CARDIOVASCULAR DISEASE

(CHAPTERS 24-26 AND 28)

QUESTION 1

What is an atheroma? When do fatty streaks appear?

An **atheroma** or **atheromatous plaque** is a fatty lesion that can develop in the **tunica intima**, the innermost layer of the artery wall.

A **fatty streak** is one of the **first stages of development** leading to an atheroma.

It is formed by the gradual accumulation of **foam cells**, which are macrophages saturated with low-density lipoprotein (LDL.)

Over time, extracellular lipids accumulate within the lesion, creating a "lipid core" at which point the lesion is classified as an atheroma.

Bulging of the tunica intima causes damage to the endothelium and encourages the growth of protective scar tissue (**fibrosis**.)

If not treated, the endothelium can **rupture** from the stress exerted by the plaque underneath, leading to clotting within the artery (**thrombosis**.)

QUESTION 2

What is secretory PLA_2?

Secreted phospholipase A_2 ($sPLA_2$) is a **digestive enzyme** produced in the pancreas, responsible for breaking down dietary phospholipids.

It has a **pro-inflammatory** effect due to its involvement in the production of arachidonic acid (precursor to **prostaglandins**).

$sPLA_2$ is relevant here because high levels are a **risk factor** for **coronary artery disease** (CAD).

QUESTION 3

What is the consequence of atherosclerosis? What is its effect on blood pressure? Why?

Bulging of the tunica intima due to plaque formation results in the **narrowing** of the arterial lumen.

This **increases** systemic vascular resistance (SVR) thus **increasing** blood pressure.

Plaques can interfere with blood delivery to the tissues, leading to **ischemia**.

In severe cases, plaques can **rupture**, creating blood clots in the circulation (thrombosis) which can lead to a heart attack or stroke.

QUESTION 4

What characterizes a complicated lesion?

Complicated lesions occur when an advanced atheromatous plaque breaks through or **ruptures** the endothelium, triggering the intrinsic clotting pathway.

Formation of a thrombus at the site of the rupture further narrows the arterial lumen, and is at risk of breaking free to form a **thromboembolism**.

QUESTION 5

What is the inflammatory marker of choice in heart disease?

A high sensitivity **C-reactive protein** test (hs-CRP) is first-line for detecting the possible presence of atherosclerosis.

CRP is a protein **produced in the liver** which acts as part of the **complement system**, binding to damaged cells to promote phagocytosis.

Note that CRP is a **generic** inflammatory marker, and is not **unique** to atherosclerosis (CRP elevation can also be observed due to infection, cancer, etc.)

QUESTION 6

List some of the risk factors for atherosclerosis and heart disease.

- **Male** patients
- Familial/genetic predisposition
- **High-fat** diet, **smoking**
- **Obesity** and **lack of exercise**
- Chronic **stress**
- **Hypertension**

QUESTION 7

List the normal values for serum lipids. What is the normal ratio of LDL to HDL?

Total cholesterol **below** 200 mg/dl

Low-density lipoprotein (LDL) **below** 130 mg/dl

High-density lipoprotein (HDL) **above** 40 mg/dl

Triglycerides **below** 150 mg/dl

The normal ratio of LDL to HDL is about **4:1**.

QUESTION 8

What is the least conservative method to prevent heart disease?

Treatment for cardiovascular disease covers a spectrum from **conservative** to **invasive**:

- **Excercise** – physical activity can help reduce risk
- **Statin therapy** – medication to reduce cholesterol
- **Balloon angioplasty** – minimally-invasive procedure to push arteries open from the inside
- **Atherectomy** – minimally-invasive procedure to scrape plaque off of the vessel wall
- **Coronary artery bypass graft** (CABG) – invasive surgery to route blood around occluded artery

QUESTION 9

Describe some invasive techniques to treat CAD.

Balloon angioplasty – wire is passed into artery and advanced to the site of the plaque, which then guides a balloon catheter that expands, pushing out the walls of the artery and opening up the lumen

Atherectomy - similar to angioplasty, but rather than expanding the artery, the plaque is mechanically removed and the debris vacuumed out

Coronary artery bypass graft (CABG) – arterial graft is taken from elsewhere in the body and implanted to "bridge over" the affected area

QUESTION 10

What is the usual cause of hypertension? How does hypertension damage blood vessel walls?

Hypertension is typically caused by **increased systemic vascular resistance** rather than heart problems.

Chronically high blood pressure causes smooth muscle of arteries to adapt, becoming thicker and reducing the arterial lumen, further increasing pressure.

QUESTION 11

Name some risk factors for hypertension.

- **Age**, gradually increasing through 40s and 50s
- Genetic predisposition
- Race and sex

  (Higher risk in black patients; white men more risk than white women)
- **Obesity**, **diabetes**
- High **sodium intake**

QUESTION 12

85-95% of hypertension is of which type? Does hypertension usually produce signs and symptoms?

Most cases of hypertension are **essential hypertension** which is **idiopathic** and may be related to a variety of etiologic factors.

Mild to moderate chronic hypertension usually causes **no observable symptoms**.

Symptoms of **hypertensive crisis** include headache, blurred vision, chest pain, and shortness of breath.

Let's talk about blood pressure...

Blood pressure can be represented by the equation:

$$MAP = CO \times SVR$$

(mean arterial pressure = cardiac output × systemic vascular resistance)

Blood pressure is a function of the **amount of blood** being expelled from the heart and how hard the arteries are **resisting** the flow of blood.

So how can we **lower** blood pressure? Three ways:

volume reduction – reduce the total volume of blood in the body, decreasing cardiac output

negative inotropy – reduce the strength of contraction of the heart, decreasing cardiac output

vasodilation – relax the smooth muscle of the tunica media, reducing systemic vascular resistance

QUESTION 13

How do diuretics influence blood pressure?

Diuretics **inhibit electrolyte reabsorption** in the kidney tubules, resulting in the **loss of fluid** from the body in the urine.

This decreases blood volume by directly removing water from the blood, **decreasing cardiac output** and lowering blood pressure.

QUESTION 14

How do beta blockers (β-adrenergic antagonists) influence blood pressure?

Beta blockers act on **both** the heart and the blood vessels, causing:

negative inotropy – relax the heart, causing it to contract with **less strength**

negative chronotropy – cause the heart to beat **more slowly** (longer diastole, lower MAP)

vasodilation – relax the arterial smooth muscle, lowering systemic vascular resistance

QUESTION 15

How do calcium channel blockers influence blood pressure?

Remember the crucial role of calcium in muscle fibers: bind to troponin, triggering muscle contraction

CCBs **reduce availability** of intracellular calcium by interfering with transport across the sarcolemma.

This results in a **negative chronotropic** effect, as well as **vasodilation** via relaxation of vascular smooth muscle.

QUESTION 16

How do angiotensin-converting enzyme (ACE) inhibitors influence blood pressure?

ACE inhibitors interfere with the **conversion** of angiotensin I to angiotensin II, leading to a **decrease** in angiotensin II levels.

Angiotensin II is a **vasoconstrictor**, and also stimulates the adrenal cortex to release **aldosterone**.

Blocking ACE thus results in **vasodilation** as well as a **diuretic effect** (decreased fluid retention) due to decreased aldosterone.

QUESTION 17

How do alpha blockers (α adrenergic antagonists) influence blood pressure?

Alpha blockers act **solely** on the blood vessels, reducing sympathetic tone to cause **vasodilation**.

QUESTION 18

5-10% of hypertension is due to the dysfunction of another organ. Which organ may be involved?

In a small number of cases, hypertension can be secondary to **kidney dysfunction**.

Excessive fluid retention leads to **increased blood volume**, resulting in hypertension.

QUESTION 19

Which stress hormones may be involved in hypertension, coronary artery disease (CAD,) stroke, and peripheral artery disease (PAD?)

catecholamines – epinephrine/norepinephrine

glucocorticoids – cortisol, cortisone

QUESTION 20

Compare benign and malignant hypertension.

Benign hypertension is the normal form, which develops and progresses slowly over the course of years.

Malignant hypertension (or a **hypertensive emergency**) is **acutely** and **severely** elevated BP, sometimes defined as above 180/120.

Untreated hypertensive emergencies risk serious damage to blood vessels and organs.

(Don't confuse this with **malignant hyperthermia**, an adverse reaction to general anesthesia)

QUESTION 21

Which organs are most often affected by prolonged hypertension?

brain – blood clots, stroke, vascular dementia

kidneys – damage to renal blood vessels impairs filtration

heart – increased cardiac workload leading to LVH; heart failure, CAD

QUESTION 22

Describe orthostatic hypotension.

Orthostatic hypotension is a **sudden drop** in blood pressure that occurs **after standing up** from a sitting or lying position.

Gravity causes blood to rush to the lower body, and delayed compensation by the blood vessels temporarily reduces oxygen delivery to the brain.

It can manifest as sudden **dizziness** or even **loss of consciousness**, and is more common in **older patients** due to impaired baroreceptor activity.

(Remember that this is **hypotension**, a **drop** in blood pressure.)

QUESTION 23

Where is the most common site of aneurysms? Why?

The most common type of aneurysm is the **abdominal aortic aneurysm** (AAA.)

It occurs because of the **large diameter** and **high internal pressure** of the abdominal aorta, combined with the **poor structural support** provided by the surrounding organs.

QUESTION 24

List some common manifestations of abdominal aortic aneurysm (AAA.)

Dysphagia and **dyspnea** due to pressure on internal organs

Epigastric abdominal pain (often radiating to back in dissecting AAA)

Impaired blood flow can lead to **ischemia**, particularly of the bowels (ischemic colitis)

May be able to feel bounding pulse in epigastric region

QUESTION 25

What factors promote thrombus formation? How do we reduce the development of clots in the future?

Blood **stasis** – slow blood flow promotes formation of clots in stagnant/turbulent areas (e.g. valvular dysfunction)

Atherosclerosis – endothelial changes can promote clot formation, plus risk of plaque rupture leading to thrombosis

Thrombocytosis (increased platelet count) or increased intrinsic clotting factors (I, II, IX, X, XI, XII)

QUESTION 26

Where do plaques generally form in the coronary artery circulation?

Plaques usually form at the **proximal** end of the coronary arteries (closest to the aorta.)

The most common site is the **anterior interventricular** branch of the **left** coronary artery.

QUESTION 27

Which risk factor is most closely related to coronary artery disease (CAD?)

The most significant risk factor for coronary artery disease is **hypertension**.

Other risk factors include hyperlipidemia, smoking, diabetes, and age (>45.)

QUESTION 28

Which lipoprotein is protective?

High-density lipoprotein (HDL) plays a protective role as it can **reabsorb** cholesterol from the systemic circulation, preventing it from infiltrating the endothelium and contributing to plaque formation.

QUESTION 29

Compare stable, unstable, and Prinzmetal (variant) angina.

Angina is intermittent chest pain caused by cardiac ischemia (a temporary deficit of oxygen delivered to the heart.)

It often occurs or worsens with **exertion** due to the **increased metabolic demands** of the heart.

stable angina – normal angina that occurs predictably with exertion or emotional stress, then fades

unstable angina – unpredictable angina that comes on without warning or obvious reason

Prinzmetal (variant) angina – occurs at rest due to spontaneous vasospasm of the coronary arteries

QUESTION 30

What is ST-elevation myocardial infarction (STEMI?)
What does it suggest?

A STEMI is an infarction associated with **elevation** of the **ST segment** on an EKG.

ST elevation suggests a **transmural** infarction, meaning **complete blockage** of the coronary artery "from wall to wall."

STEMIs are even **more serious** than NSTEMIs (**non**-ST elevation myocardial infarctions) due to higher level of blockage, leading to severe ischemia and extensive tissue necrosis.

QUESTION 31

What are the signs and symptoms of myocardial infarction (MI?)

Severe, prolonged **chest pain** which may radiate to the left arm

Shortness of breath

Low-grade **fever** and increased **white blood cell** count (leukocytosis)

Serology: increased cardiac **troponin** and **creatine kinase myocardial band** (CK-MB)

QUESTION 32

What are some of the complications of MI?

Dysrhythmias can develop which lead to LVF

Cardiogenic shock

Thrombosis due to stagnation of blood

QUESTION 33

What is a complication of pericarditis?

One of the main complications is **cardiac tamponade**, in which excess pericardial fluid compresses the heart from the outside, impairing its ability to function.

Tamponade is a **medical emergency**, and is one potential cause of **cardiogenic shock**, which we'll talk about in the final question.

QUESTION 34

How would inflammation of a heart valve lead to stenosis? Why is mitral or aortic valve stenosis a problem?

Valve **stenosis** is the **narrowing** of the opening of a heart valve, leading to **impaired blood flow**.

Endocarditis (valve inflammation) can lead to stenosis—often as a sequela of **rheumatic fever**.

RF is uncommon in the U.S. but can still be seen in developing countries. The immune response to RF causes valve tissue to be targeted, causing permanent damage and scarring.

Poor blood flow through the valves **limits cardiac output**, and may be associated with **regurgitation**, in which the heart valves fail to close completely and blood is ejected backwards into the atria.

Stenosis and regurgitation are two of the most common causes of **heart murmurs**, audible on auscultation of the heart.

QUESTION 35

Compare right and left heart failure (RHF/LHF.) What is cor pulmonale?

Left heart failure is more common, with **right** heart failure usually occurring as a progression of LHF.

LHF can be caused by myocardial necrosis due to an MI, or by increased SVR due to hypertension.

Cor pulmonale (pulmonary heart disease) is a common cause of RHF, in which changes in the pulmonary circulation (stenosis, pulmonary hypertension) cause the right ventricle to have difficulty pumping blood through the lungs.

QUESTION 36

Describe a third-degree heart block.

Three types of **atrioventricular block** (AV block):

- **1st degree** AV block – conduction between atria and ventricles is **slowed**, resulting in a **prolonged PR interval**
- **2nd degree** AV block – conduction is even further slowed, and some impulses **don't reach** the ventricles at all
- **3rd degree** AV block – conduction to the ventricles is **completely cut off**, resulting in an "escape rhythm"

In a third-degree AV block, the sino-atrial (SA) node no longer has **any** control over the ventricular rate, causing it to spontaneously trigger at its own (much slower) rate.

The ventricles don't **stop** due to the presence of accessory pacemakers, but the rhythms of the atria and ventricles are completely disconnected and independent of each other.

QUESTION 37

Compare atrial and ventricular fibrillation.

Ventricular fibrillation (v-fib) is the **most serious** form of cardiac dysrhythmia, occurring when the ventricles fail to contract as a single unit.

The ventricles contract one part at a time, often in circular waves, resulting in a failure to effectively move blood out of the heart.

Atrial fibrillation (a-fib) is still not good, but the ventricles are able to maintain a small fraction of their effectiveness even without the help of the atria "loading" them with blood.

The heart can still operate at 20-30% of its normal function during a-fib, as the expansion of the ventricles pulls some blood in from the atria during diastole.

Defibrillation works by depolarizing the entire heart at once, hopefully causing it to resume contraction in unison and restoring normal rhythm.

QUESTION 38

Describe the types of shock.

Shock is a general term for insufficient blood supply to the tissues of the entire body, and the resulting complications. It is categorized according to the **cause**.

cardiogenic shock – blood delivery interrupted by some form of ventricular dysfunction (acute MI, tamponade, CHF)

hypovolemic shock – lack of blood volume, particularly due to severe blood loss or dehydration

distributive shock – low BP due to severe **vasodilation**, includes:

- ↳ **neurogenic** shock – loss of sympathetic tone due to CNS damage
- ↳ **anaphylactic** shock – immune response to allergens
- ↳ **septic** shock – immune response to infection