DRUG INDUCED LUNG DISEASES
CHEMOTHERAPEUTIC AGENTS

- 1. CYTOTOXIC ANTIBIOTICS
- 2. ALKYLATING AGENTS
- 3. ANTIMETABOLITES
- 4. BIOLOGIC RESPONSE MODIFIERS
CYTOTOXIC ANTIBIOTICS

- BLEOMYCIN

1. CHRONIC PNEUMONITIS/ PULM FIBROSIS
   MOST COMMON SYNDROME
   RADIATION RECALL EFFECT
   RISK FACTORS: cumulative dose > 400u
   - oxygen therapy
   - therapeutic radiation
   - renal insuff
   - old age
2. HYPERSENSITIVITY TYPE LUNG DISEASES
Dyspnea, cough, skin rash, eosinophilia
may not occur with rechallenge

3. CHEST PAIN SYNDROME
Associated with iv infusion of the drug
MITOMYCIN C

- **1. CHRONIC PNEUMONITIS / PULMONARY FIBROSIS**
  
  most common syndrome
  
  risk factors: oxygen therapy
  
  therapeutic radiation
  
  concurrent use of other cytotoxic drugs

- **2. ACUTE DYSPNEA/ BRONCHOSPASM**
  
  NON CARDIOGENIC PULMONARY EDEMA
  
  pts receiving vinca alkaloids
3. HAEMOLYTIC UREMIC SYNDROME
microangiopathic hemolytic anemia,
thrombocytopenia, renal insufficiency,
non cardiogenic pulmonary edema
ACTINOMYCIN D

1. EXACERBATION OF RADIATION INDUCED INJURY
ALKYLATING AGENTS

BUSULFAN

1. CHRONIC PNEUMONITIS /PUMONARY FIBROSIS

toxicity may occur after several years of treatment

fibrosis may occur insidiously
CYCLOPHOSPHAMIDE

1. CHRONIC PNEUMONITIS /PULMONARY FIBROSIS

risk factors: concurrent use of

other cytotoxic drugs

therapeutic radiation
ANTIMETABOLITES

- METHOTREXATE
  1. CHRONIC PNEUMONITIS / PULMONARY FIBROSIS
  2. HYPERSENSITIVITY TYPE
  3. ACUTE CHEST PAIN SYNDROME
     often assoc with pleural effusions
  4. NON CARDIOGENIC PULMONARY EDEMA
     assoc with intrathecal route
- CYTOSINE ARABINOSIDE
  1. NON CARDIOGENIC PULMONARY EDEMA

- FLUDARIBINE
  1. HYPERSENSITIVITY RXN
  2. INTERSTITIAL PNEUMONITIS
BIOLOGIC RESPONSE MODIFIERS

- **ALLTRANS RETINOIC ACID**
  1. retinoic acid syndrome

- **INTERLEUKIN 2**
  1. pleural effusions
     - focal/ diffuse radiographic abnormalities
     - risk factors: increasing cumulative dose
       - admn of LAK cells
     - IL 2 induced cardiac toxicity
  2. NON CARDIOGENIC PULMONARY EDEMA
NON CHEMOTHERAPEUTIC AGENTS

- CARDIOVASCULAR DRUGS
- TOPICAL OPHTHALMIC AGENTS
- TOCOLYTICS
- CORTICOSTEROIDS
- ANTIBIOTICS
- ANTICONVULSANTS
- SALICYLATE
- GOLD & PENCILLAMINE
- ILLICIT DRUG USAGE
CARDIOVASCULAR DRUGS

- AMIODARONE
  incidence of pulmonary toxicity 5%
  1. alveolitis/ fibrosis syndrome
     a) chronic 2/3 rd cases
     b) subacute –fever, chest pain, alveolar/mixed infiltrates
  leucocytosis, raised ESR
  2. NON CARDIOGENIC PULMONARY EDEMA
Daily dose < 400mg is assoc with lower risk

PATHOLOGY

- accumulation of foamy macrophages
- acute intraalveolar h’age
- type 2 cell proliferation
- Hyaline membrane formation

on Electron m’scopy cytoplasm of foamy macrophages has lamellar inclusions containing indigested phospholipids
PROCAINAMIDE

- DRUG INDUCED SLE
  - ANA +ve, antihistone Ab
  - Slow acetylators develop ANA & clinical SLE rapidly
  - common symptoms: arthralgias, fever
  - Pleural effusions & pleuritic chest pain (MC pulmonary symptoms)
  - Parenchymal infiltrates
ADENOSINE

MC pulmonary side effect is acute dyspnea during infusion

Acute bronchospasm in asthma & COPD pts
- **ACE INHIBITORS**
  - chronic nonproductive cough 5-15%
  - angioneurotic edema

- **BETA BLOCKERS**
  - pulmonary fibrosis
  - drug induced SLE
  - dose dependent decrease in FEV1
TOPICAL OPHTHALMIC AGENTS

- Significant decrease in FEV1 in asymptomatic
- Acute bronchospasm
- Non specific agents – timolol
TOCOLYTIC AGENTS

- ACUTE PULMONARY EDEMA
- BRONCHOSPASM
- METABOLIC ACIDOSIS AND DYSPNEA
CORTICOSTEROIDS

LONE COUGH

MEDIASTINAL FATTY DEPOSITS (LIPOMATOSIS)

THROMBOEMBOLIC DISEASE

OPPORTUNISTIC INFECTIONS
ANTIBIOTICS

- HYPERSENSIVITY RXN
  PIE syndrome - beta lactams, sulfa drugs
  MC is loeffler’s syndrome
  c/f- dyspnea cough fever
  peripheral blood eosinophilia of acute onset
  spontaneous resolution on drug withdrawal
NITROFURANTOIN

ACUTE
Onset <1 mth after 1st
Dose; recurs with challenge
fever, dyspnea, cough,
Maculopapular rash
Mixed infiltrates
PFT-restrictive defect with
Decrease DLCO

CHRONIC
elderly pts undergoing
chronic oral therapy
cough, dyspnea,
cyanosis, fatigue
interstitial infiltrates
prognosis worse
INH INDUCED SLE
fever anemia rash arthralgias
Pleural effusions & pleuritic chest pain (MC pulmonary symptoms)
ANA+ve, anti histone Ab
ANTIBIOTIC ASSOCIATED ALVEOLAR HYPOVENTILATION AND HYPERCARBIC RESP FAILURE

AMINOGLYCOSIDES (MC DRUGS)

seen in cases of:

- post operative pts.
- myasthenia like syndromes
- unrecognized myasthenia gravis
ANTICONVULSANTS

- DIPHENYLHYDANTOIN
  1. asymptomatic physiological abnormalities
  2. hypersensitivity syndrome
  3. lymphocytic interstitial pneumonitis
  4. pseudolymphoma syndrome
SALICYLATES

- **ASPIRIN INDUCED ASTHMA**
  - aspirin sensitivity seen in 5% asthmatics
  - SAMPTER’S TRIAD- nasal polyposis, chronic sinusitis, asthma

- **SALICYLATE INDUCED PULM EDEMA**
  - 10-15% of salicylate overdosing
  - metab acidosis with resp alkalosis
  - Significant proteinuria
  - CXRAY- perihilar alveolar infiltrates with pleural effusion and cardiomegaly
**GOLD**

seen in treatment of osteoarthritis, pemphigus

Assoc with HLAB 40 & HLAB 35

typically interstitial pneumonitis
c/f cough fever skin rash peripheral blood eosinophilia

Lung biopsy- alveolar septal thickening

interstitial fibrosis

mononuclear cell infiltrate
PENCILLAMINE

1. Interstitial Lung Diseases

2. Bronchiolitis Obliterans

3. Pulmonary Renal Syndrome
COMPLICATIONS OF ILLICIT DRUG USE

- Alveolar hypoventilation & hypercarbic resp failure
- Endocarditis, septic emboli
- HIV assoc infections
- Tuberculosis
- Complications of central cannulation
  - pneumothorax
  - intravascular infections
  - arterial aneurysms and dissections
- Foreign body granulomatosis
- Opiate induced pulmonary edema
- Cocaine crack lung
  - bronchospasm
  - pneumothorax, pneumomediastinum
  - airway burns
- Non cardiac pulmonary edema
- Pulmonary infiltrates with eosinophilia
- Acute alveolar h’age syndrome
TREATMENT

- DRUG CESSATION
- CORTICOSTEROIDS
### EMPERICAL GUIDELINES FOR USE STEROIDS IN DIRD's

<table>
<thead>
<tr>
<th>Pattern of Involvement</th>
<th>Indication for Steroids</th>
<th>Duration of Treatment</th>
<th>Level of Scientific Evidence†</th>
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<tbody>
<tr>
<td>Laryngeal edema</td>
<td>Y</td>
<td>Days</td>
<td>1</td>
</tr>
<tr>
<td>Sudden severe asthma</td>
<td>Y</td>
<td>Weeks</td>
<td>1</td>
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<tr>
<td>Worsening of asthma</td>
<td>Y</td>
<td>As needed</td>
<td>2</td>
</tr>
<tr>
<td>Bronchiolitis obliterans</td>
<td>Y‡</td>
<td>Months</td>
<td>2</td>
</tr>
<tr>
<td>Classic interstitial pneumonia (NSIP)</td>
<td>Y§</td>
<td>A few weeks or months†</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary infiltrates and eosinophilia</td>
<td>Y§</td>
<td>A few weeks or months†</td>
<td>2, 3</td>
</tr>
<tr>
<td>Amiodarone lung</td>
<td>Y§</td>
<td>6 to 18 mo¶</td>
<td>3</td>
</tr>
<tr>
<td>Organizing pneumonia</td>
<td>Y§</td>
<td>A few months™</td>
<td>3</td>
</tr>
<tr>
<td>Desquamative interstitial pneumonia</td>
<td>Y</td>
<td>A few months ?</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>Y‡</td>
<td>Months</td>
<td>2, 3</td>
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<tr>
<td>Lipoid pneumonia</td>
<td>N</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>?</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>N</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Alveolar hemorrhage</td>
<td>Y?</td>
<td>Months</td>
<td>2</td>
</tr>
<tr>
<td>Hemolytic-uremic syndrome</td>
<td>Y?</td>
<td>?</td>
<td>2</td>
</tr>
<tr>
<td>Veno-occlusive disease</td>
<td>N</td>
<td>–</td>
<td>–</td>
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</tbody>
</table>
All the best..