TABLE 17-4 COMMON DRUG-INDUCED LUNG DISEASES

DRUG	DOSE RELATIONSHIP	MANIFESTATION
CHEMOTHERAPEUTIC		
Bevacizumab	Acute	Hemoptysis, pulmonary hemorrhage
Bleomycin	Acute or delayed, >450 U increases risk	Pneumonitis, fibrosis, OP, lung nodules
Busulfan	Chronic	Fibrosis, alveolar proteinosis
Cyclophosphamide	Chronic	Fibrosis, OP
Cytosine arabinoside	Acute	Pulmonary edema, ARDS
Gefitinib	Acute	Pulmonary fibrosis, interstitial pneumonitis, diffuse alveolar damage
Gemcitabine	Acute	Dyspnea, bronchospasm, capillary leak syndrome with pulmonary edema, ARDS, alveolar hemorrhage
Imatinib	Acute, chronic	Pulmonary edema, pneumonitis
Interferon alfa	Chronic	Sarcoidosis
Irinotecan	Acute	Pneumonitis
Methotrexate	Acute or chronic	Hypersensitivity pneumonitis, resolves with discontinuation, OP
Mitomycin C	Acute or delayed	Pneumonitis, ARDS, OP, hemolytic uremic syndrome
Paclitaxel and docetaxel	Acute	Interstitial and hypersensitivity pneumonitis
ANTIMICROBIAL		
Nitrofurantoin	Acute or chronic	Acute pneumonitis, chronic fibrosis
Sulfasalazine	Acute or chronic	Pulmonary infiltrates with eosinophilia, OP
CARDIOVASCULAR		
Amiodarone	Acute or chronic, >400 mg/day	Pneumonitis, fibrosis
Flecainide	Acute	ARDS, LIP
Tocainide	Weeks or months	Pneumonitis
Procainamide	Subacute or chronic	Drug-induced SLE, pleural effusions, pulmonary infiltrates
ANTI-INFLAMMATORY		
Aspirin	Acute	Pulmonary edema, bronchospasm
ILLICIT		
Opiates	Acute	Pulmonary edema
Cocaine	Acute	Pulmonary edema, diffuse alveolar damage, pulmonary hemorrhage, OP
Talc (in intravenous and inhaled illicit drugs)	Acute or chronic	Granulomatous interstitial fibrosis, granulomatous pulmonary artery occlusion, particulate embolization
TOCOLYTIC		
Terbutaline, albuterol, ritodrine	Acute	Pulmonary edema

ARDS, Acute respiratory distress syndrome; OP, organizing pneumonia; LIP, lymphoid interstitial pneumonia; SLE, systemic lupus erythematosus.

toxicities of various drugs, and it is searchable by drug name and by pattern of lung involvement.

For a deeper discussion on this topic, please see Chapter 94, "Physical and Chemical Injuries of the Lung," in Goldman-Cecil Medicine, *25th Edition.*

PULMONARY VASCULITIS AND DIFFUSE ALVEOLAR HEMORRHAGE

Diffuse Alveolar Hemorrhage

Definition and Epidemiology

Diffuse alveolar hemorrhage (DAH) syndromes encompass a diverse group of entities that are characterized by disruption of the alveolar-capillary membrane, resulting in bleeding into the alveolar spaces from the alveolar capillaries and intra-alveolar accumulation of red blood cells. DAH is a rare condition of uncertain incidence in the general population, but it occurs with increased frequency in specific patient populations, such as those after hematopoietic stem cell transplantation.

Pathology

The DAH syndromes are characterized by three distinct histologic patterns. Bland pulmonary hemorrhage is caused by alveolar hemorrhage without inflammation or destruction of the alveolar structures. This pattern is seen in conditions with elevated pulmonary capillary hydrostatic pressure, such as congestive heart failure or mitral stenosis, or with the use of anticoagulation medications.

DAH can be seen in diffuse alveolar damage (DAD), which is caused by a variety of pulmonary infections, connective tissue diseases, and medications. DAD is also seen in acute respiratory distress syndrome (ARDS) from any cause. Histologically, alveolar walls appear edematous and are lined with hyaline membranes.

The most common histologic pattern seen on lung biopsy obtained from patients with DAH is pulmonary capillaritis, which is characterized by neutrophilic infiltration of the alveolar septa. It sequentially leads to necrosis, loss of capillary structural integrity, and extravasation of red blood cells into the interstitium and alveolar spaces. This pattern is seen in a variety of connective tissue diseases and in some of the pulmonary vasculitides.

Clinical Presentation

All DAH syndromes are characterized by the abrupt onset of cough and dyspnea. Hemoptysis is common but not universal; it may be absent in up to one third of patients with DAH. Fever may occur in patients with underlying vasculitis. Physical