Appendix 7: Drug-Induced Pulmonary Disease

INTRODUCTION

TABLE A7-1

Drugs That Induce Apnea

Mechanism	Relative Frequency of Reactions
Central nervous system depression	
Narcotic analgesics	F
Barbiturates	F
Benzodiazepines	F
Other sedatives and hypnotics	I
Tricyclic antidepressants	R
Phenothiazines	R
Ketamine	R
Promazine	R
Anesthetics	R
Antihistamines	R
Alcohol	R
Levodopa	R
Oxygen	R
Respiratory muscle dysfunction	
Aminoglycoside antibiotics	I
Polymyxin antibiotics	I
Neuromuscular blockers	I
Quinine	R

Digitalis	R
Myopathy	
Corticosteroids	F
Diuretics	I
Aminocaproic acid	R
Clofibrate	R

F, frequent; I, infrequent; R, rare.

TABLE A7-2

Drugs That Induce Bronchospasm

Mechanism	Relative Frequency of Reactions
Anaphylaxis (IgE-mediated)	
Penicillins	F
Sulfonamides	F
Serum	F
Cephalosporins	F
L-Asparaginase	F
Papain	F
Pancreatic extract	I
Psyllium	I
Subtilase	I
Tetracyclines	I
Allergen extracts	I
Cimetidine	R
Direct airway irritation	
N-acetylcysteine	F
Bisulfite	F

Smoke	F
Smoke inhaled steroids	I
Acetate	R
Crromolyn	R
Precipitating IgG antibodies	
β-Methyldopa	R
Carbamazepine	R
Spiramycin	R
Cyclooxygenase inhibition	
Aspirin/NSAIDs	F
Phenylbutazone	I
Acetaminophen	R
Anaphylactoid mast-cell degranulation	
Iodinated-radiocontrast media	I
Benzalkonium chloride	I
Opioid analgesics	I
Iron-dextran complex	I
Local anesthetics	I
Steroidal anesthetics	I
Platinum	R
Pancuronium bromide	R
Ethylenediamine	R
Pharmacologic effects	
β-Adrenergic agonists	I-F
Cholinergic stimulants	I
Anticholinesterases	R

α-Adrenergic receptor blockers	R
Ethylenediamine tetraacetic acid	R
Unknown mechanisms	
ACE inhibitors	I
Monosodium glutamate	I
Anticholinergics	R
Hydrocortisone	R
Isoproterenol	R
Piperazine	R
Tartrazine	R
Sulfinpyrazone	R
Zinostatin	R
Losartan	R

ACE, angiotensin-converting enzyme; F, frequent; I, infrequent; Ig, immunoglobulin; NSAIDs, nonsteroidal anti-inflammatory drugs; R, rare.

TABLE A7-3

Tolerance of Anti-Inflammatory and Analgesic Drugs in Aspirin-Induced Asthma

Cross-Reactive Drugs	Drugs with No Cross-Reactivity
Diclofenac	Acetaminophen[a]
Diflunisal	Benzydamine
Fenoprofen	Chloroquine
Flufenamic acid	Choline salicylate
Flurbiprofen	Corticosteroids
Hydrocortisone hemisuccinate	Dextropropoxyphene
Ibuprofen	Phenacetina
Indomethacin	Salicylamide
Ketoprofen	Sodium salicylate
Mefenamic acid	
Naproxen	
Noramidopyrine	
Oxyphenbutazone	
Phenylbutazone	
Piroxicam	
Sulindac	
Sulfinpyrazone	
Tartrazine	
Tolmetin	

[a]A very small percentage (5%) of patients with aspirin-hypersensitivity react to acetaminophen and phenacetin.

TABLE A7-4

Drugs That Induce Pulmonary Edema

Mechanism	Relative Frequency of Reactions

Cardiogenic pulmonary edema	
Excessive intravenous fluids	F
Blood and plasma transfusions	F
Corticosteroids	F
β_2-Adrenergic agonists	I
Sodium diatrizoate	R
Hypertonic intrathecal saline	R
Phenylbutazone	R
Noncardiogenic pulmonary edema	
Heroin	F
Methadone	I
Morphine	I
Oxygen	I
Propoxyphene	R
Ethchlorvynol	R
Chlordiazepoxide	R
Salicylate	R
Hydrochlorothiazide	R
Triamterene + hydrochlorothiazide	R
Leukoagglutinin reactions	R
Iron–dextran complex	R
Methotrexate	R
Cytosine arabinoside	R
Nitrofurantoin	R
Dextran 40	R
Fluorescein	R

Amitriptyline	R
Colchicine	R
Nitrogen mustard	R
Epinephrine	R
Metaraminol	R
Bleomycin	R
Iodide	R
Cyclophosphamide	R
VM-26	R

F, frequent; I, infrequent; R, rare.

TABLE A7-5

Drugs That Induce Pulmonary Infiltrates with Eosinophilia (Löffler Syndrome)

Drug	Relative Frequency of Reactions
Nitrofurantoin	F
para-Aminosalicylic acid	F
Amiodarone	F
Iodine	F
Captopril	F
Bleomycin	F
L-tryptophan	F
Methotrexate	F
Phenytoin	F
Gold salts	F
Sulfonamides	I
Penicillins	I
Carbamazepine	I

Granulocyte-macrophage colony-stimulating factor	I
Imipramine	I
Minocycline	I
Nilutamide	I
Propylthiouracil	I
Sulfasalazine	I
Tetracycline	R
Procarbazine	R
Cromolyn	R
Niridazole	R
Chlorpromazine	R
Naproxen	R
Sulindac	R
Ibuprofen	R
Chlorpropamide	R
Mephenesin	R

F, frequent; I, infrequent; R, rare.

TABLE A7-6

Drugs That Induce Pneumonitis and/or Fibrosis

Drug	Relative Frequency of Reactions
Oxygen	F
Radiation	F
Bleomycin	F
Busulfan	F
Carmustine	F
Hexamethonium	F

Paraquat	F
Amiodarone	F
Mecamylamine	I
Pentolinium	I
Cyclophosphamide	I
Practolol	I
Methotrexate	I
Mitomycin	I
Nitrofurantoin	I
Methysergide	I
Sirolimus	I
Azathioprine, 6-mercaptopurine	R
Chlorambucil	R
Melphalan	R
Lomustine and semustine	R
Zinostatin	R
Procarbazine	R
Teniposide	R
Sulfasalazine	R
Phenytoin	R
Gold salts	R
Pindolol	R
Imipramine	R
Penicillamine	R
Phenylbutazone	R
Chlorphentermine	R

Fenfluramine	R
Leflunomide	R
Mefloquine	R
Pergolide	R

F, frequent; I, infrequent; R, rare.

TABLE A7-7

Possible Causes of Pulmonary Fibrosis

- Idiopathic pulmonary fibrosis (fibrosing alveolitis)
- Pneumoconiosis (asbestosis, silicosis, coal dust, talc berylliosis)
- Hypersensitivity pneumonitis (molds, bacteria, animal proteins, toluene diisocyanate, epoxy resins)
- Smoking
- Sarcoidosis
- Tuberculosis
- Lipoid pneumonia
- Systemic lupus erythematosus
- Rheumatoid arthritis
- Systemic sclerosis
- Polymyositis/dermatomyositis
- Sjögren syndrome
- Polyarteritis nodosa
- Wegener granuloma
- Byssinosis (cotton workers)
- Siderosis (arc welders' lung)
- Radiation
- Oxygen
- Chemicals (thioureas, trialkylphosphorothioates, furans)
- Drugs (see Tables A7-5, A7-6, and A7-8)

TABLE A7-8

Drugs That May Induce Pleural Effusions and Fibrosis

Mechanism	Relative Frequency of Reactions
Idiopathic	
Methysergide	F
Practolol	F
Pindolol	R
Methotrexate	R
Nitrofurantoin	R
Drug-induced lupus syndrome	
Procainamide	F
Hydralazine	F
Isoniazid	R
Phenytoin	R
Mephenytoin	R
Griseofulvin	R
Trimethadione	R
Sulfonamides	R
Phenylbutazone	R
Streptomycin	R
Ethosuximide	R
Tetracycline	R
Pseudolymphoma syndrome	
Cyclosporine	R
Phenytoin	R

F, frequent; I, infrequent; R, rare.

(*See e/Chapter 47, Drug-Induced Pulmonary Diseases, authored by Hengameh H. Raissy and Michelle Harkins, for a more detailed discussion of this topic.*)