

Human Metabolism: Macronutrients

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Time/place: Fall 2015: 10:10 -11:00 MWF / 2306 McGavran-Greenberg

Prerequisites: NUTR 400 (or CHEM/BIO 430) OR for PhD students, a biochemistry course; CHEM 261 (organic chemistry) & BIOL 252 (anatomy/physiology) or equivalents.

Course Description: Our objective is to enable UNC students to understand the relationships between macronutrient biochemistry and metabolism during specific physiological and disease states. We will cover the metabolic and physiological functions of nutrients at different levels - molecular, cellular, organ and whole body. We will focus on aspects of current research that are relevant to macronutrient-related diseases (e.g. atherosclerosis, obesity, diabetes, cancer, perinatal growth). Students will be encouraged to develop their ability to analyze current articles/ reviews/ advertising/ diet and drug recommendations related to the topics of this course.

Text: PowerPoints for the lectures will be available to you before the relevant class. I recommend that you look at the PPTs before class. Lippincott's Illustrated Reviews, 4th, 5th or 6th edition *Biochemistry* is recommended, but *optional*. You can use another biochemistry text if you prefer.

Exam questions will be based primarily on the lectures and PPTs.

A man cannot become a competent surgeon without the full knowledge of human anatomy and physiology, and the physician without physiology and chemistry flounders along in an aimless fashion, never able to gain any accurate conception of disease, practicing a sort of popgun pharmacy, hitting now the malady and again the patient, he himself not knowing which.
Sir William Osler (1849-1919)

Important Points:

1. **Practice questions** are available on page 12
2. **Cell phones** must be off in class. If yours rings, you must leave the room and not return.
3. **Plagiarism** will result in a zero for the work. Plagiarism is the use of someone else's words or ideas as your own without giving credit to that person.
4. **Sources for information:** Any source you use for an assignment must be cited AND you must tell me (briefly) why you considered this source to be a valid one. This includes the Web. If you use a poor or unreliable source, you will receive a poor grade.
5. **Exams.** No make-up exams will be given except for emergencies or illness. The latter must be documented by a letter from a physician. **Quizzes** – since you can drop your lowest quiz, there will be no quiz make-ups.
6. **Attendance is not taken.** Lectures are “captured” so that you can listen later. However, most students feel that class attendance is advisable.
7. **Sakai is used to communicate from professors and TAs to students.** For questions from students to instructors and TAs, please use email.

Accommodations. We want to ensure an optimal environment for students with physical or other disabilities. Students with a disability should contact the UNC Learning Center: <http://www.unc.edu/asp/index.html>. If you are experiencing life events or academic pressures that leave you feeling anxious, confused, lonely, angry, depressed or overwhelmed, please see a professional at the Counseling and Wellness office:

http://campushealth.unc.edu/index.php?option=com_content&task=blogcategory&id=33&Itemid=56

Assignments/Discussion sessions: The objective of these sessions and the assignments is to help you use and integrate information covered in the course. These sessions will help you understand disorders related to nutrition. You may be called on in class to discuss your answer. If you do not wish to be called on, please tell Dr. Coleman. Exams will cover information from these sessions.

Course Policy: Topics discussed in class will appear on quizzes and tests. You are responsible for knowing the due dates for assignments and tests. If you must be absent, you must hand in your assignment BEFORE the class. There are no “make-ups”. If you are sick, you must have a letter from Student Health or a physician in order to receive additional time to complete an assignment.

Late Policy: Assignments are due in class on the date specified. Assignments should be turned in during class at the front of the room. Unless you have permission, assignments turned in after class (hard copy or email) will be considered “late.” If an assignment is late, points will be deducted. Thus, for a 15 point assignment, you will receive 10 points if it is a) emailed after class begins or b) if a hard copy is received after class on the day assigned, and 5 points if it is received after midnight. These rules are in place 1) because we will discuss assignment answers in class and 2) to avoid discrepancies concerning the time a document was emailed vs. the time it was received.

Exams and Grading

Exams will contain ‘short answer’ and ‘discussion’ questions. The first part of the final exam will cover the last third of the semester and the second part will be a cumulative exam covering the first 2/3 of the course. There are no make-up exams without Dr. Coleman's permission obtained before the scheduled exam. Unless you are told otherwise, you are responsible for all material from **lectures and assignments (primary focus)** and, secondarily, from the parts of the chapters covered.

Quizzes (mostly [but not all] multiple choice) will be given weekly on material covered during the previous 2-3 lectures to ensure that everyone is keeping up. Quizzes are noted on your syllabus and will be 10 minutes long, starting precisely at 10:10 am.

Assignments are designed to enable you to think critically about nutrition and nutrient-related disorders. Some assignments will be graded in full and, for some, only a single section will be graded.

	Points	%
Exam 1	90	17
Exam 2	90	17
Quizzes (you may omit one 10 point quiz)	55	10.5
Assignments (worth 15 or 20 pts each)	90	17
Final exam	200	38
Total	525	100

These are **rough** guidelines for determining your letter grade from your numerical average. This scale assumes a final class average of ~84%. The scale may shift depending on the final average for your group (BSPH / MPH, PhD). In previous years, the vast majority of students received A, B, H, or P.

YOUR FINAL AVERAGE (%)	LETTER GRADE	YOUR FINAL AVERAGE (%)	LETTER GRADE	YOUR FINAL AVERAGE (%)	LETTER GRADE
93-100	A / H	83-85	B / P	70-74	C / L
89-92	A- / H	79-82	B- / P	66-69	C- / F
86-88	B+ / P	75-78	C+ / L	60-65	D / F

Expectations: Nutrition 600 integrates a large amount of material relevant to biology, physiology, biochemistry, metabolism, and human health. These are complex topics that require knowledge, understanding, and critical thinking, i.e. the ability to apply this knowledge to real life problems. We estimate that a student should spend about 2 to 3 hours/day outside of class reading, reviewing, and studying – in other words, 2-3 hours studying / hour of class (= 6 to 9 hours/week). **We highly recommend Study Groups.**

PLEASE: Do not try to cram the night before an exam. There is too much material and too much active learning that needs to go on in your brain to master these concepts when you are exhausted and stressed.

Collaboration: Since all graded work (including homework, quizzes, and examinations) is used to determine academic progress, no collaboration on this work is permitted unless the instructor explicitly states that some specific degree of collaboration is allowed. Students may study together and work together on assignments that are not collected.

Syllabus Changes:

The instructors reserve the right to make changes to the syllabus, including presentation dates when unforeseen circumstances occur. These changes will be announced as early as possible so that students can adjust their schedules.

Web Animations to help you understand. Let me know if any of these links do not work.

Co-transport, Sodium-Potassium Exchange Pump, Endocytosis and exocytosis, Proton pump

http://highered.mcgraw-hill.com/sites/0072437316/student_view0/chapter6/ Click on “animations”

Feedback inhibition

http://highered.mcgraw-hill.com/sites/0072437316/student_view0/chapter8/animations.html#

Hormone and G-protein (explanation of 1st and 2nd messenger)

epinephrine, cAMP, PKA and nuclear signaling

<http://www.sumanasinc.com/webcontent/animations/content/extracellularsignaling.html>

G-protein→PKC→open ion channel

<http://www.youtube.com/watch?v=A3AUhMCE9n0>

GPCR and cAMP. See: Signal amplification & Second messengers (cAMP and IP3/calcium)

http://highered.mcgraw-hill.com/sites/0072437316/student_view0/chapter7/animations.html#

Protein secretion (e.g. what happens to digestive enzymes, insulin & other peptide hormones)

<http://www.sumanasinc.com/webcontent/anisamples/molecularbilogy/proteinsecretion fla.html>

Glycolysis

<http://www.johnkyrk.com/>

TCA Cycle

<http://www.science.smith.edu/departments/Biology/Bio231/krebs.html>

<http://www.johnkyrk.com/>

Electron transport and ATP synthase

<http://www.science.smith.edu/departments/Biology/Bio231/etc.html>

<http://www.johnkyrk.com/mitochondrion.html>

http://highered.mcgraw-hill.com/sites/0072437316/student_view0/chapter9/animations.html#

Cholesterol enters cells via receptor-mediated endocytosis

<http://www.sumanasinc.com/webcontent/anisamples/molecularbiology/endocytosis.html>

DNA Structure/ synthesis

http://www.sumanasinc.com/webcontent/anisamples/molecularbiology/DNA_structure.html

DNA replication

<http://www.johnkyrk.com/DNAreplication.html>

Dynamic DNA replication

<http://www.youtube.com/watch?v=E8NHcQesYl8&mode=related&search=>

mRNA synthesis (transcription)

http://www-class.unl.edu/biochem/gp2/m_biology/animation/gene/gene_a2.html

<http://www.sumanasinc.com/webcontent/anisamples/molecularbiology/lifecyclemrna fla.html>

<http://www.youtube.com/watch?v=NJxobgkPEAo&mode=related&search=>

Splicing (optional)

<http://www.sumanasinc.com/webcontent/anisamples/molecularbiology/mRNAsplicing.html>

Protein synthesis (translation)

<http://www.sumanasinc.com/webcontent/anisamples/molecularbiology/polyribosomes.html>

DNA, RNA, protein synthesis

<https://www.youtube.com/watch?v=Kzgnl5-8Wak>

PPAR receptor and ligand

<http://vodpod.com/watch/854770-dnatube-com-ppar-modulators>

Fun : The Elements (click on 'Broadband')

<http://www.privatehand.com/flash/elements.html>

More fun: Inner life of the cell

<http://video.google.com/videoplay?docid=-252954788111451909>

Protein synthesis film from 1971, Department of Chemistry of Stanford University and imprinted with the "free love" aura of the period. Narrated by Paul Berg, 1980 Nobel prize for Chemistry.

<http://www.youtube.com/watch?v=u9dhO0iCLww&mode=related&search>

Honor Code at the University of North Carolina. The principles of academic honesty, integrity, and responsible citizenship govern the performance of all academic work and student conduct at the University as they have during the long life of this institution. Your acceptance of enrollment in the University presupposes a commitment to the principles embodied in the Code of Student Conduct and a respect for this most significant Carolina tradition. Your reward is in the practice of these principles.

Your participation in this course comes with the expectation that your work will be completed in full observance of the Honor Code. Academic dishonesty in any form is unacceptable, because any breach in academic integrity, however small, strikes destructively at the University's life and work.

I expect that all in-class exams will be taken without the assistance of books, notes, the web, other people, or looking at exams of fellow classmates. **You must sign a pledge on each exam that indicates "On my honor, I have neither given nor received unauthorized aid on this assignment."**

If you have any questions about your responsibility or the responsibility of faculty members under the Honor Code, please consult with someone in either the Office of the Student Attorney General (966-4084) or the Office of the Dean of Students (966-4041).

Schedule: This schedule is “approximate” for individual lecture topics and may be changed.

DATE	Topic	Lippincott: Chapters, pp
	Self-Review: <i>protein structure, amino acids, vitamins, nutrient and energy requirements, diet recommendations, diet and chronic disease</i>	Chapter 5
8/19 W	Metabolism: Introduction to metabolic regulation	Ch. 5 Coleman
8/21 F	Hormones 1: Glucagon & Insulin Signaling in liver, muscle, & fat	Ch. 5, 23 Coleman
8/24 M	Quiz 1: (12 min) Write the pathway (glucose → acetyl-CoA) showing the names of the <u>regulated</u> enzymes (indicate these regulated enzymes with a star *), names of intermediates, # of carbons of intermediates; steps in which NAD ⁺ and NADH are used or produced, steps in which ATP and ADP are used or produced (20 pts) Hormones 1: Glucagon & Insulin Signaling in liver, muscle, & fat	Ch. 8 Coleman Ch. 23
8/26 W	Carbohydrates 1: CHO metabolism overview & glycogen metabolism	(Review Ch. 7), Ch. 8, 11 Hursting
8/28 F	Assignment 1: Diabetes & insulin signaling (10 pts)	Ch. 25 Coleman
8/31 W	Practice Exam Question (similar to Q3 on page 12) Carbohydrates 2: Glycolysis regulation; Centrality of pyruvate; Tricarboxylic acid cycle, PDH	Coleman Ch. 9 Hursting
9/2 F	Carbohydrates 3: ETC, uncoupling protein, PPP	Ch. 6, 13 Hursting
9/4	Carbohydrates 4: Gluconeogenesis; PEPCK, G6Pase; F-1,6-bisP/ PFK Assignment 2: Lactate problem due (15 pts)	Ch. 10 Hursting
9/7 M	Labor Day	
9/9 W	Assignment 2: discuss lactate problem Carbohydrates 5: Integration of CHO metabolism	Coleman
9/11 F	Quiz 2: on carbohydrates (10 pts) Hormones 2: Overview	p. 246 Coleman
9/14 M	Exam 1: Covers all lectures & assignments AND review material on transport and enzyme kinetics Exam does not cover 9/11 “Hormones 2 overview” (90 points)	Extra rooms: 2302 MC and 2303 MC
9/16 W	Hormones 2: Peptide hormones & cell signaling Steroid hormones and cell signaling	Ch. 18 Hursting
9/18 F	Hormones 2: Amino acid-derived hormones	p. 285-6 Sheridan

9/21 M	(<u>Lipid Digestion</u> : Review on your own) Lipids 1 : Fatty acid synthesis	(Review Ch. 15) Coleman Ch. 16
9/23	Lipids 2 : PUFA, eicosanoids	pp. 213-7; pp. 362-4 Coleman
9/25 F	Assignment 3 : TBA (15 pts)	Ch. 24 Hursting
9/28 M	Lipids 3 : TAG synthesis & lipolysis; fatty acid oxidation; ketone bodies <u>Case 2</u> : More hypoglycemia	Ch. 16 Coleman
9/30 W	Cholesterol & Lipoproteins 1 : Cholesterol absorption, synthesis <u>Case 3</u> : Familial hyperlipidemia	Ch. 18 Coleman
10/2 F	Quiz 3 : on lipids (not lipoproteins) (10 pts) Cholesterol & Lipoproteins 2 : Lipoproteins	Ch. 18 Coleman
10/5 M	Amino Acids 1 : Ammonia, urea cycle, protein degradation <u>Case 4</u> : Protein malnutrition	Hursting Review pp. 245-250 Chapter 19 pp. 270-272
10/7 W	Amino Acids 2 : (Review chemistry, digestion & absorption) N metabolism, transamination, oxidative deamination, amino acid products <u>Case 5</u> : PKU	Hursting Ch. 19-21 pp. 366-9
10/9 F	Quiz 4 : on amino acids (10 pts) Metabolic Regulation 1: Starvation vs. Stress (Burns, trauma, surgery) TNF α , IL-6	Ch. 18 Hursting
10/12 M	UNIVERSITY DAY	
10/14 W	Metabolic Regulation 2: AMPK, mTOR, Autophagy, proteasome	Coleman
10/16 F	Fall Break	
10/19 M	Atherosclerosis	Hursting
10/21 W	Metabolic Regulation 3: Metabolic Syndrome (15 pts) Assignment 4 : Metabolic Syndrome	Coleman
10/23 F	Nutrients & Genes 1 : [Review transcription of eukaryotic genes, translation, protein synthesis] How nuclear transcription factors work – regulation of gene expression	[Review Ch. 30: pp. 422ff; Ch. 31] Coleman Ch. 32: pp. 454-7

10/26 W	Exam 2: Covers amino acids, lipids through 10/21 BUT NOT material from 10/23	Extra rooms: 2302, 2303, 2304 McGavran
10/28 W	Metabolic Regulation 4: Microbiome and Metabolism	Glenny
10/30 F	Nutrients & Genes 2: Nutrient control of gene expression: SREBP, PPAR	Ch. 18 Coleman
11/2 M	Nutrients & Genes 3: Nutrient control of gene expression PPAR, ChREBP, FXR	Coleman
11/4 W	Metabolic Regulation 5: Fetal growth & Pregnancy: Physiological biochemistry <u>Case 7:</u> Infant of a diabetic mother Assignment 5: TBA (15 pts)	Hursting
11/6 F	Body Weight Regulation 1: Central control of food intake Leptin, insulin	Hursting
11/9 M	Assignment 6: Diet analyses day 1 (20 points) (? 235 Rosenau Hall)	Ch. 24 Coleman
11/11 W	Assignment 6: Diet analyses day 2 (20 points) (? 235 Rosenau Hall)	Ch. 24 Coleman
11/13 F	Body Weight Regulation 2: Control of food intake, cannabinoids, appetite	Hursting Ch. 26, 27
11/16 M	Cancer 1: Cell metabolism	Hursting
11/18 W	Cancer 2: host metabolism & cachexia; mTORC1 Quiz 5: Body weight (10 pts)	Hursting
11/20 F	Metabolic Regulation 6: Ageing and Longevity (and red wine) <u>Case 8.</u> Progeria	Coleman
11/23 M	Metabolic Regulation 7: Circadian Rhythm	Coleman
11/25 W	Thanksgiving vacation	
11/27 F	Thanksgiving vacation	
11/30 M	Exercise 1: Muscle substrates, fiber types, energy	Muoio
12/2 W	Exercise 2: Muscle and metabolic adaptations	Muoio
12/11 8:00 – 11:00 am	Final Exam: Part 1 covers 10/23 - 12/2. Part 2 covers the entire course. The date of the exam is given in compliance with UNC final exam regulations and according to the UNC Final Exam calendar.	

Nutrition 600: Learning Objectives

General Objectives: Students will be able to:

1. Explain how nutrients are transported in the blood and across cell membranes.
2. Explain how hormones transmit signals that regulate metabolic pathways.
3. Explain major metabolic pathways and critical regulatory points for the metabolism of macronutrients.
4. Integrate the metabolic interconversions of lipids, carbohydrates and amino acids.
5. Explain how metabolic pathways are regulated during different dietary and physiological conditions.
6. Explain how specific nutrients alter gene expression.
7. Explain concepts of appetite control, weight regulation, RQ, thermogenesis.
8. Apply concepts about metabolic pathways and their regulation to novel situations, including current popular diets, claims of health benefits, new therapies.
9. Understand the biochemical and metabolic alterations in physiological situations, like starvation, stress, obesity, atherosclerosis, diabetes, nitrogen balance, hypoglycemia, exercise, metabolic syndrome, cystic fibrosis, thyroid disease, malnutrition, lactose deficiency, ageing, hyperlipidemia, cancer.

Review: DIGESTION AND ABSORPTION - from your prerequisite physiology course)

- Explain the digestive functions of the gastrointestinal (GI) tract (stomach, duodenum, jejunum, ileum, and colon) and associated organs (liver, gallbladder, and pancreas).
- Identify the sources and functions of secretions into the gastric and duodenal lumens.
- Define and explain the importance of zymogens.
- Describe three effects of hydrochloric acid (HCl) secretion by the stomach.
- Diagram the stepwise sequence of digestion of dietary protein in the GI tract.
- Describe the digestion of carbohydrates (CHO) in the stomach, duodenal lumen and duodenal mucosa; specify enzymes, CHO intermediates and end products.
- Identify barriers of diffusion and transport into cells for water soluble nutrients.
- Compare diffusion to facilitated and active transport with regard to concentration gradients, energy, carrier protein, and saturability.
- Describe the route by which water-soluble nutrients reach the interior of cells.
- Describe emulsification, digestion, and absorption of lipids and lipid-soluble vitamins. Specify the roles of pancreatic lipase, co-lipase, and bile salts. How do digestion, absorption, and metabolism differ for long-chain and medium-chain fatty acids?

Review: ENZYME REGULATION – from your prerequisite biochemistry course

- Describe five different mechanisms of metabolic regulation.
- Explain allosteric regulation and competitive inhibition
- Understand and use concepts like affinity, V_{max} , K_m

HORMONAL CONTROL

A. PEPTIDE HORMONES AND THEIR RECEPTORS

- Describe the general concepts of endocrine, paracrine, and autocrine, action (Review)
- Explain signal transduction and its benefits (e.g. G-proteins, cAMP, IP3, calmodulin)
- Explain the hormone cascade system: hypothalamus, pituitary, and target gland
- Explain the concept of negative feedback inhibition
- Describe the formation of a polypeptide hormone: e.g. insulin
- Describe the regulators of production and secretion of insulin, glucagon, growth hormone, ghrelin, etc.
- Describe how peptide hormones act on surface receptors of target cells to confer specificity
- Explain how insulin stimulates glucose uptake into cells and suppresses hepatic glucose production
- Explain the concept of insulin resistance
- Understand what incretins do
- Receptors: contrast tyrosine kinase receptors vs. G-protein coupled receptors (7-transmembrane). Show details of their signaling pathways.

B. NON-PEPTIDE HORMONES AND THEIR RECEPTORS

- Know organ sources of cortisol, aldosterone, progesterone, estradiol, testosterone
- Know what signals regulate the secretion of the steroid hormones listed above?
- Describe the function of the steroid hormones listed above
- Explain the mechanism by which steroid hormones act through their nuclear receptors
- Explain the synthetic pathway involved in thyroid hormone production and the role of iodine.
- Explain thyroid hormone action through its nuclear receptor
- Know the precursors of epinephrine, norepinephrine, and dopamine

C. INTRACELLULAR SIGNALING I: GENERAL MECHANISMS

- Understand the role of phosphorylation and dephosphorylation of proteins in cell signaling.
- Understand the role of cyclic nucleotides in cell signaling.
- Understand the role of intracellular calcium and phospholipids in cell signaling
- Define a "signal cascade" and tell why it is useful in amplifying a signal
- Understand the importance of signaling pathways in nutrition

D. INTRACELLULAR SIGNALING II: SPECIFIC PATHWAYS

- Understand the signaling pathways used by: insulin, glucagon, epinephrine
- Understand the function of AMP-activated kinase (AMPK) and its role in metabolism
- Understand the function and role of mTOR

CARBOHYDRATES AND INTERMEDIARY METABOLISM

- Describe glycolysis (glucose to pyruvate), identifying major regulated steps, oxidation, ATP generation
- Differentiate the metabolic circumstances under which aerobic or anaerobic glycolysis would operate; compare the means of regenerating NAD, energy yield and end products.
- Locate the entry points into glycolysis for glucose, glucose derived from glycogen, fructose, and glycerol. What are the hexose monophosphate shunt end products and what are they used for?
- Identify glycolysis "branch points" that lead to glycogen, pentoses, and glycerol.
- Explain the metabolic circumstances that direct pyruvate metabolism to acetyl-CoA, oxaloacetate, alanine, or lactate.
- In these reactions, specify the names and metabolic functions (the type of chemical reaction catalyzed) of niacin, riboflavin, thiamin, pantothenic acid, biotin and pyridoxine coenzymes.
- Outline the oxidation of pyruvic acid to acetyl-CoA and the oxidation of acetyl-CoA to CO₂ by the Krebs/ TCA cycle, indicating the reactions that (1) yield ATP directly, (2) require NAD, (3) require FAD or (4) yield CO₂. Summarize the energy (ATP) yields from glucose, from glycogen, and from pyruvate.
- Explain why it is advantageous to have a system that extracts energy from reduced fuels to regenerate ATP (regeneration of ADP to ATP).
- Summarize oxidative phosphorylation; name substrates and products; identify oxidized and reduced components and reactants, and energy equivalency of coenzymes of niacin and riboflavin.
- Explain what uncoupling protein does?
- What are the major regulated steps in glycolysis, gluconeogenesis, glycogen synthesis and glycogenolysis? How do these function during feeding, starvation, exercise, diabetes, stress, and other physiological changes?

AMINO ACIDS

- Describe the main interconversions of amino acids and how they facilitate gluconeogenesis
- Understand the urea cycle and its role during normal metabolism, protein excess, and starvation
- Know the major physiological differences between stress and starvation
- Explain the concepts: essential amino acid, ketogenic amino acid, glucogenic amino acid
- Understand the different mechanisms of protein hydrolysis (proteasome, ubiquitination, autophagy,..) and the physiological circumstances that control them

LIPIDS, LIPOPROTEINS, ENERGY STORAGE

- Describe the ACS activation step that precedes fatty acid metabolism. What is the ATP energy cost?
- Explain the mechanism by which activated fatty acids are transported from the cytoplasm into the mitochondria, why this mechanism is important, and how it is regulated.
- Describe the end products of β -oxidation; name the coenzymes involved.
- Calculate the net energy yield, after activation, from beta-oxidation of fatty acids and oxidation of resultant acetyl-CoA via the TCA cycle.
- Provide an overview of the reactions and coenzymes involved in palmitate synthesis from acetyl-CoA.
- Compare fatty acid oxidation vs. fatty acid synthesis, in terms of substrates, products, energy considerations, coenzymes.
- Describe the elongation and desaturation of palmitate. Name the primary products of lipogenesis in the liver (long chain fatty acids incorporated into VLDL-triacylglycerol).
- Describe triacylglycerol synthesis in liver and in adipose tissue, comparing the sources of glycerol and the predominant fatty acids.
- Explain why linoleic and linolenic acids are dietary essentials.
- What are the structural and regulatory roles of polyunsaturated fatty acids (PUFA)?
- Summarize the assimilation (absorption, transport and storage and/or metabolism) of dietary triacylglycerol and the disposition of excess energy from protein and carbohydrate after a meal.
- Compare the plasma lipoproteins (chylomicra, VLDL, LDL, HDL) with respect to size and the relative amounts and types of core lipids.
- Explain the functions of each plasma lipoprotein by specifying the origin, transfer mechanism and destination of core lipid and the disposition of the apoprotein shell.
- Know the regulated steps in the synthesis of cholesterol from acetyl-CoA. Describe the function of cholesterol in membranes and in embryogenesis. Identify other sterols that are synthesized from cholesterol.
- Explain how dietary cholesterol regulates endogenous cholesterol synthesis.
- Distinguish circumstances for stimulation of lipid mobilization by glucagon, cortisol or catecholamines.
- Explain how fatty acids are released from adipose stores and delivered to muscle vs. liver; describe the circumstances, tissues involved and mechanisms of ketone body production and oxidation.
- Explain how triacylglycerol synthesis and degradation are regulated under conditions of excess caloric intake or fasting/starvation
- Explain how cholesterol synthesis and lipoprotein metabolism are regulated by statin drugs and by dietary cholesterol, saturated fatty acids, and carbohydrates.

APPETITE AND SATIETY

- Diagram the systems involved in the complex behavior of food intake; the brain, adipose tissue, the GI tract, the environment, and the endocrine system.
- Identify the areas of the brain involved in the regulation of hunger and satiety.
- Specify the source and function of central nervous system controllers of food intake, NPY, MSH, and CRH.
- Identify the neurotransmitters that regulate food intake; serotonin, dopamine, norepinephrine, and cannabinoids, and describe the signaling steps involved in their synthesis.
- Describe the endocrine (peripheral) controllers of food intake; insulin, glucocorticoids, leptin, gonadal steroids.
- Distinguish between the signals that regulate short-term food intake (meal size) and long-term food intake (adipose stores).

NUTRIENTS AND GENE EXPRESSION (Review information from previous courses)

- Know the structure and function of DNA (Review)
- Understand DNA replication (Review)
- Describe the 3 types of RNA and how they are involved in protein synthesis (Review)
- Explain the difference between transcription and translation (Review)

- Understand the difference between cis and trans acting factors (Review)
- Understand and describe promoters and their function (Review)
- Understand regulatory elements and their function
- Explain how nutrients alter gene expression:
 - SREBP1 (PUFA, insulin), SREBP2 (cholesterol)
 - PPAR γ , PPAR α , PUFA (poly-unsaturated fatty acids), carbohydrate and ChREBP

EXERCISE

- Describe the nutrients used by muscle during different types of exercise
- Describe how exercise alters muscle structure and function (fiber type, blood flow, use of fuels)
- Explain how AMP kinase improves glucose metabolism in diabetic people
- Explain the regulation of different fuel use (glucose vs. fatty acid)

CLINICAL PROBLEMS

- Understand the biochemical and metabolic alterations that occur in starvation vs. stress
- Understand the relationship(s) between obesity, insulin resistance, the metabolic syndrome, diabetes, atherosclerosis, and cancer
- Understand how statins, fibrates, and PUFAs work to treat dyslipidemias
- Understand how TZDs, incretins, and metformin work in the treatment of diabetes
- Understand the biological and physiological differences between types 1 and 2 diabetes
- Understand the biochemical and histological changes that occur in atherosclerosis
- Understand what occurs during a myocardial infarction
- Describe the components of nitrogen balance and what happens during protein deficiency or excess
- Understand the physiological and biochemical responses that occur to combat hypoglycemia
- Understand the consequences of malabsorption problems (e.g. cystic fibrosis)
- Understand the causes and consequences of hypothyroidism and hyperthyroidism
- Understand the causes and consequences of lactose deficiency (Review)
- Understand recent nutritional research related to aging and longevity
- Be able to evaluate the biochemical effects of low CHO diets and low fat diets
- Be able to evaluate the pros and cons of new popular diets.
- Understand the altered metabolism of cancer cells
- Understand effects, including cachexia, of cancer cells on their host,

Typical exam questions: Judge the detail required for your answer by the number of points

1. (4 points each)

- a. Define 'substrate level phosphorylation' and give an example.
- b. Premature babies are susceptible to severe inflammation of the small intestine. If the small intestine becomes gangrenous (suffers tissue death), it is removed surgically. Briefly describe what you think the result would be on digestion and absorption of rice cereal if most of the small intestine was removed and only 10 cm was left. Briefly explain your reasoning.
- c. In an experiment performed on rats, a drug was given to increase the activity of uncoupling protein (UCP) in brown adipose tissue. Explain biochemically why the drug increased the rats' respiratory rate.
- d. Explain the difference between primary and secondary active transport
- e. Explain the difference between allosteric regulation and regulation by phosphorylation. Is one faster than the other?

2. (5 points) Enzyme A has a lower K_m for its substrate than enzyme B. Will enzyme A have a higher V_{max} , too? Explain why or why not? Draw a graph showing the substrate dependence for enzymes A and B.

3. (10 points) Jack's boat sinks in a storm and he swims to a tiny island where there is fresh water to drink but nothing to eat. When he is rescued 8 hours later, his liver glycogen stores are (circle the best answer): close to normal / increased 30% / decreased 30% / almost absent. Explain your answer by describing, in detail, the hormonal pathways and the activation and inactivation of the regulated enzymes involved in glycogen metabolism at the time of Jack's rescue. You may draw a pathway, but explain your answer in words.

4. (10 points)

Jack's friend Joe swims to another tiny island without food but is not rescued for 2 weeks. When Joe is rescued, his blood glucose is ___ (make an X at a point on the line that shows the most likely glucose concentration. The normal range for glucose is 64-126 mg/dl):

0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170

At the time Joe is rescued, describe the 2 primary hormones that are important (active and inactive) and how these hormones are working to regulate the major enzymatic steps that control the synthesis and output of glucose from Joe's liver. Remember—the inactive hormone also plays a role.

5. (6 points)

You have been hired to advise a large pharmaceutical company. Propose a new weight loss drug that works by interfering with the function of pancreatic lipase. Describe how the proposed drug would work biochemically. Why do you think this biochemical approach would be effective (discuss the mechanism)? What limitations, problems, or side effects might occur?

6. (15 points)

Sylvia Mathews Burwell, the US Secretary of Health and Human Services, was previously the president of the Global Development Program of the Bill and Melinda Gates Foundation. She has no background in nutrition or medicine or biochemistry, so you are writing a position paper for her about current research on drugs that affect glucose metabolism and diabetes. Describe the signaling pathway of insulin. If a drug were available to increase the amount of insulin secreted after a meal, what biochemical changes would you see in two (2) major regulated steps of glycolysis or glucose production by the liver? Would it be good idea to increase the amount of insulin secreted after a meal? How do incretin drugs work and why are they used?

Normal Blood Chemistries (you do **NOT** need to memorize these values, except for the glucose ranges that indicate “normal,” “pre-diabetes,” and “diabetic”)

What is called “normal” will vary in different labs. Remember, there is no point in worrying about “low normal” or “high normal” values. Values within the normal range are normal!

Normal Values

- Albumin: 3.9 to 5.0 g/dl
- Alkaline phosphatase: 44 to 147 IU/L
- ALT (alanine transaminase): 6 to 59 IU/L
- AST (aspartate aminotransferase): 10 to 34 IU/L
- Bilirubin, total: 0.2 to 1.9 mg/dl
- Bilirubin: 0.0 to 0.3 mg/dl
- BUN (blood urea nitrogen): 7 to 20 mg/dl
- Calcium - serum: 8.5 to 10.9 mg/dl
- Chloride, serum: 101 to 111 mmol/L
- Cholesterol, total: <200 mg/dl (see Athero section of syllabus)
 - HDL-cholesterol: women \geq 50 mg/dl
 - Men \geq 40 mg/dl
- CO₂ (carbon dioxide): 20 to 29 mmol/L
- Creatinine: 0.8 to 1.4 mg/dl
- GGT (gamma-glutamyl transpeptidase): 0 to 51 IU/L
- Glucose: 64 to 126 mg/dl
 - Fasting plasma glucose
 - Normal 70 - 99
 - Prediabetes 100 - 125 (impaired fasting glucose)
 - Diabetes \geq 126 (\geq 7.0 mM)
 - Oral glucose tolerance test: 75 g glucose dissolved in H₂O (peak level)
 - Normal < 140
 - Prediabetes \geq 140 - <200 (impaired glucose tolerance)
 - Diabetes \geq 200 at 2 h after glucose ingestion
- LDH (lactate dehydrogenase): 105 to 333 IU/L
- Phosphorus - serum: 2.4 to 4.1 mg/dl
- Potassium : 3.7 to 5.2 mEq/L
- Protein, total: 6.3 to 7.9 g/dl
- Sodium - serum: 136 to 144 mEq/L
- Triglycerides: <150 mg/dl
- Uric acid: 4.1 to 7.0 mg/dl

Key to abbreviations:

- IU = international unit
- L = liter
- dl = deciliter = 0.1 liter
- g/dl = gram per deciliter
- mg = milligram
- mmol = millimole
- mEq = milliequivalents