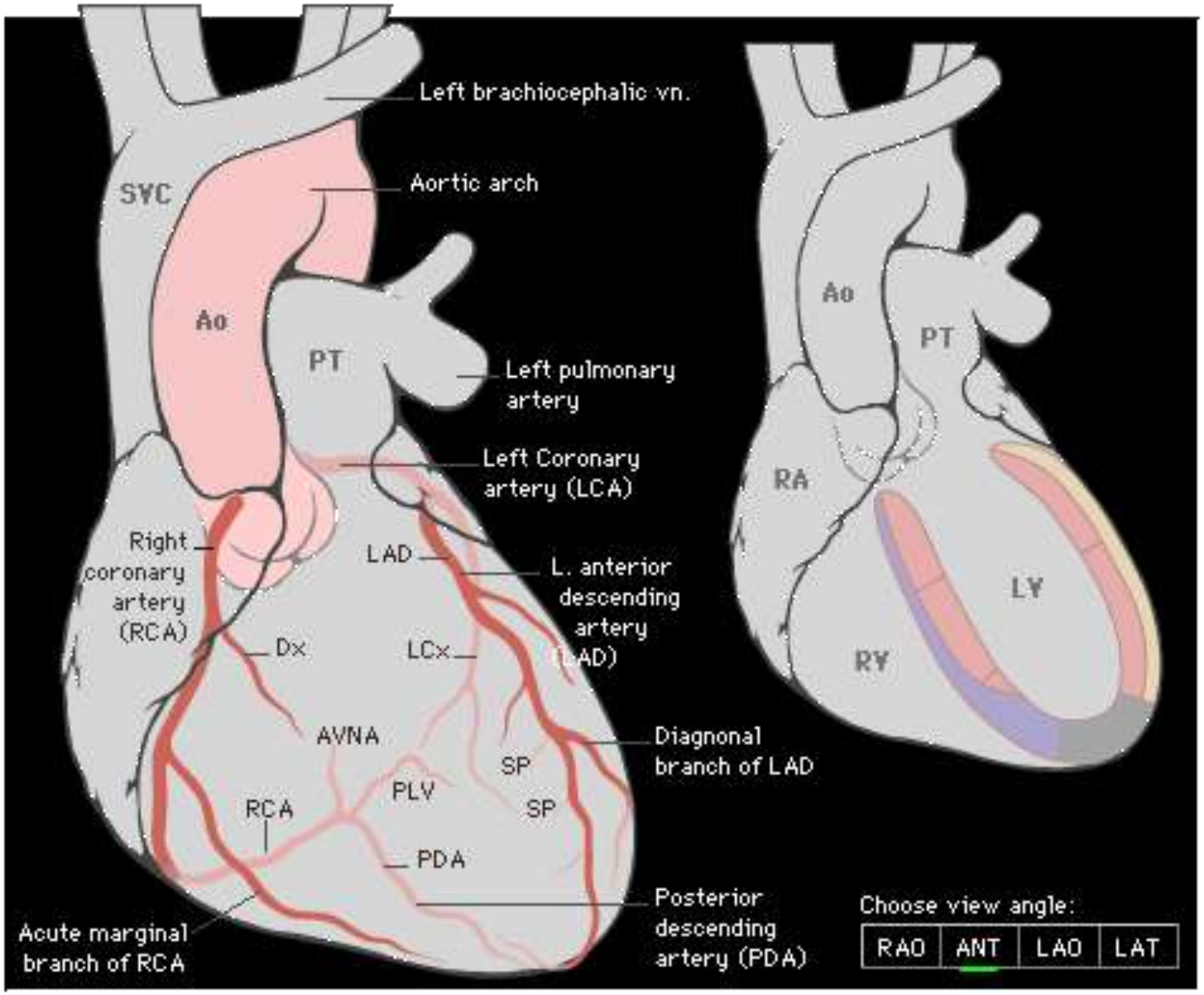
Coronary Circulation

Coronary Artery Disease

Reading

- Klabunde, Cardiovascular Physiology Concepts
  - Chapter 7 (Organ Blood Flow) pages 151-155 (Section on Coronary Circulation)
  - Chapter 4 (Cardiac Function) pages 85-88

Coronary Artery Anatomy


Left brachiocephalic vn.
SVC
Aortic arch
Ao
PT
Left pulmonary artery
Left Coronary artery (LCA)
Right coronary artery (RCA)
LAD
L. anterior descending artery (LAD)
Dx
LCx
AVNA
Diagnonal branch of LAD
SP
PLV
SP
RCA
PDA
Posterior descending artery (PDA)
Acute marginal branch of RCA
Ao
PT
RA
LV
RV
Choose view angle:
RAO
ANT
LAO
LAT

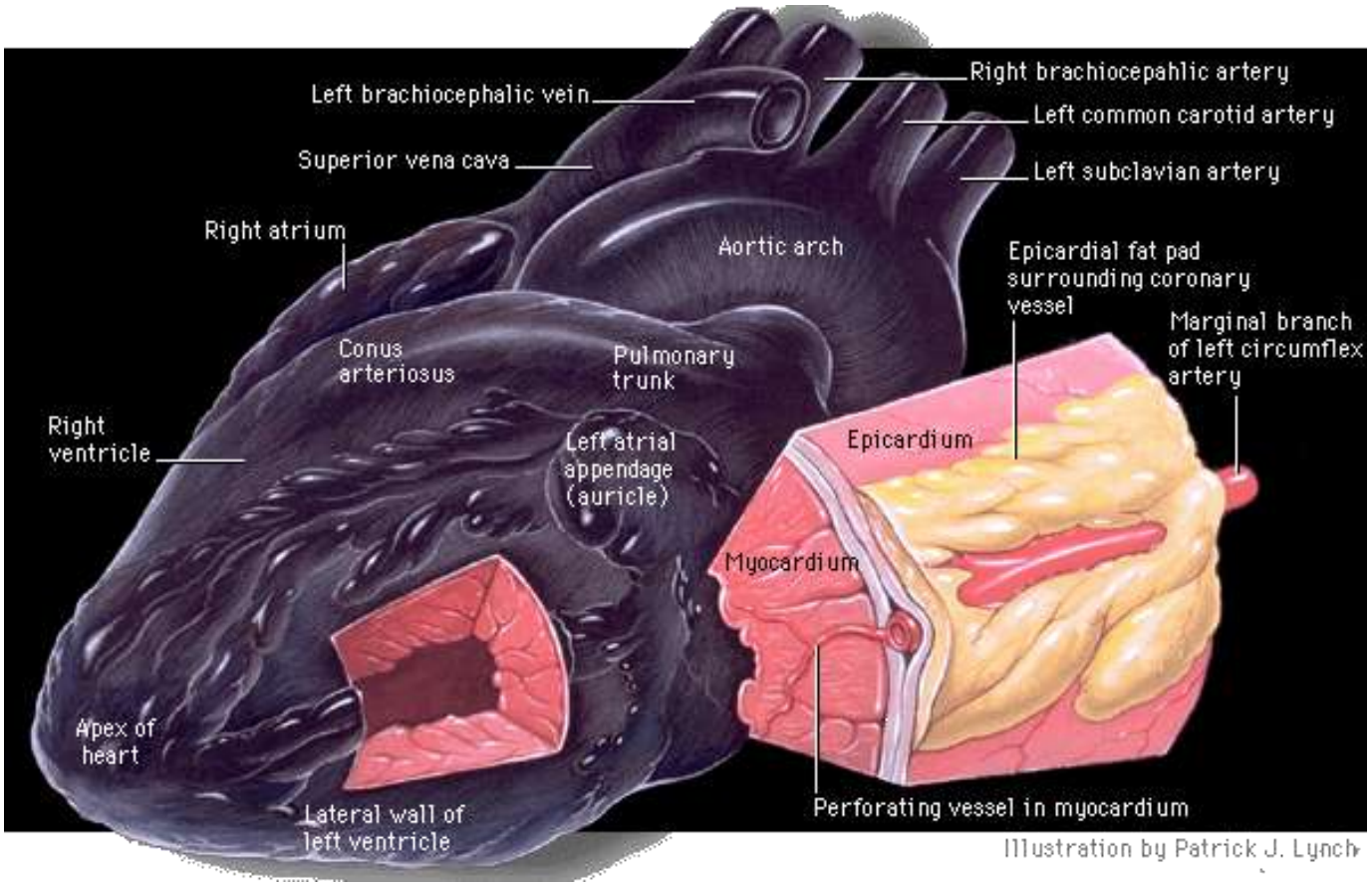
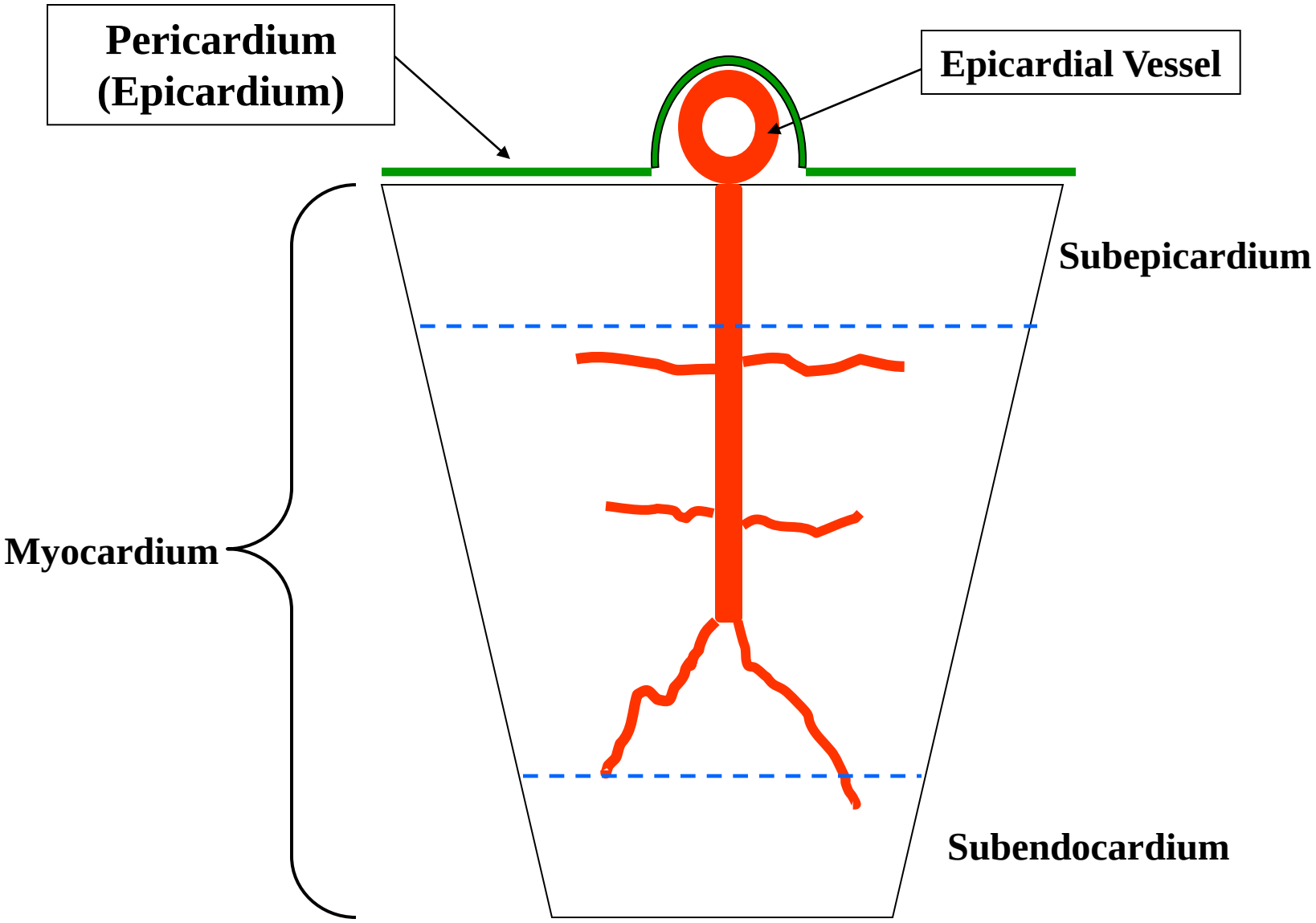


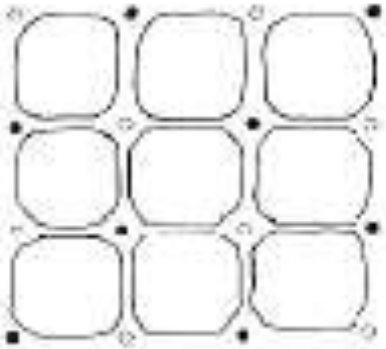
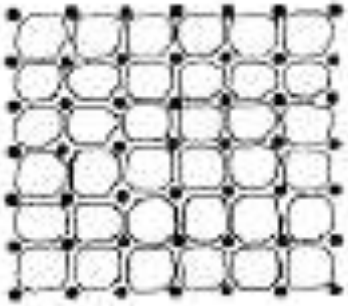
Illustration by Patrick J. Lynch


Pericardium
(Epicardium)
Epicardial Vessel
Subepicardium
Myocardium
Subendocardium

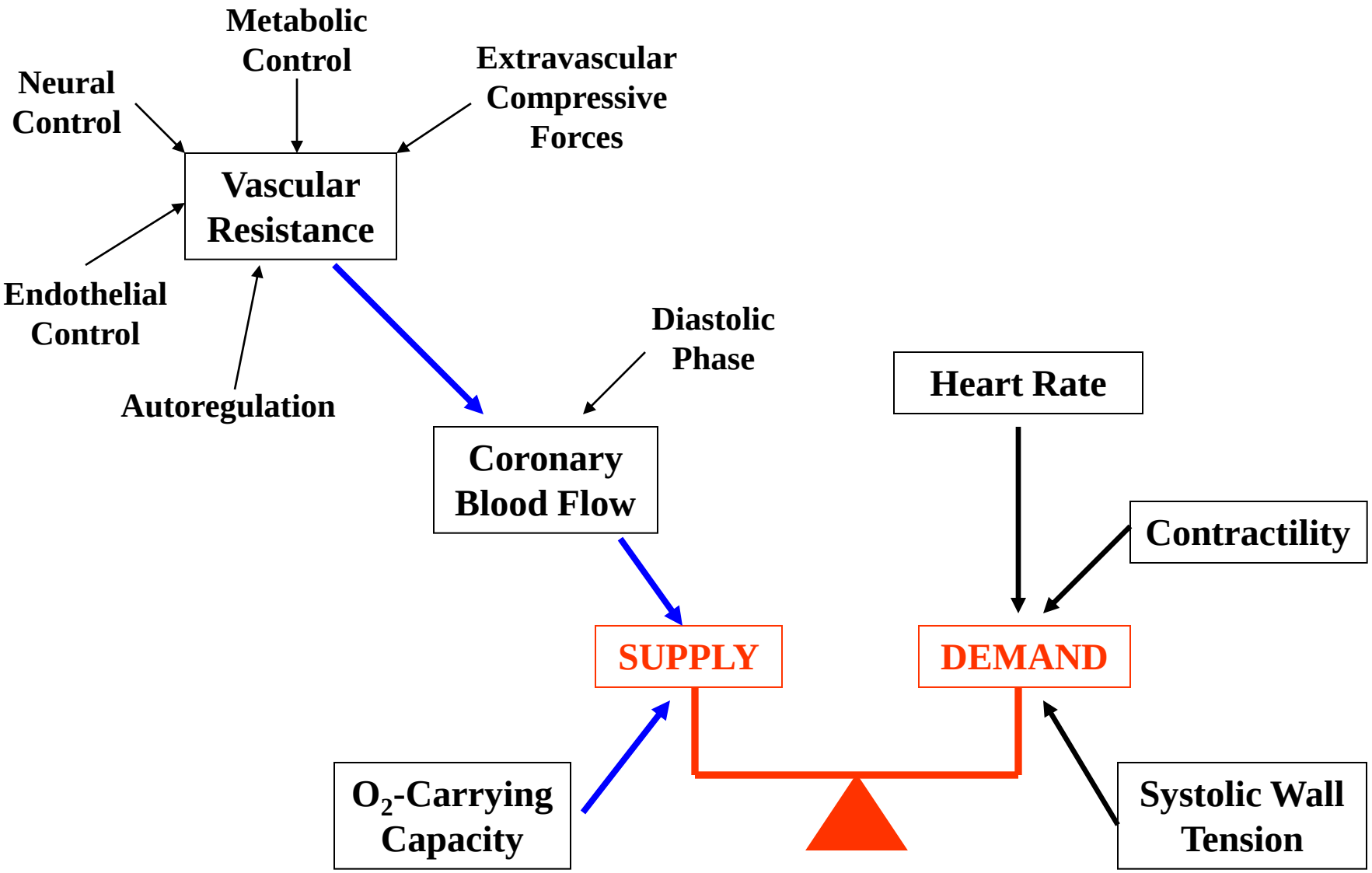
Coronary Vascular Resistance

- Epicardial conductance vessels
  - Only a small % of resistance normally
  - Stenotic lesions
- Intramyocardial vessels (arterioles)
  - Contribute most to total coronary vascular resistance

Capillary Density in the Heart

	Skeletal muscle	Cardiac muscle
		
Fibre diameter	50 µm	18 µm
Capillaries per mm^2	400	3000

Determinants of Myocardial Oxygen Supply and Demand


Metabolic Control
Neural Control
Extravascular Compressive Forces
Vascular Resistance
Endothelial Control
Autoregulation
Diastolic Phase
Heart Rate
Coronary Blood Flow
Contractility
SUPPLY
DEMAND
O_2-Carrying Capacity
Systolic Wall Tension

Myocardial Oxygen Supply

Resting O2 Consumption of Various Organs

Liver	2.0 ml/100 g/min
Kidneys	6.0 ml/100 g/min
Brain	3.3 ml/100 g/min
Skin	0.3 ml/100 g/min
Skeletal muscle	0.2 ml/100 g/min
Cardiac muscle	9.7 ml/100 g/min
Whole body	0.4 ml/100 g/min

Coronary Perfusion Pressure

- Pressure gradient that drives blood through the coronary circulation.

Coronary Perfusion Pressure =

Diastolic BP – LVEDP (or PCWP)

Myocardial Oxygen Supply
Oxygen Content of Blood

- O2 Content =

  (1.36 cc O2/g Hgb/100 ml blood x Hgb x % Saturation) + (pO2 x 0.003)

- O2 delivered to myocardium =

  O2 content x coronary blood flow

Myocardial Oxygen Supply

- Oxygen Extraction
  - **The heart extracts oxygen to a greater extent than any other organ**
  - Coronary sinus pO2 value is normally in range of 20-22 mmHg (% sat = 32-38%)
  - Can only minimally increase O2 extraction
  - Increases in O2 demand must be met by increased coronary blood flow

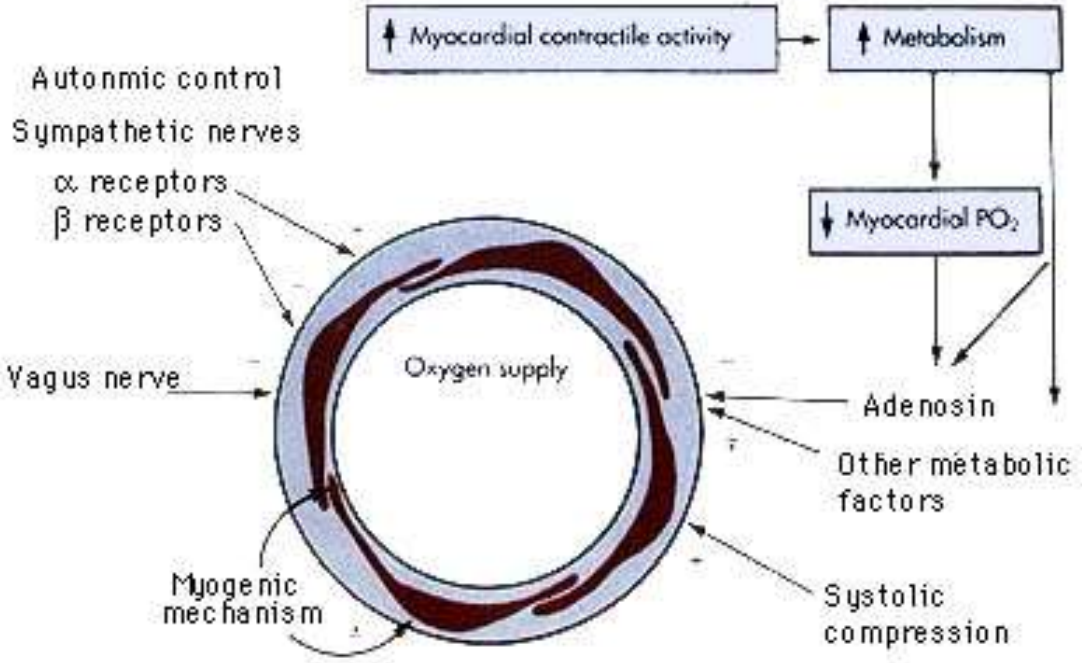
Myocardial Oxygen Supply

Regulation of Coronary Blood Flow

Coronary Blood Flow

- Metabolic control
- Autoregulation
- Endothelial control of coronary vascular tone
- Extravascular compressive forces
- Neural control

Regulation of Coronary Blood Flow

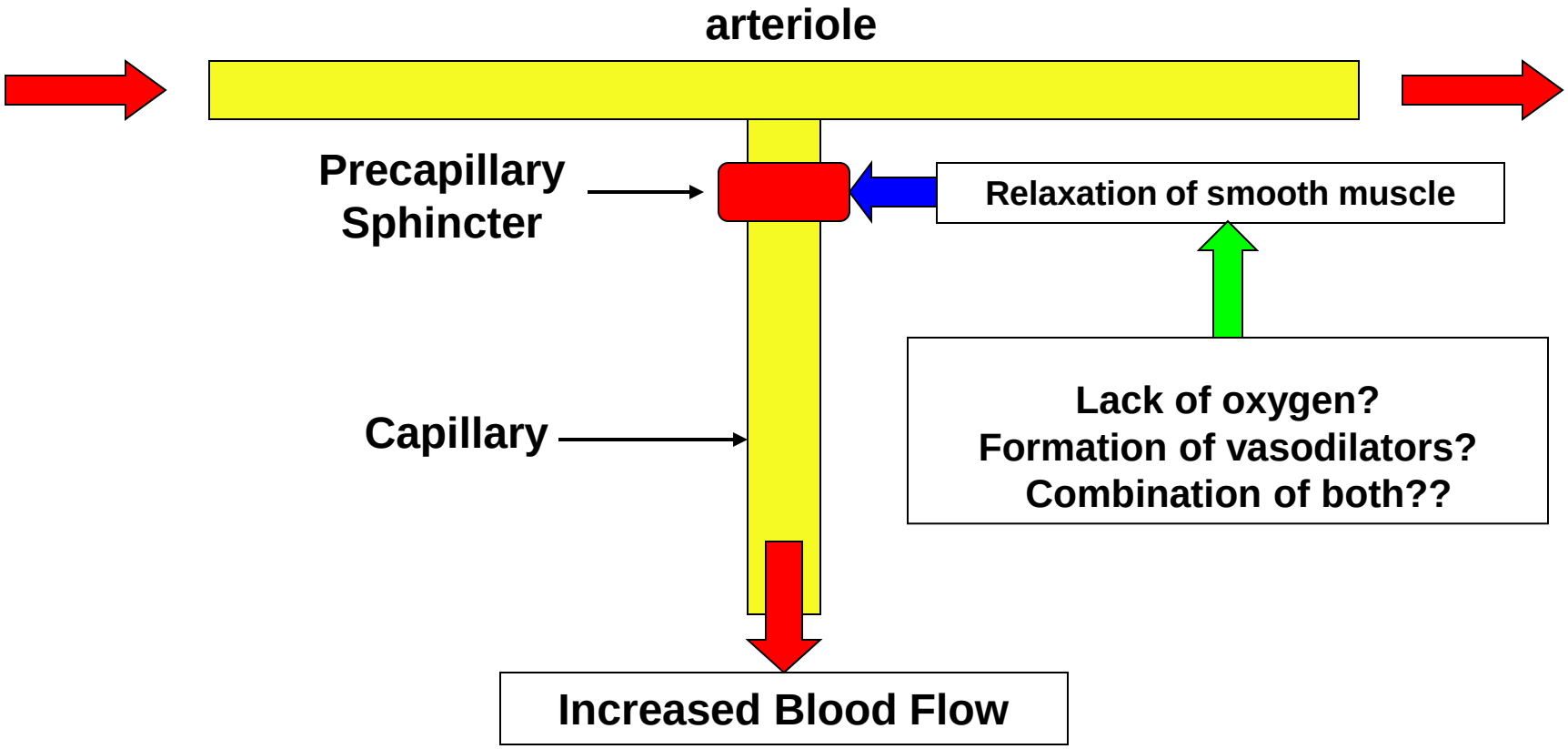


Metabolic Control

- Coronary circulation is exquisitely sensitive to myocardial tissue oxygen tension

- Increased oxygen demand results in a lower tissue oxygen tension. This causes vasodilation and increased blood flow.
  - Adenosine
  - Nitric oxide
  - Prostaglandins
  - K^+_{ATP} channels

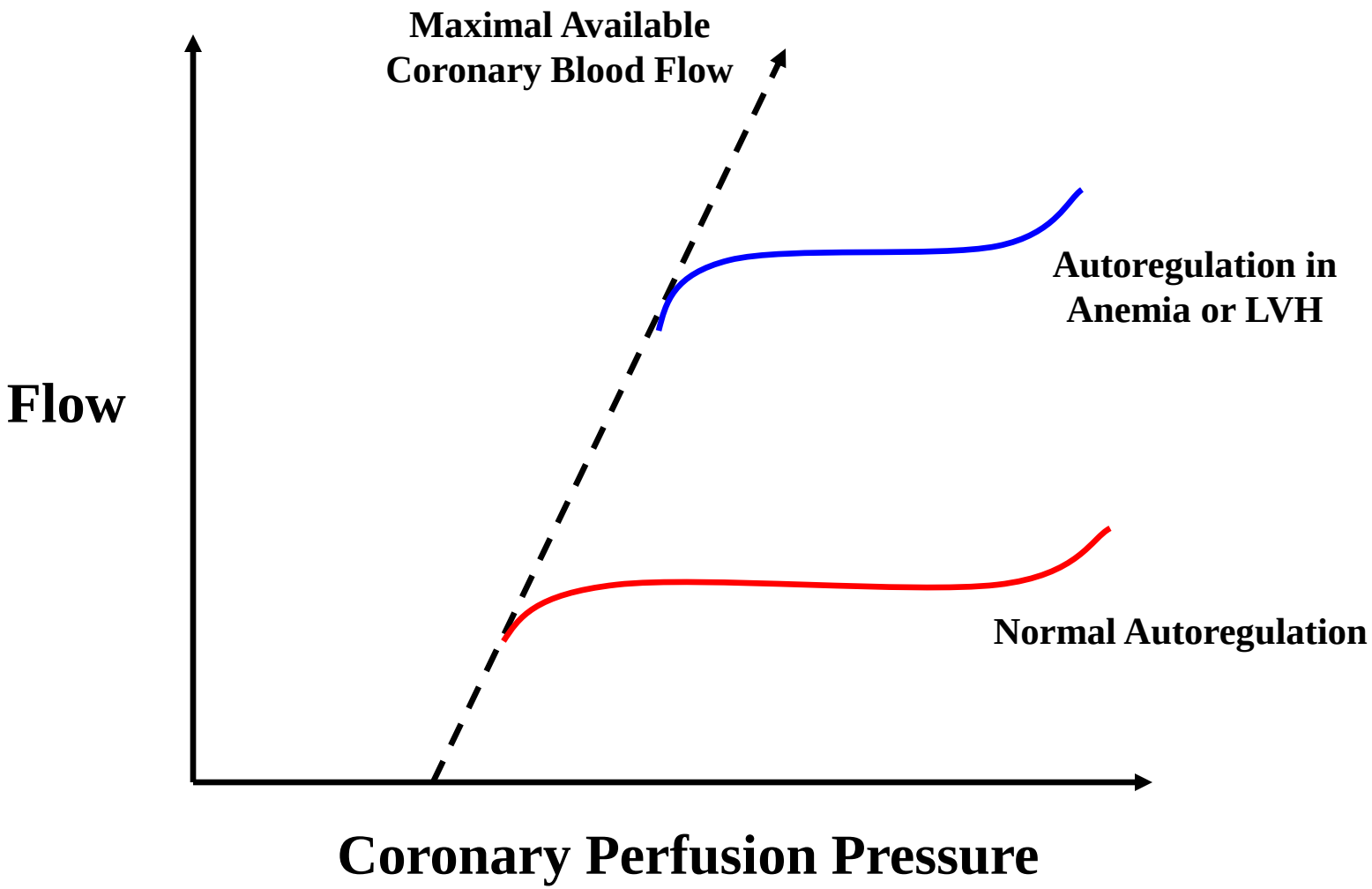
Metabolic Control of Blood Flow



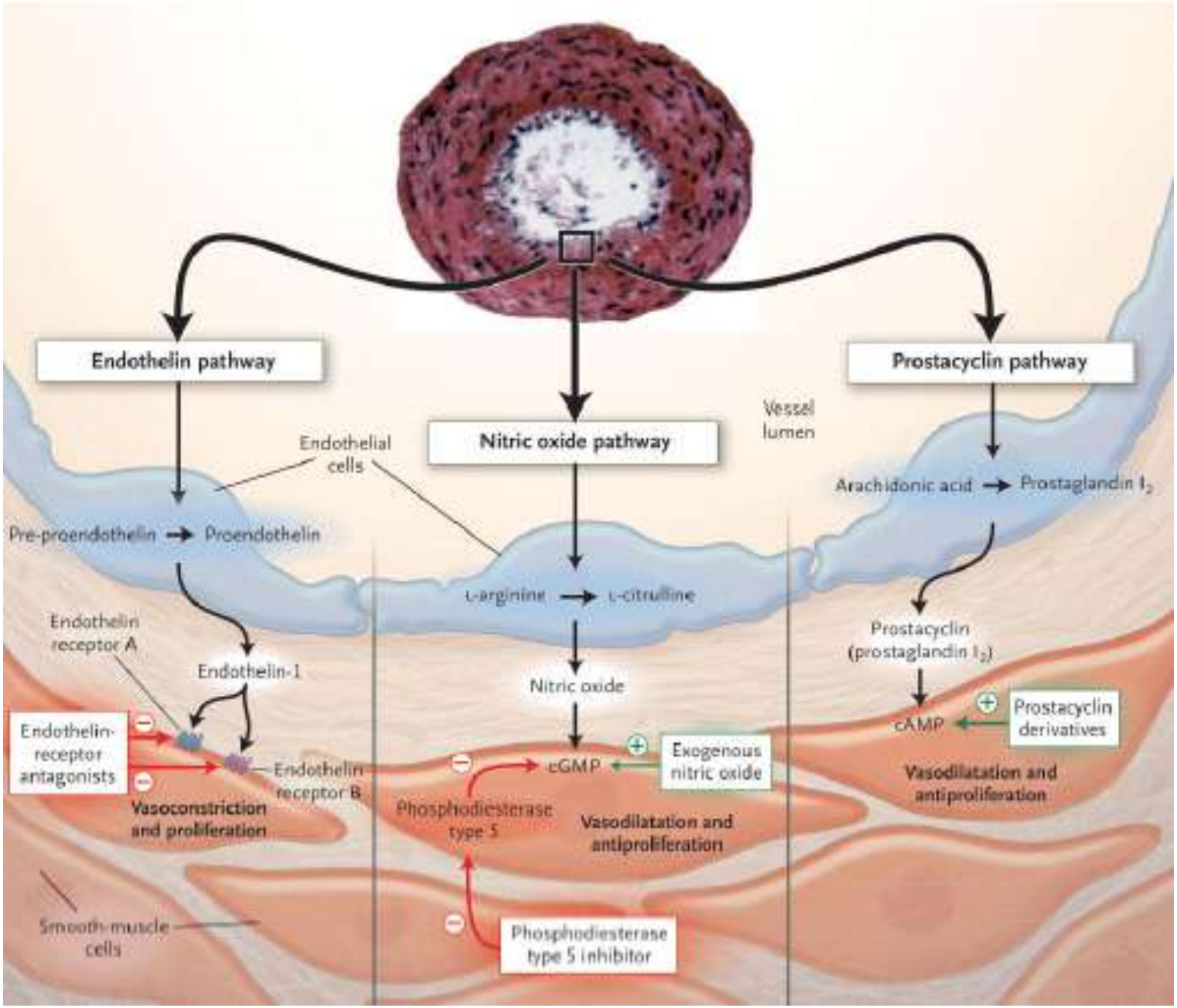
Autoregulation

- Ability of a vascular network to maintain constant blood flow over a range of arterial pressures.
- Autoregulation is an independent determinant of CBF
- The set point at which CBF is maintained depends on MVO2

Autoregulation



Endothelial Control of Coronary Vascular Tone


Endothelin pathway
Nitric oxide pathway
Prostacyclin pathway
Vessel lumen
Endothelial cells
Pre-proendothelin
Proendothelin
Endothelin receptor A
Endothelin-1
Endothelin-receptor antagonists
Endothelin receptor B
Vasoconstriction and proliferation
Smooth-muscle cells
L-arginine
L-citrulline
Nitric oxide
cGMP
Exogenous nitric oxide
Phosphodiesterase type 5
Vasodilatation and antiproliferation
Phosphodiesterase type 5 inhibitor
Arachidonic acid
Prostaglandin I2
Prostacyclin (prostaglandin I2)
cAMP
Prostacyclin derivatives
Vasodilatation and antiproliferation

When Damage to Endothelium Occurs

- Damage to endothelial cells will lead to:
  - Decreased Nitric Oxide and Prostacyclin production
  - Increased Endothelin production

- This will lead to:
  - Vasoconstriction
  - Vasospasm
  - Thrombosis

Neural Control

- Coronary blood flow is controlled predominantly by local metabolic, autoregulatory, and endothelial factors

- Neural control of the coronary circulation complements the above local effects

Neural Control

- Sympathetic Control
  - Alpha = constrict coronary vessels
  - Beta = dilate coronary vessels
    - $Beta_1$ in conduit arteries
    - $Beta_2$ in resistance arterioles
- Parasympathetic Control
  - Acetylcholine
    - Vasodilation in healthy subjects
    - Vasoconstriction in patients with atherosclerosis

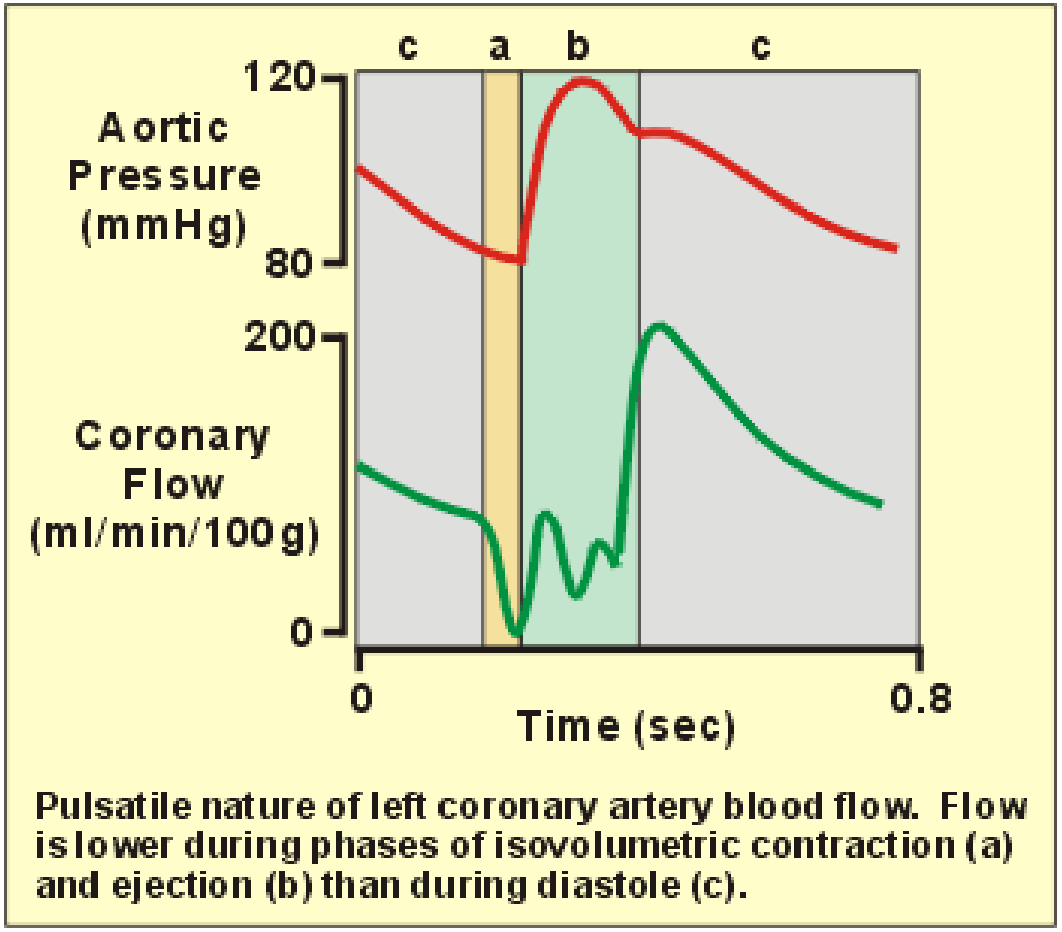
Extravascular Compressive Forces

- The heart influences its blood supply by the squeezing effect of the contracting myocardium on the blood vessels coursing through the heart

Extravascular Compressive Forces

- Left Ventricle
  - Early Systole > Initial Flow Reversal
  - Remainder of Systole > Flow follows aortic pressure curve, but at a much reduced pressure
  - Early Diastole > Abrupt pressure rise (80-90% of LV flow occurs in early diastole)
  - Remainder of Diastole > Pressure declines slowly as aortic pressure decreases

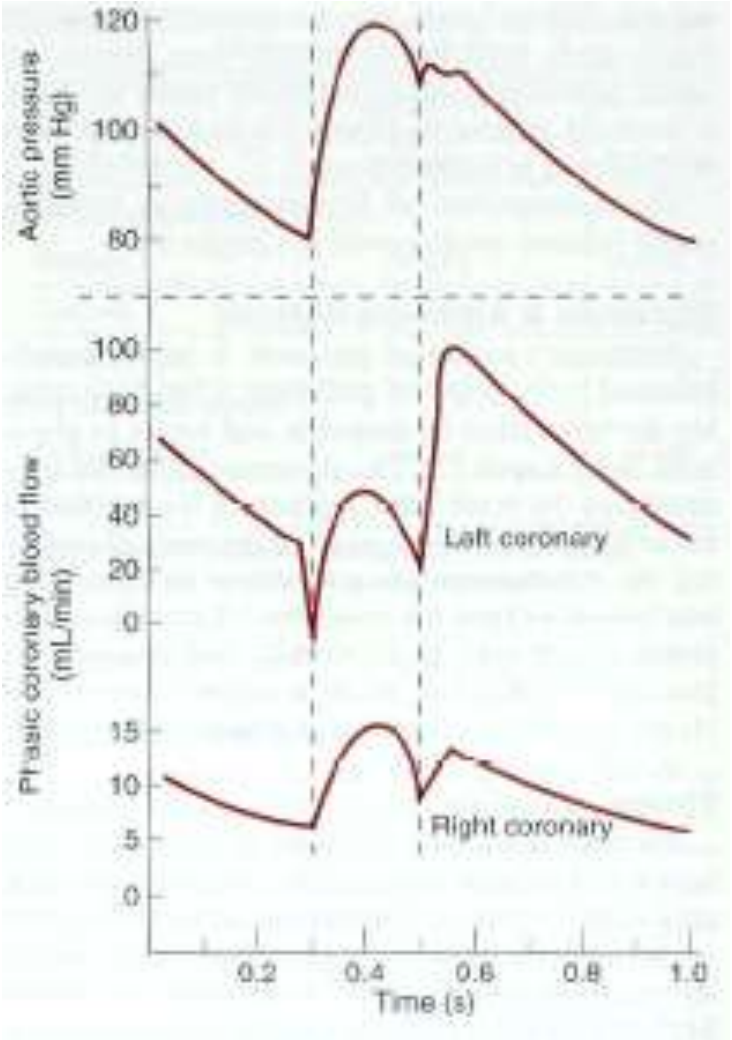
Extravascular Compressive Forces



Pulsatile nature of left coronary artery blood flow. Flow is lower during phases of isovolumetric contraction (a) and ejection (b) than during diastole (c).

Extravascular Compressive Forces

- Right Ventricle
  - Lower pressure generated by thin right ventricle in systole
  - No reversal of blood flow during early systole
  - Systolic blood flow constitutes a much greater proportion of total blood flow


Aortic pressure (mm Hg)
120
100
80
Phasic coronary blood flow (mL/min)
100
80
60
40
20
0
Left coronary
15
10
5
0
Right coronary
0.2
0.4
0.6
0.8
1.0
Time (s)

Transmural Distribution of Myocardial Blood Flow

- Extravascular compressive forces are greater in the subendocardium (inner) and least near the subepicardial layer (outer)

- Under normal resting conditions this does not impair subendocardial blood flow as increased flow during diastole compensates
  - Subendocardial to subepicardial ratio: 1.25/1
  - Due to preferential dilatation of the subendocardial vessels
  - Secondary to increased wall stress and, therefore, increased MVO2 in the subendocardium

Transmural Distribution of Myocardial Blood Flow

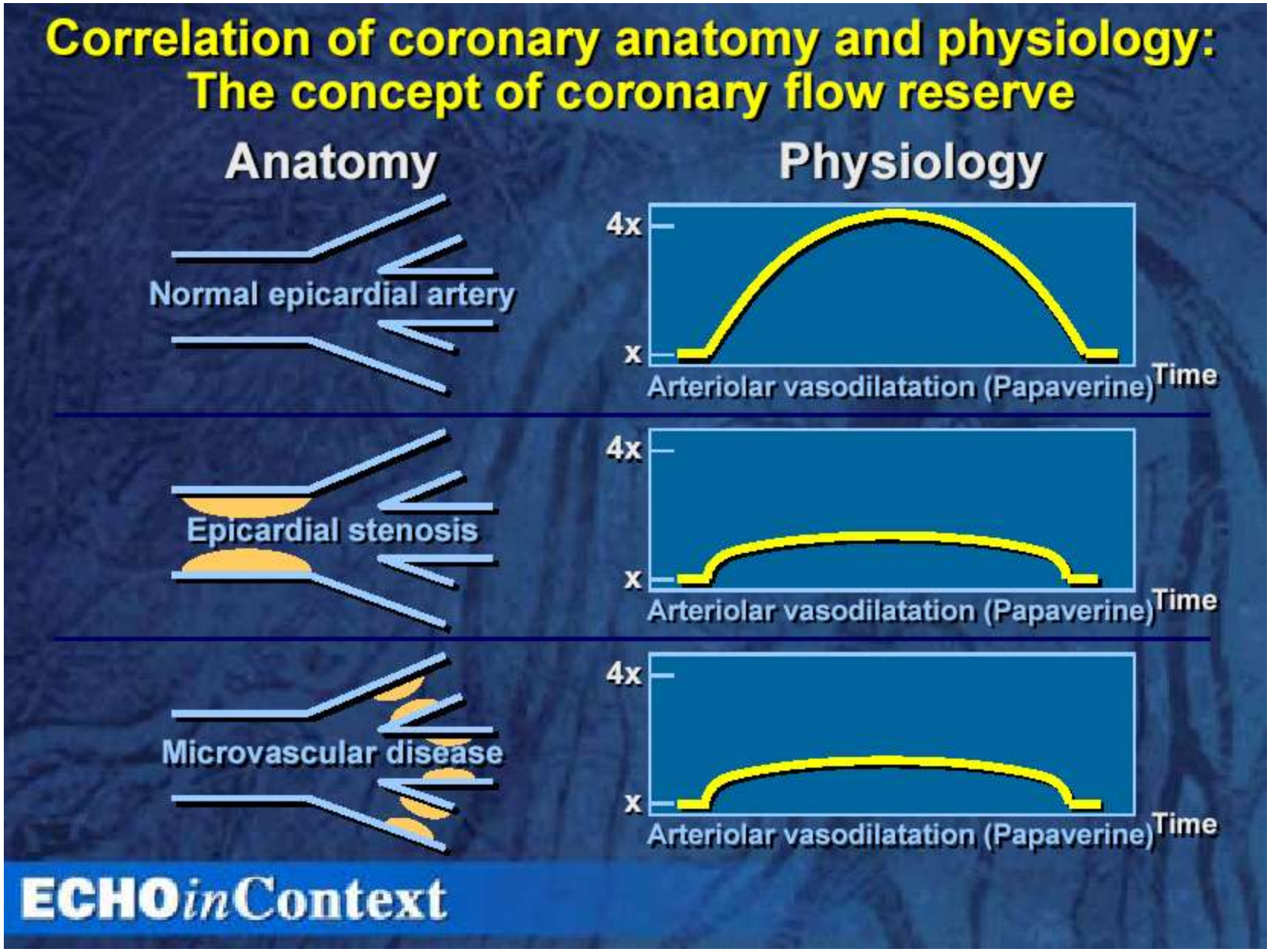
- The subendocardium is more susceptible to ischemia than the midmyocardium or subepicardium

- Epicardial coronary stenoses are associated with reductions in the subendocardial to subepicardial flow ratio

Coronary Flow Reserve

- Difference between baseline blood flow and maximal flow
  - Usually measured following pharmacologic coronary vasodilation
- In the absence of coronary artery disease, maximal flow is 4 – 5 times as great as at rest
- Coronary flow reserve decreases with increasing severity of coronary artery disease

Correlation of coronary anatomy and physiology: The concept of coronary flow reserve



ECHO*in*Context

Myocardial Oxygen Demand

Myocardial Oxygen Consumption

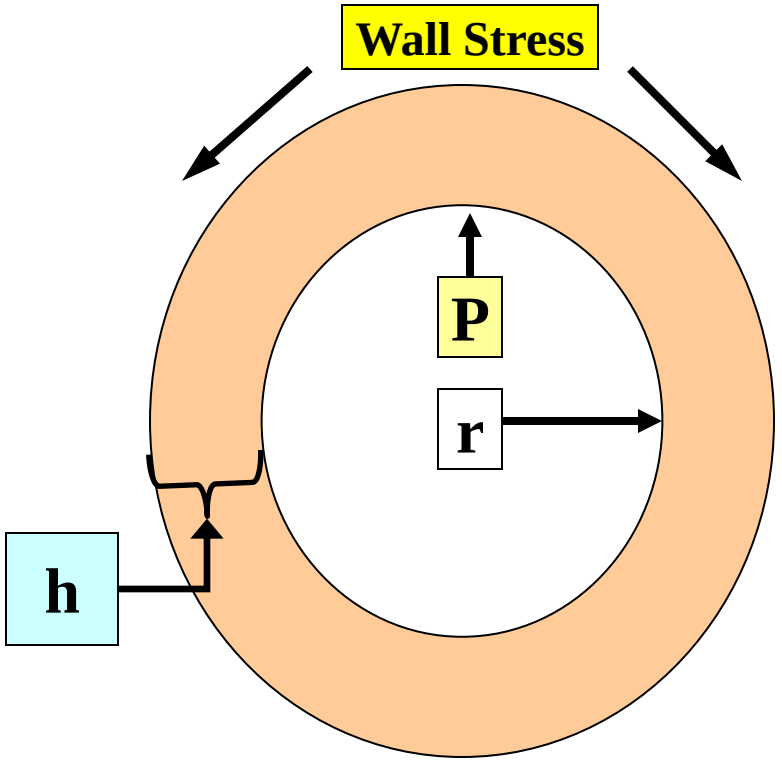
- Oxygen consumption is defined as the volume of oxygen consumed per minute (usually expressed per 100 grams of tissue weight)

Myocardial Oxygen Demand is Related to Wall Stress

- LaPlace's Law

Wall Stress

$$\sigma \propto \frac{Pr}{h}$$



Factors Increasing Myocardial Oxygen Consumption

- Increased Heart Rate
- Increased Inotropy (Contractility)
- Increased Afterload
- Increased Preload
  - Changes in preload affect myocardial oxygen consumption less than do changes in the other factors

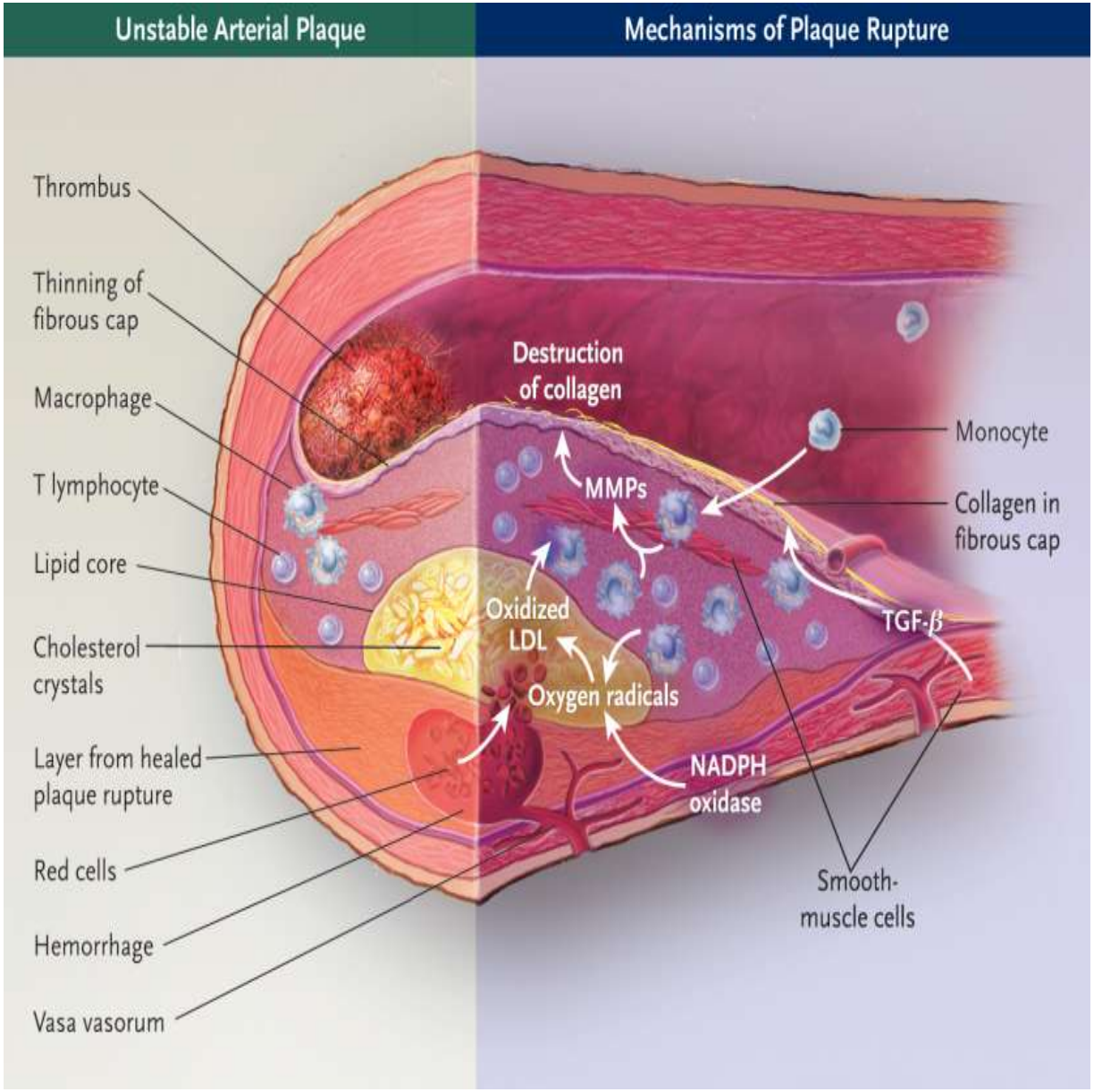
Oxygen Cost of Myocardial Work

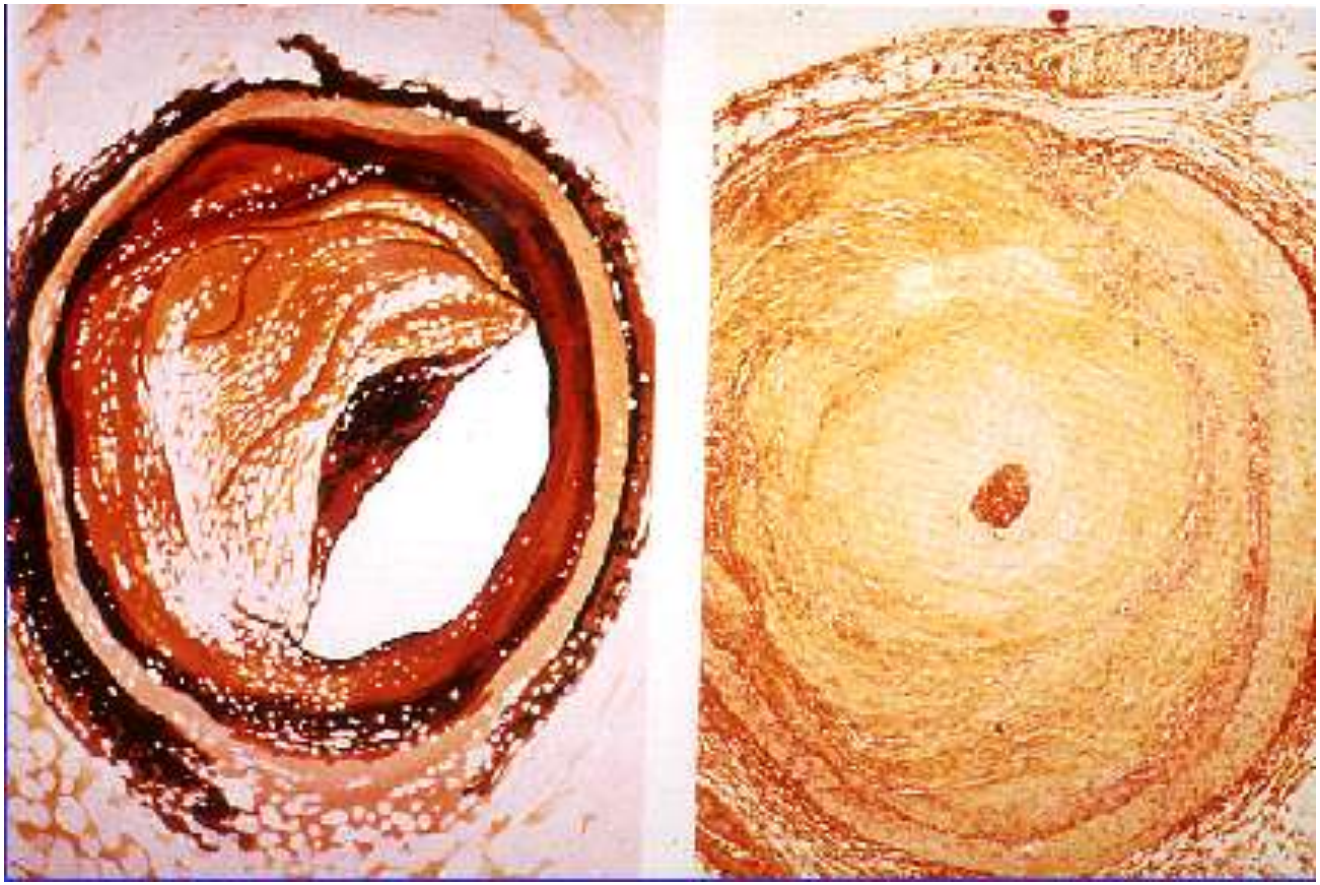
- Pressure work is much more costly than volume work for the heart
  - Pressure work = increasing arterial pressure at a constant cardiac output
  - Volume work = increasing cardiac output while maintaining a constant pressure

Coronary Artery Disease

Coronary Artery Disease

- Myocardial ischemia occurs when myocardial availability is inadequate to meet metabolic requirements.


Unstable Arterial Plaque
Mechanisms of Plaque Rupture
Thrombus
Thinning of fibrous cap
Macrophage
T lymphocyte
Lipid core
Cholesterol crystals
Layer from healed plaque rupture
Red cells
Hemorrhage
Vasa vasorum
Destruction of collagen
MMPs
Monocyte
Collagen in fibrous cap
Oxidized LDL
TGF-β
Oxygen radicals
NADPH oxidase
Smooth-muscle cells



Effects of Coronary Stenoses

Coronary Flow Reserve

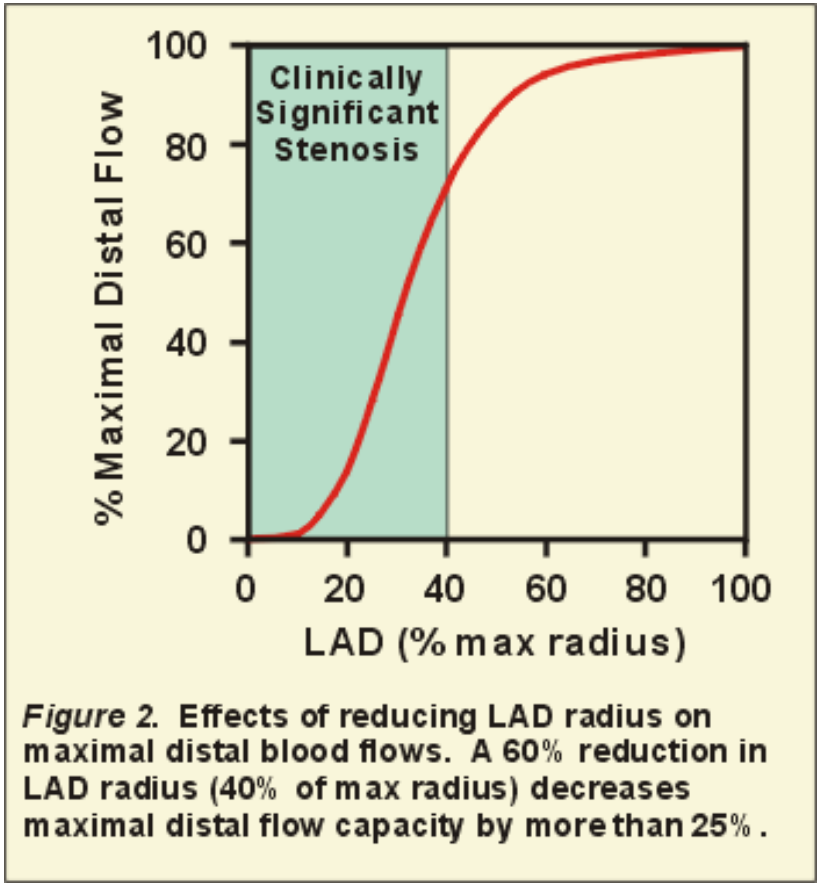
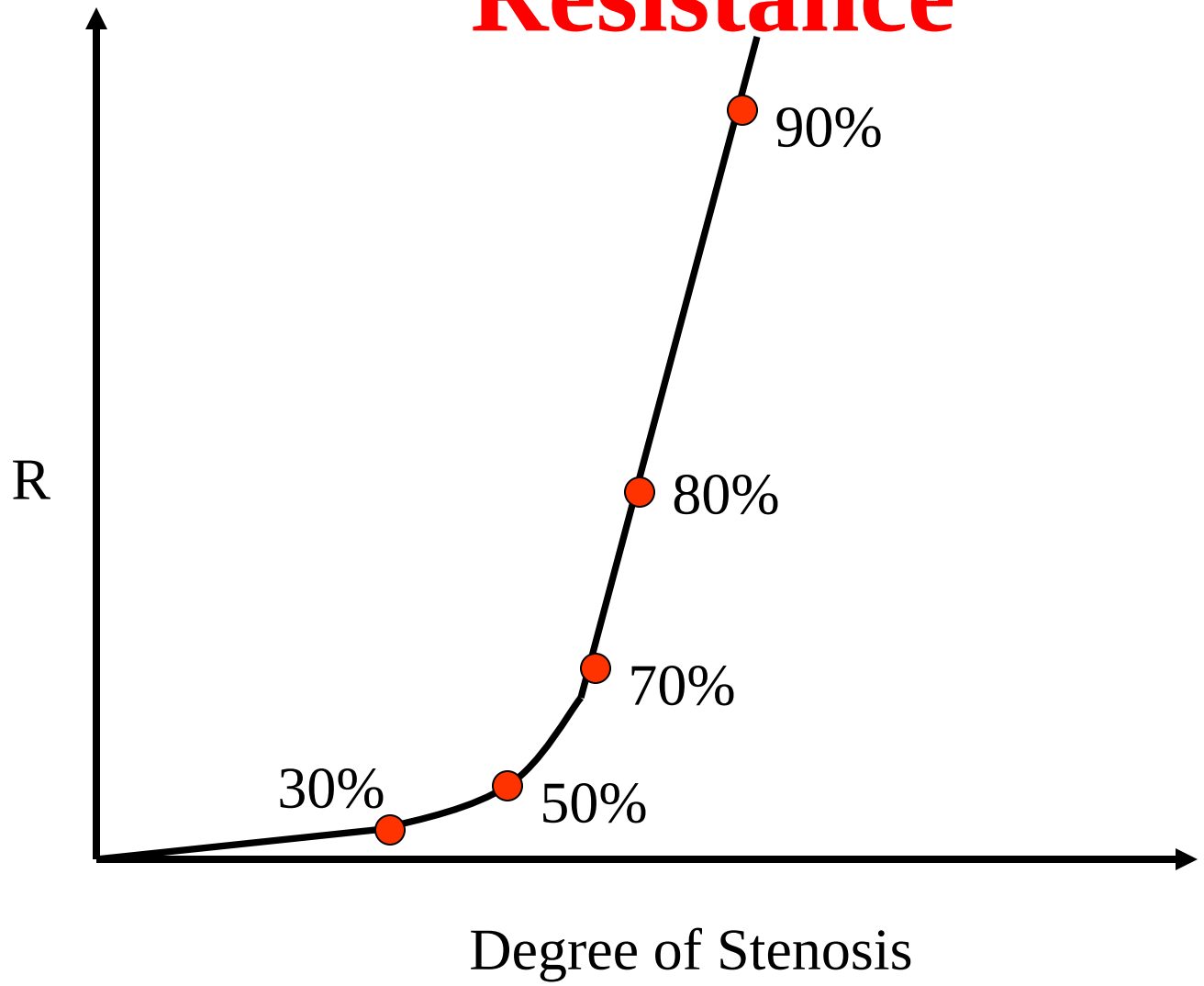
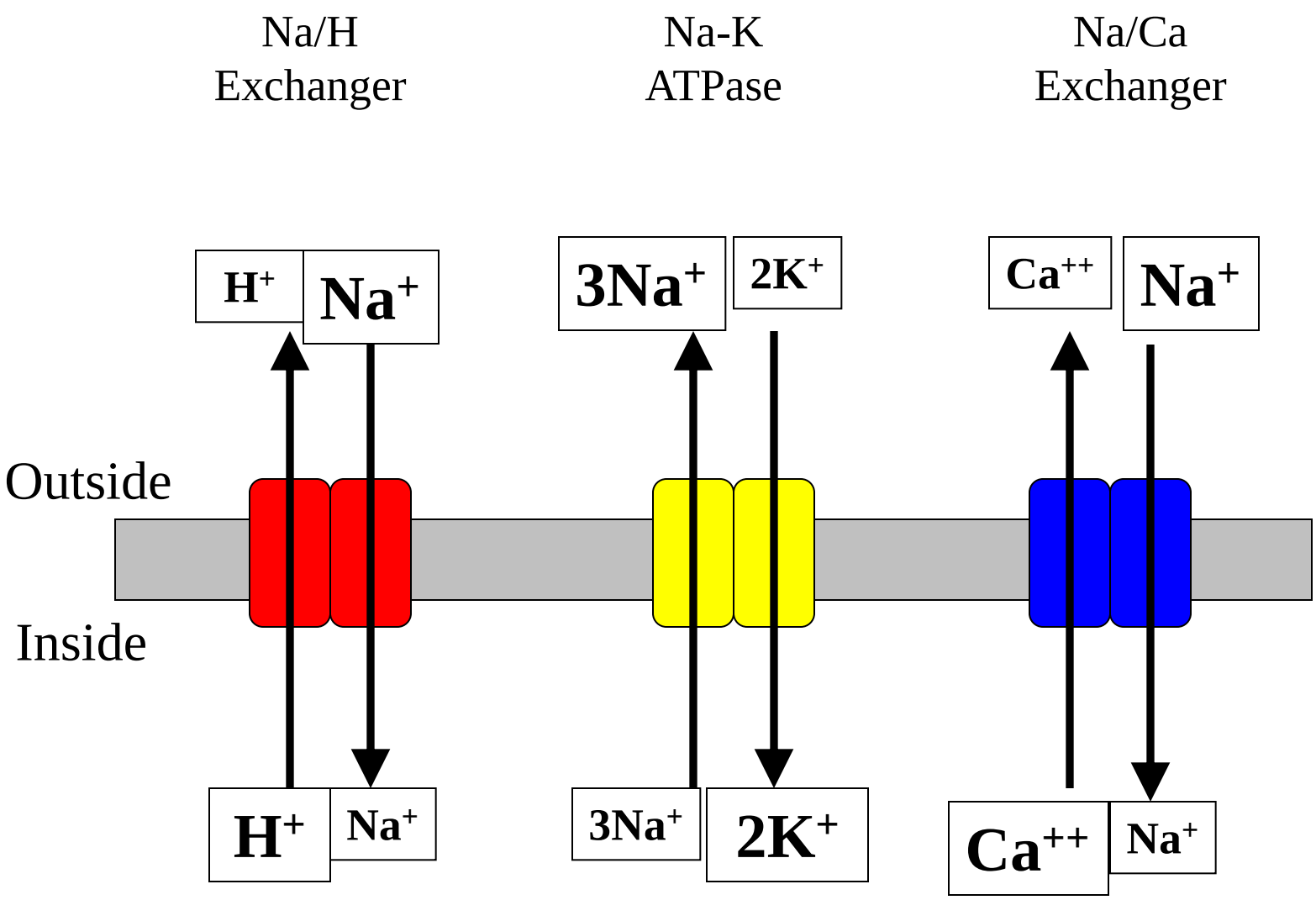


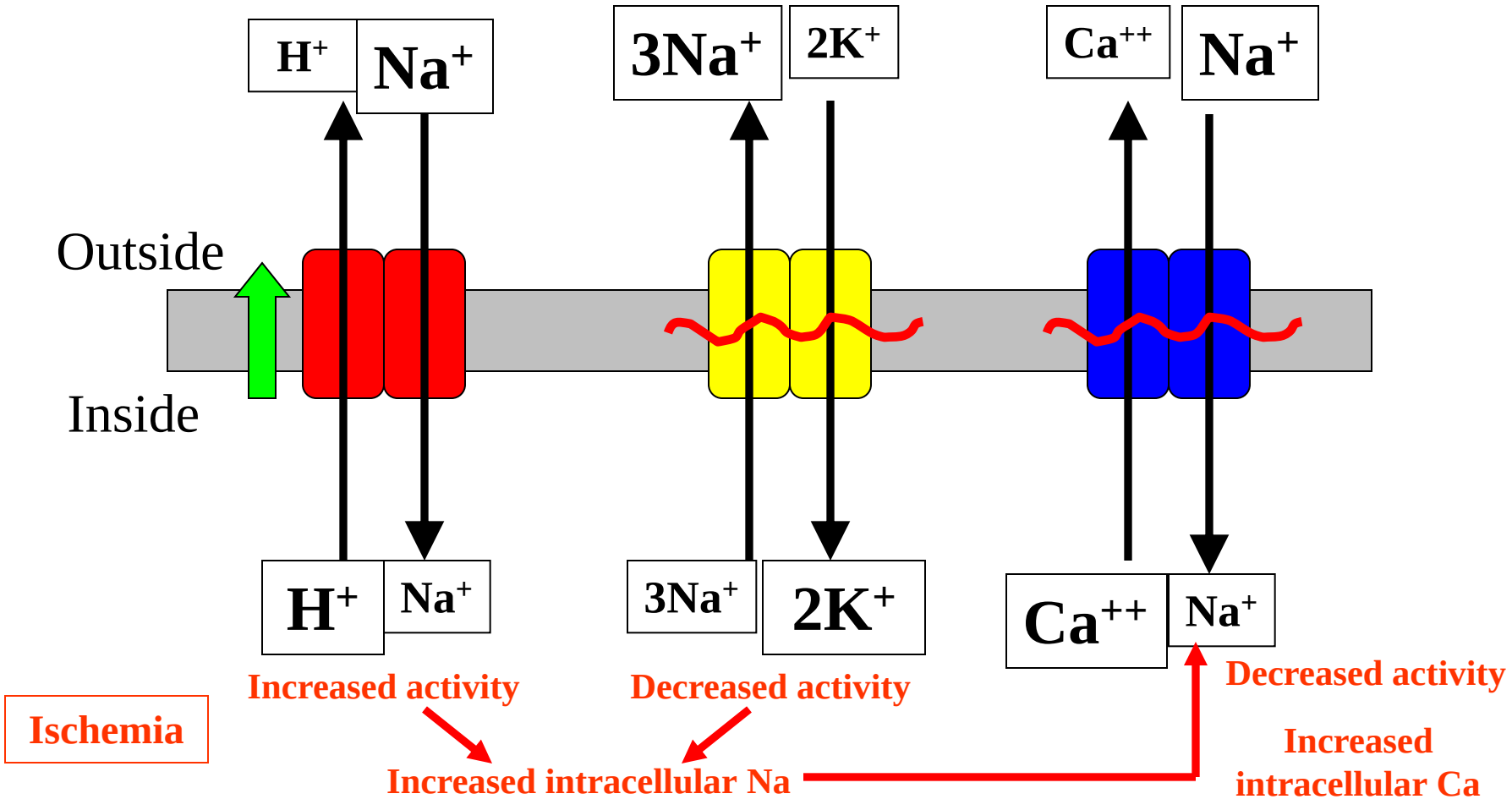
Figure 2. Effects of reducing LAD radius on maximal distal blood flows. A 60% reduction in LAD radius (40% of max radius) decreases maximal distal flow capacity by more than 25%.

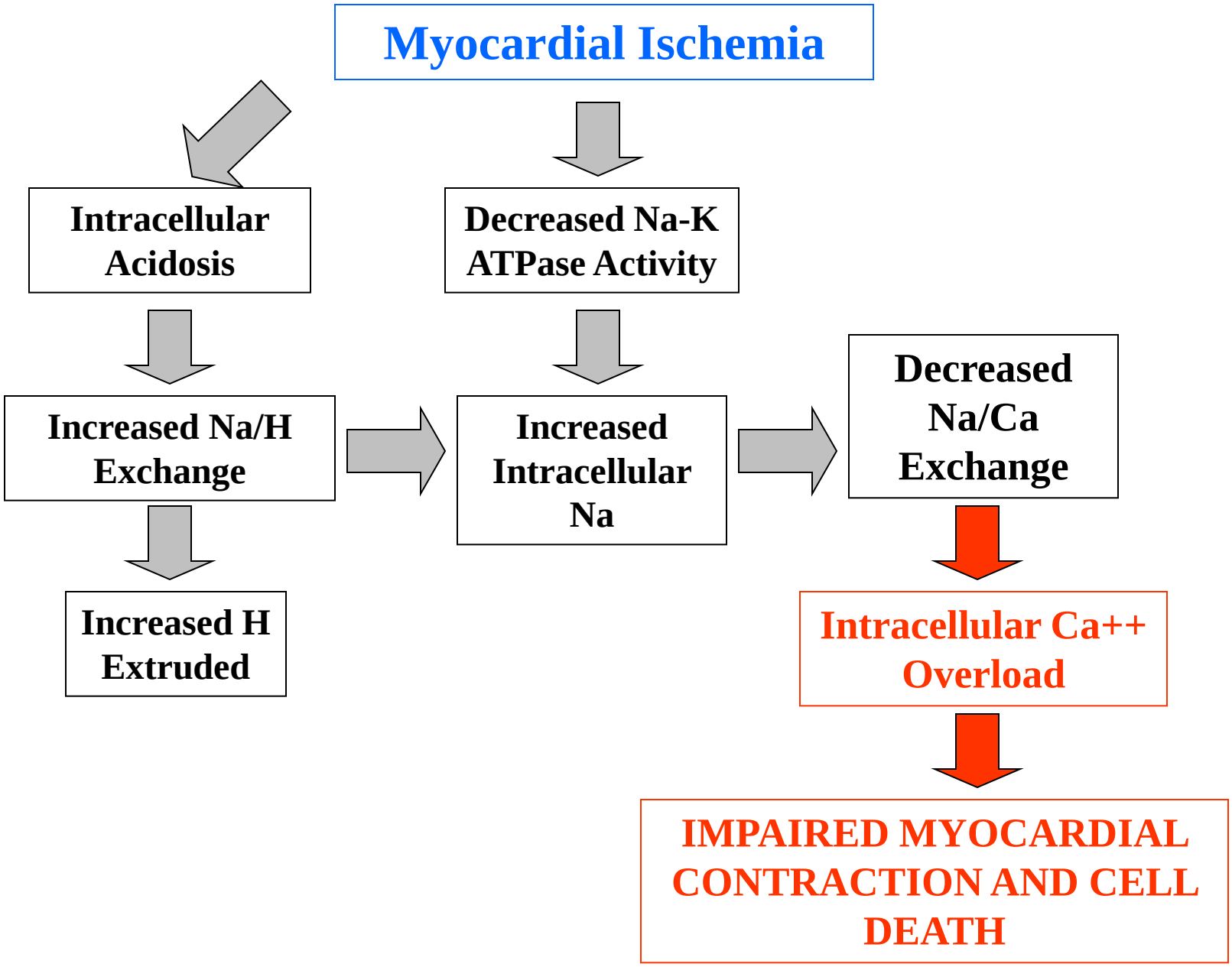
Coronary Stenosis and Resistance



Myocardial Ischemia


Na/H
Exchanger
Na-K
ATPase
Na/Ca
Exchanger
H+
Na+
3Na+
2K+
Ca++
Na+
Outside
Inside
H+
Na+
3Na+
2K+
Ca++
Na+

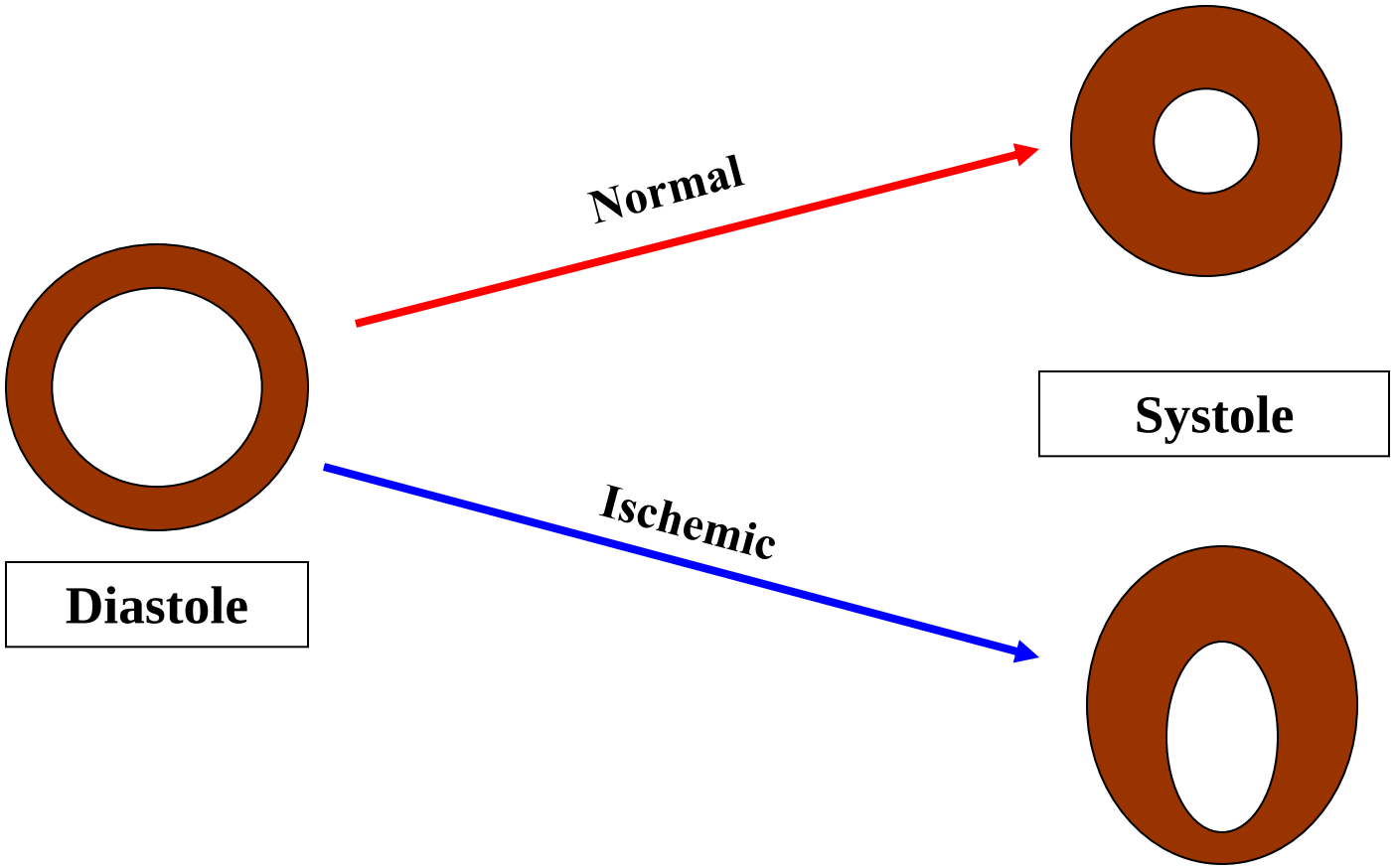

Na/H
Exchanger
Na-K
ATPase
Na/Ca
Exchanger
H+
Na+
3Na+
2K+
Ca++
Na+
Outside
Inside
H+
Na+
3Na+
2K+
Ca++
Na+
Increased activity
Decreased activity
Decreased activity
Ischemia
Increased intracellular Na
Increased
intracellular Ca


Myocardial Ischemia
Intracellular Acidosis
Decreased Na-K ATPase Activity
Increased Na/H Exchange
Increased Intracellular Na
Decreased Na/Ca Exchange
Increased H Extruded
Intracellular Ca++ Overload
IMPAIRED MYOCARDIAL CONTRACTION AND CELL DEATH

Effects of Myocardial Ischemia

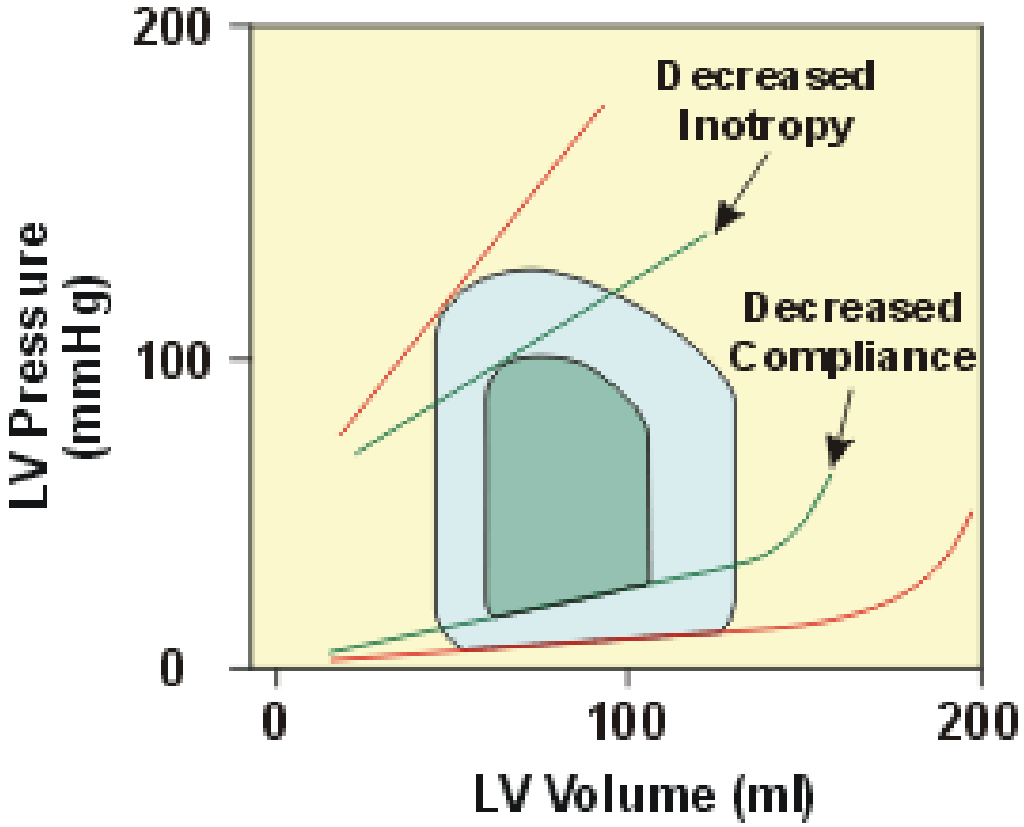
- Systolic dysfunction
  - Normal myocardium **thickens** and **shortens** during systole
  - Ischemia causes alterations that may range from minimal impairment to absence of movement (akinesis) to systolic lengthening and post- systolic shortening (dyskinesis)
  - May have compensation by surrounding areas of normal muscle

Effects of Myocardial Ischemia



Effects of Myocardial Ischemia

- Diastolic Dysfunction
  - When a sufficient amount of myocardium is rendered ischemic, then LVEDP rises
  - Relaxation is impaired, and myocardial compliance decreases

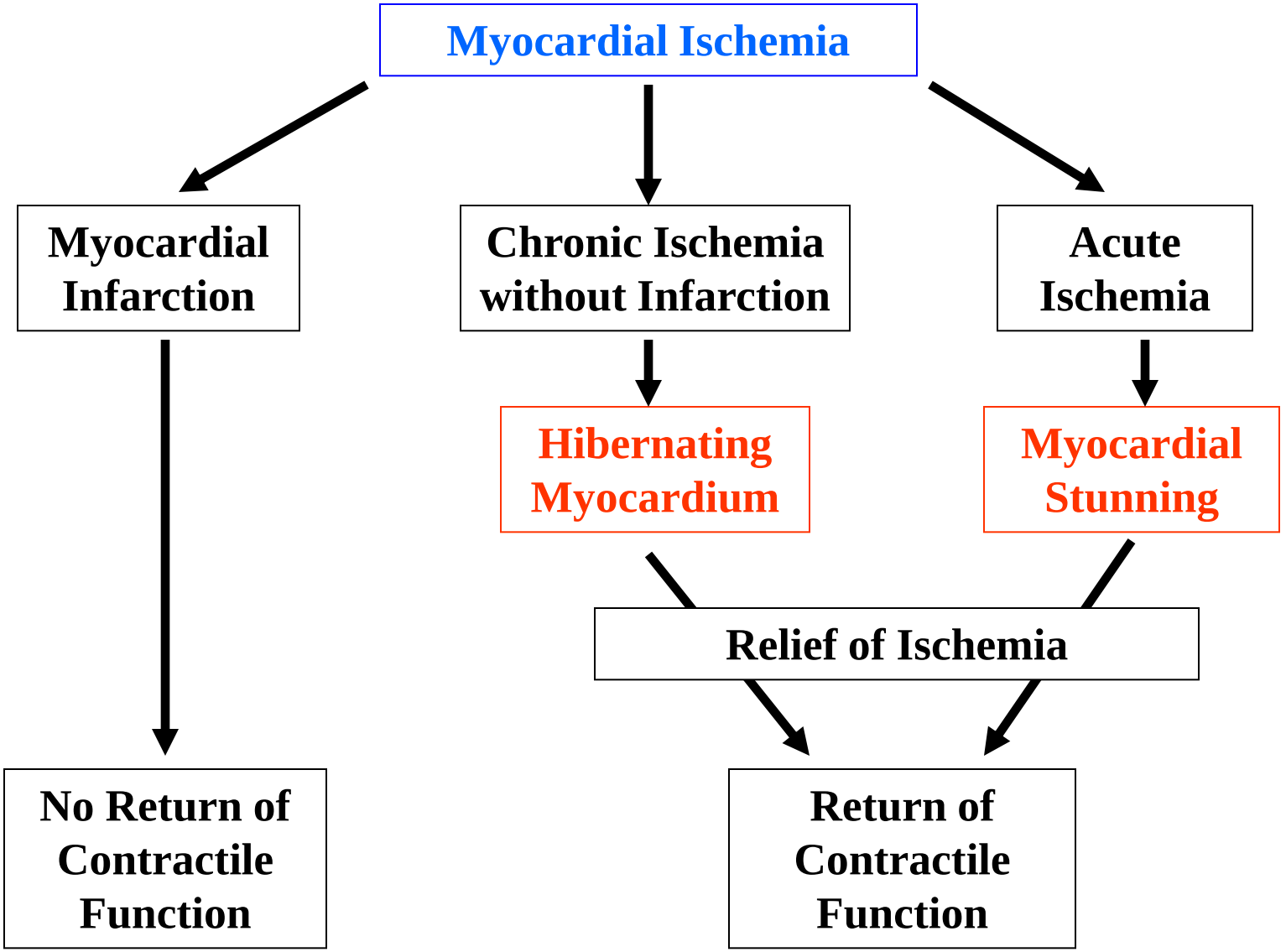


Effects of a combination of systolic dysfunction (decreased inotropy) and diastolic dysfunction (decreased compliance) on left ventricular pressure-volume loop. Heart rate and systemic vascular resistance are unchanged.

Myocardial Ischemia

- Myocardial Stunning
  - After a brief episode severe ischemia, prolonged myocardial dysfunction with gradual return of contractile activity occurs.

- Myocardial Hibernation
  - Presence of impaired resting LV function, owing to reduced CBF that can be restored toward normal by revascularization.


Myocardial Ischemia
Myocardial Infarction
Chronic Ischemia without Infarction
Acute Ischemia
Hibernating Myocardium
Myocardial Stunning
Relief of Ischemia
No Return of Contractile Function
Return of Contractile Function

Myocardial Ischemia

- Systolic and diastolic dysfunction
- Angina
- CHF or Pulmonary Edema
- Arrythmias
- Myocardial Infarction
- Ventricular Rupture or VSD
- Cardiogenic Shock
- Death

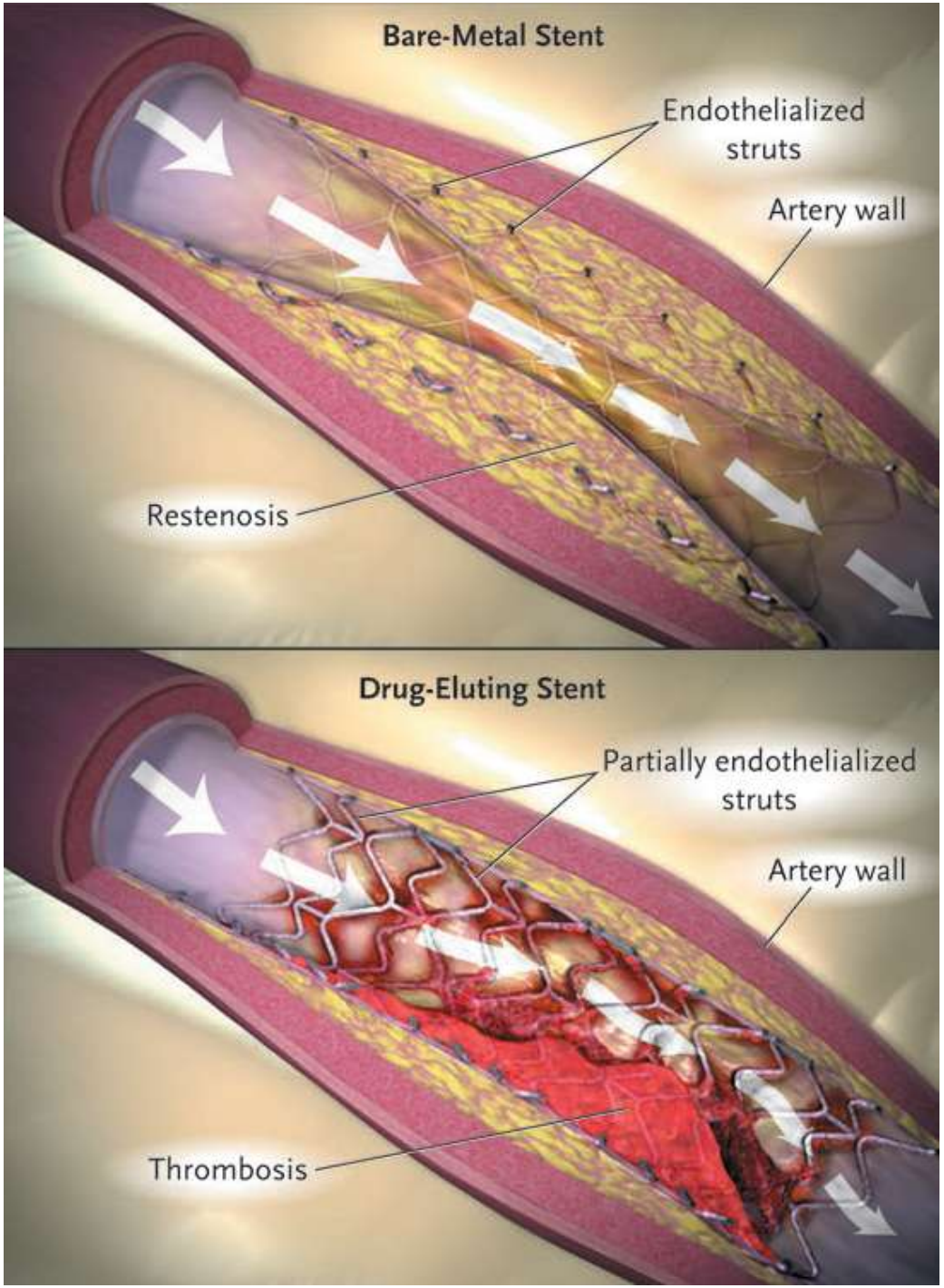
Drugs Used for Treatment of Ischemia

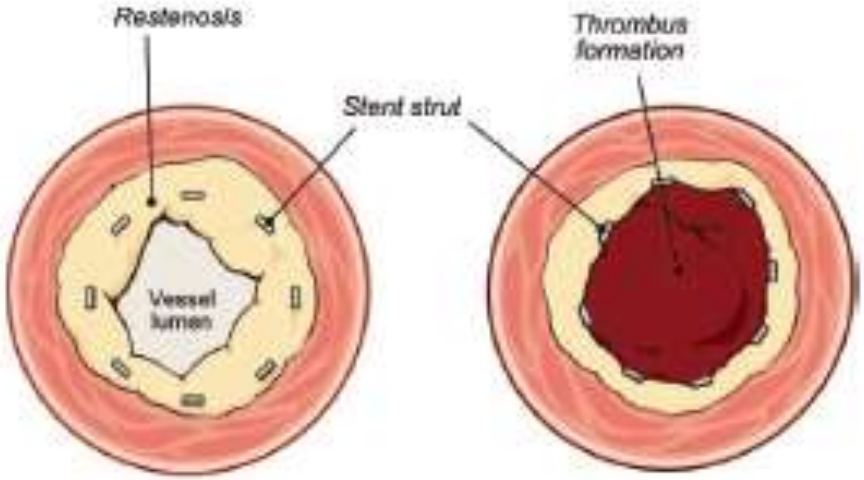
- Oxygen
- Beta-Blockers
- Nitrates
- Antiplatelet/Anticoagulant Drugs
- Analgesics
- Calcium-Channel Blockers

Interventions for the Treatment of Myocardial Ischemia

- Coronary artery bypass surgery (CABG)

- Percutaneous Coronary Interventions
  - Coronary Balloon Angioplasty
  - Bare-metal Coronary Stents
  - Drug-eluting Stents


Bare-Metal Stent
Endothelialized struts
Artery wall
Restenosis
Drug-Eluting Stent
Partially endothelialized struts
Artery wall
Thrombosis


Restenosis
Stent strut
Vessel lumen
Thrombus formation
Bare Metal Stent
Drug-eluting Stent

How long should you wait before doing elective surgery after PCI?

- Bare-metal Stent
  - Cardiac complications are lowest after 90 days
- Drug-eluting Stent
  - 1 year is recommended

Perioperative Medical Therapy

- Volatile anesthetic agents may be preferred
  - Anesthetic Preconditioning
- Beta-blockers
- Statins
  - Stabilize plaque
  - Anti-inflammatory

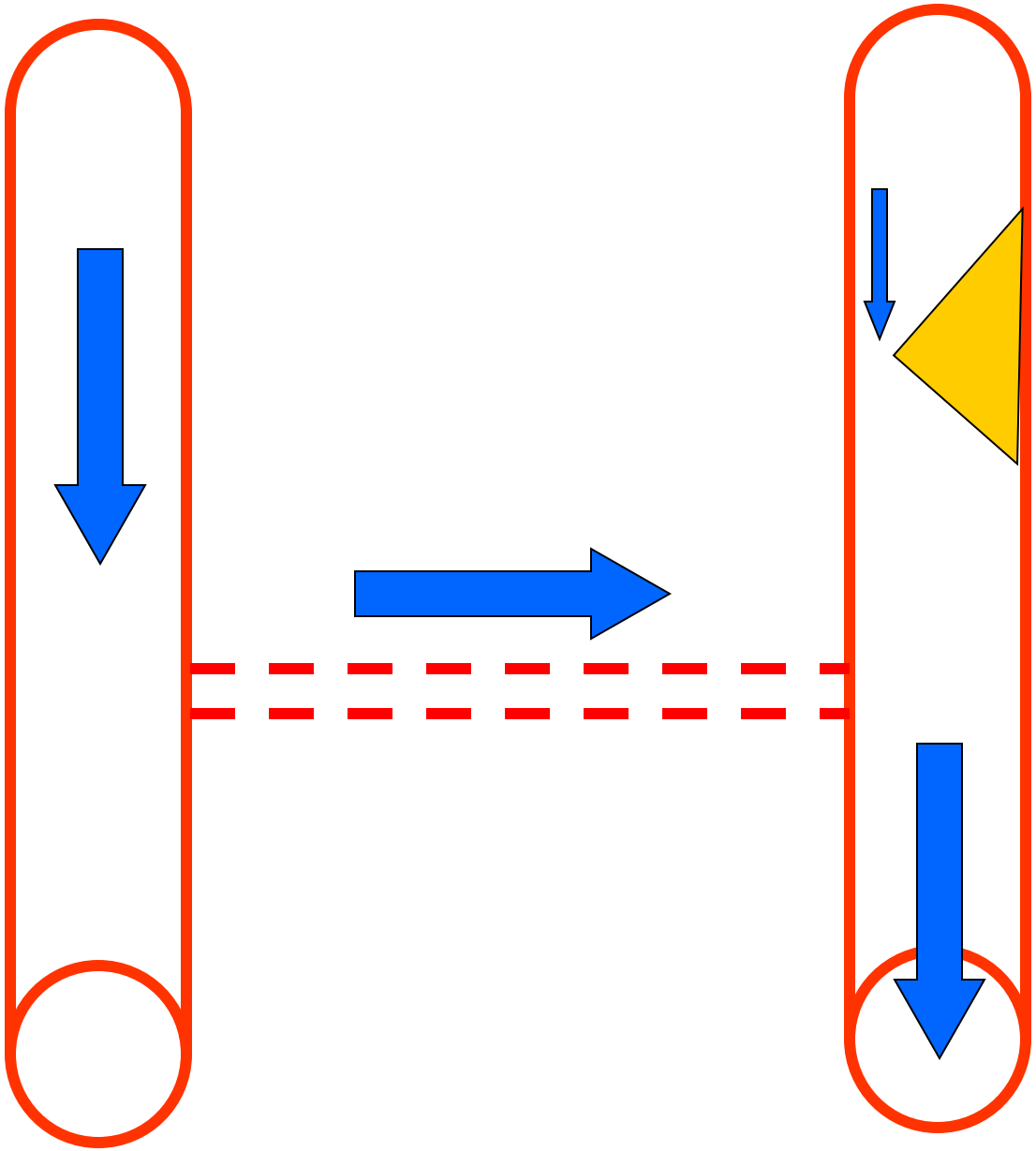
Perioperative Medical Therapy

- Alpha-2-agonists
  - Clonidine
  - Useful in patients not able to take Beta-blockers (e.g., asthmatic)
- Calcium channel blockers
- The use of Nitroglycerin as a prophylactic drug during anesthesia is unclear. No study has clearly demonstrated a change in outcome from its routine use.

Collateral Blood Flow

Collateral Blood Flow

- Coronary collateral vessels develop in response to impairment of coronary blood flow
- Collaterals develop between branches of occluded and non-occluded arteries and can contribute a significant amount of blood flow.
- They originate from pre-existing arterioles that undergo proliferative changes of the endothelium and smooth muscle.
  - Monocyte chemoattractant protein-1 (MCP-1)
  - Vascular endothelial growth factor (VEGF)



Ischemic Preconditioning

Ischemic Preconditioning

- Laboratory and clinical investigations have demonstrated that single or multiple brief periods of ischemia can be protective against a subsequent prolonged ischemic insult. The brief periods of ischemia appear to "precondition" myocardium against reversible or irreversible tissue injury, including stunning, infarction, and the development of malignant ventricular arrhythmias. This process is known as ***ischemic preconditioning*** (IPC)

- Inhaled anesthetic agents have effects that mimic IPC
  - ANESTHETIC PRECONDITIONING

- K^{+}_{ATP} channels play an important role

The End