Biochemistry Learning Objectives & Competencies: Created & Approved at the 3rd International Conference of the Association of Biochemistry Course Directors (ABCD).

BIOCHEMISTRY LEARNING OBJECTIVES AND COMPETENCIES

INTRODUCTION

To support improvements in curricula, the ABCD decided to develop competencies and learning objectives in biochemistry for students. This process started at the 2009 meeting with the generation of topic lists that should be included in medical curricula. The importance of each topic in medical, pharmacy, and dental curricula was evaluated through member surveys conducted shortly before the 2011 meeting. At the 2011 meeting, nine working groups of 8-19 faculty each produced a set of learning objectives from the existing
topics lists and sample objectives. The resulting lists of learning objectives represented the consensus opinion of each working group.

A tenth working group reviewed and refined a parallel set of overarching competencies that were conceived and mapped to the six ACGME domains of competency by several ABCD members ahead of the meeting. The entire group of conference attendees approved that list of overarching competencies, which have been recently published (Fulton TB, Ronner P, and Lindsley JE. Medical Biochemistry in the Era of Competencies: Is it Time for the Krebs Cycle to go? Med Sci Educ 22(1): 29-32, 2012).

The ABCD is now working to review, refine, and link the existing learning objectives to these competencies. In the meantime, the ABCD is making available their current draft of learning objectives, which may be used as a resource for those interested in reviewing biochemistry in their existing curriculum, or to help guide those who are in the process of developing biochemistry content into their new or revised curriculum.

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1. DNA Replication, Transcription and Translation

1. Summarize the central dogma of molecular biology, and cite exceptions to the original model.
2. Compare and contrast the structure of DNA and RNA, explaining the difference between the constituent bases, sugars, nucleosides and nucleotides.
3. Describe the double-stranded, helical, and antiparallel chain structure of DNA and how it relates to the processes of DNA replication, transcription, recombination and repair.)
4. Compare and contrast the different types of RNA.
5. Summarize the mechanism of DNA replication and why discontinuous synthesis is required.
6. Explain the process of telomere replication and relate telomere dynamics to aging and disease.
7. Describe how DNA and DNA processes can be used as therapeutic targets (e.g. anticancer and antibacterial drugs).
8. Compare and contrast polymerase proofreading, direct repair, base excision repair, nucleotide excision repair, mismatch repair, and recombination.
9. Name the different types of mutations that occur in DNA.
10. Describe the universal features of the genetic code and describe its biological relevance.
11. Use the genetic code to predict the amino acid sequence of a protein for a given nucleic acid sequence and demonstrate how nucleotide mutations can lead to alterations in the primary structure of a protein.
12. Summarize why mutations in DNA repair systems can lead to disease, including certain types of cancer.
13. Summarize the initiation, elongation, and termination of transcription, comparing and contrasting these processes in eukaryotic and prokaryotic cells.
14. Compare and contrast prokaryotic and eukaryotic gene structure.
15. Describe the posttranscriptional processing of eukaryotic mRNA, and explain how diseases may result from alterations in the processing steps and cite examples.
16. Define RNAi and describe its role in regulation of gene expression.
17. Summarize the three steps of translation: initiation, elongation, and termination. Compare and contrast these processes and their regulation in eukaryotic and prokaryotic cells.
18. Summarize the effects of various antibiotics on prokaryotic protein synthesis, and potential side-effects of these antibiotics.
19. Describe the mechanisms of gene regulation, both negative and positive, as exemplified by prokaryotic systems.
20. Describe the structure and function of chromatin, and summarize the mechanism of remodeling required to make DNA accessible for biological processes.
21. Describe the cis and trans acting elements involved in eukaryotic transcription and summarize their regulation.
22. Describe how transcriptional defects may result in diseases and how this knowledge can be used to develop therapeutics.
23. Summarize the effect of covalent modification of chromatin on gene transcription (including methylation, histone acetylation and phosphorylation).
24. Define epigenetics and describe its role in development, imprinting and disease.
25. Describe the principles, methods, and applications of Northern, Southern, Western blot, microarray, PCR, and DNA sequencing for clinical and forensic sciences.

26. Describe how recombinant DNA technology is used to clone and express genes.

2. Fundamentals, Proteins, and Enzymes

Fundamentals:

1. Define and explain pH, pK, and the dissociation constant Kd.
2. Apply the Henderson-Hasselbalch equation to solve pH problems.
3. Define and explain briefly the role of entropy, and enthalpy in biochemical reactions
4. Define and explain Gibbs free energy (ΔG), standard free energy (ΔG0), and the equilibrium constant (Keq) as it applies to biochemical reactions.
5. Apply the Gibbs free energy equation to calculate free energy and equilibrium in coupled reactions.
6. Explain what is meant by the isoelectric point (pI)
7. Examine and assess the charge on a small peptide at a given pH.
8. Define and explain the roles of Van der Waals forces, charge-charge interactions, hydrogen bonds, and hydrophobic interactions in protein and macromolecular architecture and indicate how these forces differ from covalent bonds. (see also 2 below)

Protein Structure

1. List and name the 20 amino acids that commonly occur in proteins and classify them according to chirality, polarity, size, and charge.
2. Describe the bonds and forces (peptide, disulfide, and hydrogen bonds; hydrophobic, dipole-dipole, van der Waals and electrostatic interactions) that contribute to the conformation of proteins and the interaction of proteins with other biomolecules.
3. List and match the 3 letter codes identifying amino acids, including selenocysteine with their respective amino acid.
4. Define and discuss the following terms:
peptide bond, peptide backbone, N-terminus, C-terminus, disulfide bridges, α-helices, β-sheets, β -strands, β -turns.
5. Discriminate between primary, secondary, tertiary, and quaternary protein structure.
6. Integrate the forces in (#2) above with the structure considerations in (#5) above.
7. Propose reasons why folded proteins have a finite number of conformations.
8. Compare and contrast the difference between conservative and non-conservative amino acid substitutions and be able to identify and assess invariant positions.
9. Using the information in #s 6, 7, 8, and 9, evaluate the relationship of structure to function for the proteins myoglobin and hemoglobin.
10. Explain the formation of coiled–coils and protein fibrils and compare and contrast structure-function of fibrillar proteins to globular proteins.
11. Define and explain the role of membrane proteins.
12. Compare and contrast peripheral versus integral membrane proteins.
13. List, explain, and evaluate the role of each of the terms below with regard to membrane structure: phospholipids, membrane spanning α-helices, membrane β-barrels, membrane anchors (hydrophobic amino acids, myristic acid, prenyl groups, and glycophosphatidylinositol (GPI) anchor).
14. Use the following diseases as examples of how abnormal protein structure causes disease and be able to propose the mechanisms of abnormal function:
Sickle cell anemia (β-globin), Alzheimer's disease (β-amyloid), Crutzfeldt-Jacob / Kuru / Mad Cow disease (prion proteins), Huntington disease (poly-glutamine repeat diseases), Parkinson disease (α-

synuclein), osteogenesis imperfecta (Collagen), Erlers Danlos Syndrome (Collagen).
15. List, discuss, and evaluate the major techniques used in separating proteins, including: solubility; size, dialysis, sodium dodecyl sulfate polyacrylamide electrophoresis (SDS-PAGE); charge– ion exchange chromatography, size and charge– 2 dimensional gels; specific ligand binding – affinity chromatography, antigen-antibody recognition (Western Blot, ELISA); mass spectrometry of peptides and proteomics.
16. Describe the cellular machinery for protein folding and degradation, including the role of chaperonins, and the proteosome.

Biological Membranes:

1. List and describe the physiological roles of membranes including:
compartmentation, electrochemical/membrane potential, transport, anchoring.
2. Define micelles and liposomes and describe how they are formed spontaneously from detergent, bile acids, and phospholipids.
3. List and describe the roles of each of the major components of membranes and integrate each into a working model of a generic membrane, including:
phospholipids, sphingolipids, cholesterol, and protein [for example lipid rafts and caveola].
4. Explain the role of membrane fluidity and describe how it can be altered by biological processes.
5. List the various specific types of major membrane lipids and describe the role of membrane asymmetry.
6. Describe how a membrane is synthesized by the incorporation of monoacylglycerols and their modifications.
7. Describe and assess the role of the aminophospholipid translocases in the membrane [for example, "flippases", "floppases" (ABC transporters) and "scramblases" in membrane biosynthesis].

Membrane Transport:

1. Name two examples each of passive diffusion, active transport, and facilitated transport via a channel or carrier and briefly summarize the differences between each.
2. Explain in scientific and in laymen's terms the cause of Tay-Sachs disease (Recommend move to phospholipid metabolism).
3. Name two types of molecules that pass through lipid membranes without the aid of a transporter and describe what controls the rate of transport.
4. Compare and contrast the major differences between a pore/channel and a transmembrane carrier protein and propose reasons why membranes need both.
5. Compare and contrast the major differences between V-type pumps, P-type pumps, and the ATP binding cassette (ABC) pumps.
6. Describe and evaluate the role of ion gradients, co transporters, and ATP in active transport mechanisms.

Enzymes:

1. Describe the 6 major enzyme classifications and the basic type of reaction catalyzed, including: oxidoreductases, transferases, hydrolases, lyases, isomerases, and ligases.

2. Define and describe the roles of the following enzyme-related terms: zymogen/proenzyme, coenzyme, co-factors, prosthetic group, apoenzyme, holoenzyme, and isozymes.
3. Explain how an enzyme functions as a catalyst in lowering the activation energy of reactions.
4. Propose a thermodynamic explanation of why enzymes cannot alter the equilibrium of reactions.
5. Define the term transition state and propose a role for the transition state in lowering activation energy.
6. Explain how transition state inhibitors work as drugs.
7. Explain the induced fit (conformational changes) model of enzyme catalysis.
8. Name an example and describe basic catalytic mechanisms, including: serine proteases, covalent and acid-base catalysis.
9. Define initial velocity (v_o) and explain the effect of substrate concentration on enzyme velocity for a single subunit enzyme.
10. Explain Michaelis-Menton kinetics and be able to apply the Michaelis-Menton equation to calculate velocity, maximum velocity (Vmax) and the Michaelis-Menton constant Km.
11. Describe the significance of an enzyme's Km value in metabolic systems.
12. Draw a Lineweaver-Burke plot, defining Vmax and Km and use the plot to evaluate types of inhibition, including: competitive, non-competitive, and mixed inhibition in drugs.
13. Compare and contrast the different types of inhibitors, with examples including: transition state inhibitors, suicide inhibitors, irreversible inhibitors, competitive and noncompetitive inhibitors.
14. Evaluate the difference between a competitive versus non-competitive drug inhibitor (e.g. using fomepizole and ethanol treatments for methanol poisoning.)
15. Define and draw a generic substrate versus velocity plot of a cooperative reaction.
16. Define and explain allosterism and the important physiological role of allosteric enzyme inhibition or activation.
17. Define and compare and contrast feed-back versus feed-forward regulation.
18. Explain the role of post-translational modifications in regulating enzyme activity, including: proteolysis, and reversible phosphorylation.
19. Propose why some enzyme reactions are considered irreversible in the cell.
20. Evaluate and predict the effects of partial or complete enzyme deficiency on a metabolic pathway.

Extracellular Matrix:

1. Describe the role of collagen and elastin in connective tissue.
2. Describe the synthesis, posttranslational modification and assembly of collagen into a triple helix in the ER, and into collagen fibrils in the extracellular space and the physiological significance of this assembly process.
3. Describe the role of vitamin C in assembling, maintaining, and repairing the extracellular matrix.
4. List the key symptoms of vitamin C deficiency and be able to connect the symptoms to their pathogenic mechanisms.
5. Describe the synthesis of elastin and fibrillin and the subsequent assembly of elastic fibers.
6. Describe the distinct roles of elastase and of α1-antitrypsin (elastase inhibitor) in maintaining elastic fibers and explain how α1-antitrypsin deficiency causes emphysema.
7. Define the roles of adhesive proteins (RGD sequences), laminin, and both forms of fibronectin (soluble – blood clotting; insoluble – filaments) in the structure and function of extracellular matrix.
8. Identify the characteristic properties of proteoglycans and glycosaminoglycans and to describe

their synthesis, assembly and physiological role in the extracellular matrix.
9. Describe how integrins connect cells to the extracellular matrix and their physiological role.
10. Describe the changes in extracellular matrix molecules associated with wound healing and osteoporosis. Explain the rationale for using bisphosphonate in the treatment of osteoporosis.
11. List the key symptoms of osteogenesis imperfecta and be able to connect the symptoms with their pathogenic mechanisms.
12. List the possible symptoms of Ehlers-Danlos syndrome and connect the symptoms to their mode of inheritance and pathogenic mechanism.
13. Identify the role of the major components of the basal lamina and basement membrane in maintaining their overall structure.
14. Name the defective type of protein (collagen) and describe the pathogenic mechanism of thin-basement membrane nephropathy and Alport syndrome.
15. Name the defective protein (fibrillin) and describe the pathogenic mechanism(s) of Marfan syndrome.
16. Explain the rationale for the use of chondroitin sulfate in patients who suffer from arthritis.
17. Explain how deficiencies in enzymes that degrade glycosaminoglycans cause mucopolysaccharidoses (Hurler/Scheie, Hunter syndromes).

3. Blood

Coagulation:

1. Explain how platelets adhere to a surface, are activated, and aggregate to form a platelet plug.
2. Describe the two main roles of von Willebrand Factor (vWF) in hemostasis.
3. Explain how anti-thrombotic drugs such as aspirin interfere with the aggregation of platelets.
4. Explain why damage to the liver can result in impaired coagulation.
5. Describe the roles and pathways of coagulation factors in blood plasma in activating thrombin to promote coagulation.
6. Describe the mechanisms that prevent activation of clotting in healthy blood vessels.
7. Describe the steps in formation of a stable fibrin clot from fibrinogen. Contrast the structures of fibrinogen and fibrin in explaining the differences in their solubilities in blood.
8. Explain why patients who have hemophilia A or B have impaired clotting.
9. Explain the role of vitamin K in blood coagulation.
10. Describe the mechanism of the anti-coagulation effect of warfarin, and how warfarin poisoning can be reversed.
11. Relate the structures of gla-containing factors to their affinity for Ca^{+2} and thereby, to factor activation on platelet surfaces.
12. Explain how citrate, oxalate, EDTA, and heparin prevent the coagulation of drawn blood.
13. Propose a plan to monitor the effectiveness of a patient's warfarin treatment.
14. Describe the various mechanisms by which the clotting process is turned off once clotting factors have been activated, a stable clot has formed, and blood loss has been stemmed.
15. Describe the effects of Factor V Leiden on blood clotting.
16. Describe the physiological and pharmacological activation of antithrombin, as well as the effects of activated antithrombin on coagulation.
17. Describe the use of heparin in anti-thrombotic therapy. Critique the use of low compared to high molecular weight heparins in avoiding heparin-induced thrombocytopenia (HIT).
18. Applying knowledge of amino acid structure, predict why protamines (rich in arginine) can be used to reverse the effects of heparin therapy.
19. Explain how a fibrin clot is degraded physiologically. Describe pharmacological interventions to enhance degradation of fibrin clots and their application to myocardial infarction and ischemic stroke.
20. Identify a test to estimate the rate of fibrin degradation in a patient.
21. Compare and contrast the following laboratory measurements: Platelet function test; Prothrombin Time (PT), activated partial thromboplastin time (aPTT), and International Normalized Ratio (INR).
22. Using the above measurements, propose how to differentiate between Hemophilia A or B, von Willebrand Disease, and Vitamin K deficiency or warfarin poisoning.

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Hemoglobin:

1. Explain the role of hemoglobin in the delivery of oxygen, removal of waste and buffering
2. Define the composition of normal hemoglobin at various stages of development (include proteins and prosthetic groups)
3. Describe the structural difference between hemoglobin, myoglobin and methemoglobin (oxidized hemoglobin) and compare O2 binding properties of hemoglobin, methemoglobin and myoglobin.
4. Describe the allosteric effects of temperature, H+, 2,3-BPG and CO2 on the P50 of hemoglobin for O2. Explain how these effects enable appropriate oxygen delivery to tissues, buffering of the blood, and CO2 removal.
5. Explain how oxygen is delivered from the mother to the fetus, taking into account structural differences between adult and fetal hemoglobin and O2 binding affinity.
6. Explain the deleterious effects of CO on hemoglobin function. Describe why a rise in environmental CO can lead to hypoxia. Explain why a hyperbaric chamber may be needed for treatment of CO poisoning.
7. List conditions and treatments that lead to methemoglobinemia and describe the protective effects of glutathione.
8. Use laboratory values to create a differential diagnosis for anemia.
9. Analyze the results of hemoglobin composition studies and use them to differentiate between the major hemoglobinopathies (such as sickle cell trait and disease, thalassemia, HbC, etc)
10. Compare and contrast the pathogenesis and genetics of the major hemoglobinopathies (such as sickle cell trait and sickle cell disease, thalassemia, HbC, etc.).
11. Compare and contrast pathogenesis of iron, folate and B12 deficiency anemia including dietary absorption and transport of iron, folates and B12.
12. Explain how a B12 deficiency can lead to a functional folate deficiency.
13. Use lab values to distinguish between iron deficiency, folate deficiency and B12 deficiency anemia (e.g., homocysteine, TIBC, ferritin…).
14. Explain the pathogenesis of G6PD deficiency and use lab values to distinguish this from other hemolytic anemias.
15. Describe the effects of oxidizing drugs on patients who have G6PD deficiency.
16. Distinguish the endogenous cellular precursor from the pharmacologic precursor of nitric oxide (NO). Distinguish the calcium-dependent NO synthase of endothelial cells from the calcium-independent NO synthase of macrophages and neutrophils. Distinguish the local (paracrine) action of NO from its long-range (endocrine) action via hemoglobin as a carrier (S-nitrosylation).

Heme:

1. List the major classes of proteins that have heme prosthetic groups and describe the functional role of heme in these different classes of proteins.
2. Identify the major organs/tissues that have the highest rates of heme biosynthesis.
3. Describe the pathway of heme synthesis, with particular attention to control of the rate-limiting step, and the requirement for iron.

4. Categorize the biochemical, developmental and socioeconomic basis of lead poisoning. Predict the effectiveness of, and possible toxicities associated with, available treatments for lead poisoning.
5. Describe how defective heme synthesis leads to the following three porphyrias: PCT (porphyria cutanea tarda), AIP (acute intermittent porphyria) and EPP (erythropoietic protoporphyria); and distinguish the signs and symptoms, and treatment options.
6. Explain the rationale for the use of hemin and glucose in the treatment of porphyrias.
7. Describe the conversion of heme to first, unconjugated bilirubin, and subsequently, conjugated bilirubin (heme catabolism), with particular attention to the tissues in which this occurs, the transport of the intermediates, and the color of the intermediates.
8. Describe the metabolism of bilirubin by gut bacteria and explain how stool color can be used in the diagnosis of obstructive jaundice.
9. Distinguish the causes and consequences of the following types of jaundice: neonatal, hemolytic, hepatocellular, and obstructive.
10. Explain the significance of neonatal jaundice and describe the common treatment.
11. Distinguish between direct and indirect measurements of bilirubin and its implications for distinguishing the cause of the jaundice.
12. Explain the cause of Gilbert syndrome and describe the effects of this syndrome on bilirubin laboratory values.

Iron:

1. Compare and contrast hemochromatosis and anemia of chronic disease from the perspective of iron homeostasis.
2. Identify the clinical presentation of dysregulated iron homeostasis.
3. Choose and interpret lab tests to assess or evaluate a patient's iron status.
4. Judge the utility and limitations of serum ferritin in evaluating a patient's iron status.
5. Compare and contrast the use of phlebotomy and chelation therapy in the treatment of iron overload.
6. Explain the role of iron in creating reactive oxygen species that damage organs.
7. Differentiate laboratory values that are associated with iron deficiency or restriction due to insufficient dietary intake, bleeding, chronic inflammation, or cancer.
8. Explain the roles of the Iron Responsive Element (IRE) and the Iron Responsive Factor (IRF) in regulating the synthesis of transferrin receptor and ferritin. Predict the consequences of iron deficiency and hemochromatosis on the synthesis of transferrin receptor and ferritin.

4. Carbohydrate Metabolism

Nomenclature, Structure, Digestion, and Uptake:

- Identify the major monosaccharides, disaccharides, and polysaccharides found in the human body and diet
- Explain why ingested disaccharides and polysaccharides must be broken down into monosaccharides and describe how this is accomplished
- Draw a diagram of how glucose is transported across intestinal epithelial cells and into the bloodstream and describe the proteins involved
- Explain the biochemical basis of the efficacy of oral hydration therapy in the treatment of cholera
- Describe the role of glucose transporters (GLUTs) in the transport of glucose into and out of cells, and tissue specific differences in the expression and regulation of GLUTs
- Describe the common biochemical and clinical features of GLUT-2 deficiency
- Explain the biochemical basis for the symptoms seen in lactose intolerance

Glycolysis:

- Describe the overall purpose of glycolysis, its reactants and products, its cellular localization, and its tissue distribution
- Describe the roles of hexokinase/glucokinase, phosphofructokinase-1 (PFK-1), and pyruvate kinase in glycolysis and predict the biochemical and potential clinical consequences in deficiencies of these enzymes
- Compare and contrast the mechanisms for regulating glycolysis including allostery, hormonal regulation and covalent modification
- Differentiate the roles of hexokinase and glucokinase in blood glucose regulation
- Compare and contrast aerobic and anaerobic glycolysis in terms of the tissues in which they occur, reactants and products, purposes, and the conditions in which they occur
- Explain the concept of substrate level phosphorylation and why it is important
- Describe the purpose of the reaction catalyzed by lactate dehydrogenase, its reactants and products, cellular and tissue localization, and how it is regulated
- List conditions (inherited genetic defects in various pathways; drugs) that increase the risk of lactic acidosis
- Describe the role and fate of the cytosolic NADH produced in glycolysis
- Explain the biochemical basis of the hemolytic anemia observed in deficiency of erythrocyte pyruvate kinase
- Predict the results of a complete blood count (CBC) and iron studies in a person with pyruvate kinase deficiency who is in hemolytic crisis

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Gluconeogenesis:

- Describe the overall purpose of gluconeogenesis, its reactants and products, its cellular localization, and its tissue distribution
- Differentiate the enzymes involved in glycolysis vs gluconeogenesis
- Explain the contribution of gluconeogenesis to blood glucose regulation
- Describe the roles of pyruvate carboxylase, PEPCK, fructose 1,6 bisphosphatase and glucose 6-phosphatase in gluconeogenesis, and predict the biochemical and potential clinical consequences in deficiencies of these enzymes
- Evalute the relative importance of different precursors for gluconeogenesis in feeding, fasting, and exercise
- Explain how the activities of glycolysis and gluconeogenesis are regulated in response to fatty acid metabolism and protein metabolism, and in response to insulin and glucagon
- Explain the biochemical basis for the effects of alcohol ingestion on gluconeogenesis

Metabolism of Fructose and Galactose:

- Explain how fructose and galactose feed into the glycolytic pathway
- Describe the roles of fructokinase and hexokinase in catabolism of fructose and galactose
- Identify diseases that arise from defects in the metabolism of fructose and galactose
- Metabolism in muscle vs liver
- Describe the biochemical basis for the symptoms seen in aldolase B deficiency (hereditary fructose intolerance)
- Compare and contrast the symptoms seen in deficiency of galactokinase and galactose-1-phosphate uridyl transferase (GALT) deficiency and explain their biochemical basis
- Appraise and present current scientific evidence related to the contribution of fructose to obesity and risk for heart disease

Pentose Phosphate Pathway:

- For different tissue types, compare and contrast the overall purpose of the pentose phosphate pathway, its reactants and products, and its cellular localization
- Describe the role of reduced glutathione in the body, and the contribution of NADPH to its formation
- Explain the biochemical basis of the drug-induced hemolytic anemia observed in glucose 6-phosphate dehydrogenase deficiency
- Select laboratory tests used to diagnose glucose 6-phosphate dehydrogenase deficiency
- Predict the results of a CBC and iron studies in a person with G6PD deficiency who is in hemolytic crisis
- Explain the function of transketolase in the non-oxidative branch of the pentose phosphate pathway

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Pyruvate Dehydrogenase (PDH) Complex and the Tricarboxylic Acid (TCA) Cycle:

- Describe the overall purpose of the pyruvate dehydrogenase (PDH) complex, its reactants and products, its cellular localization, and its tissue distribution
- Compare the general structure, regulation, and required cofactors/vitamins of the PDH complex to that of alpha-ketoglutarate dehydrogenase and the branched-chain alpha-keto acid dehydrogenase complex
- Describe the overall purpose of the TCA cycle, its cellular localization, and its tissue distribution
- Describe the reactants and products of the TCA cycle, as related to the fates of the breakdown products of carbohydrates, fatty acids, and amino acids
- Describe the roles of citrate synthase, isocitrate dehydrogenase, alpha-ketoglutarate dehydrogenase, succinyl-coA synthetase, succinate dehydrogenase, and malate dehydrogenase in the TCA cycle and predict the biochemical and potential clinical consequences of deficiencies of these enzymes
- Explain the effect of the following parameters on the activity of the TCA cycle and the mechanism(s) by which the effect occurs: mitochondrial NADH:NAD ratio, ADP:ATP ratio, succinyl CoA concentration
- Describe the central role of the TCA cycle in connecting glycolysis, gluconeogenesis, oxidative phosphorylation, fatty acid metabolism, and amino acid metabolism
- Describe the role of TCA cycle intermediates as sources of reactants for biosynthetic pathways
- Describe the clinical result of severe thiamin deficiency, and connect the symptoms to the biochemical role of thiamin in the PDH complex and TCA cycle
- Explain the rationale for providing thiamin along with glucose to patients with suspected hypoglycemia

Oxidative Phosphorylation:

- Compare the mitochondrial content of different tissues and relate this characteristic to the function of the particular tissue (e.g. parietal cells, which utilize an ATP-requiring proton pump, have high mitochondrial content)
- Describe the purpose of the electron transport chain (particularly complexes I, III, and IV) and ATP synthase, their substrates and products, their cellular localization, and their tissue distribution
- Explain how electron transport and ATP synthase are functionally coupled
- Explain how the process of oxidative phosphorylation is influenced by the availability of oxygen and NADH
- Explain how the cellular ATP:ADP ratio regulates the rate of ATP production by oxidative phosphorylation
- Discuss how succinate dehydrogenase, mitochondrial glycerol 3-phosphate dehydrogenase and electron-transferring-flavoprotein dehydrogenase transfer electrons to ubiquinone from succinate, cytosolic NADH and fatty acid dehydrogenases, respectively.
- Explain the biochemical basis for generation of heat by brown fat and discuss the role of brown fat in infants and the possible role in adults

- Describe the effects of electron transport chain inhibitors, ATP synthase inhibitors, and uncouplers on oxidative phosphorylation, and predict the effects of these agents on glycolysis, the citric acid cycle, and lactate production
- Describe the biochemical and clinical features associated with ingestion/overdose of electron transport inhibitors (e.g. industrial exposure to cyanide and sodium azide) and uncouplers (e.g. aspirin, phthalate plasticizers) of oxidative phosphorylation
- List known mutations that cause defects in oxidative phosphorylation which result in myopathies and neuropathies (including exercise intolerance) and explain the pathophysiologic basis and genetics of each mitochondrial disease
- Compare and contrast the activities of glycolysis and oxidative phosphorylation in cancer cells to those of non-cancerous cells

Glycogen Metabolism:

- Describe the overall purpose of glycogenesis and glycogenolysis, their reactants and products, their cellular localization, and their tissue distribution
- Explain the contribution of glycogenesis and glycogenolysis to blood glucose regulation during the fed state, the fasting state, and exercise
- Describe the roles of glycogen synthase and branching enzyme in glycogenesis, and predict the biochemical and potential clinical consequences in deficiencies of these enzymes
- Explain how glycogen synthesis and glycogenolysis are regulated by insulin, glucagon, and catecholamines
- Describe the roles of glycogen phosphorylase, debranching enzyme, and glucose 6-phosphatase in glycogen breakdown, and predict the biochemical and potential clinical consequences in deficiencies in these enzymes glucose 6-phosphatase – explicitly ask about absence in muscle
- Compare and contrast the purpose and regulation of glycogenolysis in hepatocytes vs skeletal muscle
- Distinguish the symptoms that arise from glycogen storage diseases that affect the muscle, the liver, and lysosomes and explain their biochemical basis
- Select laboratory tests that would contribute to the diagnosis of glycogen storage diseases
- Describe the commonly used treatments for glycogen storage diseases and the biochemical basis for their efficacy

Glycoproteins, Proteoglycans, and Glycolipids:

- Define the following terms and explain their relationships to one another: glycosaminoglycan (GAG), glycoprotein, proteoglycan, and glycolipid
- Describe the biochemical basis and common clinical features of the mucopolysaccharidoses and glycosphingolipidoses
- Distinguish between N- and O-glycoproteins
- Describe the role of dolichol in N-linked glycolprotein synthesis
- Differentiate between the ER and Golgi in terms of sites of glycoprotein syntheses
- Describe the biochemical basis of I-cell disease
- Explain the role of glycans in determining blood groups

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Ethanol Metabolism:

- Identify the metabolic products of ethanol metabolism including acetyl coenzyme A.
- Evaluate the metabolic effects and clinical significance of ethanol and its metabolites.

Higher level, more comprehensive objectives:

- Generate a problem list with potential biochemical causes of hypoglycemia, hepatomegaly, or lactic acidosis
- Create a diagram that shows the ways that the following branch point intermediates can be generated and utilized: glucose 6-phosphate, pyruvate, acetyl CoA

5. Lipid Metabolism

Overview of Lipid Metabolism:

A. Differentiate the contribution of diet and endogenous synthesis to lipid levels.
B. Differentiate the role of dietary omega-3 versus omega-6 fatty acids in the formation of polyunsaturated fatty acids and the consequences for eicosanoid production.
C. Distinguish the effects of the feeding, fasting, exercise and hormonal regulation on body lipids.

Fatty Acid and Triglyceride Biosynthesis:

A. Describe the pathway of fatty acid synthesis and in particular the role of malonyl-CoA carboxylase and fatty acid synthase.
B. Outline short-term and long-term regulation of fatty acid synthesis.
C. Explain the concepts of elongation and desaturation of the fatty acid chain.
D. Describe the synthesis of triglycerides.
E. Describe endocrine function of adipose tissue.

Beta-Oxidation & Ketone Body Formation:

A. Describe the mechanism for activation and transport of fatty acids into mitochondria for catabolism.
B. Outline the sequence of reactions involved in oxidation of fatty acids in mitochondria.
C. Describe the general features of pathways for oxidation of unsaturated odd-chain and branched-chain fatty acids.
D. Explain the mechanism for the formation of ketone bodies and identify the physiological and pathological roles of those molecules.
E. Describe the mechanism by which hormonal activation of lipolysis in adipose tissue is coordinated with activation of gluconeogenesis in liver during fasting.
F. Describe the composition of triglycerides and complex phospho- and glycolipids.
G. Show how diacylglycerol serves as an intermediate in more than one pathway of lipid synthesis.
H. Contrast different strategies used in the synthesis of phosphatidyl compounds.
I. Identify the action of different phospholipases.

Synthesis & Degradation of Sphingolipids:

A. Distinguish the composition of different sphingolipids.
B. Explain how specific enzyme deficiencies can result in the inborn errors of metabolism known as sphingolipidoses.

Cholesterol & Bile Acid Metabolism:

A. Compare and contrast the structure and function of cholesterol and cholesterol esters.

B. Distinguish the mechanisms by which cholesterol biosynthesis is regulated by energy availability, hormones, food intake and pharmacological manipulation.
C. Interpret the effect of up-regulating or down-regulating plasma cholesterol levels on the intracelleular synthesis of choleserol, and the transcriptional regulation of genes that are involved in cholesterol homeostasis.
D. Summarize the process of cholesterol breakdown and elimination from the body.

Lipoprotein Metabolism:

A. Compare and contrast the life cycle of the various lipoprotein particles with respect to their composition, metabolism and transport.
B. Categorize the different hyperlipidemias.
C. Summarize the different biochemical pathways that could potentially be targeted pharmacologically in the management of heart disease i.e. high LDL, low HDL.
D. Describe the increasing incidence of obesity and diabetes and its impact on atherosclerosis.
E. Describe the risk factors of the metabolic syndrome and its specific lipid abnormalities.
F. Identify the statins as the main therapeutic intervention in dyslipidemia/atherosclerosis and interpret their action in terms of the inhibition of HMG CoA reductase.

6. Signaling, Hormones, and Diabetes

Basics of Signal Transduction:

1. Describe the properties of receptor-ligand interactions
2. Provide examples of each of the following major classes of receptors and compare and contrast their mechanism of signaling and termination: receptor tyrosine kinases, cytokine receptors, serine/threonine linked receptors, G-Protein coupled receptors, cytoplasmic/nuclear receptors and guanylyl cyclase linked receptors, channel receptors.
3. Describe the role of these signal transduction pathways in controlling normal cellular, systemic and organismal functions.
4. Describe how alterations in signal transduction pathways can lead to human disease.
5. Describe how signal transduction pathways can be used as targets for disease therapy.

Hormones related to blood glucose levels and diabetes:

1. Explain how insulin is processed and why C-peptide is a useful measure of insulin secretion in diabetic patients.
2. Summarize the process by which insulin is secreted.
3. Compare and contrast how each of the following affects insulin secretion: glucose, amino acids, ketone bodies, epinephrine.
4. Describe the properties of the insulin receptor and outline the molecular events which, after ligand binding, lead to IRS activation.
5. Describe the effect of insulin on the processes and pathways that regulate blood glucose homeostasis.
6. Compare and contrast the characteristics of insulin-dependent and non-insulin-dependent glucose transporters.
7. Compare and contrast the effect of insulin on the metabolic events which follow glucose uptake in liver, muscle and adipose tissue.
8. Describe the clinical presentation of a patient with an insulinoma (sporadic or MEN) or autoimmune hypoglycemia.
9. Compare and contrast how each of the following affects glucagon secretion: glucose, amino acids, ketone bodies, epinephrine.
10. Describe the effect of glucagon on metabolic processes in the liver and how this hormone functions to regulate blood glucose homeostasis.
11. Define the roles of glucagon-like peptides 1 and 2 in regulation of glucose homeostasis.

Diabetes:

1. Compare and contrast type 1 and type 2 diabetes mellitus with respect to incidence, age of onset and distinguishing characteristics.
2. Recognize the clinical presentation of type 1 diabetes mellitus and discuss established diagnostic criteria.
3. Describe abnormalities in blood glucose homeostasis in patients with type 1 diabetes.
4. Compare and contrast postprandial blood glucose changes in a patient with type 1 diabetes with someone who does not have diabetes.

5. Compare and contrast the available therapeutic options for type 1 diabetes mellitus.
6. Discuss the metabolic derangements leading to diabetic ketoacidosis.
7. Describe the classical presentation of a patient with diabetic ketoacidosis; include expected laboratory values and treatment options.
8. List the long-term complications associated with poorly controlled blood glucose levels and the organs and tissues that are affected.
9. Define metabolic syndrome and insulin resistance.
10. Discuss how lifestyle factors impact the development of type 2 diabetes.
11. Compare and contrast the available therapeutic options for type 2 diabetes mellitus.

Thyroid hormones:

1. Describe the synthesis and secretion of thyroid hormones T_4, rT_3 and T_3 noting the steps that occur exclusively in the thyroid gland and those in peripheral tissues.
2. Explain how the secretion of thyroid hormones is regulated by Thyroid Releasing Hormone (TRH) and Thyroid Stimulating Hormone (TSH).
3. Discuss the regulation of iodine uptake by the thyroid gland and the effects of iodine deficiency
4. Describe the molecular basis of thyroid hormone action
5. Discuss the normal physiological effects of thyroid hormone on the cardiovascular, GI and musculoskeletal systems.
6. Discuss the etiology of common diseases that cause hyper and hypothyroidism, their common presentation and treatments.

7. Amino Acid Metabolism

Digestion of proteins:

1. Describe the dynamics of the free amino acid pool, including (A) inputs from diet, body protein breakdown, and de novo synthesis (B) outputs to protein synthesis, urea production, synthesis of specialized products and other metabolic processes.
2. Describe factors affecting nitrogen balance in health and disease.
3. Describe the importance of dietary protein quality in the maintenance of health, and the consequences of protein-energy malnutrition (e.g. Marasmus and Kwashiorkor).
4. Describe the role of gastric hormone gastrin and paracrine hormone histamine in promoting secretion of HCl and pepsinogen, and the activation of pepsinogen to pepsin. Describe pepsin action in the digestion of peptides. Describe the symptoms and potential problems associated with hypochlorhydria or achlorhydria.
5. Describe the roles of secretin, bicarbonate and cholecystokinin in the neutralization of duodenal pH, and the release of bile and pancreatic zymogens.
6. Describe the activation of pancreatic zymogens and the roles of the active enzymes in protein digestion.
7. Describe the consequences of pancreatic insufficiency.
8. Describe the uptake of peptides and amino acids from the gastrointestinal tract. Note: in neonates the absorption of intact proteins.
9. Identify defects in the uptake of amino acids (e.g. Hartnup disease) or peptides that lead to clinical symptoms (failure to thrive, edema, various vitamin deficiencies).

Protein turnover:

1. Compare and contrast degradation of body protein via ubiquitin-mediated proteolysis, and lysosomes, and explain their regulation.
2. Describe how aberrations of the ubiquitin-mediated proteolytic pathway can lead to disease.

Urea cycle:

1. Explain the rationale of the urea cycle in ammonia excretion.
2. Describe the interconversion between ketoacids and amino acids, including the requirement of pyridoxal phosphate (PLP) as a cofactor.
3. List specific examples of ketoacid/amino acid transamination reactions (pyruvate/alanine, oxaloacetate/aspartate, α-ketoglutarate/glutamate), including the names of the enzymes, and apply the measurement of aminotransferase activity to the diagnosis of liver (and other) diseases.
4. Describe the importance of the reactions catalyzed by (A) glutamine synthetase, (B) glutaminase, and (C) glutamate dehydrogenase.
5. List the two subcellular compartments used by the urea cycle.
6. Describe the roles of arginine and ornithine in metabolic pathways other than the urea cycle (in NO and synthesis, respectively).

7. Describe the reactions of the Urea Cycle, including the (A) specific enzymes, (B) the input substrates (NH_4, HCO_3, ornithine, and aspartate), and (C) energy requirements.
8. Describe urea cycle regulation by allosteric effectors, substrate availability, and enzyme levels.
9. List the causes for hyperammonemia, its consequences, and treatments to reduce blood ammonia levels.
10. Identify the connections and common intermediates between the Urea Cycle and TCA cycle.

Amino Acid Synthesis:

1. Define essential, conditionally essential, and nonessential amino acids, and list them accordingly.
2. Explain how certain nonessential amino acids become essential in certain conditions and states.
3. Integrate amino acid synthesis with specific precursors from glycolysis, citric acid cycle and the pentose phosphate pathway.
4. Explain the role of transamination reactions in amino acid synthesis and identify the vitamin essential for this reaction (tie in to urea cycle).
5. Describe the roles of folic acid, cobalamin and S-adenosylmethionine (SAM) in the transfer of one carbon units between molecules, and apply their relevance to certain conditions and disease states.

Conversion of Amino Acids to Specialized Products:

1. Describe porphyrin and heme synthesis, including normal regulation, lead inhibition, and the clinical manifestations of specific porphyrias (deficient enzyme, tissue specificity, metabolite build up, photosensitivity).
2. Describe heme catabolism, including the different tissues in which different reactions occur, and the difference between total, direct and indirect bilirubin.
3. Compare and contrast the clinical settings involved in different forms of jaundice (hemolytic, hepatocellular, obstructive and neonatal), and relate them to the different metabolites of heme catabolism.
4. Compare and contrast between a deficiency of phenylalanine hydroxylase and tetrahydrobiopterin in the cause and treatment of classical PKU and hyperphenylalaninemia.
5. Discuss the role of tyrosine in catecholamine synthesis.
6. Compare and contrast dopamine levels (or dopamine receptor function) in Parkinson's disease versus schizophrenia.
7. Explain how (levodopa/cardiodopa) is used to treat Parkinson's disease.
8. Define the role of tetrahydrobiopterin in the synthesis of tyrosine, catecholamines, and indolamines, and how a deficiency in tetrahydrobiopterin regeneration or synthesis can lead to decreased catecholamine and serotonin synthesis.
9. List the amino acid precursors of γ-aminobutyrate (GABA), carnitine, polyamines, glutathione, serotonin, histamine, ubiquinone, melanin, and creatine.
10. Describe the role of tyrosinase in albinism.

Biochemistry Learning Objectives & Competencies: Created & Approved at the 3rd International Conference of the Association of Biochemistry Course Directors (ABCD).

Amino acid degradation:

1. Define ketogenic and glucogenic amino acids, and list them as exclusively ketogenic, glucogenic, or both.
2. List which amino acids are precursors to citric acid cycle intermediates and identify the specific intermediates (in addition to Acetyl-CoA and Acetoacetyl-CoA).
3. Distinguish the following disease states associated with Inborn Errors of Metabolism, including (A) the deficient enzyme, (B) relation of the deficiency to the buildup of secondary metabolites, and (C) clinically relevant information related to the disease state (vitamin deficiencies, symptoms, diagnosis, pathology and treatments - diseases are listed in order of most common to least common).
    a. Cystinuria
    b. Histidinemia
    c. Phenylketonuria (PKU) – know difference between classical, atypical and maternal PKU.
    d. Methylmalonyl CoA mutase deficiency
    e. Albinism (with lesser priority to vitiligo and Menke disease).
    f. Homocystinuria
    g. Alcaptonuria
    h. Maple syrup urine disease (branched chain amino acids; tie in with pyruvate dehydrogenase complex and alpha-ketoglutarate dehydrogenase complex, and the requirement for thiamine, lipoic acid, niacin, riboflavin and pantothenate).
    i. Cystathioninuria
    j. Tyrosinemia

8. Nucleotides, Folates, and One Carbon Metabolism

Medical Knowledge:

1. Name the major purine and pyrimidine bases and identify amino acid and one-carbon metabolites that contribute to the synthesis of these ring structures.
2. Integrate the terminology and defining structural features that distinguish different classes of nucleotide metabolites (such as purine vs. pyrimidine, bases vs. nucleoside vs. nucleotide, and ribo- vs. deoxyribo-).
3. Describe the biosynthesis of the purine and pyrimidine nucleotides with emphasis on the key regulated steps.
4. Explain the purine salvage pathways and discuss the central role of hypoxanthine phosphoribosyltransferase (HPRT) under physiological (such as steady-state purine nucleotide synthesis) and pathophysiological (such as gout in partial and complete HPRT deficiencies) conditions, and in pharmacotherapy (anti-purine chemotherapy).
5. Explain the salvage pathways for uracil and thymine and their relevance to pharmacotherapy (such as for the treatment of cancer or herpes infections).
6. Connect the pentose phosphate pathway to 5'phosphoribosyl-1-pyrophosphate (PRPP) synthesis and explain the central role of this metabolite in nucleotide metabolism.
7. Differentiate the interplay and relative contributions of the de novo and salvage pathways in maintaining steady-state purine and pyrimidine nucleotide levels.
8. Explain the role of adenylate kinase in nucleotide interconversion and connect this to adenine nucleotide catabolism during periods of increased demand or reduced supply of ATP.
9. Summarize purine nucleotide catabolism and explain the significance of alternate adenine nucleotide catabolic pathways under physiological (such as intense anaerobic exercise) and pathophysiological (such as myocardial ischemia) conditions.
10. Identify inborn errors of purine metabolism (such as deficiencies of HPRTase and adenosine deaminase) and compare and contrast their primary clinical presentations.
11. Describe the ribonucleotide reductase reaction and its regulation, and explain its role in cancer chemotherapy and in adenosine deaminase deficiency.
12. Summarize folate metabolism and explain its connection to nucleotide metabolism (such as the synthesis of thymidine and IMP).
13. Compare and contrast the effects of 5-flurouracil (5-FU) and methotrexate (MTX) on the synthesis of thymidine.
14. Explain the mechanisms by which antifolates interfere with bacterial growth. Discuss the roles of antifolates in treating bacterial infections.
15. Describe the synthesis of S-adenosylmethionine and its role in methylation reactions.
16. Explain how a cobalamin deficiency leads to a secondary folate deficiency.

Patient Care: Clinical Testing:

1. Distinguish between hyperuricemia and gout and identify physiological and pathophysiological effectors of circulating uric acid levels.
2. Explain the relationship between uric acid insolubility and gout and discuss the differential diagnosis of this disorder.

3. Distinguish between xanthine dehydrogenase/oxidase and explain how allopurinol and febuxostat inhibit uric acid formation.
4. Compare and contrast the management of acute vs. chronic gout.
5. Compare and contrast the benefits and drawbacks of approved therapies for gout (such as allopurinol vs febuxostat vs pegylated uricase) and ADA-SCD (such as gene therapy vs pegylated ADA).
6. Describe conditions that lead to elevated orotic acid and interpret urine orotic acid concentration for the diagnosis of defects of the urea cycle or pyrimidine biosynthesis.
7. Interpret laboratory data (such as serum folic acid, cobalamin, and methylmalonic acid) to distinguish between primary and secondary folate deficiency.
8. Select lab tests that would contribute to the diagnosis of pernicious anemia.

9. Nutrition

1. Select, justify, and interpret the results of clinical tests in order to identify likely molecular and metabolic causes of nutritionally-related disease states and conditions. For example, metabolic panel, CBC, UUN, urinalysis, B-12/folate, anthropometrics, DEXA scan, lipid panel, prealbumin, serum iron; transferrin, non-glucose-reducing substances, neonatal screen, urine organic acids, serum amino acids, fecal fat test, 25-OH vitamin D, creatine-height index, delayed hypersensitivity skin test, PT/INR, serum magnesium.
2. Based on patient history, physical exam, medical record, and/or laboratory test results, develop differential diagnoses for molecular and metabolic causes of disease states For example, genetically inherited causes of metabolic acidosis, jaundice (indirect or direct hyperbilirubinemia), hypoglycemia, hyperammonemia, hemolysis.
3. Interpret presenting symptoms associated with a primary deficiency or toxicity of micronutrients and trace elements, such as osteopenia, nyctalopia, microcytic anemia, and megaloblastic anemia.
4. Identify the diagnostic criteria for syndromes associated with malnutrition and disordered eating.
5. Interpret neonatal genetic and laboratory measures consistent with the diagnosis of inborn errors of metabolism, such as PKU, MSUD, and cysteinuria.
6. Interpret laboratory and radiological data associated with common nutritional disorders, such as hematological indices and DEXA.
7. Identify the genetic and lifestyle (nutritional) causes of dyslipidemias, obesity-related disorders such as type II diabetes, and metabolic syndrome.
8. Identify nutrient-drug interactions including symptoms associated with nutritional deficiencies caused by drug abuse.
9. Select and apply preventive, curative, and/or palliative strategies for the management of conditions or disease states with a nutritional basis/component. For example, aging, pregnancy, diabetes, hypercholesterolemia, galactosemia, glucose 6-phosphate dehydrogenase deficiency, glycogen storage diseases, urea cycle disorders, lysosomal storage diseases, hyperuricemia/gout, fatty acid oxidation deficiencies, PKU, alcoholism, toxic exposure (iron, methanol, ethylene glycol).
10. Predict the effectiveness of, and possible adverse effects associated with, interventions for conditions or diseases with a nutritional basis predicated on knowledge of molecular and cellular regulatory mechanisms. (For example: reduction of dietary trans fats for dyslipidemia, increased exercise for insulin resistance, Olestra, Orlistat/Alli, carbohydrate absorption inhibitors, artificial sweeteners, antibiotics (vitamin K; intestinal fauna/flora), laxatives, lactase (lactase persistence, lactose intolerance), niacin (flushing, prickling, liver damage), bariatric surgery (B12), excessive use of antioxidants, drug nutrient interactions (metformin-folate), Atkin's and renal failure, IEMs and diet, low-fat diets, etc).
11. Describe the roles of micro- and macronutrients.
12. Apply the principles of homeostasis to an understanding of nutrient processing and storage.
13. Define calorie, basal metabolic rate, respiratory quotient, and daily energy expenditure, and describe how these values are measured or calculated.
14. Identify individuals, populations or communities at risk for nutritional imbalances as a result of genetic, environmental, demographic or socio-cultural influences.
15. Explain the nutritional basis for the major chronic and metabolic conditions and diseases.

For example: obesity, cardiovascular disease, hypertension, diabetes, PKU, anemias

16. Describe common biochemical and clinical features of nutritional disorders.
17. Describe the general characteristics of a healthy diet.
18. Define nitrogen balance and explain how it is affected by dietary intake, growth and metabolic stress.
19. Define essential and list examples of essential, conditionally and non-essential nutrients.
20. List major sources of micro- and macronutrients.
21. Recognize the contribution of bacterial metabolism for nutrient availability.
22. Describe the consequences of disease on human nutritional requirements.
23. Evaluate the molecular and metabolic plausibility of nutritional claims made in the medical and lay public literature based on appraisal of scientific evidence and biochemical reasoning.
24. Demonstrate effective use of nutrition and dietetic counseling and referral services.

Competency Domain	Proposed biochemistry competency	Sample learning objective
Medical Knowledge	Apply and integrate molecular and metabolic knowledge of conditions and disease states for clinical problem solving (e.g., diabetes, carcinogenesis, mental illness).	Explain the biochemical basis of (disease).
	Apply molecular and metabolic reasoning to evaluate clinical and translational research.	Describe how the development of effective therapies is based on an understanding of the molecular or metabolic nature of (disease).
Patient Care Sub-Domain: Clinical Testing	Select, justify, and interpret the results of clinical tests in order to identify likely molecular and metabolic causes of disease states (e.g., PCR, complete blood count, comprehensive metabolic panel).	Predict the results of (specific lab tests) for a patient with (specific disease/condition).
Patient Care Sub-Domain: Diagnosis	Based on patient history, physical exam, medical record, and/or laboratory test results, develop differential diagnoses for molecular and metabolic causes of disease states (e.g., metabolic acidosis, hyperbilirubinemia, hypoglycemia, hemolysis).	Prioritize and justify diagnoses that explain a (presenting symptom, physical exam finding, lab test).
Patient Care Sub-Domain: Clinical Intervention	Select and apply preventive, curative, and/or palliative strategies for the management of conditions or disease states with a molecular or metabolic basis (e.g., hypercholesterolemia, Lynch syndrome, hemoglobinopathies, glucose 6-phosphate dehydrogenase deficiency, PKU, poisoning).	Explain the biochemical basis of the use of (specific clinical intervention) in the treatment of (specific disease/condition).
	Predict the effectiveness of, and possible adverse effects associated with, interventions for conditions or diseases based on knowledge of molecular, genetic and cellular regulatory mechanisms (e.g., reduction of dietary trans fats for dyslipidemia, insulin analogs for hyperglycemia, allopurinol for hyperuricemia).	Explain the biochemical basis of (specific toxicities) seen with (specific clinical intervention).
Practice-Based Learning and Improvement	Evaluate the molecular and metabolic plausibility of claims made in the medical and lay public literature based on appraisal of scientific evidence and biochemical reasoning.	Produce a written or oral evaluation of an advertisement for a (drug, nutritional supplement, etc.), citing current literature.
	Demonstrate curiosity about the molecular and biochemical basis for the maintenance of health and the causation of disease.	Formulate a question, the answer to which could improve diagnosis and/or treatment of patients.
	Demonstrate knowledge and appropriate use of information literacy for the clinical diagnosis, testing, and understanding of biochemistry-based conditions.	Conduct a literature search and identify the most relevant articles or other forms of information regarding (disease).
	Based on assessment data and feedback related to biochemistry, reflect on one's own performance to identify strengths and challenges, set learning and improvement goals, and engage in appropriate learning activities to meet those goals.	Document evidence of reflection on progress toward learning goals.
Interpersonal and Communication Skills	Effectively explain to patients from a variety of backgrounds the molecular and metabolic basis of conditions and disease states and how lifestyle and/or therapeutic interventions can alter their manifestations.	Explain the molecular basis of (disease) to a standardized patient.
	Communicate biochemical reasoning effectively with peers, medical school staff and faculty, and other members of the health care team.	Teach a peer about (biochemical process) and ensure that the peer meets the relevant learning objectives.
	Communicate enthusiasm for knowledge to patients and professional colleagues.	Ask thoughtful questions regarding how we know what we know, and how we can learn more.

Table 1. *Proposed biochemistry competencies and sample learning objectives*

Professionalism	Demonstrate empathy and respect towards patients regardless of the biochemical nature of their disease and with sensitivity to diversity (e.g., obesity, depression, alcoholism).	Reflect about your personal biases regarding the causes of (disease).
	Demonstrate respect, accountability, and reliability in interactions with patients, families, peers, and other healthcare professionals.	Arrive on time to required sessions and meet deadlines without reminders.
	Demonstrate ethical behavior and integrity in one's work.	Cite resources appropriately.
Systems-Based Practice	Demonstrate effective use of nutrition, lifestyle and genetic counseling referral services.	Identify when to consult a dietitian or genetics counselor.
	Contain healthcare costs by selecting and justifying diagnostic measures and treatments.	Prioritize and justify the use of (specific diagnostic test) for patients with (specific signs and symptoms).

Table 1 (cont.). *Proposed biochemistry competencies and sample learning objectives*

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