MEDICAL EDUCATION RESOURCE

Plasma Proteins

Plasma Proteins :

Serum Electrophoretic Pattern — Normal & Abnormal

(All points grounded in the retrieved text)

Normal Pattern

- Serum proteins separate into **5 major fractions** on agar electrophoresis:
  Albumin ? ?1 ? ?2 ? ? ? ?
  (Albumin has the **maximum mobility**, ?-globulins have **minimum mobility**)

- **Gamma globulins** contain **immunoglobulins** (antibodies).
  ?1 mainly contains **?1-antitrypsin**.
  ?2 mainly contains **?2-macroglobulin**.
  ? contains **LDL**.

Abnormal Electrophoretic Patterns

- **Chronic infections:** smooth, wide-based **?-globulin increase**.

- **Multiple myeloma:** sharp **M-spike** due to monoclonal immunoglobulins.

- **Plasma (instead of serum): Fibrinogen** forms a prominent band in ? region (may mimic M-band).

- **Primary immune deficiency:** reduced ?-globulin fraction.

- **Nephrotic syndrome:** massive loss of small proteins ? **prominent ?2 band** (macroglobulin retained).
- **Cirrhosis:** low albumin, wide ? band; **?–? bridging**.
- **CLL:** reduced ?-globulins.
- **?1-antitrypsin deficiency:** thin or missing ?1 band.

Albumin

(Grounded in PDF lines)

- Major plasma protein; synthesized in liver.
- Single polypeptide chain; molecular weight ~69,000 Da.
- Present in **CSF and interstitial fluid** because it can leave circulation.
- **Half-life:** ~20 days; liver synthesizes ~12 g/day (25% of hepatic protein synthesis).
- Important functions:
  - Maintains **oncotic pressure**
  - Transports numerous substances (fatty acids, bilirubin, drugs, Ca^{2}?, hormones).

Transport Proteins (Carrier Proteins)

(Based on Table 28.1)

Major Transport Proteins & Their Functions

- **Albumin:** transports fatty acids, bilirubin, calcium, drugs like aspirin, sulphonamides.
- **Prealbumin (Transthyretin):** transports steroid hormones, thyroxine, retinol.
  Short half-life (1 day).
- **Retinol Binding Protein (RBP):** transports vitamin A; indicator of protein turnover.
- **Thyroxine Binding Globulin (TBG):** transports T3, T4.
- **Transcortin (CBG):** transports cortisol and corticosterone; increased in pregnancy.
- **Haptoglobin:** binds free hemoglobin; low in hemolysis; acute phase protein.
- **Transferrin:** transports iron; prevents iron loss.
- **Hemopexin:** binds free heme; prevents iron loss.
- **HDL / LDL:** lipoprotein carriers for cholesterol & lipids.

Polymorphism

(Grounded in PDF)

- A protein shows **different phenotypes in a population**; only one form seen in each person.
- Seen in:
  - **Haptoglobin** (Hp1-1, Hp2-1, Hp2-2)

    - **Transferrin**
    - **Ceruloplasmin**
    - **?1-Antitrypsin**
    - **Immunoglobulins**
- Useful for **genetic and anthropological studies**.

Acute Phase Proteins

- Levels increase **50–1000 fold** during **inflammation, infection, trauma, neoplasia**.
- Synthesized mainly by the **liver** under cytokine stimulation (IL-6, IL-1, TNF-?).
- Rise early in inflammation and fall early during recovery.

Major Acute Phase Proteins

- **C-Reactive Protein (CRP)**
- **Ceruloplasmin**
- **Haptoglobin**
- **Fibrinogen**
- **?1-Antitrypsin**
- **Complement proteins**

C-Reactive Protein (CRP)

- Named for its reaction with **C-polysaccharide** of pneumococci.
- A **?-globulin**, molecular weight **115–140 kDa**.
- Synthesized in the **liver**.
- Activates **complement** and enhances **phagocytosis**.
- Rises rapidly and falls rapidly (faster response than ESR).
- High-sensitivity CRP correlates with **coronary artery disease risk**.

Ceruloplasmin

- A **blue-colored ?2-globulin** containing **6–8 copper atoms** per molecule.
- Molecular weight ~160 kDa.
- Synthesized mainly in the **liver**; copper incorporated during intracellular processing.
- Plasma **half-life: 4–5 days**.

Functions

- Acts as **ferroxidase** (oxidizes Fe^{2}? ? Fe^{3}? for transferrin binding).
- Major **antioxidant** in plasma.
- Carries **90% of plasma copper** (rest loosely bound to albumin).

Decreased Levels

- **Wilson’s disease**
- Malnutrition
- Nephrotic syndrome
- Cirrhosis

Increased Levels

- Active hepatitis
- Biliary cirrhosis
- Pregnancy
- Estrogen therapy
- Obstructive biliary disease
- Inflammatory states and malignancy

Alpha-1-Antitrypsin (A1AT)

- Major component of the **?1-globulin** fraction.
- A **protease inhibitor**, especially against **neutrophil elastase**.

Electrophoresis Finding

- In A1AT deficiency ? **thin or absent ?1 band**.

Clinical Importance

- Deficiency causes:
  - **Early-onset emphysema/COPD** (due to unchecked elastase activity).
  - **Cholestatic liver disease/cirrhosis** (due to A1AT accumulation in hepatocytes).
- It is also an **acute phase protein**, so levels may rise in inflammation.

Alpha-2-Macroglobulin (A2M)

- A major protein component of the **?2-globulin** fraction.
- Very **large molecular weight (~725 kDa)**, hence **cannot pass the glomerular filter** easily.

Functions

- Acts as a **pan-protease inhibitor**: inhibits *trypsin, chymotrypsin, plasmin, kallikrein*.
- Binds and inactivates proteases by trapping them inside its structure.
- Transports **cytokines and growth factors**.
- Helps in **immune modulation** and **inflammation control**.

In Electrophoresis

- Produces a **prominent ?2 band** because of large size.
- In **nephrotic syndrome**, smaller proteins are lost in urine, but A2M is retained ? **?2 band becomes markedly increased**.

Clinical Significance

- **Increased** in:
  - Nephrotic syndrome (classic)
  - Diabetes mellitus
  - Hyperestrogenic states (pregnancy, estrogen therapy)
- **Decreased** in:
  - Acute pancreatitis
  - Severe liver disease

Negative Acute Phase Proteins

*(Proteins whose levels **decrease** during inflammation)*

During inflammation, the liver shifts toward synthesis of **positive acute phase proteins**, causing a **drop** in the synthesis of certain normal plasma proteins. These are called **negative acute phase proteins**.

Major Negative Acute Phase Proteins

1. **Albumin**

- Falls because liver prioritizes acute phase proteins.
- Also decreases due to increased capillary leakage.

2. **Prealbumin (Transthyretin)**
   - Sensitive indicator of **nutritional status**.
   - Drops rapidly in inflammation.
3. **Transferrin**
   - Decreases because iron sequestration reduces iron transport.
   - Helps reduce availability of iron to pathogens.
4. **Retinol Binding Protein (RBP)**
   - Decreases in inflammation and malnutrition.
5. **Apolipoproteins (A-I, A-II)**
   - Mild decrease.

Clinical Utility

- Helps differentiate **acute inflammation** from chronic states.
- Low albumin + high CRP indicates **acute phase response**.
- Prealbumin & transferrin reductions help monitor **malnutrition** vs **inflammation**.

Clotting Factors (Coagulation Factors)

There are **13 factors**, mostly made in the **liver**. Many require **vitamin K** for synthesis (II, VII, IX, X).

List of Clotting Factors

1. **Factor I** – Fibrinogen
2. **Factor II** – Prothrombin
3. **Factor III** – Tissue factor (Thromboplastin)
4. **Factor IV** – Calcium ($Ca^{2?}$)
5. **Factor V** – Proaccelerin
6. **Factor VII** – Proconvertin
7. **Factor VIII** – Antihemophilic factor A
8. **Factor IX** – Christmas factor / AHF B
9. **Factor X** – Stuart–Prower factor
10. **Factor XI** – Plasma thromboplastin antecedent
11. **Factor XII** – Hageman factor
12. **Factor XIII** – Fibrin-stabilizing factor

Coagulation Pathways

- **Intrinsic pathway:** XII ? XI ? IX ? VIII

- **Extrinsic pathway:** Tissue factor (III) + VII
- Both converge on **common pathway:** X ? V ? Prothrombin ? Thrombin ? Fibrinogen ? Fibrin ? XIII (crosslinking)

Vitamin K–dependent factors

- **II, VII, IX, X** + **Protein C & Protein S**

Anticoagulants

Substances that **prevent clot formation** in vitro or in vivo.

Natural Anticoagulants

1. **Heparin**
    - Enhances **antithrombin III** ? inactivates IIa (thrombin), Xa, IXa.
2. **Antithrombin III**
    - Inhibits thrombin and factors IXa, Xa, XIa, XIIa.
3. **Protein C**
    - Vitamin K–dependent; activated by thrombin–thrombomodulin complex.
4. **Protein S**
    - Cofactor for Protein C.
5. **TFPI** (Tissue factor pathway inhibitor)

- Inhibits tissue factor–VIIa complex.

Clinical Anticoagulants

1. **Heparin**
   - Immediate effect.
   - Monitored by **aPTT**.
2. **Warfarin**
   - Inhibits vitamin K recycling.
   - Affects II, VII, IX, X.
   - Monitored by **PT/INR**.
3. **Direct Oral Anticoagulants** (DOACs)
   - Dabigatran (IIa inhibitor), Rivaroxaban/Apixaban (Xa inhibitors).

In Vitro Anticoagulants

- **EDTA** – binds calcium
- **Citrate** – binds calcium (used in coagulation studies)
- **Oxalate** – precipitates calcium
- **Heparin** – used for arterial blood gas samples

Fibrinolysis

Process that **breaks down fibrin clots**.

Key Components

- **Plasminogen** – inactive precursor
- **Plasmin** – active fibrinolytic enzyme
- Converts fibrin into **Fibrin Degradation Products (FDPs)**, including **D-dimer**.

Activation of Plasminogen

1. **tPA (tissue plasminogen activator)** – endothelial origin
2. **Urokinase**
3. **Factor XIIa**

Inhibitors of Fibrinolysis

- **?2-antiplasmin** – inhibits plasmin
- **PAI-1** – inhibits tPA and urokinase

Clinical Use

- Elevated **D-dimer** ? DIC, thrombosis, pulmonary embolism.
- **Thrombolytic drugs:**
    - Streptokinase

- Alteplase (tPA)
- Tenecteplase (TNK)

Hemophilia

Hemophilia A

- **Deficiency of Factor VIII**.
- **Most common** inherited coagulation disorder.
- X-linked recessive.
- Prolonged **aPTT**, normal PT & platelet count.
- Clinical:
  - Hemarthrosis
  - Deep muscle bleeds
  - Prolonged bleeding after injury

Hemophilia B

- **Deficiency of Factor IX** (Christmas disease).
- X-linked recessive.
- Similar presentation to hemophilia A.

Hemophilia C

- **Factor XI deficiency**, autosomal recessive.
- Mild bleeding tendency.

Diagnosis

- Prolonged **aPTT**
- Mixing test corrects aPTT
- Specific factor assays confirm diagnosis

Treatment

- Factor VIII/IX concentrates
- Desmopressin (DDAVP) for mild Hemophilia A (releases stored Factor VIII & vWF)
- Avoid intramuscular injections & NSAIDs

Important Points to Remember — Plasma Proteins

- Plasma proteins are synthesized mainly in the **liver**, except **immunoglobulins**, which are formed by **plasma cells**.
- Serum electrophoresis shows **5 major bands**:
  Albumin ? ?1 ? ?2 ? ? ? ?
- **Albumin** has the **highest mobility** and contributes most to **oncotic pressure**.

- **Gamma globulin** fraction contains **immunoglobulins (IgG, IgA, IgM, IgD, IgE)**.
- **Nephrotic syndrome** shows ? albumin, ? ?1, ? ?, and **marked ? ?2** (due to ?2-macroglobulin retention).
- **Cirrhosis** shows **?–? bridging** due to increased IgA.
- **Multiple myeloma** shows a sharp **M-band** in ? region.
- **Albumin** transports fatty acids, bilirubin, Ca²?, drugs; low albumin occurs in liver disease, nephrotic syndrome, malnutrition.
- **Prealbumin (transthyretin)** is a sensitive marker of **protein-energy malnutrition**.
- **Transferrin** is a negative acute phase protein; ? in iron deficiency anemia.
- **Haptoglobin** decreases in **hemolysis** due to binding hemoglobin.
- **Ceruloplasmin** contains **6–8 copper atoms**; low in **Wilson's disease**.
- **C-Reactive Protein (CRP)** rises rapidly in inflammation; **high-sensitivity CRP** predicts **coronary artery disease risk**.
- **Alpha-1-antitrypsin (A1AT)** is a protease inhibitor; deficiency causes **early-onset emphysema**.
- **Alpha-2-macroglobulin** is massively increased in **nephrotic syndrome** (cannot be filtered due to large size).
- **Negative acute phase proteins:** albumin, prealbumin, transferrin, RBP.
- **Clotting factors:** II, VII, IX, X are **vitamin K–dependent**.

- **Factor VIII deficiency? Hemophilia A**, X-linked recessive.
- **Fibrinolysis** is mediated by **plasmin**, activated by **tPA**, urokinase, streptokinase.
- **D-dimer** increases when fibrin is degraded ? used to detect thrombosis & DIC.

FAQs — Plasma Proteins (Viva-oriented)

1. What are the major fractions seen on serum electrophoresis?

Albumin, ?1, ?2, ?, ?.

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2. Which fraction is largest in normal serum?

Albumin (50–60% of total proteins).

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3. What causes ?1 band to disappear?

Alpha-1-antitrypsin deficiency.

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4. What causes a marked increase in ?2 band?

Nephrotic syndrome (retention of ?2-macroglobulin).

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5. What is ?–? bridging and where is it seen?

Fusion of ? and ? region; seen in **cirrhosis**.

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6. Which condition shows an M-spike on electrophoresis?

Multiple myeloma.

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7. Name the major transport proteins in plasma.

Albumin, prealbumin, RBP, TBG, CBG, transferrin, hemopexin.

8. What is the function of haptoglobin?

Binds free hemoglobin; ? in hemolysis.

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9. What is the main function of ceruloplasmin?

Copper transport and **ferroxidase** activity ($Fe^{2?}$? $Fe^{3?}$).

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10. Where is CRP synthesized and when does it rise?

Synthesized in the **liver**; rises in **acute inflammation**.

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11. What are negative acute phase proteins?

Proteins that **decrease** during inflammation—albumin, prealbumin, transferrin, RBP.

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12. What is the clinical significance of alpha-1-antitrypsin deficiency?

Causes **early-onset emphysema** due to unopposed elastase activity.

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13. Why is alpha-2-macroglobulin high in nephrotic syndrome?

Large size prevents filtration ? accumulates in plasma.

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14. Which clotting factors are vitamin K–dependent?

II, VII, IX, X, Protein C, Protein S.

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15. What activates plasminogen?

tPA, urokinase, streptokinase.

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16. What is elevated in active fibrinolysis?

D-dimer.

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17. What is the defect in Hemophilia A?

Factor VIII deficiency, X-linked recessive.

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18. What happens to prothrombin time in liver disease?

PT becomes prolonged (liver synthesizes most clotting factors).

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19. What is the carrier protein for retinol?

Retinol Binding Protein (RBP).

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20. Which protein has the role of anti-oxidant and copper carrier?

Ceruloplasmin.

MCQs — Plasma Proteins

1. The major protein fraction seen on serum electrophoresis is:

A. ?1-globulin
B. ?2-globulin
C. Albumin
D. ?-globulin
Answer: C

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2. A sharp M-band in the ? region suggests:

A. Cirrhosis
B. Nephrotic syndrome
C. Multiple myeloma
D. Hemolytic anemia
Answer: C

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3. ?–? bridging in electrophoresis is characteristic of:

A. Acute inflammation
B. Cirrhosis
C. Nephrotic syndrome
D. Primary immune deficiency
Answer: B

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4. The ?1 region mainly contains:

A. Haptoglobin
B. Ceruloplasmin
C. Alpha-1-antitrypsin
D. Fibrinogen
Answer: C

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5. In nephrotic syndrome, the fraction that becomes markedly elevated is:

A. Albumin
B. ?1
C. ?2
D. ?
Answer: C

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6. Which plasma protein transports the highest proportion of copper?

A. Albumin
B. Transferrin
C. Ceruloplasmin
D. Hemopexin
Answer: C

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7. Low ceruloplasmin levels are seen in:

A. Wilson’s disease
B. Hemochromatosis

C. Pregnancy

D. Estrogen therapy

Answer: A

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8. Which protein rises rapidly and falls rapidly during inflammation?

A. Albumin

B. CRP

C. TBG

D. Transferrin

Answer: B

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9. Negative acute phase proteins include:

A. CRP

B. Haptoglobin

C. Albumin

D. Fibrinogen

Answer: C

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10. Alpha-2-macroglobulin is typically increased in:

A. Liver cirrhosis

B. Hemolytic anemia

C. Nephrotic syndrome

D. Multiple myeloma

Answer: C

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11. Retinol Binding Protein is a transporter of:

A. Vitamin D

B. Vitamin A

C. Thyroxine

D. Cortisol

Answer: B

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12. A thin or absent ?1 band on electrophoresis indicates:

A. Hypoalbuminemia
B. A1AT deficiency
C. Wilson’s disease
D. IgA deficiency
Answer: B

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13. Which is a vitamin K–dependent protein?

A. Fibrinogen
B. Ceruloplasmin
C. Factor VII
D. Factor VIII
Answer: C

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14. CRP belongs to which fraction in electrophoresis?

A. Albumin
B. ?1
C. ?
D. ?
Answer: C

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15. The main ferroxidase in plasma is:

A. Transferrin
B. Ceruloplasmin
C. Hemopexin
D. Ferritin
Answer: B

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16. Haptoglobin decreases in:

A. Obesity
B. Hemolysis

C. Nephrotic syndrome

D. Hypothyroidism

Answer: B

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17. Which of the following increases in pregnancy and estrogen therapy?

A. ?1-antitrypsin

B. Transferrin

C. Ceruloplasmin

D. Albumin

Answer: C

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18. Factor VIII deficiency leads to:

A. Hemophilia B

B. Hemophilia A

C. Hemophilia C

D. Von Willebrand disease

Answer: B

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19. Plasmin breaks down fibrin to produce:

A. Ferritin

B. D-dimer

C. Reticulin

D. Heme

Answer: B

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20. Which transport protein binds cortisol?

A. CBG (Transcortin)

B. TBG

C. Albumin

D. Hemopexin

Answer: A

Clinical Case–Based Questions — Plasma Proteins

Case 1 — M-band in ? region

A 58-year-old man presents with bone pain and recurrent infections. Serum electrophoresis shows a **sharp M-spike in the ? region**.
Q: What is the most likely diagnosis?

Answer: Multiple myeloma
Explanation: Monoclonal Ig production creates a narrow M-band.

Case 2 — ?–? Bridging

A 45-year-old male with long-standing alcoholism shows **merging of ? and ? bands** on electrophoresis.
Q: What condition does this pattern suggest?

Answer: Liver cirrhosis
Explanation: Increased IgA causes ?–? bridging.

Case 3 — Nephrotic pattern

A child presents with pitting edema. Serum electrophoresis shows **high ?2 band** and **very low albumin**.
Q: What disorder is most likely?

Answer: Nephrotic syndrome
Explanation: Loss of smaller proteins in urine; large ?2-macroglobulin is retained ? ?2 spike.

Case 4 — Thin ?1 band

A 20-year-old nonsmoker develops early-onset emphysema. Serum electrophoresis shows **absent ?1 band**.
Q: Which protein is deficient?

Answer: Alpha-1-antitrypsin
Explanation: A1AT deficiency ? absent ?1 region.

Case 5 — Low ceruloplasmin

A 14-year-old boy presents with tremors and Kayser–Fleischer rings. Lab reports show **very low ceruloplasmin**.
Q: What is the most likely diagnosis?

Answer: Wilson's disease
Explanation: Defective copper incorporation ? low ceruloplasmin.

Case 6 — Elevated CRP

A 30-year-old woman develops fever and joint swelling. CRP is markedly elevated but ESR is normal.
Q: What does this imply?

Answer: Very early acute inflammation
Explanation: CRP rises before ESR.

Case 7 — High haptoglobin

A patient recovering from intravascular hemolysis shows increasing haptoglobin levels.
Q: What does low haptoglobin indicate during active hemolysis?

Answer: Binding and clearance of free hemoglobin
Explanation: Haptoglobin decreases because it binds Hb-released in hemolysis.

Case 8 — High transferrin

A 28-year-old woman with fatigue shows **high transferrin** and **low ferritin**.
Q: What condition is most likely?

Answer: Iron deficiency anemia
Explanation: Transferrin increases to capture more iron.

Case 9 — Copper overload signs absent

A pregnant woman shows **high ceruloplasmin**, but no neurologic signs.
Q: What explains this elevated ceruloplasmin?

Answer: Physiological rise during pregnancy
Explanation: Estrogen increases ceruloplasmin synthesis.

Case 10 — Elevated ?2-globulin without edema

A diabetic patient's electrophoresis shows mildly elevated **?2-macroglobulin** but normal albumin.
Q: Why may ?2-macroglobulin be elevated in diabetes?

Answer: Compensatory increase due to glycation & inflammation
Explanation: Chronic hyperglycemia increases A2M synthesis.

Case 11 — Severe malnutrition

A child with severe protein-energy malnutrition has very low **prealbumin** and **RBP**.
Q: Why are these low?

Answer: Short half-life & rapid fall during malnutrition
Explanation: Prealbumin (2 days) and RBP (12 hours) drop quickly.

Case 12 — Prolonged PT/INR

A patient with jaundice has prolonged PT/INR but normal platelet count.
Q: What major plasma proteins are affected in liver failure?

Answer: Clotting factors (II, VII, IX, X)
Explanation: Liver synthesizes vitamin K–dependent factors ? PT prolongs.

Case 13 — D-dimer elevation

A 45-year-old man presents with sudden dyspnea; D-dimer is high.
Q: What does this indicate?

Answer: Active fibrinolysis due to thrombosis/PE
Explanation: Plasmin degrades fibrin ? D-dimer formation.

Case 14 — Hemarthrosis in a child

An 8-year-old boy has recurrent joint bleeding. aPTT is prolonged; PT normal.
Q: What is the likely diagnosis?

Answer: Hemophilia A or B
Explanation: Intrinsic pathway factors (VIII or IX) are deficient.

Case 15 — Low albumin, but normal globulins

A 50-year-old patient with chronic liver disease shows very low albumin but normal ?-globulins.
Q: Why are gammaglobulins preserved?

Answer: Produced by plasma cells, not the liver
Explanation: Liver failure reduces albumin but immunoglobulins remain.

Viva Voce — Plasma Proteins (Short Q&A)

1. What is the major plasma protein?

Albumin.

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2. Where are most plasma proteins synthesized?

Liver.

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3. Which plasma proteins are NOT synthesized in the liver?

Immunoglobulins (made by plasma cells).

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4. What is the normal albumin level?

3.5–5.0 g/dL.

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5. What is the main function of albumin?

Maintains **oncotic pressure** and **transports** many molecules.

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6. Which band moves fastest on electrophoresis?

Albumin band.

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7. What does ?–? bridging indicate?

Liver cirrhosis.

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8. What does an M-band represent?

Monoclonal immunoglobulin (multiple myeloma).

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9. Which band contains ?1-antitrypsin?

?1-globulin band.

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10. Which fraction is markedly increased in nephrotic syndrome?

?2-globulin (due to ?2-macroglobulin).

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11. What is the function of haptoglobin?

Binds **free hemoglobin**.

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12. Why is haptoglobin low in hemolysis?

It is **consumed** while binding Hb.

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13. What is the function of transferrin?

Iron transport.

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14. Which transporter carries vitamin A?

Retinol Binding Protein (RBP).

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15. What is the major copper-carrying protein?

Ceruloplasmin.

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16. What enzyme activity does ceruloplasmin have?

Ferroxidase activity ($Fe^{2?}$? $Fe^{3?}$).

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17. Low ceruloplasmin is seen in which disease?

Wilson’s disease.

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18. Which protein rises rapidly in acute inflammation?

C-Reactive Protein (CRP).

---

19. Name two negative acute phase proteins.

Albumin, Transferrin.

---

20. Name two vitamin K–dependent factors.

II and VII (also IX, X).

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21. Which factor deficiency causes Hemophilia A?

Factor VIII.

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22. Which factor deficiency causes Hemophilia B?

Factor IX.

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23. What is the role of plasmin?

Breaks down fibrin ? **fibrinolysis**.

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24. What test detects fibrin degradation?

D-dimer test.

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25. What activates plasminogen physiologically?

tPA (tissue plasminogen activator).

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26. What is the main inhibitor of plasmin?

?2-antiplasmin.

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27. What happens to PT in liver failure?

PT is **prolonged**.

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28. Which plasma protein has the shortest half-life?

RBP (12 hours).
Prealbumin is next (~2 days).

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29. What causes absent ?1 band on electrophoresis?

Alpha-1-antitrypsin deficiency.

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30. Why is ?2-macroglobulin high in nephrotic syndrome?

Large size ? **cannot be filtered** ? accumulates.