# Cardiovascular Drugs Our Patients Take


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## Conflict of Interest Disclosure Statement

- Dr. Ojeda Díaz reports no conflicts of interest associated with this course.
- Dr. Huber has done consulting work for Procter & Gamble and serves on the dentalcare.com Advisory Board.

## Introduction - Cardiovascular Drugs

Cardiac risk associated with dental treatment depends on procedure-specific and patient-specific factors. Important co-determinants of patient-specific risk factors include disease-related factors, including therapeutic variables. Cardiovascular Drugs Our Patients Take presents relevant information for oral healthcare providers, predicated on the mechanisms of action and indications for the use of cardiovascular drugs.

## Course Contents



## Overview

This course (1) presents an overview of cardiovascular pharmacology, (2) identifies prevalent cardiovascular diagnoses in ambulatory settings based on the mechanisms of action of cardiovascular drugs dispensed by U.S. community pharmacies, and (3) discusses key points for practice.

## Learning Objectives

**Upon completion of this course, the dental professional should be able to:**

- Recognize cardiovascular drugs by name.
- Discuss the mechanisms of action of cardiovascular drugs.
- Identify prevalent cardiovascular diseases.
- Discuss key points for practice.

## Introduction

A patient's overall health status determines the patient's ability to undergo and respond to dental care. Consequently, patient-specific problems that may interfere with the clinical process must be identified. In determining perioperative risk, clinicians must consider multiple factors, including past and present illnesses; major hospitalizations; adverse drug reactions; the prescription and OTC medication profile; special diets; vital signs; and functional capacity.[1]

In the United States there are approximately 500 Food and Drug Administration (FDA)-approved active ingredients, i.e., therapeutic agents, available in several thousand different formulations.[2] **ClinCalc DrugStats** provides prescription drug utilization data estimates based on the annual Medical Expenditure Panel Survey (MEPS).[2] The most recently published report reflects prescriptions for the year 2020. The Top 300 Prescription Drugs represent 60% of all available therapeutic agents and 97% of all prescription drugs dispensed by U.S. community pharmacies.[2]

## Cardiovascular Drugs in the Top 300

Therapeutic agents in the Top 300 Prescription Drugs dispensed by U.S. community pharmacies indicated for the treatment of cardiovascular diseases fall into 6 major categories: (1) drugs that regulate cholesterol and lipoprotein metabolism, (2) drugs that regulate extracellular fluid volume, (3) drugs that regulate vascular tone, (4) drugs that regulate cardiac rhythm, (5) drugs that regulate cardiac contractility, and (6) drugs that affect hemostasis, i.e., platelet function and coagulation.[2-9]

Oral healthcare providers (OHCPs) need to (1) recognize medications by name (generic and/or brand name); (2) know their mechanisms of action and indications for use; (3) be aware of the spectrum of their ADRs and be actively involved in monitoring for and reporting such adverse effects; (4) have access to reliable informational resources. **DailyMed** is the official repository for FDA-approved individual drug-related clinically relevant data and it is a useful online resource for clinicians.[10]

The Council of International Organizations of Medical Sciences in their publication "Reporting Adverse Drug Reactions: Definitions of Terms and Criteria for Their Use" codified ADRs under 21 major headings and defined 179 conditions considered reportable.[11] ADRs range from mild to severe and can lead to hospitalization, permanent disability, and even death. The issue of identifying and addressing ADRS cannot be overstated. ADRs occur in up to 35% of older outpatients and 44% of older inpatients. Patients taking 7 or more medications have an 80% risk of experiencing an ADR and ADRs account for 10% of all emergency department visits.[12]

Adverse drug effects may be explained by one of five mechanisms: (1) "on-target" adverse reactions, (2) "off-target" adverse reactions, (3) cytotoxic reactions, (4) immune-mediated reactions, and (5) idiosyncratic reactions, i.e., reactions of unknown mechanisms.[13] A discussion of mechanisms of ADRs, common ADRs associated with drugs dispensed by U.S. community pharmacies, and less common ADRs that may manifest in the head and neck area is presented elsewhere.[13-15]

## Drugs that Regulate Lipoprotein Metabolism

Lipoproteins, differentiated on the basis of density, size, and protein content, are essential for the biogenesis of plasma membranes and maintenance of their integrity. They also serve as sources of energy, hormone precursors, and signaling molecules.[3] In blood, lipoproteins transport cholesterol and triglycerides. Abnormalities of lipoprotein metabolism appear to be the result of genetic factors, which modify the sensitivity of individuals to adverse dietary habits and to sedentary lifestyles.

Elevated cholesterol-rich low-density lipoproteins (LDLs) and lipoproteins that are rich in triglycerides (TGs), and decreased levels of high-density lipoproteins (HDLs) are strongly associated with **atherosclerosis**.[3] Diet and exercise can reduce total plasma cholesterol concentrations by as much as 25%. If this approach is insufficient to normalize lipid levels drug therapy is initiated. Drugs in the top 300 that regulate lipoprotein metabolism (Table 1) fall into four major classes.[2,3,10]

## Drugs that Regulate Extracellular Fluid Volume

About ⅔ of total body water is intracellular and ⅓ is extracellular. Nearly ¾ of the extracellular fluid (ECF) resides in the interstitial space. The remaining ¼ of the ECF, a determinant of tissue perfusion, i.e., the distribution of O2 and nutrients, is in plasma. Depletion of plasma volume (1) activates the renin-angiotensin-aldosterone system (RAAS), (2) promotes antidiuretic hormone release, and (3) increases renal sympathetic activity.[4] Volume overload promotes the release of natriuretic peptides.[4]

**Table 1. Drugs that Affect Cholesterol and Lipoprotein Metabolism.[2,3,10]**

| Drugs (Rank/300) | Mechanisms of Action | Common Indications |
|---|---|---|
| **Inhibitors of cholesterol synthesis**<br>• Atorvastatin (1)<br>• Simvastatin (13)<br>• Rosuvastatin (17)<br>• Pravastatin (34)<br>• Lovastatin (99) | **Inhibit HMG-CoA reductase, the rate-limiting enzyme in cholesterol synthesis**<br>• Decrease LDL<br>• Decrease TG<br>• Increase HDL | • Hypercholesterolemia<br>• Prophylaxis for coronary atherosclerosis |
| **Inhibitors of cholesterol absorption**<br>• Ezetimibe (100) | **Decrease cholesterol transport into enterocytes**<br>• Decrease LDL<br>• Decrease TG | • Hypercholesterolemia |
| **Fibrates**<br>• Fenofibrate (95)<br>• Gemfibrozil (189) | **Agonists of peroxisome proliferator-activated receptor α (PPARα) in hepatocytes**<br>• Decrease LDL<br>• Decrease TG<br>• Increase HDL | • Hypertriglyceridemia |
| **Omega-3 fatty acids**<br>• Omega-3-acid ethyl ester (199) | **Regulate hepatic nuclear transcription factors to reduce TG synthesis and increase fatty acid oxidation**<br>• Reduces TG | • Hypertriglyceridemia |

Excessive Na+ and H2O retention, primarily a result of renal abnormalities, is responsible for **volume-based hypertension**.[4] Pathological Na+ and H2O retention can also lead to **transudative edema associated with heart failure, cirrhosis of the liver, and nephrotic syndrome**[4] Drugs in the top 300 that regulate extracellular fluid volume (Table 2) can be divided into three broad classes: (1) agents that act directly on the nephron to increase renal Na+ excretion, (2) drugs that modulate the RAAS, and (3) drugs that modulate the natriuretic peptide (NP) system.[2,4,10,16]

## Drugs that Regulate Vascular Tone

Vascular tone is another key determinant of tissue perfusion. Vascular smooth muscle cells are the functional regulatory units that integrate a variety of signals initiated by (1) local factors (e.g., $H^+$, $CO_2$, stretch), (2) endothelium-derived signaling molecules (e.g., nitric oxide, prostacyclin), (3) neurotransmitters (e.g., epinephrine), and (4) hormones (e.g., vasopressin) to optimize vascular tone.[5] Ultimately, vascular smooth muscle tone is determined by the intracellular $Ca^{2+}$ ion concentration.

Drugs in the top 300 that regulate vascular tone (Table 3) include (1) $Ca^{2+}$ channel blockers, (2) β1-adrenoceptor antagonists, (3) α1-adrenoceptor antagonists, (4) α2-adrenoceptor agonists, (5) $K^+$ channel openers, (6) nitric oxide donors, and (7) late sodium current blockers.[2,5,6,10] TThese drug categories are intended for the management of **systemic and pulmonary hypertension, ischemic heart disease** (i.e., chronic coronary artery disease and acute coronary syndromes), and **congestive heart failure**.[5,6]

## Drugs that Regulate Cardiac Rhythm

The heart is both a mechanical and an electrical organ. The electrical component controls the rhythm of the heart. Under the influence of the autonomic nervous system, the sinoatrial (SA) node initiates action potentials, i.e., paces the heart at normal resting rates between 60 and 100 beats per minute.[1] Other pacemaker cell are found in the atrioventricular (AV) node, and the ventricular conducting system. Abnormal impulse generation and/or impulse conduction underlie **cardiac arrhythmias**.[6,7]

The most common cause of cardiac arrhythmias is chronic coronary artery disease; less commonly, arrhythmias may be related to cardiomyopathies, valvular and congenital heart disease, primary electrophysiological disorders, and genetically determined ion-channel abnormalities.[1,7] Drugs in the top 300 that regulate cardiac rhythm (Table 4) include: (1) $Na^+$ channel blockers, (2) $\beta_1$-adrenoceptor antagonists, (3) $K^+$ channel blockers, (4) $Ca^{2+}$ channel blockers, and (5) cardiac glycosides.[6,7,10]

## Drugs that Regulate Cardiac Contractility

Cardiac muscles contract when action potentials depolarize plasma membranes. Decreased cardiac contractility is associated with dysregulation of calcium homeostasis, changes in cAMP-dependent regulation of contractile proteins, and alterations in β-adrenoceptor activity.[8] The most common causes of contractile dysfunction include coronary artery disease resulting in myocardial infarction, systemic hypertension, and valvular disease. Progressive contractile dysfunction leads to **heart failure** (HF).[8]

The central role of intracellular $Ca^{2+}$ and cAMP in cardiac muscle contraction provides a basis for the classification of agents with positive inotropic effects as (1) cardiac glycosides, (2) $\beta_1$-adrenoceptor agonists, and (3) phosphodiesterase inhibitors.[8] Currently, the cardiac glycoside digoxin, is the only drug in the top 300 that regulates cardiac contractility (Table 4).[2,8,10] It inhibits $Na^+/K^+$-ATPase and thereby increases intracellular $Ca2^+$ concentration in myocytes and exerts a positive inotropic effect.[8]

## Drugs that Affect Hemostasis

A well-regulated hemodynamic system keeps blood fluid and clot-free in normal vessels and forms a localized clot rapidly in response to vessel injury.[9] The first step in the formation of a localized clot at the site of vessel injury is vasoconstriction. This is followed by platelet aggregation and the formation of a primary hemostatic plug. Secondary hemostasis, also known as the coagulation cascade, leads to the formation of a stable, durable clot. An abnormal extension of hemostasis is thrombosis.[9]

**Thrombosis** is characterized by the uncontrolled enlargement of clots that occlude blood vessels

## Table 2. Drugs that Regulate Volume.[2,4,10]

| Drugs (Rank/300) | Mechanisms of Action | Common Indications |
|---|---|---|
| **Thiazide diuretics**<br>• Hydrochlorothiazide (11)<br>• Chlorthalidone (133) | **Inhibit $Na^+$ reabsorption by cells of the distal convoluted tubule** | • Edema<br>o Congestive heart failure<br>o Cirrhosis of the liver<br>o Corticosteroid and estrogen therapy<br>o Renal disease<br>• Hypertension |
| **Loop diuretics**<br>• Furosemide (19)<br>• Torsemide (213)<br>• Bumetanide (270) | **Inhibit $Na^+$ reabsorption by cells of the Loop of Henle** | • Edema<br>o Congestive heart failure<br>o Cirrhosis of the liver<br>o Renal disease<br>• Hypertension |
| **Neprilysin inhibitor**<br>• Sacubitril* | **Inhibit the degradation of natriuretic peptide thereby increasing vasodilation** | • Heart failure |
| **Mineralocorticoid receptor antagonist (MRA) diuretics**<br>• Spironolactone (51)<br>• Triamterene** | **Spironolactone inhibits $Na^+$ reabsorption by inhibiting aldosterone action**<br><br>**Triamterene inhibits $Na^+$ reabsorption by principal cells of the collecting duct** | • Primary hyperaldosteronism<br>• Edema<br>o Heart failure<br>o Cirrhosis of the liver<br>o Nephrotic syndrome<br>• Hypertension<br>• Hypokalemia |
| **Angiotensin converting enzyme (ACE) inhibitors**<br>• Lisinopril (4)<br>• Benzapril (141)<br>• Ramipril (196)<br>• Quinapril (253) | **Inhibit the conversion of angiotensin (AT) I to AT II thereby decreasing**<br>• Arteriolar vasoconstriction<br>• Aldosterone synthesis<br>• $Na^+$ reabsorption by cells of renal proximal tubule<br>• ADH release<br><br>**Inhibit the degradation of bradykinin and thereby increasing vasodilation** | • Hypertension<br>• Heart failure<br>• Acute myocardial infarction |
| **Angiotensin II receptor blockers**<br>• Losartan (9)<br>• Valsartan (123)<br>• Olmesartan (139)<br>• Irbesartan (148)<br>• Telmisartan (248) | **Antagonize the action of AT II at $AT_1$ receptors**<br><br>**May indirectly increase $AT_2$-receptor-related vasodilation** | • Hypertension<br>• Nephropathy in type 2 diabetic patients |
| **Sodium-glucose cotransporter 2 (SGLT2) inhibitor**<br>• Empagliflozin (102)<br>• Dapagliflozin (217) | **Inhibit $Na^+$ reabsorption by cells of the distal convoluted tubule** | • Type 2 diabetes<br>• Congestive heart failure |

*Not available as single agent; see Table 6 Combination Cardiovascular Drugs

**Not a top 300 single agent; see Table 6 Combination Cardiovascular Drugs

**Table 3. Drugs that Regulate Vascular Tone.**[2,5,6,10]

| Drugs (Rank/300) | Mechanisms of Action | Common Indications |
|---|---|---|
| **Calcium channel blockers**<br>• Amlodipine (5)<br>• Diltiazem (76)<br>• Nifedipine (135)<br>• Verapamil (151) | **Block voltage-gated L-type $Ca^{2+}$ channels and thereby cause**<br>• Vasodilation<br>• Depressed cardiac contractility<br>• Depressed SA-node automaticity<br>• Depressed AV-node conduction velocity | • Hypertension<br>• Stable angina pectoris<br>• Vasospastic angina<br>• Unstable angina pectoris |
| **$\beta_1$-adrenoceptor antagonists**<br>• Metoprolol (6)<br>• Carvedilol (26)<br>• Atenolol (53)<br>• Propranolol (88)<br>• Labetalol (210)<br>• Nebivolol (239)<br>• Bisoprolol (267) | **Block $\beta_1$-adrenoceptors**<br>• Propranolol and nadolol also block $\beta_2$-adrenoceptors<br>• Labetalol and carvedilol also block $\beta_2$- and $\alpha_1$-adrenoceptors | • Hypertension<br>• Angina pectoris<br>• Post-MI syndrome<br>• Heart failure |
| **$\alpha_1$-adrenoceptor antagonists**<br>• Prazosin (190)<br>• Doxazosin (209)<br>• Terazosin (211) | **Block the binding of catecholamines to $\alpha_1$-adrenoceptors** | • Benign prostatic hypertrophy<br>• Hypertension |
| **$\alpha_2$-adrenoceptor agonists**<br>• Clonidine (75)<br>• Guanfacine (300) | **Selectively activate central $\alpha_2$-adrenoceptors and thereby inhibit sympathetic outflow from the CNS** | • Hypertension |
| **$K^+$ channel openers**<br>• Hydralazine | **Open $K^+$ channels in the plasma membrane of vascular smooth muscles thereby preventing the opening of $Ca^{2+}$ channels causing arterial vasodilation** | • Hypertension |
| **Nitric oxide donors**<br>• Isosorbide (114)<br>• Nitroglycerin (165)<br>• Isosorbide dinitrate (299) | **Release NO, which activates guanylyl cyclase and increases dephosphorylation of myosin light chain in vascular smooth muscle causing vasodilation** | • Acute angina pectoris (nitroglycerin)<br>• Prophylaxis for angina pectoris due to ischemic heart disease (isosorbide and isosorbide dinitrate) |
| **Late sodium current blocker**<br>• Ranolazine (258) | **Inhibits late inward Na current in myocardium, decreasing $Na^+$ and $Ca^{2+}$ overload, resulting in less diastolic stiffness** | • Chronic angina pectoris |

**Table 4. Drugs that Affect Cardiac Rhythm and Cardiac Contractility.**[2,6-8,10]

| Drugs (Rank/300) | Mechanisms of Action | Common Indications |
|---|---|---|
| **Class IC antiarrhythmics**<br>• Flecainide (188) | **Block voltage-gated $Na^+$ channels in ventricular myocytes** | • Sustained ventricular tachycardia<br>• Paroxysmal supraventricular tachycardia<br>• Paroxysmal atrial fibrillation/flutter |
| **Class II antiarrhythmics**<br>• Propranolol (88) | **Block $\beta_1$-adrenoceptors in SA and AV nodal cells** | • Supraventricular and ventricular arrhythmias precipitated by sympathetic stimulation |
| **Class III antiarrhythmics**<br>• Amiodarone (198)<br>• Sotalol (296) | **Block $K^+$ channels and prolong repolarization**<br><br>**Sotalol exhibits both β-adrenoreceptor blocking and cardiac action potential duration prolongation** | • Recurrent and unstable ventricular arrhythmias<br>• Maintain normal sinus rhythm in patients with symptomatic atrial flutter or atrial fibrillation |
| **Class IV antiarrhythmics**<br>• Diltiazem (76)<br>• Verapamil (151) | **Block voltage-gated L-type $Ca^{2+}$ channels and thereby**<br>• Decrease excitability of SA nodal cel<br>• Prolong AV nodal conduction | • Paroxysmal supraventricular tachycardias |
| **Cardiac glycosides**<br>• Digoxin (237) | **Inhibit $Na^+/K^+$-ATPase leading to increased $Ca^{2+}$ concentration in myocytes**<br>• Positive inotropic effect<br><br>**Prolong refractory period at AV node**<br>• Slow conduction velocity | • Systolic heart failure<br>• Supraventricular arrhythmias<br>o Atrial flutter<br>o Atrial fibrillation<br>o Paroxysmal atrial tachycardia |

as a result of (1) injury of the endothelium associated with hyperlipidemia and hypertension; (2) abnormal blood flow, i.e. turbulence or stasis associated with atherosclerosis, arrhythmias, valvular problems, and heart failure, and (3) genetic or acquired hypercoagulability.[9] Drugs in the top 300 that affect hemostasis (Table 5) fall into two major categories: antiplatelet agents and anticoagulants.[2,9,10]

## Key Points for Practice

In 2020, there were 52 single cardiovascular agents and 8 combination agents (see Table 6) that were in the top 300 prescription drugs dispensed by U.S. community pharmacies.[2] Predicated on the mechanisms of action of these drugs, the most common cardiovascular conditions encountered in ambulatory settings include **hypertension** (HTN); **ischemic heart disease** (IHD), i.e., chronic coronary artery disease (CAD) and acute coronary syndromes (ACS); **cardiac arrhythmias**; **heart failure** (HF); and **thromboembolic complications**.[2-10,17]

### Hypertension

Blood pressure (BP), the lateral pressure exerted by blood in a unit area of the blood vessel wall, is a function of cardiac output and peripheral vascular resistance.[1] When the blood volume exceeds the limited volume capacity of the vascular compartment because of volume expansion or increased vascular resistance the patient develops **hypertension** (HTN). BP is classified as normal (<120/80

**Table 5. Drugs that Affect Hemostasis and Thrombosis.**[2,9,10]

| Drugs (Rank/300) | Mechanisms of Action | Common Indications |
|---|---|---|
| **Cyclooxygenase inhibitors**<br>• Aspirin (36) | **Inhibit platelet cyclooxygenase, thereby blocking thromboxane $A_2$-dependent platelet aggregation** | • Prophylaxis against<br>o Transient ischemic attacks<br>o Myocardial infarction<br>o Thromboembolic disorders<br>o Reocclusion in coronary revascularization procedures and stent implantation |
| **ADP receptor pathway inhibitors**<br>• Clopidogrel (29)<br>• Ticagrelor (247) | **Block platelet ADP receptors thereby inhibiting ADP-dependent platelet activation**<br>• Clopidogrel irreversibly blocks ADP receptors<br>• Ticagrelor reversibly blocks ADP receptors | • Acute coronary syndromes<br>• Prevention of stent thrombosis in combination with aspirin<br>• Secondary prevention of atherosclerotic events in patients with recent MI, stroke, or peripheral vascular disease |
| **Traditional anticoagulants**<br>• Warfarin (58) | **Inhibit hepatic peroxide reductase that catalyzes the regeneration of reduced vitamin K, which is required for the synthesis of biologically active coagulation factors II, VII, IX, and X** | **Prophylaxis and treatment**<br>• Pulmonary embolism<br>• Deep vein thrombosis<br>• Systemic embolism<br>o Post-MI<br>o Atrial fibrillation<br>o Prosthetic heart valve |
| **Selective Factor Xa inhibitors**<br>• Apixaban (48)<br>• Rivaroxaban (86) | **Competitively inhibit factor Xa by binding to the active side on the enzyme** | • Prophylaxis against<br>o Systemic embolism with atrial fibrillation<br>o Deep vein thrombosis and pulmonary embolism associated with hip or knee replacement surgery<br>• Prophylaxis and treatment<br>o Deep vein thrombosis and pulmonary embolism |

mmHg), elevated (120-129/<80 mmHg), stage 1 HTN (130-139/80-89 mmHg), or stage 2 HTN (≥140/90 mmHg).[18]

HTN is known as the "silent killer" because signs and symptoms, i.e., flushed face, restlessness, headache, dizziness, tinnitus, visual disturbances, dyspnea, and a hammering pulse are not observed until the systolic BP is ≥180 mmHg or the diastolic BP ≥110 mmHg; or until evidence of target organ damage manifests.[19] Target organ damage may include renal insufficiency and end-stage renal disease; CAD, left ventricular hypertrophy, and HF; stroke; peripheral vascular disease; and hypertensive retinopathy.[19]

The treatment of HTN may include (1) diuretics to reduce blood volume, (2) ACE inhibitors or AT

**Table 6. Combination Cardiovascular Drugs.**[2,9,10]

| Combinations (Rank/300) | Common Indications |
|---|---|
| Hydrochlorothiazide / Lisinopril (50) | • Hypertension |
| Losartan / Hydrochlorothiazide (93) | • Hypertension<br>• Hypertension with heart left ventricular hypertrophy |
| Hydrochlorothiazide / Triamterene (131) | • Hypokalemia associated the hydrochlorothiazide use |
| Amlodipine / Benazepril (169) | • Hypertension |
| Sacubitril / Valsartan (219) | • Heart failure |
| Hydrochlorothiazide / Valsartan (235) | • Hypertension |
| Hydrochlorothiazide / Olmesartan (281) | • Hypertension |
| Bisoprolol / Hydrochlorothiazide (290) | • Hypertension |

II receptor antagonists to modulate the RAAS, (3) β1-adrenoceptor antagonist, $\alpha_1$-adrenoceptor antagonists, and central $\alpha_2$-adrenoceptor agonists to reduce sympathetic tone, and (4) $Ca^{2+}$ channel blockers and $K^+$ channel activators to reduce vascular tone[4-6,17] Frequently, two or more agents from different drug classes may be required to reach target BP in a particular patient.

BP >180/110 mmHg is a minor independent risk factor for a major adverse cardiac event (MACE) in association with dental procedures performed under local dental anesthesia.[19] However, high BP is associated with an increased stroke risk and is a useful marker for the presence of significant CAD. HTN is associated with several diseases to include adrenal disorders, dyslipidemia, diabetes mellitus, obesity, renal disease, and thyroid disorders. Contributory behavioral factors include a sedentary lifestyle and exposure to alcohol and tobacco.[18,19]

**Hypertensive urgency** is characterized by a gradual elevation of BP in patients with chronic, slowly progressive end-organ damage.[17] Clinically it may manifest as stroke or myocardial infarction (MI).[17] Common signs of stroke include unilateral paralysis or numbness affecting the face or an extremity; vision loss; slurred speech; and / or confusion. Perioperatively, when a conscious patient experiences chest pain and the BP drops from baseline the diagnosis of MI should be considered. In contrast, when a conscious patient experiences chest pain and a

rise in BP from baseline the diagnosis of acute angina pectoris is more likely.

**Hypertensive emergency** is a rare life-threatening condition characterized by severe, acute BP elevation associated with acute vascular injury.[17] The vascular injury manifests clinically as retinal hemorrhage, papilledema, encephalopathy, acute renal insufficiency, and acute left ventricular (LV) failure. The treatment of patients with hypertensive emergency mandates rapid reduction of BP in a hospital setting to prevent irreversible end-organ damage.[17]

Signs and symptoms of **hypotension**, defined as BP <90/60 mmHg, include dizziness, and fainting (syncope); rapid, shallow breathing; fatigue, lack of concentration, and depression: cold, clammy, and pale skin; and thirst.[19] Causes range from impaired homeostatic mechanisms of BP regulation as in old age, dehydration, and antihypertensive therapy.[19]

### Ischemic Heart Disease

I**schemic heart disease** (IHD) is characterized by an imbalance in myocardial oxygen supply and demand primarily as a result of atherosclerotic plaques in coronary arteries and endothelial dysfunction-associated vasoconstriction and thrombus formation.[17] It can be classified into two broad categories: **chronic coronary artery disease** (CAD), i.e., stable angina pectoris; and **acute coronary syndromes** (ACS), i.e., unstable angina pectoris and MI, each with a distinct pathogenesis.

Chronic CAD is associated with subintimal atheromas in the coronary arteries.[17] Its principal clinical manifestation is **chronic stable angina pectoris**. Atherosclerotic plaques in patients with chronic stable angina are overlaid by a thick, fibrous cap that resists disruption. The fibrous cap reduces vessel lumen diameter and causes inappropriate vasoconstriction resulting in acute myocardial ischemia and chest pain at reproducible workloads, e.g., walking up a flight of stairs.[17]

All patients with chronic CAD require aggressive lipid lowering therapy, BP control and focused therapy intended to reduce oxygen demand. Commonly prescribed drugs include: (1) $\beta_1$-adrenoceptor antagonists to reduce heart rate and contractility,(2) $Ca^{2+}$ channel blocking agents decrease cardiac contractility and systemic vascular resistance, and (3) nitric oxide donors decrease preload and dilate peripheral capacity veins.[3,5,6,17] Nitroglycerin is used to treat acute symptoms.

Acute coronary syndromes are caused by the rupture of unstable atherosclerotic plaques that lead to vasoconstriction, platelet aggregation, and thrombus formation. Downstream blockage by the thrombus results in acute myocardial ischemia and, potentially, irreversible myocardial injury (myocyte necrosis).[17] The principal clinical manifestation of ACS is **unstable angina pectoris** (UA) characterized by increased frequency and severity of chest pain that may occur even at rest.[17] Patients with UA are at high risk for MI.

An unstable plaque that abruptly ruptures and partially occludes the lumen of a coronary artery is termed **non-ST elevation MI** (NSTEMI).[17] Because there is a persistent prothrombotic surface at the site of plaque rupture, the patient is at high risk for recurrent ischemia. The goals of prevention and treatment of both UA and NSTEMI are (1) to relieve ischemic symptoms, i.e., β1-adrenoceptor antagonists; and (2) to prevent additional thrombus formation, i.e., antiplatelet agents and/or an anticoagulant.[3,6,9,17]

Complete coronary artery occlusion, unless perfusion is reestablished, is termed a **ST elevation MI** (STEMI).[17] The treatment of STEMI is the same as that of UA and NSTEMI. When pharmacological strategies are insufficient to reestablish perfusion, patients with STEMI require either coronary artery bypass grafts or percutaneous coronary intervention, i.e., balloon angioplasty or stent placement.[17] Ischemia-induced electrical instability of the myocardium can lead to **sudden cardiac death.**

The functional consequences of MI vary greatly among patients; thus, post-MI therapeutic regimens are individualized. Commonly prescribed agents include (1) aspirin (clopidogrel if aspirin is contraindicated); (2) aspirin and another anti-platelet agent

following percutaneous coronary intervention; (3) a $\beta_1$-adrenoceptor antagonist; (4) an ACE inhibitor for patients with HF, hypertension, and diabetes; (5) an aldosterone antagonist for patients with left ventricular dysfunction; and (6) lipid-lowering agents.[17]

## Cardiac Arrhythmias

The primary pacemaker of the heart is the sinoatrial (SA) node.[1] Electrical impulses generated by the SA node at a normal frequency of 60 to 100 beats per minute spread rapidly through the atria and enter the atrioventricular (AV) node. After a brief delay at the AV node, the impulses continue to propagate over the Bundle of His and converge on the Purkinje system as depolarization progresses over the ventricles in an anatomically synchronous and hemodynamically effective fashion.[1] When impulse generation and/or impulse conduction malfunctions, the patient develops cardiac arrhythmias.[7]

**Sinus bradycardia** - Impulses originate from the sinoatrial node (SA) at a rate <60 beats per minute under the influence of increased parasympathetic (vagal) tone.[1] The rhythm is regular. Sinus bradycardia is common in athletes, in patients with hypothyroidism, in patients with increased intracranial pressure, and during treatment with drugs with negative chronotropic action (e.g., $\beta_1$-adrenergic receptor antagonists, calcium channel blocking agents, and digoxin). The patient may be asymptomatic or experience weakness, palpitation, chest discomfort, dyspnea, and syncope.

**Sinus tachycardia** - Impulses originate from the SA node at a rate of 100 to 180 beats per minute under the influence of increased sympathetic tone or vagal blockade.[1] The rhythm is regular. Sinus tachycardia is found in patients after exercise or smoking; in patients with hyperthyroidism, anxiety, toxic states, fever, anemia, and acute or chronic heart diseases; and in patients consuming stimulants such as tea, coffee, and medications with positive chronotropic effects (e.g., epinephrine). The patient may be asymptomatic or experience weakness, palpitation, chest discomfort, dyspnea, and syncope.

**Atrial flutter** - Impulses originate from a single abnormal atrial focus at a rate of 250 to 300 beats per minute.[1] The rhythm is regular. Because the pace of atrial firing is rapid, some of the impulses reach the AV node during its refractory period. These impulses are not transmitted to the ventricles, and the ventricular rate is slower than the atrial rate. The ratio of atrial to ventricular firing rate is typically 2:1, i.e., the ventricular rate is between 125-150 beats per minute. The patient may be asymptomatic or experience weakness, palpitation, chest discomfort, dyspnea, and syncope.

**Atrial fibrillation** - Impulses originate from multiple abnormal atrial foci at a rate of 350 to 450 beats per minute.[1] Impulses in the atria travel in a random manner and the rhythm is irregular. The AV node is unable to transmit all of the impulses and the ventricular rate is between 120 to 180 beats per minute. Turbulence and/or stasis of blood in the fibrillating atrium can lead to clot formation. Systemic embolization may lead to stroke or stroke-like illness characterized by sudden confusion: acute, painful, pulseless limbs: and an acute abdomen.

**Premature ventricular contractions** (PVCs) are characterized by a pronounced pause in an otherwise normal rhythm.[1] Impulses originate from an ectopic ventricular focus. PVCs may be an occasional finding in otherwise healthy adults and the incidence increases with age, fatigue, emotional stress, and the use of coffee and tobacco. PVCs are considered benign if fewer than six such pauses are noted per minute. PVCs are significant in a patient with a history of cardiovascular diseases, i.e., ischemic heart disease, valvular disease, hypertension, and congestive heart failure.

**Ventricular tachycardia** (VT) usually evolves from an ectopic focus in a ventricle, which generates ventricular extrasystoles at a rate of 120 to 220 beats per minute.[1] VT occurs in patients with organic heart disease and may be precipitated by drugs such as digoxin and tricyclic antidepressants. A patient with sustained VT is almost always

symptomatic experiencing fatigue, palpitation, light-headedness, and syncope. VT is a serious arrhythmia, if left untreated, it may lead to ventricular fibrillation manifested as loss of consciousness and sudden cardiac death.

**Ventricular fibrillation** (VF) - The heart rate is 350-450 beats per minute and the rhythm is irregular.[1] The myocardium depolarizes in a chaotic manner. Coordinated ventricular activity ceases. The heart ceases to pump, the blood pressure falls, and unconsciousness occurs. If left untreated, death will follow in about three to five minutes. CAD-associated ischemia-induced electrical instability of the myocardium is the most common cause of VF and it is the main cause of **sudden cardiac death**, which occurs most frequently in the first few hours after a MI.

**Atrioventricular** (AV) blocks are characterized by a delay or failure in impulse conduction from the atria to the ventricles.[1] It occurs at three levels: first degree, with a delay in impulse conduction; second degree, with an intermittent failure in conduction; and third degree, with permanent failure in conduction. First degree AV block is usually asymptomatic. Second degree AV block may be asymptomatic or manifest as light-headedness and syncope. Third degree or high-grade AV block is characterized by fatigue, light-headedness, syncope and, if left untreated, leads to HF.

Generally, to restore synchronous myocardial contraction, Class I and Class III antiarrhythmic agents are used to treat both supraventricular tachycardias (SVTs) and ventricular tachycardias (VTs), Class II and Class IV antiarrhythmic agents are used to treat SVTs, and cardiac glycosides such as digoxin are used to treat atrial flutter and atrial fibrillation.[7] In addition, antiplatelet drugs and/or anticoagulants are prescribed to prevent thromboembolic complications.[9] If pharmacological strategies fail, a patient with cardiac arrhythmias requires a pacemaker or an implanted cardiac defibrillator.

## Heart Failure

Heart failure (HF) is a chronic contractile dysfunction characterized by myocyte loss and increased interstitial collagen deposits associated with structural cardiac diseases.[8,17,20] Cardiac output is decreased resulting in reduced renal perfusion. Reduced renal perfusion leads to increased renin-angiotensin-aldosterone synthesis. Decreased hepatic perfusion leads to decreased aldosterone clearance. Increased aldosterone concentrations lead to coronary artery and renovascular fibrosis, endothelial cell and baroreceptor dysfunction, and decreased myocardial norepinephrine uptake.

The most common cause of HF is **left ventricular (LV) dysfunction**.[17,20] LV dysfunction develops as a complication of HTN, CAD, cardiomyopathy, and most forms of congenital heart defects. It may manifest as tachycardia, fatigue on exertion, dyspnea on mild exercise, and intolerance to cold. Paroxysmal nocturnal dyspnea and nocturnal cough reflect the redistribution of excess fluid into the lungs with the recumbent position. Occasionally, bronchospasm, wheezing and hemoptysis are present.

**Right-ventricular (RV) dysfunction** is usually a consequence of either LV dysfunction, tricuspid valve regurgitation, valve stenosis (mitral or pulmonary), pulmonary hypertension, or pulmonary emboli.[17,20] Cardinal symptoms include fatigue; an awareness of fullness in the neck, i.e., jugular vein distension; fullness in the abdomen with an enlarged liver with tenderness in the right upper quadrant; and, in advanced cases, abdominal swelling secondary to ascites and pitting edema of the lower extremities.

The clinical classification of HF, i.e., New York Heart Association Class I, II, III, and IV, is based on the patient's functional capacity (FC).[20] FC is expressed in metabolic equivalents (METs).[20] One MET equals the resting or basal oxygen requirement (i.e., 3.5 ml of O2 per kg per minute) of a 40–year-old, 70-kg man. FC can be classified as excellent (>10 METs), good (7-10 METs), moderate (4-7 METs), and poor (<4 METs).[21-23] A functional capacity <4 METs is predictive of increased cardiac risks in association with noncardiac procedures.[24]

Patients with **Class I heart failure** are typically asymptomatic at rest and ordinary physical activities do not cause fatigue, dyspnea, palpitations, or acute angina pectoris. These

patients can complete physical activities requiring a FC of ≤7 METs, e.g., run a short distance; do heavy work around the house such as scrubbing floors or moving furniture; and participate in recreational activities such as golfing, bowling, dancing, or playing basketball.

Patients with **Class II heart failure** are typically asymptomatic at rest; however, ordinary physical activities can cause fatigue, dyspnea, palpitations, or acute angina pectoris. These patients can only complete physical activities requiring a FC ≤5 METs, e.g., do light work around the house such as dusting and washing dishes; garden; climb a flight of stairs or walk up a hill; walk on level ground at 4 mph (6.4 km per h): and run a short distance.

Patients with **Class III heart failure** are typically asymptomatic at rest; however, ordinary physical activities can cause fatigue, dyspnea, palpitations, or acute angina pectoris. These patients can only complete physical activities requiring a FC ≤2 METs, e.g., walk indoors around the house, dress, eat, and use the toilet. Patients with **Class IV heart failure** are typically symptomatic at rest and either cannot complete or perform physical activities requiring a FC ≤2 METs.

The treatment of HF includes: (1) an angiotensin receptor neprilysin inhibitor (ARNI), ACE inhibitor, or ARB, (2) a βeta-blocker, (3) a mineralocorticoid receptor antagonist (MRA), and (4) an a SGLT2 inhibitor. If the patient is volume overloaded, a diuretic is added. Black patients recalcitrant to initial therapy are often prescribed isosorbide dinitrate and hydralazine.[25] When pharmacological strategies fail, a patient with HF becomes a candidate for heart transplantation.

### Thromboembolic Complications

A blood clot, or thrombus, that forms in a blood vessel or heart chamber may be either venous or arterial in origin. **Venous thrombi** develop in areas of slow blood flow, e.g., in a lower extremity. The clot forms rapidly and lacks organization. Although venous occlusion does occur, a far greater concern is the tendency of small emboli to detach from venous thrombi.[9] These emboli tend to travel to and wedge into pulmonary arteries, preventing deoxygenated blood from entering the lungs.[9]

An **arterial thrombus** forms when platelets aggregate and become surrounded by fibrin and erythrocytes.[9] Arterial thrombi cause coronary artery thrombosis, coronary artery rethrombosis after thrombolysis, occlusion of coronary artery grafts and lead to unstable angina pectoris, MI, recurrent MI, and sudden cardiac death. Arterial thrombi also contribute to systemic embolization in patients with atrial fibrillation or prosthetic heart valves and cause transient ischemic attacks and stroke.[9]

To prevent and/or treat thromboembolic complications patients are prescribed antiplatelet agents and/or anticoagulants.[9] It is of note that antithrombotic therapy should not be interrupted for most dental procedures.[26,27] The risk of perioperative and postoperative bleeding complications in patients in whom antiplatelet and anticoagulation therapy is continued is exceedingly small and is outweighed by the small risk of serious and sometimes fatal embolic events when antithrombotic therapy is interrupted.

## Summary

Familiarity with the top 300 prescription drugs dispensed by U.S. community pharmacies provides an insight into prevailing disease trends in the U.S. population. In 2020, 20% of the top 300 drugs dispensed in the United States were prescribed to address cardiovascular diseases such as HTN, IHC (i.e., chronic CAD and ACS), cardiac arrhythmias, heart failure, and thromboembolic complications.

The risk of a major adverse cardiac event (MACE), defined as myocardial infarction, heart failure, or sudden cardiac death, occurring in the dental treatment scenario is predicated on multiple factors such as the cardiovascular / overall health of the patient and the extent of dental procedural stress. The stress associated with an outpatient dental procedure under local anesthesia is typically not associated with an increased risk of MACE. Presenting medical conditions such as advanced age, atrial fibrillation, stroke, uncontrolled HTN, chronic stable angina pectoris, previous MI (>60 days), compensated HF, diabetes mellitus, and renal insufficiency

are generally not associated with an increased risk of MACE.

The risk of MACE is significantly increased in a patient presenting with one of the following conditions: unstable angina pectoris, recent MI (<60 days), decompensated HF, severe valvular disease, or significant arrhythmia. The risk is independent of the level of dental procedural stress.

It is important to always estimate the patient's perioperative risk for MACE. If the combined procedure- and patient-specific variables predict a low-risk for MACE and the patient's FC is ≥4 METs no further preoperative evaluation may be needed. If the FC is <4 METs and/or the risk for MACE is elevated, the practitioner should refer the patient for appropriate medical evaluation, before undergoing elective dental care.

## Course Test Preview

To receive Continuing Education credit for this course, you must complete the online test. Please go to: *www.dentalcare.com/en-us/ce-courses/ce581/start-test*

**1. All of the following drug categories may be prescribed to manages cardiovascular diseases, EXCEPT for one. Which one is the exception?**

A. Drugs that regulate intracellular fluid volume
B. Drugs that regulate vascular tone
C. Drugs that regulate cardiac rhythm
D. Drugs that affect hemostasis

**2. Drugs taken by our patients are associated with at least 10,000 potential ADRs ranging from mild to severe illness and can lead to hospitalization, permanent disability, and even death; consequently, OHCPs are expected to have access to reliable informational resources.**

A. True
B. False

**3. All of the following statements related to lipoproteins are correct, EXCEPT for one. Which one is the exception?**

A. In blood, lipoproteins transport cholesterol and triglycerides.
B. Abnormalities of lipoprotein metabolism appear to be the result of genetic factors, which modify the sensitivity of individuals to adverse dietary habits and to sedentary lifestyles.
C. Low levels of low-density lipoproteins (LDLs) and low levels of triglycerides (TGs) and high levels of high-density lipoproteins (HDLs) are strongly associated with atherosclerosis.
D. Diet and exercise can reduce total plasma cholesterol concentrations by as much as 25%, if this approach is insufficient to normalize lipid levels drug therapy is initiated.

**4. Which of the following classes of drugs are prescribed for the treatment of hypercholesterolemia and prophylaxis for coronary atherosclerosis?**

A. Inhibitors of cholesterol synthesis, i.e., the "statins, which inhibit HMG-CoA reductase, the rate-limiting enzyme in cholesterol synthesis.
B. Fibrates e.g., fenofibrate, an agonist of peroxisome proliferator-activating receptor α (PPARα) in hepatacytes
C. Inhibitors of cholesterol absorption, e.g., ezetimibe, which decreases cholesterol transport into enterocytes.
D. Omeda-3 fatty acids, which regulate nuclear transcription factors to reduce TG synthesis and increase fatty acid oxidation.

**5. All of the following statement related to plasma volume depletion are correct, EXCEPT for one. Which one is the exception? Plasma volume depletion _____**

A. Activates the renin-angiotensin-aldosterone system (RAAS)
B. Promotes the release of natriuretic peptides
C. Promotes antidiuretic hormone release
D. Increases renal sympathetic activity

**6. Excessive Na+ and H2O retention, primarily a result of renal abnormalities, is responsible for volume-based hypertension and can also lead to transudative edema associated with heart failure, cirrhosis of the liver, and nephrotic syndrome.**

A. True
B. False

**7. All of the following statements related to drugs indicated for the treatment of hypertension and/or as adjuncts in chronic edema states, and/or as adjuncts in the prevention and treatment of MI, HF, or diabetic nephropathy are correct EXCEPT for one? Which one is the exception?**

A. Thiazide diuretics, e.g., hydrochlorothiazide, inhibit Na+ reabsorption by cells of the distal convoluted tubule.
B. Loop diuretics, e.g., furosemide, inhibit Na+ reabsorption by cells of the Loop of Henle.
C. Spironolactone, a collecting duct (potassium sparing) diuretic, inhibits Na+ reabsorption by inhibiting aldosterone action.
D. Angiotensin II receptor antagonists, i.e., the "artans", inhibit the conversion of angiotensin (AT) I to AT II and the degradation of bradykinin.

**8. Vascular smooth muscle cells are the functional regulatory units responsible for maintaining vascular tone, which is ultimately is determined by the intracellular Ca2+ ion concentration.**

A. True
B. False

**9. All of the following statements related to drugs that regulate vascular tone are correct, EXCEPT for one. Which one is the exception?**

A. Calcium channel blockers, e.g., amlodipine, block voltage-gated L-type Ca2+ channels and are indicated for the treatment of hypertension, anginal pectoris, and cardiac arrhythmias.
B. Beta-adrenoceptor blocking agents such as metoprolol selectively block β1-adrenoceptors, propranolol and nadolol also block β2-adrenoceptors, and labetalol and carvedilol also block β2- and α1- adrenoceptors.
C. Alpha2-adrenoceptor agonists, e.g., clonidine, selectively activate central α2-adrenoceptors, thereby increasing sympathetic outflow from the CNS.
D. Nitric oxide donors, e.g., nitroglycerin, are indicated for the treatment of acute angina pectoris and or prophylaxis for ischemic heart disease.

**10. All of the following statements related to cardiac arrhythmias are correct, EXCEPT for one? Which one is the exception?**

A. Under the influence of the autonomic nervous system, the sinoatrial (SA) node paces the heart at normal resting rates between 60 and 100 beats per minute.
B. The atrioventricular (AV) node and the ventricular conducting system contain pacemaker cells.
C. Abnormal impulse generation and/or impulse conduction underlie cardiac arrhythmias.
D. The most common cause of cardiac arrhythmias is primary electrophysiological disorders and genetically determined ion-channel abnormalities.

**11. All of the following statements related to drugs that affect cardiac rhythm are correct, EXCEPT for one. What is the exception?**

A. Class IC antiarrhythmics such as flecainide block voltage-gated Na+ channels in ventricular myocytes.
B. Class II antiarrhythmics, i.e., β1-adrenoceptor antagonists, block β1-adrenoceptors in SA and AV nodal cells.
C. Class IV antiarrhythmics, i.e., Ca2+ channel blocking agents, decrease excitability of SA nodal cell and prolong AV nodal conduction.
D. Cardiac glycosides, e.g., digoxin reduce the refractory period at AV nodal cell and thereby increase conduction velocity.

**12. Cardiac glycosides, e.g., digoxin, inhibit Na+/K+-ATPase and thereby increase intracellular Ca2+ concentration in myocytes exerting a positive inotropic effect and are indicated for the treatment of heart failure.**

A. True
B. False

**13. All of the following statements regarding drugs used to reduce thrombosis are correct, EXCEPT for one. Which one is the exception?**

A. Ticagrelor irreversibly blocks ADP receptors.
B. Aspirin acts to inhibit platelet cyclooxygenase, thereby blocking thromboxane A2-dependent platelet aggregation.
C. Rivaroxaban competitively inhibits factor Xa by binding to the active site on the enzyme.
D. The action of warfarin ultimately inhibits the synthesis of biologically active coagulation factors II, VII, IX, and X.

**14. All of the following statements regarding blood pressure assessment are true, EXCEPT for one. Which one is the exception?**

A. The upper limit of normal blood pressure is defined as 120 / 80 mmHg.
B. Elevated blood pressure is defined as 120-129/<80 mmHg.
C. Stage 1 HTN 130-139/80-89 mmHg.
D. Stage 2 HTN (≥140/90 mmHg).

**15. HTN is known as the "silent killer" because signs and symptoms, are not observed until the systolic BP is ≥180 mmHg or the diastolic BP ≥110 mmHg or until evidence of target organ damage manifests.**

A. True
B. False

**16. All of the following statements related to the top 300 cardiovascular-oriented combination drugs prescribed in 2020 are correct EXCEPT for one. Which one is the exception?**

A. Most of the combination drugs contain hydrochlorothiazide.
B. Sacubitril is only available as a combination with Valsartan.
C. All of the combination drugs were prescribed to manage hypertension.
D. The hydrochlorothiazide / Triamterene combination agents reduce hypokalemia risk.

**17. All the following statements related to hypertension are correct, EXCEPT for one. Which one is the exception?**

A. BP >180/110 mmHg is a major independent risk factor for a major adverse cardiac event (MACE) in association with dental procedures performed under local dental anesthesia
B. Hypertensive urgency is characterized by gradual elevation of BP in patients with chronic, slowly progressive end-organ damage that perioperatively may manifest as stroke or myocardial infarction.
C. Hypertensive emergency is a rare life-threatening condition characterized by severe, acute BP elevation associated with acute vascular injury that perioperatively may manifests as retinal hemorrhage, papilledema, and altered mental state.
D. Hypertension is associated with an increased risk of stroke.

**18. In addition to aggressive lipid lowering therapy and BP control, focused therapy in patients with chronic coronary artery disease, i.e., chronic stable angina pectoris may include all of the following, EXCEPT for one. Which one is the exception?**

A. β1-adrenoceptor antagonists reduce heart rate and contractility
B. Ca2+ channel blocking agents decrease cardiac contractility and systemic vascular resistance
C. nitric oxide donors to decrease preload and dilate peripheral capacity veins
D. α2-receptor agonists to increase sympathetic outflow from the CNS.

**19. All of the following statements related to acute coronary syndromes (ACS), i.e., unstable angina pectoris (UA) and MI are correct EXCEPT for one. Which one is the exception?**

A. Acute coronary syndromes are caused by the rupture of unstable atherosclerotic plaques that result in vasoconstriction, platelet aggregation, and thrombus formation.
B. The principal clinical manifestation of UA is chest pain at reproducible workloads, e.g., walking up a flight of stairs.
C. The goals of prevention and treatment of ACS are to relieve ischemic symptoms, i.e., β1-adrenoceptor antagonists; and to prevent additional thrombus formation, i.e., antiplatelet agents and/or an anticoagulant.
D. If pharmacological strategies are not sufficient to reestablish perfusion patients with STEMI require coronary artery bypass grafts or percutaneous coronary intervention.

**20. All of the following statements related to cardiac arrhythmias are correct, EXCEPT for one. Which one is the exception?**

A. In patients with atrial fibrillation systemic embolization may present clinically as a stroke-like illness characterized by sudden confusion.
B. A patient with sustained VT is almost always symptomatic and if left untreated it may lead to ventricular fibrillation.
C. Ventricular fibrillation, if left untreated, leads to death within about three to five minutes.
D. First degree AV block is almost always symptomatic, while third degree AV block is rarely symptomatic.

**21. The goals in treating cardiac arrhythmias are to restore synchronous myocardial contraction and to prevent thromboembolic complications. When pharmacological strategies fail, a patient with cardiac arrhythmias requires a pacemaker or implanted cardiac defibrillator.**

A. True
B. False

**22. All of the following statements related to HF are correct, EXCEPT for one. Which one is the exception?**

A. Heart failure (HF) is a chronic contractile dysfunction characterized by myocyte loss and increased interstitial collagen deposits associated with structural cardiac diseases.
B. Patients with Class I heart failure are typically asymptomatic at rest and ordinary physical activities do not cause fatigue, dyspnea, palpitation, or acute angina pectoris; these patients can complete physical activities requiring a FC of ≤7 METs.
C. Patients with Class II heart failure are typically asymptomatic at rest but ordinary physical activities can cause fatigue, dyspnea, palpitation, or acute angina pectoris; these patients can only complete physical activities requiring a FC ≤5 METs.
D. Patients with Class IV heart failure are typically asymptomatic; however, ordinary physical activities can cause fatigue, dyspnea, palpitation, or acute angina pectoris; these patients can only complete physical activities requiring a FC ≤2 METs.

**23. All of the following statements regarding the pharmacological management of HF are correct, EXCEPT for one. Which one is the exception?**

A. An SGLT2 inhibitor is prescribed to inhibit Na+ reabsorption by cells of the distal convoluted tubule.
B. The use of an ACE inhibitor or ARB is preferred over the use of an ARNI.
C. A mineralocorticoid receptor antagonist such as spironolactone is prescribed to inhibit aldosterone activity.
D. Black patients recalcitrant to initial therapy are often prescribed isosorbide dinitrate and hydralazine.

**24. All of the following statements related to thromboembolic complications are correct, EXCEPT for one. Which one is the exception?**

A. Venous thrombi develop in areas of slow blood flow, e.g., in a lower extremity, small emboli tend to detach and travel to and wedge into pulmonary arteries preventing deoxygenated blood from entering the lung.
B. Arterial thrombi cause coronary artery thrombosis, coronary artery rethrombosis after thrombolysis, occlusion of coronary artery grafts and lead to unstable angina pectoris, MI, recurrent MI, and sudden cardiac death.
C. Arterial thrombi contribute to systemic embolization in patients with atrial fibrillation or prosthetic heart valves and cause transient ischemic attacks and stroke.
D. The risk of perioperative and postoperative bleeding complications in patients in whom anticoagulation therapy is continued far outweighs the small risk of serious and sometimes fatal embolic events when antithrombotic therapy is interrupted.

**25. All of the following statements regarding the preoperative assessment of the patient with cardiovascular disease are true, EXCEPT for one. Which one is the exception?**

A. A major adverse cardiac event (MACE) is defined as myocardial infarction, heart failure, or sudden cardiac death.
B. The stress associated with an outpatient dental procedure under local anesthesia is frequently associated with an increased risk of MACE.
C. If the FC is <4 METs and/or the risk for MACE is elevated, the practitioner should refer the patient for appropriate medical evaluation, before undergoing elective dental care.
D. The risk of MACE is significantly increased in a patient presenting with unstable angina pectoris.

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## Additional Resources

- No Additional Resources Available

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