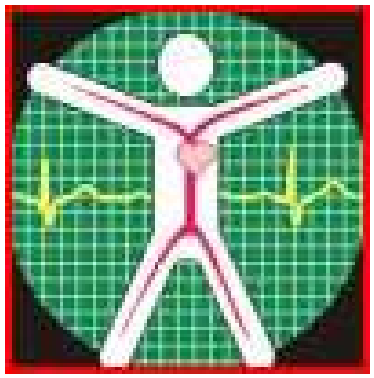

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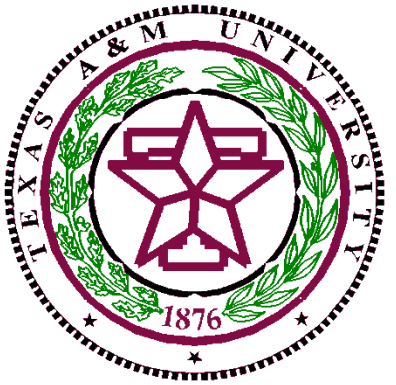


Section 3

Non-ischemic Heart Disease and Pharmacology for the Clinical Physiologist

Exercise Testing & Prescription for Special Populations

These lectures will cover the pathophysiology as well as implications for exercise testing and prescription for the following health concerns

- Hypertension
- Heart Failure and Valvular Heart Disease
- Peripheral Vascular Disease

Hypertension

- **Types of Hypertension**
  - **Primary (essential) hypertension**
    - 95% of cases have no identifiable primary cause but may be related to:
      - heredity - accounts for up to 50% of the variability in BP
        - a gene has been identified that influences sodium balance
        - CNS abnormalities → ↑ circulating catecholamines → ↑ TPR
      - stress
      - obesity / insulin resistance
      - low levels of nitric oxide (EDRF - a vasodilator)
        - more prevalent in African-Americans
      - aging → ↓ arterial elasticity (arteriosclerosis) → ↑ TPR
  - **Secondary hypertension**
    - Caused by specific endocrine, metabolic, or renal diseases
      - renal artery stenosis → ↑ renin → ↑ sodium & fluid retention → ↑ BP
        - most common cause of secondary hypertension
      - tumors of the adrenal gland → ↑ circulating catecholamines → ↑ TPR

Hypertension

- **Effects on the physiological response to acute exercise**
  - **Usually, hypertensives have a normal ↑ in BP from baseline levels**
    - BP responses to exercise may be exaggerated or diminished in a few cases
    - pre-existing hypertension → absolute ↑ in BP may increase enough to be classified as a hypertensive response to exercise (SBP > 225 mmHg)

- **Effects of exercise training on hypertension**
  - **10 mmHg ↓ in SBP for mild to moderate hypertensives**
    - possible ↓ in circulating NE and ↑ in plasma vasodilator substances
    - possible ↑ in insulin sensitivity → ↓ BP (less insulin → less Na^+ retention)

- **Implications for exercise testing**
  - **Standard ACSM guidelines apply to hypertensives**
    - SBP > 200 and / or DBP > 110 is a relative contraindication to testing
    - SBP > 250 and / or DBP > 115 is a relative indication to terminate test
      - those exhibiting a hypertensive response to exercise may be at high risk for developing hypertension at rest

Hypertension

- **Implications for exercise prescription**
  - **Those with BP > 180/110 should be medicated before exercising**
  - **Normal Exercise Rx parameters may be used**
    - consider starting at a low intensities and durations
  - **Resistance exercise has not consistently been shown to ↓ BP**
    - pressor responses to lifting heavy weights may ↑ SBP to dangerous levels
    - "circuit" types of training with lighter weights and higher reps are preferred

Heart Failure (Acute & Chronic)

- **Pathophysiology**
  - **↓ LV contractile capability → ↓ $\dot{Q}$ …… due to:**
    - Prolonged untreated hypertension
    - Myocardial infarction (acute heart failure or CHF possibly resulting from accumulated MI plus hypertension damage)
    - Cardiomyopathy (malformed malfunctioning heart muscle)
    - Valvular heart disease
      - aortic stenosis & regurgitation
      - coarctation of aorta (narrowing of aortic outflow tract)
      - mitral stenosis & regurgitation
    - Myocardial infection & inflammation (myocarditis, restrictive pericarditis)

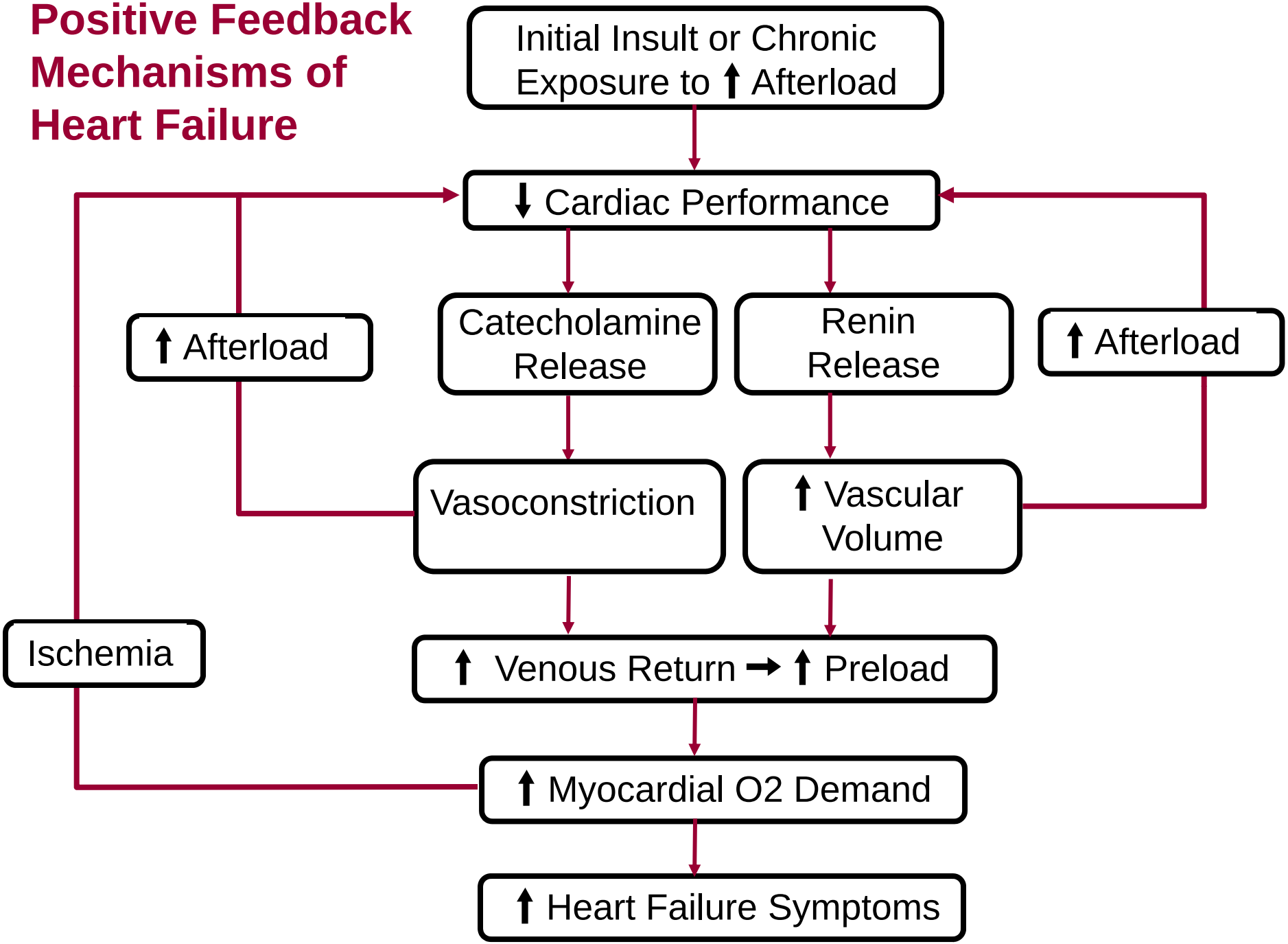
Heart Failure (Acute & Chronic)

- **Pathophysiology**
  - **The body can compensate for the ↓ $\dot{Q}$ (compensated HF)**
  - **(consequences of compensation in red)**
    - ↑ tissue O_2 extraction - almost 100% of O_2 is extracted (↑ AVO2-difference)
    - ↑ β sympathetics → ↑ TPR → ↑ venous return & preload (↑ afterload)
    - ↓ renal perfusion → ↑ blood vol → ↑ venous return & preload (↑ afterload)
      - ↑↑ preload → (ventricular dilation - max stretch on LV fibers)
    - Myocardial hypertrophy occurs in response to pressure / volume overload
      - Volume overload (↑↑ preload) → eccentric hypertrophy
      - Pressure overload (↑↑ afterload) → concentric hypertrophy
      - Hypertrophy → ↓ ventricular contractility + ↓ ventricular compliance
        - usually, both systolic function and diastolic function are affected

Heart Failure (Acute & Chronic)

- **Pathophysiology**
  - **Summary of pathological changes due to heart failure**
    - ↓ $\dot{Q}$ during exercise and, in severe cases, at rest
    - ↑ afterload due to ↑ α & β symp. mediated ↑ in TPR and fluid retention
    - ↑ preload - due to diastolic dysfunction & fluid retention
    - ↑ left atrial pressure → exertional dyspnea
    - destructive changes in organs due to lack of perfusion: muscles, kidneys….
- **Effects on the physiological response to acute exercise**
  - **↓ HR + ↓ SV → ↓ $\dot{Q}$**
  - **↓ max HR**
  - **↓ O_2 delivery + muscle lactate buildup → fatigue + hyperventilation**
    - sometimes occurs before the onset of CHF related dyspnea symptoms
  - **↓ exercise tolerance due to**
    - inability to ↑ $\dot{Q}$
    - ↓ oxidative metabolism → ↑ dependence on glycolysis
    - muscle atrophy
  - **Poor redistribution of blood flow during exercise**

Positive Feedback Mechanisms of Heart Failure



Heart Failure (Acute & Chronic)

- **Signs & symptoms of left ventricular heart failure**
  - **Dyspnea (pulmonary edema)**
    - ↓ contractility of LV → pressure "backs up" in pulmonary circulation
      - fluid leaks into alveoli → ↓ gas exchange, cough, dyspnea
    - mismatch of $\dot{V}_E : \dot{Q}$ → ↑ physiologic dead space in lungs → dyspnea
  - **Fatigue & weakness ("heaviness" in arms and legs)**
    - caused by ↓ perfusion to the muscles
  - **Dizziness, confusion, anxiety, memory loss,**
    - caused by ↓ perfusion to the brain
- **Signs and symptoms of right ventricular heart failure**
  - **Jugular venous distension**
    - pressure "backed up" behind RV into the major veins → venous distension
  - **Ascending peripheral edema**
    - ↑ venous pressure → edema in distal extremities - progresses to thighs
      - weight gain: patients may be monitored daily for gain in water weight
  - **Hepatomegaly & ascites (fluid in peritoneal cavity)**
    - ↑ venous pressure → blood engorged liver + fluid leaks into peritoneum

Heart Failure (Acute & Chronic)

- **<u>Treatment strategies in CHF</u>: main goal: ↓ cardiac workload**
  - **Angiotensin converting enzyme (ACE) inhibitors:**
    - ↓ angiotensin II → ↓ arterial vasoconstriction → ↓ afterload
    - ↓ angiotensin II → ↑ venodilation → ↓ preload
    - ↓ Na^+ retention → ↓ H2O retention → ↓ blood vol → ↓ preload
      - only drug shown to both improve symptoms and prolong life in CHF
  - **Diuretics + dietary salt restriction**
    - ↓ H2O retention → ↓ blood vol → ↓ preload
  - **Positive inotropic agents: digitalis, sympathomimetics, PD inhibitors**
    - digitalis → ↑ contractility → ↑ $\dot{Q}$ → ↓ CVP → ↓ preload
    - sympathomimetics: ↑ contractility → ↑ $\dot{Q}$ → ↓ CVP → ↓ preload
    - PD inhibitors → ↑ cyclic AMP in myocardium and vascular smooth muscle
      - ↑ contractility + ↑ arterial & venous dilation → ↓ preload & afterload
  - **Arterial and venous dilators**
    - nitrates → ↑ venodilation → ↓ preload
    - nitrates → ↑ arterial dilation → ↓ afterload
  - **Antiarrhythmics - CHF is the most arrhythmogenic CVD (V-tach)**

Heart Failure (Acute & Chronic)

- **Implications for exercise testing:**
  - **Unstable or decompensated CHF is a contraindication to testing**
  - **Maine goals of exercise testing in CHF patients:**
    - identify the severity of CHF (precisely quantify functional capacity - $\dot{V}O_{2max}$)
    - test the efficacy of various interventions
    - evaluate the possibility of other disease (CAD, PVD, VHD, arrhythmias, etc.)
  - **Make sure testing protocol, equipment, and staff are appropriate**
    - begin protocol at < 3 METS with small stage workload increments
    - be prepared for hypotension, arrhythmias, and chronotropic incompetence
    - use respired gas measurements if possible
      - breathing can be assessed for efficiency, T-vent can be determined
  - **Observe conservative test endpoints**
    - fatigue, weakness, pallor → ↓ $\dot{Q}$
    - CNS symptoms (dizziness, unsteady gait) → ↓ cerebral perfusion
    - ST-segment changes (especially if accompanied by symptoms)
    - PVC's & ventricular ectopy (especially in aortic stenosis patients)
    - atrial flutter or fibrillation accompanied by a fast ventricular response

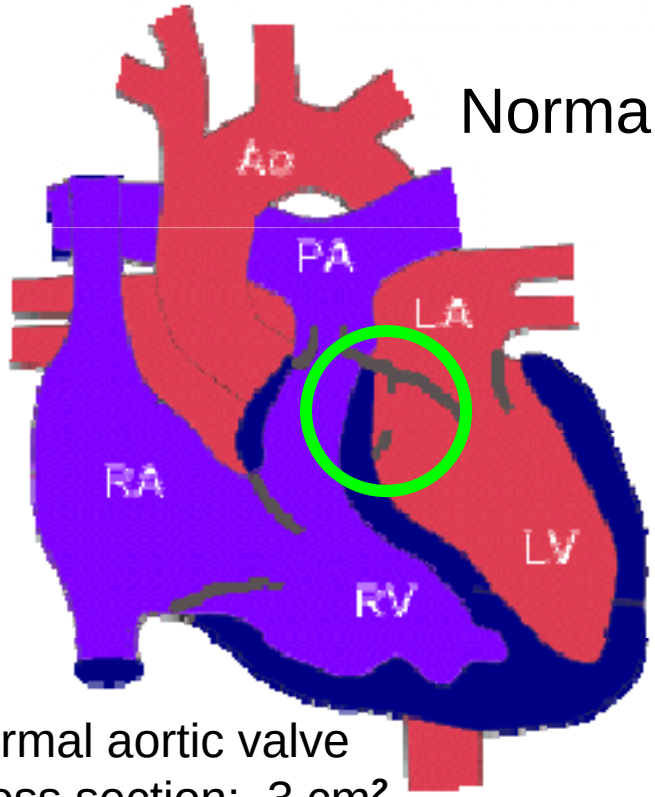
Heart Failure (Acute & Chronic)

- **Implications for exercise Rx:**
  - **Observe conservative contraindications to training:**
    - decompensated CHF, LV outflow tract obstruction, unstable arrhythmias
  - **Maine goals of exercise training in CHF patients:**
    - ↓ symptoms + ↑ functional capacity ($\dot{V}O_{2peak}$) & T-vent → ↑ quality of life
  - **Make sure exercise Rx and patient monitoring is appropriate**
    - prolong warm-up and cool-down sessions
    - use RPE and dyspnea scales instead of THR or absolute workload targets
    - begin at a low workload (Borg 11-13) - always below point of symptoms onset
      - workload should be less than that which produces:
        - LV wall motion abnormalities or a drop in ejection fraction
        - an excessive left atrial pressure
        - anaerobic threshold (ventilatory threshold)
    - progress by advancing the duration of the bout
    - avoid isometric exercise
      - valsalva maneuver → ↑ thoracic pressure → ↑ afterload
    - CHF patients may deteriorate rapidly → frequent re-assessment of symptoms

Valvular Heart Disease: Aortic Stenosis

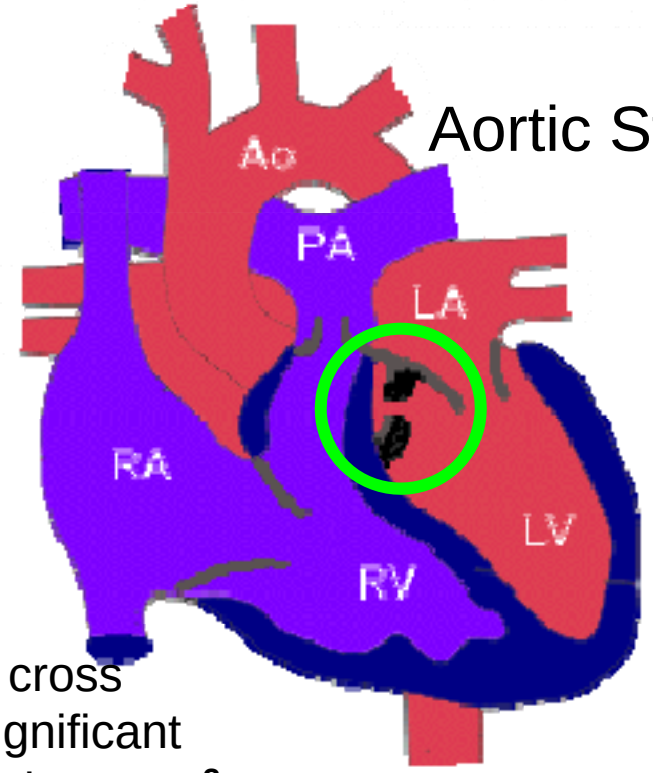
- **Pathophysiology**
  - Narrowing of the aortic outflow tract at, above, or below the valve due to valve fibrosis & calcification, congenital abnormality, or damage from rheumatic fever
  - Idiopathic hypertrophic subaortic stenosis (form of cardiomyopathy)
    - asymmetric hypertrophy of the ventricular septum → ↓ outflow

Normal Heart



normal aortic valve cross section: 3 cm^2

Aortic Stenosis



aortic valve cross section in significant aortic stenosis: 1 cm^2

Valvular Heart Disease: Aortic Stenosis

- **Pathophysiology (continued)**
  - **↑ pressure required to eject blood into aorta → ↑ LV muscle mass**
    - the thickened LV eventually dilates, stiffens, and begins to fail
  - **In some cases the normal tricuspid valve is abnormally bicuspid**
  - **Usually occurs in children (congenital) or after age 70**
  - **Pressure gradient across the valve is critical diagnostic factor**
    - mild AS: peak LVSP is 10 - 40 mmHg higher than aortic pressure
    - severe AS: peak LVSP is > 60 mmHg higher than aortic pressure
- **Symptoms**
  - **Fatigue & syncope**
  - **Dyspnea (with exertion and at night)**
  - **Anginal type chest pains**
  - **Sudden death**

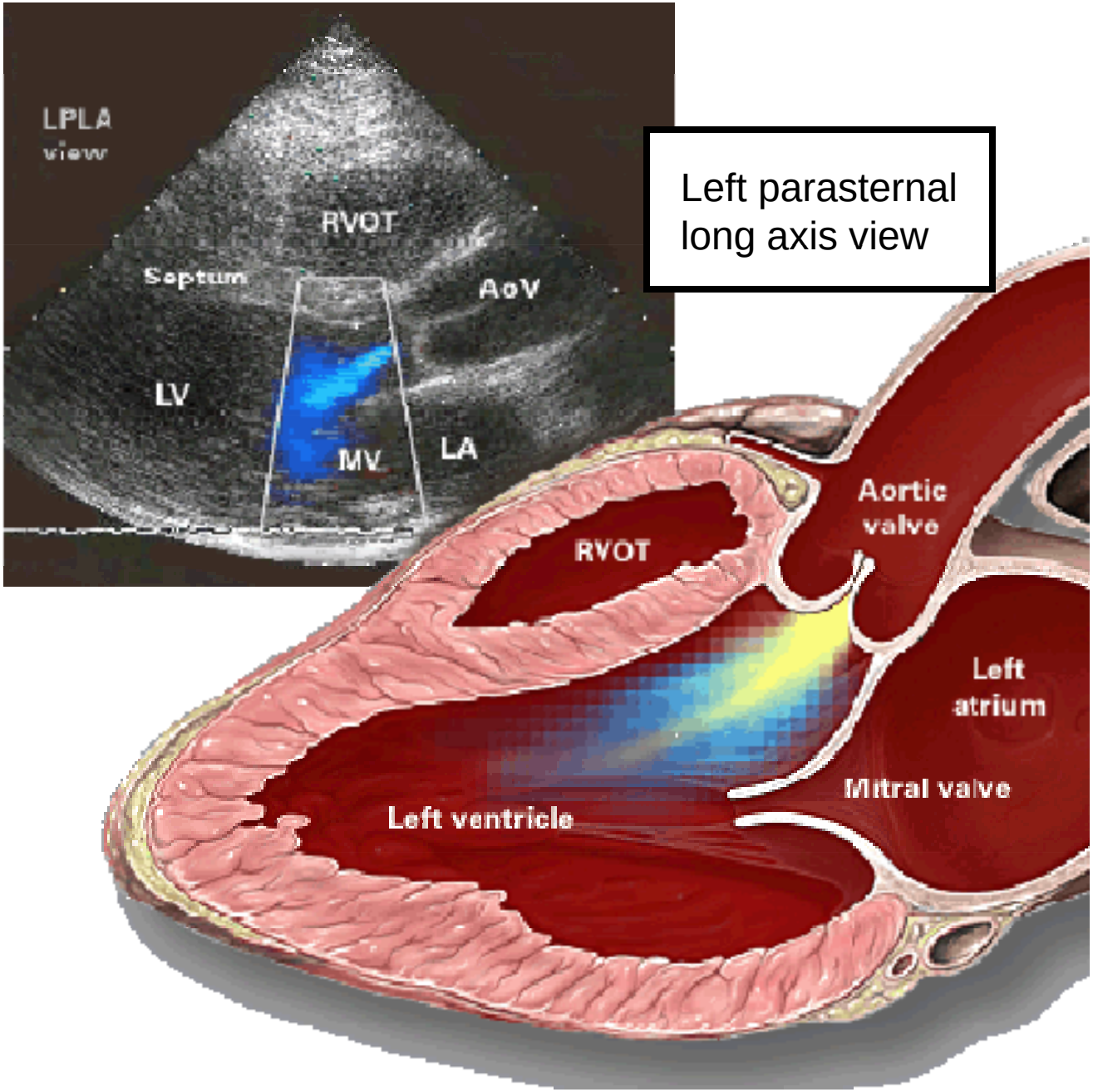
Valvular Heart Disease: Aortic Stenosis

- **Treatment**
  - **Balloon valvuloplasty - "stretching" the aortic valve opening**
    - may improve condition for a period of time, but procedure is not curative
  - **Valve replacement surgery - artificial valve or autograft valve**
    - Ross Operation - autografted valve can grow with the child
      - patient's pulmonary valve grafted into aortic valve
      - donor valve replaces transplanted pulmonary valve
- **Implications for exercise testing**
  - **Severe aortic stenosis is an absolute contraindication to testing**
    - aortic stenosis is associated with ventricular arrhythmias & sudden death
  - **Sometimes GXT 's are done to quantify functional capacity**
    - ST-segment depression is often seen
    - important to use low stage increments so FC can be accurately identified
    - important to closely monitor pressure for falloffs

Valvular Heart Disease: Aortic Stenosis

- **Implications for exercise training**
  - **Clinically mild AS can be prescribed exercise - normal parameters**
    - asymptomatic, negative GXT should be secured before exercise begins
    - begin at low intensities and durations
  - **Patients with gradients > 40 mmHg should not do intense exercise**
    - exercises with high cardiac demands should be avoided
      - no competitive activities
  - **Surgery is usually recommended when gradient exceeds 60 mmHg**

Aortic Regurgitation (Insufficiency)



Valvular Heart Disease:
Aortic Regurgitation (Insufficiency)

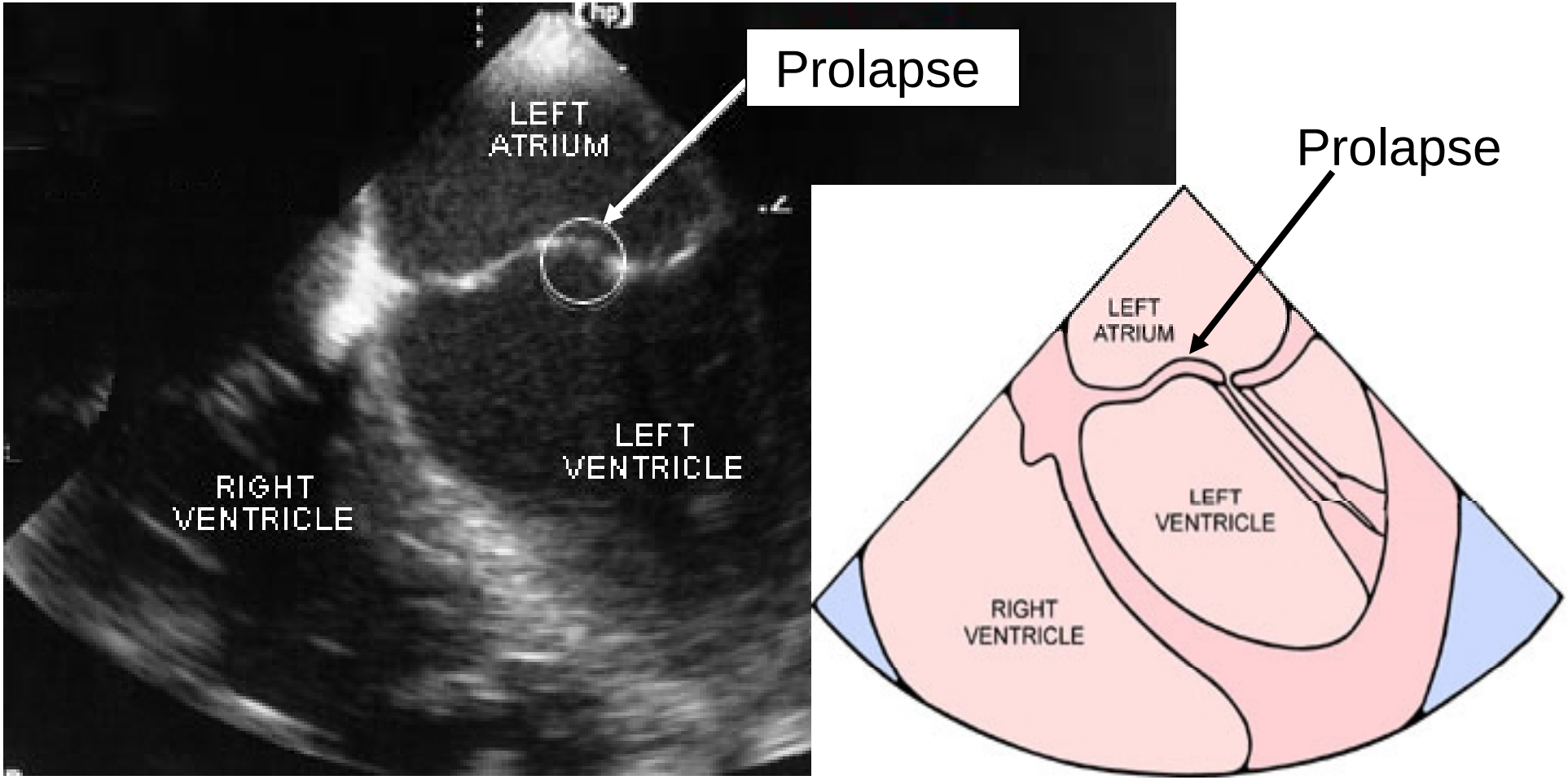
- **Pathophysiology**
  - **Retrograde flow from the aorta back into the LV**
  - **Usually caused by:**
    - rheumatic fever or bacterial endocarditis
    - congenital valve defect (valve is bicuspid instead of tricuspid)
    - Marfan's syndrome: composition defects in connective tissue → ↓ stiffness
  - **Heart must pump normal EDV + regurgitant volume**
    - pressure & volume overload → eventual LV failure
    - acute AR → ↑ left atrial pressure → pulmonary edema (EMERGENCY)
- **Signs & Symptoms - note that most are reflective of heart failure**
  - **Fatigue, syncope, dyspnea (with exertion and at night)**
  - **Sensation of forceful heartbeat**
  - **Chest pain**
  - **Arrhythmias**

Valvular Heart Disease:
Aortic Regurgitation (Insufficiency)

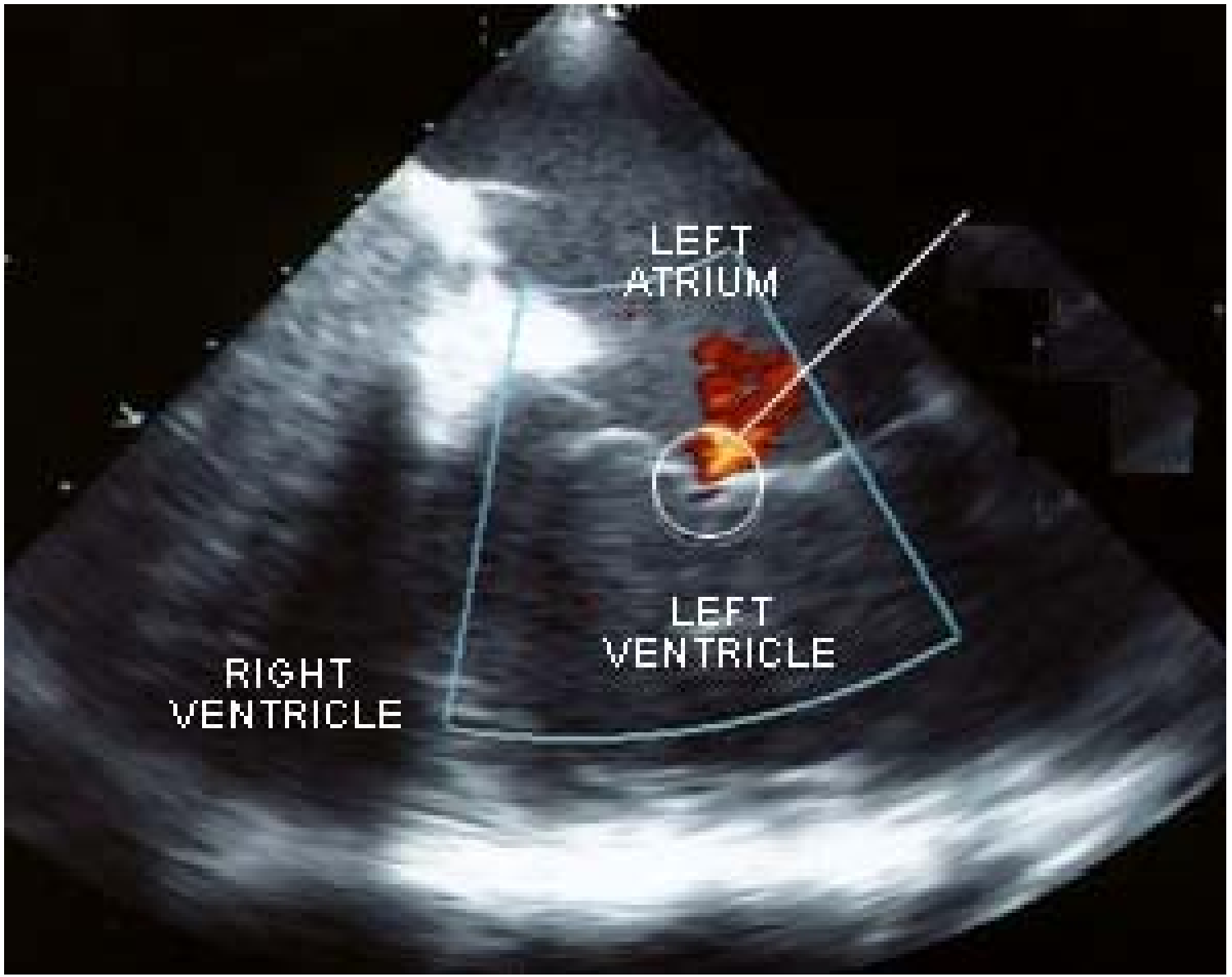
- **Treatment**
  - **Mild / asymptomatic cases**
    - appropriate antibiotic prophylaxis
    - vasodilator drugs to reduce afterload
  - **Acute or severe chronic cases**
    - valve replacement surgery
      - should be done before irreversible damage is done to the heart
- **Implications for exercise testing & RX**
  - **Same precautions & guidelines as in heart failure**
  - **Strenuous or competitive exercise should be avoided**

Valvular Heart Disease: Mitral Valve Prolapse

- **Pathophysiology**
  - **MV leaflet "prolapses" (bulges) back into left atrium during systole**



Valvular Heart Disease: Mitral Valve Regurgitation



Valvular Heart Disease:
Mitral Valve Prolapse - Regurgitation

- **Pathophysiology (continued)**
  - **5% - 10% of US population has some degree of MV prolapse**
  - **Most common in women ages 40 to 50**
  - **Severe MV prolapse will lead to MV regurgitation**
    - retrograde blood flow back into the left atrium
- **MVP Symptoms - most patients are asymptomatic**
  - **Chest palpitations**
  - **Arrhythmias**
  - **Fatigue & anxiety**
  - **Sharp chest pains (possible related to strain on papillary muscle)**
  - **Resting & Orthostatic hypotension**

  SIGNIFICANT REGURGITATION → HEART FAILURE SYMPTOMS:
  - **Dyspnea (with exertion and at night while in prone position)**

Valvular Heart Disease:
Mitral Valve Prolapse - Regurgitation

- **Treatment**
  - For asymptomatic MV prolapse: antibiotic prophylaxis
  - β-blockers or Ca^{++} channel blockers may relieve chest palpitations
  - Severe MV prolapse / regurgitation: valve repair or replacement
    - should be done before irreparable damage is done to LV
- **Implications for exercise testing and Rx**
  - Exam should be performed to rule out other valve problems
  - Normal parameters for exercise testing - symptoms limited test
  - Normal exercise Rx parameters in most asymptomatic patients
  - Patients may be sensitive to exercise induced hypovolemia
  - Patients that should avoid strenuous/competitive/contact sports:
    - moderate to severe regurgitation
    - history of arrhythmogenic syncope or exercise induced tachycardias
    - family history of sudden death or embolism associated with MVP

Valvular Heart Disease: Mitral Valve Stenosis

- **Pathophysiology**
  - **Narrowing of the mitral valve - usually due to rheumatic fever**
    - thickening & calcification of the valve leaflets
    - normal valve area 4 - 6 cm^2 - pressure gradient occurs when area < 2 cm^2
  - **Women have MV stenosis 4 X more than men:**
    - first symptoms may occur during pregnancy
  - **↑ LA pressure transmitted back to lungs → ↑ pulmonary edema**
    - LA becomes dilated → conduction fibers are stretched → A-fib may occur
    - essentially, patients have left sided heart failure without LV dysfunction
- **Signs & Symptoms**
  - **Exertional dyspnea is most common symptom in mild MS**

CONDITION PROGRESSES (VALVE AREA OF 1 CM^2 OR LESS)

- **Marked fatigue & dyspnea due to pulmonary congestion**
- **Paroxysmal nocturnal dyspnea**
- **Cough or hoarseness**
- **Stagnation of LA blood flow → ↑ risk of thrombi formation**

Valvular Heart Disease: Mitral Valve Stenosis

- **Treatment**
  - **For asymptomatic MV stenosis: antibiotic prophylaxis**
  - **β-blockers used to slow HR and ↑ diastolic filling time**
  - **Mild pulmonary congestion can be treated with diuretics**
  - **A-fib patients require antiarrhythmics and anticoagulants**
  - **Severe MS requires valve replacement or balloon valvuloplasty**
- **Implications for exercise testing and Rx**
  - **SV may fall during exercise due to inadequate ventricular filling**
    - exercise → ↑ HR → ↓ diastolic filling time → ↓ SV → ↓ $\dot{Q}$ → ↓ SBP
    - ↓ $\dot{Q}$ → ↓ muscle perfusion → ↑ lactate → ↓ functional capacity
    - pulmonary congestion → ↑ work of breathing → dyspnea is limiting factor
  - **Normal parameters for exercise testing - symptoms limited test**
    - use precautions similar to those for heart failure patients
  - **For exercise Rx, use same precautions as in heart failure patients**
  - **Strenuous / competitive / contact sports should be avoided**

Peripheral Arterial Disease (PAD)

- **Peripheral Arterial Disease - atherosclerotic obstruction of peripheral arteries**
  - **Signs & Symptoms**
    - claudication (usually earliest & most common symptom):
      - cramping in the hips, thighs, & especially the calves
      - caused by skeletal muscle ischemia
    - numbness, weakness, or heaviness of lower extremity muscles
    - severe cases ➞ burning - aching pain at rest in feet & toes
    - pale color & palpable coldness of lower extremities
    - diminished or absent peripheral pulses (tibial & dorsalis pedis pulses)
  - **Risk Factors**
    - Hypertension, Diabetes, Age, CAD, Smoking (similar to CAD risk markers)
  - **Diagnosis**
    - ratio of ankle SBP to brachial SBP (AB index) is less than 0.9
    - doppler assessments of flow
    - angiography
    - treadmill testing to assess functional capacity (time to claudication)

Peripheral Arterial Disease (PAD)

- **Treatment**
  - **Exercise → ↑ vascularization and blood flow + ↑ pain tolerance**
    - may double time to claudication or exertion level before it appears
  - **Cilostazol - helps to relieve PAD symptoms**
    - PDE III inhibition → ↑ C-amp → ↓ Ca++ in smooth muscle → vasodilation
    - ↓ platelet aggregation
  - **Pentoxifylline (TRENTAL)**
    - ↓ blood viscosity → ↑ blood flow
  - **Dipyridamole (PERSANTINE), PLAVIX**
    - inhibition of platelet adhesion → ↑ blood flow
  - **Warafin Sodium (COUMADIN)**
    - inhibition of vitamin K dependent coagulation factors → ↑ blood flow
  - **Aspirin & other platelet inhibitors → ↓ platelet aggregation**
  - **Angioplasty (to place stents in large peripheral arteries)**
  - **Lower limb bypass surgery**

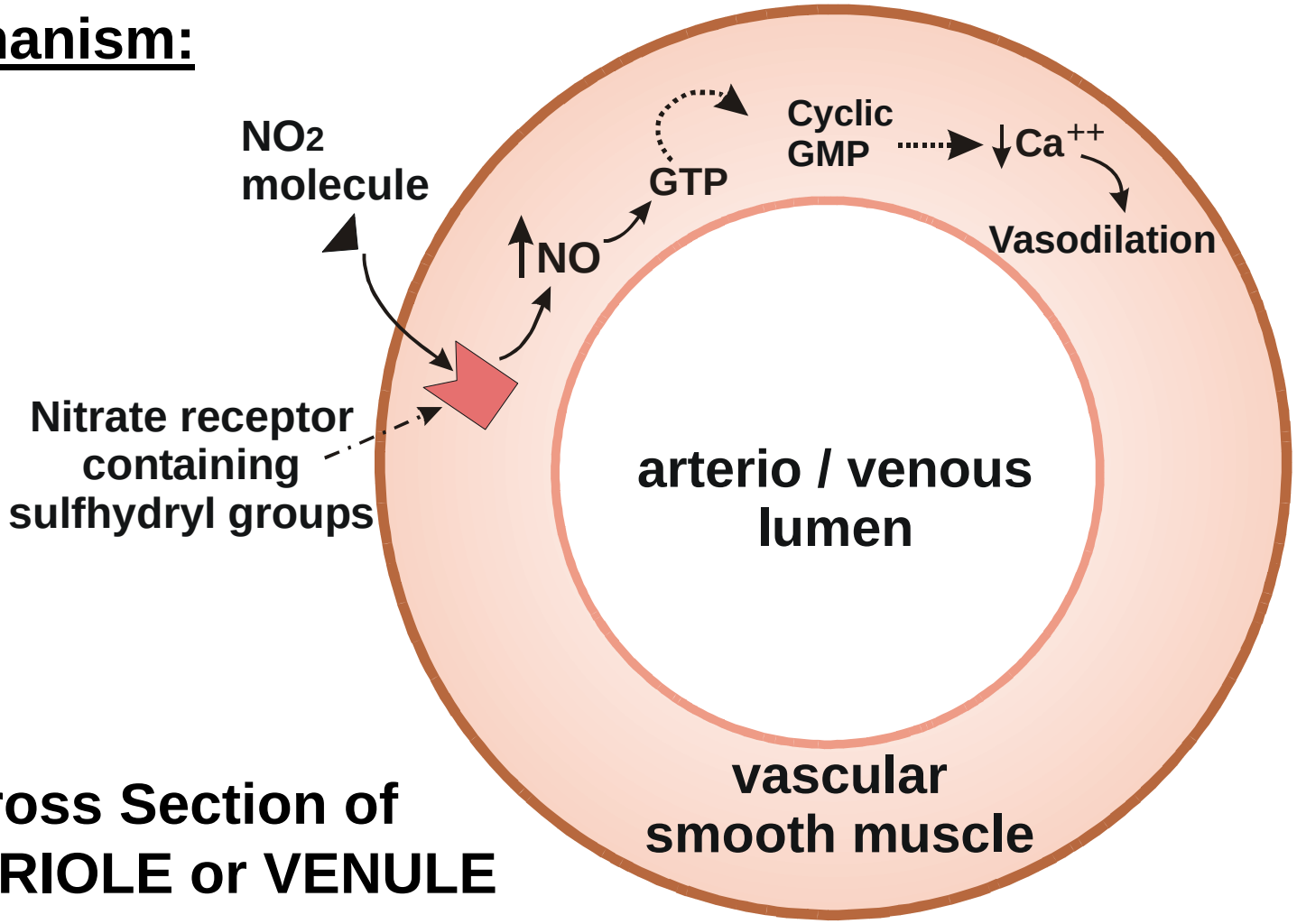
Peripheral Arterial Disease (PAD)

- **Implications for exercise testing and Rx**
  - **Exercise Testing**
    - ABI's are assessed pre & post exercise
    - gradual stage workload increments are used to precisely assess FC
    - pain scale of 1-4 is used to assess claudication pain throughout GXT
    - record elapsed time from volitional termination to symptoms disappearance
    - closely monitor patients for signs of CAD
      - 50% - 80% of PAD patients have CAD
  - **Exercise Rx**
    - Mode: treadmill (walking), stair climbing
    - Frequency: minimum 3 days per week
    - Intensity: 3 on a 4 point pain scale (≅ 40% Karvonen to start)
    - Duration: 20 minutes - exercise to point of pain tolerance, rest, repeat
      - usually, 5 minutes of exercise will produce severe claudication
      - allow full recovery between bouts
      - increase duration before intensity
    - Progression: 40 - 60 minutes of intermittent exercise within 6 months

Nitrates (NO_2) - anti-anginal medication

Nitrates provide exogenous source of Endothelial Derived Relaxation Factor (EDRF) now known to be Nitrous Oxide (NO)

Mechanism:



Cross Section of ARTERIOLE or VENULE

Nitrates

TRIDIL ISORDIL SORBITRATE DILATRATE CARDILATE ISMO MONOKET

Indications

- angina (stable angina management)
- ↓ coronary artery spasm

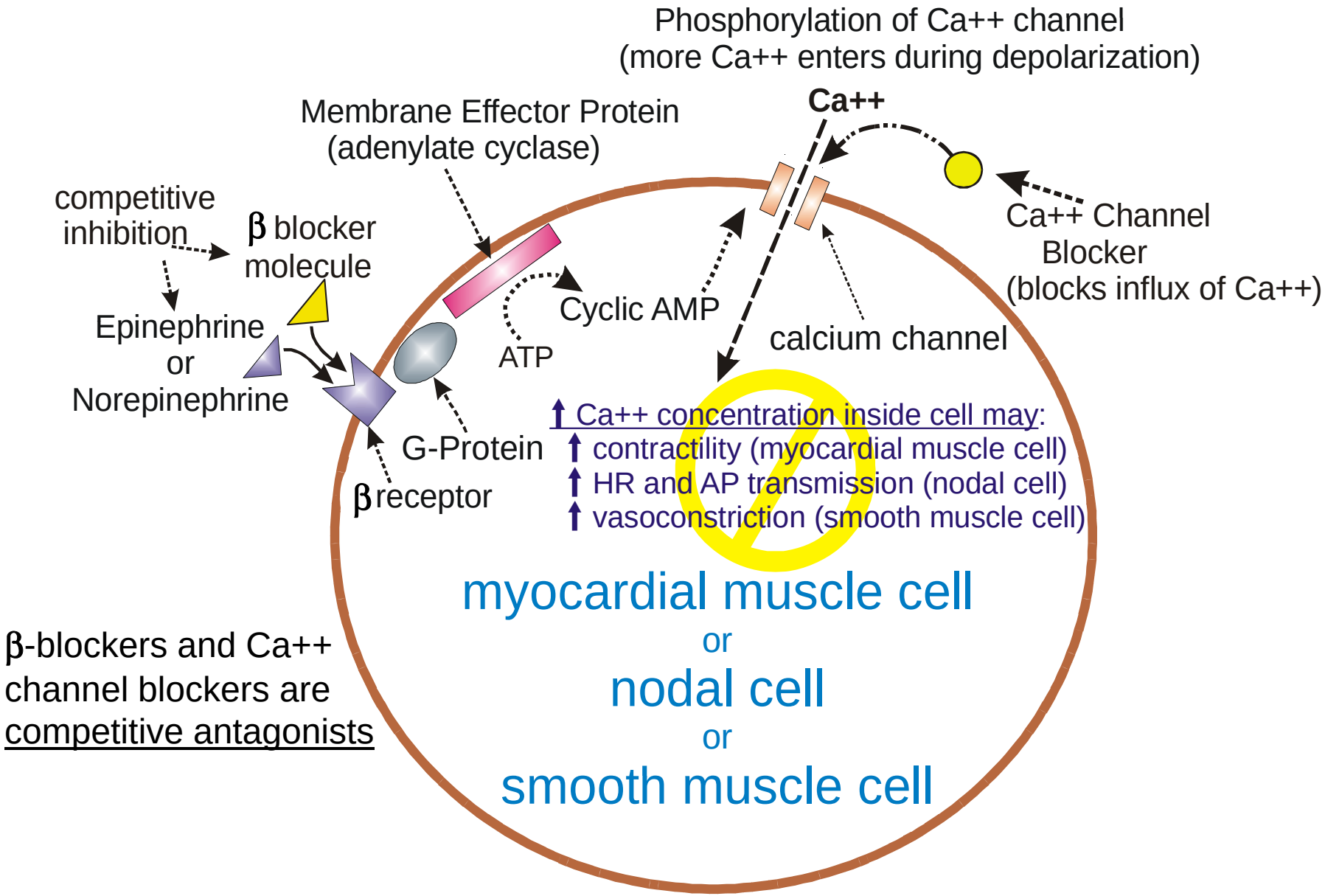
Effects

- venous & arterial vasodilator
- ↓ preload
- ↓ afterload
- ↑ myocardial O2 supply
- ↓ myocardial O2 demand
- ↓ BP
- ↑ HR (via baroreceptor)
- ↑ exercise angina threshold

Adverse Reactions

- dizziness & syncope (↓↓ BP)
- orthostatic hypotension
- tolerance can be built up which means that, over time, more of the drug must be used to achieve the desired effect

β - blocker and Calcium Channel Blocker Mechanisms



β-blockers and Ca++ channel blockers are <u>competitive antagonists</u>

β-blockers

INDEROL, VISKIN, BLOCADREN, CORGARD, COREG Carvedolol, BYSTOLIC

Indications:

- angina
- hypertension (not a 1st line drug for hypertension)
- ventricular & supraventricular arrhythmias
- congestive heart failure & cardiomyopathies
- treatment of MI's

Effects

- ↓ HR & contractility → ↓ $\dot{Q}$ → ↓ BP
- ↑ O_2 supply + ↓ O_2 demand
- ↑ exercise angina threshold
- ↓ functional capacity
- ↓ susceptibility to ventr. arrhyth.

Adverse Reactions

- lethargy (↓ functional capacity)
- ↓ signs of hypoglycemia in diabetics
- ↓ cold tolerance
- depression
- vivid & bizarre dreams

Notes: Some β-blockers are <u>cardioselective</u>, meaning they have greater affinity for β1 (heart) receptors:

BREVIBLOC Esmolol, LOPRESSOR TOPROL-XL Metaprolol

Calcium Channel Blockers

CALAN (Verapamil), CARDAZEM (Diltiazem), PROCARDIA (Nifedipine), CARDENE (Nicardipine), NIMOTOP, NORVASC, PLENDIL, VASCOR, SULAR

Indications:

- hypertension (1st line drug for hypertension)
- PSVT , atrial fibrillation & flutter
- angina
- coronary artery spasm

Effects

- ↓ HR & contractility → ↓ $\dot{Q}$ → ↓ BP
- ↑ O_2 supply + ↓ O_2 demand
- ↑ exercise angina threshold
- ↓ arterial vasoconstriction → ↓ BP
- ↓ PSVT
- ↓ atrio-ventricular conduction rate
- ↓ coronary artery spasm
  - drug of choice for variant angina

Adverse Reactions

- headaches
- flushing
- ↓ cold tolerance
- depression
- vivid & bizarre dreams

Diuretics

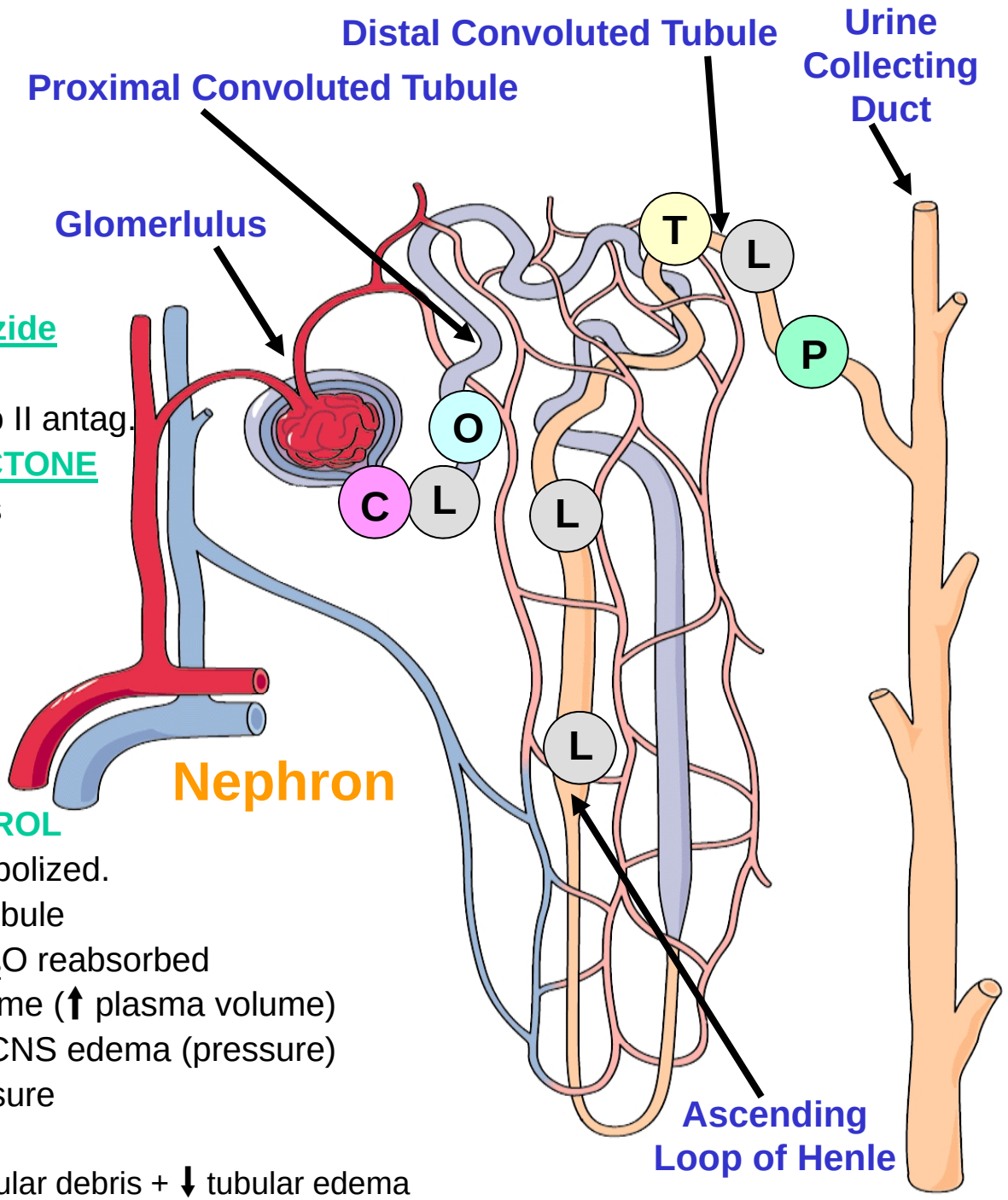
L - **Loop diuretics** **Furosemide LASIX**
- Block reabsorption of Na^+ & Cl^-
- Fast acting - edema removal
- Used to treat CHF

T - **Thiazide diuretics** **Hydrochlorothiazide**
- Block reabsorption of Na^+ & Cl^-
- Combined with ACE inhib. & Angio II antag.

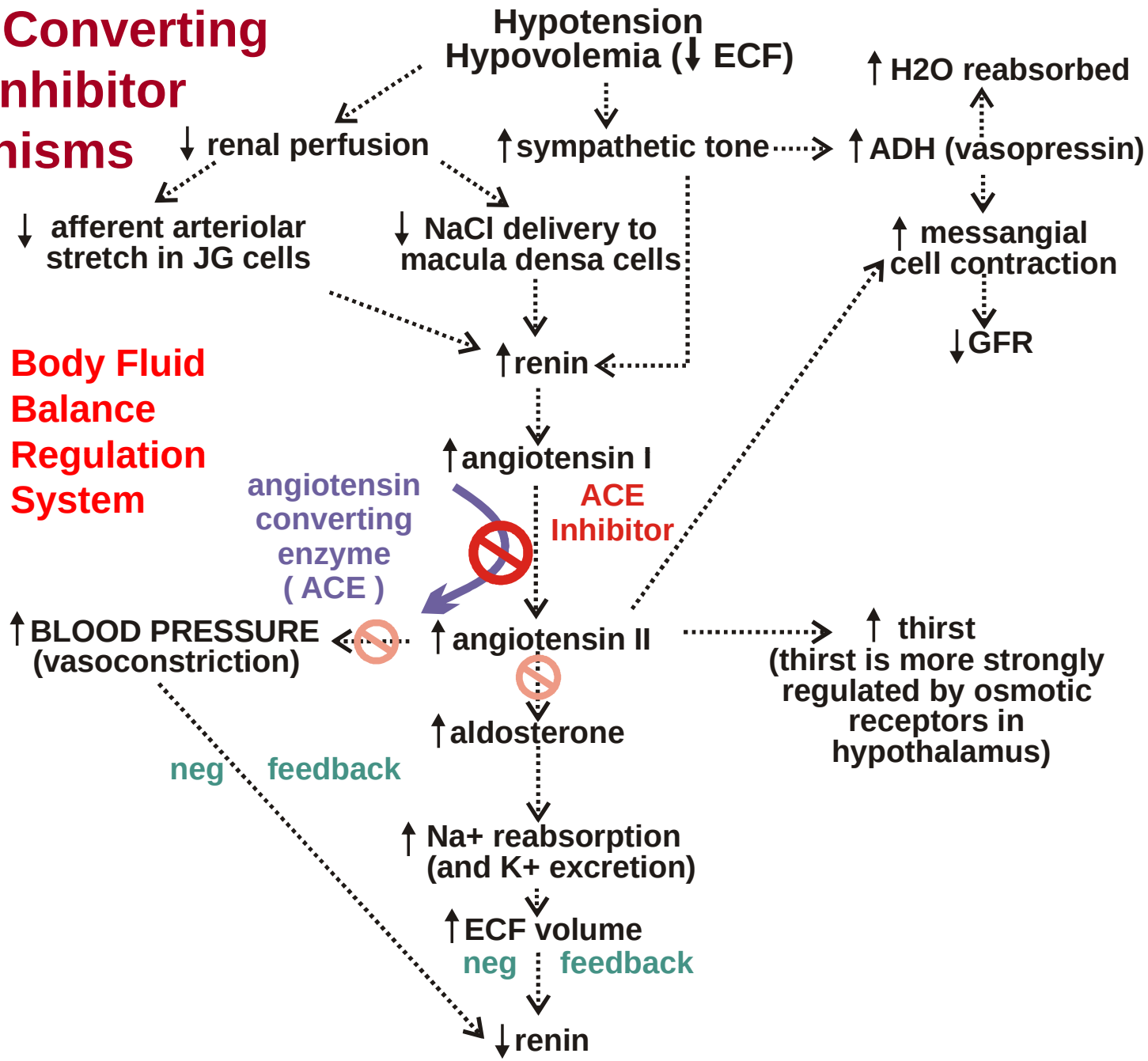
P - **K^+ sparring** **Spironolactone ALDACTONE**
- Some are aldosterone antagonists
- Others are thiazides
- All have antikaliuretic properties

C - **Carbonic anhydrase inhibitors**
- ↓ HCO_3 resorption → mild ↓ H_2O
- Primarily used to treat glaucoma
- ↓↓ production of aqueous humor

O - **Osmotic diuretics** **Mannitol OSMITROL**
- 6-C sugar alcohol that is not metabolized.
- Filtered through glomerulus into tubule
- ↑ osmolarity of tubular fluid →↓ H_2O reabsorbed
- ↑ plasma osmolarity → ↓ ICF volume (↑ plasma volume)
- Primarily used to ↓ intracranial & CNS edema (pressure)
- Can be used to ↓ intraocular pressure
- Can be used to treat renal failure
  - ↑ fluid flow rate flushes out cellular debris + ↓ tubular edema



Angiotensin Converting Enzyme Inhibitor Mechanisms



Drugs Affecting the Renin-Angiotensin System

1. Angiotensin Converting Enzyme Inhibitors

VASOTEC CAPOTEN ZESTRIL ACCUPRIL MONOPRIL LOTENSIN LISINOPRIL

Indications:

- Hypertension (1st line drug for hypertension – along with Ca^{++} blockers)
- Congestive heart failure

Effects:

- ↓ blood (plasma) volume
- ↓ vasoconstriction
- ↓ preload & afterload
- ↑ cardiac effciency & ↓ edema
  - drug of choice for CHF patients

Adverse effects:

- cough
- hypotension

2. Angiotensin II Antagonists COZAAR BENICAR DIOVAN

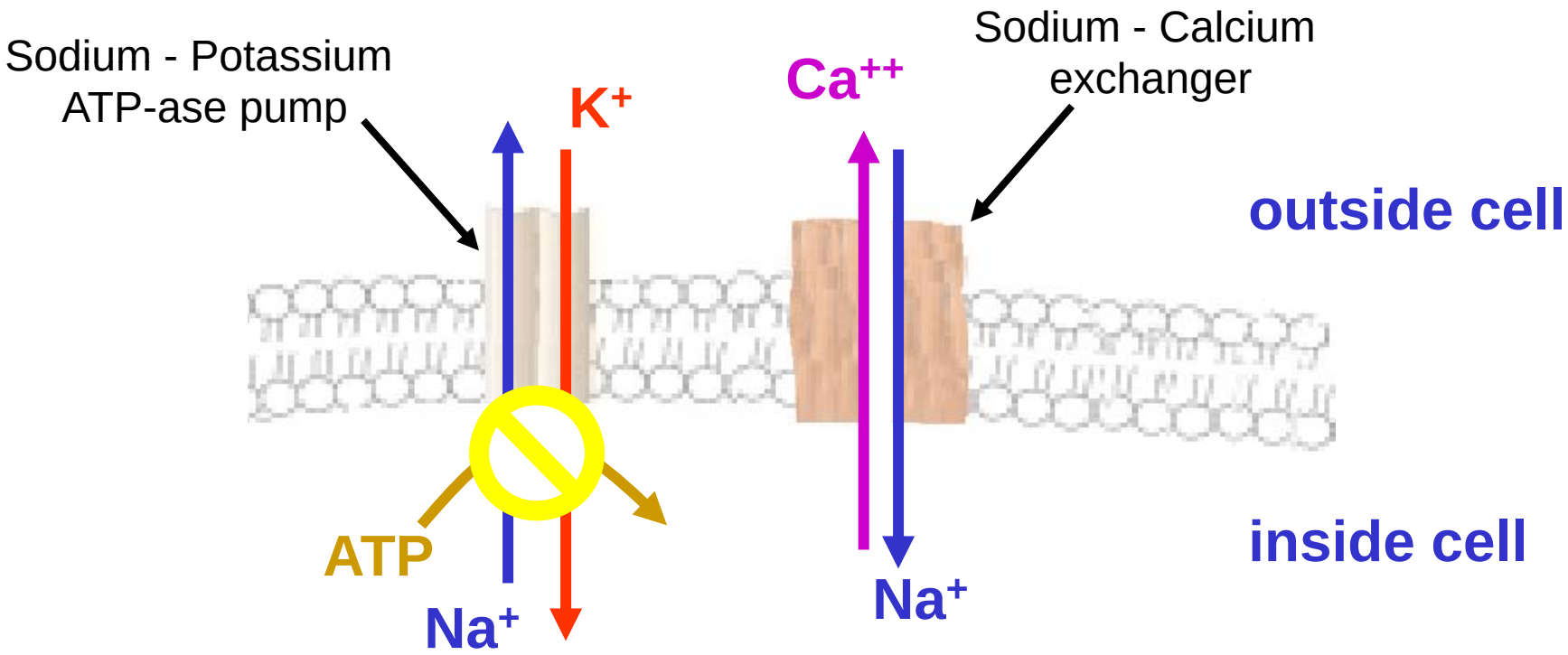
Competitive antagonist of Angiotensin II:

- ↓ aldosterone production and ↓ angiotensin II mediated vasoconstriction

DIGITALIS DIGOXIN, LANOXIN

Poisons the $Na^+ K^+$ ATP-ase pump

- ↑ [Na^+] inside cell → ↓ activity of exchanger → ↑ Ca^{++} inside cell
- ↑ Ca^{++} inside cell → ↑ myocardial contractility



Ca^{++} extrusion is passively linked to Na^+ extrusion from repolarizing cells. This process involves active transport and requires energy

Anti-platelet Drugs: Thienopyridines

PLAVIX (Clopidogril) TICLID (Ticlopidine)

- **Inhibits platelet aggregation (stops platelets from sticking together)**
  - ↓ platelet aggregation → ↓ clot formation (↓ atherothroembolic events)
  - often used in conjunction with Aspirin
  - often used after CABG surgery, angioplasty / stent placement
- **Indications:**
  - helps prevent MI's, Strokes, TIA's
  - used to prevent clots in valvular heart disease or during various surgeries
- **Precautions & side effects:**
  - major side effects: ↑ gastrointestinal and other bleeding, ↓ neutrophil number
    - ↑ time for coagulation to take place → ↑ bleeding or bruising from trauma
      - use NSAID's with caution due to the compounding effect of the drugs
  - FDA has issued updated warnings:
    - ↑ risk for heart problems & unsubstantiated claims of effectiveness

Anti-platelet Drugs: Phosphodiesterase (PDE3) Inhibitors

PERSANTINE (Dipyridamole) AGGRENOX (Dipyridamole + Aspirin)

Cilostazol (PLETAL)

- **Inhibits Phosphodiesterase → ↓ breakdown of C-AMP + ↑ Adenosine**
  - **↑ Cyclic-AMP in the platelet → ↓ platelet aggregation**
  - **↑ adenosine → relaxation of arterial smooth muscle → vasodilation**
  - **↑ contractility + ↑ stroke volume + ↓ afterload & preload**
    - **used to treat congestive heart failure**

- **Indications:**
  - used propholactically to prevent throboembolic events, PAD, CHF
  - used as an adjunct to other anticoagulants in the prevention of postoperative thromboembolic complications of cardiac valve replacement