CAUSES OF DISEASE

(CHAPTER 10)

PART 1, QUESTION 1

How are anatomy and physiology the same?

aná (up)

témnō (to cut)

ANATOMY

"the study of the body's *physical structures*"

phúsis (nature)

-logía (study)

PHYSIOLOGY

"the study of the body's *internal functions*"

Form and **function**.

What the body *is* versus *how it works*.

However...

Physiologic processes **can't occur** without the anatomical structures that make them possible.

At a molecular scale, it all comes down to chemistry—**here, A&P are indistinguishable**.

PART 1, QUESTION 2

What are the causes of disease?

In a diseased state, the body malfunctions because **cells** malfunction.

This results in **altered physiology**, which we observe as signs and symptom of disease.

Five main causes of disease:

- Injury
- Adaptation
- Cellular death
- Neoplasia
- Aging

Cellular injury results from a disruption of normal cellular functions. Something goes wrong, causing the cell's homeostasis to be disrupted.

Cellular adaptation is an *intentional* physiologic change by a cell in response to external stressors.

Cellular death is the complete and irreversible destruction of cells, either intentionally as a protective measure, or unintentionally due to external influence.

Neoplasia is an abnormal and excessive growth of new tissues (tumors.) Neoplasms can be either benign or malignant.

Aging can disturb many of the body's normal physiologic processes, although the mechanism of these changes are not always well-understood.

PART 1, QUESTION 3

When cells are injured, what are the stages of injury? Describe them.

First stage: **reversible** injury

Reversible injury is **adaptive**—the body is trying to compensate for an imbalance caused by disease.

When the stimulus goes away, the cells will eventually return to their normal state.

However, there is a limit to how much injury a cell can handle. Eventually, one of two things will happen...

apó (away from)

ptôsis (falling)

APOPTOSIS

"programmed (physiologic) cell death"

Body **intentionally** signals cells to "explode."

Internal enzymes are activated which cleave the cell membrane from within, and the cell falls apart.

nékrōsis (death)

NECROSIS

"unintentional (non-physiologic) cell death due to external factors"

Apoptosis and necrosis represent the second stage, **irreversible** cellular injury.

In irreversible injury, the cells die rather than simply changing, meaning that they cannot return to their original state.

PART 1, QUESTION 4

Describe some signs of cellular injury. Are they reversible or irreversible?

Two examples of cellular injury: **hydropic swelling** and **cellular inclusions**.

Both are typically reversible (unless they progress to cellular death.)

Hydropic swelling of renal tubules results from malfunction of Na^+/K^+ exchange pump, causing osmotic gradient which pulls water **into** the cell.

If the root cause is addressed, water will leave the cell and it will return to normal.

Cellular inclusions vary in type and cause, but one example is fatty liver disease, where lipids build up *inside* the cytoplasm of the hepatic cells.

FLD can be reversed with lifestyle changes: avoiding alcohol, lowering dietary fat, etc.

Eventually, lipid export via VLDL will improve and begin to clear the excess fat from the liver.

PART 1, QUESTION 5

The whole body controls the internal environment.
The stability of that environment is called...

HOMEOSTASIS

"steady state; equilibrium"

PART 1, QUESTION 6

Describe the stages of the general adaptation syndrome.

General adaptation syndrome refers to the response to stress experienced **by an organism**.

Don't get confused; we're not talking about **cellular** adaptation here!

Stressors could include:

- Physical exertion (fight or flight)
- Cold temperatures
- Illness, such as an infection
- Even psychological stressors!

(Anything demanding that makes your body work extra hard to adapt)

alarm → resistance → exhaustion

Alarm (or **compensation**) is the first stage, in which the body begins to adapt to a new stressor.

This results in an **onset shock** as the expenditure of resources increases.

In the **resistance** stage, the body begins to mobilize resources to support the increased demands.

This stage continues for as long as the body is able to keep up with the costs, then...

Exhaustion (or **decompensation**) when the body finally runs out of steam and can't continue the adaptive response.

Hopefully, the stressor goes away before we get to this point, and recovery is possible.

PART 1, QUESTION 7

Describe the types of tissue adaptation.

Get ready for a lot of defintions!

a- (not)

trophé (nourishment)

ATROPHY

"reduction in the **size** or **number** of cells to decrease resource consumption"

hupér (excessive)

trophḗ (nourishment)

HYPERTROPHY

"an increase in the **size** of individual cells"

hupér (excessive)

plásis (formation)

HYPERPLASIA

"an increase in the total **number** of cells"

metá- (succession, change)

plásis (formation)

METAPLASIA

"an adaptive change in which cells **change form** to become another type of cell"

dus- (bad)

plásis (formation)

DYSPLASIA

"an increased number of **abnormal** cells"

(Also called **atypical hyperplasia**)

Atrophy is an decrease in the size or number of cells due to disuse or the inability to support their needs.

Cells either die, resulting in fewer cells, or make themselves smaller through **autophagy**.

Caused by a deficit of resources, or by those resources being intentionally "bugdeted" elsewhere.

Can be caused by:

- Disuse
- Denervation
- Ischemia
- Nutrient starvation
- Hormonal changes
- Persistent cellular injury

EXAMPLES OF ATROPHY

Disuse: Muscle cells use a LOT of protein and are expensive for the body to maintain

If not in use, protein will be budgeted to more important things, e.g. energy for the brain

EXAMPLES OF ATROPHY

Denervation: Similar concept. Muscles without good nerve control aren't worth maintaining, resources will be budgeted elsewhere instead.

Think paraplegia, carpal tunnel syndrome, etc.

EXAMPLES OF ATROPHY

Ischemia: Every cell in the body needs O_2 for aerobic metabolism. If they don't get enough, growth is impaired and some cells may die.

This can happen anywhere in the body, especially due to poor circulation!

EXAMPLES OF ATROPHY

Nutrient starvation: Cells also need other resources (protein, glucose) for normal function, and can atrophy if there is a systemic deficit of these nutrients.

Caloric malnutrition → **marasmus**

Protein malnutrition → **kwashiorkor**

EXAMPLES OF ATROPHY

Hormonal changes: Many tissues' growth rate signaled by hormones—change in hormone level results in change in tissue growth.

Decreased androgens → muscular atrophy

Decreased estrogen → endometrial atrophy

EXAMPLES OF ATROPHY

Persistent cellular injury: Atrophy can also be caused by direct damage to the cells themselves.

Good example: Duchenne muscular dystrophy (DMD.) Lack of a specific structural protein causes sarcolemma to lose adherence, resulting in damage.

Hypertrophy is an increase in the **size** of cells.

Examples include:

- Left ventricular hypertrophy (LVH)
- Calf hypertrophy in toddlers with DMD
- Hypertrophy of hepatic cells in fatty liver disease

Hyperplasia is an increase in the **number** of cells, which can be compensatory, protective, or non-adaptive.

Compensatory: **hepatomegaly**

Protective: **calluses**

Non-adaptive: **benign prostatic hyperplasia (BPH)**

Metaplasia is a *change* from one type of cell to another, as a protective response to cellular damage.

Examples:

- Barrett's esophagus:

  stratified squamous → simple columnar
- Squamous metaplasia of the airways in smokers:

  pseudostratified ciliated columnar → stratified squamous

Dysplasia, also known as **atypical hyperplasia** is different—arguably *not* an adaptation, but evolves from hyperplasia.

Characterized by **abnormal** changes in the size, shape, and organization of cells

Can sometimes progress to cancer, but not always; still reversible at this stage

PART 2, QUESTION 1

Describe a consequence of benign prostatic hyperplasia.

Often occurs in men ages 40 and up, increasing in prevalence with age. Main symptoms are related to urination due to pressure on the urethra which runs through the prostate.

Frequent urination, urinary urgency, urge incontinence, dysuria, etc...

PART 2, QUESTION 2

Describe a consequence of alcoholic liver disease.

Compensatory hyperplasia → hepatomegaly.

In response to impaired liver function due to injury, liver begins producing **more cells** to compensate, resulting in an **enlarged** liver.

PART 2, QUESTION 3

Describe a form of normal hyperplasia driven by hormones.

Usually linked to **estrogen**. Examples include breast development during puberty, uterine hyperplasia during pregnancy, ovarian follicle development in response to FSH.

(Can also be abnormal if triggered inappropriately – endometriosis)

PART 2, QUESTION 4

Describe a form of abnormal proliferation.

Hemangioma – benign tumor formed by excessive proliferation (hyperplasia) of vascular tissue. Results in red mark visible on skin, sometimes raised.

Plus, the obvious example of **malignant neoplasm** (cancer)... more on this in the next question.

PART 2, QUESTION 5

Compare dysplasia with anaplasia.

DYSPLASIA

"an increased number of **abnormal** cells"

(Also called **atypical hyperplasia**)

aná (backward)

plásis (formation)

ANAPLASIA

"the **de-differentiation** of dysplastic cells, commonly seen in malignancy"

hyperplasia → dysplasia → anaplasia

Dysplasia is *reversible* and *does not* indicate malignancy. Cells are abnormal but still fairly well differentiated.

May progress to anaplasia, or may resolve on its own over time

Anaplasia is **NOT** reversible and is strongly associated with malignancy.

Cells regress to a less-mature state, becoming more "stem cell-like."

PART 2, QUESTION 6

Define metaplasia and give an example.

METAPLASIA

"an adaptive change in which cells **change form** to become another type of cell"

Remember our examples of metaplasia from earlier: **Barrett's esophagus** (associated with GERD) and **squamous metaplasia** of the airways in smokers.

PART 2, QUESTION 7

Which of these are reversible?

Dysplasia & metaplasia – **reversible**

Anaplasia – **not reversible**

PART 2, QUESTION 8

What is the consequence of hypoxic injury?

Major adaptation due to ischemia is **atrophy**. Remember atrophy can occur in response to a shortage of vital resources—such as oxygen.

Cellular swelling can also occur due to shutdown of transport pumps due to lack of ATP, resulting in an osmotic gradient.

PART 2, QUESTION 9

How can an overactive defense cause injury?

Immmune system can cause injury in many ways. **Granulomas** are collections of macrophages that form surrounding infected tissue in an attempt to isolate the infection.

Seen in many infectious diseases: TB, rheumatic fever, Crohn's disease, etc.

PART 2, QUESTION 10

Describe some physical agents that cause injury. How can this occur? At what temperature does death ensue?

Extreme temperature (hot or cold) is very harmful to proteins in the body and can cause them to denature.

Cells begin to die at above 105 degrees Fahrenheit, but can malfunction at ~101 degrees.

PART 2, QUESTION 11

How does ear damage occur in an explosion?

Pressure. Shockwave pushes on tympanic membrane, potentially rupturing it or even disrupting the bones of the middle ear.

PART 2, QUESTION 12

How does fast decompression injure tissue?

High pressure causes gases to dissolve into body fluids. As pressure rapidly decreases, gases come out of solution and form bubbles within tissues, causing physical damage.

Bubbles can also form in the bloodstream and impede blood flow, resulting in poor oxygenation, especially to the brain.

PART 2, QUESTION 13

How does a hyperbaric chamber function in infection?

Certain bacteria, such as *Clostridium tetani*, are considered **obligate anaerobes** and cannot survive in the presence of oxygen.

High pressure, such as in a hyperbaric chamber, causes gases such as oxygen to dissolve into body fluids, potentially killing any oxygen-intolerant bacteria.

PART 2, QUESTION 14

Describe how ionizing radiation injures cells. Which cells and which tissues are most susceptible?

Radiation knocks electron off of a molecule, creating positively-charged and highly reactive "free radical." Can cause mutations by binding to DNA.

Most-affected cells are those which divide rapidly. This is why radiation therapy works well for some cancers!

PART 2, QUESTION 15

Describe some injuries that lead to cellular inclusions. How do these inclusions disrupt function?

- Hydropic degeneration: excess water in cell due to electrolyte imbalance
- Fatty liver disease: excess lipid in cell due to impaired VLDL production
- Soft tissue calcification, calcification of atherotic plaques

PART 2, QUESTION 16

Describe the types of necrosis and where they might occur.

NECROSIS

"unintentional (non-physiologic) cell death due to external factors"

Six basic types of necrosis:

- Coagulative
- Liquefactive
- Caseous (a type of coagulative necrosis)
- Gangrenous (a type of coagulative necrosis)
- Fat (a type of liquefactive necrosis)
- Fibrinoid (immune-mediated; not covered in this course)

Coagulative necrosis: Most common type, occurring in many tissues as a result of ischemia. Cells die, but the tissues maintain their original structure.

Liquefactive necrosis: After cell death, enzymes liquefy the dead cells resulting in a viscous liquid abcess.

Occurs primarily in the **brain** but can also occur in the **lungs** as well.

Caseous necrosis: Literally means "cheese-like". Most commonly associated with tuberculosis and found at the center of granulomas.

Gangrenous necrosis: Caused by infection or ischemia, most commonly in the hands and feet. Most common cause is poor peripheral blood supply.

Fat necrosis: Occurs after the death of adipose tissue, most commonly in the breast and around the pancreas. Enzymes break down extracellular fat, resulting in "soapy" accumulation.