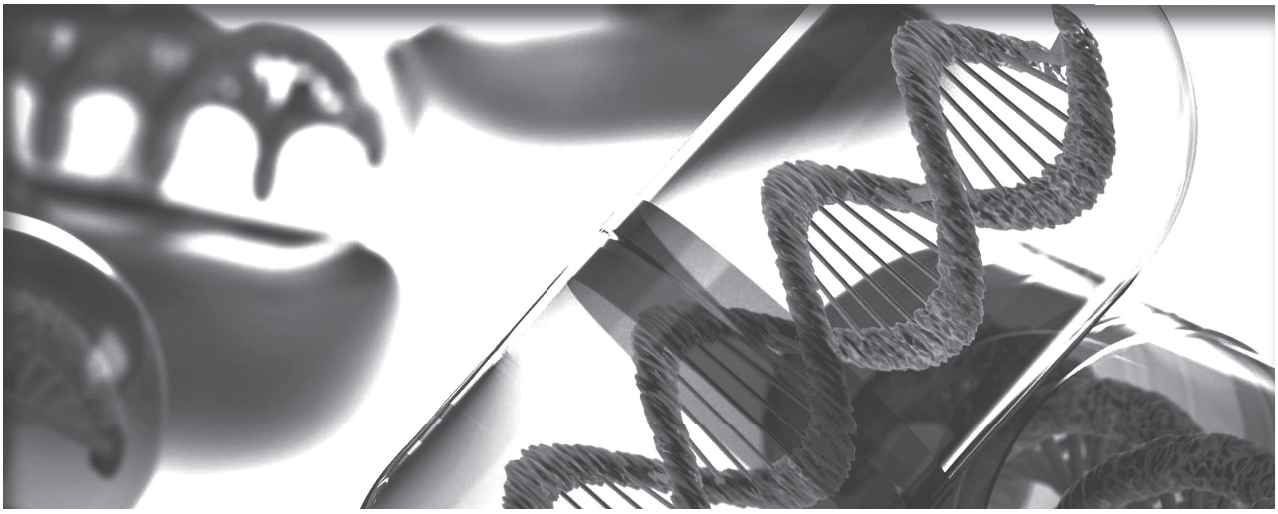

CHAPTER 29

Valvular and Pericardial Heart Disease

Sarah A. Spinler and Frank E. Silvestry

Although cardiovascular disease is the leading cause of death in the United States, valvular and pericardial disease remain relatively uncommon as compared with other cardiovascular diseases such as hypertension and ischemic heart disease. Valvular heart disease accounts for approximately 3.1% of all cardiovascular deaths in the United States.[1] Pericarditis is responsible for approximately 5% of emergency department visits for chest pain and results in 0.1% of hospital admissions.[2] Drug therapy may result in a wide variety of cardiovascular complications, including valvular heart disease and pericardial disease. Although more commonly a result of degenerative or rheumatic processes, valvular heart disease (which includes aortic, mitral, and tricuspid regurgitation) has been reported to occur in association with or as a result of drug therapy. Pericardial disease associated with drug therapy includes pericarditis due to drug-induced systemic lupus erythematosus (SLE)-like syndrome (with or without cardiac tamponade), acute pericarditis, constrictive pericarditis, and hemopericardium. This chapter will review the manifestations of drug-induced valvular and pericardial heart disease.

CAUSATIVE AGENTS

Drugs that have been reported to induce valvular or pericardial heart disease are listed in **Table 29-1**.[3-156] Three main drug classes that have been associated with the development of new valvular or pericardial heart disease are: ergot alkaloids (for migraine headache), ergot-derived dopamine agonists (for Parkinson disease), and 5-hydroxytryptamine (5-HT or serotonin) uptake regulators/inhibitors for weight loss. The earliest reports of drug-induced valvular heart disease appeared in the 1960s, in association with the ergot alkaloids ergotamine and methysergide.[16,17,23,62,63] The anorectic agents fenfluramine and its D-isomer dexfenfluramine, as well as fenfluramine in combination with phentermine, a combination commonly referred to as "fen-phen," have been associated with left-sided regurgitant valvular lesions.[4-15,18-21] Both fenfluramine and dexfenfluramine were withdrawn from the U.S. market in 1997, after reports of valvular heart disease associated with these agents began to appear.[8,19] The ergot-derived dopamine agonists bromocriptine, cabergoline, and pergolide, used to treat Parkinson disease, have

Table 29-1 Agents Implicated in Drug-Induced Valvular and Pericardial Heart Disease

Drug	Incidence	Level of Evidence[a]
AORTIC REGURGITATION		
Bromocriptine[3,97,125]	NK	B
Cabergoline[77,79,80,86-91,97,126,127]	16.7–68.8%	B
Dexfenfluramine[4-15]	6.6–38%	B
Dexfenfluramine in combination with phentermine[4-15]	6.6–38%	B
Ergotamine[16,17]	NK	C
Fenfluramine[4-15,18-21]	6.6–38%	B
Fenfluramine in combination with phentermine[5-15,18-21]	6.6–38%	B
MDMA[98]	14%	B
Methysergide[59,62,63]	0.02%	B
Pergolide[22,76-78,80,81,82-88,90-97,127]	0.005–67%	B
MITRAL REGURGITATION		
Bromocriptine[3,97,125]	NK	C
Cabergoline[77,80,86-91,97,126,127]	28.6–68.8%	B
Dexfenfluramine[4-15]	1.3–3.5%	B
Dexfenfluramine in combination with phentermine[4-15]	1.3–3.5%	B
Ergotamine[16,17,23]	NK	C
Fenfluramine[4-15,18-21]	1.3–3.5%	B
Fenfluramine in combination with phentermine[4-15,18-21]	1.3–3.5%	B
MDMA[98]	14%	B
Methysergide[59,62,63]	0.02%	B
Pergolide[22,76-78,80-88,90-97,127]	0.005–75%	B
TRICUSPID REGURGITATION		
Bromocriptine[3,97,125]	NK	C
Cabergoline[80,88,126,127]	NK	B
Ergotamine[16,23]	NK	C
MDMA[98]	NK	C
Methysergide[59,62,63]	0.02%	B
Pergolide[22,76-78,80-88,90-97,127]	0.005–78%	B
MITRAL STENOSIS		
Ergotamine[16,17,23]	NK	C
Methysergide[59,62,63]	NK	B
ACUTE EFFUSIVE PERICARDITIS		
Adalimumab[155,156]	NK	C
Azactidine[124]	NK	C
Balsalazide[137,138]	NK	C
Busulfan[24,25]	NK	C
Clozapine[99-109,156-159]	NK	B
Cromolyn sodium[26]	NK	C
Cyclophosphamide[24,27,28,141]	NK	C
Cytarabine[24,29-31]	NK	C
Dantrolene sodium[32,33]	NK	C