

Pharmacology of Cardiovascular Agents for Physical Therapists



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- **What you (should) already know...**
 - Physiology of the cardiovascular (CV) system
 - Basic pathophysiology of cardiovascular conditions
- **What we will discuss today:**
 - Drugs for hypertension (HTN) and angina
 - Drugs for dyslipidemia
 - Drugs for anticoagulation and thrombolysis
- **What you should be able to do after the lecture...**
 - Recognize brand and generic names for representative drug(s)
 - Describe the mechanism of action for representative drug(s)
 - When presented with a medication list, explain how adverse effects may affect PT therapy

Outline

- **HTN, Angina, and more**
 - ACE inhibitors
 - Angiotensin receptor blockers
 - Diuretics
 - Alpha-2 agonists
 - Beta blockers
 - Calcium channel blockers
 - Nitrates
- **Cholesterol lowering**
 - Statins

- **Oral anticoagulants**
 - Vitamin K antagonist
 - Direct Thrombin Inhibitor
 - Factor Xa Inhibitors
- **Injectable anticoagulants**
 - Unfractionated heparin
 - Low molecular weight heparins
 - Factor Xa inhibitors
- **Thrombolytics**

**How these cardiovascular medications
relate to physical therapy treatments**

Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers

ACE-I = lisinopril (Zestril); ARB = losartan (Cozaar)

- **Mechanism of action**

- Both effect RAAS system (renin-angiotensin-aldosterone)
 - ACE-I: block *angiotensin converting enzyme*
 - ARB: block *angiotensin II*

- **Effect**

- Decrease salt & water retention
- Decrease blood pressure (BP)

- **Place in therapy**

- First line agents for HTN

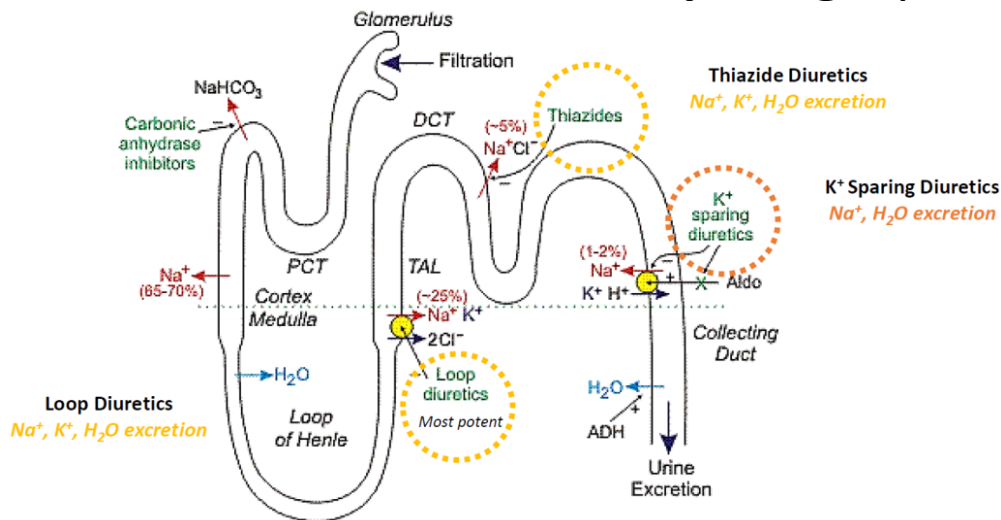
Shared adverse effects
• Dizziness • Orthostatic hypotension • Hyperkalemia (watch out for K+ levels!)
ACE-I >> ARB
• Dry hacking cough (30% of pts) • Angioedema (rare)

Diuretics

Loop diuretics: *furosemide (Lasix)*

Thiazides: *hydrochlorothiazide (Diuril)*

K⁺ sparing: *spironolactone (Aldactone)*



• Effect

- Decrease BP
- Decrease salt retention

• Place in therapy

- HTN, Heart Failure, and more

<http://cvpharmacology.com/diuretic/diuretics>

<http://www.mayoclinic.org/diseases-conditions/gynecomastia/multimedia/gynecomastia-enlarged-male-breast-tissue/img-20007324>

[gynecomastia/multimedia/gynecomastia-enlarged-male-breast-tissue/img-20007324](http://www.mayoclinic.org/diseases-conditions/gynecomastia/multimedia/gynecomastia-enlarged-male-breast-tissue/img-20007324)

Shared adverse effects

- Dizziness
- Orthostatic hypotension
- ↑ Urination
- Electrolyte abnormalities

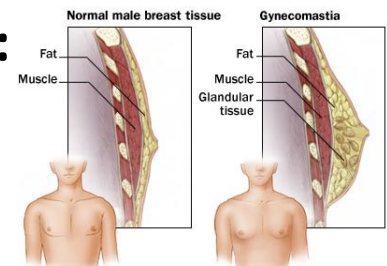
Unique adverse effects

Loop and thiazide diuretics:

- Hypokalemia
- Hyperglycemia
- Hyperuricemia

K⁺ sparing diuretics:

- Hyperkalemia
- Gynecomastia



Alpha-2 Agonists

clonidine (Catapres)

- **Mechanism of action**

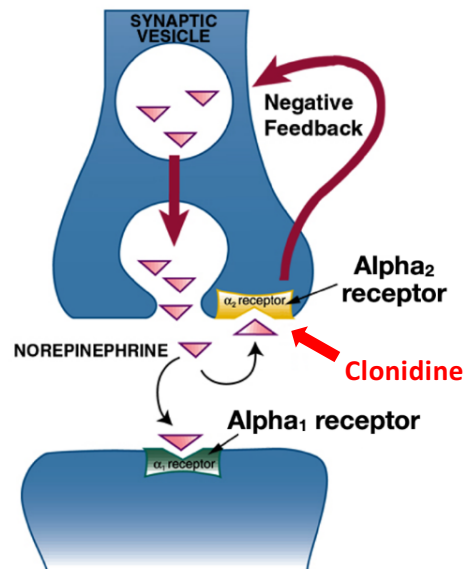
- Stimulates α_2 receptor
- Reduced sympathetic outflow from CNS

- **Effect**

- Decrease in HR
- Vasodilation

- **Place in therapy**

- Refractory HTN



Adverse effects

- Dry mouth, eyes
- Sedation
- Mental depression
- Bradycardia
- Orthostatic hypotension
- Sexual dysfunction
- Rebound HTN (if stopped abruptly)

Beta Blockers (BB)

metoprolol (Lopressor)

- **Mechanism of action**

- Block B₁ or B₁ and B₂ receptors

- **Effect**

- B₁ blockade: ↓HR, ↓contractility, ↓BP

- Decreased force of contraction

- **Place in therapy**

- HTN, angina, myocardial infarction (MI), HF

Adverse effects

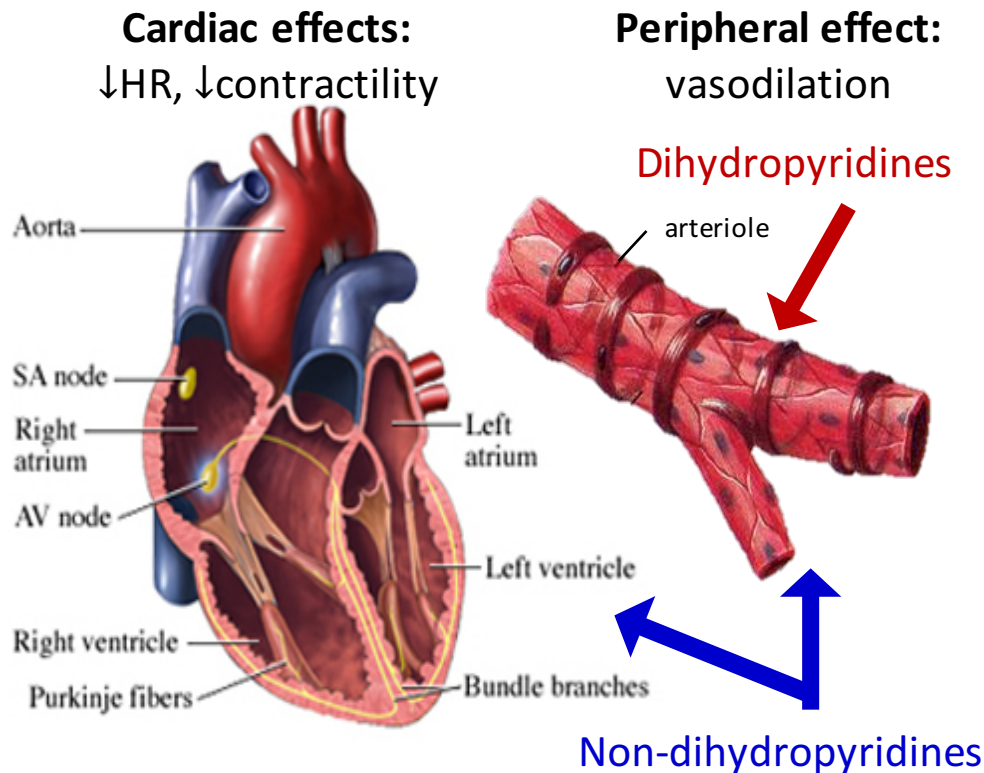
- Dizziness
- Orthostatic hypotension
- Bradycardia
- ↓ Exercise tolerance
- Rebound HTN (if stopped abruptly)

Special cautions

- Masks most hypoglycemia symptoms – check BG before aerobics if on hypoglycemics
- May antagonize asthma therapies
- HR cannot be used as marker of exertion - use perceived exertion instead

Calcium Channel Blockers (CCB)

DHP: amlodipine (*Norvasc*); Non-DHP: diltiazem (*Cardizem*)



Shared adverse effects

- Headache
- **Dizziness**, Hypotension
- Flushing
- Constipation

Unique adverse effects

- **DHP: reflex tachycardia, edema**
- **Non-DHP: bradycardia**

Special cautions

- HR cannot be used as marker of exertion - use perceived exertion instead

<http://faculty.stcc.edu/AandP/AP/AP2pages/Units18to20/vessels/artries.htm>

<http://www.bidmc.org/Centers-and-Departments/Departments/Medicine/Divisions/Cardiovascular-Medicine/For-Patients/Diseases-and-Conditions/Arrhythmias/Bradycardia-or-Low-Heart-Rate.aspx>

Nitrates

nitroglycerin (Nitrostat), isosorbide mononitrate (Imdur)

- **Mechanism of action**
 - NO release in smooth muscle
- **Effects**
 - Coronary vasodilation
 - Venodilation
- **Place in therapy = angina**



- Nitroglycerin: acute use PRN angina, onset 1-3 min, duration 30 min, sublingual tablet (SL)
- Isosorbide mononitrate: chronic daily use to prevent angina, onset 30-60 min, duration 6-12 hr, oral tablet (PO)

Adverse effects

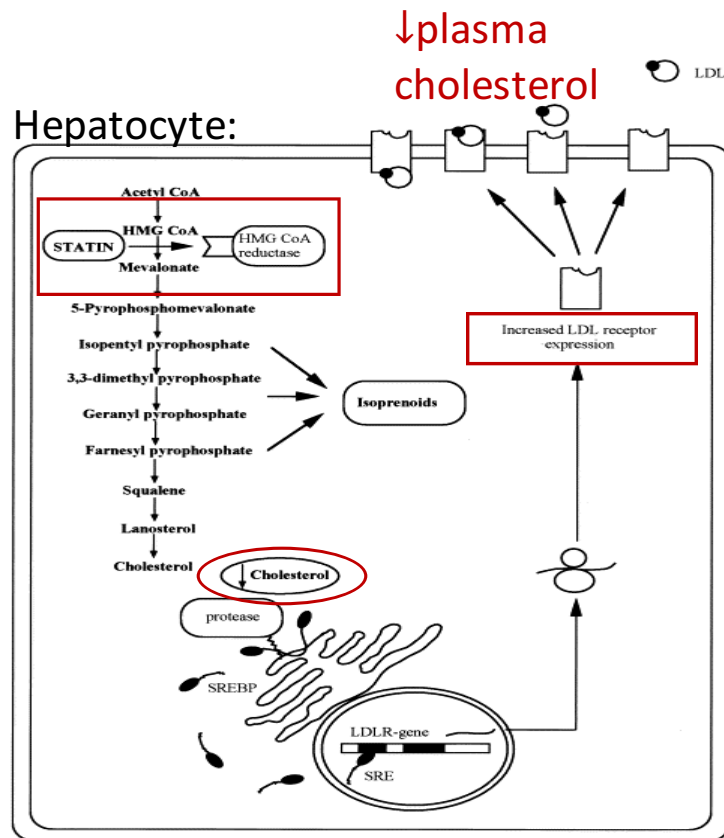
- Headache
- Dizziness
- Hypotension
- Orthostatic Hypotension
- Reflex Tachycardia

Place in physical therapy

- SL NTG prior to aerobic activity of wound debridement can prevent chest pain in pts w/ exertional angina

Other formulations: transdermal patch, topical ointment, sublingual spray

HMG-CoA Reductase Inhibitors – aka “Statins” like *atorvastatin (Lipitor)*



- **Place in Therapy** = high cholesterol

Adverse effects

- Hyperglycemia
- Reversible amnesia
- Arthralgia (4-12%)
- Myalgia (3-8%)
- Severe myopathy (0.1%)
- Rhabdomyolysis (0.01%) -> renal failure

Place in physical therapy

- PT are uniquely positioned to differentiate exercise-induced vs. statin-induced myopathy

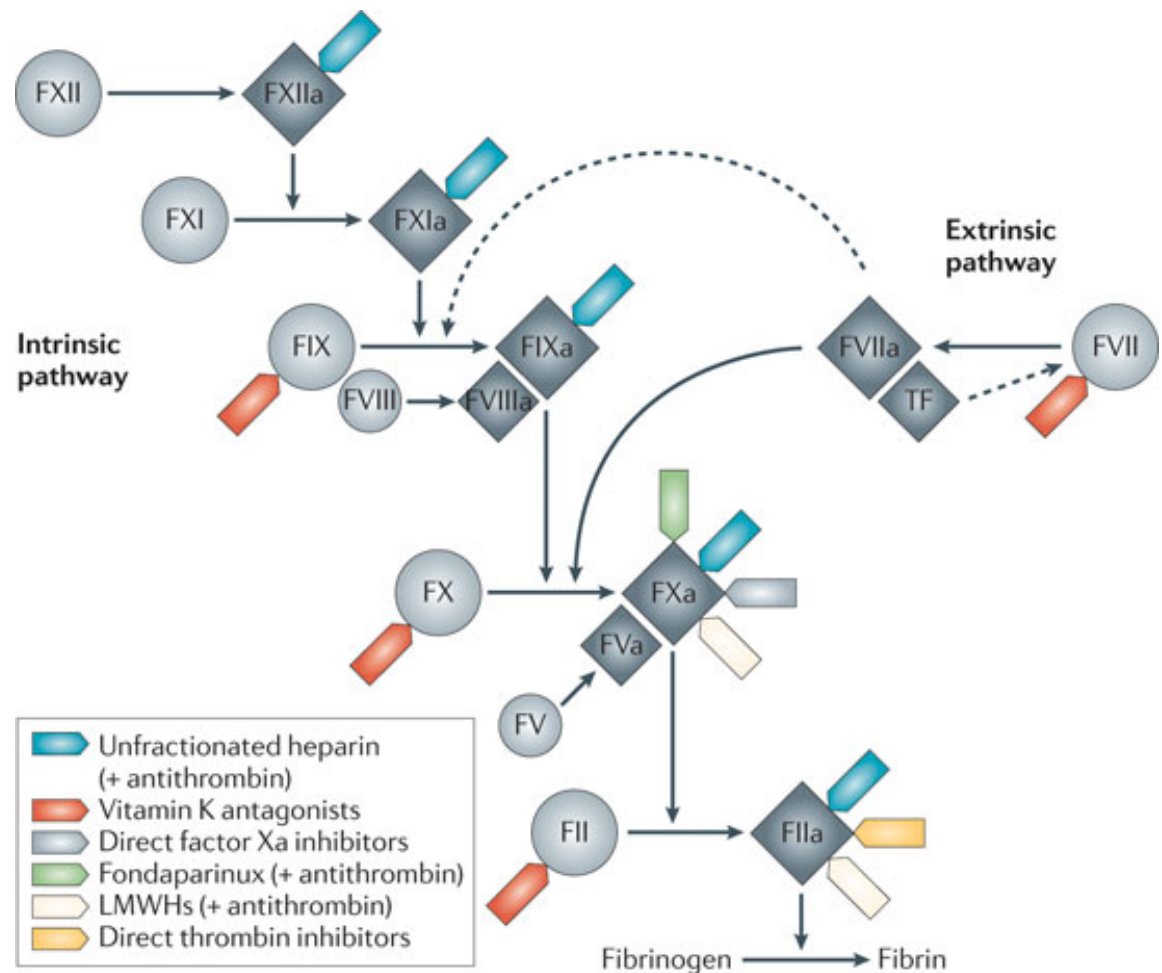
Anticoagulants

- **Place in therapy**

- Used for the prevention and/or treatment of clotting

- **Agents differ in:**

- Formulation
- Pharmacokinetics
- Reversibility



Oral Anticoagulants

Vitamin K Antagonist (VKA): Warfarin (*Coumadin*)
Direct Thrombin Inhibitor (DTI): Dabigatran (*Pradaxa*)
Factor Xa Inhibitor (FXa inhibitor): Rivaroxaban (*Xarelto*)

Shared adverse effects	Unique cautions
• Easy bruising • Risk of more serious bleeding 	VKA: • Narrow therapeutic index (NTI) drug • Many drug and food interactions • Regular INR monitoring necessary Reversibility: • FXa inhibitors: no specific reversal agent • Warfarin antidote = vitamin K • DTI antidote = idarucizumab (<i>Praxbind</i>)

Injectable Anticoagulants

Unfractionated Heparin (UFH): heparin
Low Molecular Weight Heparins (LMWH): enoxaparin (*Lovenox*)
Factor Xa Inhibitor (FXa inhibitor): fondaparinux (*Arixtra*)

Shared adverse effects	Unique cautions
• Easy bruising • Injection site pain, irritation • Risk of more serious bleeding • Thrombocytopenia	UFH: • Heparin-induced thrombocytopenia (HIT) • Hyperkalemia, osteoporosis (long-term use) • Frequent monitoring required (aPTT blood test) Reversibility: • UFH>LMWH>FXa inhibitors (heparin antidote=protamine)

Thrombolytics “Clot Busters”

aka Tissue plasminogen activators (tPA) like alteplase (Activase)

- **Mechanism of action**
 - Actively degrade clots by converting plasminogen to plasmin
- **Effect**
 - Dissolves the clot
- **Place in therapy**
 - Used in select patients with STEMI, acute ischemic stroke, pulmonary embolism

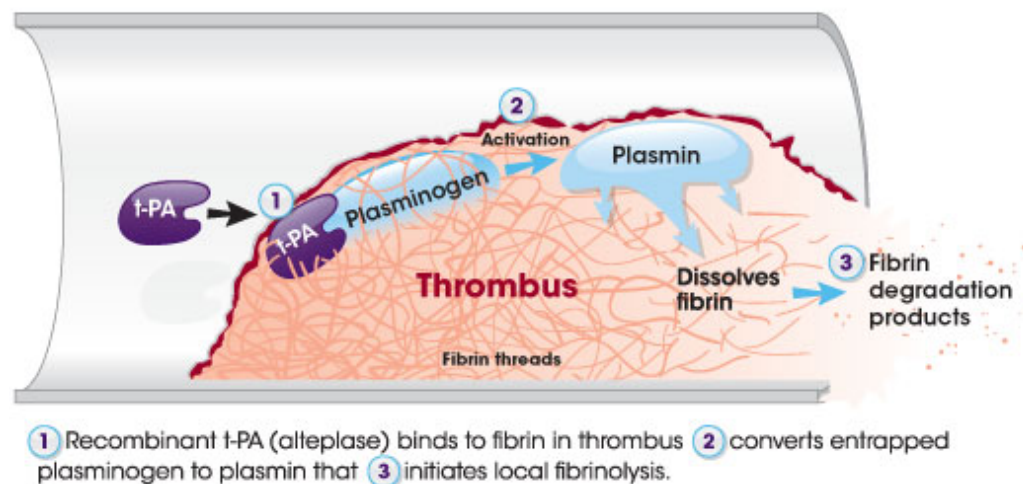
Adverse effects

- Bleeding

Unique cautions

- Patient confined to bedrest during and after infusion

Cathflo—a fibrin-specific* MOA



CARDIOVASCULAR AGENTS:

Clinical Relevance for Physical Therapy

Pts treated w/ antihypertensive, anti-angina, cholesterol-lowering, anticoagulant, and thrombolytic drugs may be in rehabilitation for many reasons.

Physical therapists should:

- Recognize adverse effects affecting exercise tolerance and monitor patients closely during physical therapy sessions
- Be aware of myalgia risk with statins and bleeding risk with anticoagulants/thrombolytics

Physical Therapy Focus

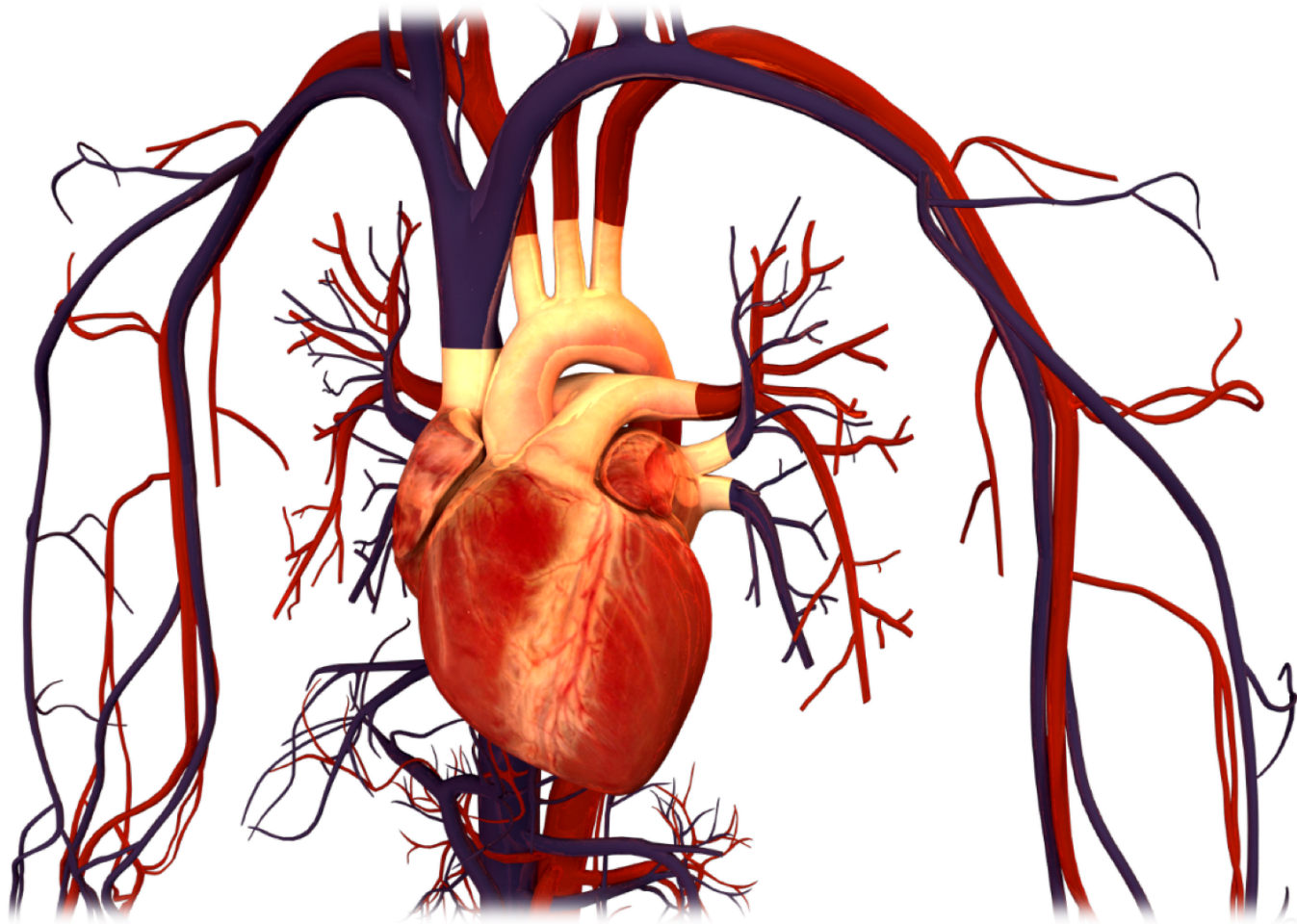
Adverse Drug Reactions	Effects on Rehabilitation
Orthostatic hypotension	• Assist pts w/ positional changes and when exiting warm pool • Always provide cool-down period
↓ Cardiac output	• Monitor BP and HR prior, during, and following aerobic activity • Exercise prescriptions based on exercise testing (while drug in effect)
Altered K ⁺ levels	• Paresthesias, ↓muscle function, ↑cramps, ↑risk cardiac dysfxn • Review recent labs and med list to determine if contributory
Statin-induced myopathy	• Use Stair Climbing Test and Six-Minute Walk Test to investigate persistent muscle weakness not involved in strength training
↑ Risk bleeding	• ↑Risk vertebral artery damage during upper cervical manipulation • Check that clotting time is within normal limits; ↓velocity and force of manipulation

Panus PC, Katsung B, Jobst E, Tinsley SL, Masteres BS, Tervor AJ. Pharmacology for the Physical Therapist. New York: McGraw Hill Medical, 2009.

Placzek JD, Boyce DA. Orthopaedic Physical Therapy Secrets. Hanley & Belfus; 2006.

Phys Ther. 2010;90:1530-1542.

Questions?



http://commons.wikimedia.org/wiki/File:Human_Heart_and_Circulatory_System.png

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