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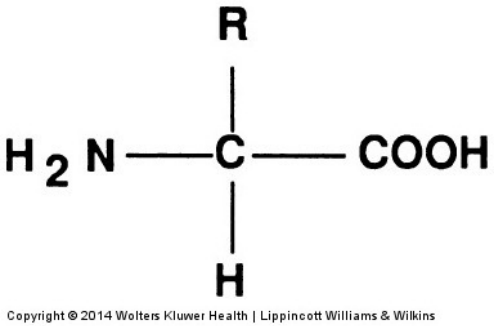
Chapter 11: Amino Acids and Proteins

By Deborah E. Keil

Amino Acids



- Basic Structure
  - At least 1 of both amino & carboxylic acid functional groups
  - Chain of amino acids = polypeptide; large polypeptide = protein
- Metabolism
  - 10 amino acids needed by humans can be synthesized by body.
  - 10 others (essential) must be supplied in proteins in food.
- Essential Amino Acids
  - Arg, His, Ile, Leu, Lys, Met, Phe, Thr, Trp, Val *(learning the functions of each essential amino acid is required. Read the book)*

Amino Acids (cont'd)

- Non-Essential Amino Acids
  - Ala, Asn, Asp, Cys, Glu, Gln, Gly, Pro, Ser, Tyr *(learning the functions of each essential amino acid is required. Read the book)*
- Amino acids are used to make proteins, and the synthesis of nonprotein nitrogen-containing compounds such as purines, pyrimidines, porphyrins, creatine, histamine, thyroxine, epinephrine, and the coenzyme NAD.
- Two New Amino Acids
  - Selenocysteine (Sec), pyrrolysine (Pyl) are encoded by UGA (a stop codon)

Metabolism

- The amino group is removed by either deamination or transamination resulting in the production of ketoacids
- Ketoacids can enter then common metabolic pathway with carbohydrates and fats
- **Glucogenic amino acids** generate precursors of glucose, such as pyruvate or a citric acid cycle intermediate (e.g.., Ala, Arg, Asp)
- **Ketogenic amino acids** generate ketone bodies from acetyl-CoA or acetoacetyl-CoA (e.g., Leu, Lys)
- Some amino acids are both ketogenic and glucogenic.
- The ammonium ion that is produced during deamination of the amino acids is converted into urea via the urea cycle in the liver.

Amino Acids (cont'd)

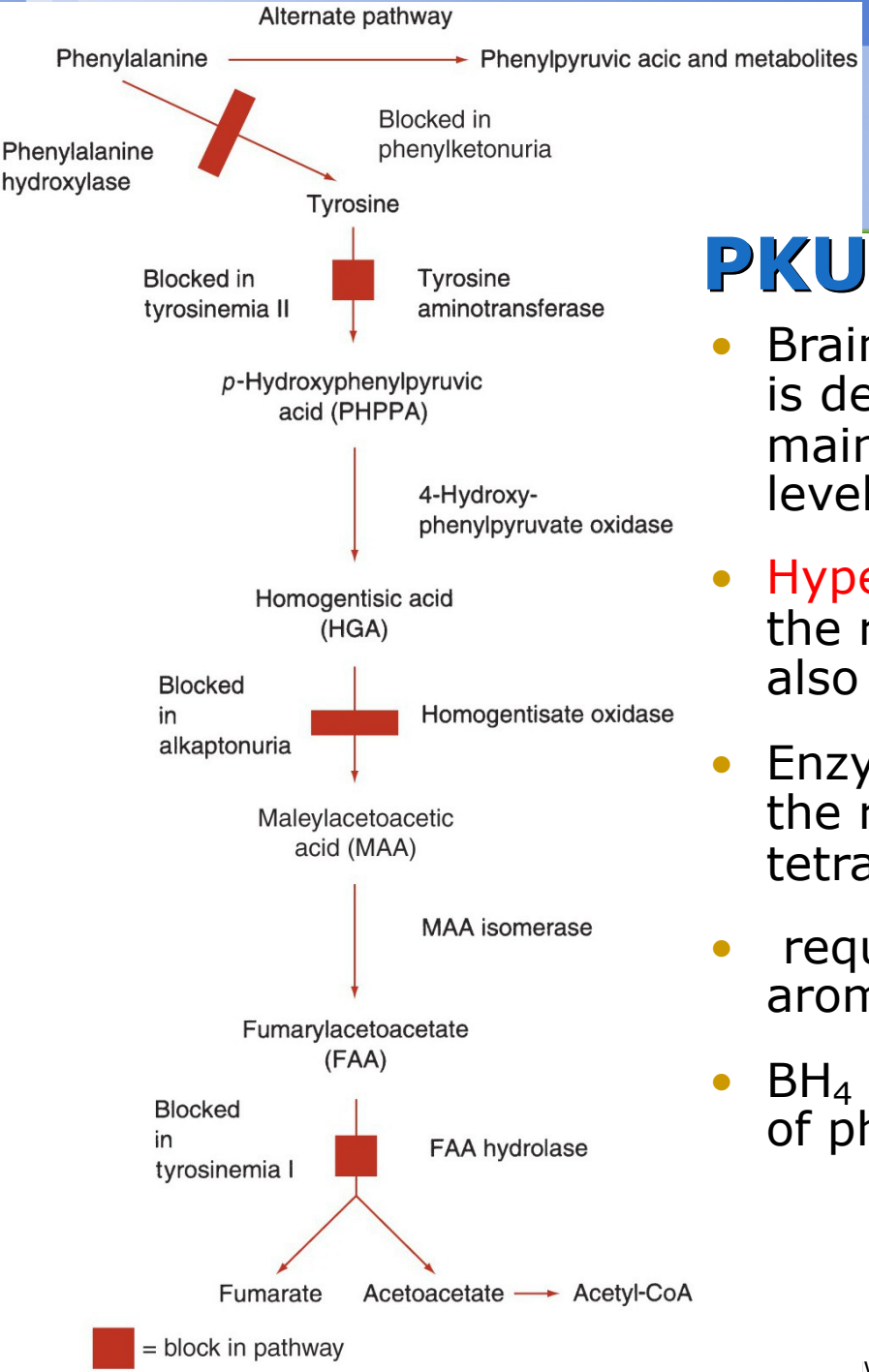
- Aminoacidopathies
  - Inherited enzyme defects that inhibit metabolism of certain amino acids
  - Exist either in activity of specific enzyme in metabolic pathway or in membrane transport system for amino acids
  - Some states require screening for up to 26 amino acids.
  - Over 100 diseases result from aminoacidopathies.
  - Cause severe medical complications due to build-up of toxic amino acids & byproducts of amino acid metabolism in blood

Amino Acids (cont'd)

- Aminoacidopathies
  - Phenylketonuria (PKU)
  - Tyrosinemia
  - Alkaptonuria
  - Maple syrup urine disease (MSUD)
  - Isovaleric acidemia
  - Homocystinuria
  - Citrullinemia
  - Argininosuccinic aciduria
  - Cystinuria

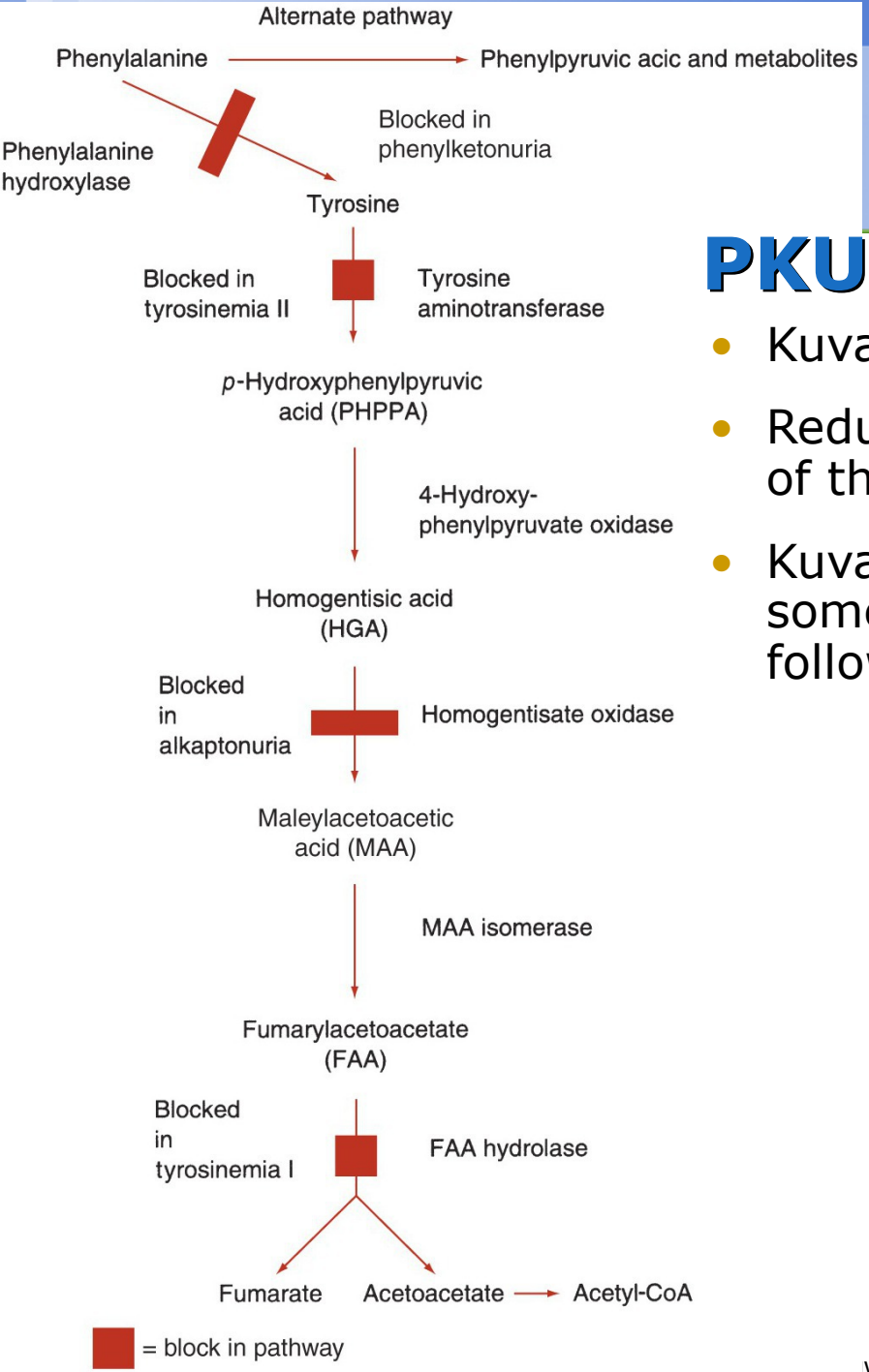
PKU

- Autosomal recessive trait and occurs in about 1 in 15,000 births
- Absence of activity of the enzyme phenylalanine hydroxylase (PAH), which catalyzes the conversion of phenylalanine to tyrosine
- Phe levels are usually greater than 1,200 µmol/L
- Chronically high levels of phenylalanine and some of its metabolites (e.g., phenylpyruvate, and phenyllactic acid) can cause significant brain problems (retarded mental development and microcephaly).
- Present in urine and blood → musty odor of urine



PKU

- Brain damage can be avoided if the disease is detected at birth and the infant is maintained on a diet containing very low levels of phenylalanine.
- Hyperphenylalaninemia cases that are not the result of the lack of the PAH enzyme also occur.
- Enzymatic deficiency in the pathways for the regeneration and synthesis of tetrahydrobiopterin (BH_4)
- required cofactor for hydroxylation of the aromatic amino acids
- BH_4 deficiency results in higher blood levels of phenylalanine and deficient



PKU

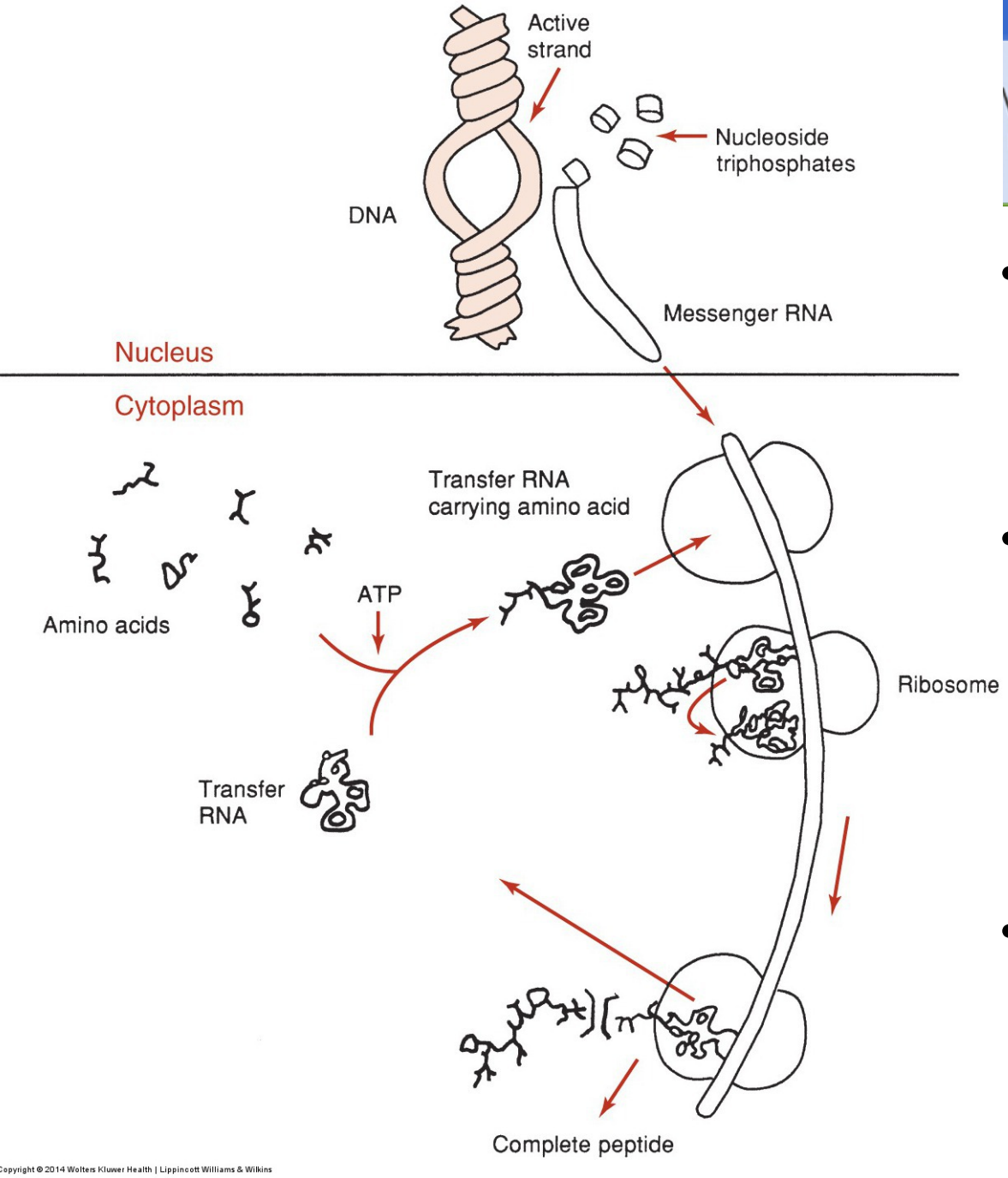
- Kuvan, the first drug to help manage PKU.
- Reduce Phe levels by increasing the activity of the PAH.
- Kuvan is effective only in patients who have some PAH activity and who continue to follow a phenylalanine-restricted diet.

Amino Acids (cont'd)

- Amino Acid Analysis
  - Blood samples should be drawn after at least a 6- to 8-hour fast.
  - Sample is collected in a heparin tube & plasma removed promptly from cells.
  - Take care not to aspirate platelet & white cell layer, no hemolysis.
  - Deproteinization within 30 minutes of sample collection
  - Analysis performed immediately or sample frozen at –20°C to –40°C
  - Urinary analysis performed on random specimen for screening
  - Method of choice for screening is thin-layer chromatography.

Proteins

- Importance
  - Every function in living cell depends on proteins: motion, biochemical reactions, cell structure, transport, antibodies.
- Molecular Size
  - Macromolecules; typical protein has 200–300 amino acids; can range in molecular mass from 6,000 to several million
- Synthesis
  - Occurs in liver (most proteins) or plasma cells (immunoglobulins)
- Structure
  - **Four levels:** primary, secondary, tertiary, quaternary



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- Protein synthesis occurs at the rate of ~ 2-6 peptide bonds per second.
- The hormones that assist in controlling protein synthesis are *thyroxine*, *growth hormone*, *insulin*, and *testosterone*.
- The hormones that assist in controlling protein catabolism are *glucagon* and *cortisol*.

Catabolism & Nitrogen Content

- Nitrogen has no designated storage depots in the body.
- Insufficient dietary quantities of even one amino acid can quickly limit the synthesis and lower the body levels of many essential proteins.
- A balance exists between protein anabolism (synthesis) and catabolism (breakdown).
- Turnover ~ about 125 to 220 g of protein each day
  - Plasma proteins and most intracellular proteins are rapidly degraded, half-lives ~ hours or days.
  - Structural proteins, such as collagen, are metabolically stable and have half-lives of years.
- Normal, healthy adults are in nitrogen balance, with intake and excretion being equal.
- +ve nitrogen balance: Pregnant women, growing children, and adults recovering from major illness
- -ve nitrogen balance: starvation; tissue destruction, burns

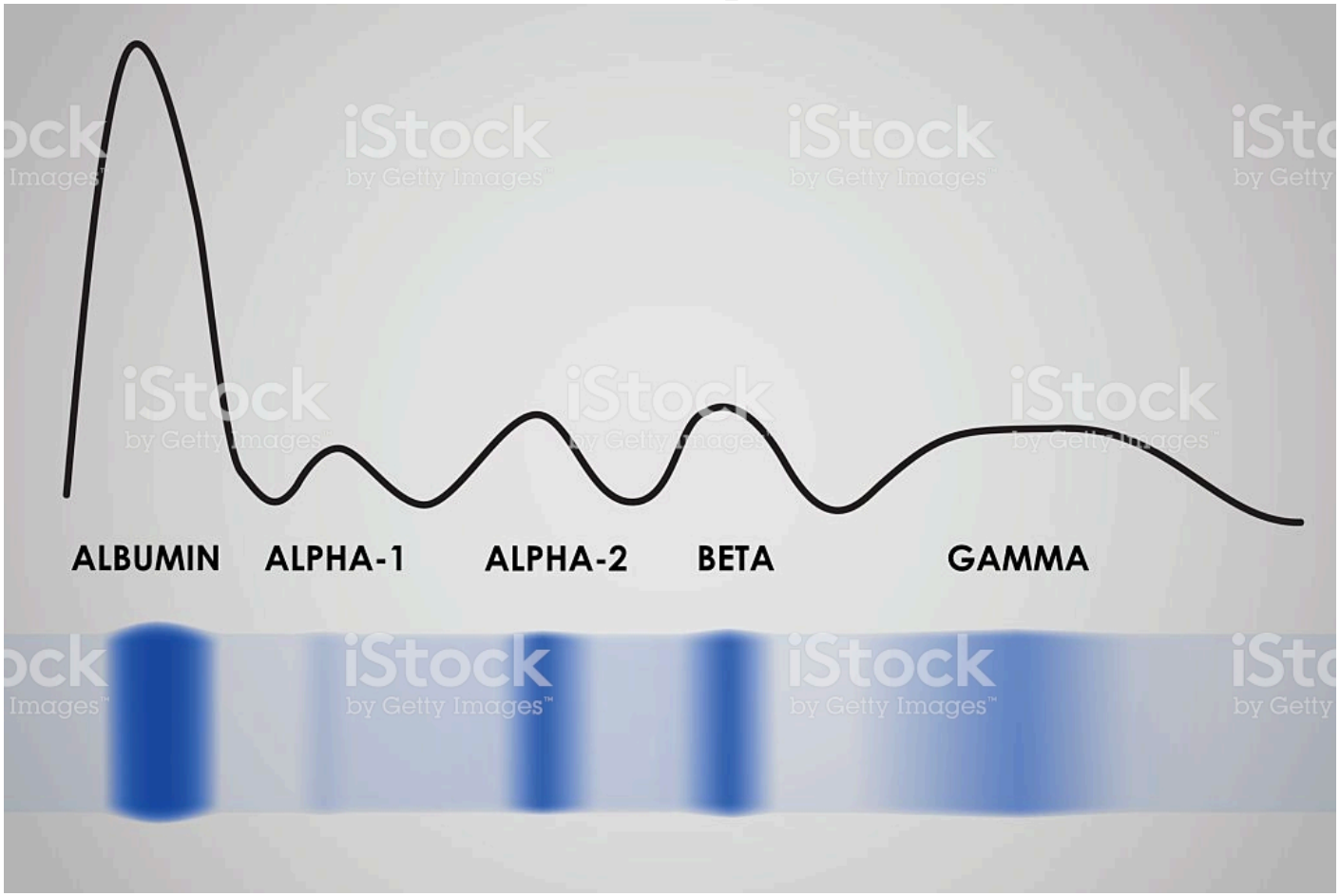
Proteins (cont'd)

- **Nitrogen Content:** 16% in serum protein
- Charge & Isoelectric Point
  - **Isoelectric point (pI):** pH at which protein has no net charge
  - If pH > pI, charge is negative; if pH < pI, charge is positive.
- **Solubility:** > charge = > solubility in water
- Classification
  - **By function:** enzyme, hormone, transport, immunoglobulin, structural, storage, energy source, osmotic force
  - **By structure:** database (manual & automated), simple, conjugated

Plasma Proteins

- Most frequently analyzed of all proteins
- Two main groups: albumin & globulins'
- A typical blood panel will provide 4 different measurements—total protein, albumin, globulins, and the albumin/globulin (A/G) ratio.
- Prealbumin (transthyretin)
  - Migrates ahead of albumin in classic electrophoresis of proteins
  - Transport protein for thyroxine & triiodothyronine
- Albumin
  - Protein present in highest concentration in plasma
  - Provides 80% of colloid osmotic pressure of intravascular fluid, buffers pH, is a negative acute phase reactant protein, binds substances in blood

SerumProtein Electrophoresis



Globulins

- The globulin group of proteins consists of α1, α2, β, and γ fractions
- **Acute-phase reactants:**
  - Proteins that are significantly increased in plasma during the acute phase of the inflammatory process.
  - Most serum globulins are from this category

Globulins

- Alpha$_1$-Antitrypsin (AAT)
  - Glycoprotein mainly synthesized in liver (90% of total α1)
  - Inhibition of the protease *neutrophil elastase*. Neutrophil elastase is released from leukocytes to fight infection, but it can destroy alveoli → emphysema.
  - Increased levels in inflammatory reactions, pregnancy, and contraceptive use.
- Alpha$_1$-Fetoprotein (AFP)
  - Synthesized in the developing embryo (levels decrease after birth)
  - No known function in adults. Binds estradiol in fetuses.

Globulins

- α_1-Acid Glycoprotein (AAG)
  - May regulate immune response (similarity between AAG and immunoglobulin in aa sequence)
  - It is elevated following stress, inflammation and tissue damage, acute myocardial infarction, trauma, pregnancy, cancer, pneumonia, rheumatoid arthritis, and surgery.
  - Binds drugs
- α_1-Antichymotrypsin
  - Serine proteinase inhibitor, inhibiting the activity of cathepsin G, pancreatic elastase, mast cell chymase, and chymotrypsin
  - Produced in the liver and is increased during inflammation.
  - Deficiency in liver disease; Parkinson disease and COPD

Globulins

- Inter-α-Trypsin Inhibitor (ITI)
  - Serine protease inhibitor
  - Assembled from two proteins: a light chain (bikunin) and either one or two heavy chains.
  - Only one type of light chain, there are five different homologous heavy chains (ITIHs). Roles in inflammation and carcinogenesis.
  - Elevations are seen in inflammatory disorders.
- Gc-globulin (Group-Specific Component; Vitamin D–Binding Protein)
  - Major carrier protein of vitamin D
  - Elevations in third trimester of pregnancy
  - Low levels in severe liver disease and protein-losing syndromes.

Globulins

- Haptoglobin (Hp)
  - Tetramer of two α and two β chains.
  - Elevated in many inflammatory diseases, such as ulcerative colitis, acute rheumatic disease, heart attack, and severe infection.
  - Binds free hemoglobin to prevent its loss (and Fe) in urine.
  - Suicide protein: When haptoglobin and hemoglobin attach, spleen cells remove the complex from circulation and destroy the proteins recycling Fe and amino acids.
- Ceruloplasmin
  - Synthesized in the liver. Elevated in inflammation, severe infection, and tissue damage and in some cancers.
  - >90% of total serum copper (10% in albumin).

Globulins

- α_2-Macroglobulin (A2M)
  - Major component of the α2 band in electrophoresis.
  - Homo tetramer
  - Inhibits proteases (trypsin, thrombin, kallikrein, and plasmin)
  - Increased in nephrosis, diabetes and liver disease and while using contraceptive medications
- Transferrin (Siderophilin)
  - Major component of the β-globulin fraction
  - Fe transport and Fe loss prevention through the kidney.
  - Low transferrin can impair Hb synthesis leading to anemia.
  - Hemochromatosis: excess Fe deposits in tissues due to increased Fe binding to transferrin (low plasma Tf)

Hemochromatosis- Mystery Diagnosis

- https://www.youtube.com/watch?v=_203ET0lkSw

Globulins

- Hemopexin
  - Heme scavenger (binds heme with the highest affinity)
  - Protects the body from the oxidative damage caused by free heme can cause.
  - Binds heme released from breakdown of Hb, Mb or catalase in a 1:1 ratio, goes to the liver and is destroyed.
  - Low hemopexin levels → hemolytic anemia.
- Lipoproteins
  - Carriers of lipids in the blood
- β_2-Microglobulin (B2M)
  - Light chain component of the MHC, HLA
  - Elevated serum levels are the result of impaired clearance by the kidney or overproduction of the protein that occurs in many inflammatory diseases

Globulins

- Complement
  - Complement is increased in inflammatory states and decreased in malnutrition and hemolytic anemia.
  - Decreased levels of C3 are associated with autoimmune disease, neonatal respiratory distress syndrome, bacteremia, tissue injury, and chronic hepatitis.
  - Decreased levels of C4 may indicate disseminated intravascular coagulation, acute glomerulonephritis, chronic hepatitis.
- Fibrinogen
  - One of the largest proteins in blood plasma. Forms fibrins clot when activated by thrombin; no fibrinogen in serum.
  - Increased levels in inflammation and pregnancy.
  - Decreased values reflect extensive coagulation.

Globulins

- C-Reactive Protein (CRP)
  - One of the first acute-phase proteins to rise in response to inflammatory disease.
  - Rises sharply whenever there is tissue necrosis
  - CRP bound to bacteria and fungi promotes the binding of complement, which facilitates their uptake by phagocytes (***opsonization***).
  - Causal relationship between CRP levels and CVD.
  - Interventions such as weight loss, diet, exercise, and smoking cessation and administration of pharmacologic agents such as statins all lead to both reduced CRP levels and reduced vascular risk.

Globulins

- High sensitivity CRP (hs-CRP)
  - Monoclonal antibody–based tests that can detect CRP at levels below 1 mg/L.
  - Using the hsCRP assay, levels of less than 1, 1 to 3, and greater than 3 mg/L correspond to low-, moderate-, and high-risk groups for future cardiovascular events.
- Immunoglobulins (Igs)
  - Produced by B cells
  - Five classes (IgG, IgA, IgM, IgD, and IgE)
  - IgG is the most abundant. Acts on bacteria, fungi, viruses, and foreign particles by agglutination, by opsonization by activating complement, and by neutralizing toxins. IgG is increased in liver disease, infections, etc.

CASE STUDY 11-2

Immediately following the birth of a baby girl, the attending physician requested a protein electrophoretic examination of the mother's serum. This was done on a sample that was obtained on the mother's admission to the hospital the previous day. An electrophoretic examination was also performed on the cord-blood specimen. Laboratory reports are shown in CASE STUDY TABLE 11-2.1.

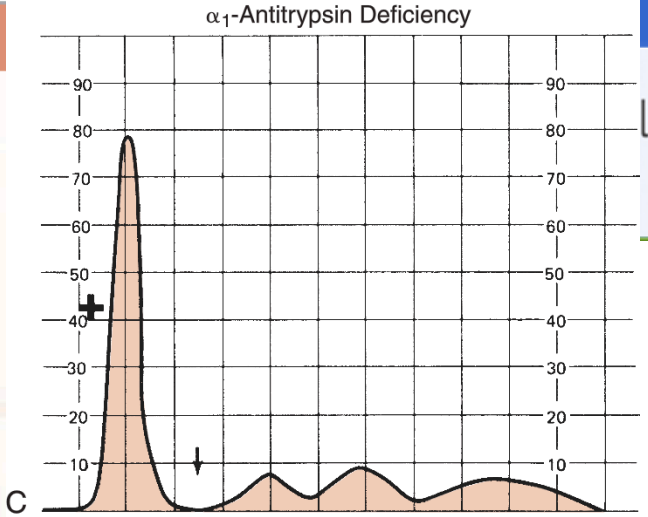
The appearance of the mother's electrophoretic pattern was within that expected for a healthy person. The electrophoretic pattern of the cord-blood serum resembled the one shown in Figure 11-9C.

CASE STUDY TABLE 11-2.1
ELECTROPHORESIS VALUES (g/dL)

	ADULT REFERENCE VALUES	MOTHER'S SERUM	CORD BLOOD
Albumin	3.5–5.0	4.2	3.3
α_1-Globulins	0.1–0.4	0.3	0.0
α_2-Globulins	0.3–0.8	1.2	0.4
β-Globulins	0.6–1.1	1.3	0.7
γ-Globulins	0.5–1.7	1.3	1.0

Questions

1. What protein fraction(s) is/are abnormal in the mother's serum and the cord-blood serum?
2. An abnormality in this/these fraction(s) is/are most often associated with what disease?
3. What other test(s) may be done to confirm this abnormality?



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1. *The mother has an increased level of α2-globulin, which may be a result of a residual increase of ceruloplasmin and α2-macroglobulin that occurred in pregnancy. The cord- blood serum (the baby) has an abnormally low α1-globulin fraction. This is associated with α1-antitrypsin deficiency.*

2. *The baby had an α1-antitrypsin deficiency. Term newborns have concentrations of α1-antitrypsin in the range of adult levels. This deficiency is associated with juvenile pulmonary emphysema and infantile hepatitis. Most babies with α1-antitrypsin deficiency, however, do not develop symptoms until later in life, when the predisposition to pulmonary emphysema materializes.*

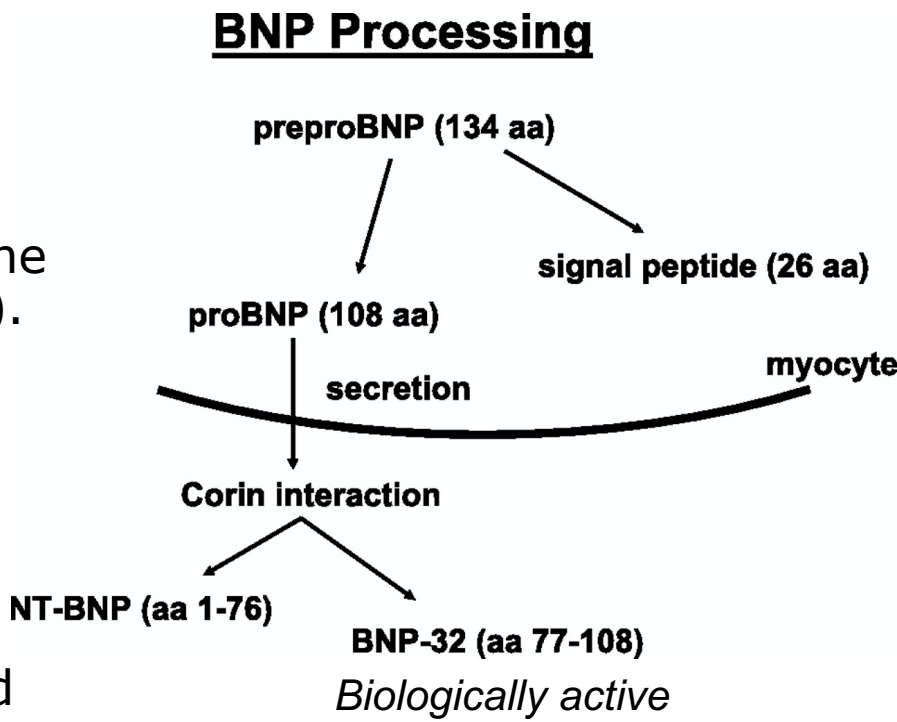
3. *Other tests can be performed to confirm the α1-antitrypsin deficiency such as quantitation by radial immunodiffusion and phenotyping of α1-antitrypsin by isoelectric focusing.*

Other Proteins of Importance

- Myoglobin
  - 153 amino acids containing heme. Oxygen-storage protein in striated skeletal and cardiac muscle. Most of it is dissolved in the cytoplasm.
  - Used to diagnose heart attacks as a cardiac biomarker with troponin
  - Released Mb after an AMI occurs within 2-3 h and reaches peak concentration in 8-12 h. Mb is easily filtered by the kidneys, allowing levels to return to normal in 18 to 30 hours after AMI
- Cardiac Troponin (cTn)
  - Complex of regulatory proteins including troponin I and troponin T that are specific to heart muscle.
  - Troponin I rises within 3 to 6 hours after myocardial damage and remains elevated for up to 10 days.
  - Used in conjunction with CK, CK-MB and Mb to diagnose myocardial injury.
  - If CK, CK-MB, and myoglobin concentrations are normal but troponin levels are increased, then it is likely that either a lesser degree of heart injury is present or that the injury took place more than 24 h in the past.

Other Proteins of Importance

- B-Type Natriuretic Peptide (BNP) and N-Terminal BNP (NT-BNP)
  - Highest concentrations of NT-proBNP and BNP are in the left ventricular myocardium (also detectable in atrial tissue and in the myocardium of the right ventricle).
  - BNP is a popular marker for congestive heart failure.
  - The natriuretic peptides are neurohormones that affect body fluid homeostasis (through natriuresis and diuresis) and blood pressure (through decreased angiotensin II and norepinephrine synthesis), both major components in the pathology of congestive heart failure.



Other Proteins of Importance

- Fibronectin
  - Roles in cell adhesion, tissue differentiation, growth, and wound healing.
  - Found in plasma and on cell surfaces and can be synthesized by
  - hepatocytes, endothelial cells, macrophages, and fibroblasts.
  - Plasma fibronectin is a nutritional marker.
  - Fetal fibronectin (fFN) is used to help predict the short-term risk of premature delivery.
- Adiponectin
  - Produced by adipocytes.
  - Inverse correlation between body mass index and adiponectin values.
  - Lower levels of adiponectin correlate with an increased risk of heart disease, type 2 diabetes, metabolic syndrome, and obesity.

Other Proteins of Importance

- β-Trace Protein
  - An accurate marker of CSF leakage.
  - A potential marker in detecting impaired renal function, although not more sensitive than cystatin C.
- Cystatin C
  - It is produced and destroyed at a constant rate, making it a new marker for the early assessment of changes to the glomerular filtration rate.
  - When the rate at which the fluid filtrate is formed is reduced, indicating decreased kidney function, blood levels of substances removed by them (such as cystatin C) increase and are an indication of kidney function.

Other Proteins of Importance

- Amyloid
  - Insoluble fibrous protein aggregates
  - Amyloidosis refers to a variety of conditions in which amyloid proteins are abnormally deposited in organs and/or tissues. Amyloid fibrils may infiltrate many organs, including the heart and blood vessels, brain and peripheral nerves, kidneys, liver, spleen, and intestines, causing localized or widespread organ failure.
  - In conjunction with Tau protein, amyloid test can be used to differentiate Alzheimer's disease from other forms of dementia.

Total Protein Abnormalities

- Hypoproteinemia
  - Total protein level less than reference interval
  - Occurs in any condition where a negative nitrogen balance exists
  - Can be caused by excessive loss (excretion in the urine in renal disease; leakage into GI tract in inflammation of the digestive system; loss of blood in open wounds), decreased intake (malnutrition), decreased synthesis (liver disease), or accelerated breakdown of proteins (burns, trauma, or other injuries)
- Hyperproteinemia
  - An increase in total plasma proteins
  - Occurs in dehydration, when concentration of proteins is elevated due to decreased volume of solvent water
  - Also results from excessive production of some proteins (γ-globulins)

CASE STUDY 11-3

A 76-year-old woman was admitted to the hospital with gangrene of her right toe. She was disoriented and had difficulty finding the right words to express herself. On evaluation, it was revealed she lived alone and was responsible for her own cooking. A daughter who lived in the area said her mother was a poor eater, even with much encouragement. An ECG, performed on admission, showed possible ectopic rhythm with occasional premature supraventricular contractions. The cardiologist suspected a possible inferior myocardial infarction of undetermined age. Laboratory results are shown in CASE STUDY TABLE 11-3.1.

CASE STUDY TABLE 11-3.1
LABORATORY RESULTS

DAY 1	RESULTS	REFERENCE RANGE
CK total	187 U/L	40–325 U/L
CK-MB mass	6 µg/L	<8 µg/L
Troponin I	16.3 µg/L	0–2 µg/L
NT-proBNP	60 pmol/L	2–50 pmol/L (generic cutoff)
Prealbumin	15 mg/dL	17–42 mg/dL
Albumin	2.7 g/dL	3.7–4.9 g/dL
REPEAT (5 H LATER)		
CK total	180 U/L	
CK-MB mass	5.4 µg/L	
Troponin I	17.5 µg/L	
NT-proBNP	100.5 pmol/L	
DAY 2		
CK total	177 U/L	
CK-MB mass	4.5 µg/L	
Troponin I	13.7 µg/L	
NT-proBNP	143 pmol/L	
Myoglobin	>500 µg/L	(<76)

Questions

1. In this patient, what is the clinical value of the troponin I measurements?
2. What is a possible explanation for the elevated myoglobin?
3. What condition is indicated by the low prealbumin value?

1. *Troponin I is a late marker for myocardial infarction. Troponin I rises within 3 to 6 hours after myocardial damage and remains elevated for up to 10 days, whereas CK-MB returns to normal in 2 to 3 days and total CK in 3 to 4 days. Although troponin I is elevated in other heart abnormalities, such as chronic heart disease, the degree of elevation in this patient (8 times the upper reference limit) points to myocardial infarction that occurred longer than 3 days before hospital admission.*

2. *Myoglobin rises when muscle tissue is damaged. In myocardial infarction, the myoglobin returns to normal levels within 18 to 30 hours. With the age of the infarction in this patient, the kidney would have already cleared the myoglobin that originated from the heart muscle. The source of myoglobin in this instance is likely from muscle destruction arising from the gangrenous toe.*

3. *The low prealbumin level is an indication of protein–calorie malnutrition. Chronically inadequate food intake, as indicated in this patient, or malabsorption leads to depletion of skeletal muscle and catabolism of visceral and plasma proteins. The low total serum protein is almost entirely a result of a low albumin level and is sometimes partially obscured by a relatively high level of γ-globulins. Albumin, however, is a poor indicator of recent malnutrition because of its long half-life. Albumin is also lowered by several other conditions independent of nutritional status. In contrast, prealbumin, with a short half-life, responds rapidly to changes in protein–calorie intake.*

Methods of Analysis

- Total Nitrogen
  - Measures all chemically bound nitrogen in a sample (i.e., plasma or urine) using chemiluminescence
  - Useful in assessing nitrogen balance
- Total Proteins
  - Most often measured in serum
  - **Reference interval:** 6.5–8.3 g/dL (65–83 g/L) in ambulatory adults
  - **Methods of measurement:** Kjeldahl, refractometry, biuret, dye binding

Methods of Analysis (cont'd)

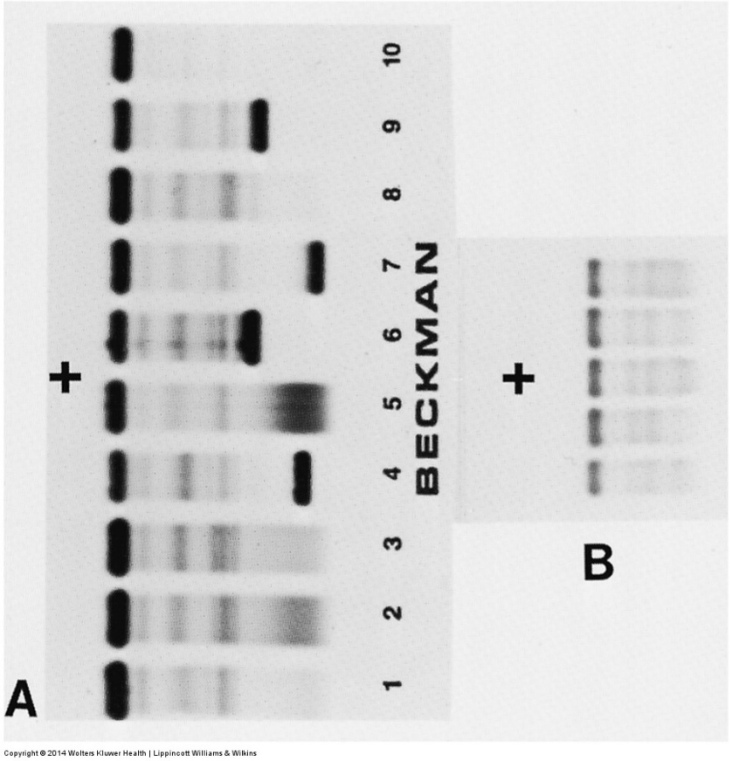
- Fractionation, Identification, & Quantitation of Specific Proteins
  - **Salt fractionation:** use of sodium salt to cause precipitation of globulins, leaving behind albumin, which can be measured
  - **Albumin:** binding of positively charged albumin with anionic dye by electrostatic forces
  - **Total globulins:** measurement of total globulin level in serum by direct colorimetric method using glyoxylic acid; albumin can then be calculated by subtracting globulin from total protein
  - **Electrophoresis:** separation of proteins on basis of electric charge densities

Methods of Analysis (cont'd)

- Serum Protein Electrophoresis
  - Serum samples are applied close to cathode end of support medium that is saturated with an alkaline buffer.
  - Support medium is connected to 2 electrodes & current is passed through medium to separate proteins.
  - Protein fractions are fixed by immersing support medium in an acid solution to denature & immobilize proteins.
  - Proteins are stained & appear as bands on support medium.
  - Membrane is inspected visually or with a scanning densitometer.
  - Most significant finding is monoclonal immunoglobulin.

Methods of Analysis (cont'd)

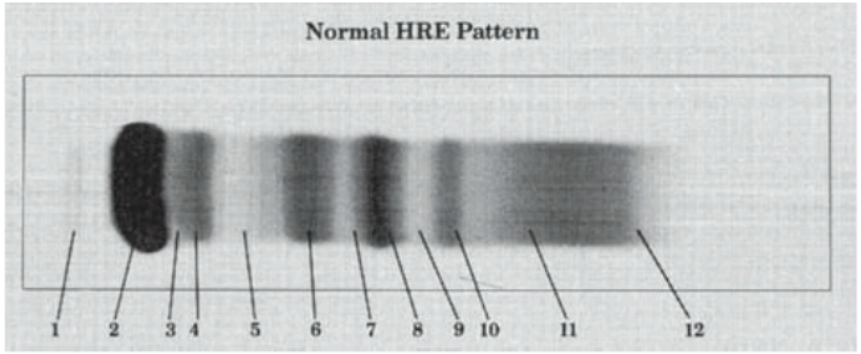
- Serum protein electrophoretic patterns on agarose & cellulose acetate



(Courtesy of Department of Laboratory Medicine, The University of Texas M.D. Anderson Hospital, Drs. Liu, Fritsche, and Trujillo, and Ms. McClure, Supervisor.)

Methods of Analysis (cont'd)

- High-Resolution Protein Electrophoresis
  - Allows further separation of proteins into as many as 12 bands
  - Uses higher voltage, cooling system, & more concentrated buffer
- Capillary Electrophoresis
  - Separation of molecules takes place in silica capillaries.
- Isoelectric Focusing
  - Zone electrophoresis that separates proteins on basis of pI
- Immunochemical Methods
  - Reaction of protein & antibody is measured by immunochemical assays.



Zones	Serum proteins found in zones
1. PREALBUMIN ZONE	-Prealbumin
2. ALBUMIN ZONE	-Albumin
3. ALBUMIN-α_1 INTERZONE	-α-Lipoprotein (α-Fetoprotein)
4. α_1 ZONE	-α_1-Antitrypsin, α_1-Acid glycoprotein
5. α_1-α_2 INTERZONE	-Gc-globulin, inter-α-trypsin inhibitor, α_1-antichymotrypsin
6. α_2 ZONE	-α_2-Macroglobulin, Haptoglobin
7. α_2-β_1 INTERZONE	-Cold insoluble globulin, (Hemoglobin)
8. β_1 ZONE	-Transferrin
9. β_1-β_2 INTERZONE	-β-Lipoprotein
10. β_2 ZONE	-C3
11. γ_1 ZONE	-IgA (Fibrinogen), IgM (Monoclonal Igs, light chains)
12. γ_2 ZONE	-IgC (C-reactive protein) (Monoclonal Igs, light chains)

Proteins listed in ( ) are normally found in too low a concentration to be visible in a normal pattern.

Proteins in Other Body Fluids

- Urinary Protein
  - Plasma proteins appear in urine because they have passed through renal glomerulus & not been reabsorbed by renal tubules.
  - **Methods of measurement:** qualitative with reagent test strip, precipitation, dye-binding, immunochemical
- Cerebrospinal Fluid Proteins
  - Abnormally increased levels occur in conditions in which there is an increased permeability of capillary endothelial barrier through which ultrafiltration occurs.
  - **Conditions include:** bacterial, viral, & fungal meningitis; traumatic tap; multiple sclerosis; obstruction; neoplasm; disk herniation; & cerebral infarction.

CASE STUDY 11-7

An 84-year-old woman resident of a nursing home was admitted to the hospital for treatment of lower back pain resulting from a fall. Radiologic examination revealed a vertebral compression fracture. Because she demonstrated signs of general deterioration, further medical evaluation was performed. A neurologic examination and CT scan were normal. Serologic examinations for collagen vascular disease were also negative, although the CRP showed a modest increase. Serum protein electrophoresis was done to rule out multiple myeloma. The serum protein fractions were as follows: albumin, 3.2 g/dL; α_1-globulins, 0.31 g/dL; α_2-globulins, 1.59 g/dL (elevated in a tight band); β-globulins, 0.72 g/dL; and γ-globulins, 0.96 g/dL.

Questions

1. What would the next step be in the evaluation of this patient?
2. Given the following additional result (haptoglobin: 416 mg/dL), what condition would explain her abnormal protein electrophoresis pattern?
3. What other proteins would you expect to be abnormal?

1. *Identification of the specific protein causing the elevation of the α2 spike would be required for accurate diagnosis.* ***The proteins making up this zone include haptoglobin, α2-macroglobulin, and ceruloplasmin.***

2. *The elevation in haptoglobin was most likely a result of an* ***acute phase reaction*** *to her recent traumatic experience.*

3. *It would be expected that other acute phase proteins would be affected. Specifically, the proteins in addition to haptoglobin that tend to rise in response to tissue damage or inflammation include* ***α1-antitrypsin, α1-acid glycoprotein, ceruloplasmin, C-reactive protein, and complement****. The proteins that tend to decrease in these conditions (negative acute phase reactants) include* ***prealbumin, albumin, and transferrin****.*