Exam 1 Review

Cell Injury

Can you describe what this diagram is trying to show?

Cell Injury – General Mechanisms

- Four very interrelated cell systems are particularly vulnerable to injury:
  - Membranes (cellular and organellar)
  - Aerobic respiration
  - Protein synthesis (enzymes, structural proteins, etc)
  - Genetic apparatus (e.g., DNA, RNA)

Summary: Dr. Dolan slides 4-25

- Cell injury starts with mitochondrial injury.
  - ↓
  - Sodium and calcium accumulate inside cell.
- Free radicals damage cell membrane.
- The ultimate reasons the cell dies are: membrane damage and cytoplasmic calcium accumulation.

Summary: Dr. Dolan slides 4-25

- Things you see in reversible injury:
  - Mitochondrial densities
  - Cellular swelling
  - Cytoskeletal disruption (microvilli loss, blebs)
- Things you see in irreversible injury:
  - All of the reversible changes, plus:
  - Increased eosinophilia (pink color) in cells
  - Bigger mitochondrial densities
  - Nuclear changes (pyknosis, karyolysis, karyorrhexis)

What single word could you use to describe the brain on the right (compared to the normal brain on the left)?

Atrophy!

If the uterus on the right is normal, what single word could you use to describe the uterus on the left?

Hypertrophy!

Which of these microscopic sections belongs to the uterus on the left (in the previous slide)?

The left section belongs to the left uterus on the previous slide.
The right section is of normal myometrium.

The glandular tissue on the left is normal. At the point indicated by the arrow, it turns into squamous tissue. What is this process called?

Metaplasia.

What kind of necrosis is this?

Coagulative.

What kind of necrosis is this?

Liquefactive. Usually happens in abscesses (like this one in the kidney) or in the CNS.

What kind of necrosis is this?
(Assume this is lung, and the whitish lesion is cheesy in texture.)

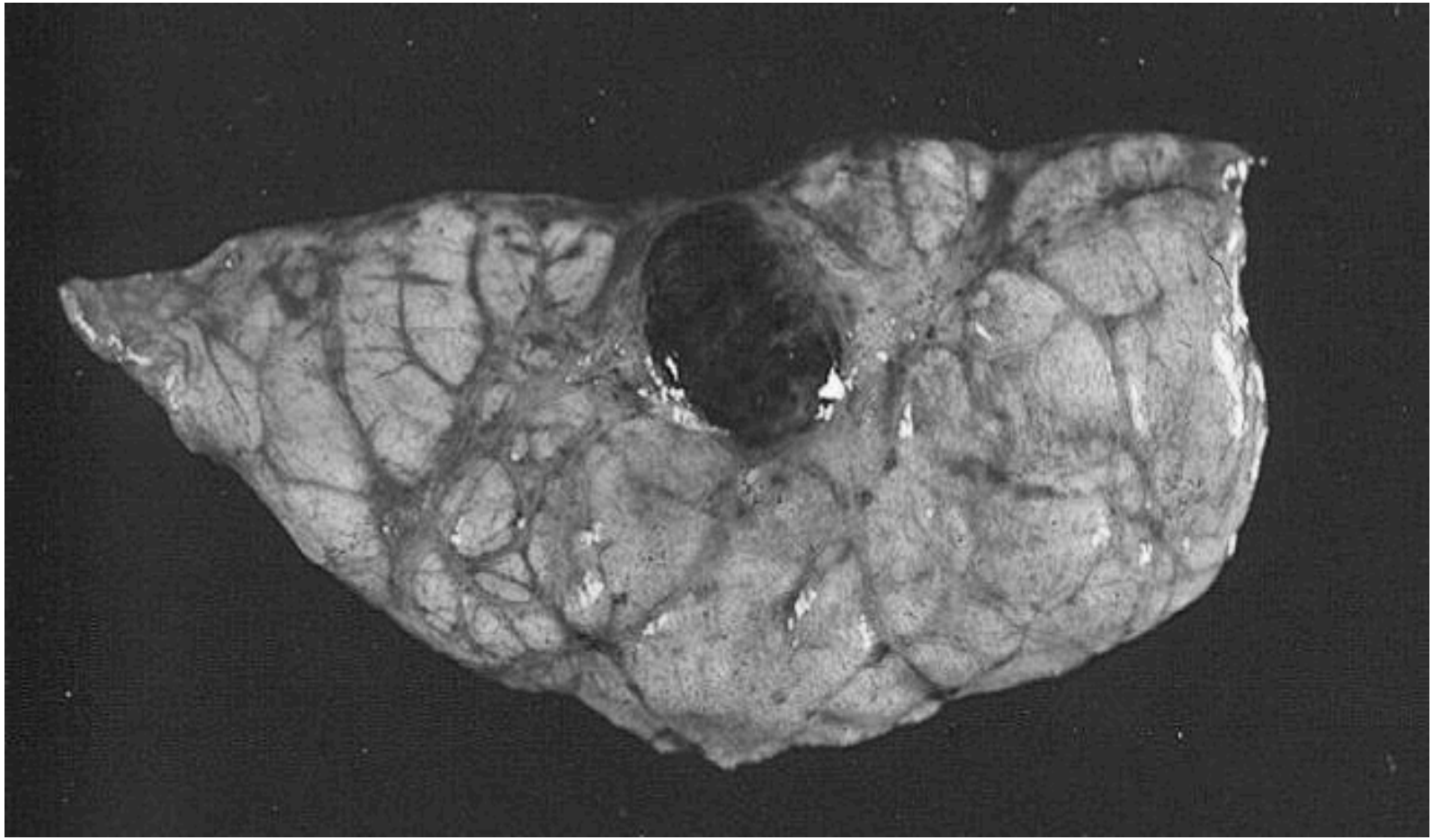
Caseous. This is probably a lung from a patient with TB.

What kind of necrosis is this? (Assume the organ in the photo is pancreas.)

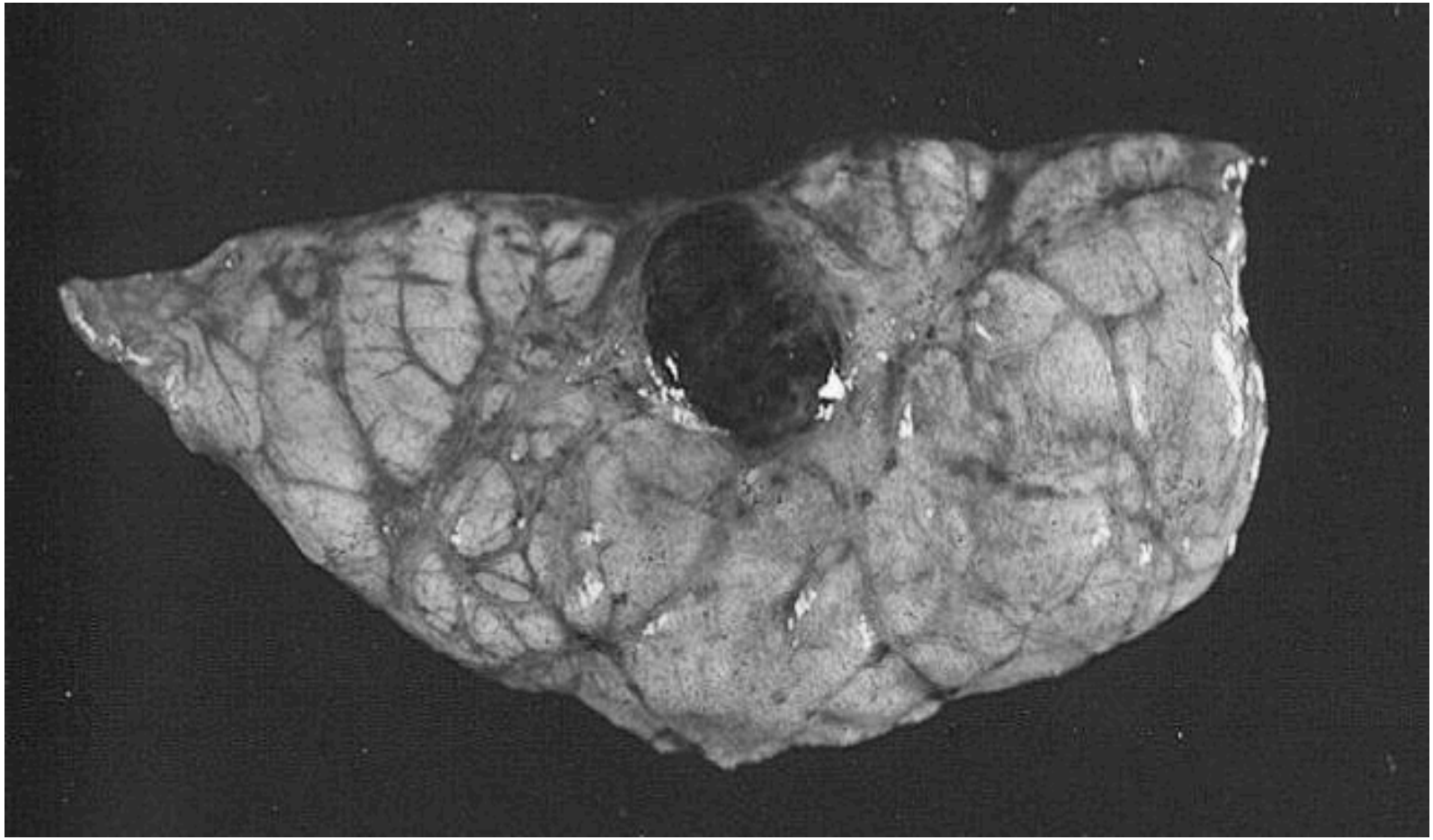
Fat necrosis.

What kind of necrosis is this?

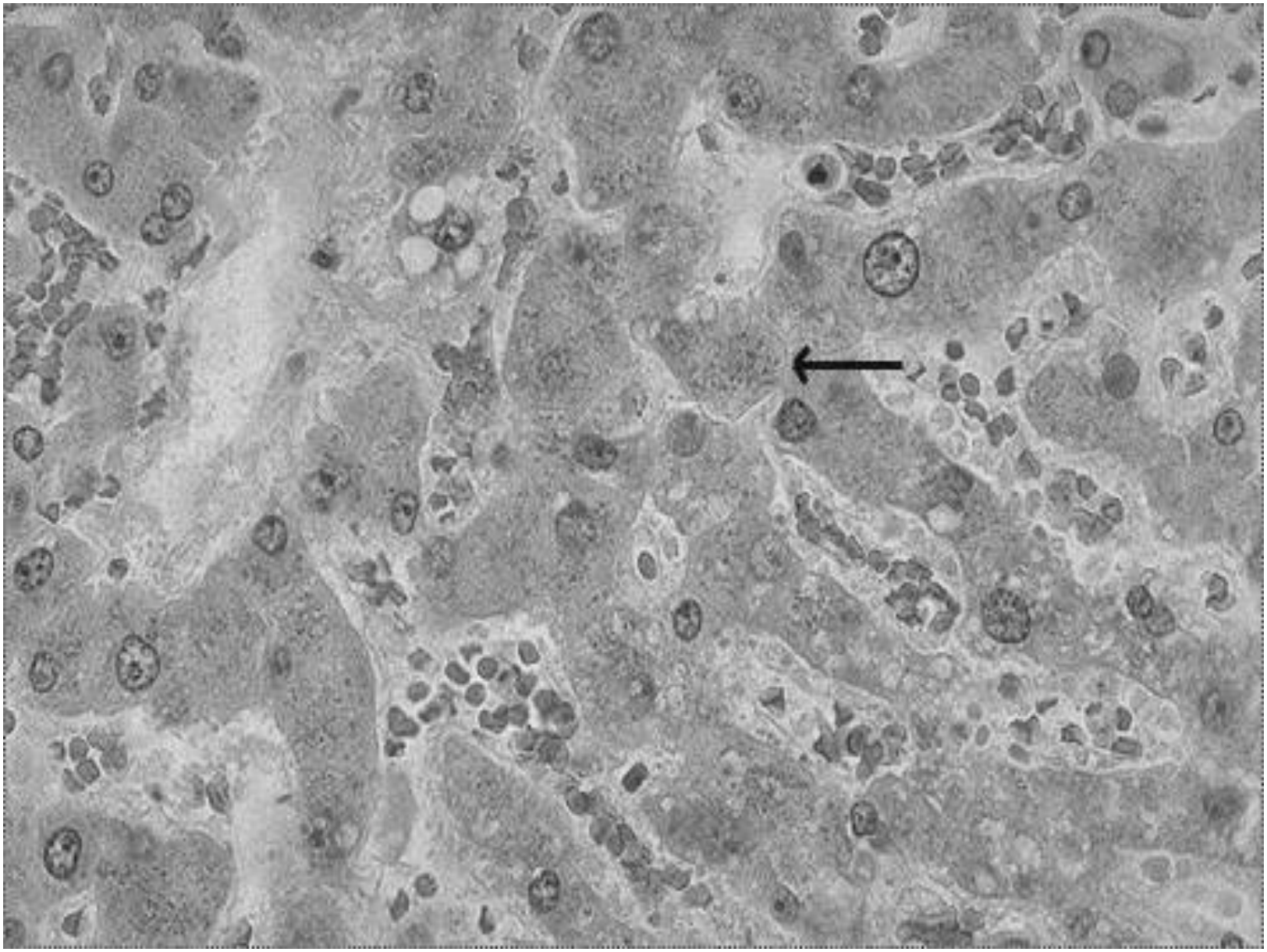
Gangrenous.



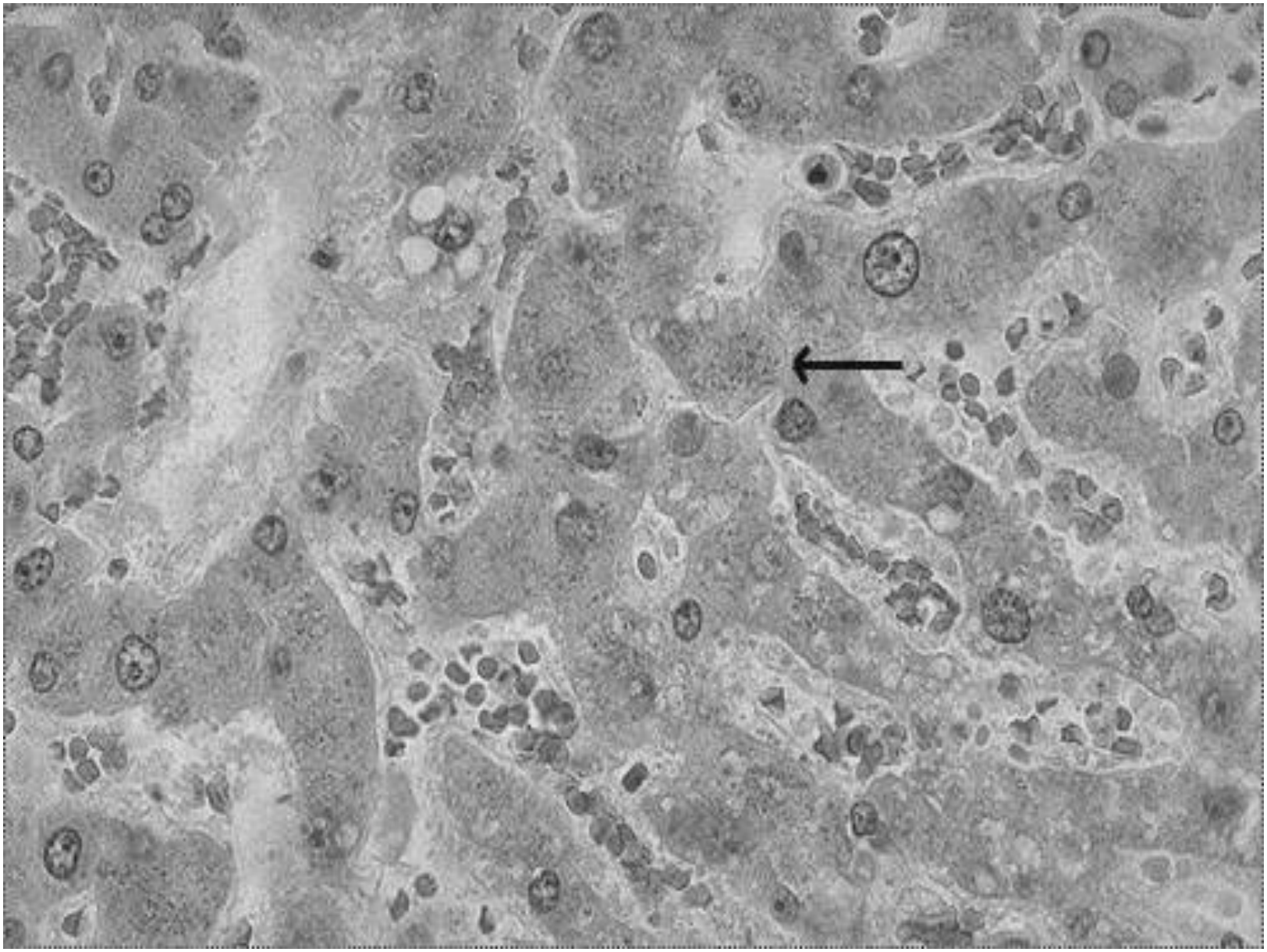
This lymph node was an incidental finding in a 60-year-old male who had lived in Los Angeles for his whole life. What's the pigment?



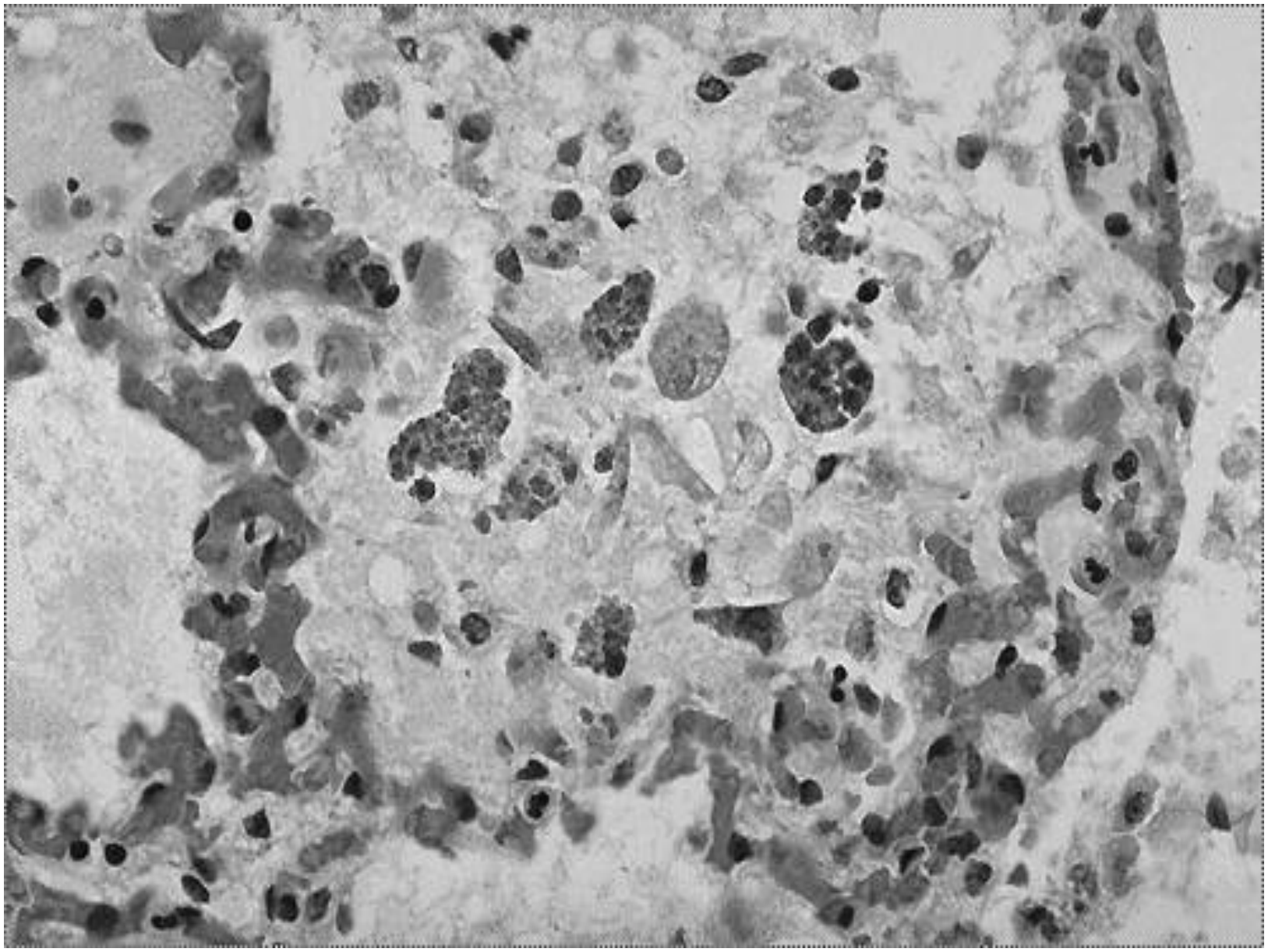
Anthracotic pigment. Commonly occurs in people who live in big cities – represents all the carbon crap we breathe in every day.



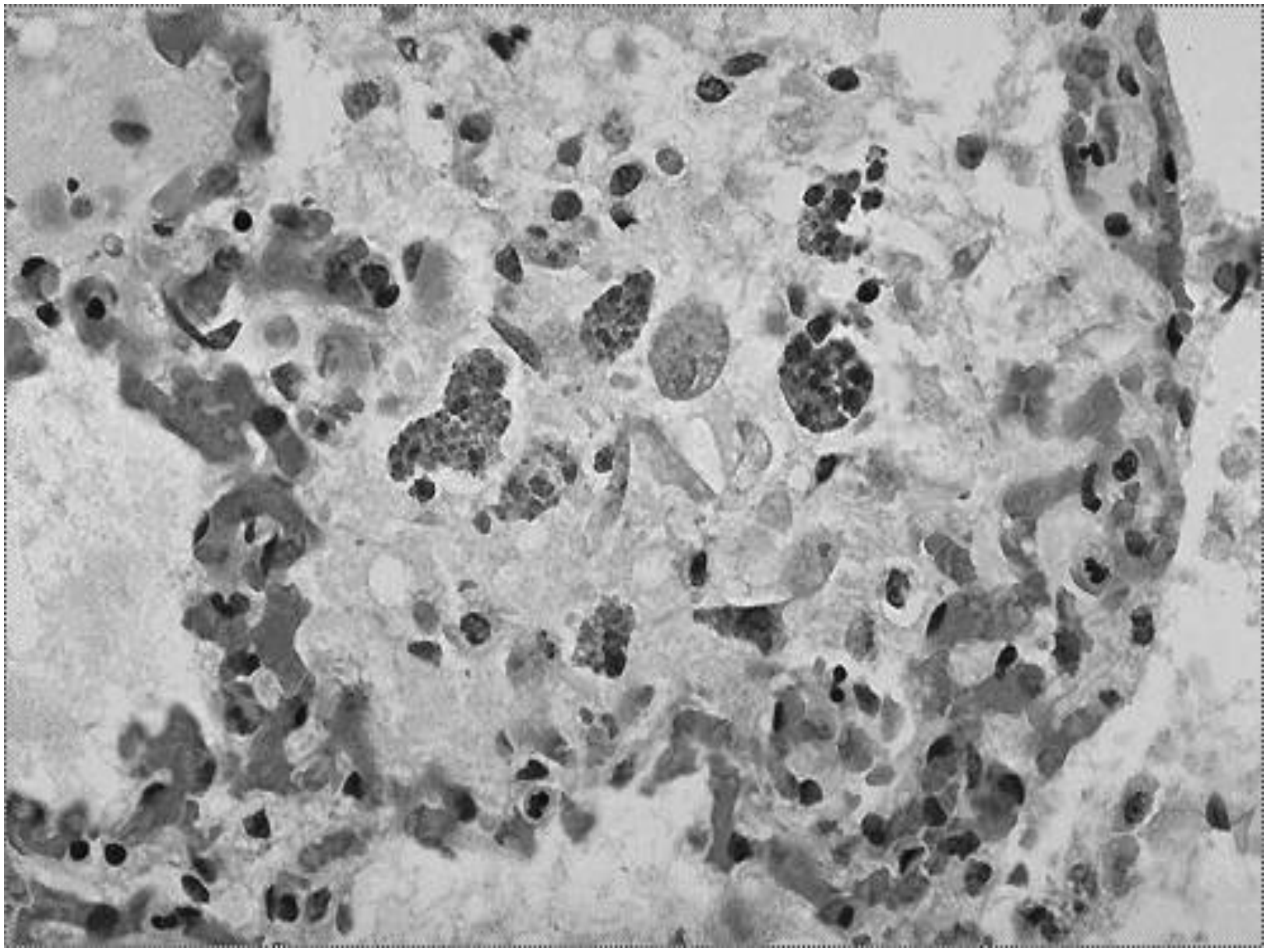
This section of liver is from a healthy elderly person.
What's the pigment?



Lipofuscin (sometimes called the aging pigment, because it increases with age).



This slide shows a resolving, hemorrhagic lung lesion.
What's the pigment?



Hemosiderin

This is a pathologic lesion of the skin. What's the pigment?

Melanin. This is a melanoma.

Inflammation

This is a section of heart taken several hours after an acute myocardial infarction. What kind of inflammation is this? What's the main cell type in this type of inflammation?

Acute inflammation. PMNs.

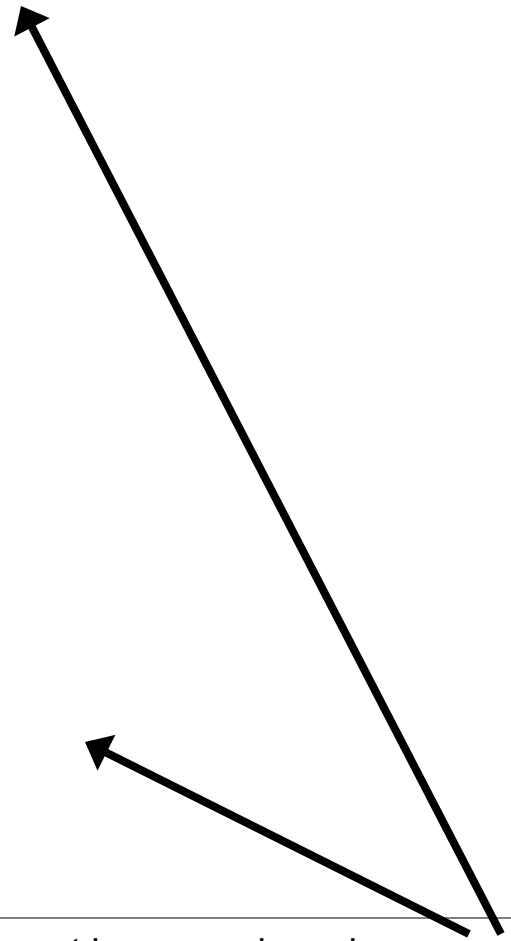
Here's the same heart, only now it's many days after the myocardial infarction.
What kind of inflammation is this? What's the main cell type in this type of inflammation?

Chronic inflammation. Lymphocytes.

Here's an intra-abdominal abscess (note goopy pus, arrow). If you looked at a section of this abscess under the microscope, what type of inflammatory cell would you see?

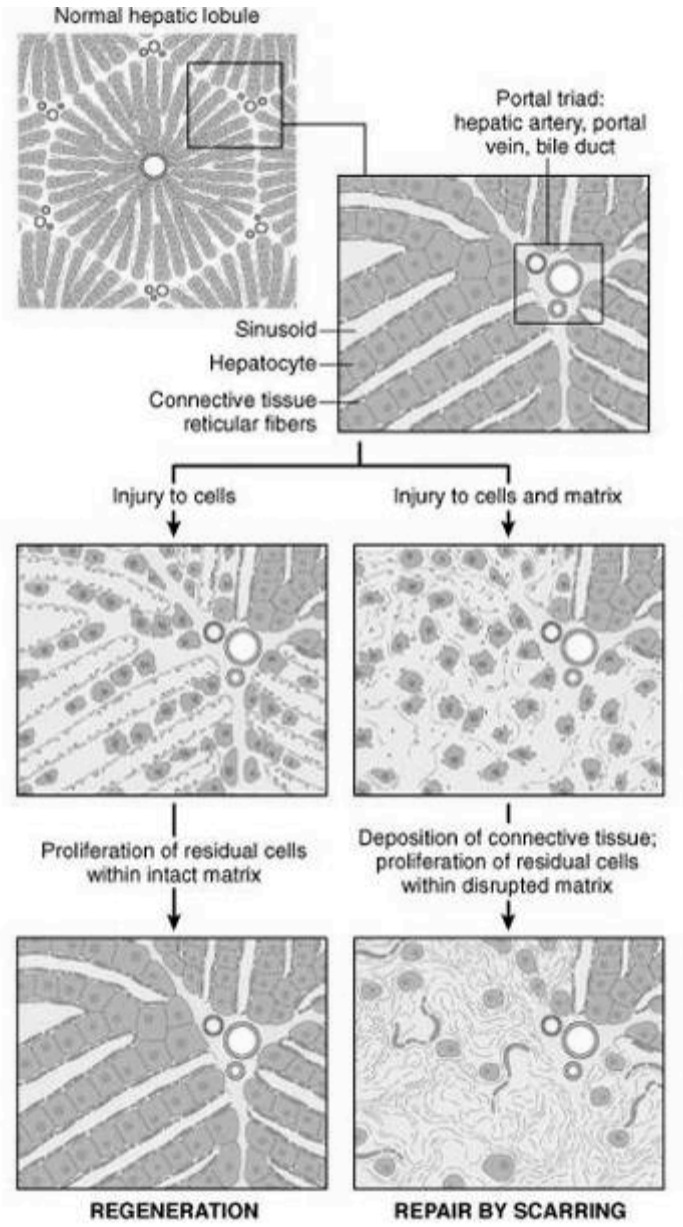
PMNs.

What kind of inflammation is this? What kinds of cells are present?
What's probably in the center of the field (though you can't see it)?



Granulomatous inflammation. The characteristic cell present in a granuloma is a macrophage (bigger cells with lots of pink cytoplasm in the middle of the field. Some of them are multinucleated.). There are also a few lymphocytes (around the edges).

Wound Healing and Repair



When tissues are injured, they can go down one of two pathways: regeneration or repair. Do you remember the differences between the two?

Three kinds of tissues

- Labile tissues
- Stable tissues
- Permanent tissues

1. What is the definition of each of the above terms?
2. What are some examples of each?
3. Why does it matter?

Three kinds of tissues

- Labile tissues
  - Bone marrow
  - Skin
  - GI epithelium
  - Oral mucosa
- Stable tissues
- Permanent tissues

Labile tissues have cells that are always proliferating.

Three kinds of tissues

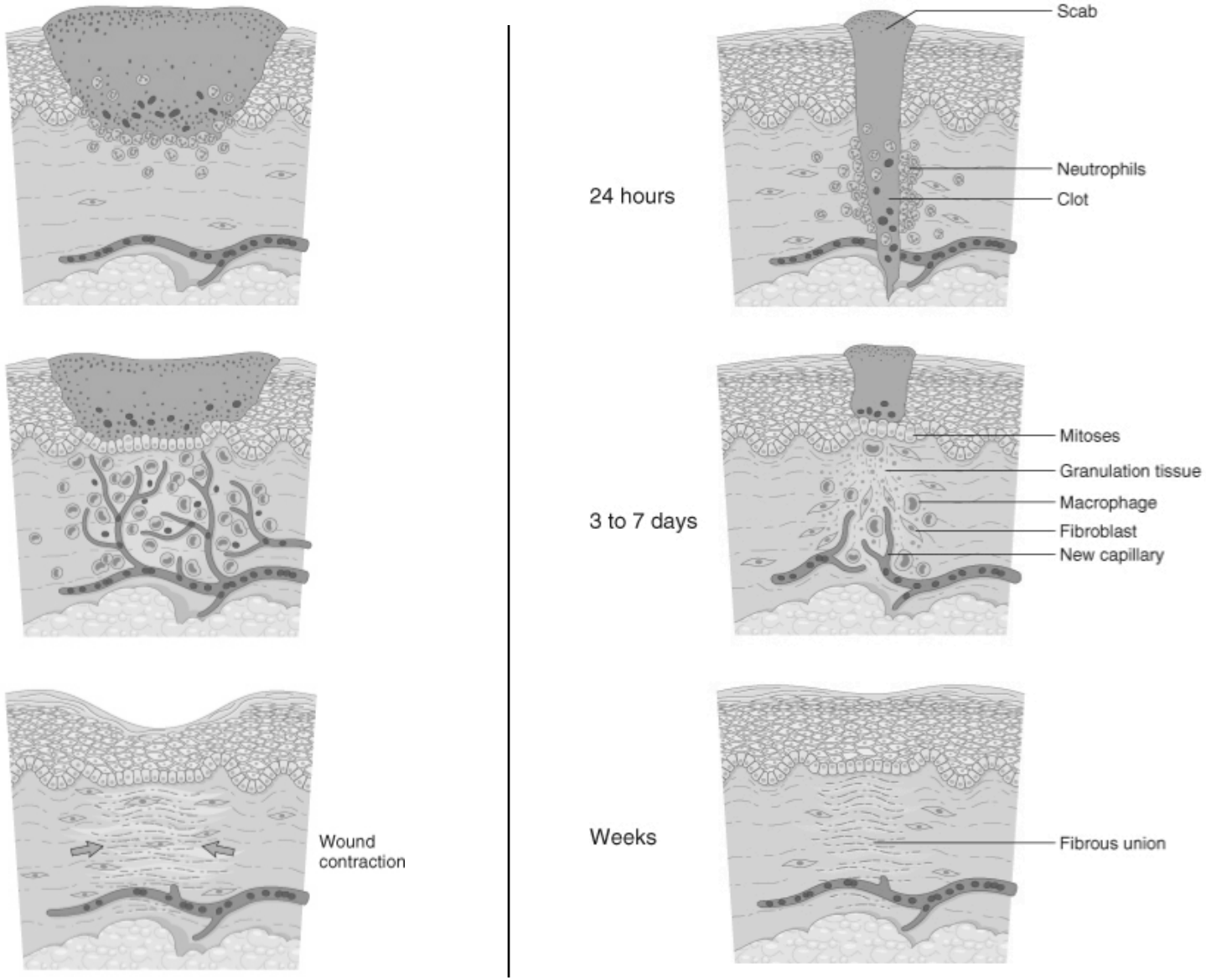
- Labile tissues
- Stable tissues
  - Liver
  - Kidney
  - Pancreas
- Permanent tissues

Stable tissues are those in which cells are usually in resting phase,
but can proliferate if necessary.

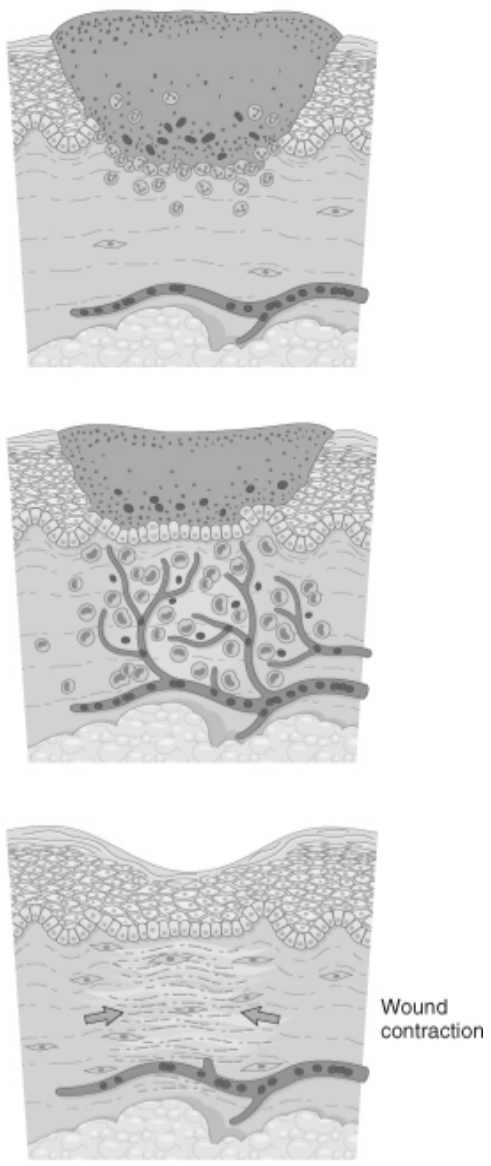
Three kinds of tissues

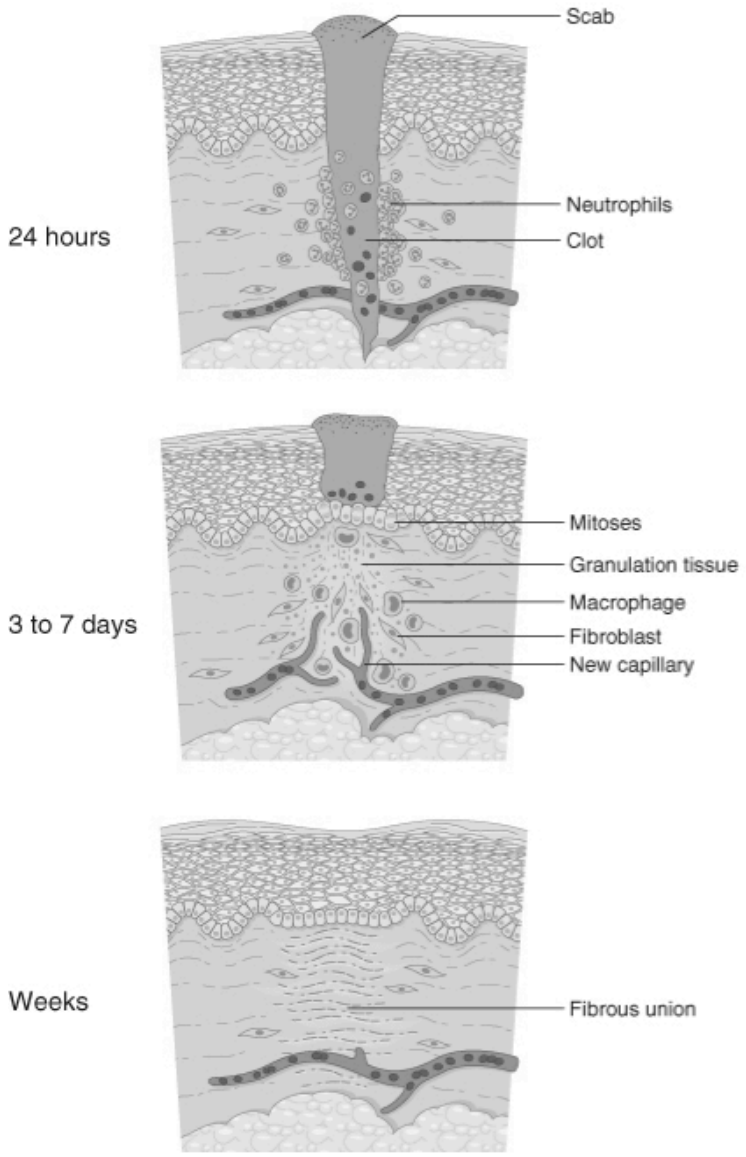
- Labile tissues
- Stable tissues
- Permanent tissues
  - Neurons
  - Cardiac muscle

Permanent tissues have cells that are totally out of the cell cycle permanently. These cells cannot proliferate at all. It's important to know these three types of tissues, because if there's an injury, you can predict whether the tissue will undergo 1) regeneration or 2) repair with scarring.



What are the main differences between healing by first and second intention?
Which side depicts healing by first intention?



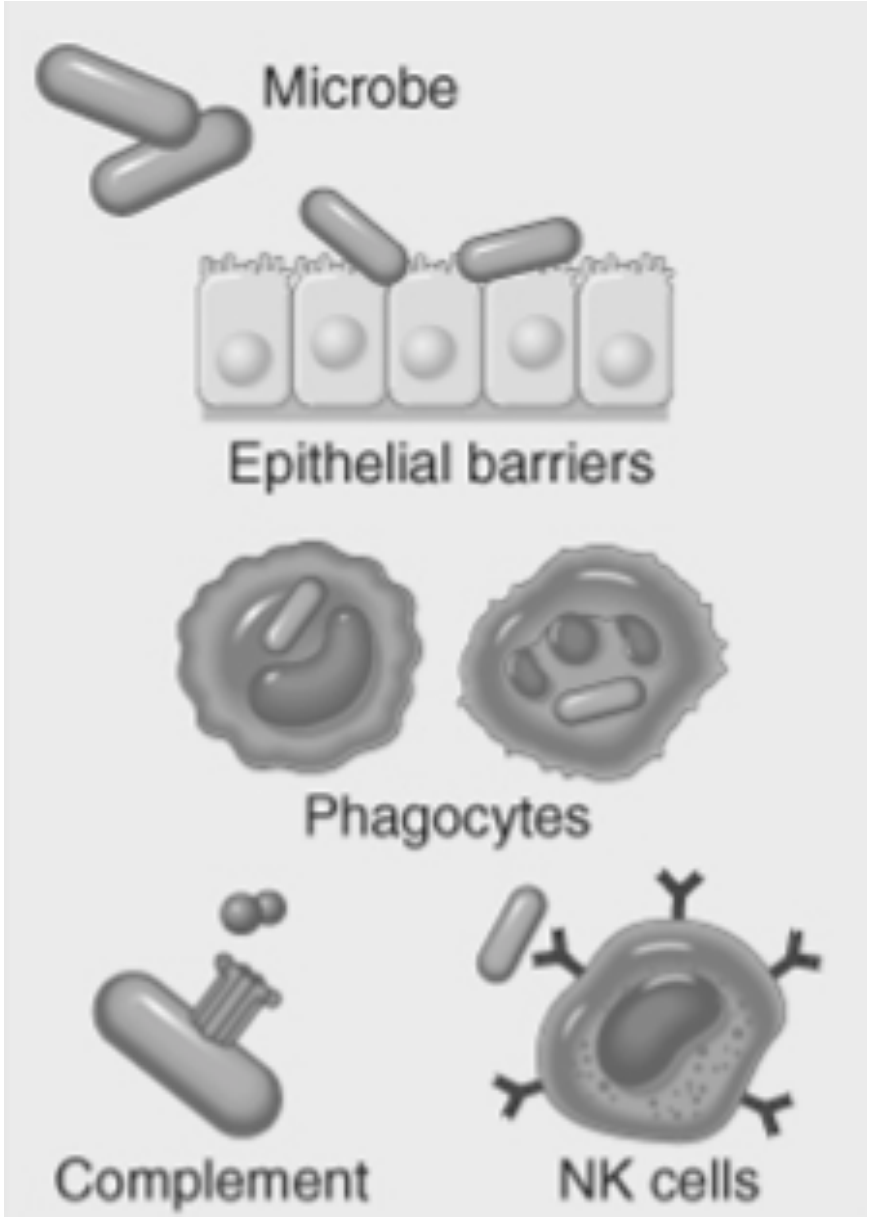


First intention is shown on the right. Second intention healing happens in bigger wounds. It takes longer, and there is more granulation tissue, inflammation, and scarring.

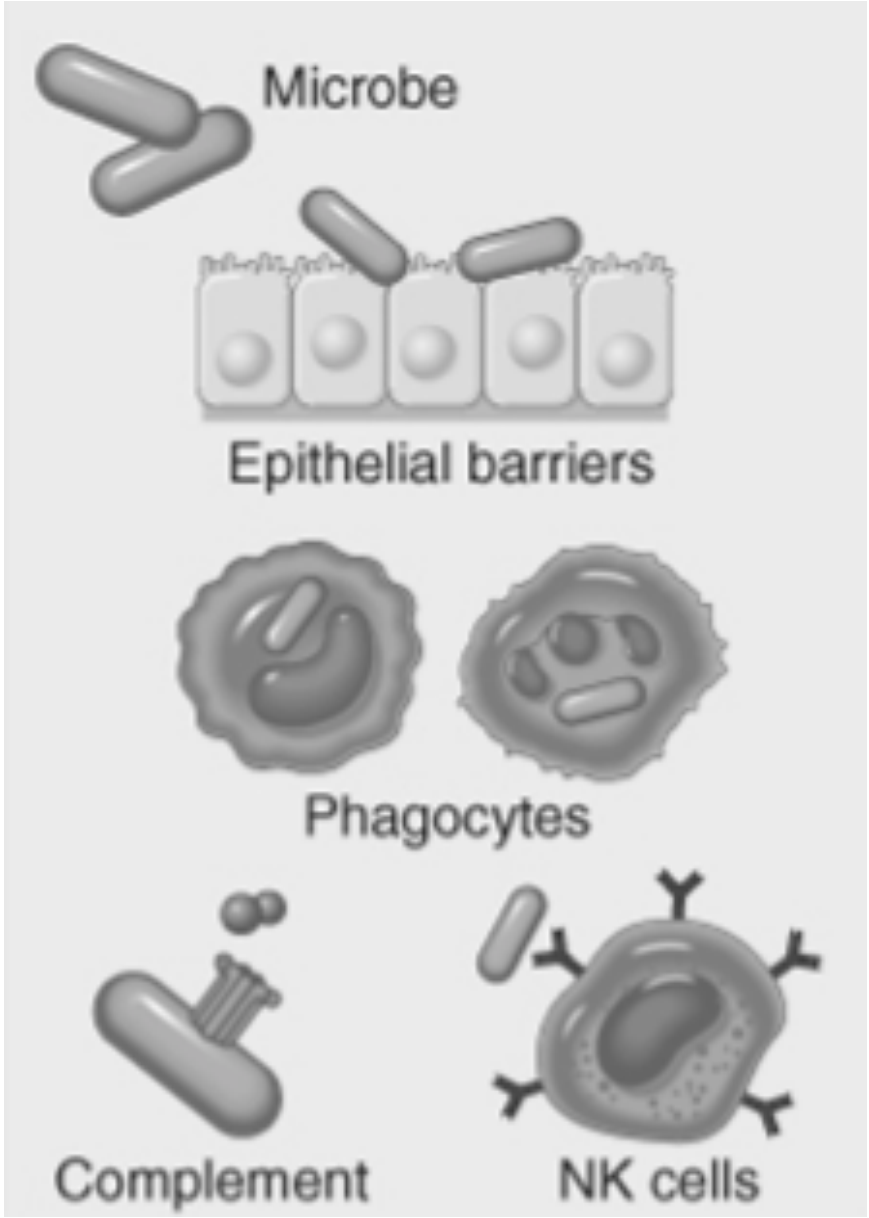
What is this stuff? What is it composed of?

Oh, please. Granulation tissue: blood vessels and fibroblasts in a loose extracellular matrix.

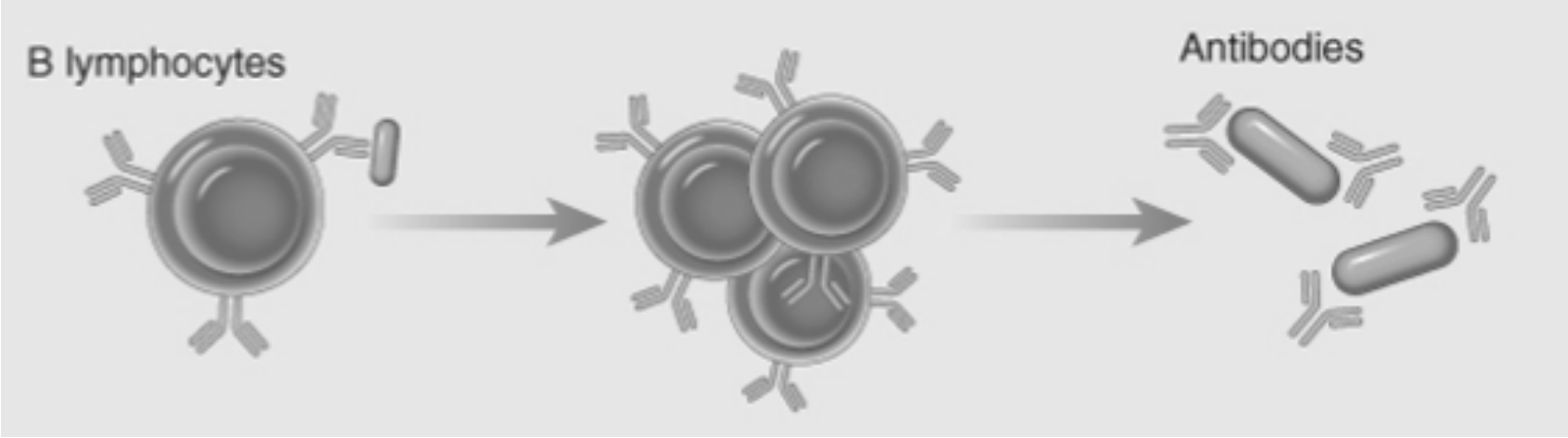
Immunology Overview



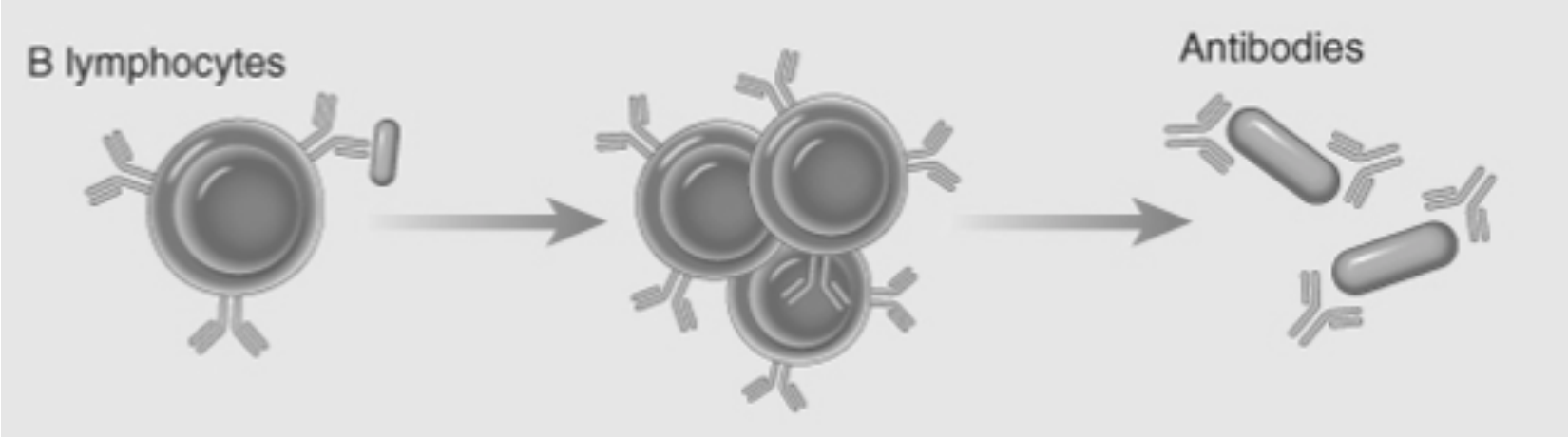
What arm of the immune system has the above components?
What's the point of this arm of the immune system?



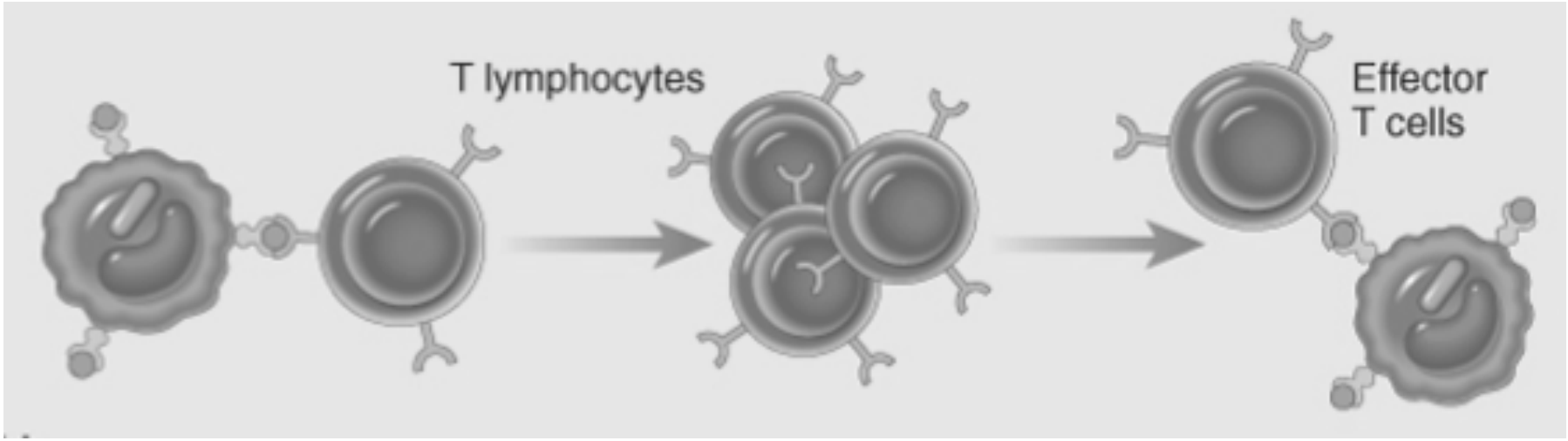
This is innate immunity. The goals of this arm are to kill stuff (mostly bacteria), and to help activate the adaptive system.



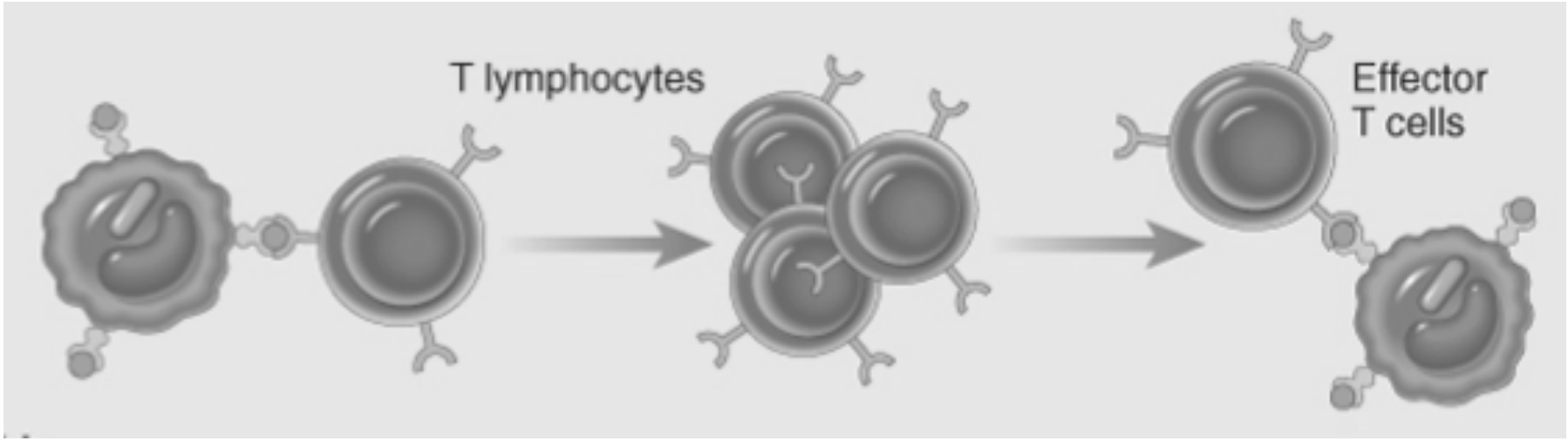
What is the name of this part of the immune system?
How does it get activated, and what's the end result?



Humoral immunity. Activated by exposure to antigen (and aided by T helper cells). End result: production of antibodies, which:
1) bind to ("neutralize") bugs, 2) opsonize bugs, and 3) activate complement.



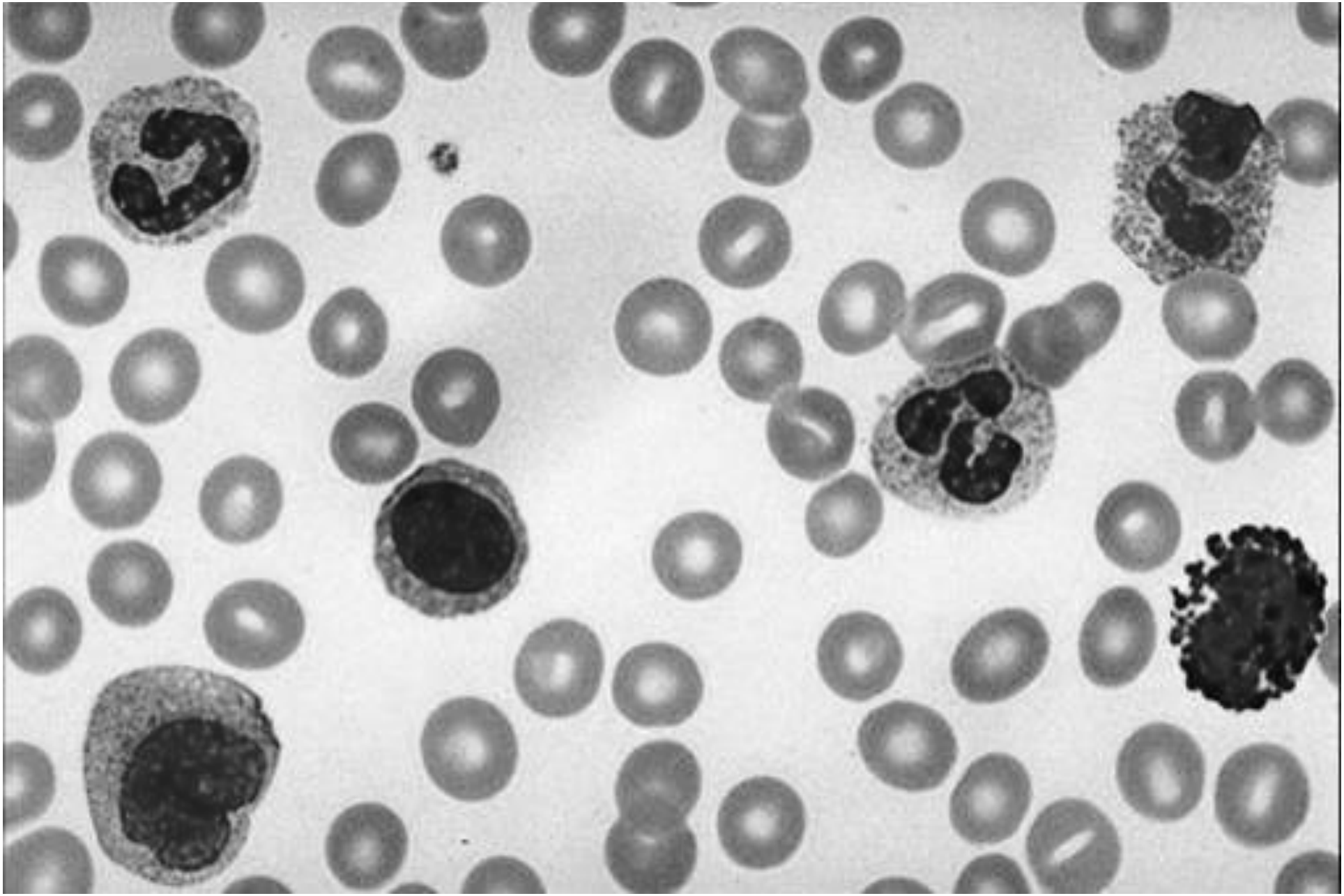
What is the name of this part of the immune system?
How does it get activated, and what are the end results?



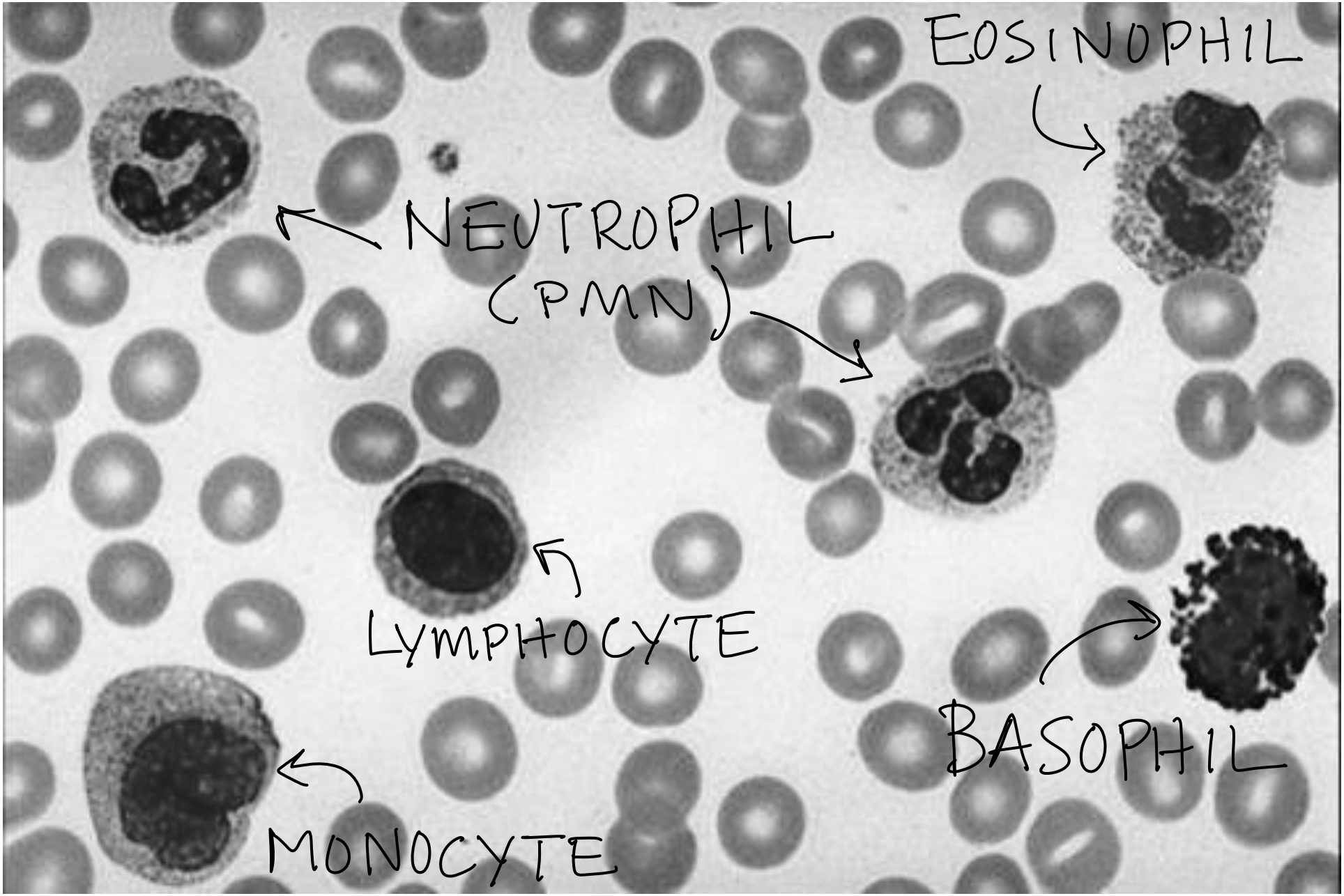
Cell-mediated immunity. Activated by exposure to antigen.

Antigen must be bound to MHC I (for cytotoxic T cells) or
MHC II (for helper T cells) receptors for the T cell to “see” it.

End result: production of 1) T helper cells (that help other cells,
like B cells and macrophages) do their jobs, and
2) T cytotoxic cells (that kill infected cells or tumor cells).



Name each of the cells. What is the main purpose of each?



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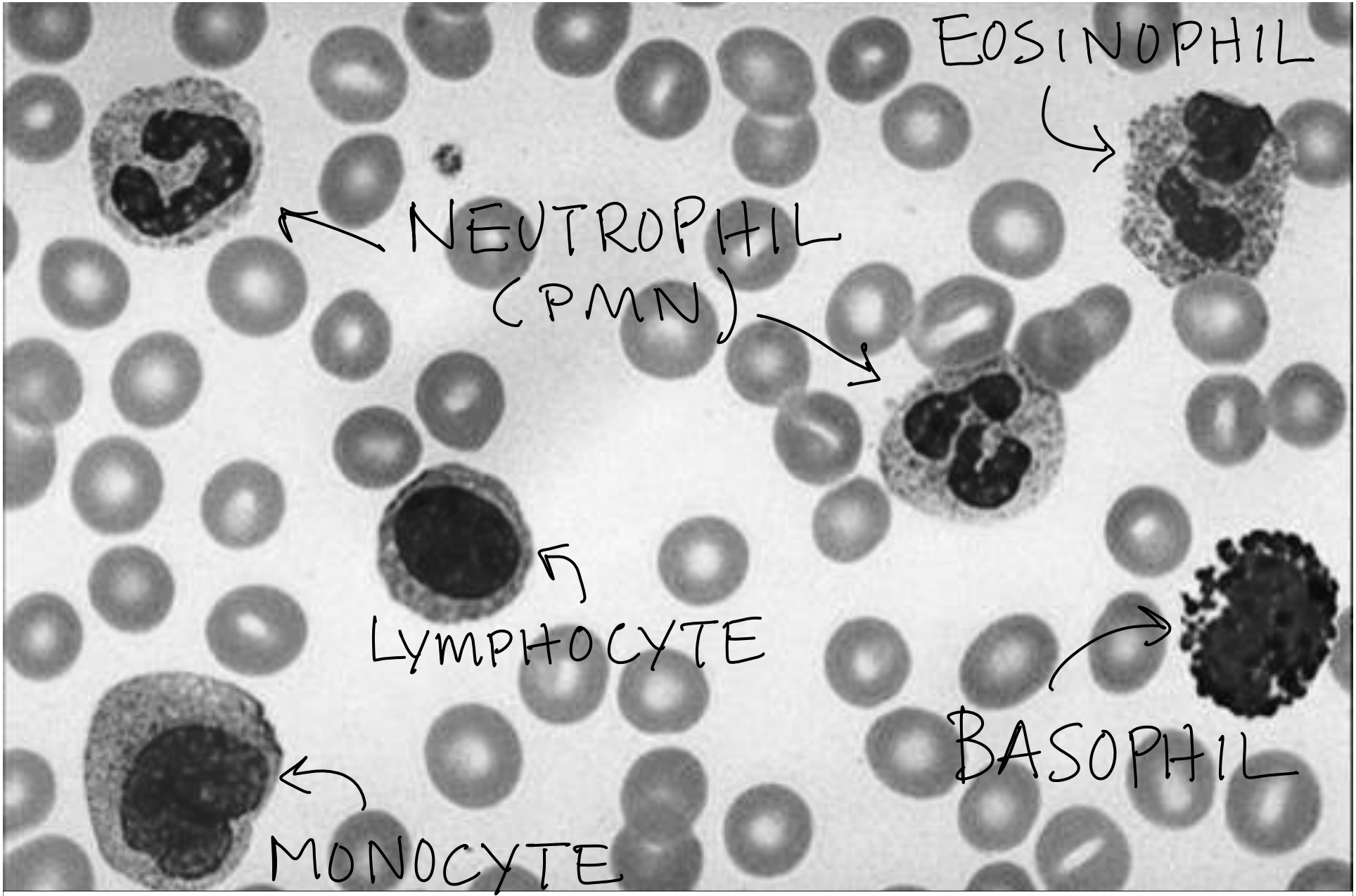
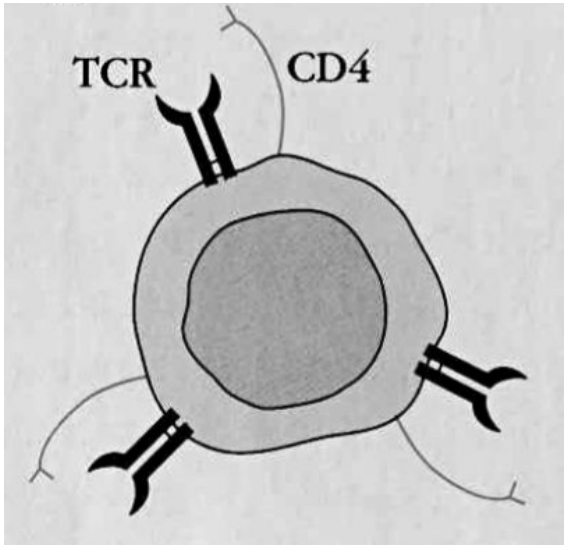
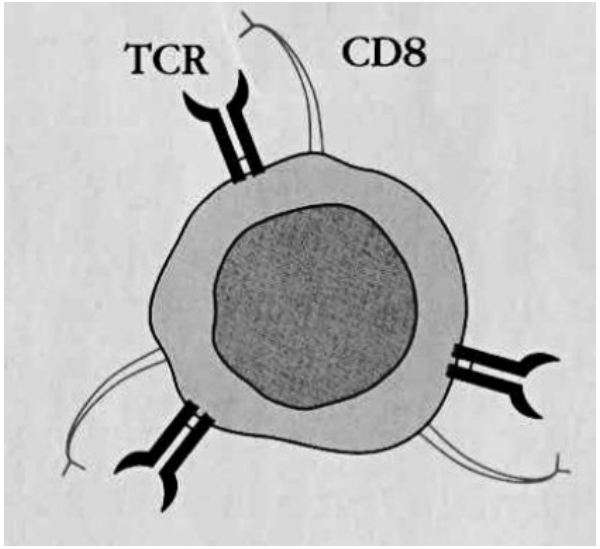
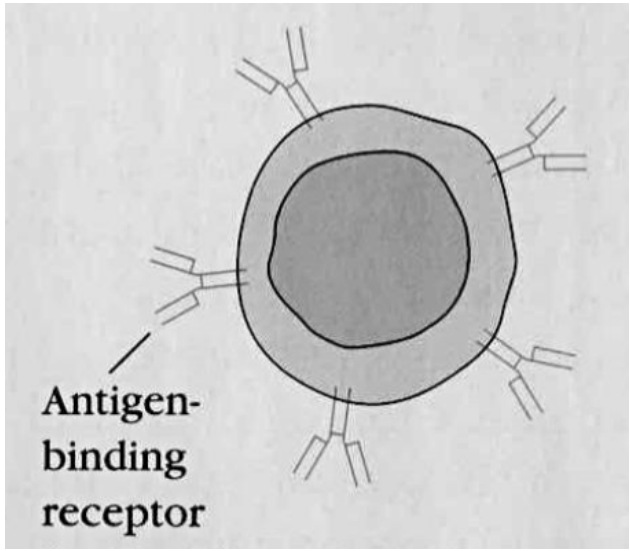


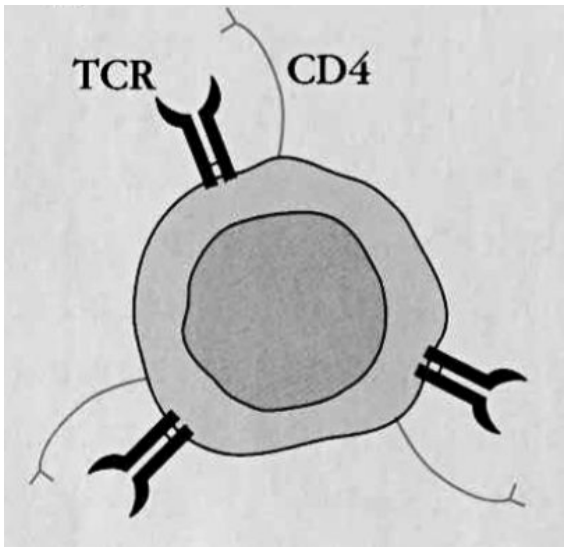
Neutrophil: fights bacterial infections (eat bugs and release cytokines). Eosinophil: participates in type I hypersensitivity reactions (good against parasites; also the mechanism of allergies). Basophil: participates in allergic reactions. Lymphocyte: participates in immune reactions (duh); fights viral and bacterial infections. Monocyte: can eat stuff as-is, in the blood. Also, in tissues, turn into macrophage, which participates in immune reactions as an antigen presenting cell and as a bug-eating machine.

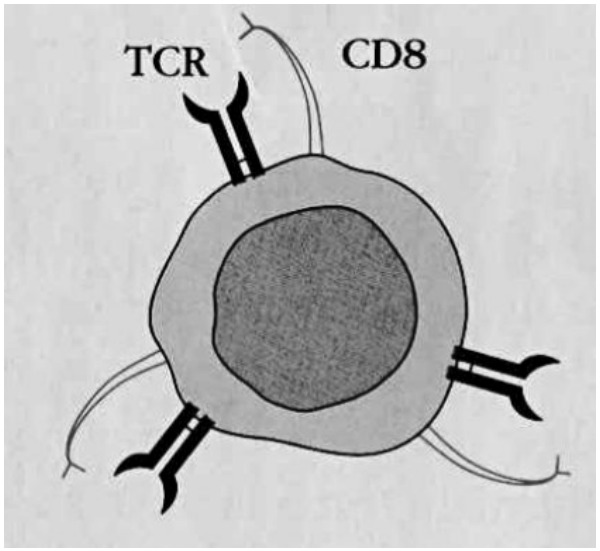


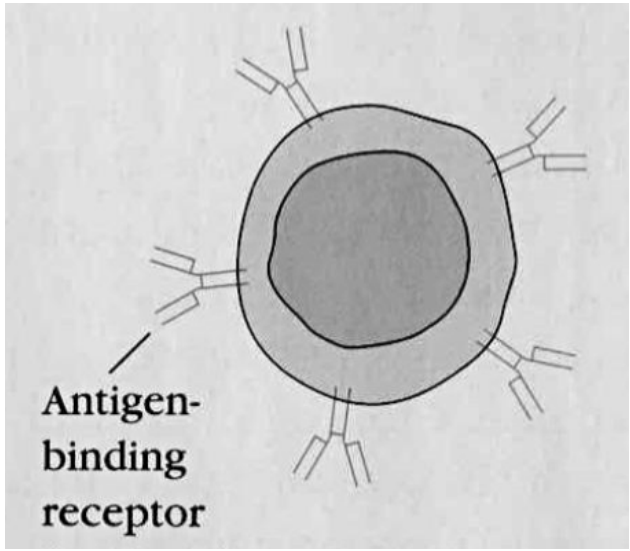




What are these cells? What do they do? How are they activated?





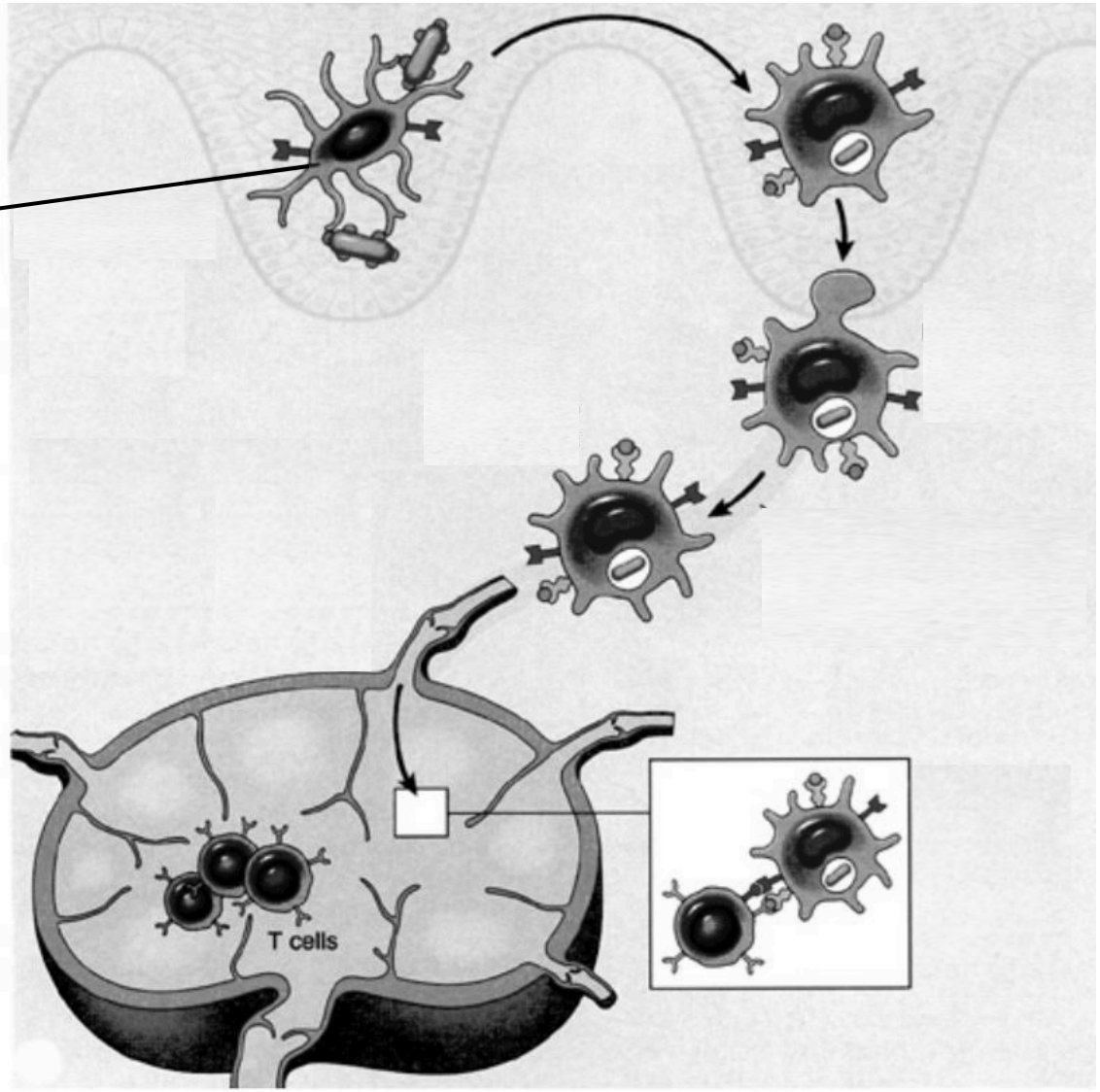


T helper cell on left. Helps other cells (B cells, macrophages) do their jobs.

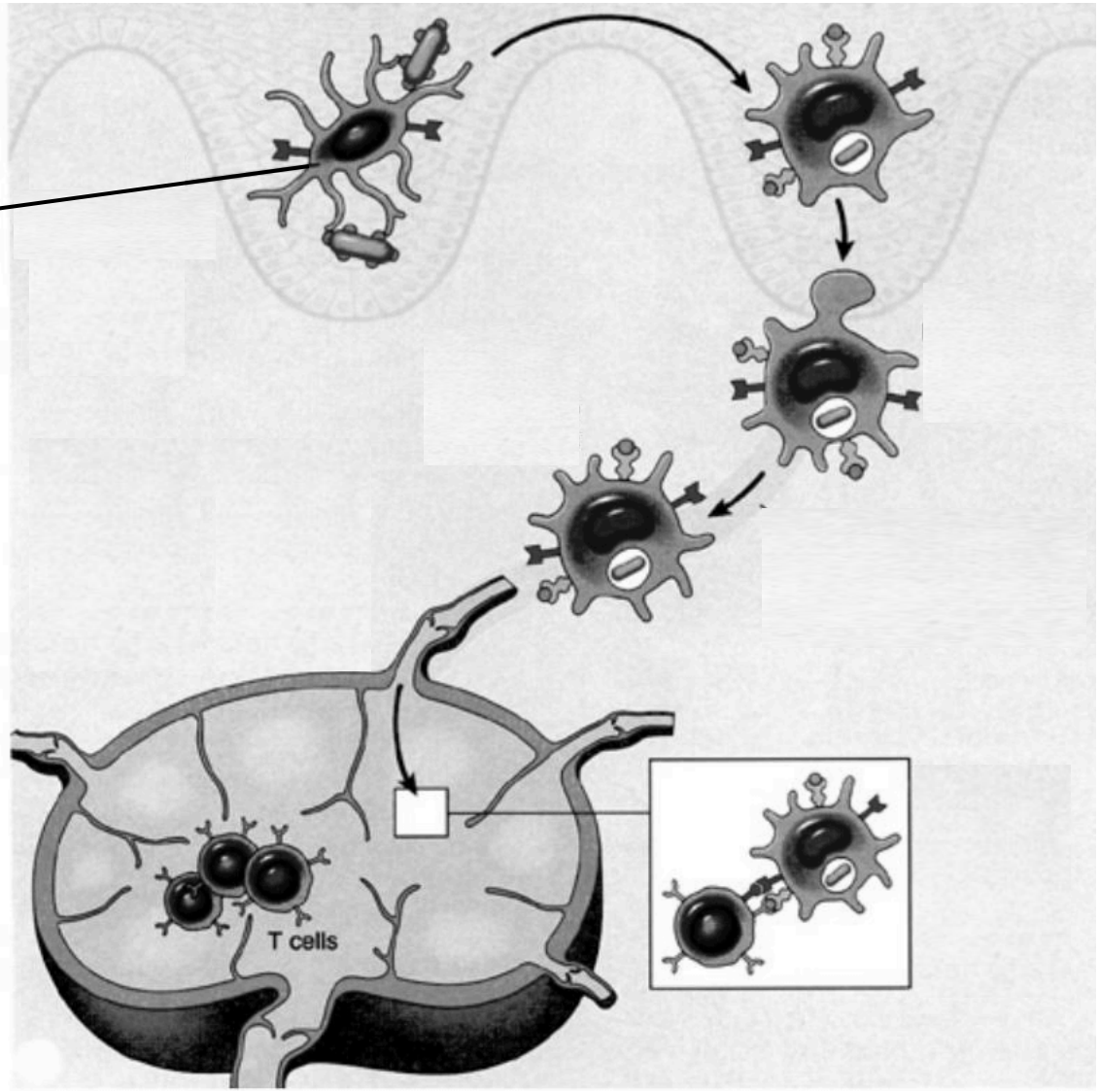
T cytotoxic cell in the middle. Kills virus-infected or tumor cells.

B cell on right. Makes antibodies that fight bacterial infections.

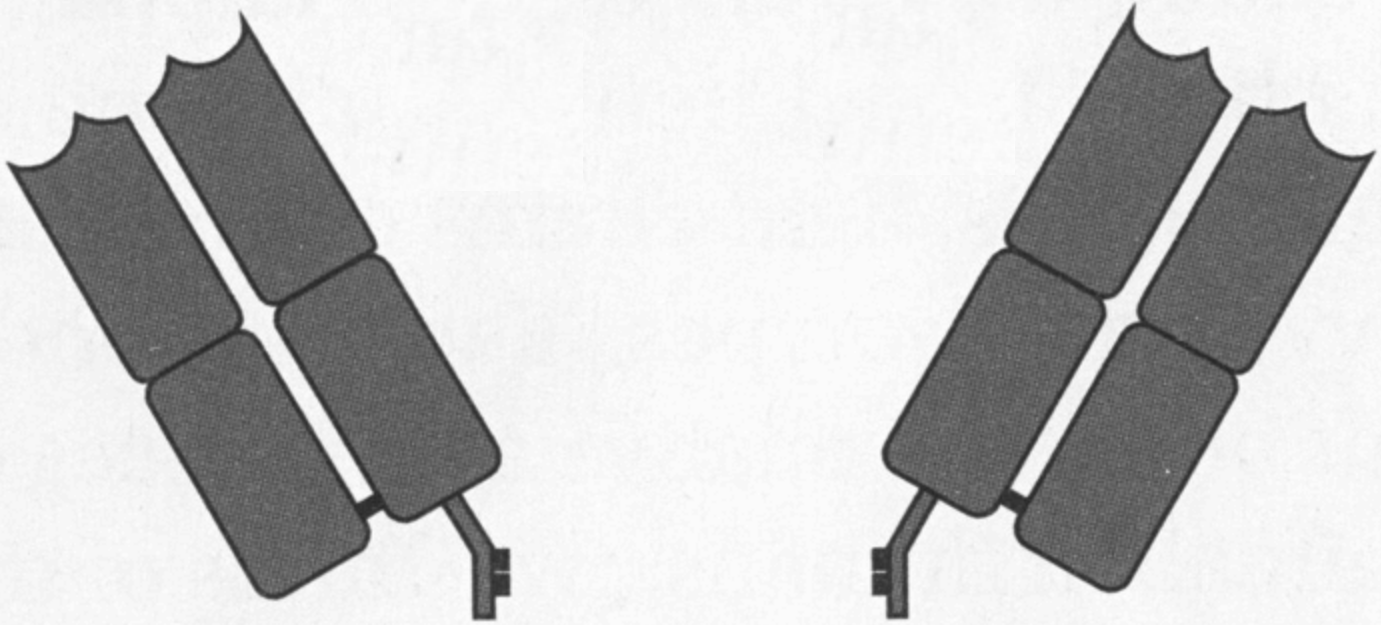
What is this cell? What does it do?



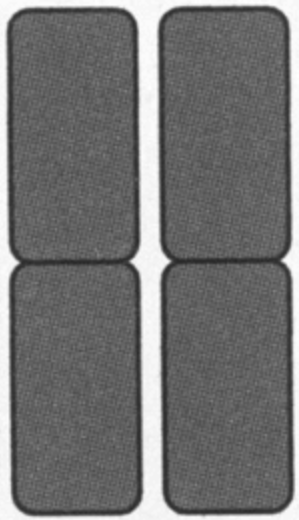
Dendritic cell. Eats bugs, carries them to lymph node and presents them to T cells.

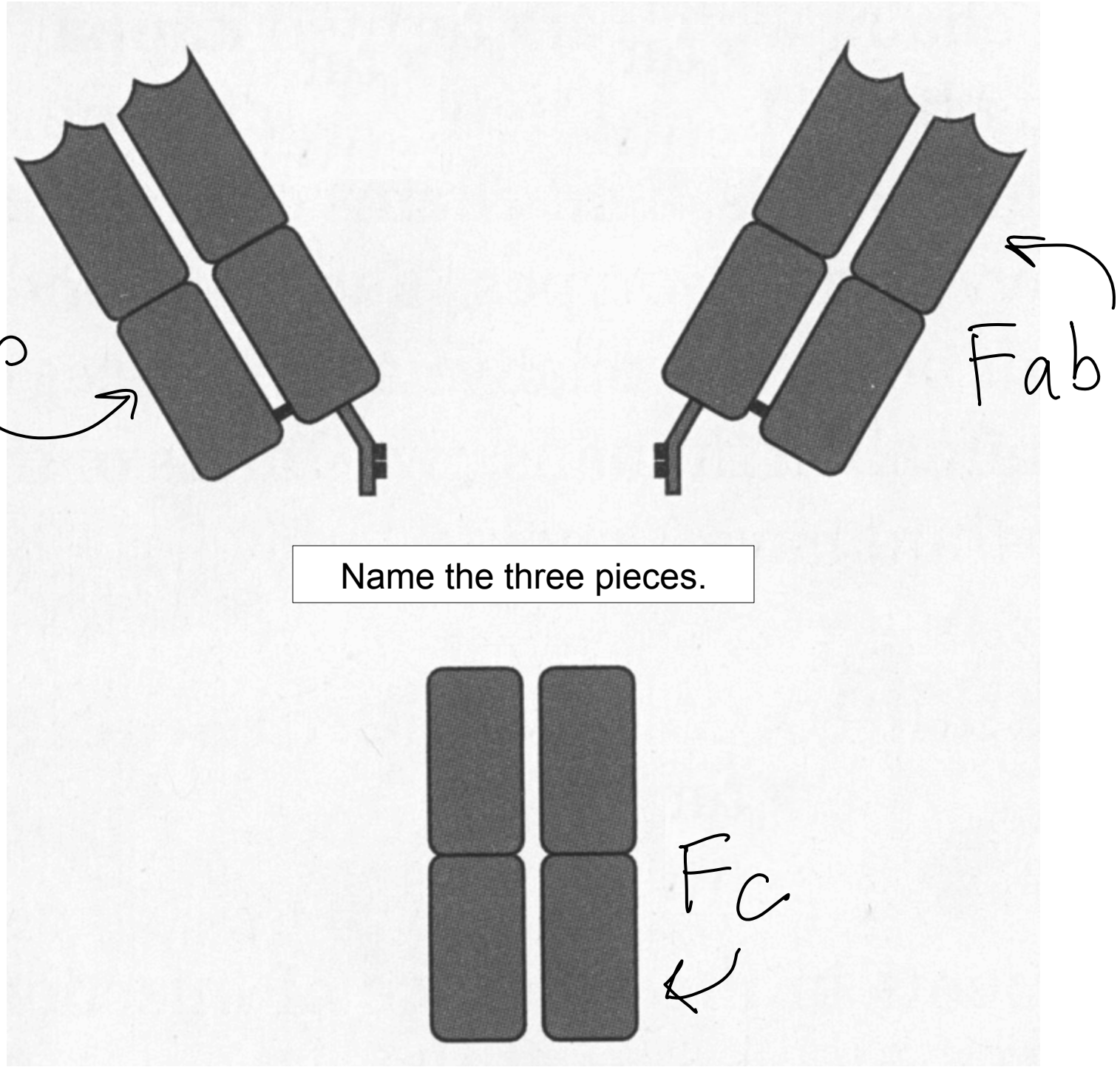


No question on this one. Just take a look at the diagram again, now that you know a bit about immunology, and see if you think it makes sense.

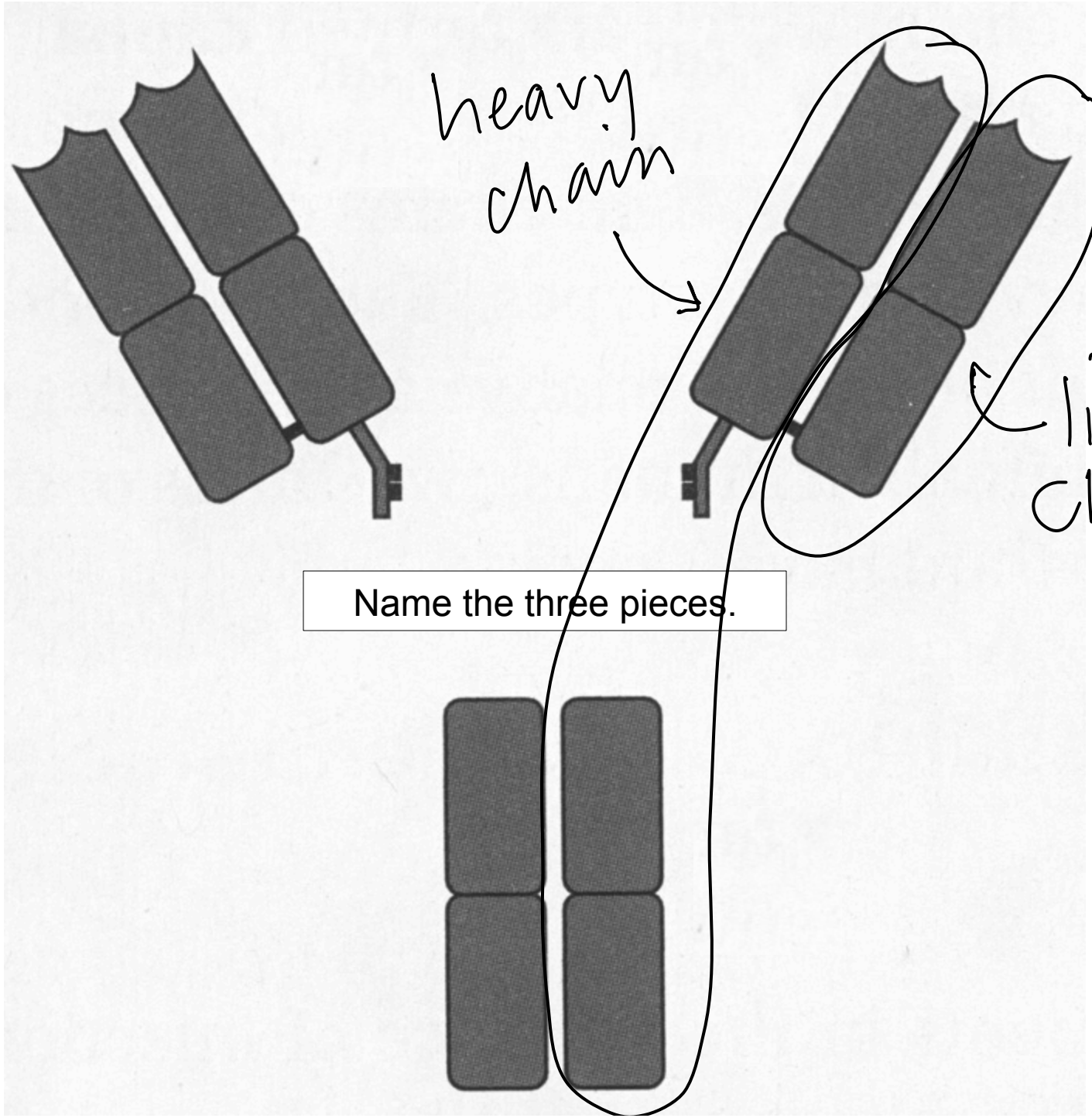


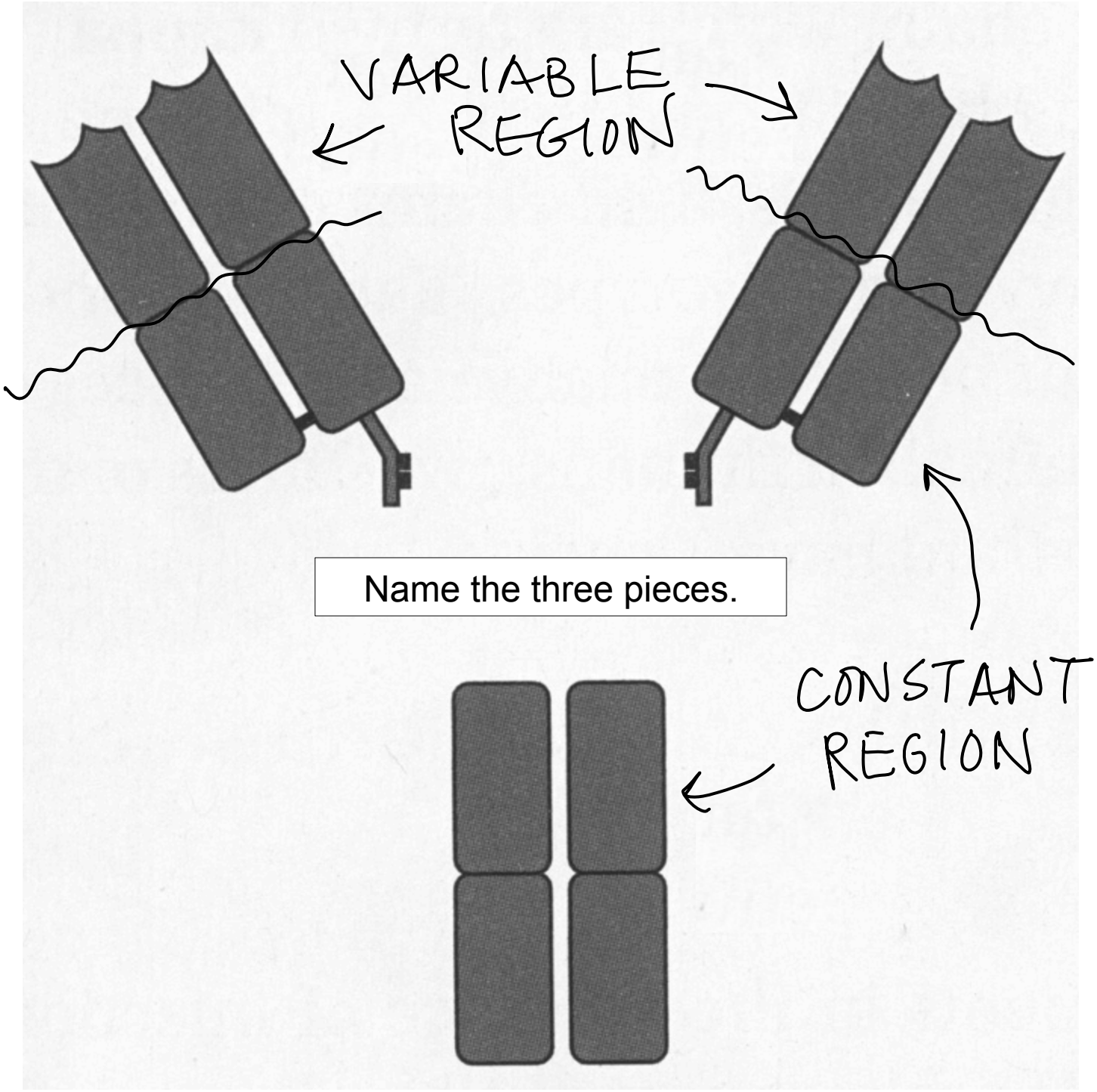
Name the three pieces.

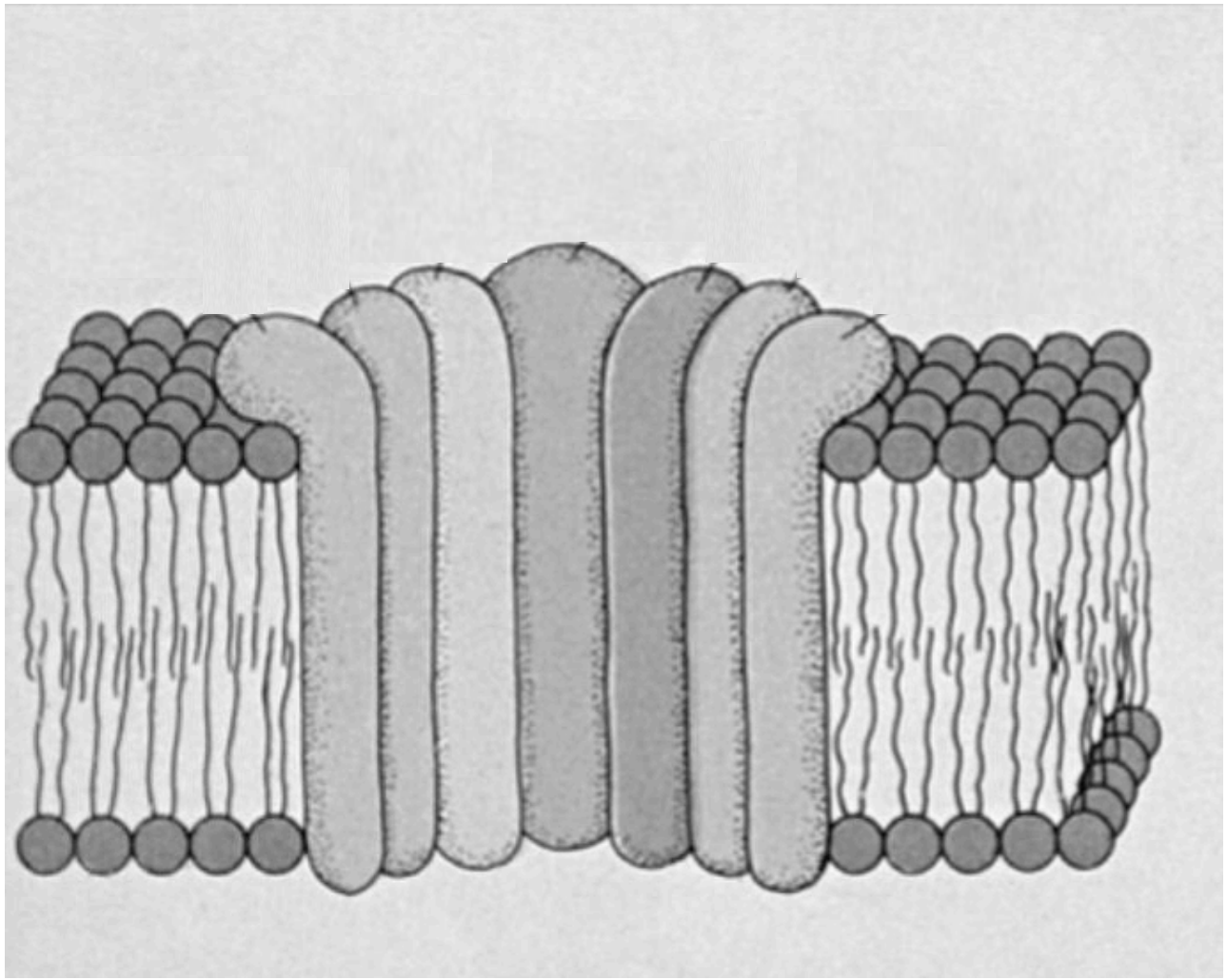




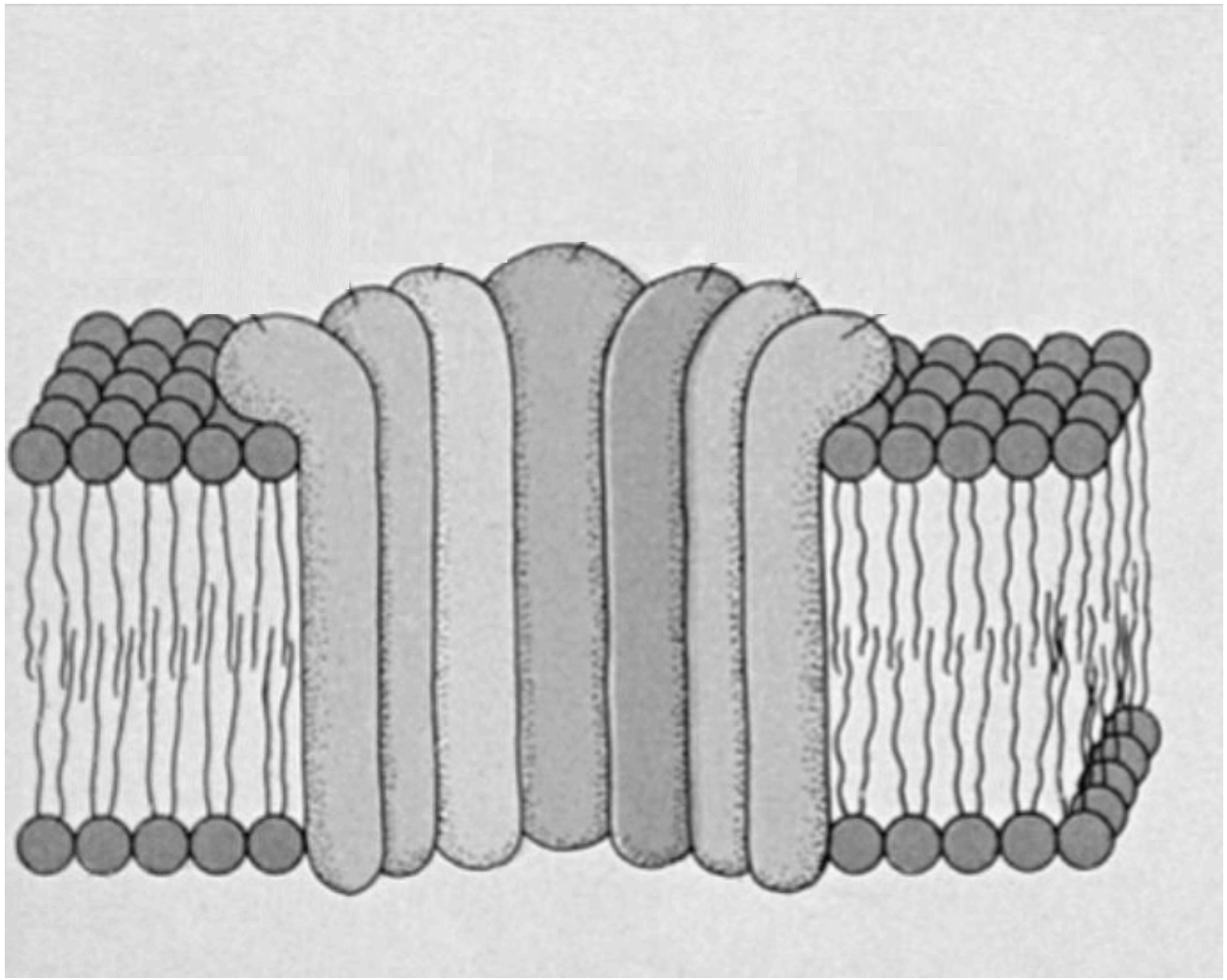
Name the three pieces.


heavy chain
light chain
Name the three pieces.


VARIABLE REGION
Name the three pieces.
CONSTANT REGION



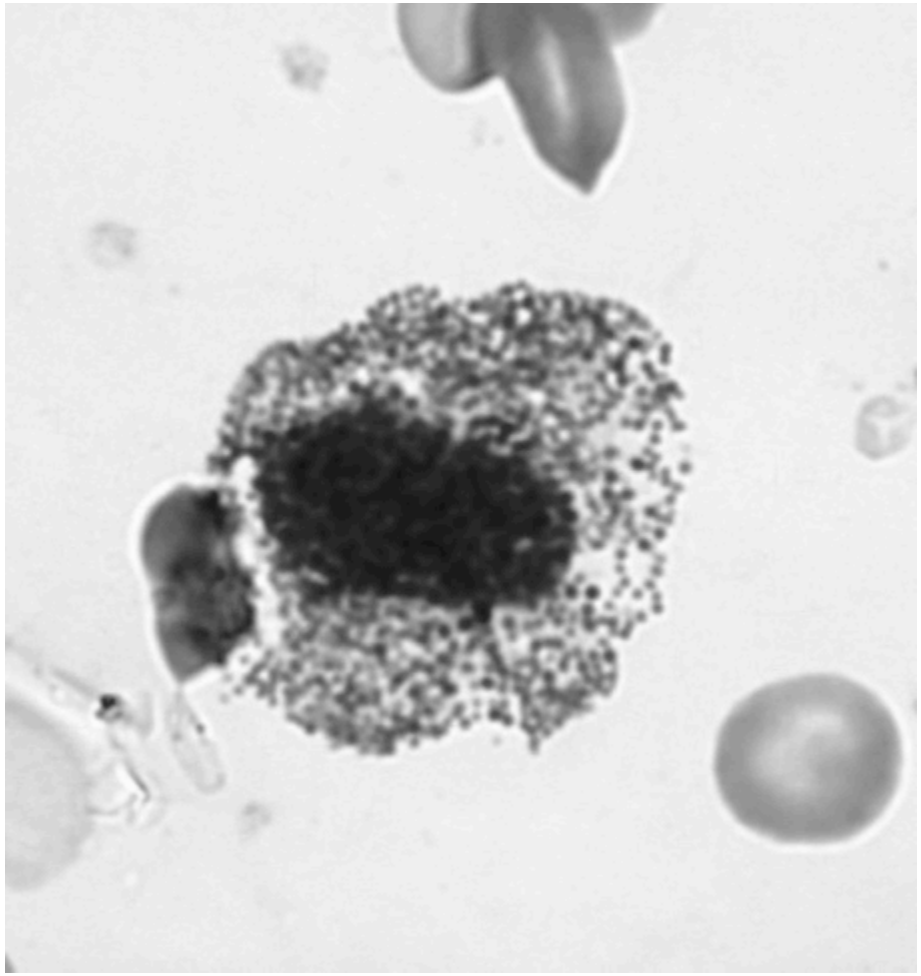
What is this group of proteins called? What are its 3 basic functions?

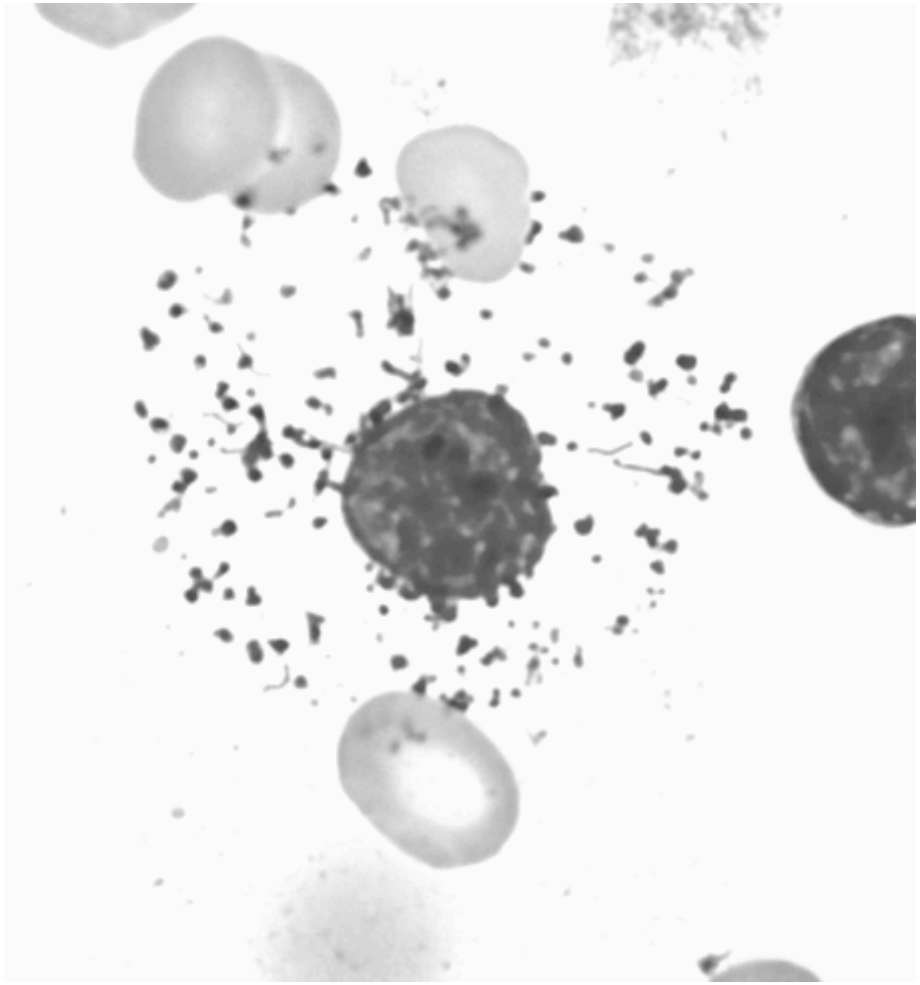


Complement. Three functions:

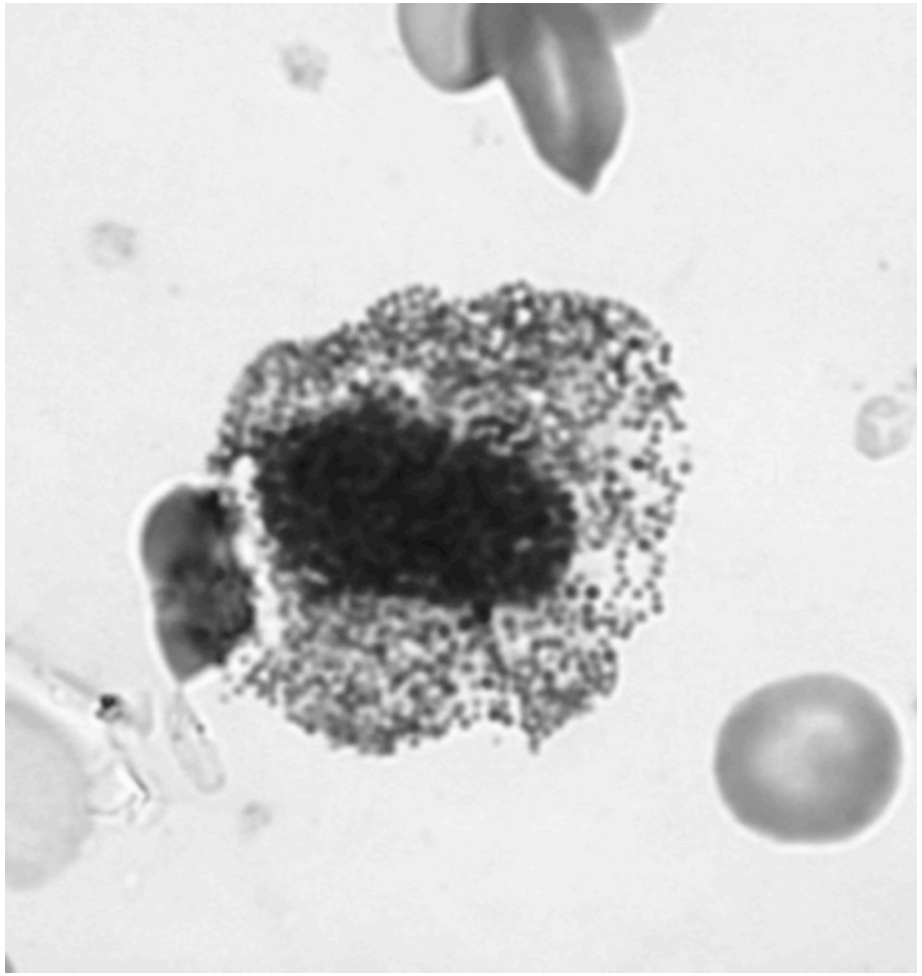
1) cell lysis (pokes holes in membranes), 2) opsonization, 3) chemotaxis

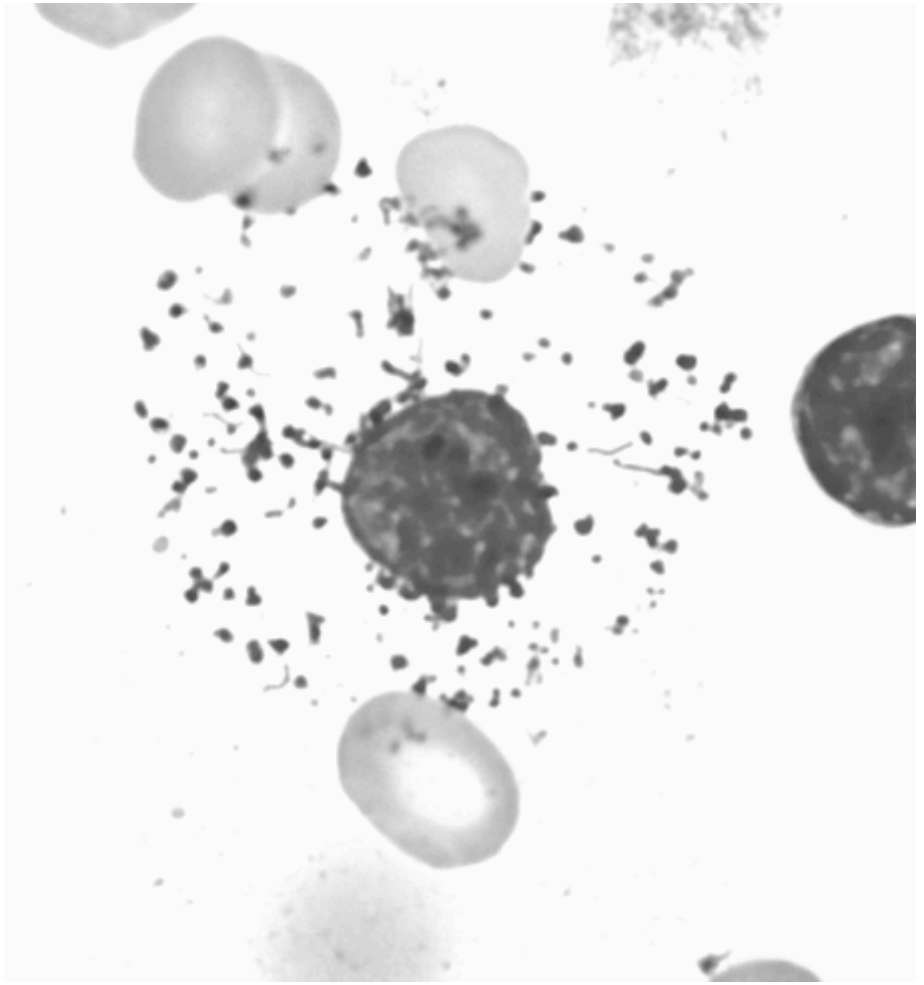
Hypersensitivity Reactions



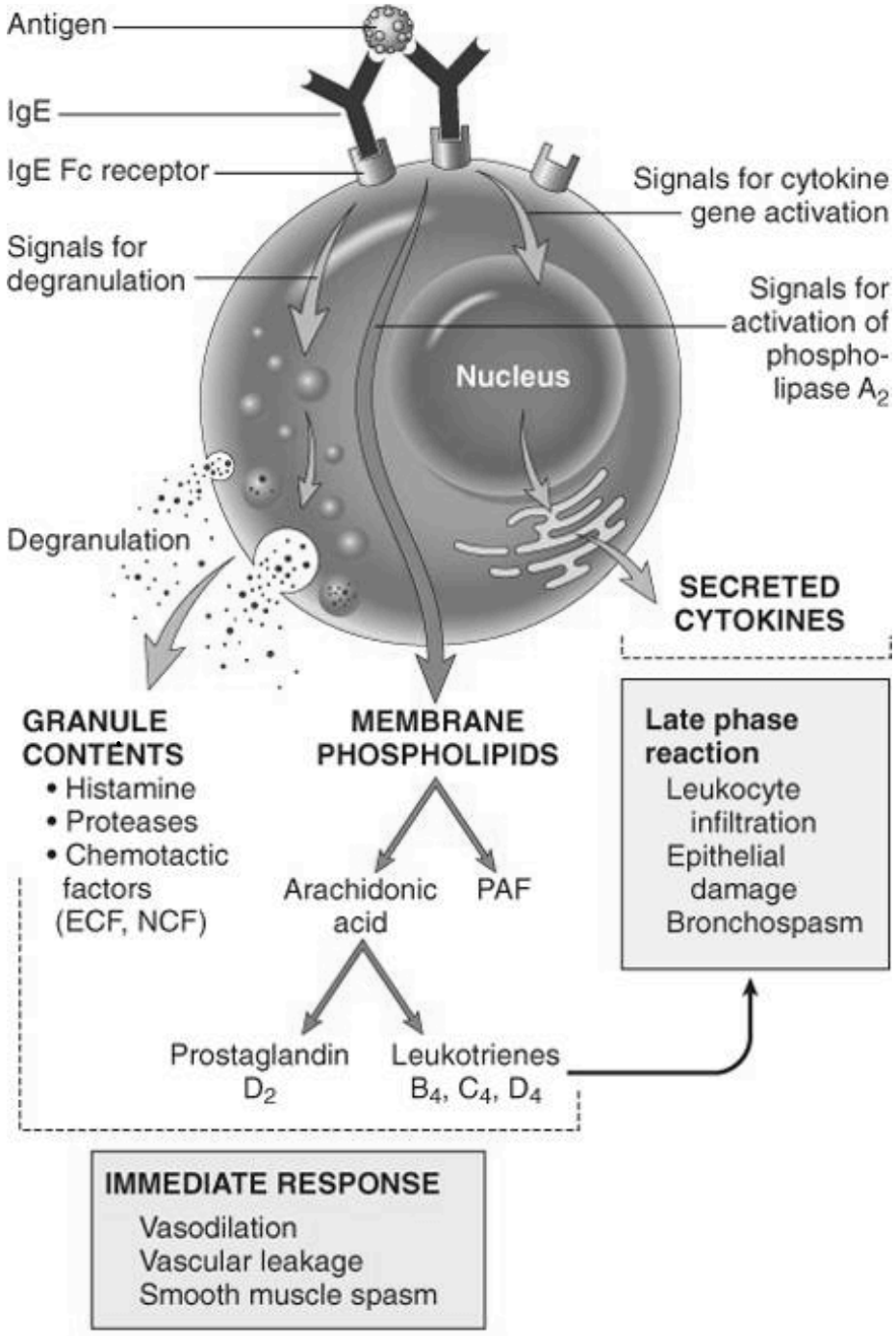


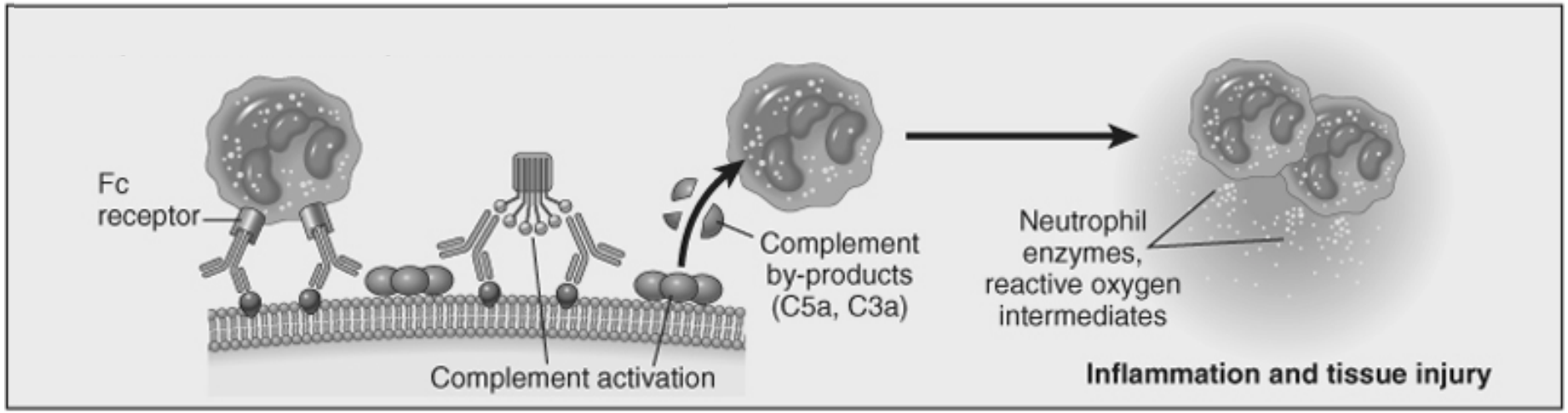
What type of cell is this? In what hypersensitivity reaction does it play a role?
What does it have on its surface, and what does it have inside?





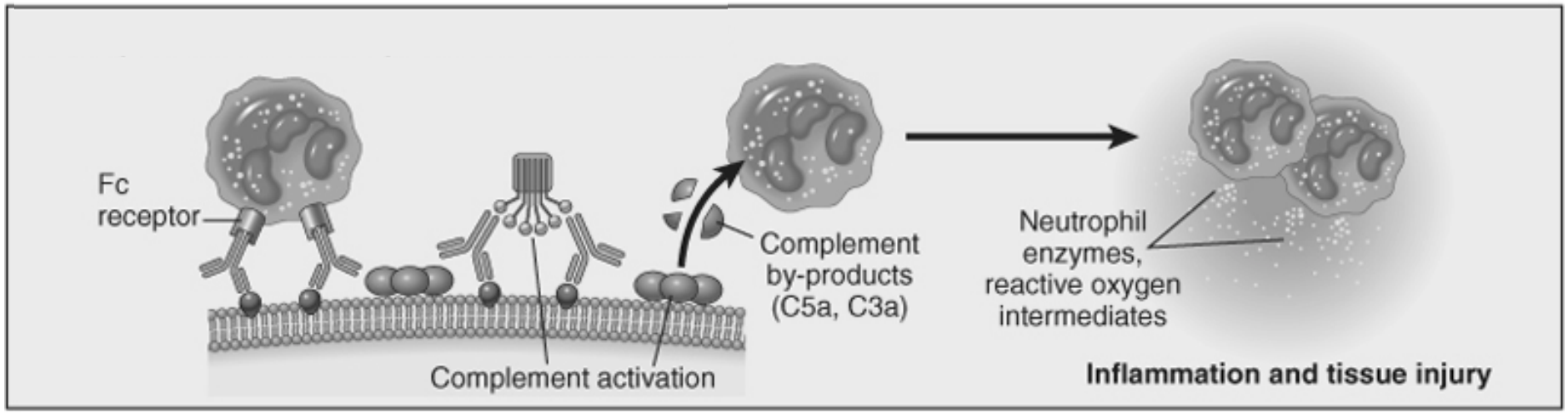
Mast cell. Type I hypersensitivity. In a type I hypersenstivity reaction, the mast cell has IgE on its surface. When an allergen comes along, it binds to the IgE, and the mast cell busts open, releasing its contents, mostly histamine.


Antigen
IgE
IgE Fc receptor
Signals for degranulation
Signals for cytokine gene activation
Signals for activation of phospho-lipase A_2
Nucleus
Degranulation
SECRETED CYTOKINES
GRANULE CONTENTS
• Histamine
• Proteases
• Chemotactic factors (ECF, NCF)
MEMBRANE PHOSPHOLIPIDS
Arachidonic acid
PAF
Prostaglandin D_2
Leukotrienes B_4, C_4, D_4
Late phase reaction
Leukocyte infiltration
Epithelial damage
Bronchospasm
IMMEDIATE RESPONSE
Vasodilation
Vascular leakage
Smooth muscle spasm



What type of hypersensitivity reaction is this?

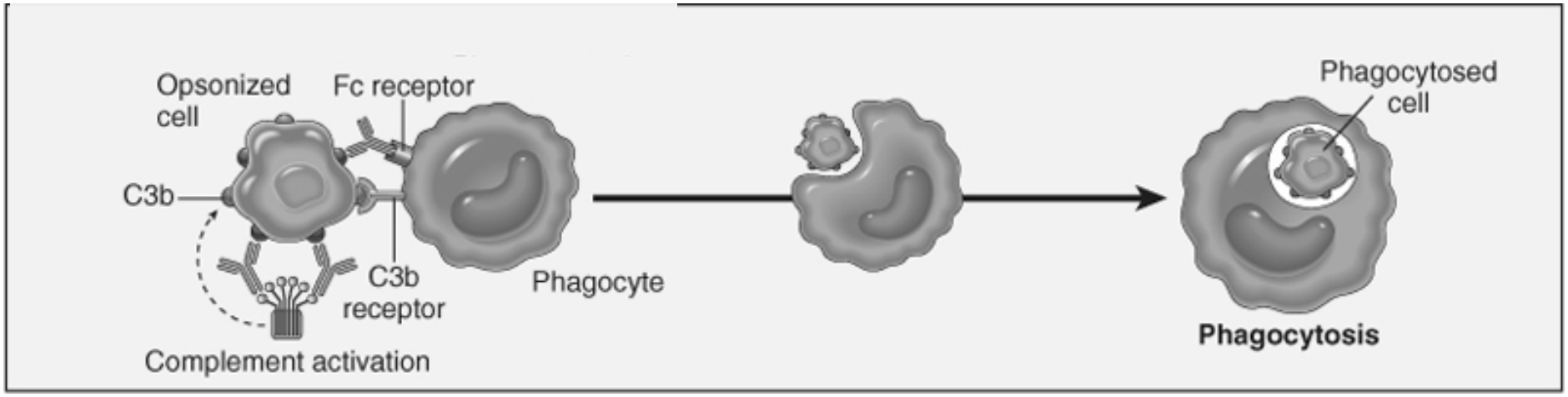
What are some examples of diseases featuring this mechanism?

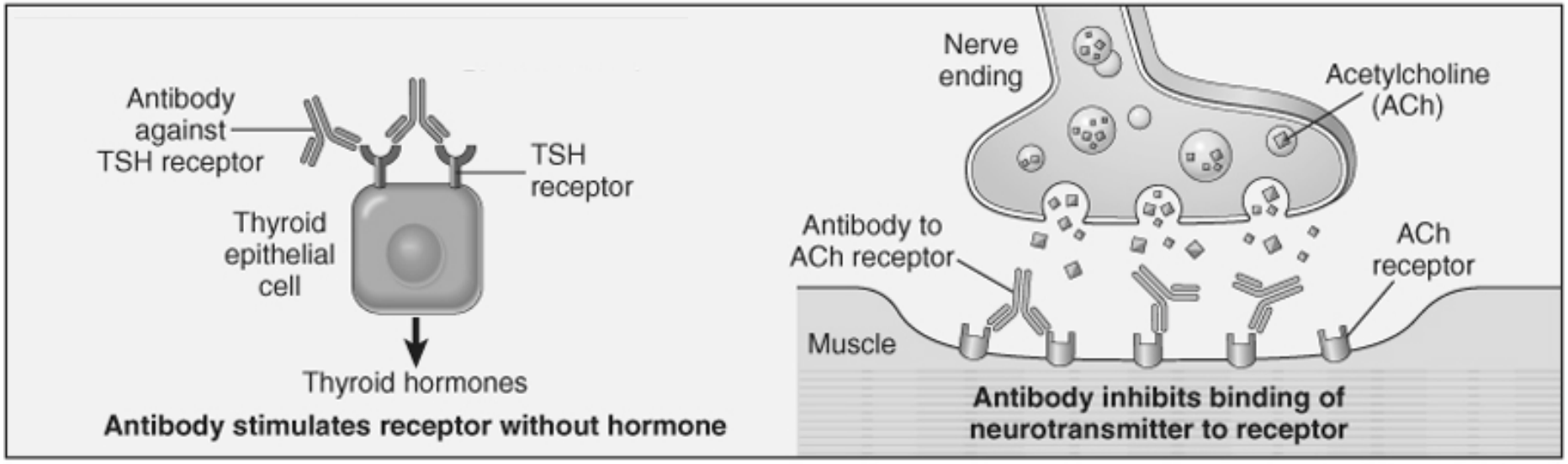


Type II hypersensitivity. Antibodies bind to fixed antigens on cell surfaces.

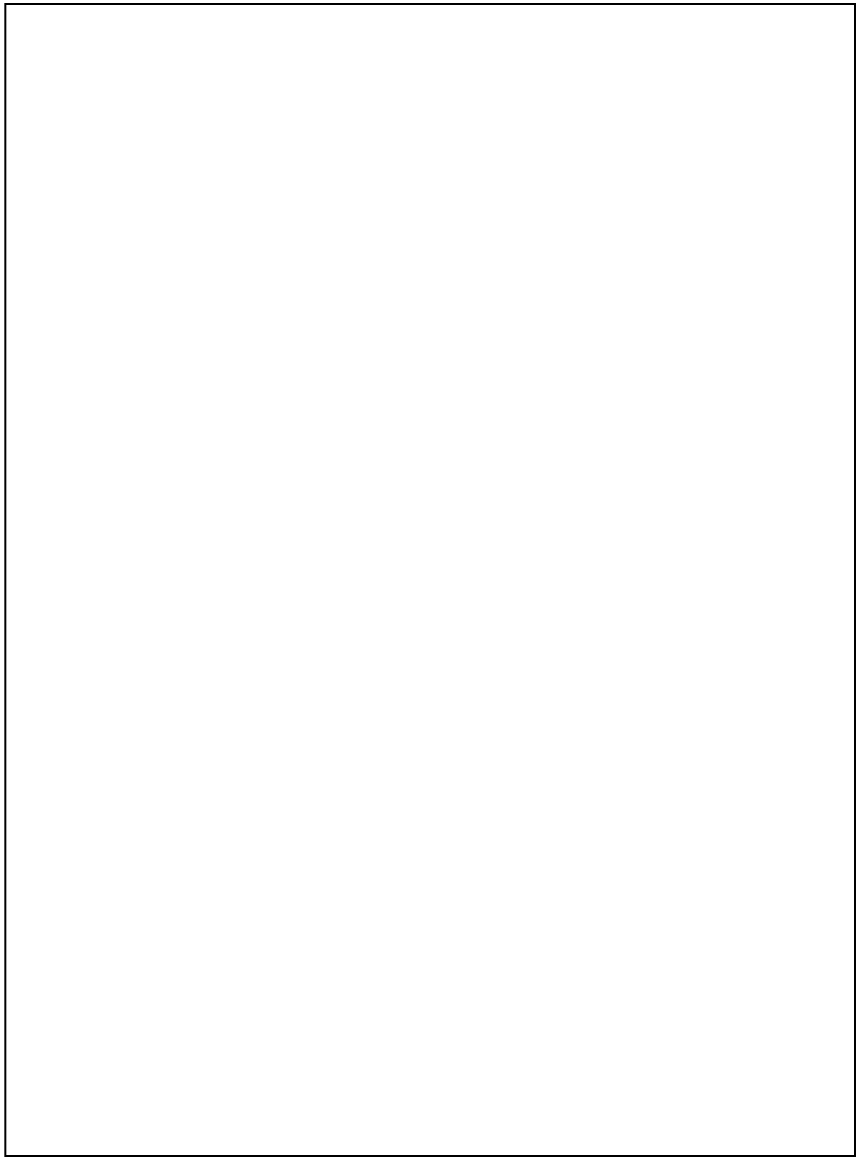
One of three things happens: 1) opsonization and phagocytosis, 2) inflammation (shown here), 3) cellular dysfunction.

Diseases that have type II hypersensitivity include autoimmune hemolytic anemia, myasthenia gravis, and Graves disease.

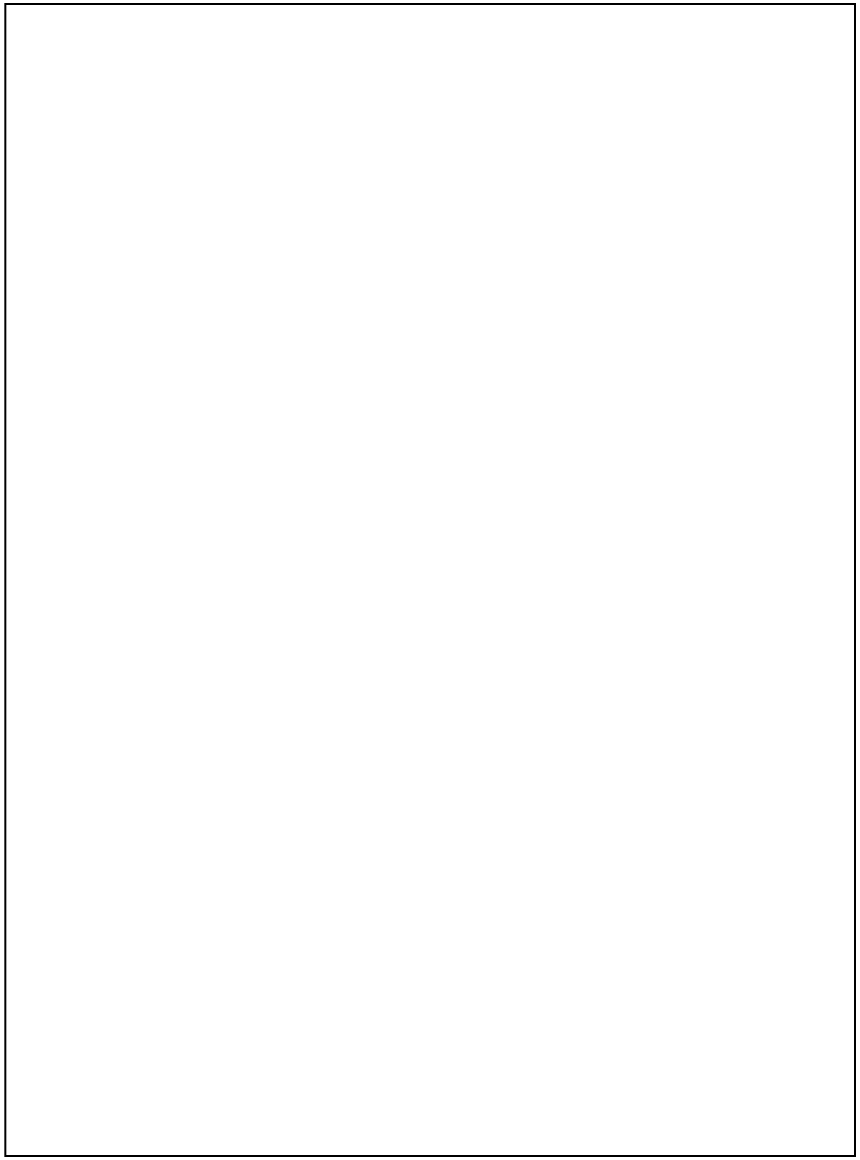




Here are the two other bad things that happen as a result of antibodies binding to cell surface antigens: opsonization and phagocytosis (top) and cellular dysfunction (bottom).

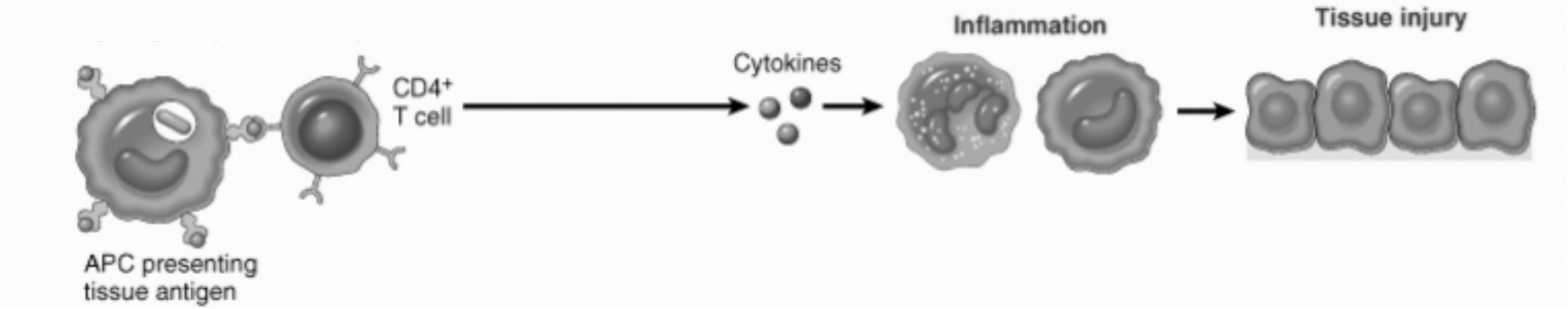


This person was frolicking in the bushes (having frolicked in same bushes months earlier). He got these lesions on his hands, and perhaps elsewhere.
What type of hypersensitivity reaction does this represent?



Type IV hypersensitivity. Specifically, delayed-type type IV.♪

Delayed-Type Hypersensitivity (DTH)



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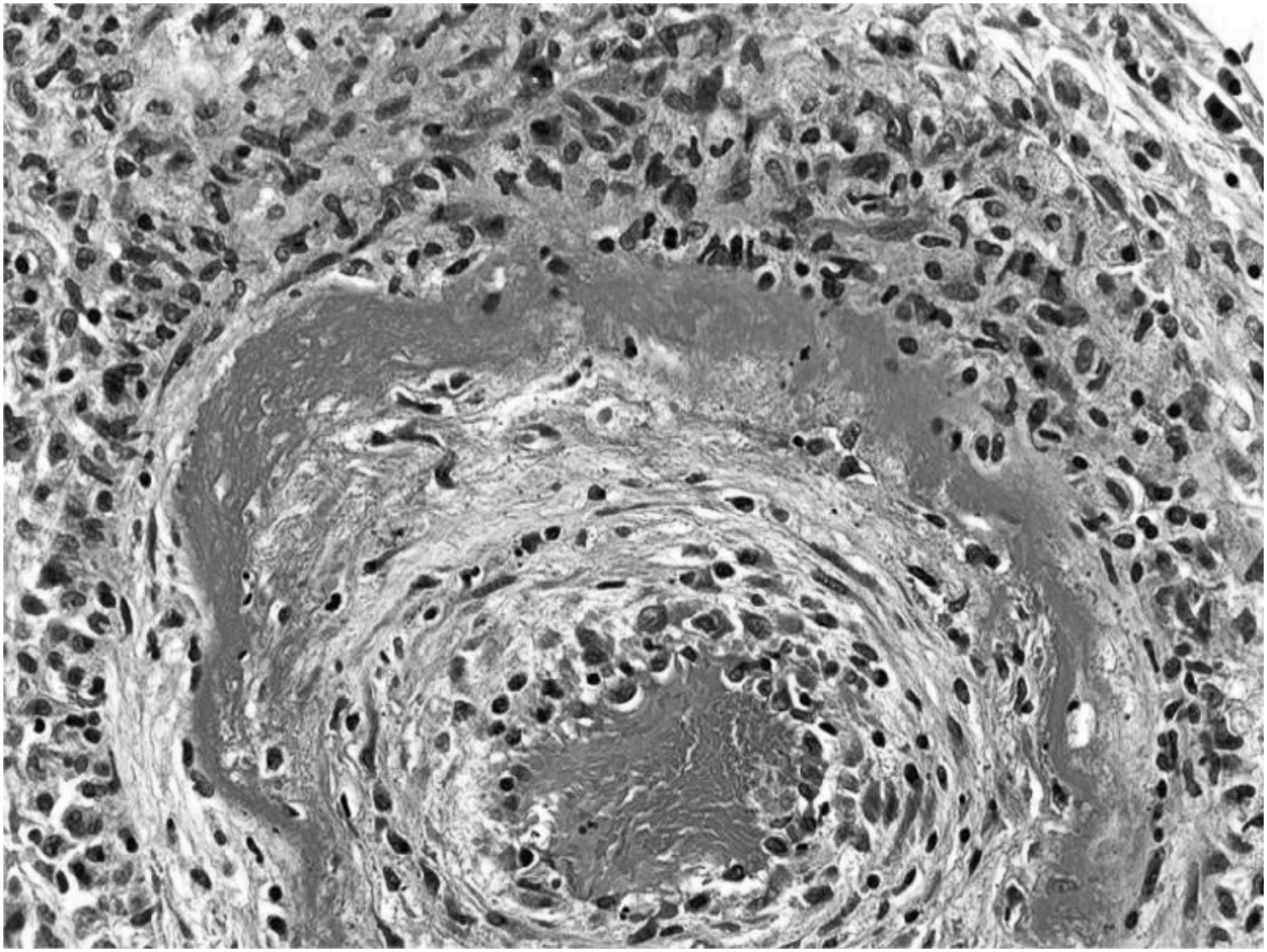
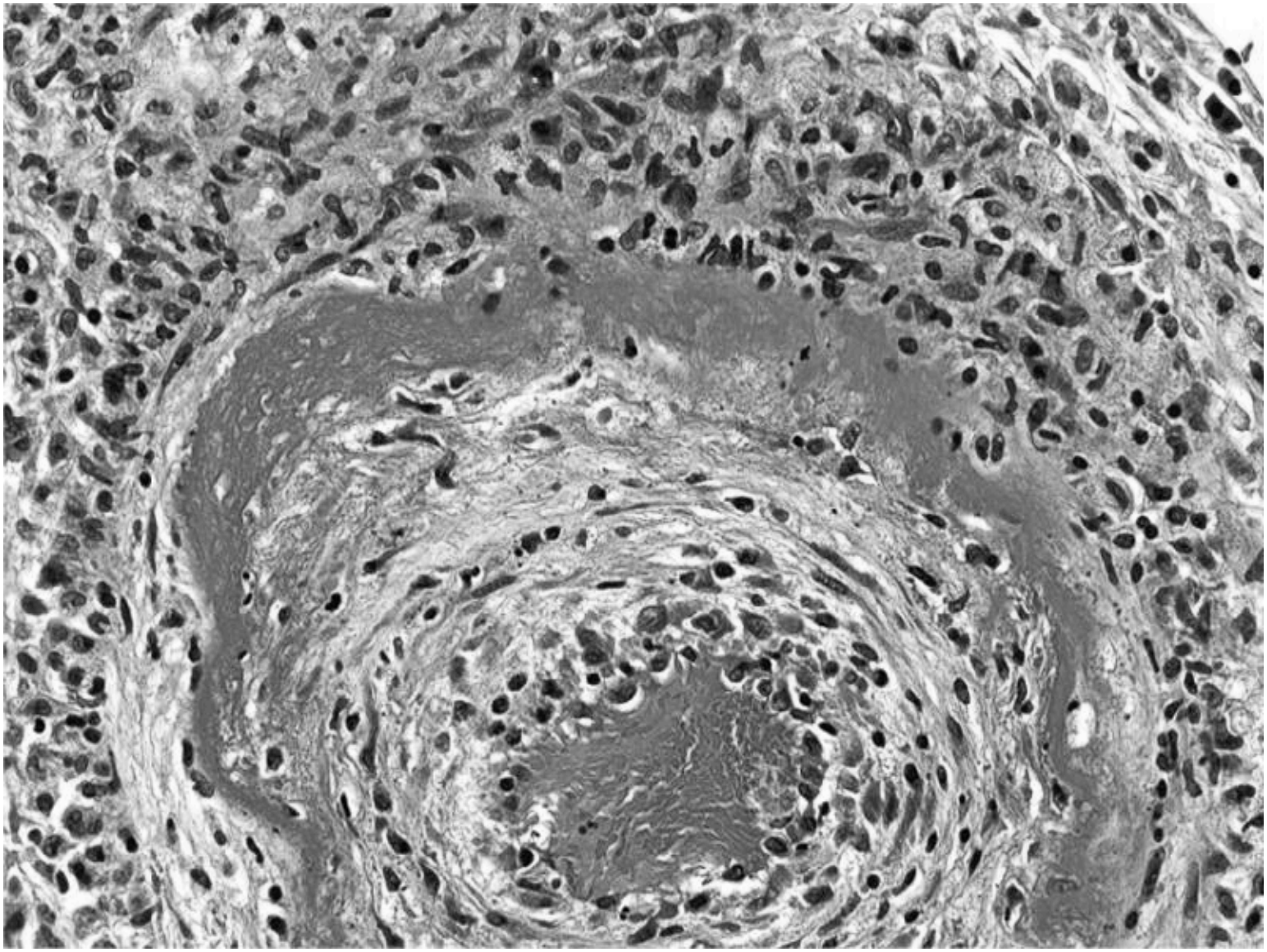
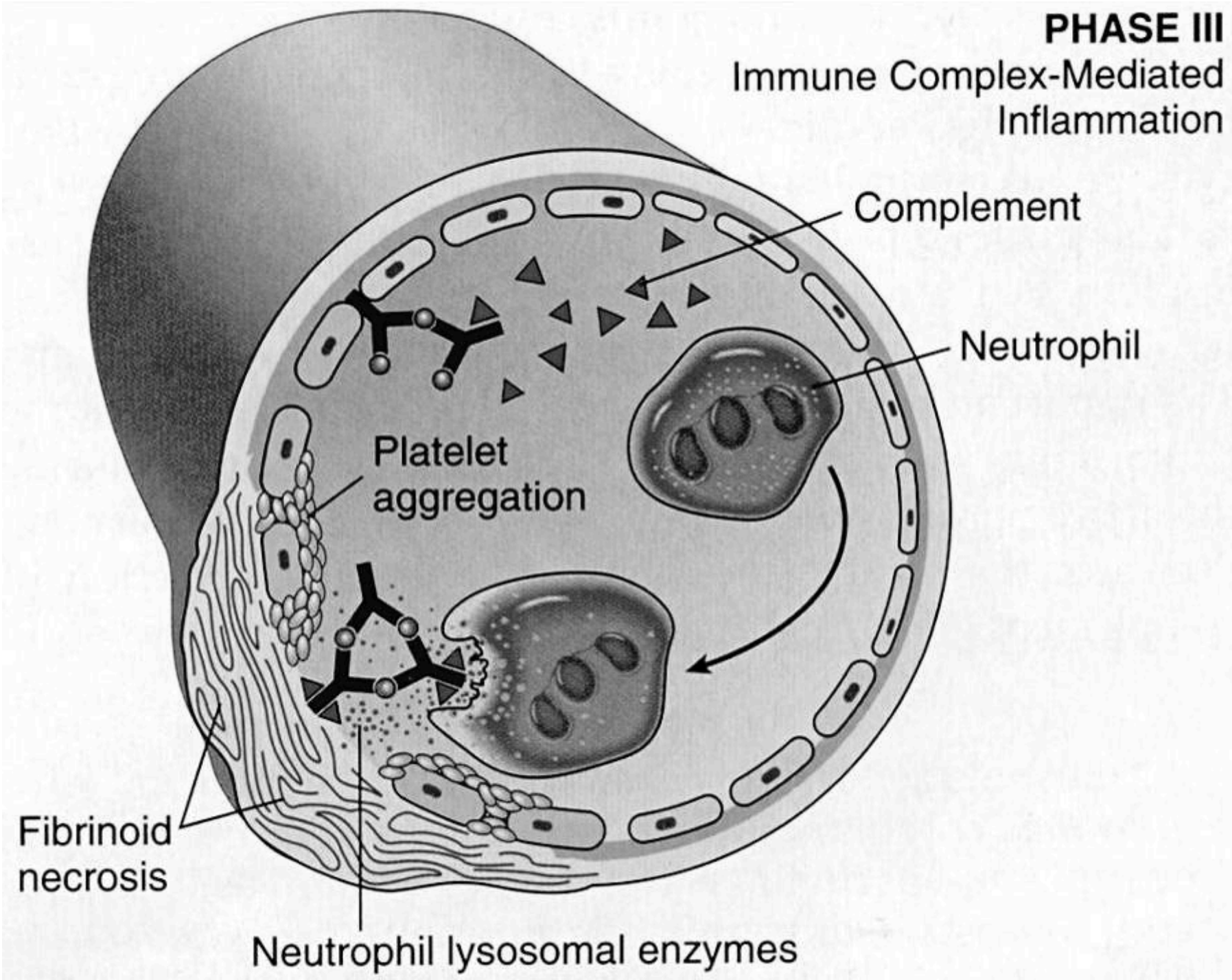


What is the pink stuff in this vessel wall called?
What kind of hypersensitivity reaction might be going on here?
What are a couple diseases in which vessels like this might be found?

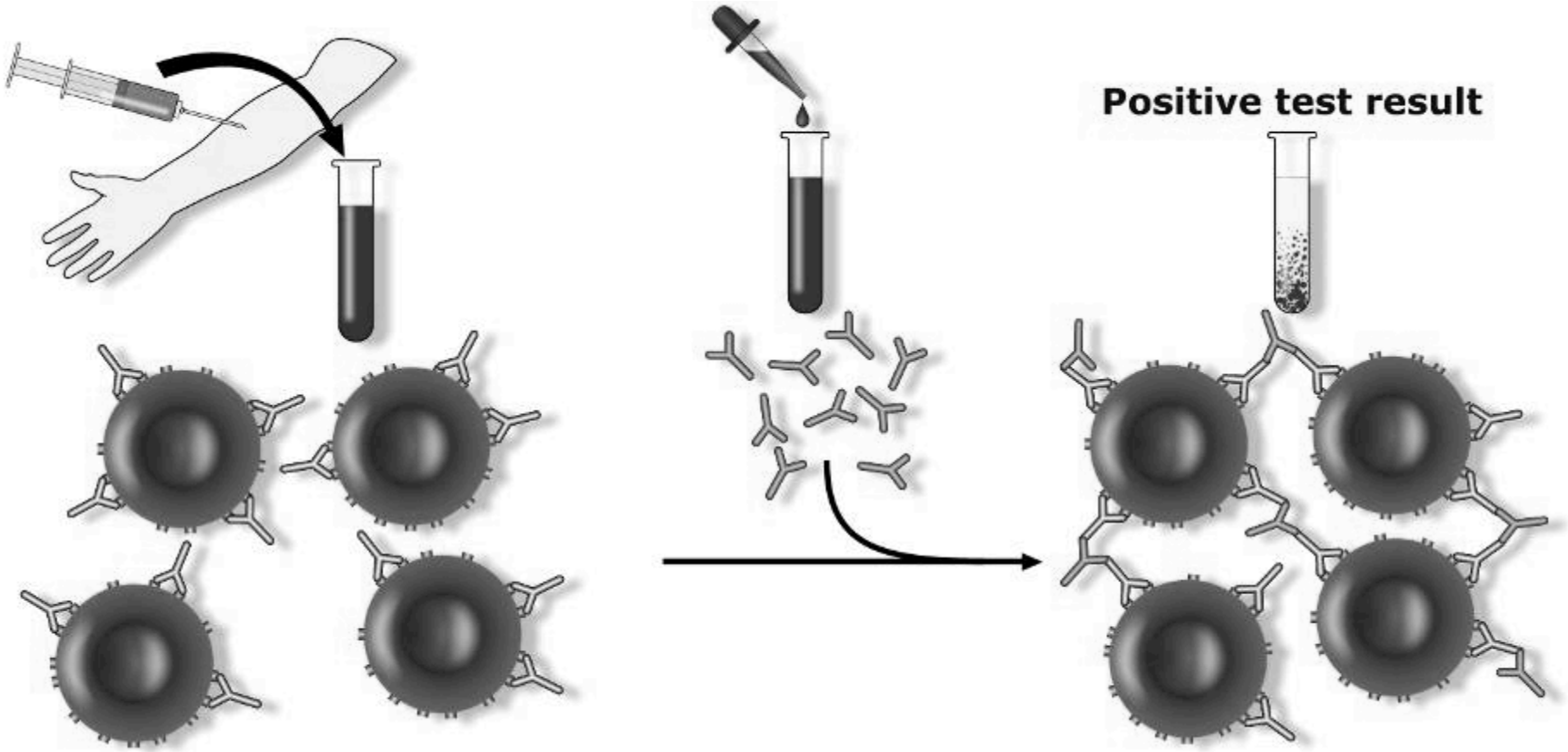


Pink stuff is fibrinoid necrosis. Type III hypersensitivity reaction.

Diseases include lupus, serum sickness, Arthus reaction.

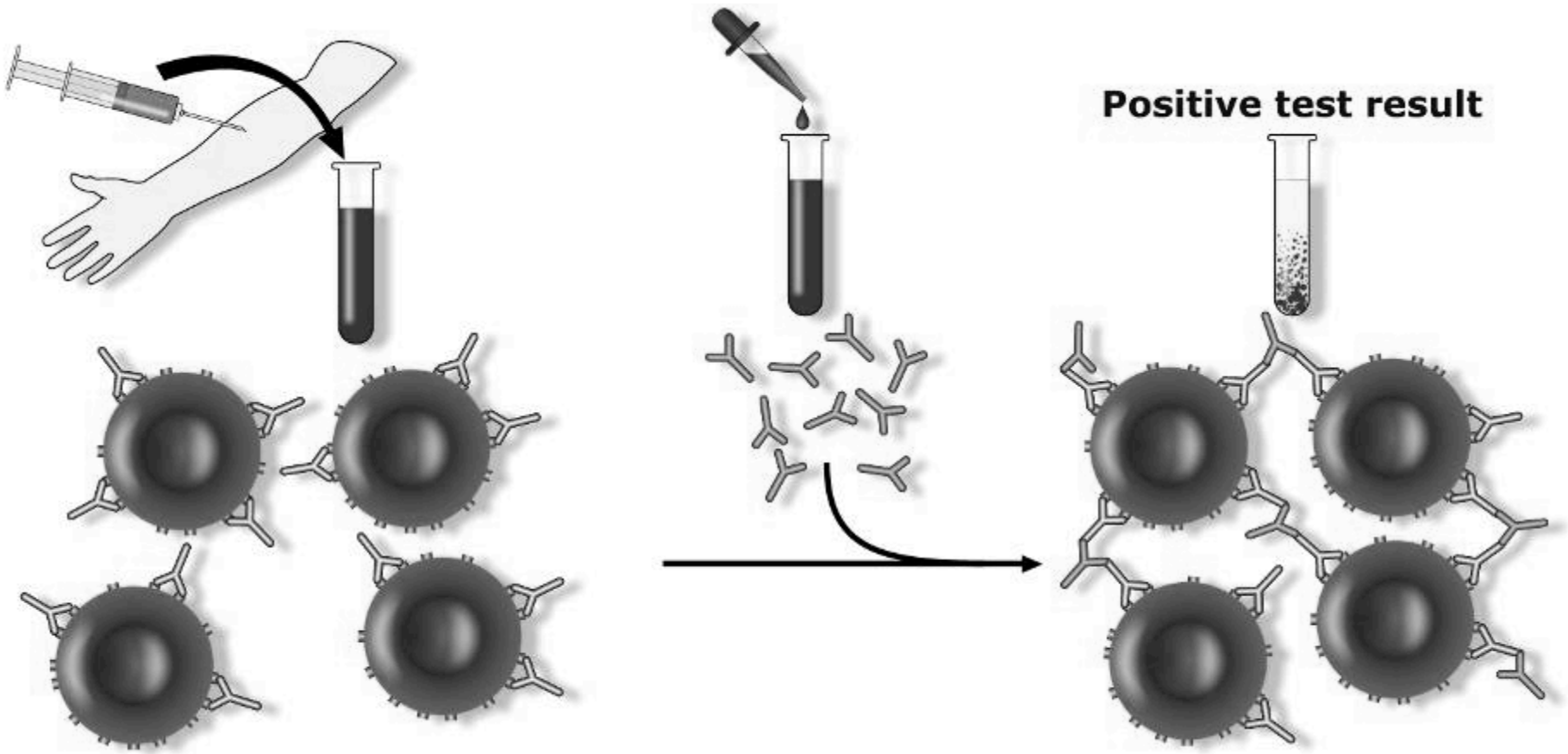

PHASE III
Immune Complex-Mediated
Inflammation
Complement
Neutrophil
Platelet
aggregation
Fibrinoid
necrosis
Neutrophil lysosomal enzymes

Immunologic Lab Tests



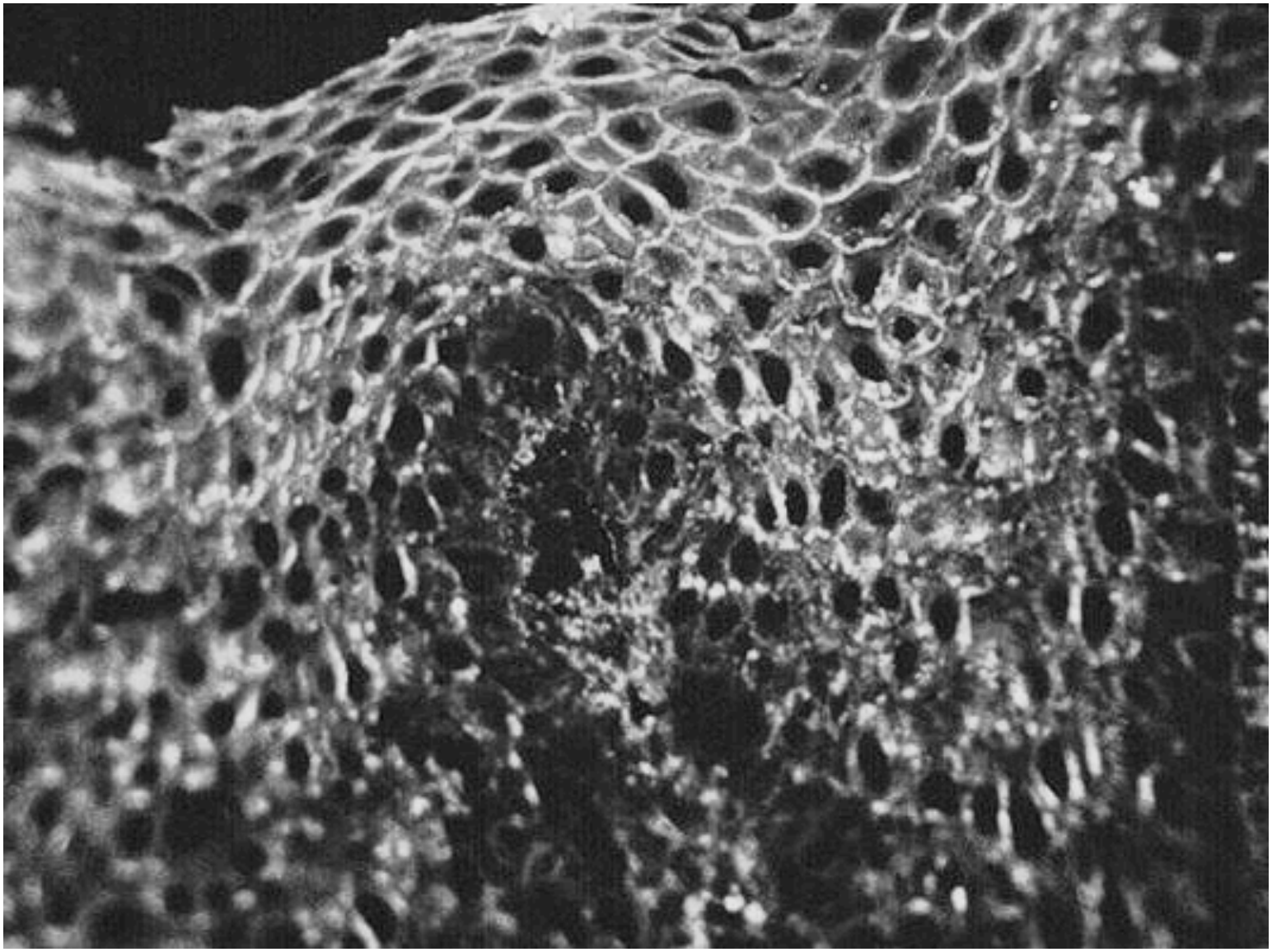
patient red cells + AHG = agglutination

This test is essential for diagnosing a particular disease. Which one?

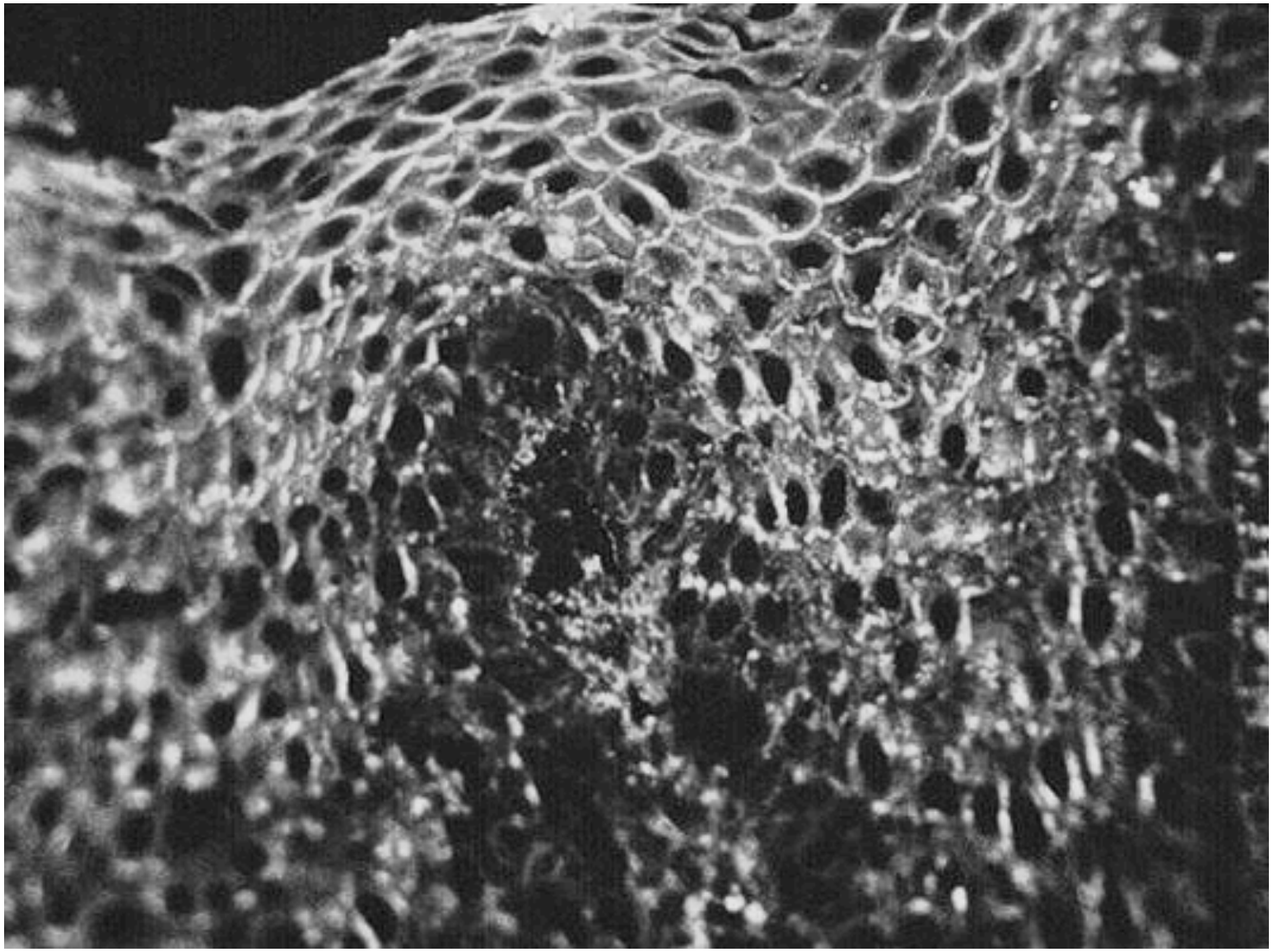


patient red cells + AHG = agglutination

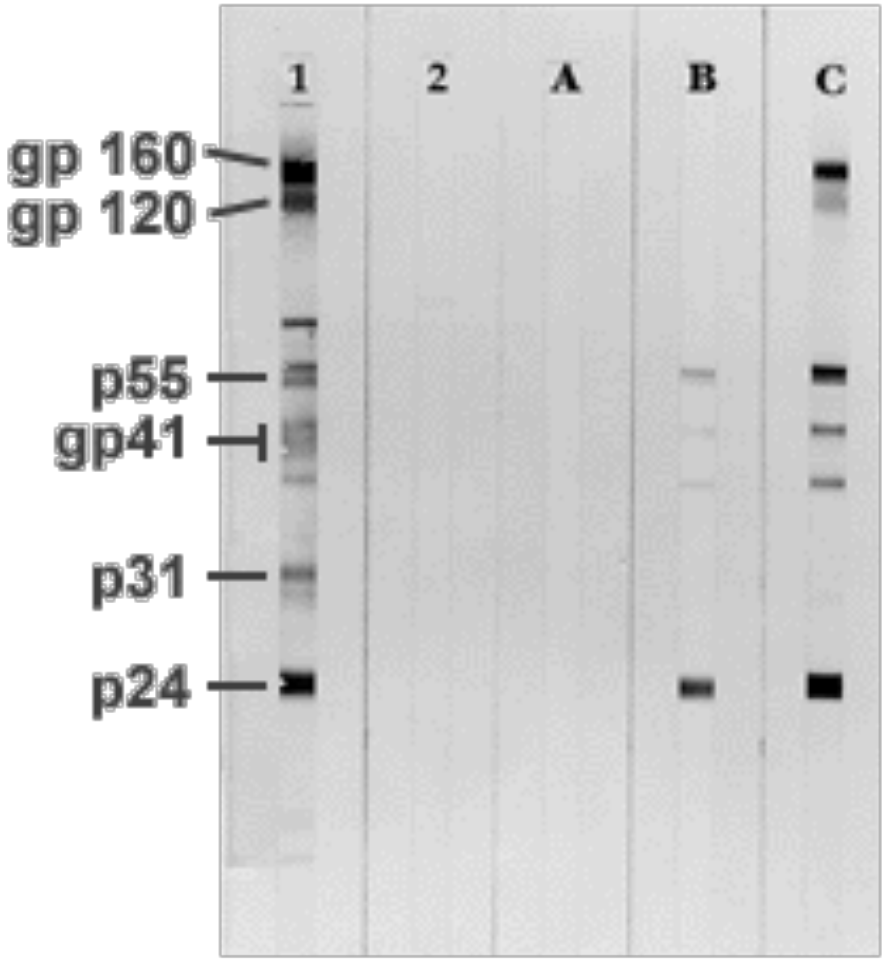
Autoimmune hemolytic anemia. The DAT (this test) tells you whether there are antibodies coating your patient's red blood cells. If there are, it means that the anemia is related to some immunologic mechanism (which is important to know for treatment). Such anemias are called "autoimmune hemolytic anemias" and we'll discuss them in the lecture on anemia.



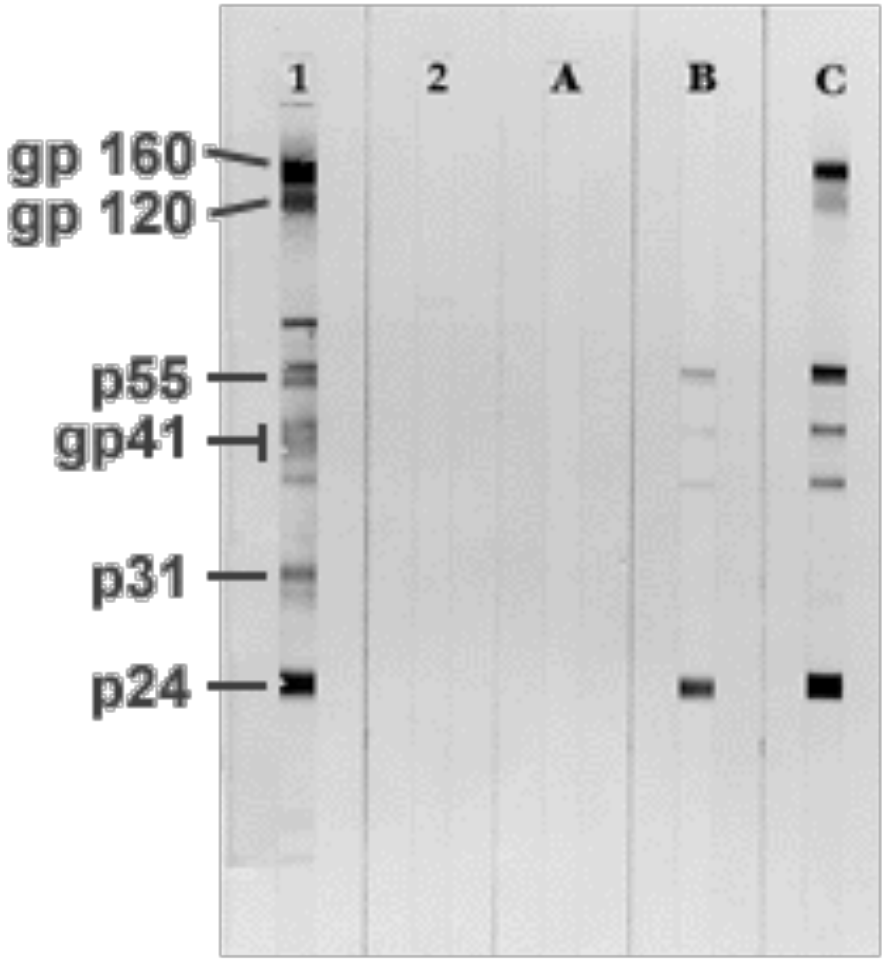
What kind of immunologic test is this?
What is lighting up in the linear spaces between the cells?



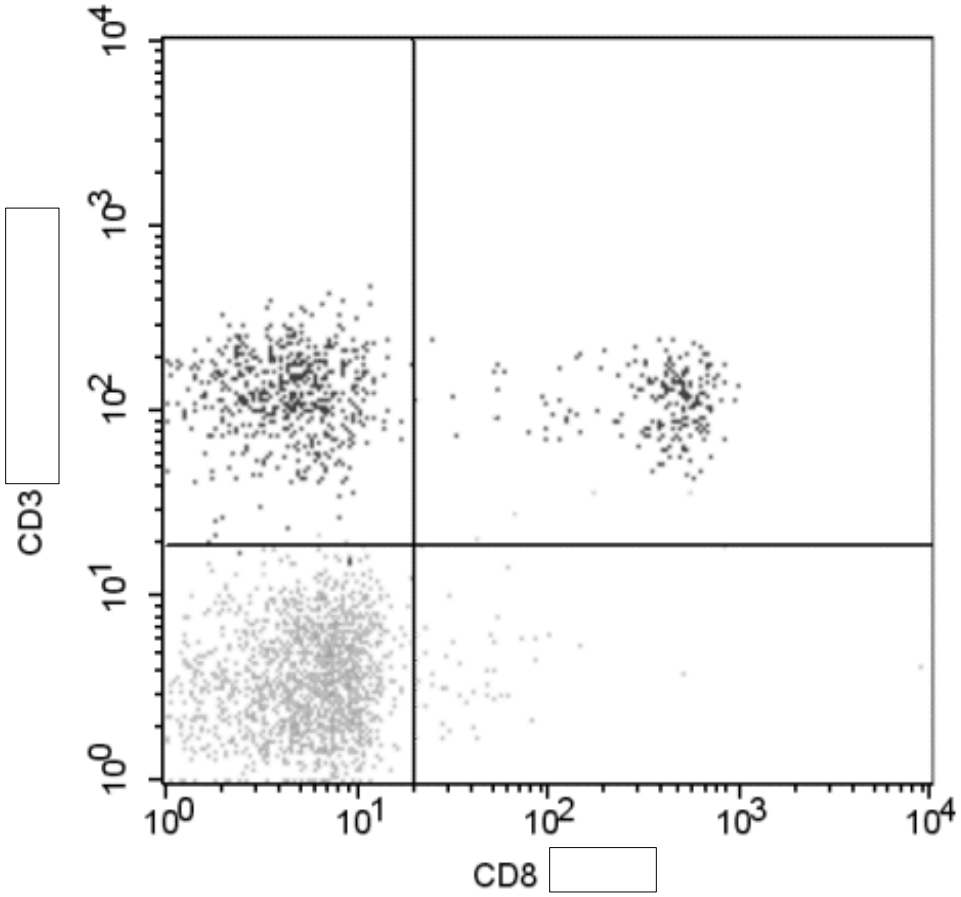
Immunofluorescence test. In this disease (pemphigus vulgaris; you'll learn about it in the lectures on skin diseases), patients make antibodies to a protein that connects squamous cells. The immunofluorescent antibodies in this test are binding to the antigen-antibody complexes sitting between the squamous cells.



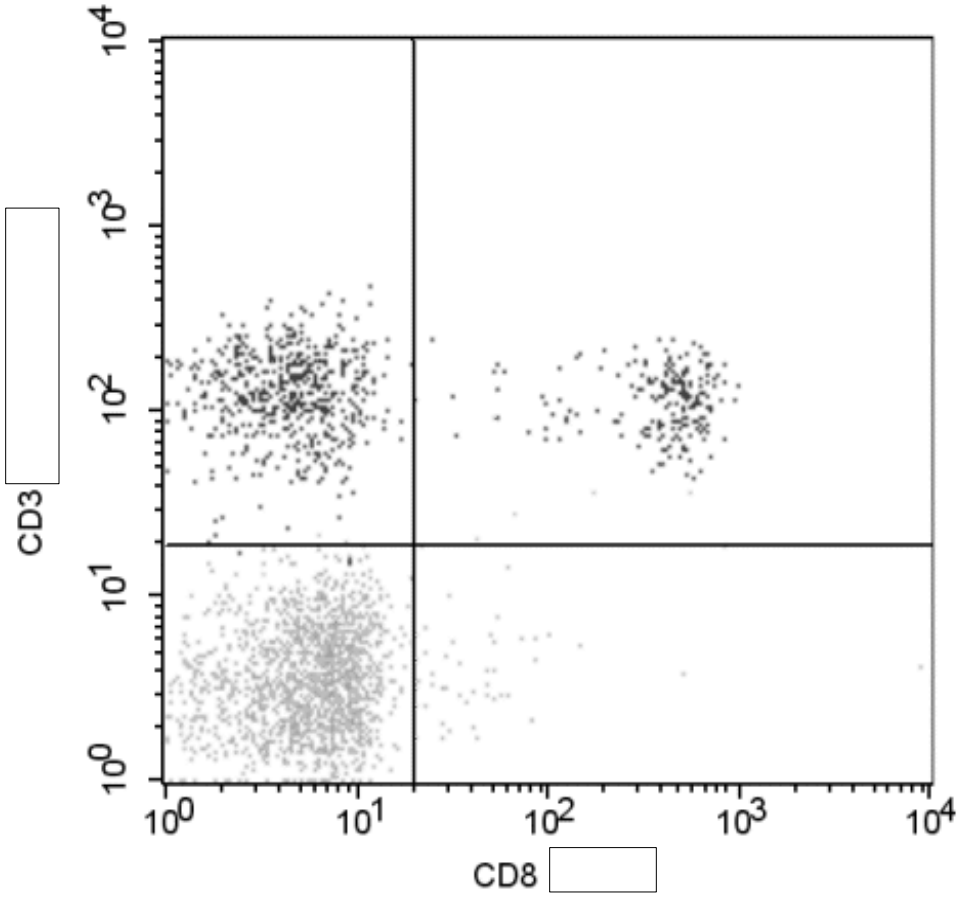
This is an electrophoresis gel, and the bands represent proteins of different charges. What kind of immunologic test is this? Name one use for this test.



Western blot. Confirmation of a positive HIV screening test.

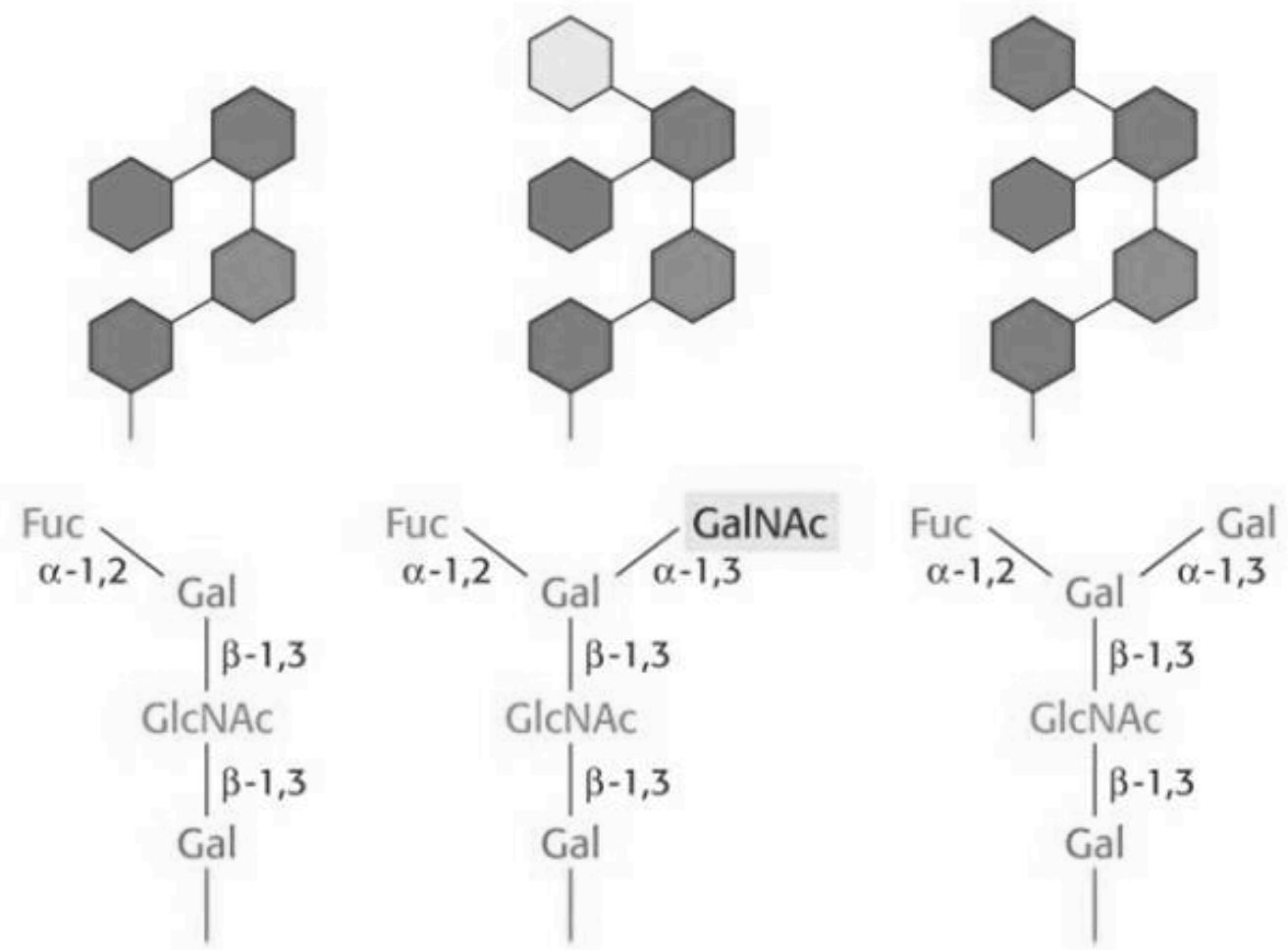


What kind of immunologic test gives you this kind of data?
Which color of dots represents cytotoxic T cells?

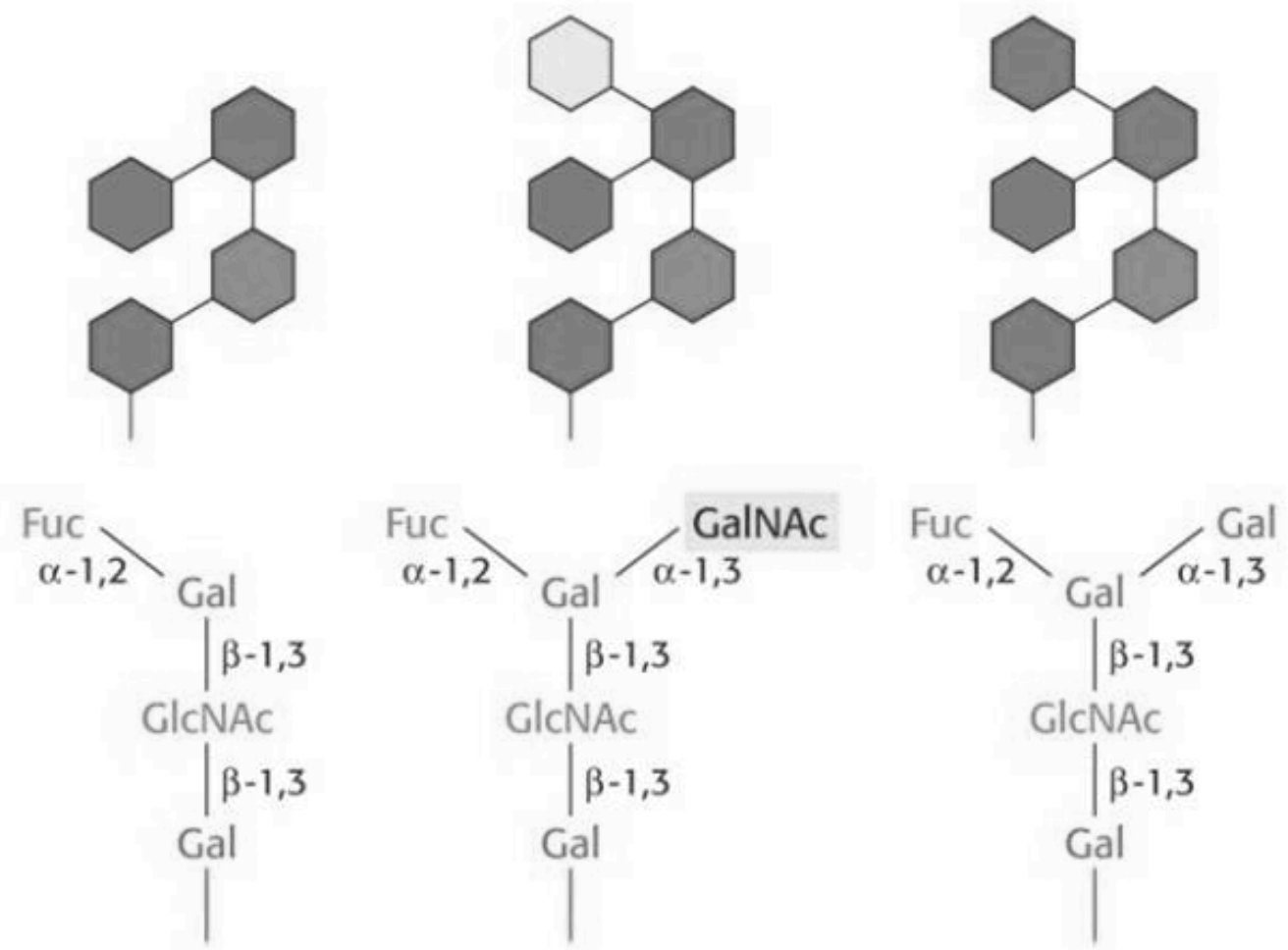


Flow cytometry. The purple dots represent cytotoxic T cells because they are CD3 positive (CD3 is a pan-T-cell marker – it's present on all T cells) and CD8 positive.

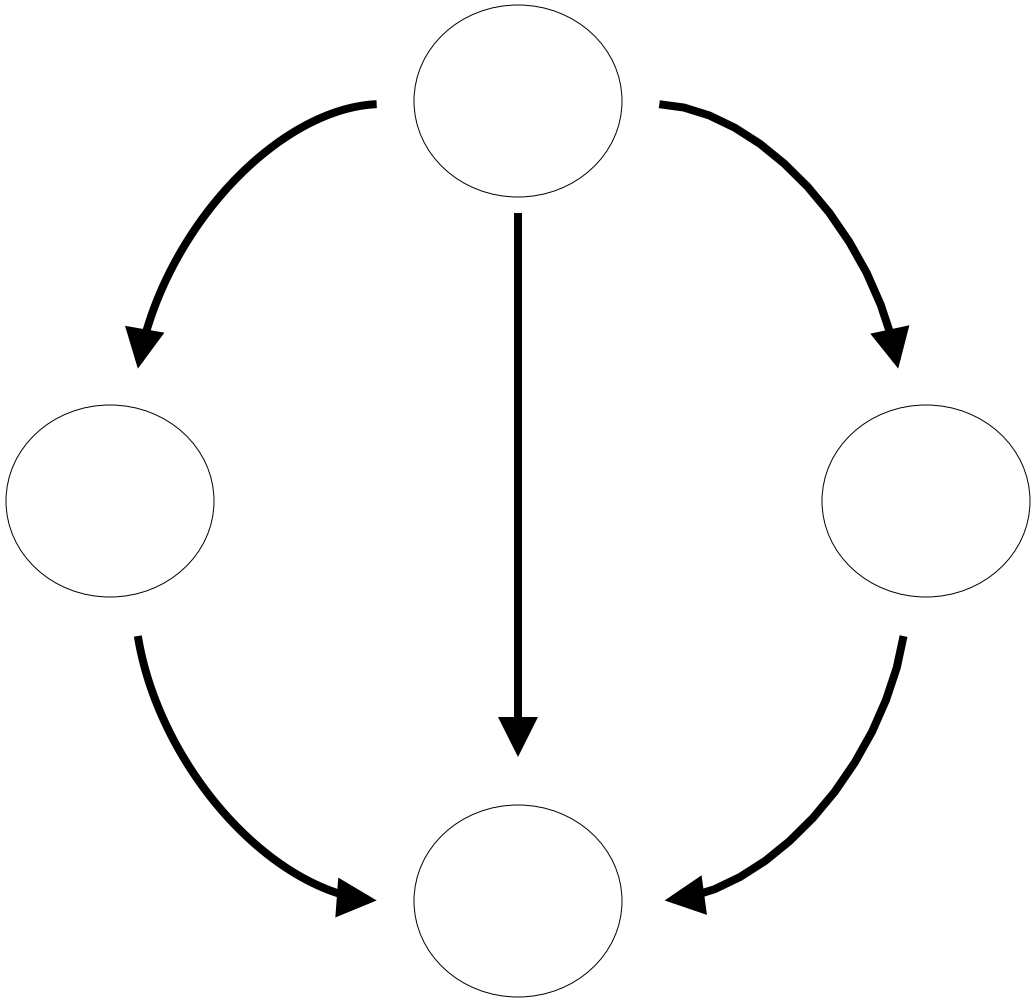
Transfusion Pathology



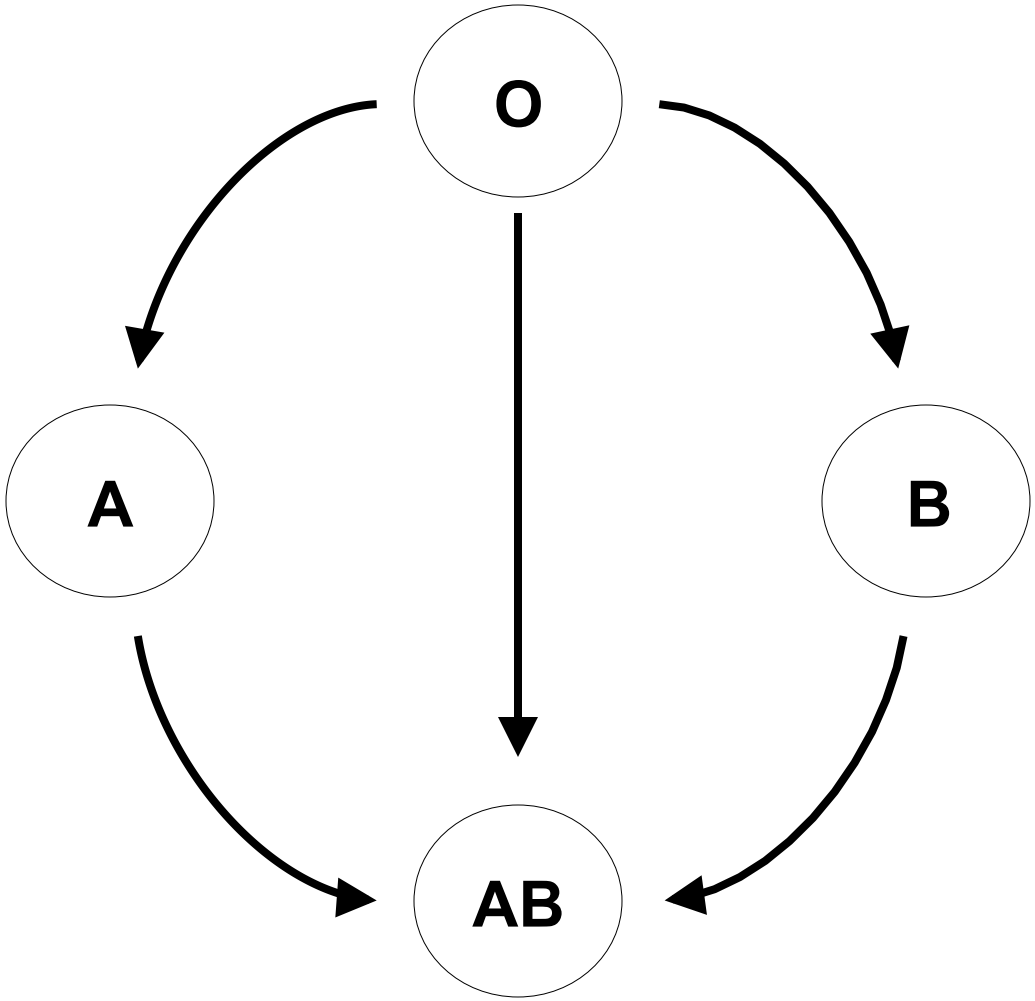
Which one of these is the H antigen? What is the gene that encodes it?
What percentage of the population has this antigen on their red cells?



The H antigen is the one on the left. The H gene encodes it.
Virtually everybody (99.something %) has the H antigen.
People with the very rare Bombay phenotype do not.

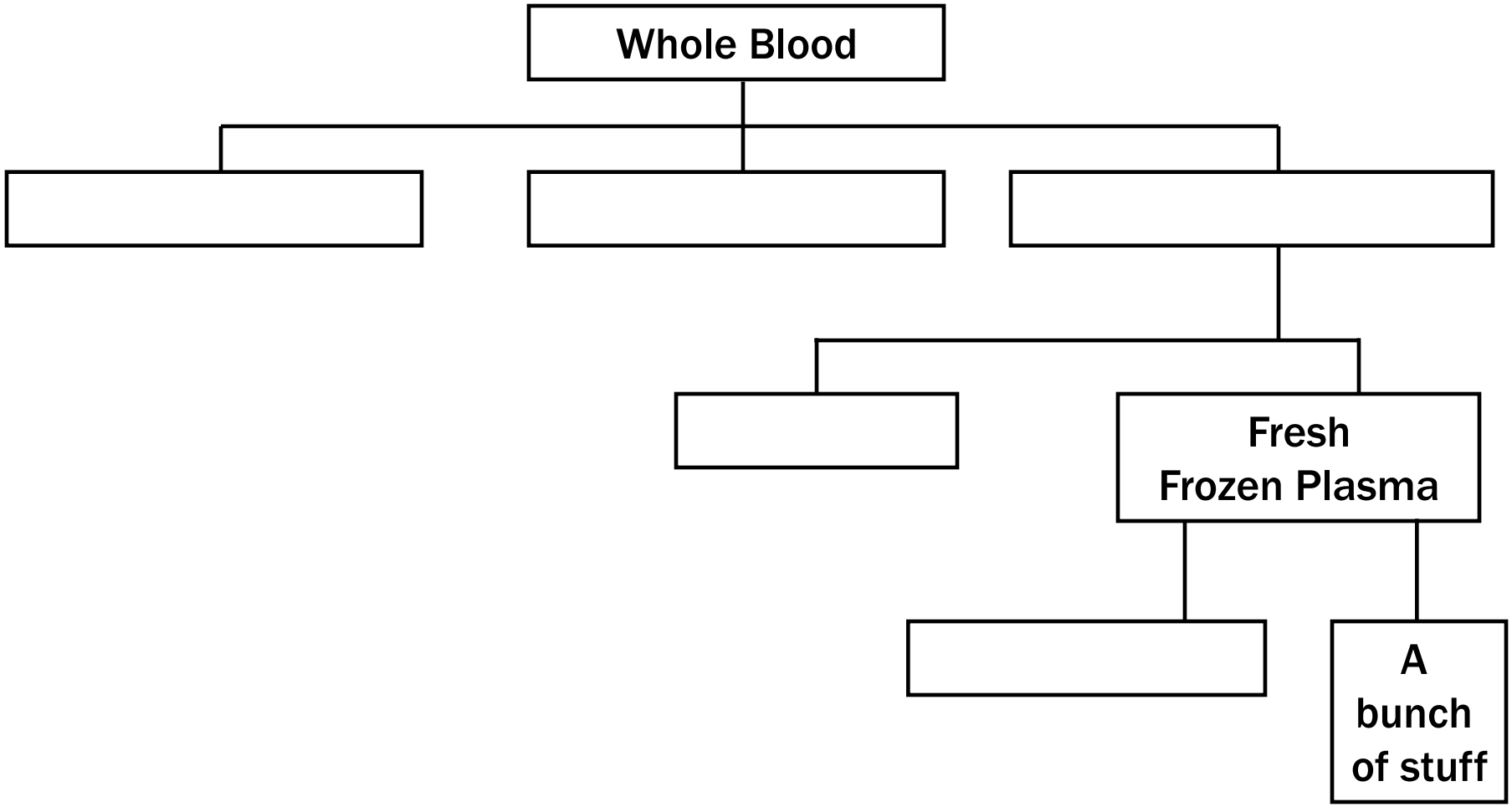


Fill in each circle with a blood type so that the diagram shows who can donate to whom.



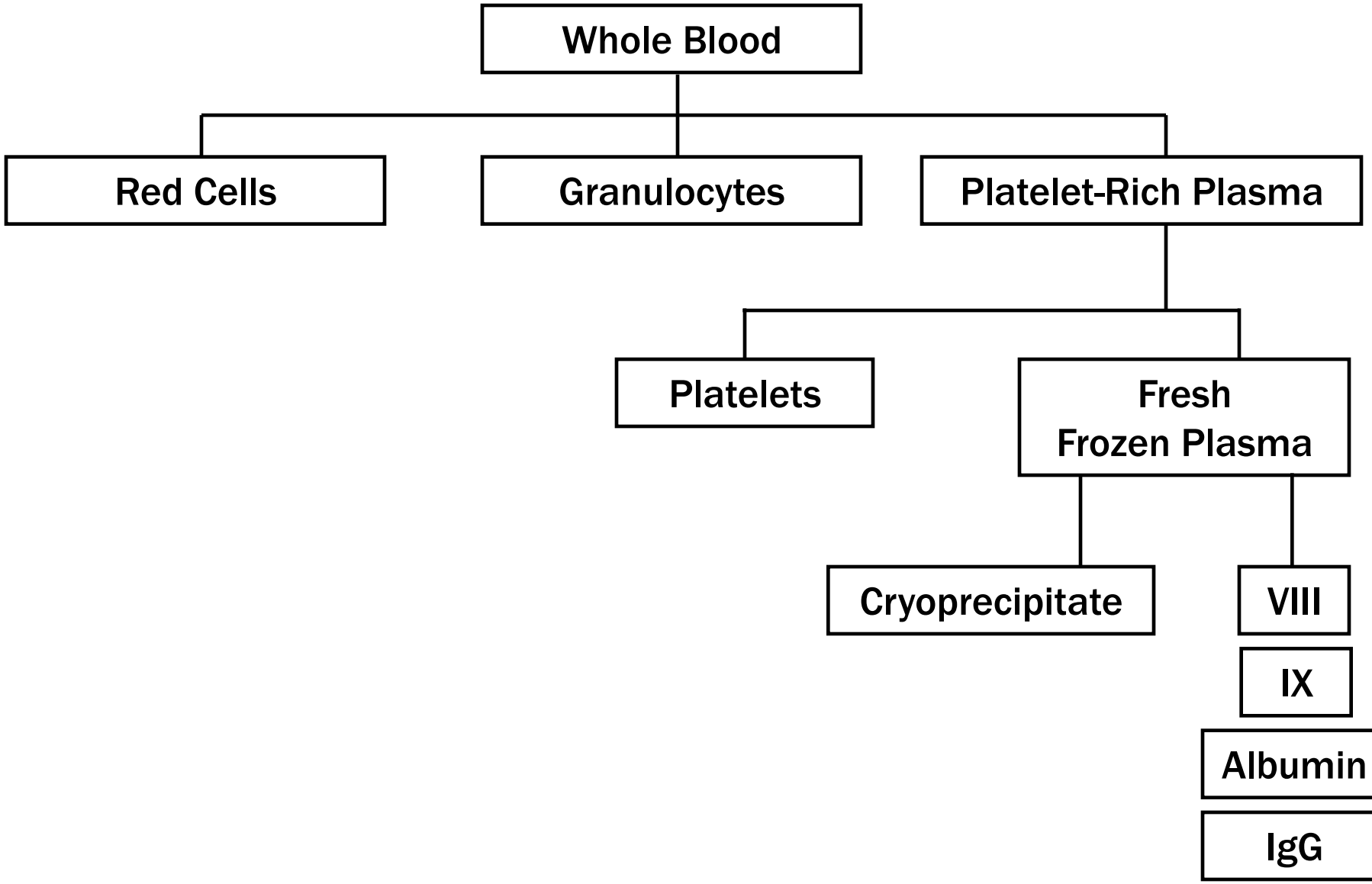
Fill in each circle with a blood type so that the diagram shows who can donate to whom.

BLOOD PRODUCTS



Fill in the boxes with blood products. What might each be used for?

BLOOD PRODUCTS



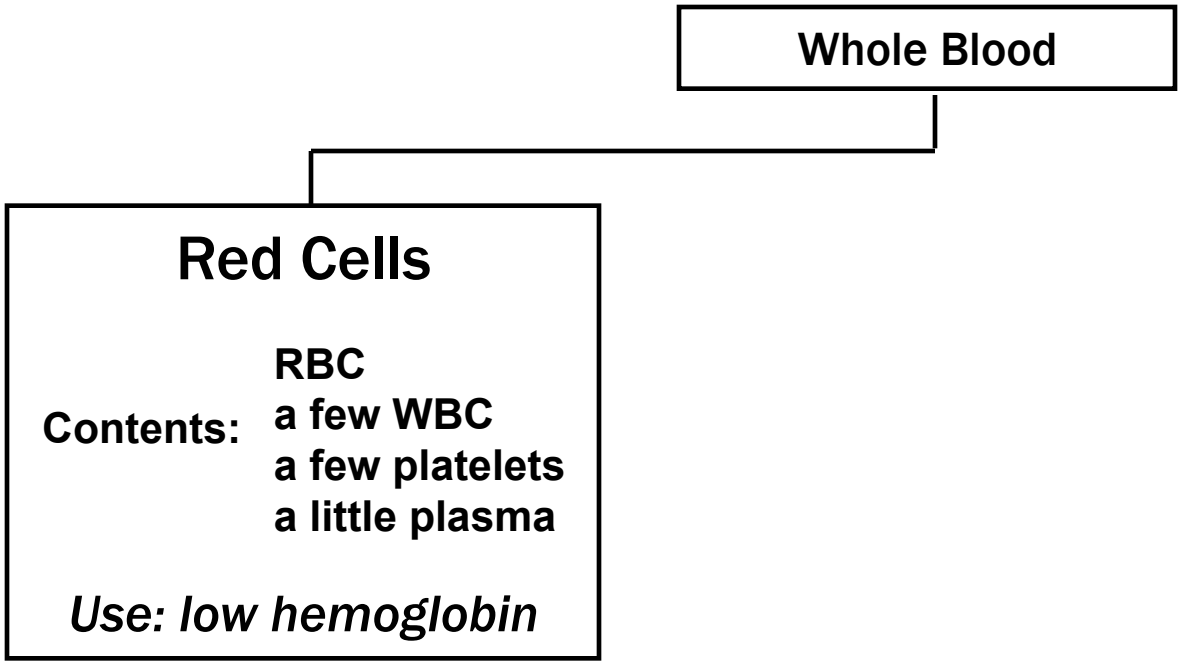
INDICATIONS

Whole Blood

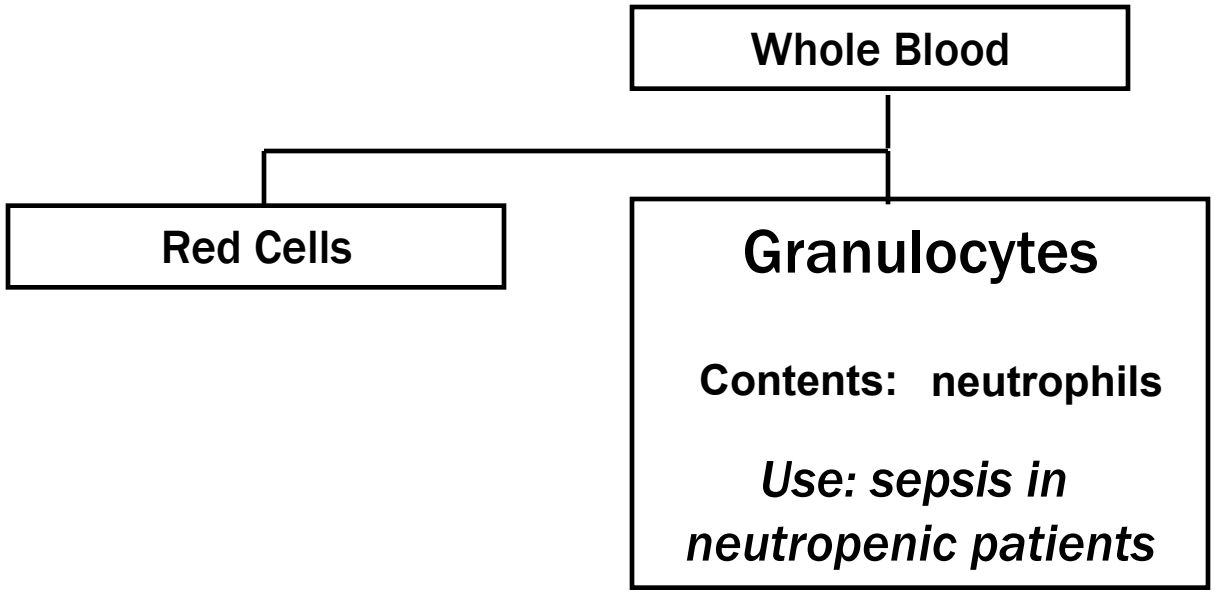
Contents:
- **RBC**
- **WBC**
- **platelets**
- **plasma**

Use: massive hemorrhage

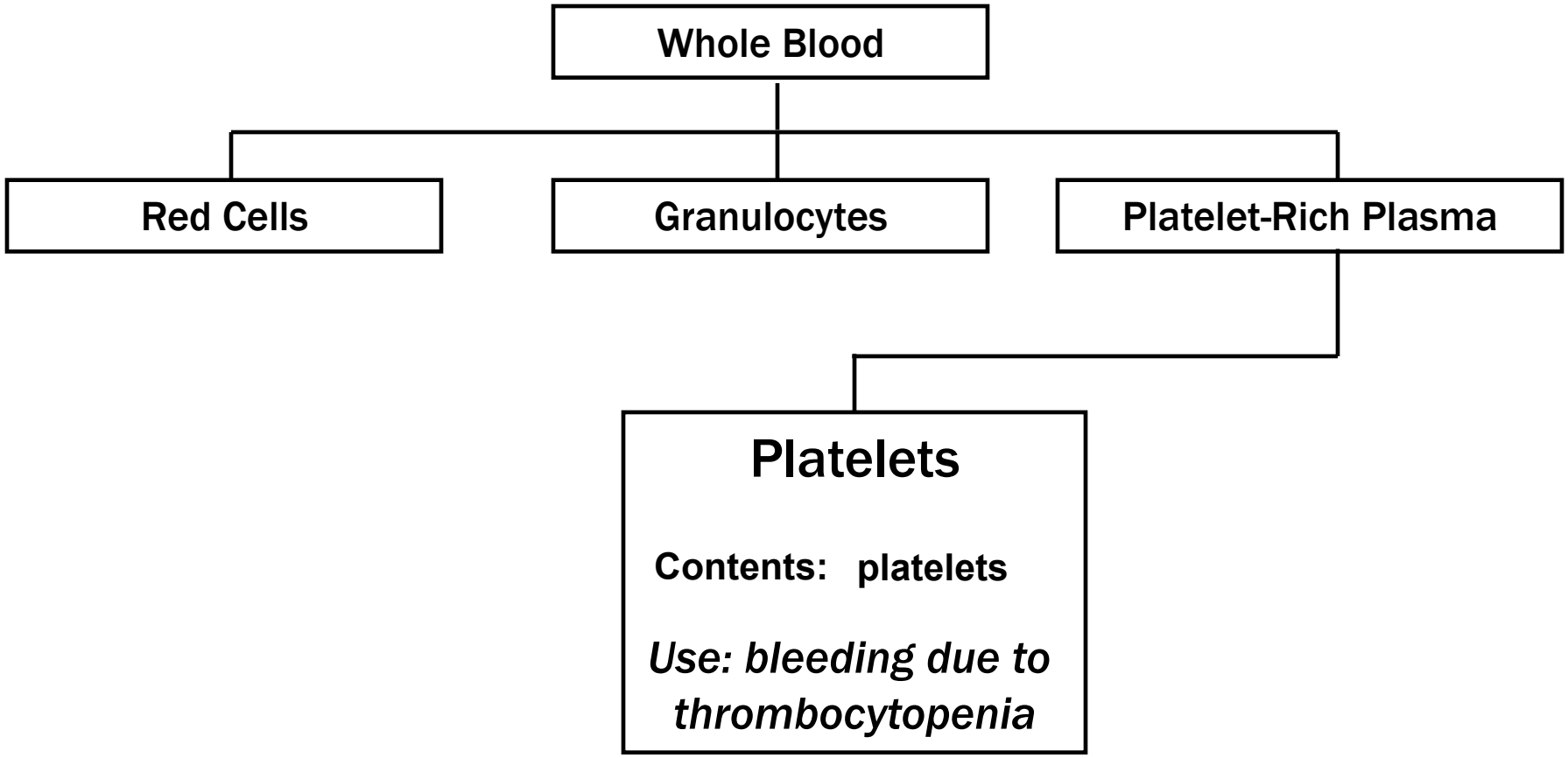
INDICATIONS



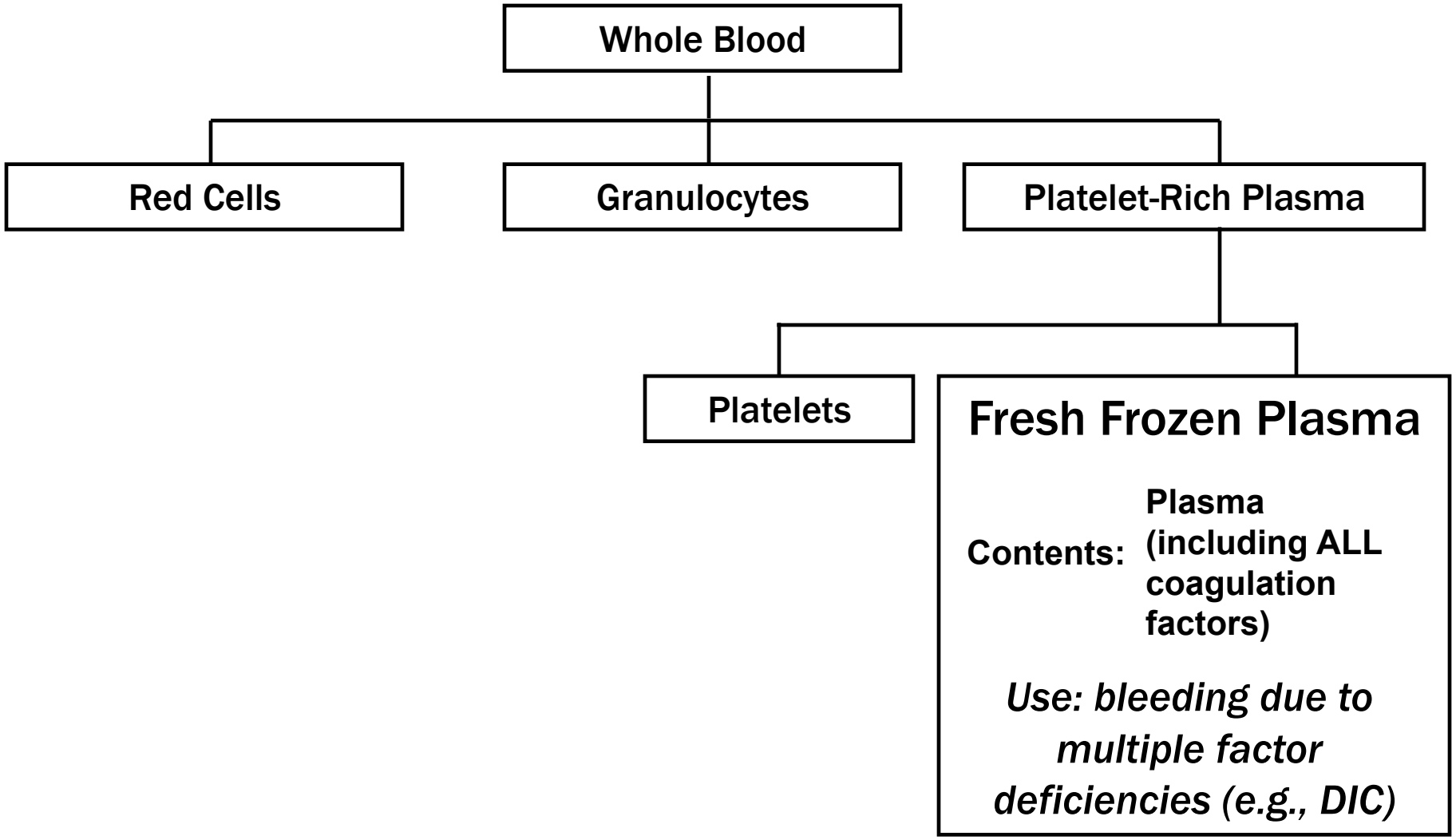
INDICATIONS



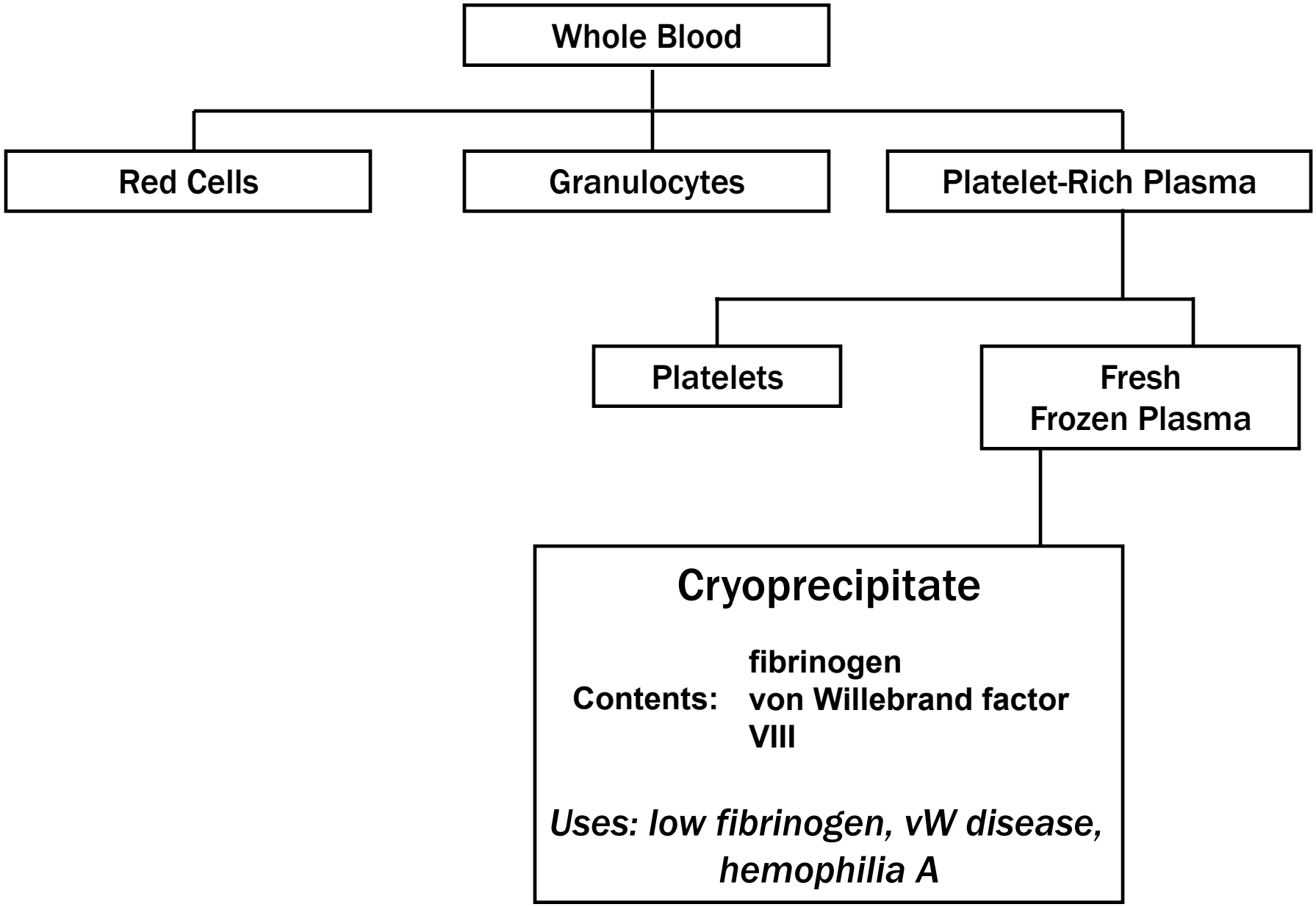
INDICATIONS



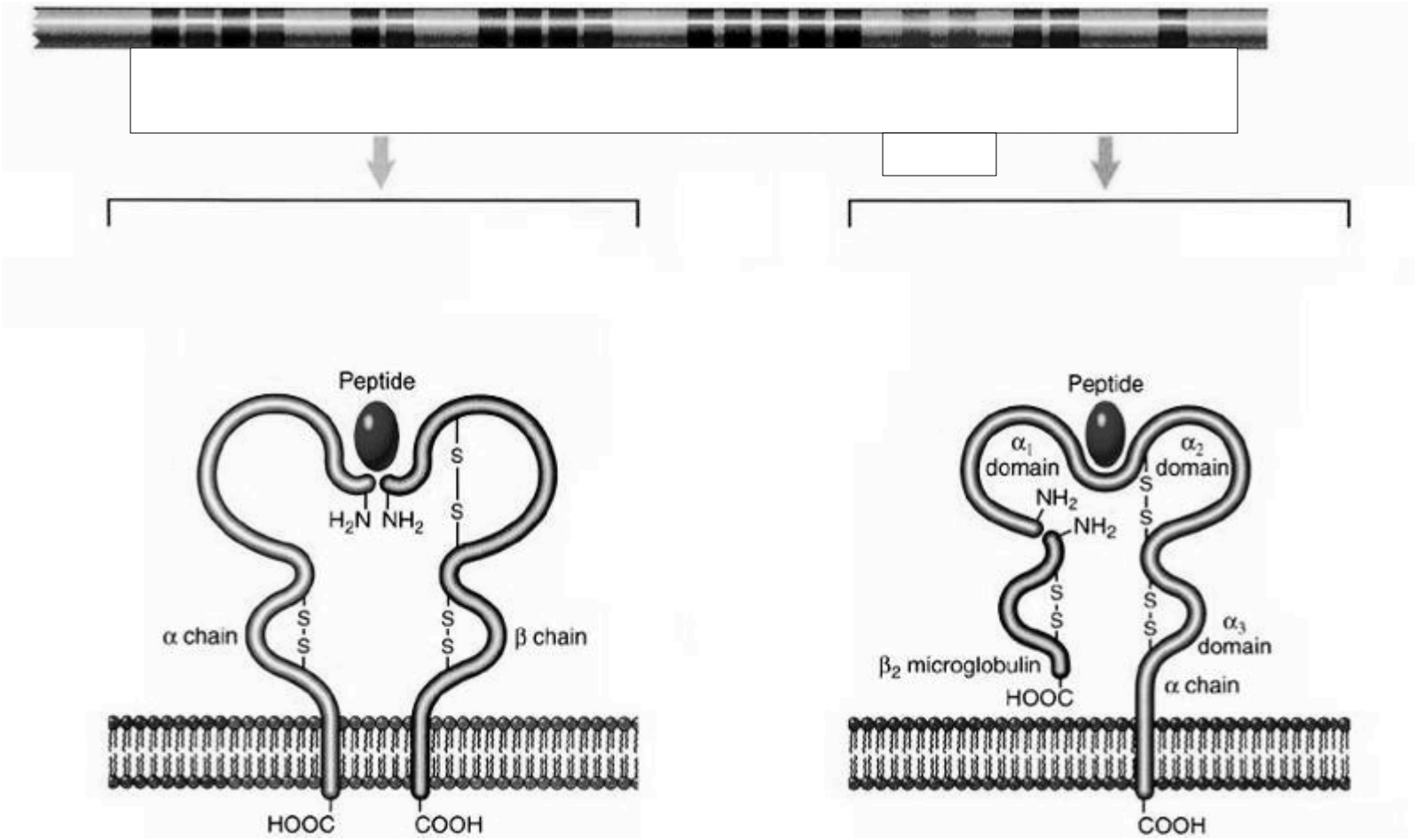
INDICATIONS



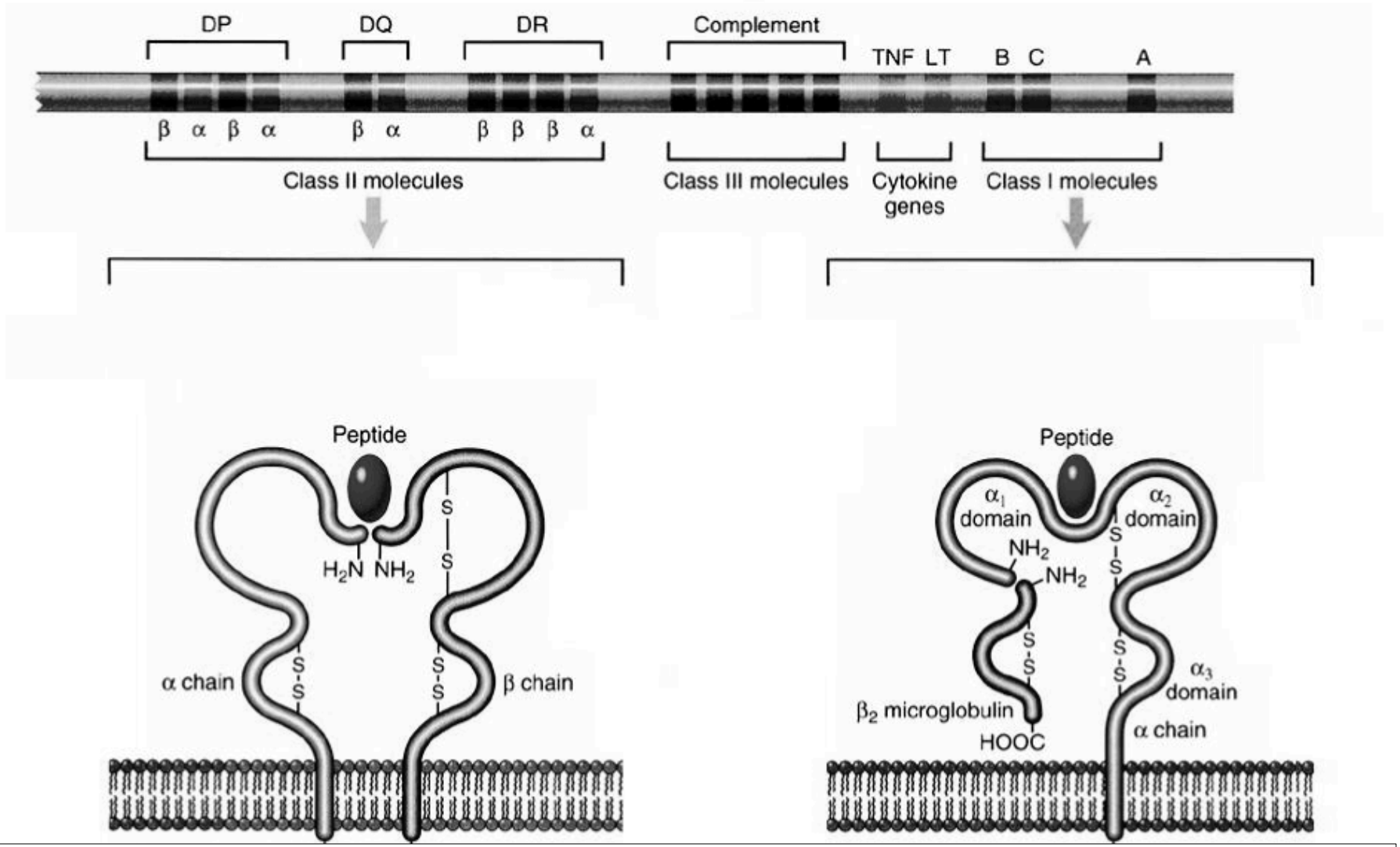
INDICATIONS



Transplantation Pathology



For old times' sake: What is the long thing at the top called?
What are the three regions within it called, and what does each encode?
What are the molecules on the bottom (you don't need to know which is which), and on what types of cells is each one found?



MHC (or in us humans, HLA) complex at the top. Class I region encodes class I MHC molecules (duh), which are present on nearly every cell in the body. The class II region encodes class II molecules, which are present only on antigen-presenting cells. The class III region encodes complement and cytokines.

	A	B	C	DR	DQ	DP
a	1	7	w3	2	1	1
b	2	8	w2	3	2	2
c	3	44	w4	4	1	3
d	11	35	w1	7	3	4

What do the A, B, C, DR, DQ, and DP represent?
What official word could you use to describe a, b, c, or d?
What word would you use to describe what the numbers represent?
Are my numbers the same as yours?

	A	B	C	DR	DQ	DP
a	1	7	w3	2	1	1
b	2	8	w2	3	2	2
c	3	44	w4	4	1	3
d	11	35	w1	7	3	4

A, B, C, DR, DQ, and DP are genes within the HLA complex.
a, b, c, and d are haplotypes.
The numbers represent alleles.
No, our alleles are not the same. Unless you and I are long-lost identical twins.

These lesions developed in a patient who recently underwent bone marrow transplantation. What disease is this? Could it happen with a kidney transplant?

GVHD. This only happens with bone marrow transplants, not with solid organ transplants, because only bone marrow transplants have enough graft T cells to start doing damage to the host.

Immune Diseases

This facial lesion is characteristic of which autoimmune disorder?
Can you name three other signs or symptoms that you, as a dentist, might notice in this patient?

Lupus

Things a dentist might see

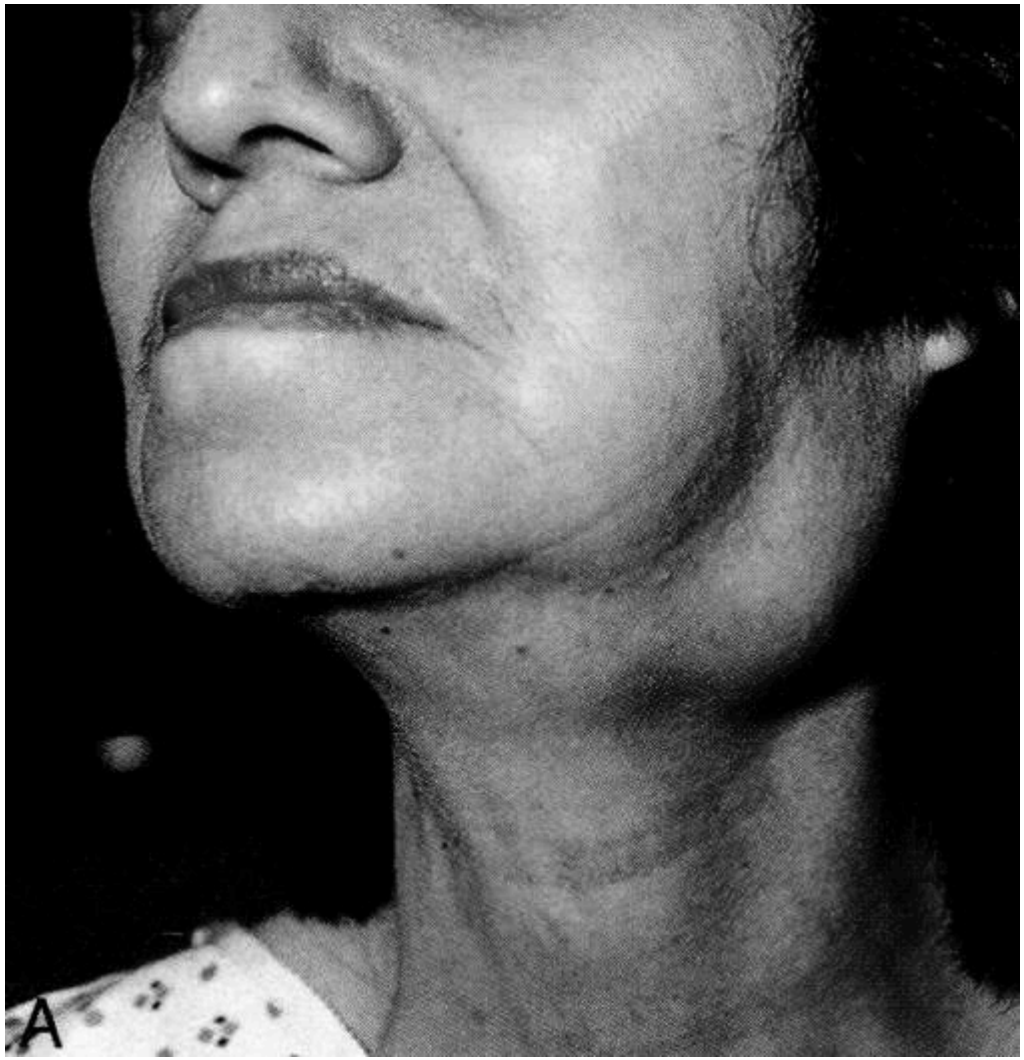
- Young woman with polyarthritis and a butterfly (or other) skin rash
- Sensitivity to sunlight
- Oral lesions: nonspecific, red-white, erosive
- Headaches, seizures, or psychiatric problems
- Pleuritic chest pain
- Unexplained fever

What autoimmune disease does this patient have? Name three organ systems that could be affected in this patient, and describe the possible findings in each.

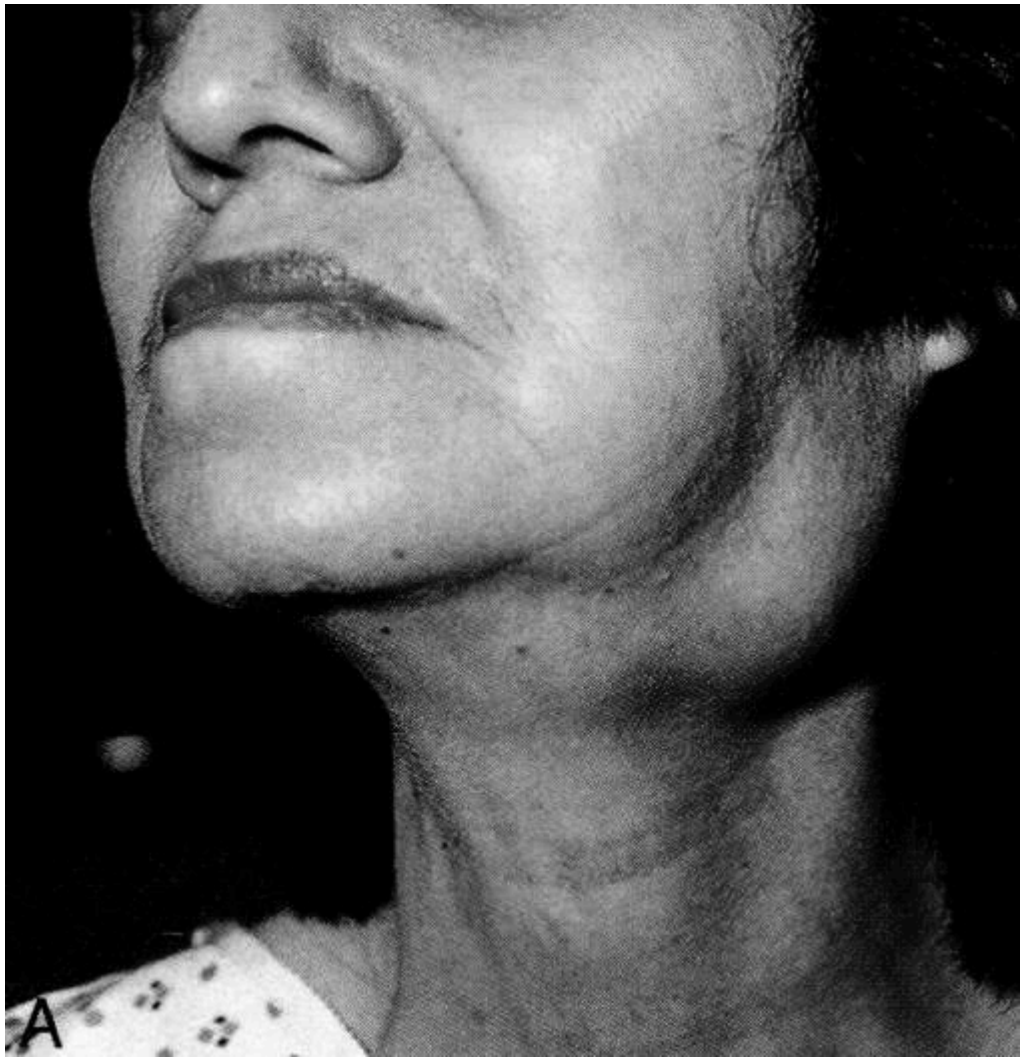
Systemic Sclerosis (Scleroderma)

Organs involved

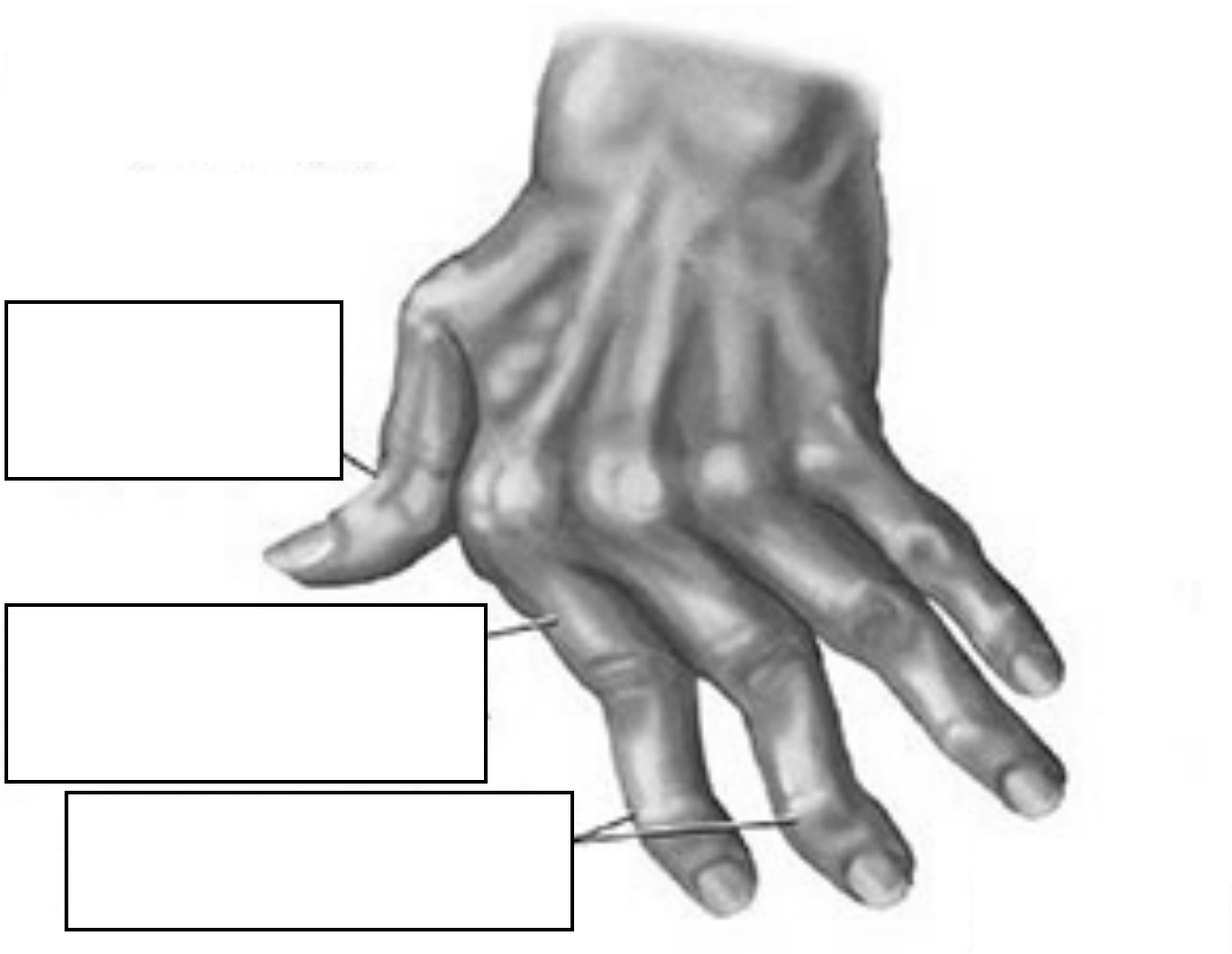
- Skin: diffuse, sclerotic atrophy. Fingers first.
- GI: “rubber-hose” lower esophagus
- Lungs: fibrosis, pulmonary hypertension
- Kidneys: narrowed vessels, hypertension
- Heart: myocardial fibrosis



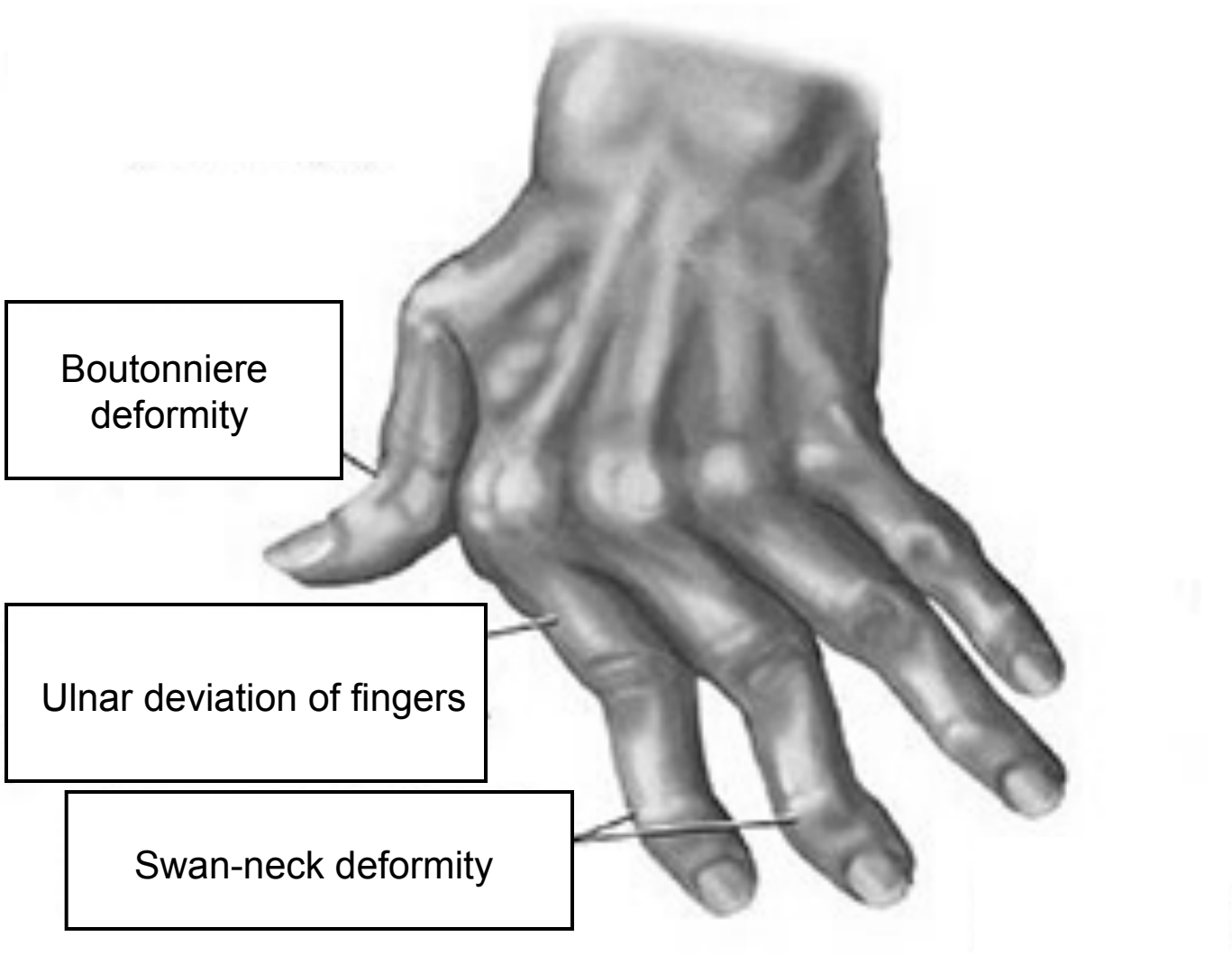
This patient came to you because she has lots of “sore teeth”. You notice her mouth is very dry. Thinking back to your favorite class during dental school – pathology - you believe this patient may be suffering from which autoimmune disease?



Sjögren syndrome.



Fill in the boxes to describe the deformities present in this hand.
What autoimmune disease does this patient most likely have?
How would the patient describe her symptoms associated with her hands?



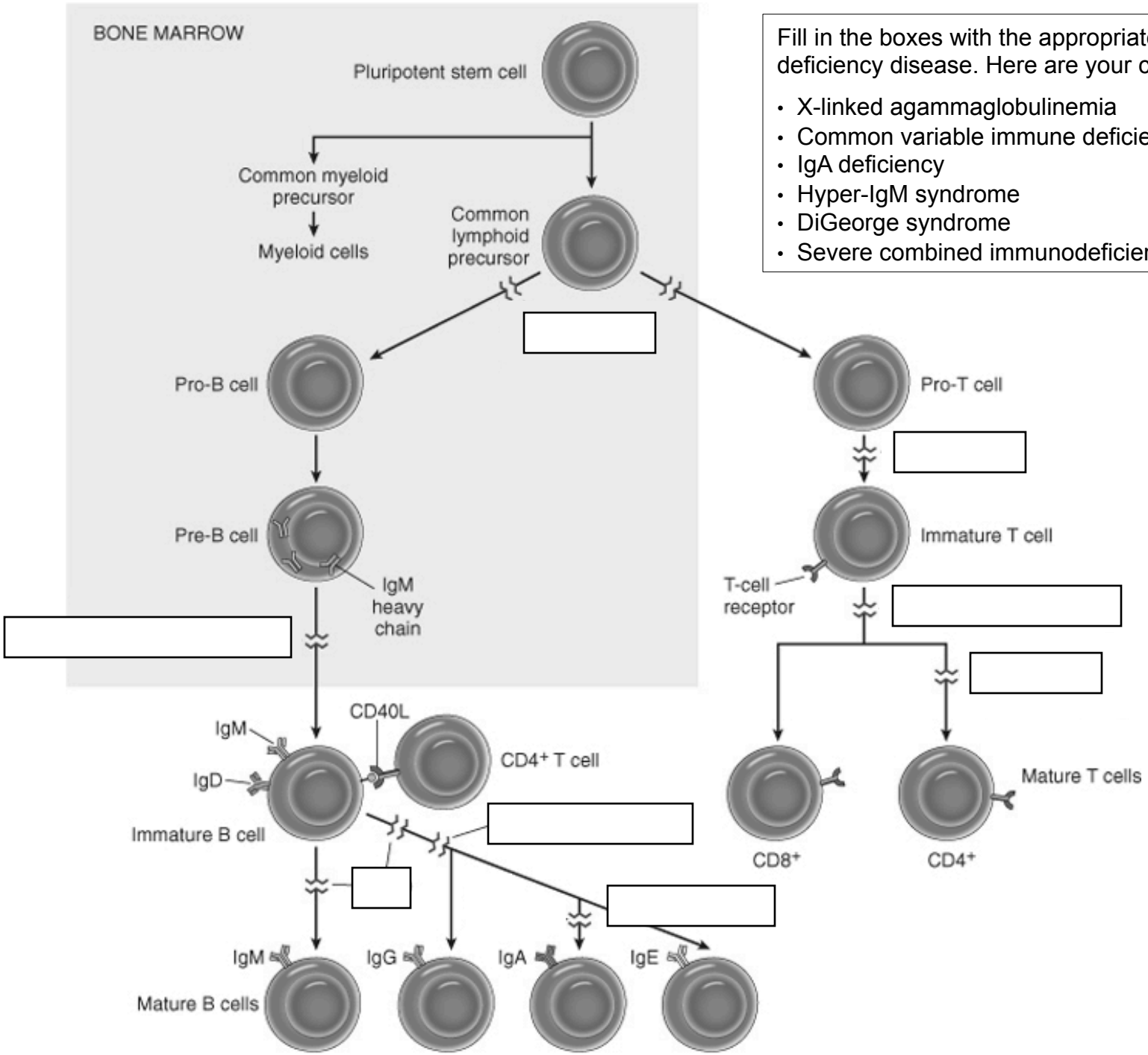
This patient has rheumatoid arthritis.
She would probably describe her symptoms as being symmetric (in the same joints on both hands), with achy pain and stiffness that is worst in the morning.

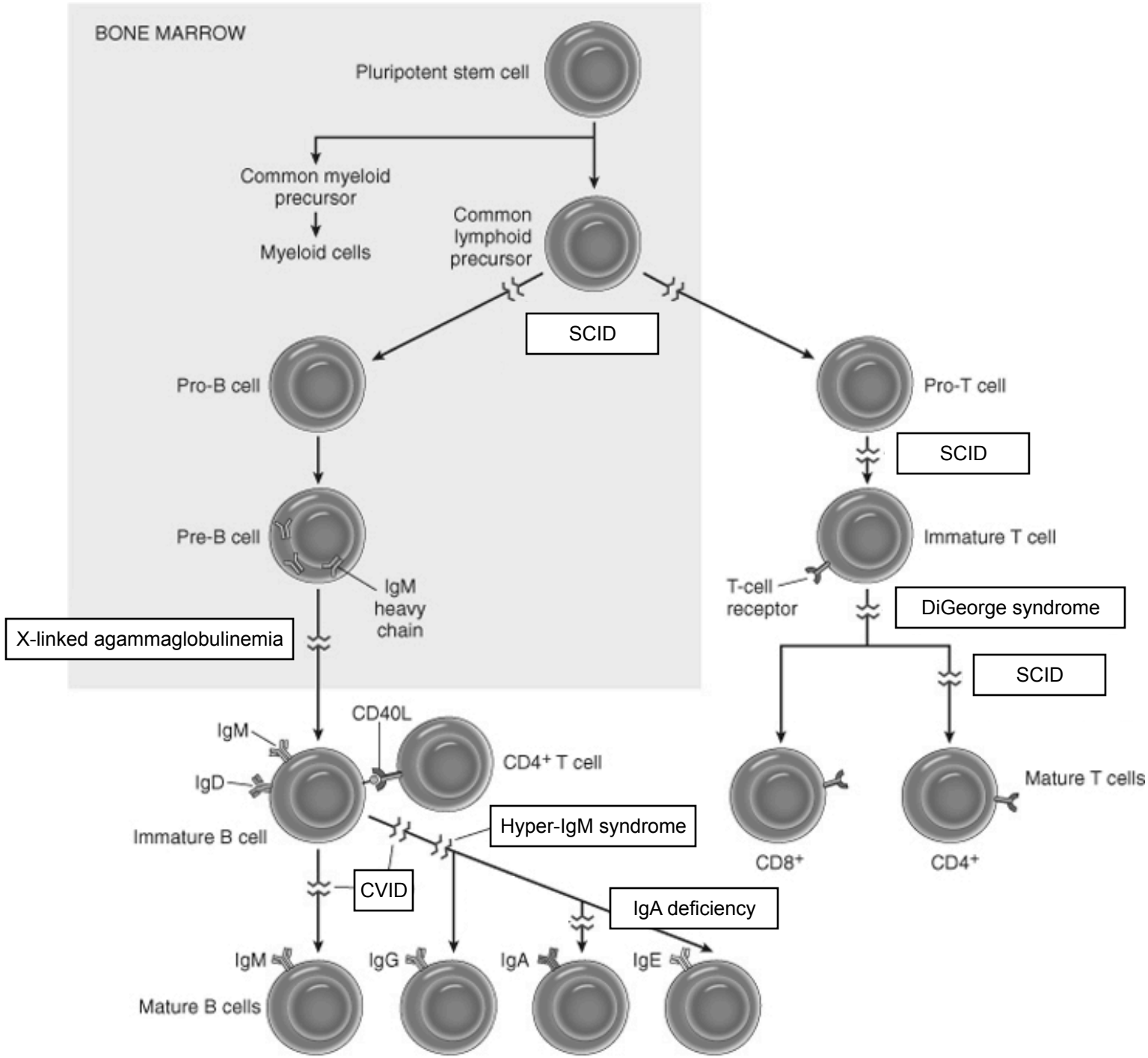
What is this phenomenon? Is it always associated with an autoimmune disease?

Raynaud phenomenon. Most of the time, it is primary (not associated with any underlying disease). In a small number of patients, it is secondary (associated with another disease, often scleroderma, but sometimes lupus or other diseases).

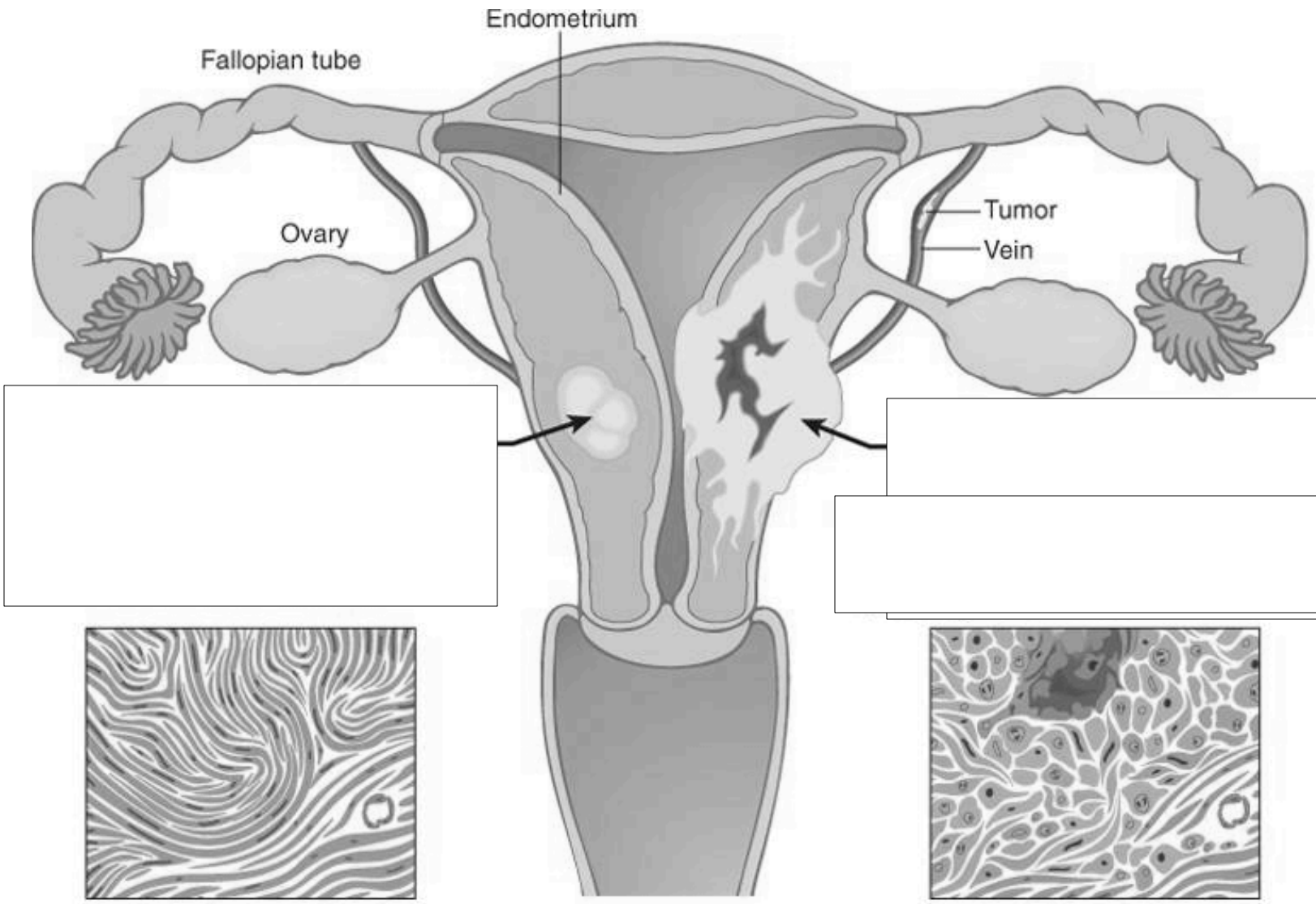
Fill in the boxes with the appropriate immune deficiency disease. Here are your choices:

- X-linked agammaglobulinemia
- Common variable immune deficiency
- IgA deficiency
- Hyper-IgM syndrome
- DiGeorge syndrome
- Severe combined immunodeficiency

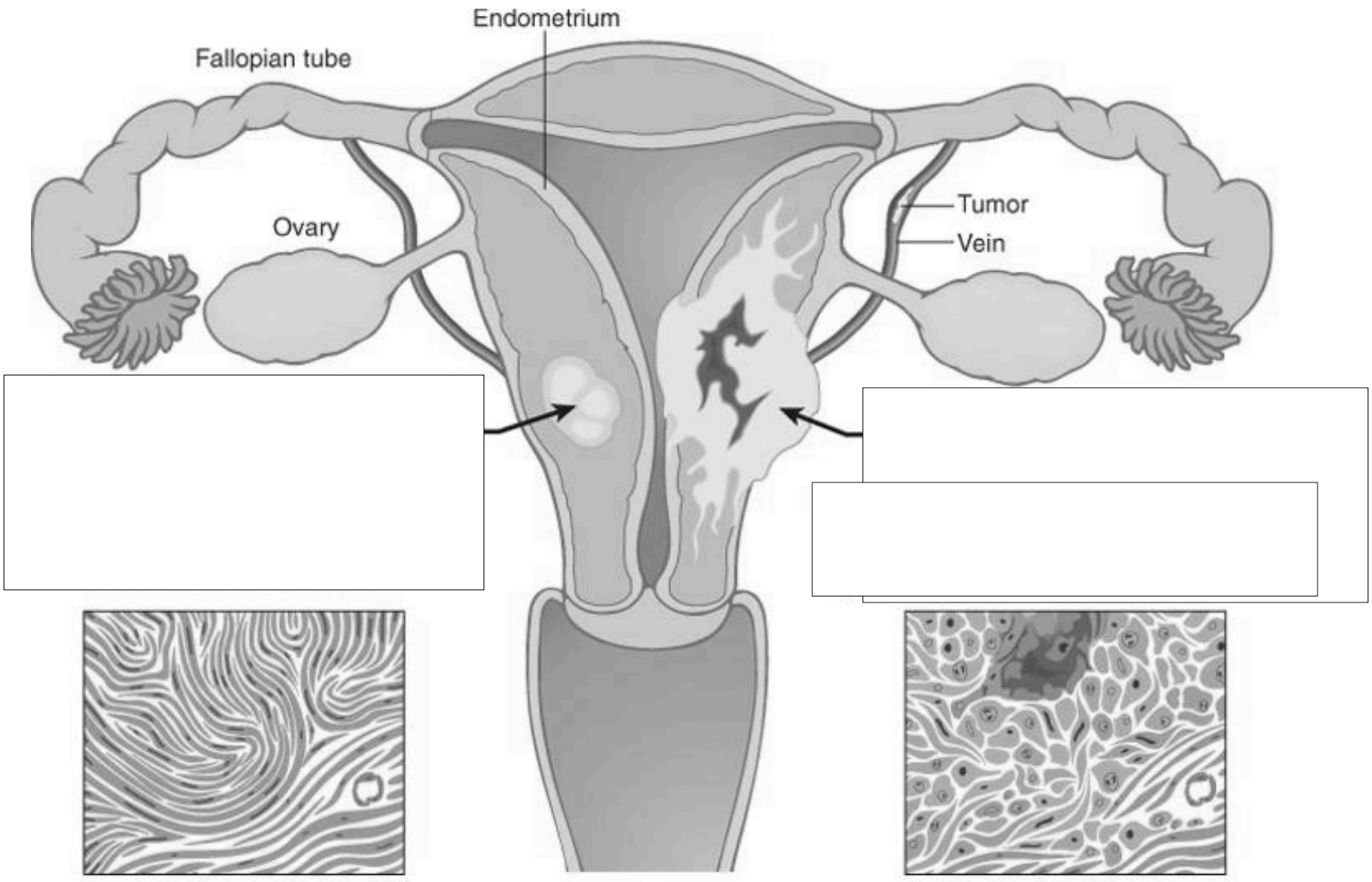



BONE MARROW
Pluripotent stem cell
Common myeloid precursor
Myeloid cells
Common lymphoid precursor
SCID
Pro-B cell
Pro-T cell
SCID
Pre-B cell
Immature T cell
IgM heavy chain
T-cell receptor
DiGeorge syndrome
X-linked agammaglobulinemia
SCID
CD40L
IgM
IgD
CD4+ T cell
Mature T cells
Immature B cell
Hyper-IgM syndrome
CD8+
CD4+
CVID
IgA deficiency
IgM
IgG
IgA
IgE
Mature B cells

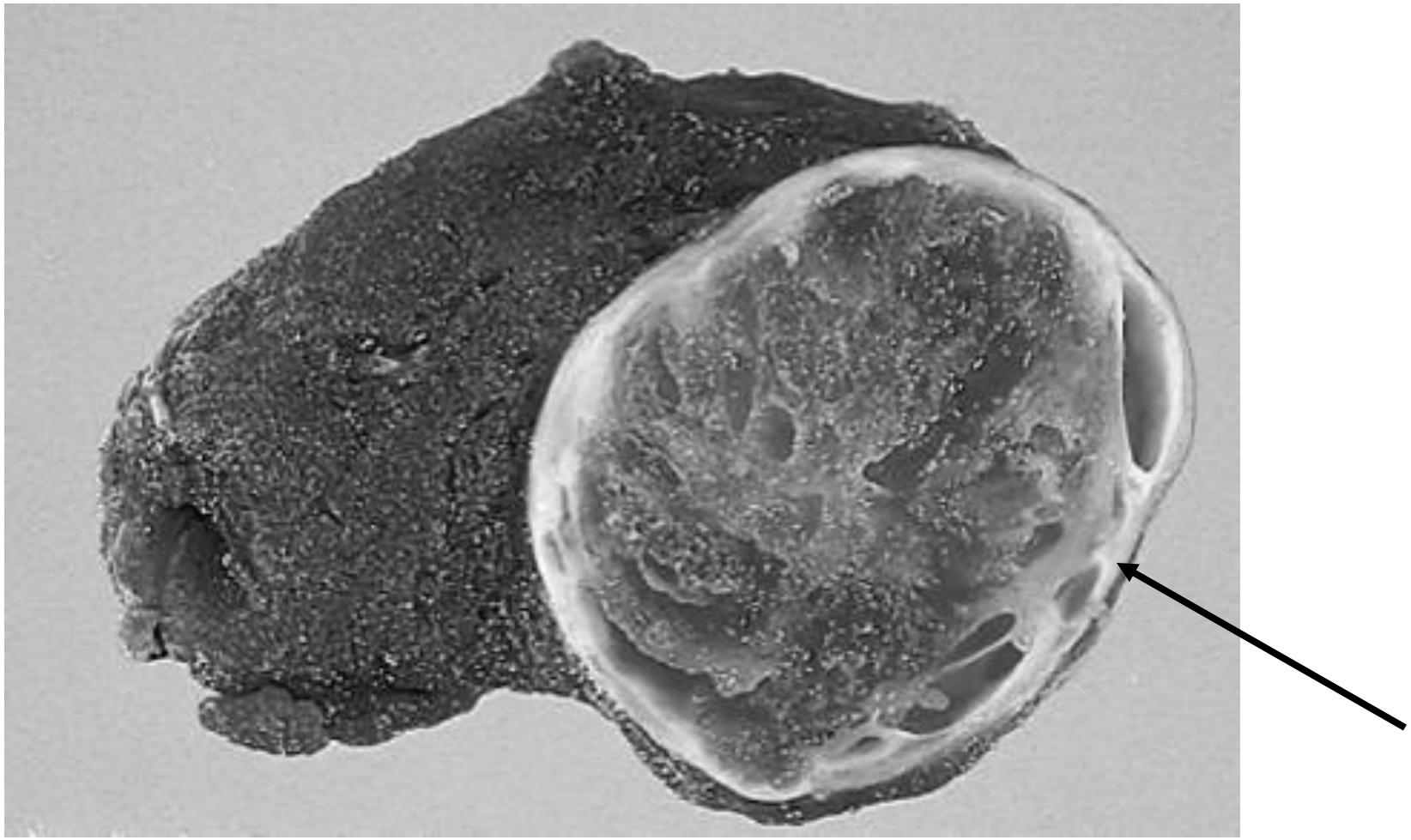
Neoplasia



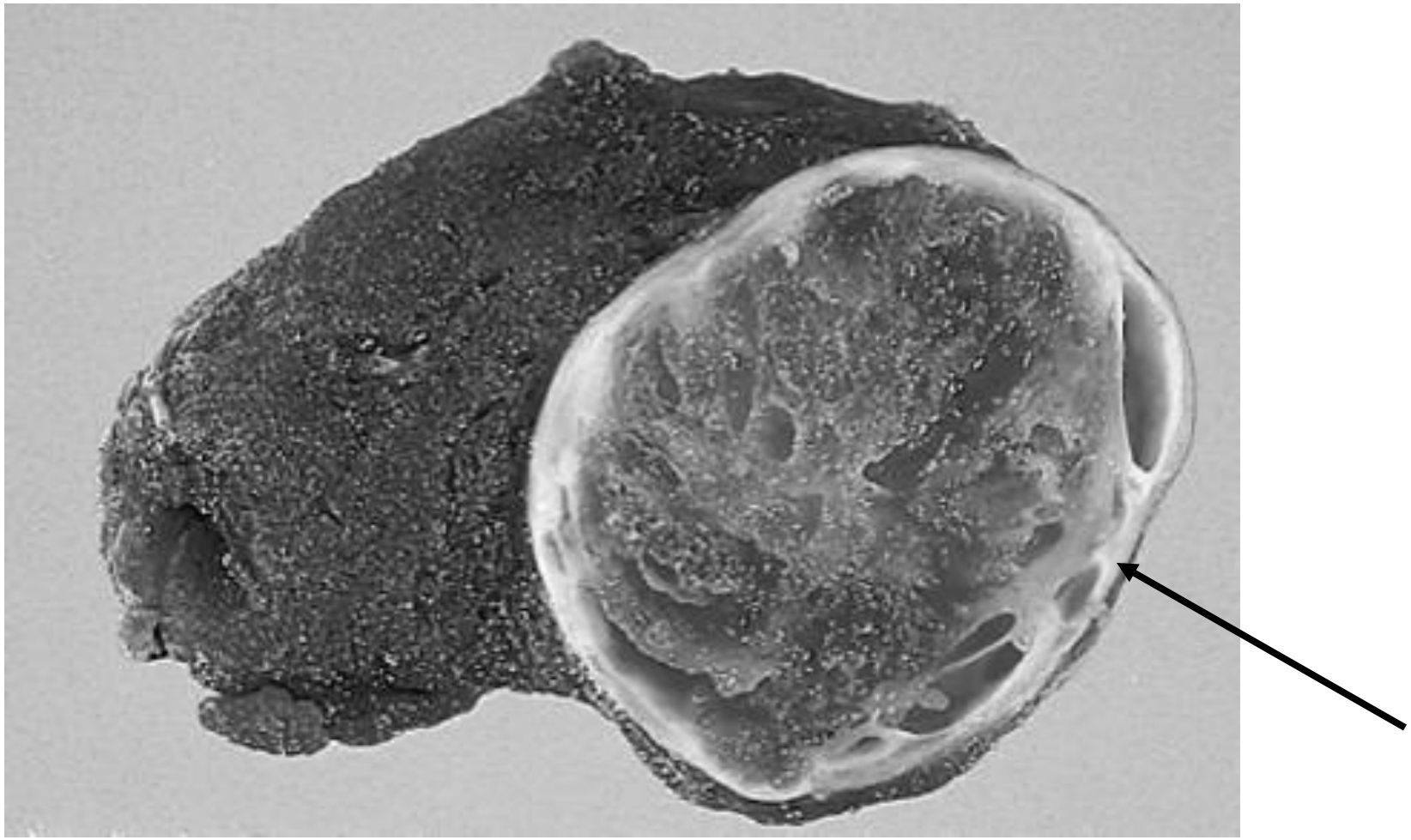
Which side has the benign tumor? Why?



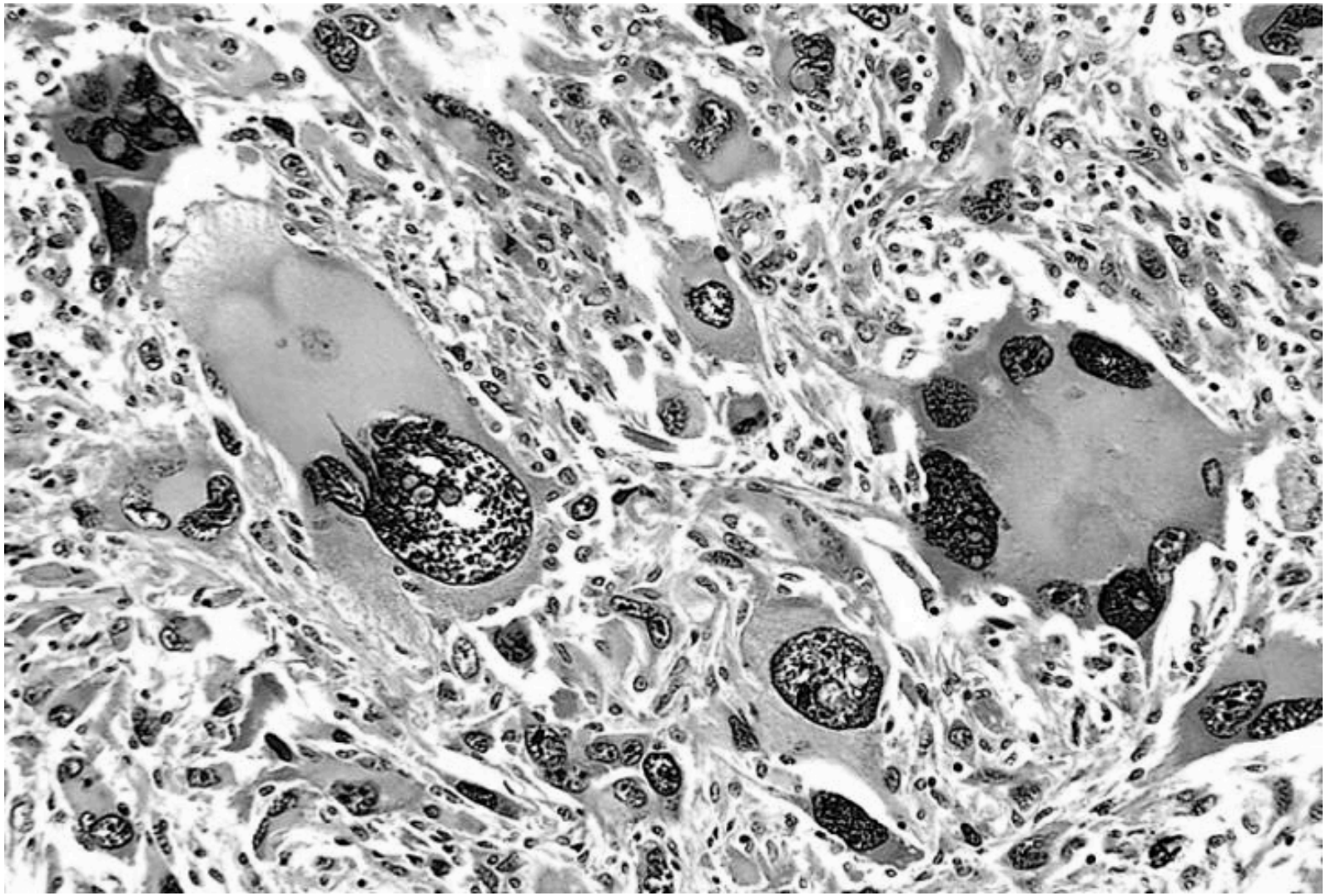
Left side. Smaller, non-invasive, and histology looks well-differentiated. Also, most importantly, the tumor on the right side has metastasized (it's in a vein).



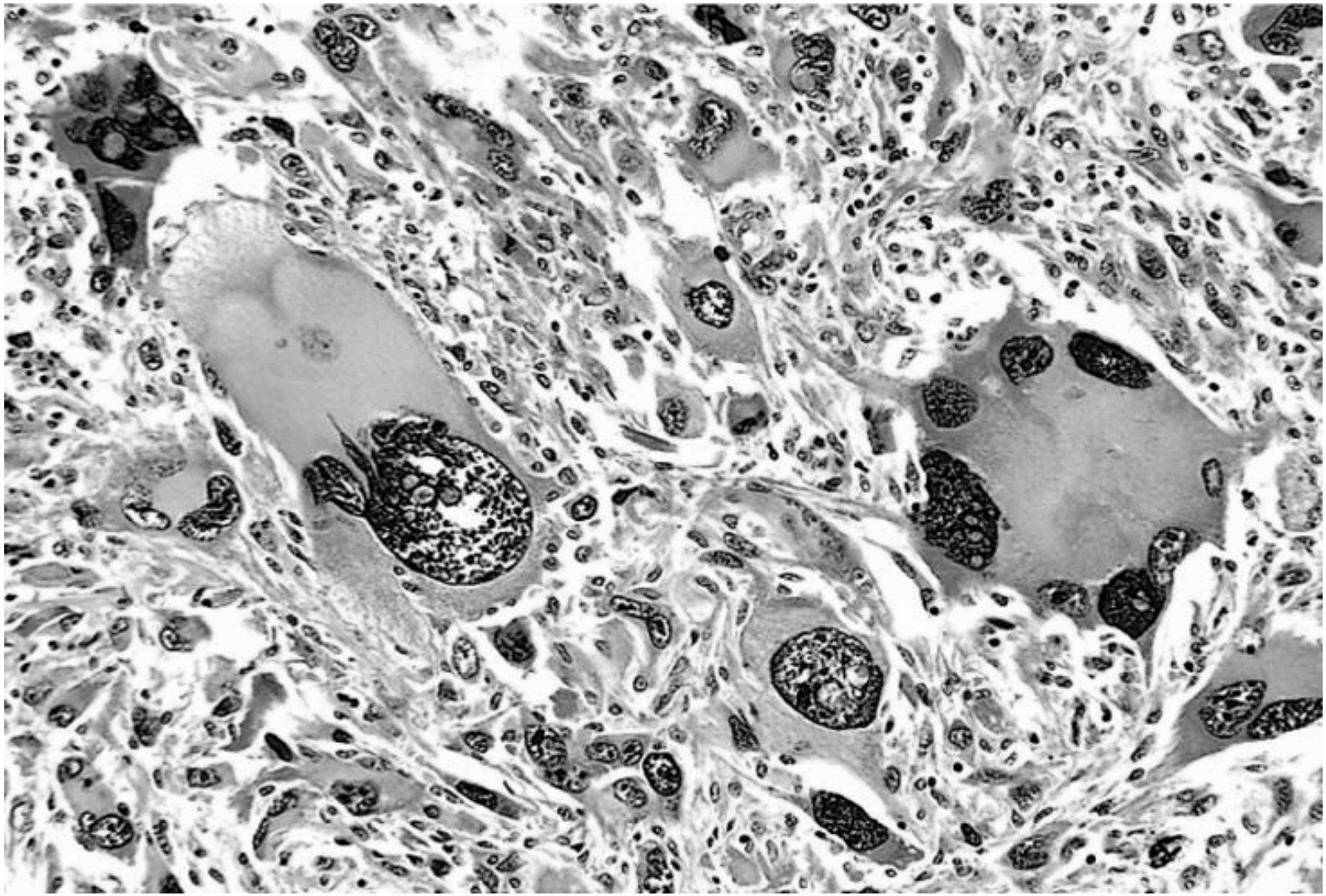
Do you think this tumor is benign or malignant?
What do you call the thing the arrow is pointing at?



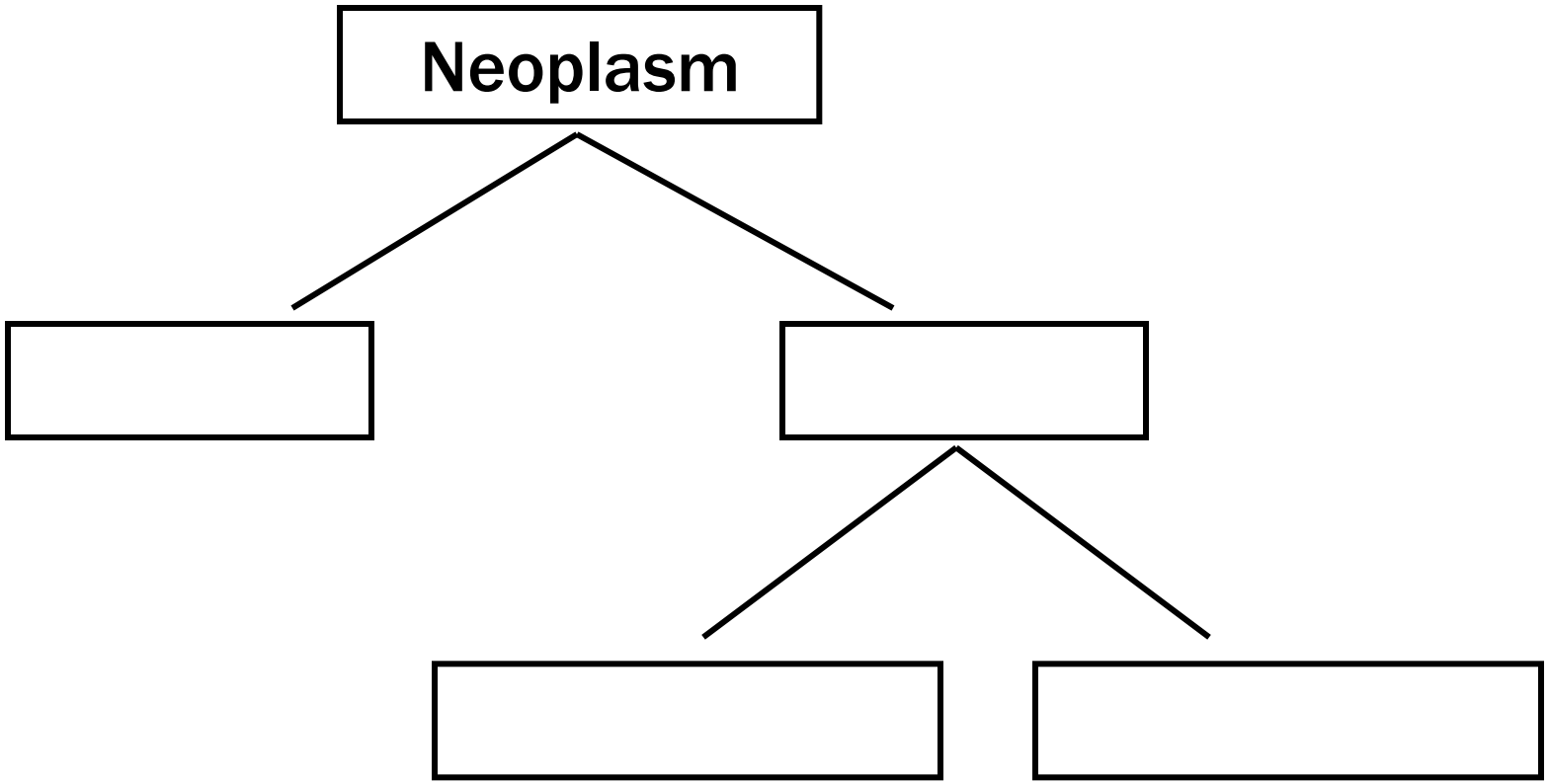
Benign. Arrow is pointing at the capsule – a good (though not foolproof) indicator of benignity.



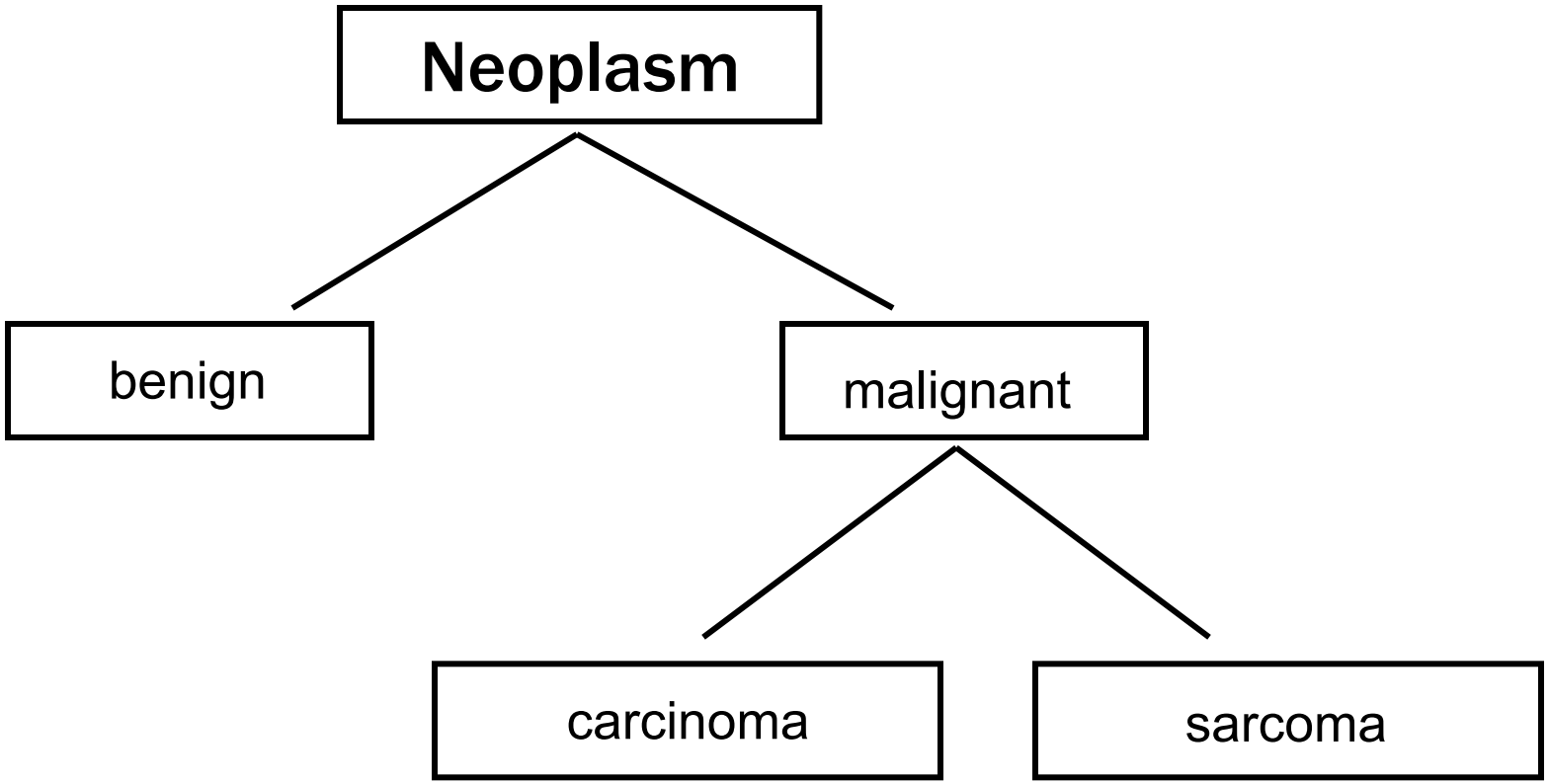
Benign or malignant?
What word would you use to describe these cells (besides ugly)?



Malignant. The cells are anaplastic.



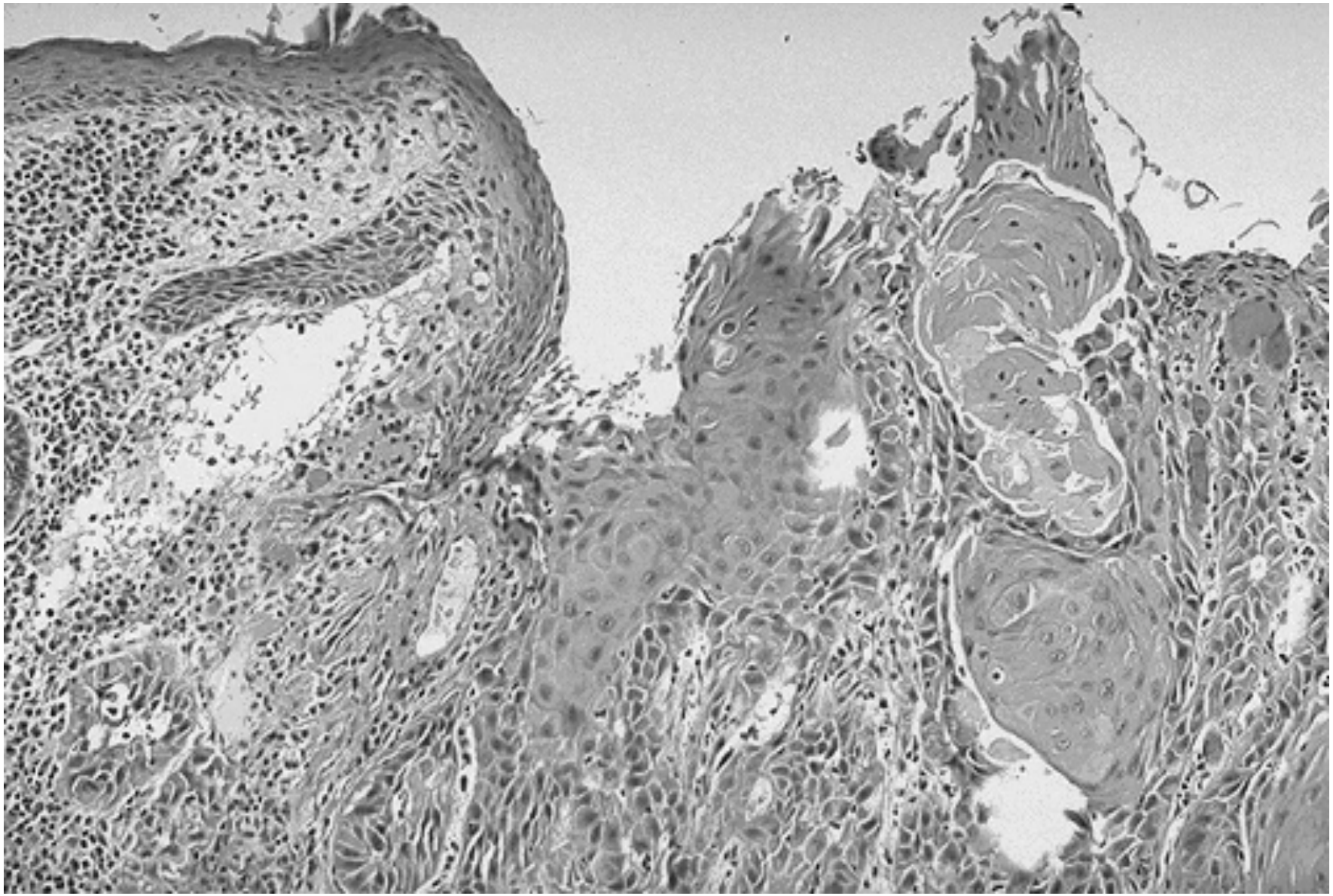
Fill in the boxes with the following words: benign, malignant, carcinoma, sarcoma.
Name as many specific tumors as you can for each of the red boxes.



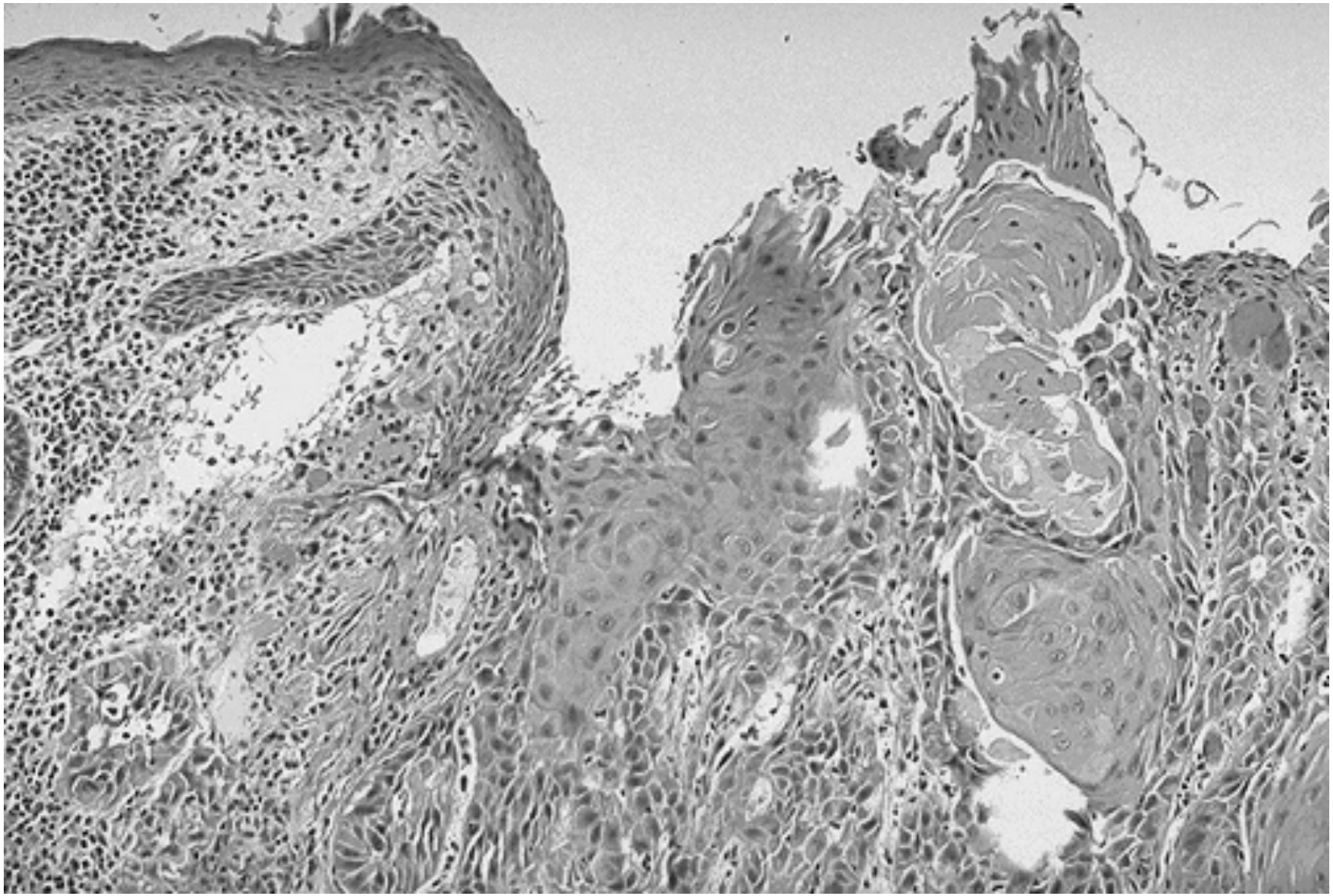
Fill in the boxes with the following words: benign, malignant, carcinoma, sarcoma.
Name as many specific tumors as you can for each of the red boxes.

Know these names!

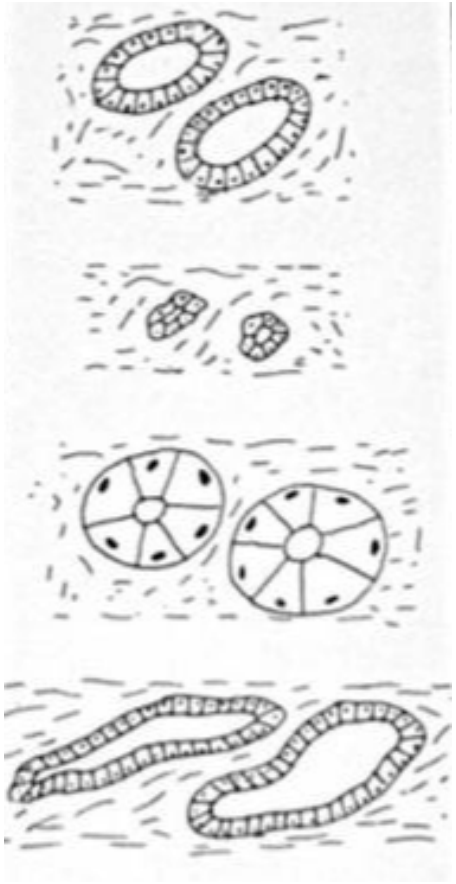
Tissue of origin	Benign	Malignant
Fibrous tissue	Fibroma	Fibrosarcoma
Fat	Lipoma	Liposarcoma
Cartilage	Chondroma	Chondrosarcoma
Bone	Osteoma	Osteogenic sarcoma
Blood vessels	Hemangioma	Angiosarcoma
Mesothelium		Mesothelioma
Hematopoietic cells		Leukemia
Lymphoid cells		Lymphoma
Squamous epithelium	Squamous cell papilloma	Squamous cell carcinoma
Glandular epithelium	Adenoma Papilloma Cystadenoma	Adenocarcinoma Papillary adenocarcinoma Cystadenocarcinoma
Smooth muscle	Leiomyoma	Leiomyosarcoma
Skeletal muscle	Rhabdomyoma	Rhabdomyosarcoma
Melanocytes	Nevus	Melanoma

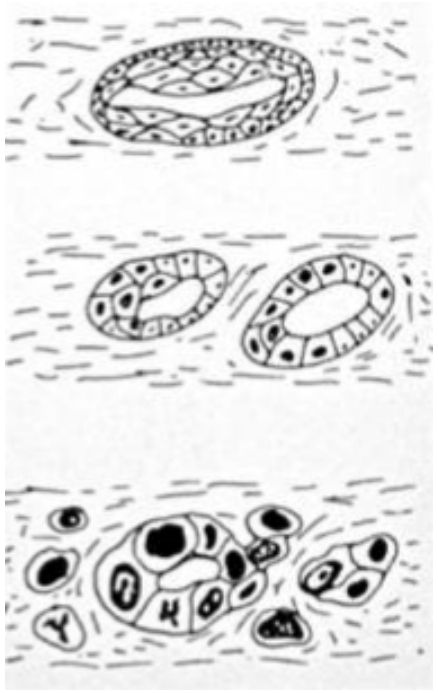


Do you think this squamous cell carcinoma is well-differentiated, moderately-differentiated, or poorly-differentiated? What does this mean for this patient's prognosis?

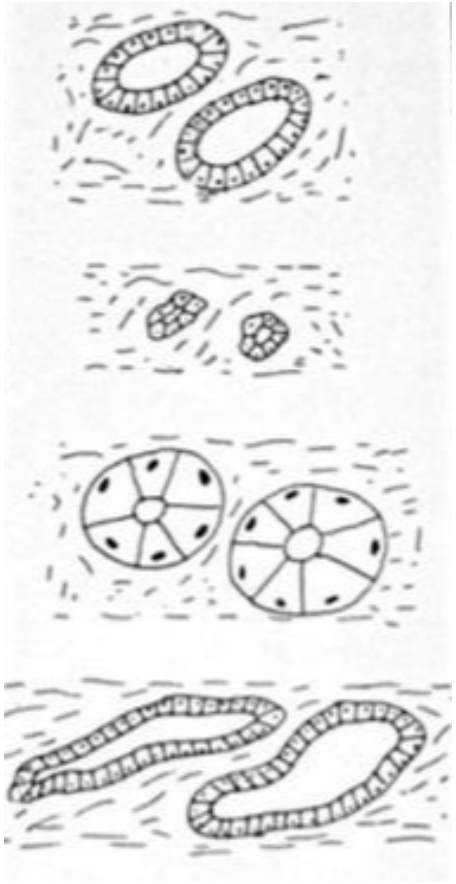


Well-differentiated. This portends a better prognosis for the patient than if the tumor were poorly-differentiated.





Fill in the blanks.

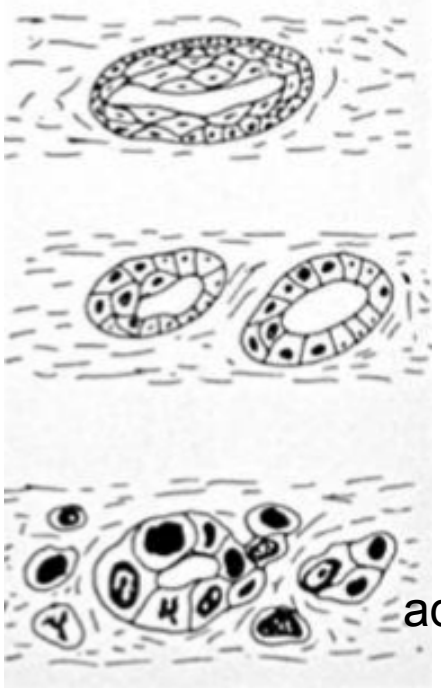


normal

atrophy

hypertrophy

hyperplasia

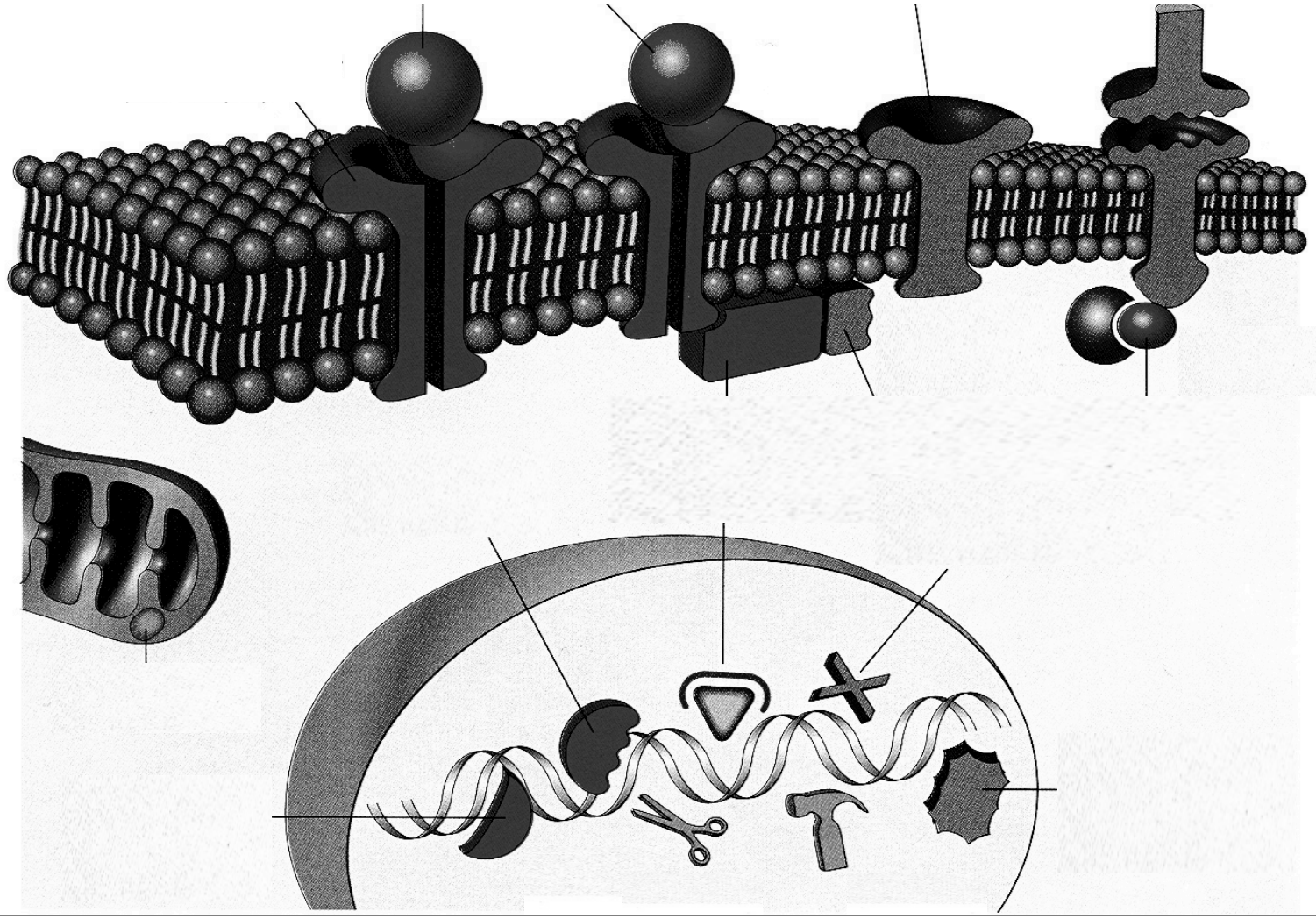


metaplasia

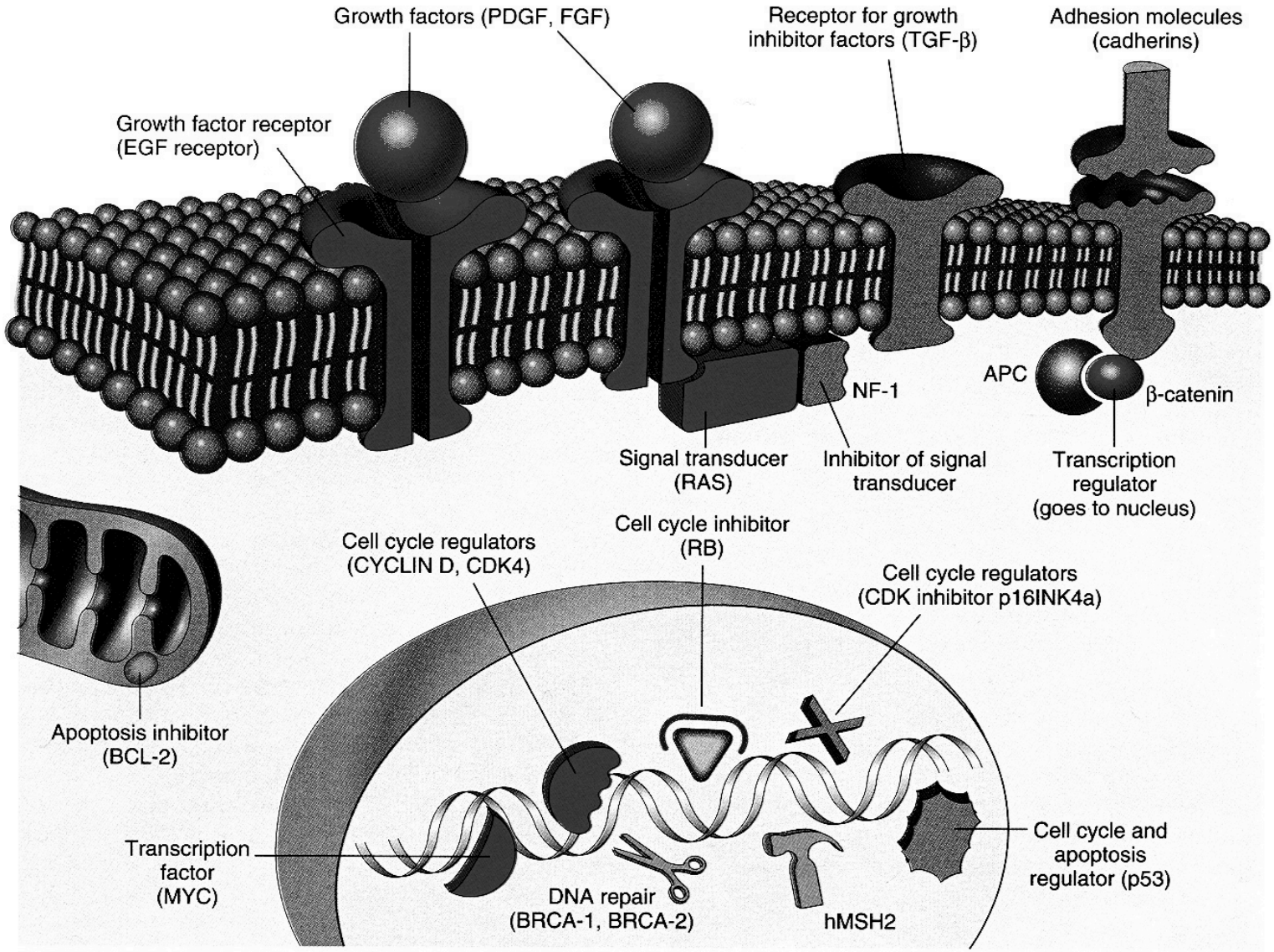
dysplasia

invasive adenocarcinoma

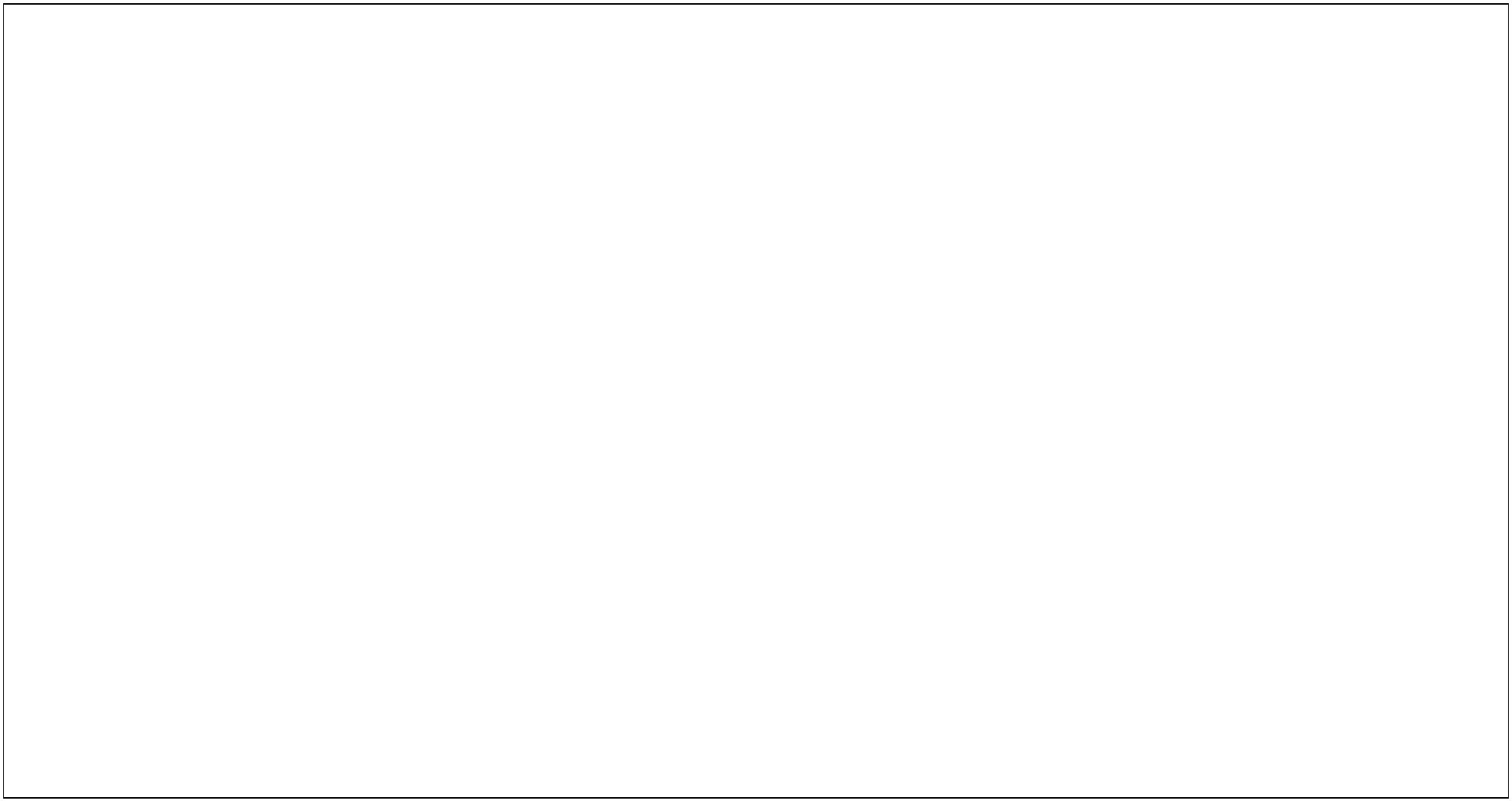
Fill in the blanks.



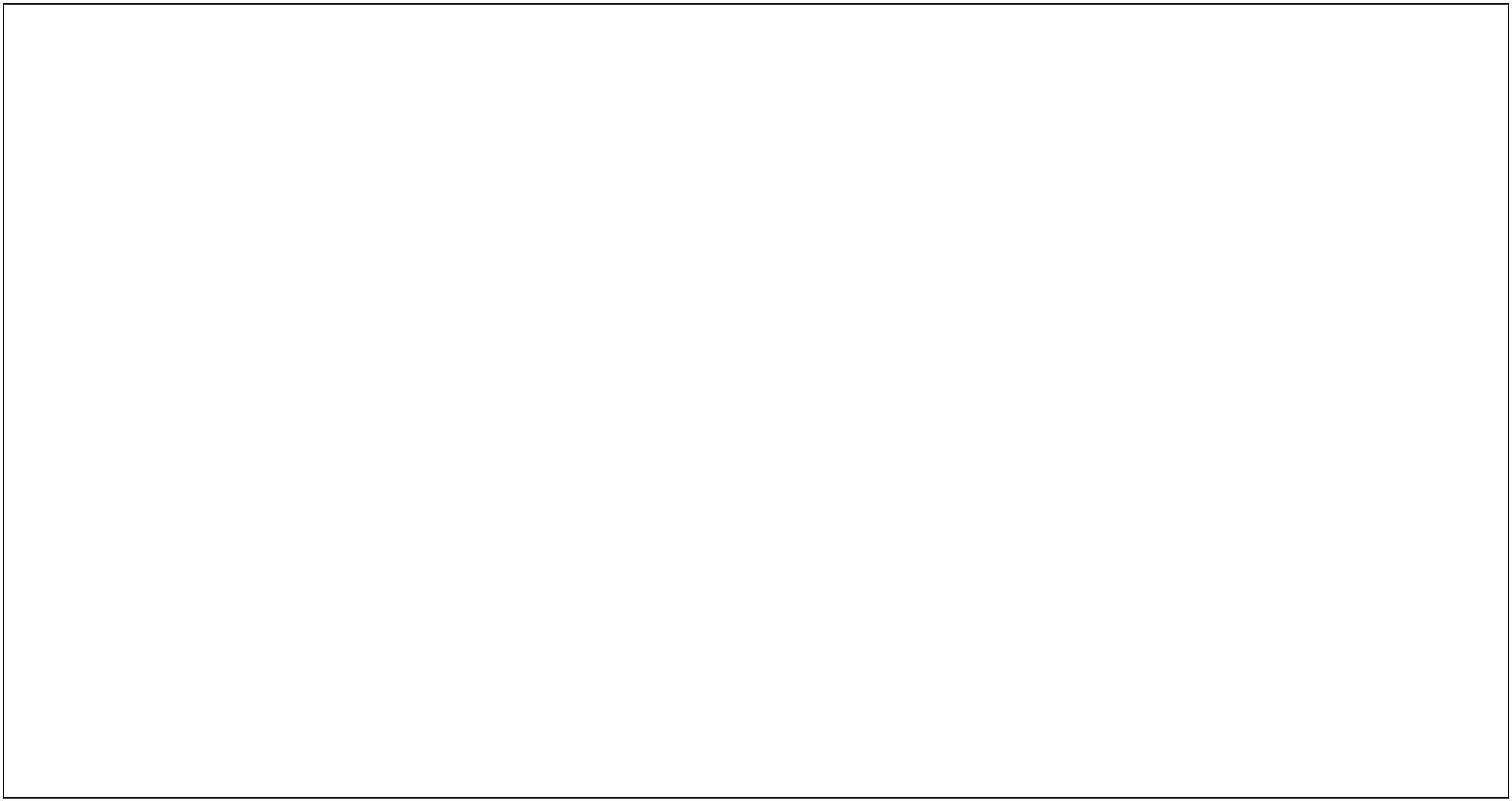
Point out the following: growth factor, growth factor receptor, signal transduction molecule, cell cycle regulators, cell cycle inhibitors, transcription factor, and cell cycle and apoptosis regulator. Where do p53, RAS, RB, cyclin D, and Myc fit in?
Curse your pathology professor for making you memorize this crap.



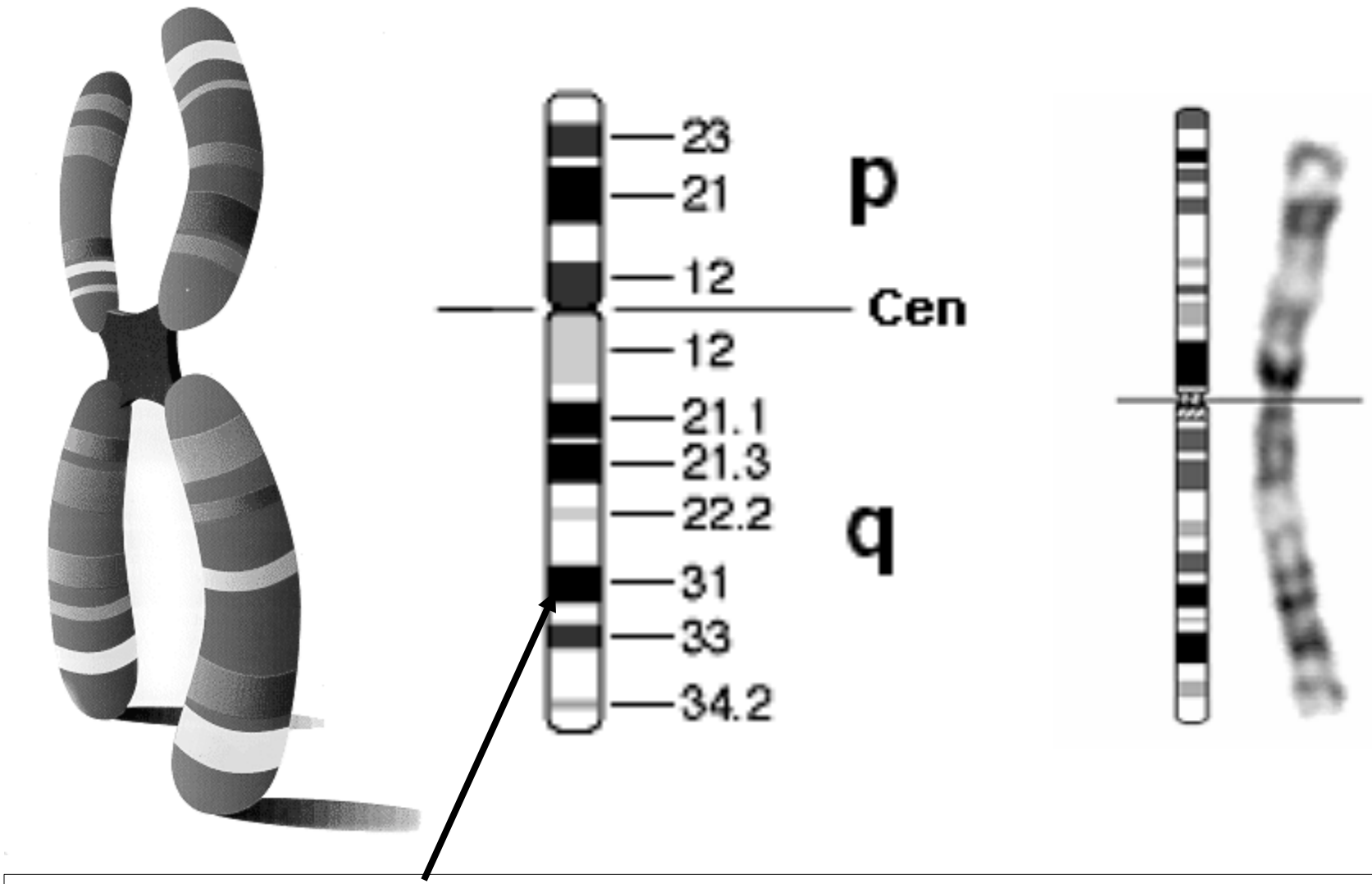
Point out the following: growth factor, growth factor receptor, signal transduction molecule, cell cycle regulators, cell cycle inhibitors, transcription factor, and cell cycle and apoptosis regulator. Where do BCL-2, p53, RAS, RB, cyclin D, and Myc fit in? Curse your pathology professor for making you memorize this crap.



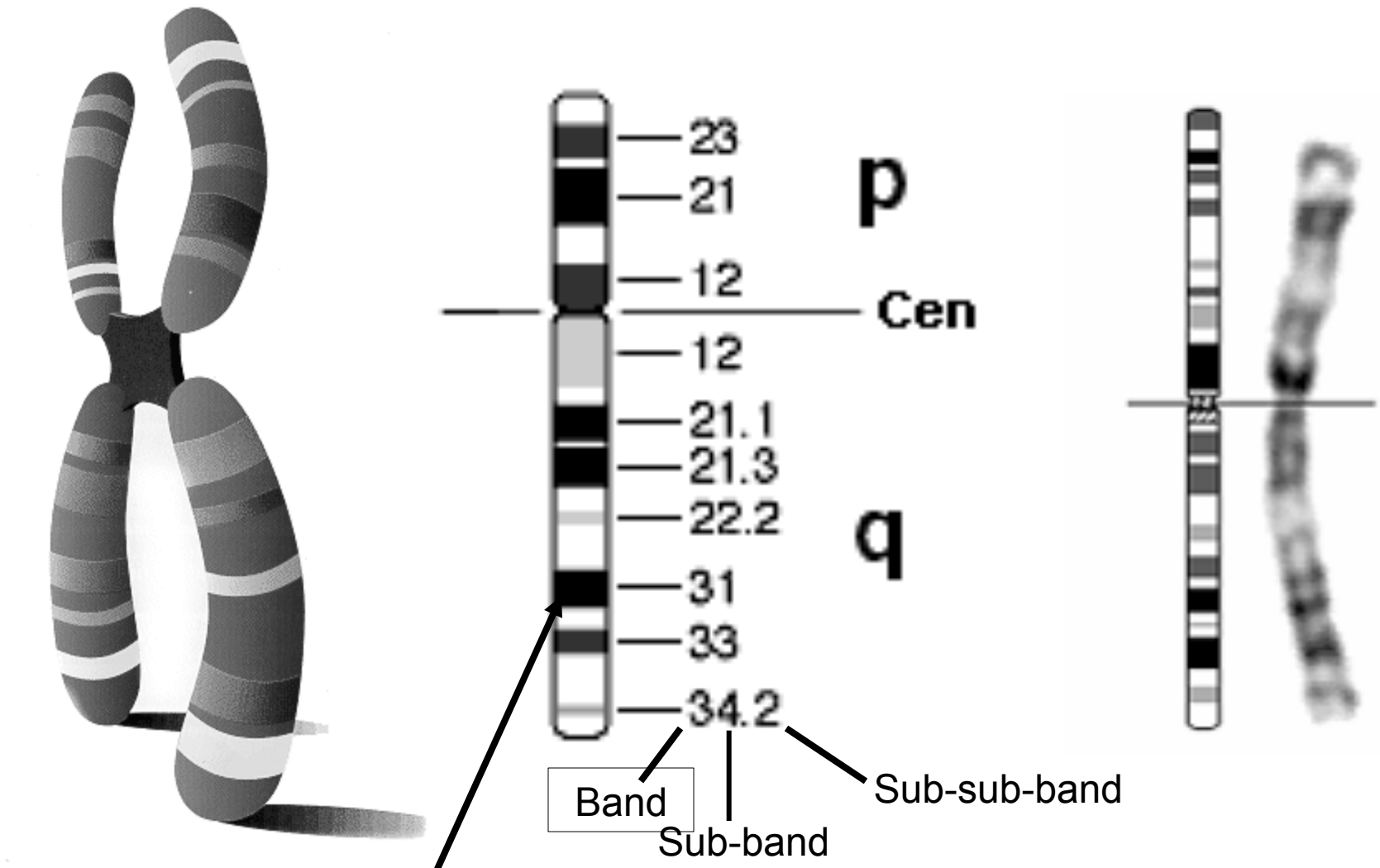
What are the reddish things on the end of the chromosome called?
What do they have to do with neoplasia?



Telomeres. These get shorter with each division of a normal cell – until they get so short that the DNA repair enzymes think there's been a double-stranded DNA break, and the cell stops dividing. Cancer cells use telomerase to maintain nice, long telomeres.

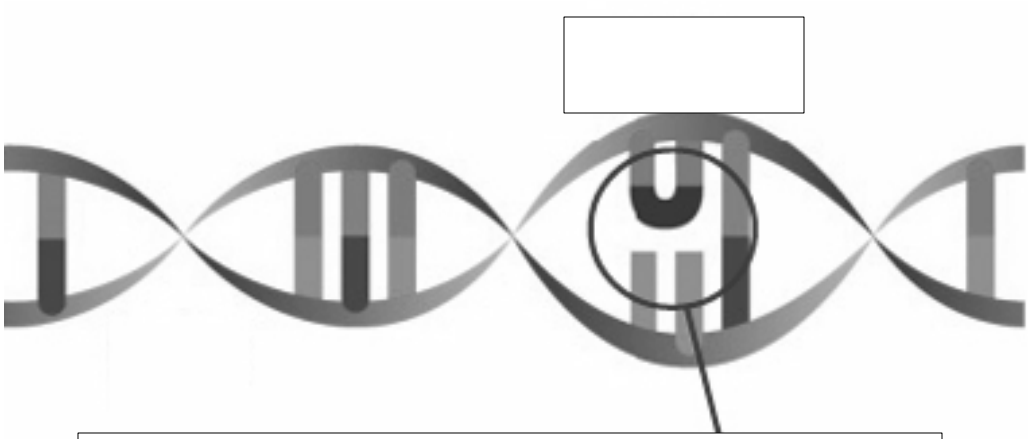


What are these things called? How does the numbering work?



Bands. Each band is labeled with a number, starting at the centromere and working out. There are also sub-bands, numbered in the same way, and sub-sub-bands, also numbered in the same way.

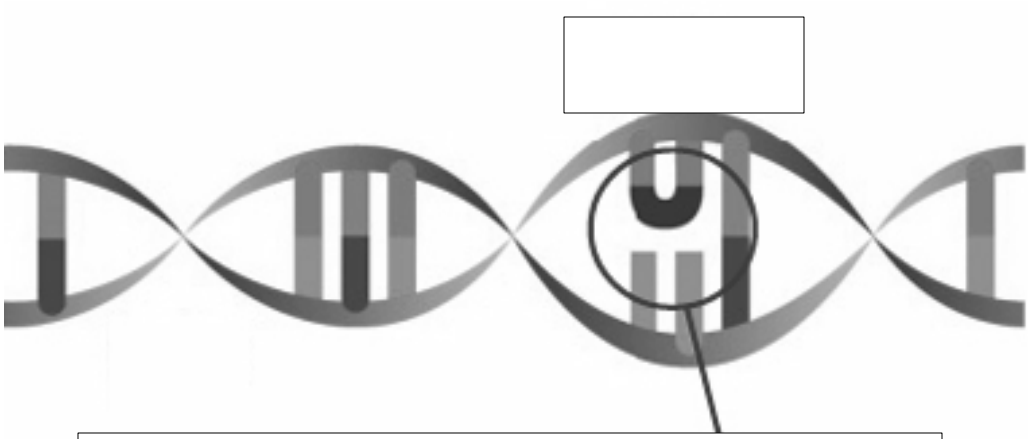
normal DNA



DNA with pyrimidine dimers

What causes the thing in the red circle to happen?

normal DNA



DNA with pyrimidine dimers

UV light. Use sunscreen!