COAGULATION DISORDERS

(CHAPTER 22)

QUESTION 1

Describe some activation problems that can result in hypercoagulation.

Activation disorders refer to the inappropriate formation of clots in the absence of injury (the clotting cascade is activated when it shouldn't be.)

This can include arterial or venous **stasis**, **roughened endothelium** as seen in atherosclerosis, or **hyperproduction** of clotting factors.

QUESTION 2

Describe some regulation problems and breakdown problems.

Fibrinolysis (breakdown of fibrin in blood clots) begins immediately as a clot forms, both to regulate the speed of clot formation and to eventually break down the clot fully once the injury is healed.

If this system fails, **decreased inhibition** of clotting can result in excessive coagulation.

QUESTION 3

Describe some complications of abnormal clotting.

Abnormal clotting interferes with normal circulation, often resulting in decreased perfusion of tissues and ultimately ischemic damage, such as...

deep vein thrombosis (DVT) – blood clot in the veins of the lower leg, blocking blood return to the heart

pulmonary embolism (PE) – blood clot in the circulation of the lungs, classically presenting as chest pain and SOB

myocardial infarction (MI) – blood clot in the coronary artery circulation, causing ischemia to the heart

stroke (CVA/TIA) – clot blocking blood flow to the brain, resulting in neurological symptoms and often permanent brain damage

QUESTION 4

How can clotting be an acquired condition? Give some examples.

Many non-hereditary factors can influence clotting:

- **venous stasis** – caused by long periods of bed rest or immobility
- **antiphospholipid syndrome** (APS) – autoimmune disorder that can cause hypercoagulation
- **cancer**
- **PICC lines**, **pregnancy**, side effect of **drugs** including contraceptives
- **Circulatory issues**: heart failure, a-fib, etc.

QUESTION 5

How is vitamin B_{12} involved in coagulation?

Vitamin B_{12} and folate are closely linked with **homocysteine**, an inflammatory substance which can be a risk factor for endothelial damage.

Low B_{12} levels impairs the body's ability to recycle homocysteine, leading to increased levels in the blood and increased risk of clotting.

QUESTION 6

Describe some inherited clotting disorders.

The **factor V Leiden** mutation is an abnormal form of clotting factor V (proaccelerin) which is "immune" to the normal regulatory mechanisms that inhibit clot formation.

The **prothrombin g20210a** mutation (factor II mutation) is a mutation leading to the overproduction of factor II (prothrombin,) which likewise leads to a hypercoagulative state.

QUESTION 7

What is dysfibrinogenemia?

Dysfibrinogenemia is an **inherited condition** caused by a mutation in the gene that codes for fibrinogen.

This abnormal fibrinogen forms a different kind of fibrin that is not as effectively broken down by plasmin, leading to hypercoagulation.

QUESTION 8

What is hemophilia? Compare hemophilia A and B.

Hemophilia is a group of **hereditary bleeding disorders** due to deficiency of clotting factors, which result in impaired coagulation.

Mild symptoms include **bruising**, **epistaxis** (nosebleeds,) increased **bleeding time**, etc.

More pronounced symptoms include severe **internal bleeding** and **hemarthrosis** (bleeding into the joint space.)

Hemophilia **A** is linked to impaired production of clotting factor VIII (anti-hemophilic factor/AHF,) whereas hemophilia **B** is due to impaired production of factor IX (Christmas factor.)

Hemophilia A is about **6 times** as common as hemophilia B. Both occur **almost exclusively** in male patients.

QUESTION 9

Why are those affected by hemophilia almost exclusively male?

The mutation that causes hemophilia is a **recessive** mutation on the **X chromosome** (X-linked recessive mutation.)

Men (XY) only have **one X chromosome**, so an abnormal gene on this chromosome will **always** be expressed.

Women (XX) have **two X chromosomes**, so the mutation will only be expressed if **both** chromosomes have the mutation.

In other words: women are protected by their "backup copy" of the X chromosome. If a woman inherits hemophilia from only one parent, she will be a **carrier** for the abnormal gene, but will not suffer from the disease.

Only by inheriting hemophilia from **both** parents can a woman actually develop the disease (extremely rare.)

QUESTION 10

What function does von Willebrand factor (vWF) serve in hemostasis?

von Willebrand Factor (vWF) is a glycoprotein in the blood which plays an important role in **platelet adhesion** during the early stages of clot formation.

The underproduction of vWF is known as **von Willebrand Disease** (vWD,) which is also hereditary, but unlike hemophilia, affects men and women equally.

Symptoms of vWD are similar to those of hemophilia, although the most common forms of vWD tend to have only mild symptoms such as bruising and epistaxis (nosebleeds.)

Internal bleeding, such as bleeding into the joints, is uncommon in most forms of von Willebrand disease but can occur in the more severe types.