

# Plasma proteins

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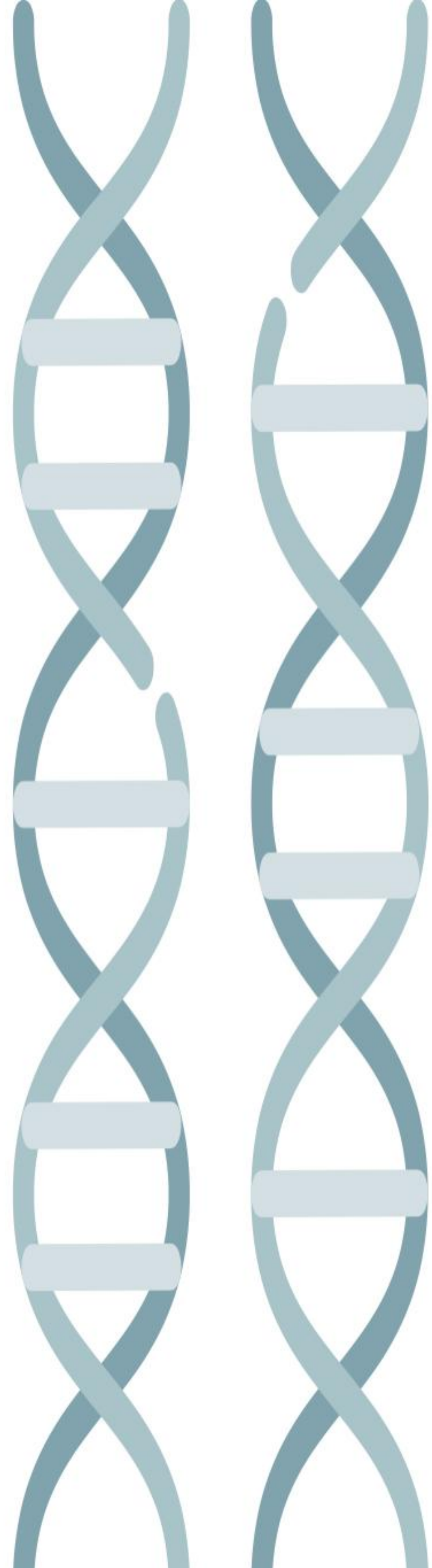
- Main Text
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# Objectives

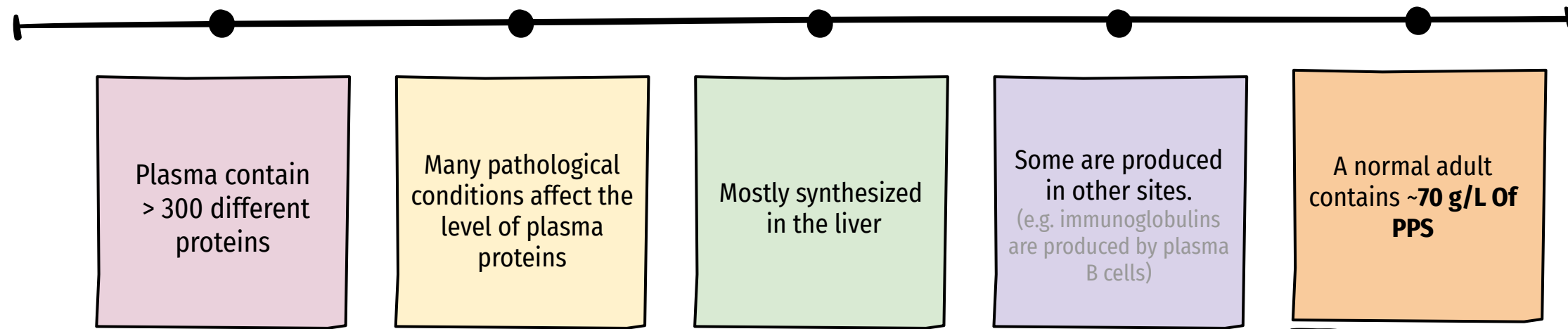
- 🗨️ Identify Types and various functions of plasma proteins .
- 🗨️ Discuss the role of plasma proteins in the diagnosis of diseases and conditions
- 🗨️ Interpret the normal and abnormal electrophoretic patterns of plasma proteins .
- 🗨️ Identify the role positive and negative acute phase proteins in various diseases .

# Overview

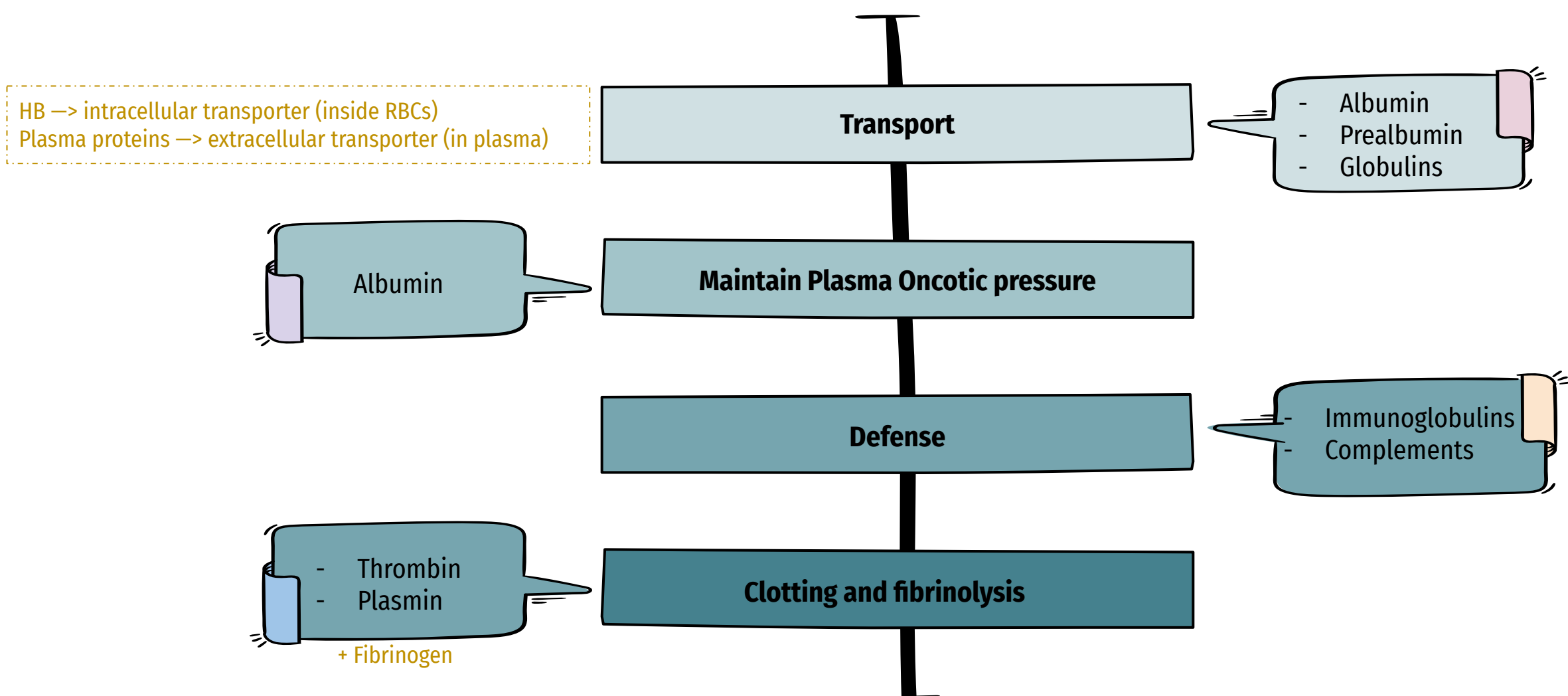
- Functions and characteristics of plasma proteins.
- Measurement of plasma proteins and diagnosis of diseases.
- Electrophoretic patterns of plasma proteins.
- Acute phase proteins.



# Plasma Proteins (PPS)



# Plasma Proteins Functions



# Measurement Of Plasma Proteins

## 1- Quantitative measurement of a specific protein:

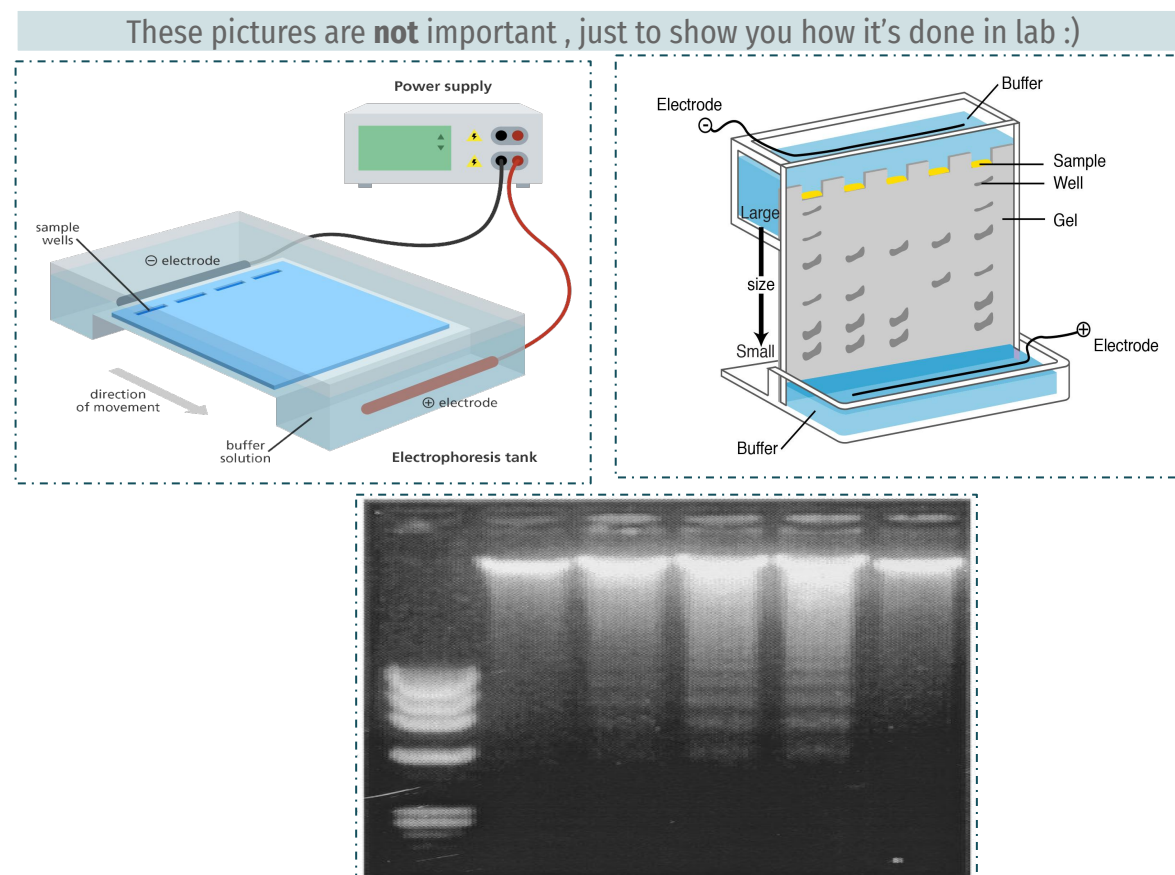
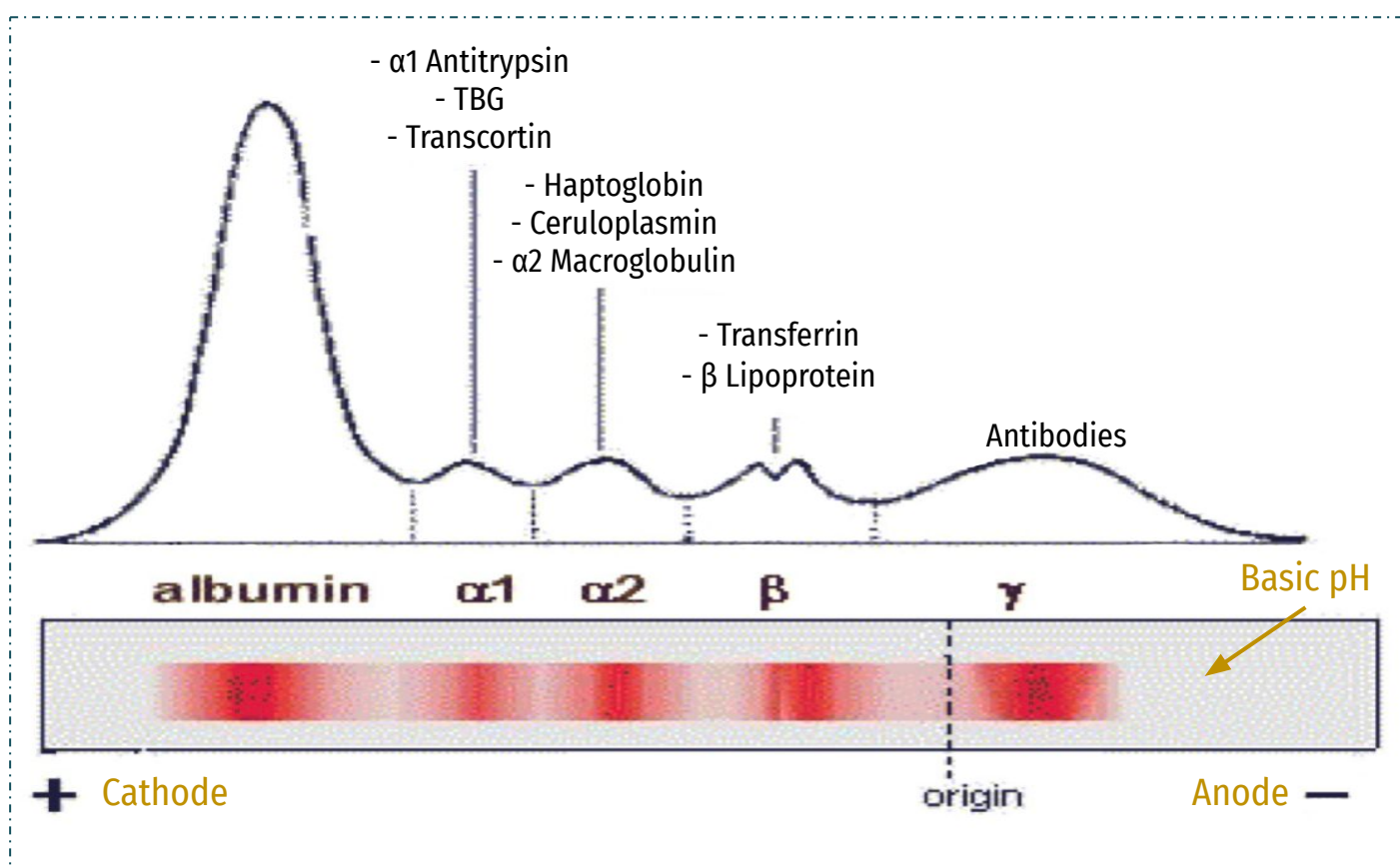
- Chemical or immunological reactions

## 2- Semiquantitative measurement by electrophoresis:

- Proteins are separated by their electrical charges in electrophoresis
- **Five separate bands of proteins are observed**
- These Bands change in disease
- Gives you a general idea about the amount but not exact.
- Using a device called Densitometer.



# Normal Pattern of Plasma Protein Electrophoresis



**Dr explanation:**

The sample is put in an alkaline buffer gel and then you run a current through it. Remember, Currents move from -ve to +ve.

**The Test separates the proteins in the blood based on their Electrical charge & Molecular weight:**

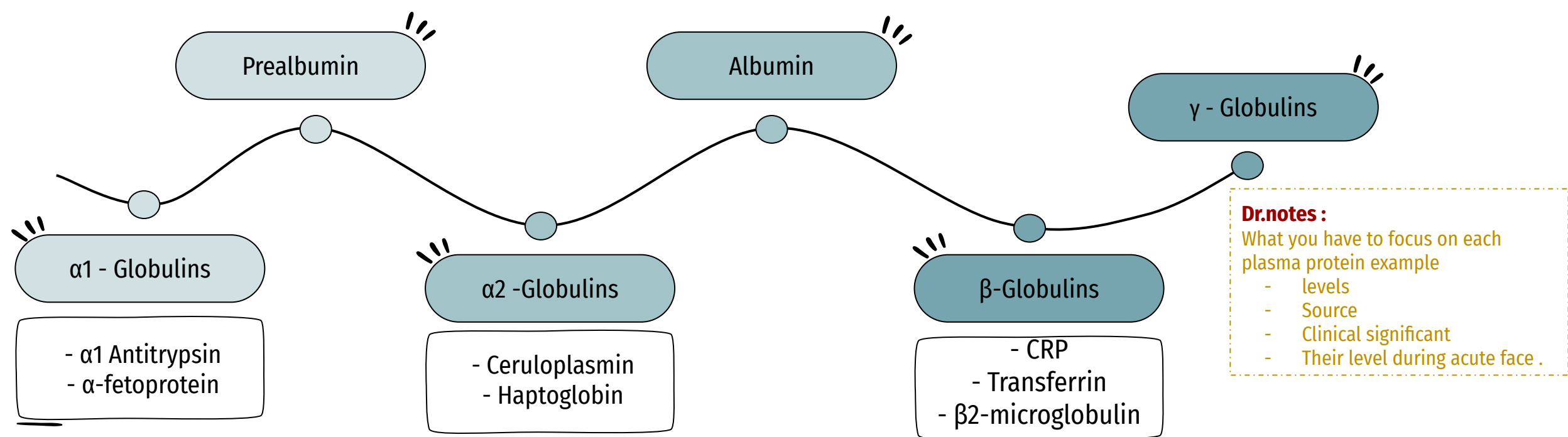
- More negativity → faster to arrive the cathode part
- Less in molecular weight → faster to arrive the cathode part

**So, lighter proteins move further than heavier ones. Producing this ladder like appearance.**

in the graph:

- ❖ **Albumin:** comes 1st (fastest) cause it has the smallest size.
- ❖ **Gamma (γ):** comes last (slowest) cause it's the largest.

## Types of Plasma Proteins



**Dr.notes:**  
What you have to focus on each plasma protein example

- levels
- Source
- Clinical significant
- Their level during acute face.

## Prealbumin (Transthyretin):

It's not albumin precursor!!!  
They are not chemically related, it called because it appears before albumins in Electrophoresis but we don't see it because it's very small (low amount).

Information	Function	Lowered Levels In:
<ul style="list-style-type: none"> <li>• Migrates faster than albumin in electrophoresis</li> <li>• Separated by immunoelectrophoresis</li> <li>• Short half-life (2 days)</li> </ul>	<p>A transport protein for:</p> <ol style="list-style-type: none"> <li>1. Thyroid Hormone <i>that's why we call it transthyretin.</i></li> <li>2. Retinol (vitamin A)</li> </ol>	<ol style="list-style-type: none"> <li>1- Liver disease <b>because they can't produce prealbumin.</b></li> <li>2- Nephrotic Syndrome</li> <li>3- Acute phase inflammatory response <b>-ve acute phase protein</b></li> <li>4- malnutrition</li> </ol>

# Albumin

Information	Function
<p>1- most abundant plasma protein (~40 g/L) in normal adult. <b>It resembles 65% of plasma protein in our body and 35% resembles the rest proteins.</b></p> <p>2- Synthesized in the <b>liver</b> as <b>preproalbumin</b> and <b>secreted as albumin.</b></p> <p>3- Half-life in the plasma: 20 Days. <b>longer than prealbumin</b></p> <p>4- Decreases rapidly in injury, infection and surgery.</p>	<p>1- Maintains oncotic pressure:</p> <ul style="list-style-type: none"> <li>- The osmotic pressure exerted by plasma proteins that pulls water into the circulatory system.</li> <li>- maintains fluid distribution in and outside cells and plasma volume.</li> </ul> <p>2- <b>80 % of plasma oncotic pressure is maintained by albumin, therefore this is the main function of Albumin.</b></p> <p>3- A non-specific carrier of: Hormones, Calcium, Free fatty acid, drugs, etc.</p> <p>4- Tissue cell can take up albumin by pinocytosis (<b>cellular drinking</b>) where it is hydrolyzed to amino acids.</p> <p>5- Useful in treatment of liver diseases, hemorrhage, shock and burns. <b>in burns: patients lose their skin and lose a lot of amount of plasma, Therefore Albumin will be the treatment in this situation.</b></p>

## Abnormalities:

### 1- Hypoalbuminemia

#### Causes:

- 1- Decrease Albumin synthesis (liver cirrhosis, malnutrition)
- 2- Increased losses of albumin:
  - Increased catabolism in infections
  - Excessive excretion by the kidneys (Nephrotic syndrome) **there's no filtration of Albumin so Albumin excreted in urine.**
  - Excessive loss in bowel (bleeding)
  - Severe burns (plasma loss in the absence of skin barrier)

#### Effects:

- 1- Edema due to low oncotic pressure
  - Albumin levels drops in liver disease causing low oncotic pressure **albumin is the main plasma protein and it's the one mainly responsible of oncotic pressure so when albumin level decrease water will shift to tissue and cause edema.**
  - Fluid moves into the interstitial spaces causing edema.
- 2- Reduced transport of drugs and other substances **that are binding with Albumin in plasma in low level of Albumin drugs that transport in blood by Albumin will take more time and increase half life of the drug.**
- 3- Reduced protein-bound calcium
  - Total plasma calcium level drops
  - Ionized calcium level may remain normal **because it's not bound to Albumin.**

**Dr. notes:** We have two types of drugs or the hormones or any substances in plasma:

- Bioavailable (e.g drug) → Free of Albumin
- Non bioavailable (e.g drug) → Bind to Albumin

Why we call the ones that bind to Albumin non bioavailable? because it's present in plasma but it can NOT go to the cell and do its action because of its binding with Albumin.

(وظيفة الألبومين عبارة عن ديدة والديدة مانقدر نوصلها وسط الحوش لازم تكون برا تنزل الحمولة وتمشي فالتالي اذا كانت الديدة مو راضية تنزل الحمولة البضاعة ماراح تقدر تدخل وسط الحوش)

Low Albumin → Decrease the non-bioavailable & increase bioavailable. (sometimes bioavailability of drug when it increased too much it will cause side effects and toxicity)

- ❖ Usually the proteins that responsible for defense are the ones raise during acute phase. And other proteins responsible for other things like transport are decrease.

### 2- Hyperalbuminemia

1- **No clinical conditions are known** that cause the liver to produce large amounts Of albumin

2- The only cause of hyperalbuminemia is **dehydration.**

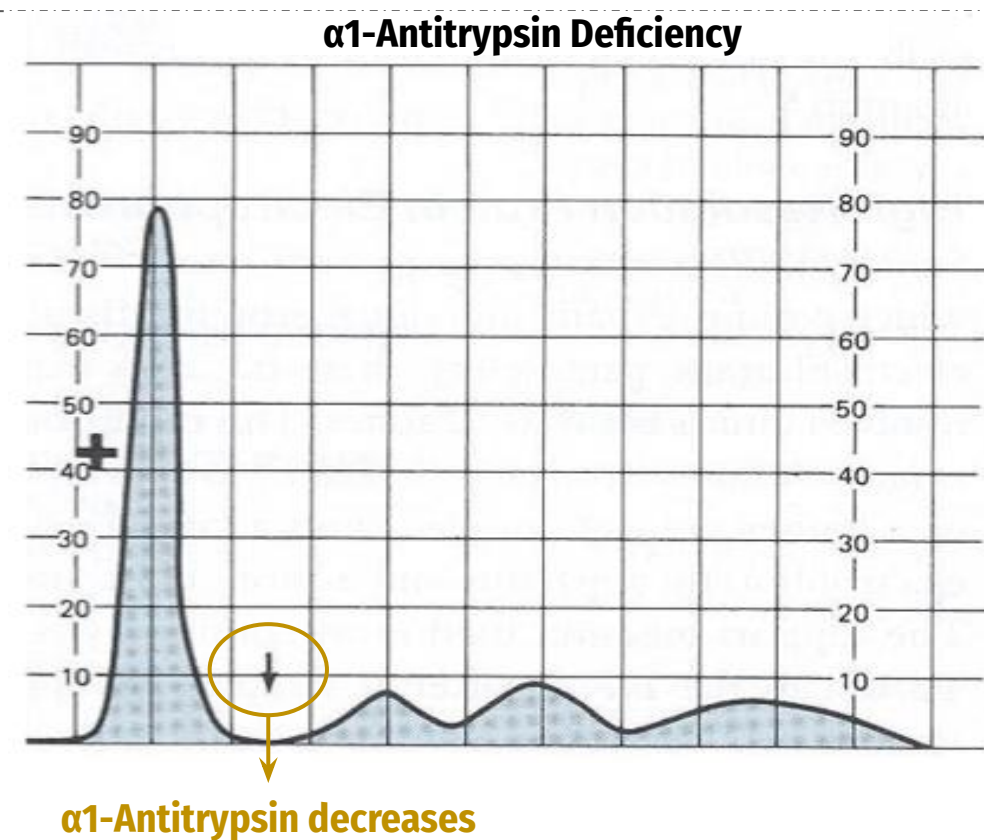
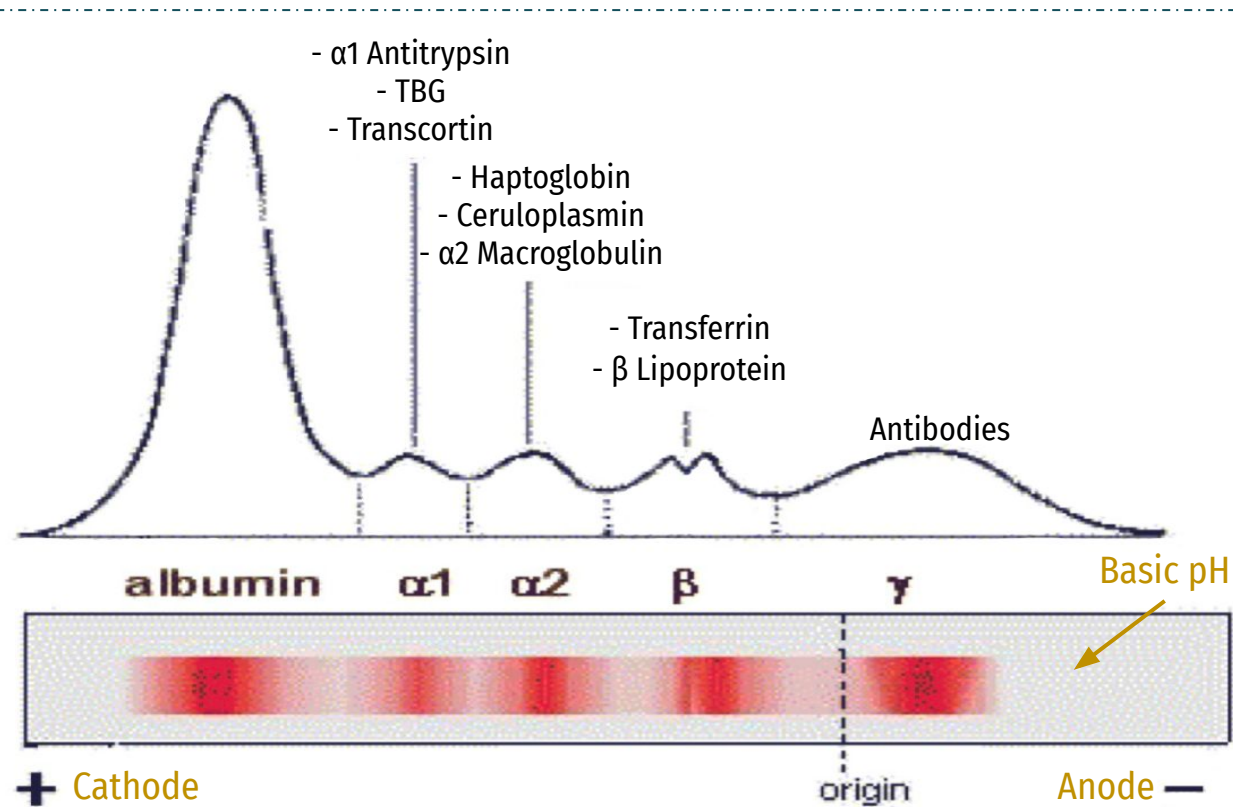
**If there is dehydration → Intravascular fluid will decrease → Albumin amount will be high → Hyperalbuminemia.**



# α1-Antitrypsin

Information	Function	Genetic Deficiency <small>Mainly associated with z type</small>
<ol style="list-style-type: none"> <li>Synthesized by the liver and macrophages.</li> <li>Over 30 types are known.</li> <li>The most common is <b>M type</b></li> </ol>	<ol style="list-style-type: none"> <li>An Acute-phase protein that inhibits <b>proteases</b> <small>(Protease enzymes that produced by organisms to destroy tissues)</small></li> <li>proteases are produced endogenously and from leukocytes and bacteria. <ul style="list-style-type: none"> <li>Digestive enzymes (trypsin, chymotrypsin)</li> <li>Other proteases (elastase, thrombin)</li> </ul> </li> <li>Infection leads to protease release from bacteria and from leukocytes.</li> </ol>	<ol style="list-style-type: none"> <li>Synthesis of the defective α1-Antitrypsin occurs in the liver but it <b>can not secrete the protein.</b></li> <li>α1-Antitrypsin accumulates in hepatocytes and is deficient in plasma.</li> </ol> <p>يتصنع بالكبد وتمام الوضع ولكن ما يصير له افراز في التالي راح يتراكم بالكبد وينقص بالبلازما وهذا راح يؤدي الى:</p> <p style="text-align: center;">↓</p>

Laboratory Diagnosis	Clinical Consequences of α1-Antitrypsin Deficiency
<ol style="list-style-type: none"> <li>Lack of α1-Antitrypsin band in protein electrophoresis</li> <li>Quantitative measurement of α1-Antitrypsin by: <ul style="list-style-type: none"> <li>Radial immunodiffusion</li> <li>isoelectric focusing</li> <li>nephelometry</li> </ul> </li> </ol> <p><small>(Male Dr: Only know the names of these techniques you don't have to know any more information rather than this, we will study the electrophoresis only)</small></p>	<ul style="list-style-type: none"> <li>Neonatal jaundice with evidence of cholestasis.</li> <li>Childhood liver cirrhosis → <b>synthesis then accumulated in body so it start to damage liver</b></li> <li>Pulmonary emphysema<sup>1</sup> in young adults <b>specially smokers.</b></li> <li><b>These things happen because of the unopposed protease.</b></li> </ul> <p>1: This happens because there is <b>no α1 Antitrypsin</b> that inhibits protease in bacterial infection conditions so protease will damage the alveoli cells in the lung and cause pulmonary emphysema.</p>



- ❖ Picture 1 shows a normal Serum Electrophoresis Pattern.
- ❖ Pictures 2 shows α1-Antitrypsin \ α1-globulin is gone. which means the patient has no α1-Antitrypsin.

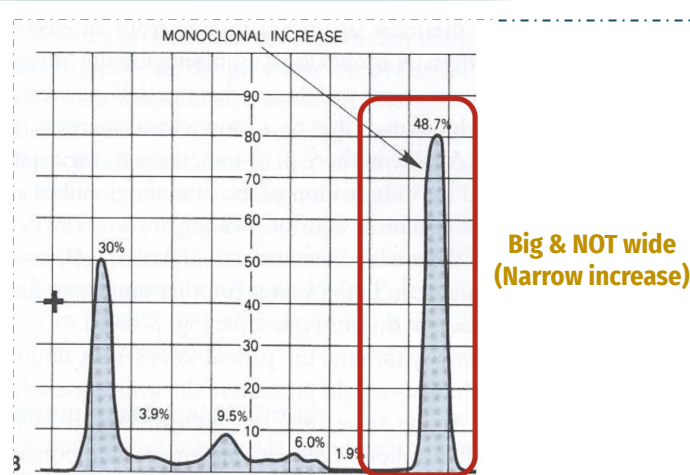
Plasm protein	About	pathology
<b>a-Fetoprotein (AFP)</b>	<ul style="list-style-type: none"> <li>Synthesized in the <b>developing embryo and fetus</b> by the parenchymal cells of the liver.</li> <li>AFP levels decrease gradually during intra-uterine life and reach adult levels at birth. <i>يكون عالي في مرحلة تكوّن الجنين ويبدأ يقل عند الولادة</i></li> <li>Function is unknown but it may protect fetus from immunologic attack by the mother &amp; no known physiological function in adult.</li> </ul>	<ul style="list-style-type: none"> <li><b>Elevated</b> maternal AFP levels are associated with: <ul style="list-style-type: none"> <li>- <b>Neural tube defect (spina bifida), anencephaly</b></li> </ul> </li> <li><b>Decreased</b> maternal AFP levels are associated with: <ul style="list-style-type: none"> <li>- Increased risk of <b>Down's syndrome</b></li> </ul> </li> <li>AFP is a <b>tumor marker</b> for: <ul style="list-style-type: none"> <li>- <b>Hepatoma and testicular cancer.</b></li> </ul> </li> </ul>
<b>Ceruloplasmin</b>	<ul style="list-style-type: none"> <li>Synthesized by the liver &amp; <b>contains &gt;90% of serum copper</b> so it related to copper transporting.</li> <li>An oxidoreductase that inactivates ROS causing tissue damage in acute phase response, <b>so we can consider Ceruloplasmin as Antioxidant.</b></li> <li>Important for iron absorption from the intestine <b>BUT it's not the main transporter for Iron</b>, the main one will talk about it <i>يعني ناقل مساعد موب اساسي</i></li> </ul>	<ul style="list-style-type: none"> <li><b>Wilson's disease:</b> Due to low plasma levels of ceruloplasmin, copper is accumulated in the liver and brain. <i>because as we said the copper binds to ceruloplasmin in plasma so if there's no ceruloplasmin in the plasma the copper will not be transported then it will be accumulated in liver and brain.</i></li> </ul>
<b>Haptoglobin</b>	<ul style="list-style-type: none"> <li>Synthesized by the liver &amp; binds to free hemoglobin to form complexes that are metabolized in the reticuloendothelial system (RES).</li> <li>Limits iron loss by preventing Hb loss from kidneys <i>Free Hemoglobin is the hemoglobin that located outside the cell. When the RBCs destroyed, our body doesn't want to loss the content (Iron) that found in HB therefore Haptoglobin comes to plasma to bind with free HB and destroy it and take the iron from HB, Now there is preventing loss of Iron from kidneys.</i></li> </ul>	<ul style="list-style-type: none"> <li>Plasma level <b>decreases</b> during <b>hemolysis.</b> <i>ليه؟ لان اذا صار فيه hemolysis يصير فيه تكسير كثير لل RBCS وبالتالي يصير فيه كمية فري هيمغلوبين عالية فراح يُستهلك ال Haptoglobin عشان يرتبط بالهيمغلوبين ويكسره وياخذ ال Iron حقه.</i></li> </ul>
<b>β2-Microglobulin</b> <i>Very small protein</i>	<ul style="list-style-type: none"> <li><b>A component of human leukocyte antigen (HLA)</b> &amp; present on the surface of lymphocytes and most nucleated cells.</li> <li>Filtered by the renal glomeruli due to its small size but most (&gt;99%) is reabsorbed.</li> </ul>	<ul style="list-style-type: none"> <li><b>Elevated</b> serum levels are found in: <ul style="list-style-type: none"> <li>- Overproduction in disease; severe inflammation (infections, SLE, and rheumatoid arthritis)</li> </ul> </li> <li>May be a <b>tumor marker</b> for: <ul style="list-style-type: none"> <li>- <b>Leukemia, lymphomas, multiple myeloma.</b></li> </ul> </li> </ul>
<b>Transferrin</b> <i>its function related to Transporting</i>	<ul style="list-style-type: none"> <li><b>A major iron-transport</b> protein in plasma 30% saturated with iron &amp; Iron deficiency results in increased hepatic synthesis <b>because liver try to compensate.</b></li> <li><b>A negative</b> acute phase<sup>1</sup> protein. (means decrease in acute phase).</li> </ul>	<ul style="list-style-type: none"> <li>Plasma level <b>drops</b> in: <ul style="list-style-type: none"> <li>- Malnutrition, liver disease, inflammation, malignancy.</li> </ul> </li> </ul>
<b>C-Reactive Protein(CRP)</b>	<ul style="list-style-type: none"> <li><b>A Positive</b> acute-phase<sup>1</sup> protein synthesized by the liver &amp; Important for <b>phagocytosis</b> by cover the bacteria so <b>macrophages deal with it</b>.</li> </ul> <p><small>1- Acute phase proteins will be discussed in next slide.</small></p>	<ul style="list-style-type: none"> <li><b>High</b> plasma levels are found in many inflammatory conditions such as <b>rheumatoid arthritis.</b></li> <li><b>A marker for ischemic heart disease.</b></li> </ul>

## Hypergammaglobulinemia

### Monoclonal Hypergammaglobulinemia (Paraproteinemia)

- Proliferation of a **single B-cell** clone produces a **single type of Ig**.
- Appears as a separate dense band (**paraprotein or M band**) in electrophoresis.
- Paraproteins are characteristic of **malignant B-cell proliferation.**
- Clinical condition:**
  - **multiple myeloma.**
  - **3M: Monoclonal - M band - Multiple myeloma**

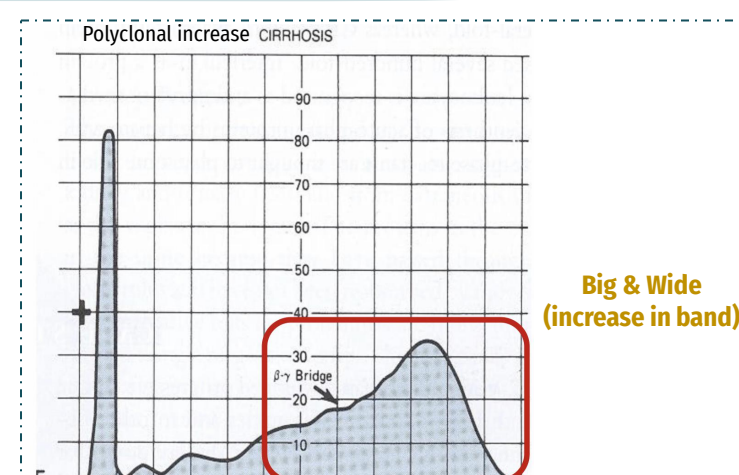
#Med438



### Polyclonal Hypergammaglobulinemia (B cells)

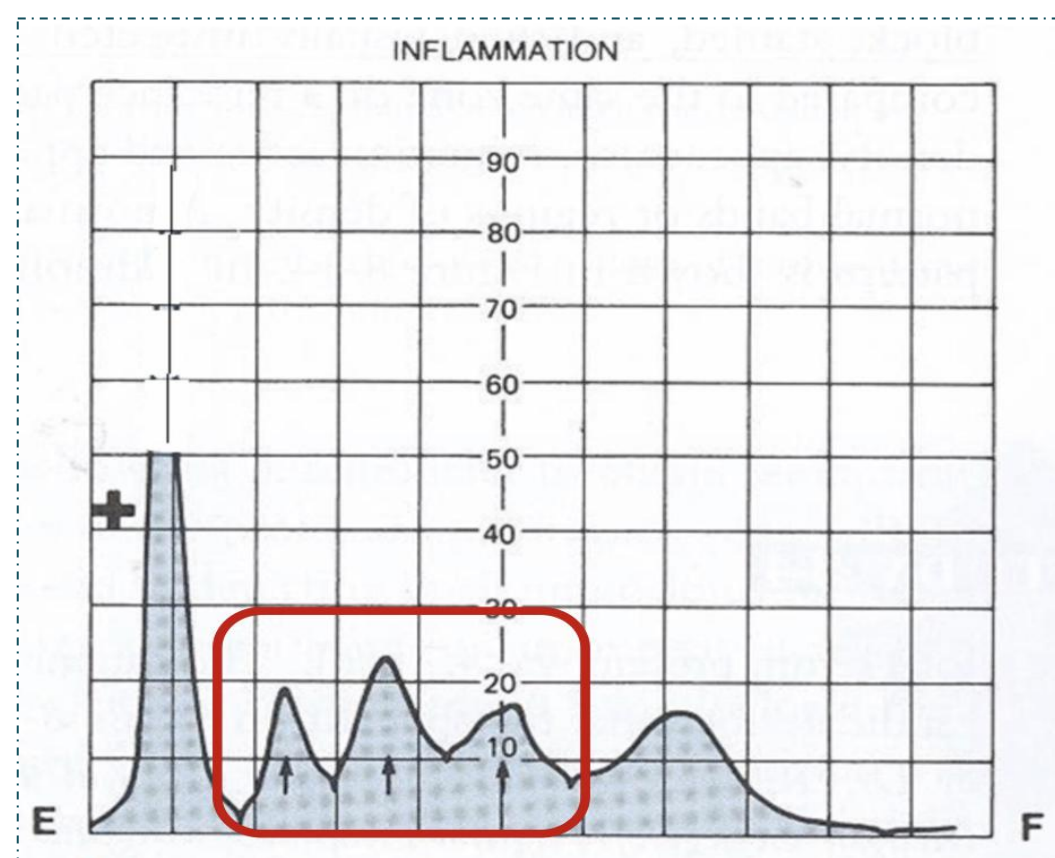
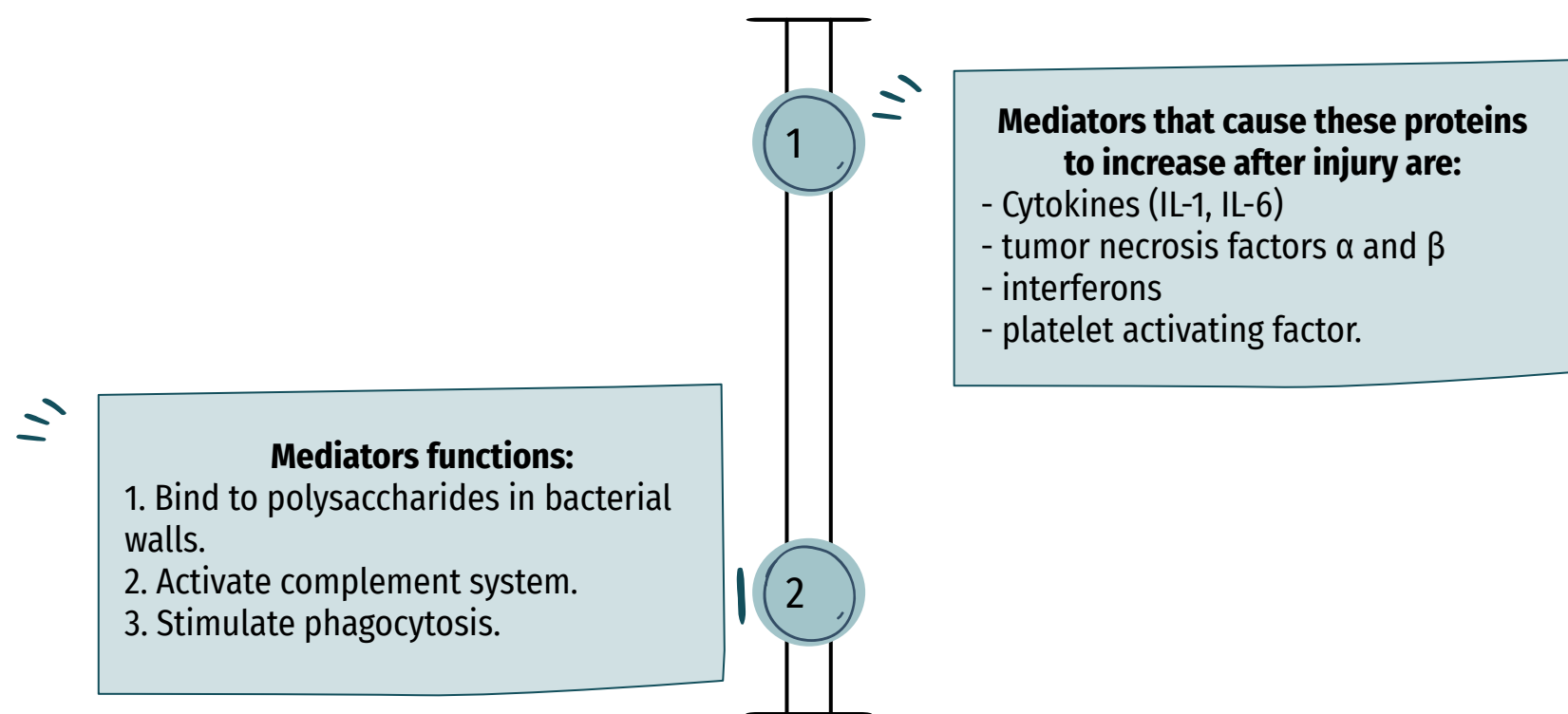
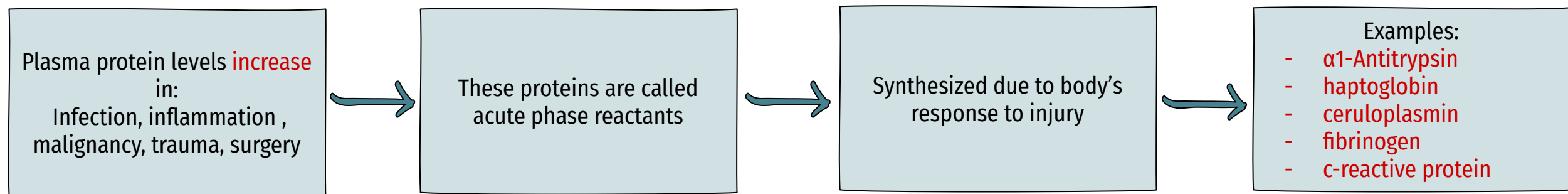
- Stimulation of **many clones of B-cells** produce a **wide range of antibodies** (IgM, IgA, IgG, IgE, IgD).
- γ-globulin band** appears **large** in electrophoresis.
- Clinical conditions:
  - **Acute and chronic infections**
  - **Autoimmune diseases**
  - **Chronic liver diseases** (Like Cirrhosis).

Polyclonal means: أكثر من نوع من الالتي بوتي (IgM, IgA, IgG, IgE, IgD)

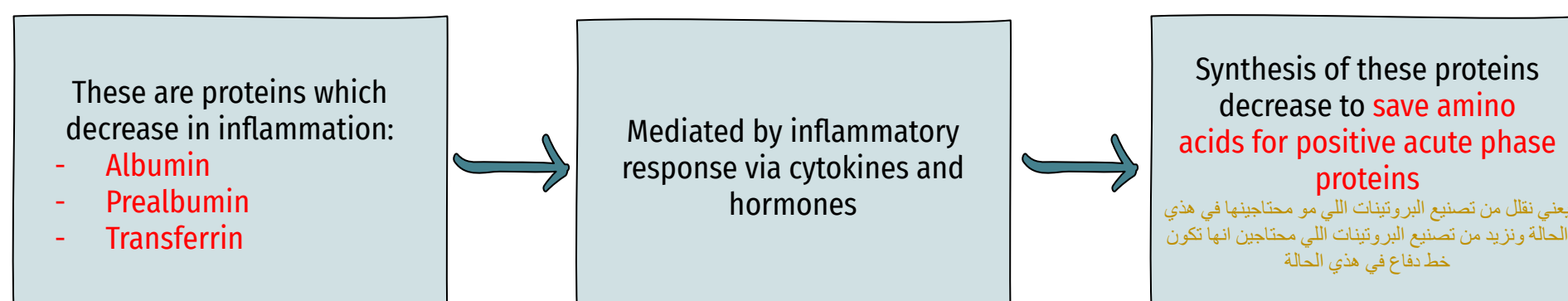




# Positive Acute Phase Proteins (PAPP)



# Negative Acute Phase Proteins



**Dr. note:**

Acute phase inflammatory response is the first response that you will have within 24 hours of an acute insult/infection. your body will try to fight the insult by synthesizing certain proteins in increased amounts (Positive Proteins) while decreasing the amounts of other proteins (Negative proteins).



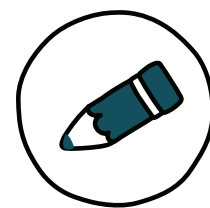
# Take Home Messages



Plasma proteins play essential roles in a number of cellular functions.



They possess diagnostic significance in identifying various pathological conditions.



## Summary

Protein	Function
PreAlbumin	Transport protein to thyroid hormone and Retinol.
Albumin	Responsible for colloid osmotic pressure; major contributor to blood viscosity; transports lipids, hormones, calcium, and other solutes; buffer blood PH.
$\alpha$ 1-Antitrypsin	Anti proteases.
A- fetoprotein	Unknown but it May protect fetus from immunoglobulin attack by the mother.
Ceruloplasmin	contains >90% of serum copper also it's Important in iron absorption from intestine.
Haptoglobin	Limits iron loss by preventing Hb loss from kidneys (recycling).
$\beta$ 2-Microglobulin	-
Transferrin	It's a major iron-transport protein in plasma 30% saturated with iron.
C-Reactive Protein(CRP)	Important for phagocytosis.



# MCQs

**1- Which of the following is a positive acute phase protein synthesized by the liver and important for phagocytosis:**

- |                            |                |               |                |
|----------------------------|----------------|---------------|----------------|
| A- C-Reactive protein(CRP) | B- Transferrin | C-Haptoglobin | D- Antitrypsin |
|----------------------------|----------------|---------------|----------------|

**2- Which of the following causes Hyperalbuminemia:**

- |                    |                           |                |          |
|--------------------|---------------------------|----------------|----------|
| A- Liver cirrhosis | B- Increased albumin loss | C- Dehydration | D- Burns |
|--------------------|---------------------------|----------------|----------|

**3- Lowered Prealbumin (Transthyretin) levels can be seen in which of the following cases:**

- |                |          |                              |                       |
|----------------|----------|------------------------------|-----------------------|
| A- Dehydration | B- Burns | C- Childhood liver cirrhosis | D- Nephrotic syndrome |
|----------------|----------|------------------------------|-----------------------|

**4-Proliferation of a single B-cell clone produces a single type of Ig and appearance of M band**

- |                                     |                  |                                     |                |
|-------------------------------------|------------------|-------------------------------------|----------------|
| A-Polyclonal hypergammaglobulinemia | B- Down syndrome | C-Monoclonal Hypergammaglobulinemia | D-None of them |
|-------------------------------------|------------------|-------------------------------------|----------------|

**5- Transferrin is A major iron-transport protein in plasma which is a:**

- |                                 |                                |                               |                |
|---------------------------------|--------------------------------|-------------------------------|----------------|
| A- Negative acute phase protein | B-Positive acute phase protein | C-Neutral Acute phase protein | D-None of them |
|---------------------------------|--------------------------------|-------------------------------|----------------|

**6-Decreased maternal alpha Fetoprotein levels & low plasma levels of Ceruloplasmin respectively indicate:**

- |                                      |                                       |                        |                                 |
|--------------------------------------|---------------------------------------|------------------------|---------------------------------|
| A-Wilson's disease & Down's syndrome | B- Down's syndrome & Wilson's disease | C-Leukemia & Hemolysis | D-Neural tube defect & Hepatoma |
|--------------------------------------|---------------------------------------|------------------------|---------------------------------|

Answers key

- 1- A      2- C      3- D      4- C      5-A      6- B



## SAQs

### 1- Name two of the the clinical consequences of $\alpha$ 1-Antitrypsin deficiency ?

Answer:

- 1- Neonatal jaundice with evidence of cholestasis
- 2- Childhood liver cirrhosis

### 2- Mention Positive and Negative Acute Phase Proteins? And which of them decreases and why?

Answer:

Positives: $\alpha$ 1-Antitrypsin, haptoglobin, ceruloplasmin, fibrinogen, c-reactive protein

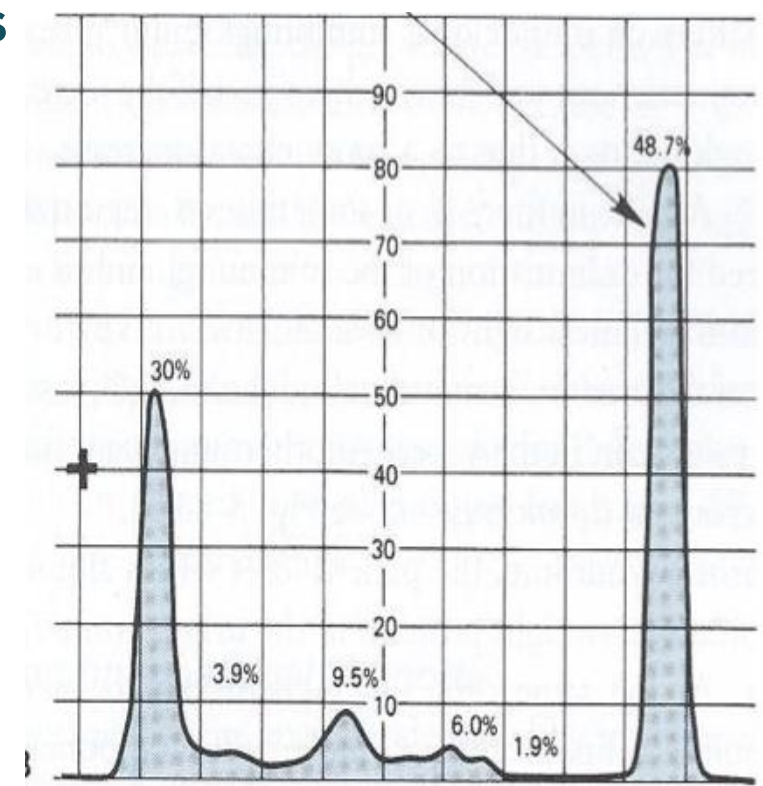
Negatives:Albumin, prealbumin, transferrin

Negative Acute Phase Proteins are the one to decrease to save amino acids for positive ones

### 3- Based on the Electrophoresis on the right, answer the following: 1)what is probably the condition of this patient? 2)what do you observe? 3)What malignant cell causes it?

Answer:

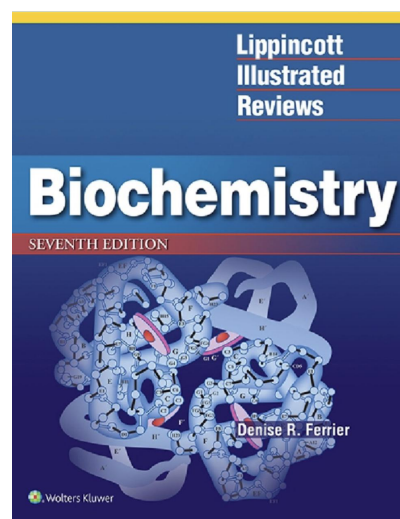
- 1)multiple myeloma 2)Appears as a separate dense band (paraprotein or M band) in electrophoresis. 3)malignant B-cell proliferation.



## Resources



Click on the book to download the resource





## Leaders



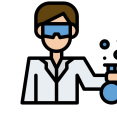
**Albandari Alanazi**



**Sara Alharbi**



**Abdulaziz Alrabiah**



**Khalid Almutlaq**

## Reviser

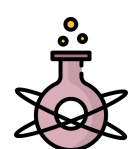
**Abdulaziz Alghuligah**

## NoteTakers

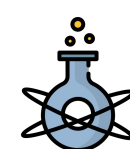
**Asma Alamri**

**Homoud Algadheb**

## Members



**Noura Bamarei**



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**Alaa Alsulmi**



Special thanks to Fahad AlAjmi for designing our team's logo.