulation defects

- Drugs : Anticoagulants → Pulmonary haemorrhage
- Treatment : Withdrawal of the drug, Corticosteroids
- Chemotherapeutic agents → Direct epithelial injury and damage to alveolar capillary basement membrane.

OXYGEN TOXICITY

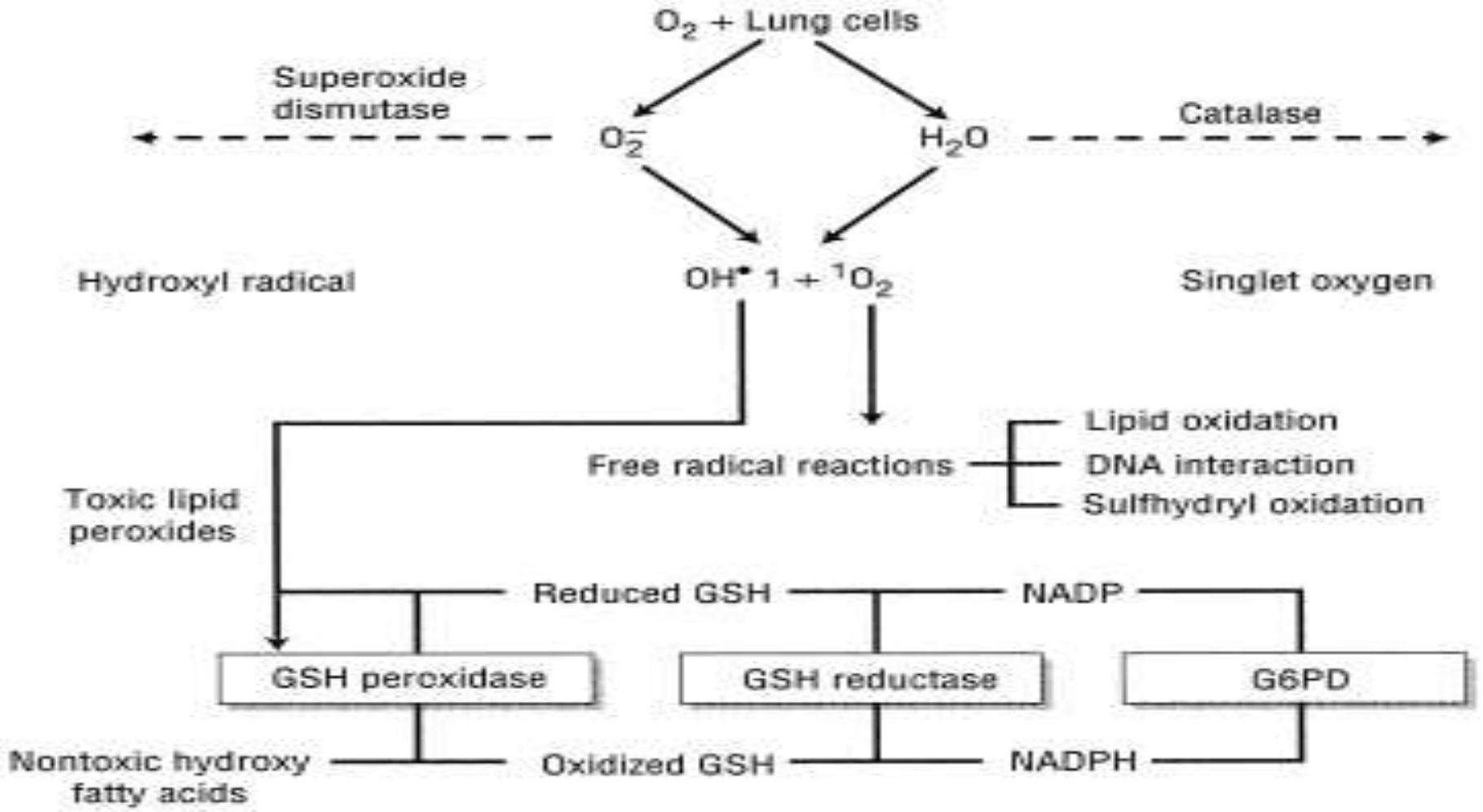


FIGURE 29–1. Schematic of the interaction of oxygen radicals and the antioxidant system. GSH = glutathione; G6PD = glucose-6-phosphate dehydrogenase; NADP = nicotinamide-adenine dinucleotide phosphate; NADPH = reduced NADP.

OXYGEN TOXICITY

- Drugs induce Lung toxicity by

Production of oxidants

e.g. of drugs include Bleomycin, Nitrofurantoin,Cyclophosphamide.

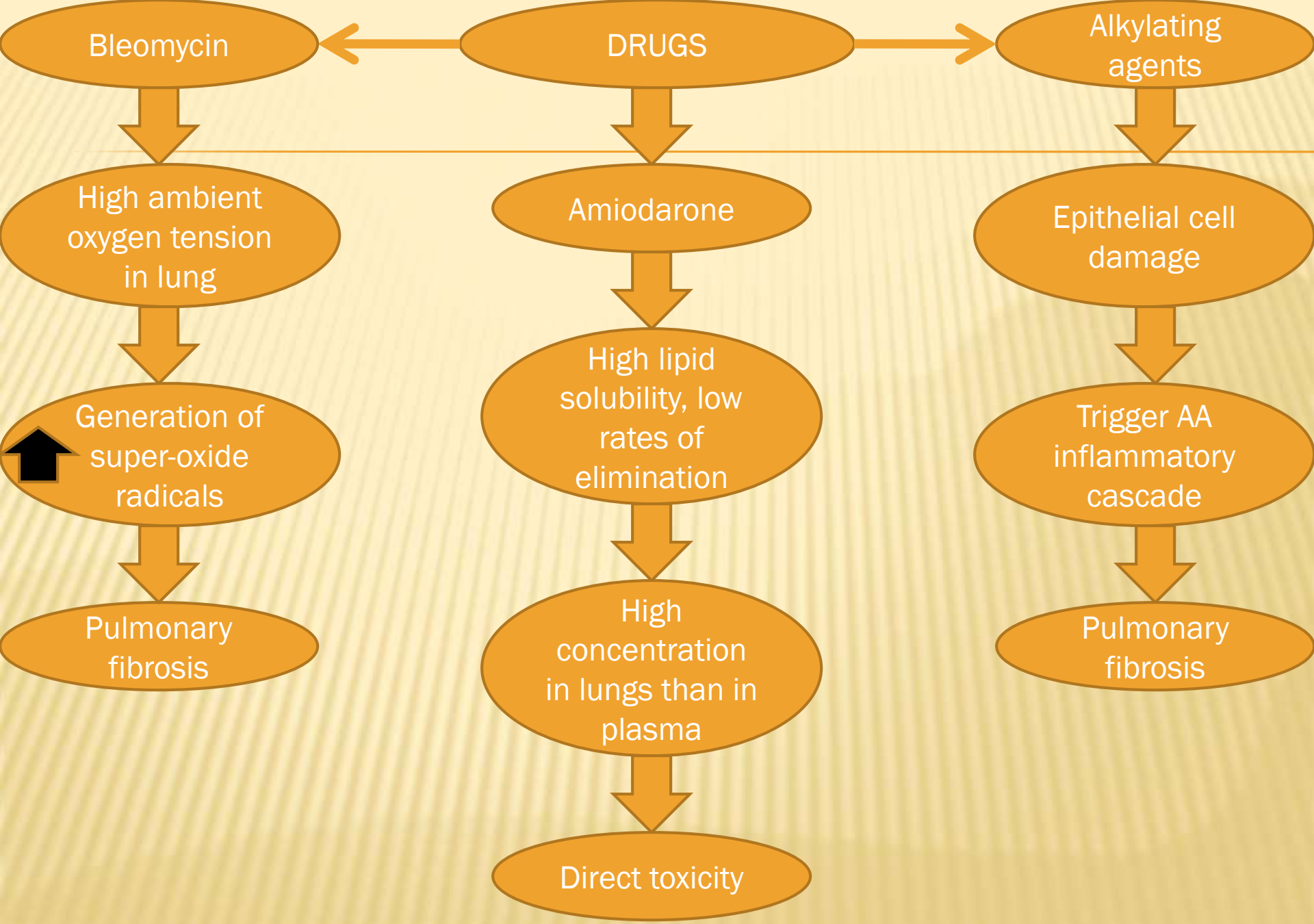
By inhibiting antioxidant system

e.g. of drugs include Nitrofurantoin.

PULMONARY FIBROSIS

- Predisposing factors : Cumulative dose, patient's age, Renal dysfunction, previous radiotherapy, Oxygen administration, concurrent cytotoxic therapy .

- Signs and symptoms : Dry cough, Fever, breathlessness developing and progressing over a period of several weeks or months.


DRUGS
Bleomycin
Alkylating agents
High ambient oxygen tension in lung
Amiodarone
Epithelial cell damage
Generation of super-oxide radicals
High lipid solubility, low rates of elimination
Trigger AA inflammatory cascade
Pulmonary fibrosis
High concentration in lungs than in plasma
Pulmonary fibrosis
Direct toxicity

- Amiodarone is an amphiphillic molecule, responsible for phospholipid, storage disorders in the lungs by inhidition of lysosomal phospholipases.

- **Treatment :** Prednisolone, Corticosteroid therapy in severe conditions.

REFERENCES

- Clinical pharmacy and therapeutics by Roger Walker
- Pharmacotherapy by Dipiro
- Applied therapeutics by Koda Kimble
- Pathologic basics of disease by Robbins and cotran

THANK YOU