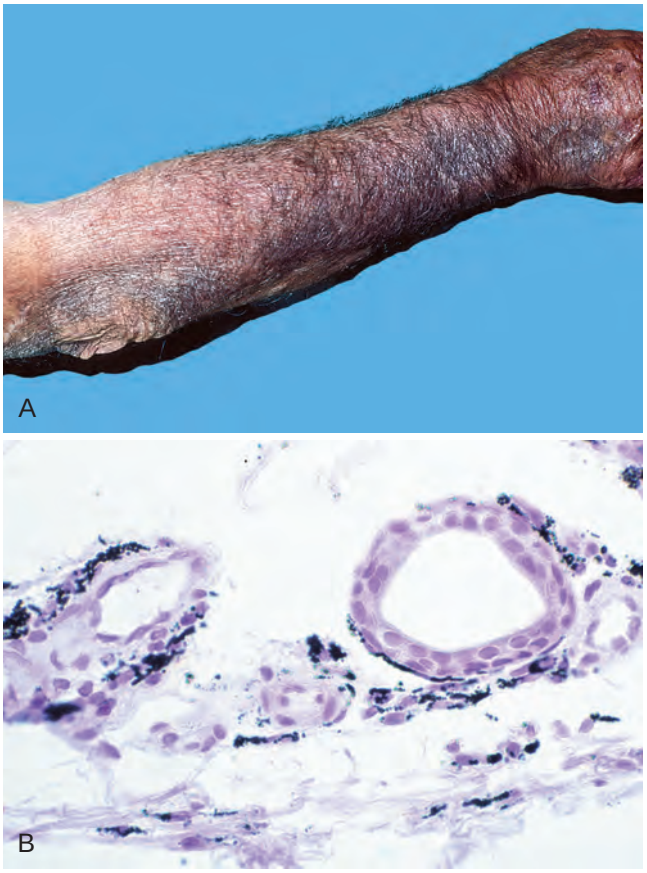

Figure 9-13 Adverse drug reaction. Skin pigmentation caused by minocycline, a long-acting tetracycline derivative. **A,** Diffuse blue-gray pigmentation of the forearm; **B,** Deposition of drug metabolite/iron/melanin pigment particles in the dermis. (Courtesy Dr. Zsolt Argenyi, Department of Pathology, University of Washington, Seattle, Wash.)

Much more common are drug reactions that are due to direct actions of the drug or to immunologically based hypersensitivity reactions. Drug-induced hypersensitivity reactions most commonly present as skin rashes, but they may also mimic autoimmune disorders such as systemic lupus erythematosus (Chapter 6), hemolytic anemia, and immune thrombocytopenia (Chapter 13). Adverse drug reactions affect almost 10% of patients admitted to a hospital.

The number of fatal adverse drug reactions is debated, but by some accounts may be as high as 140,000 deaths per year. Table 9-5 lists common pathologic findings in adverse drug reactions and the drugs most frequently involved. Many of the drugs that produce adverse reactions, such as antineoplastic agents, are highly potent, and the adverse reactions are accepted risks of the treatment. In this section, adverse reactions to commonly used drugs are examined, first discussing the unwelcome effects of anticoagulants, menopausal hormone therapy (MHT), oral contraceptives (OCs), and anabolic steroids and then discussing the effects of acetaminophen and aspirin, because all are commonly used.

Anticoagulants

In 2011, the two drugs that most frequently caused adverse reactions reported to the Food and Drug Administration were the oral anticoagulants warfarin and dabigatran. Warfarin is an antagonist of vitamin K, and dabigatran is a direct inhibitor of thrombin. The principal complications associated with both of these medications are bleeding, which can be fatal, and thrombotic complications such as embolic stroke stemming from undertreatment. Warfarin is inexpensive and its effects are easy to monitor, but many drugs and foods rich in vitamin K either interfere with its metabolism or abrogate its function. As a result, maintaining anticoagulation in a relatively safe therapeutic range can be problematic. Pharmacologic interactions of drugs with dabigatran metabolism have not been described, but many bleeding complications nevertheless occur. It is primarily used to prevent thromboembolism in patients

Table 9-5 Common Adverse Drug Reactions and Their Agents

Reaction	Major Offenders
Bone Marrow And Blood Cells*	
Granulocytopenia, aplastic anemia, pancytopenia	Antineoplastic agents, immunosuppressives, chloramphenicol
Hemolytic anemia, thrombocytopenia	Penicillin, methyldopa, quinidine, heparin
Cutaneous	
Urticaria, macules, papules, vesicles, petechiae, exfoliative dermatitis, fixed drug eruptions, abnormal pigmentation	Antineoplastic agents, sulfonamides, hydantoins, some antibiotics, and many other agents
Cardiac	
Arrhythmias	Theophylline, hydantoins, digoxin
Cardiomyopathy	Doxorubicin, daunorubicin
Renal	
Glomerulonephritis	Penicillamine
Acute tubular necrosis	Aminoglycoside antibiotics, cyclosporin, amphotericin B
Tubulointerstitial disease with papillary necrosis	Phenacetin, salicylates
Pulmonary	
Asthma	Salicylates
Acute pneumonitis	Nitrofurantoin
Interstitial fibrosis	Busulfan, nitrofurantoin, bleomycin
Hepatic	
Fatty change	Tetracycline
Diffuse hepatocellular damage	Halothane, isoniazid, acetaminophen
Cholestasis	Chlorpromazine, estrogens, contraceptive agents
Systemic	
Anaphylaxis	Penicillin
Lupus erythematosus syndrome (drug-induced lupus)	Hydralazine, procainamide
Bleeding	Warfarin, dabigatran
Central Nervous System	
Tinnitus and dizziness	Salicylates
Acute dystonic reactions and parkinsonian syndrome	Phenothiazine antipsychotics
Respiratory depression	Sedatives

*Affected in almost half of all drug-related deaths.