Bio40C schedule

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Lecture Exam 1
- Covers Ch 24 and 25 – digestion and metabolism
- Multiple choice and short answer
- 100 pts
- Bring scantron and #2 pencil
- Review sheets on my website

Lab quiz 1
- 50 pts
- Covers labs 1-3 (digestive tract)
  - Identify anatomical structures on models
    - listed on “scavenger hunt” and in lab ppt
    - A “spelling list” of structures will be provided
  - Questions based on Ex38 review sheet
    - These will focus on function
  - Take home question: Case study 2 (5 pts)

MALT and GALT
- MALT (mucosa-associated lymphatic tissue)
  - Diffuse system of small concentrations of lymphoid tissue (contain immune system cells)
  - Present all along the GI tract, especially in the tonsils, small intestine, appendix and large intestine (p.924)
- GALT (gut-associated lymphatic tissue)
  - Subdivision of MALT, includes the Peyer’s patches in the small intestine

Chapter 25: Metabolism and Nutrition

Cellular respiration

How cells make ATP by catabolizing food
How cells produce ATP

- Cells use oxygen to harvest the chemical energy of food molecules.
- In a series of chemical reactions called cellular respiration, cells convert organic molecules to ATP.
- Cells use ATP (chemical energy) to do work.

The Overall Equation for Cellular Respiration

- Glucose is a common fuel molecule for cellular respiration.

\[
\text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2 \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O} + \text{Energy}
\]

Carbohydrate metabolism

- The fate of glucose depends on the needs of body cells.
  - Glucose →
    - ATP production → cellular work
    - Amino acid synthesis → proteins
    - Glycogen synthesis → store glucose
    - Triglyceride synthesis → store energy

How does glucose get into cells?

- GluT transporters in the plasma membrane bring glucose into the cell.
- Insulin increases insertion of these transporters into the plasma membrane, increasing rate of glucose entry into cells.
- Phosphorylation traps glucose in cells.
- Glucose can be metabolized by glycolysis to produce ATP.

An overview of cellular respiration

- Cells break down glucose and capture the released energy as ATP.
  - 3 steps:
    1. Glycolysis
       - occurs in the cytoplasm
       - Produces ATP
    2. Krebs cycle
       - occurs in mitochondria
       - Produces ATP
    3. Electron transport
       - occurs in mitochondria
       - Generates most ATP

Glucose catabolism

- Glucose oxidation is also called cellular respiration.
- It occurs in every cell of the body (except red blood cells, which lack mitochondria).
- Provides the cell’s chief source of energy.
Cellular respiration begins with Glycolysis

- Glucose (6-carbon) is split into 2 molecules of pyruvic acid (3-carbon)
- Metabolic pathway consumes 2 ATP but generates 4 ATP
- Occurs in the cytoplasm
- Anaerobic – do not require oxygen
- Fate of pyruvic acid depends on oxygen availability
  - If oxygen is scarce (anaerobic), it’s converted to lactic acid
  - If oxygen is plentiful (aerobic), cells convert pyruvic acid to acetyl coenzyme A

The 10 reactions of glycolysis

- Pyruvic acid links glycolysis (in the cytoplasm) with the Krebs cycle (in the mitochondria)
- If oxygen is plentiful (aerobic conditions), pyruvic acid enters the mitochondria, is converted to acetyl coenzyme A, a two-carbon compound, and then enters the Krebs cycle

The Krebs cycle

- Occurs in the mitochondria
- Series of 8 reactions
- Generate 1 ATP molecule by substrate-level phosphorylation
- 2 reactions release CO$_2$
- Exhaled in the lungs
- The most important outcome: the energy originally in glucose is in the reduced coenzymes NADH and FADH$_2$
- Transfer energy to the electron transport chain

Electron transport chain

- Electron transport
  - Series of electron carriers in inner mitochondrial membrane
  - Carry out a series of oxidation-reduction reactions
  - As electrons are passed through the chain, there is a stepwise release of energy for the generation of ATP
  - Final electron acceptor is molecular oxygen (O$_2$)
Electron transport chain

- Hydrogen ion movement
  - Carriers also move protons ($H^+$) from the matrix into the space between the inner and outer mitochondrial membranes
  - Creates $H^+$ concentration gradient and an electrical gradient

- ATP production
  - Protons flow back into the matrix through the $H^+$ channel in ATP synthase
  - ATP synthase uses the energy to synthesize ATP
  - Called chemiosmosis

- Recap: cellular respiration
  - Glycolysis
    - occurs in the cytoplasm
    - does not require oxygen
    - anaerobic
    - generates ATP and NADH
  - Krebs cycle
    - occurs in mitochondria
    - requires oxygen
    - aerobic
    - generates ATP, NADH and FADH$_2$
  - Electron transport
    - occurs in inner membrane
    - requires oxygen
    - Generates most of the ATP

Electron transport chain

Adding up the ATP from cell respiration

- In the process of cellular respiration, the glucose molecule is entirely consumed
- the energy from its chemical bonds is transformed into high-energy molecules
- 4 ATP molecules
- 10 NADH electron carriers
- 2 FADH$_2$ electron carriers

Glucose metabolism

- Most glucose is catabolized to generate ATP
- Synthesis of glycogen: glycogenesis
  - Glucose is stored as glycogen, the only stored carbohydrate in humans
  - Glycogen is stored in liver and skeletal muscle
  - Glycogenesis occurs in the liver and is stimulated by insulin
- Glycogen breakdown: glycogenolysis
  - Glycogen stored in liver is broken down into glucose and released into blood
  - Occurs between meals

Some of the deadliest poisons disrupt electron transport

- Both carbon monoxide and cyanide kill by blocking the transfer of electrons to oxygen and disrupting ATP synthesis.
**Glycogenolysis and Glycogenesis**

Glucose can be synthesized from fats and proteins
- Glycerol (part of triglycerides), lactic acid, and many amino acids can be converted into glucose by the liver
- **Gluconeogenesis**
  - "Newly formed" glucose
  - Stimulated by cortisol and glucagon

**Lipid metabolism:**
- **Transport of lipids by lipoproteins**
  - Most lipids are hydrophobic
  - To be transported in blood, lipids are made more water-soluble by combining with proteins
  - **Lipoproteins**
    - Lipid transport vehicles
    - Outer layer of proteins, phospholipids, cholesterol
    - Core of lipids
  - Proteins in outer shell called apoproteins (apo A, apo B, etc)
  - Help solubilize the lipoprotein
  - Each has specific functions

**Lipoproteins – lipid transport vehicles**

- Categorized according to density
- 4 major classes of lipoproteins:
  - **Chylomicrons**
    - Form in small intestinal mucosal cells
    - Transport dietary lipids to adipose tissue
  - **Very low-density lipoproteins (VLDLs)**
    - Form in hepatocytes
    - Transport endogenous lipids to adipocytes
  - **Low-density lipoproteins (LDLs)** – "bad" cholesterol
    - Carry 75% of total cholesterol in blood
    - Deliver it to cells throughout the body
    - When present in excess, deposit cholesterol in artery wall → fatty plaques
  - **High-density lipoproteins (HDLs)** – "good" cholesterol
    - Remove excess cholesterol from body cells
    - Deliver cholesterol to liver for elimination

**Plaque buildup in arteries**
- Excess LDLs deposit cholesterol around smooth muscle fibers in arteries → fatty plaques
- Increases the risk of coronary artery disease
- A heart attack or stroke occurs when an area of plaque (atherosclerosis) ruptures and a clot forms at the site, blocking the flow of blood to the tissue

**Lipid Metabolism: cholesterol**

- 2 sources of cholesterol
  - Foods
  - Most is synthesized by liver
- Normal level of total cholesterol
  - <200 mg/dl
- As total blood cholesterol increases, risk of coronary artery disease begins to rise
  - Treated with exercise, low fat diet
  - Drugs
    - Promote excretion of bile in the feces
    - Block cholesterol synthesis
Lipid metabolism and storage

- Dietary fat is absorbed in GI tract as chylomicrons
- Part is metabolized to provide ATP
- The rest enters the liver and adipose tissue for storage
- Triglycerides in adipose tissue constitute 98% of all body energy reserves
- Adipose tissue supplies energy to skeletal & heart muscle
- The liver is an important site for energy conversion, exchanging energy sources from one form to another
  - Glycogen → glucose
  - Glucose → lipids
  - Amino acids → lipids

Lipids can be

- Oxidized to produce ATP
- Stored in adipose tissue
- Used as structural molecules
  - Phospholipids of plasma membranes
  - Lipoproteins that transport cholesterol
  - Thromboplastin for blood clotting
- Cholesterol is used to synthesize bile salts and steroid hormones

Triglyceride storage

- Triglycerides are stored in adipose tissue, mostly in the subcutaneous layer.
- Fats in adipose tissue are not inert.
- They are catabolized and mobilized constantly throughout the body

Lipid synthesis: lipogenesis

- Lipid synthesis (lipogenesis)
  - Occurs when more calories are consumed than needed for ATP production
  - Liver cells and adipose cells can convert glucose or amino acids into lipids

Lipid catabolism: lipolysis

- Muscle, liver and adipose tissue can breakdown lipids to form ATP
- Triglycerides are split into glycerol and fatty acids

Lipid catabolism (lipolysis)

- Glycerol and fatty acids: two different catabolic pathways
  - Glycerol → pyruvic acid enters the Krebs cycle
  - Fatty acids → β oxidation to Acetyl CoA → Krebs cycle
- In β oxidation, carbon atoms are removed in pairs from fatty acid chains. The resulting molecules of acetyl coenzyme A enter the Krebs cycle.
**Energy interconversion**

- Excess carbohydrates, proteins, and fats all have the same fate: they are converted into lipids.
- Liver and adipose cells synthesize lipids from glucose or amino acids.
- Lipogenesis
- Liver cells form ketone bodies as a normal part of fatty acid catabolism.
- Ketone breakdown occurs in most body cells.

**Ketosis**

- Liver converts lipids into fatty acids and ketone bodies.
- Level of ketone bodies in blood is normally very low because other tissues use them for ATP production.
- When few carbs are available for catabolism (in fasting or starvation), concentration of ketone bodies in blood rises above normal – a condition called ketosis.
- Most ketone bodies are acids and must be buffered.
- Prolonged ketosis can lead to acidosis.

**Test your understanding**

- Which type of lipoprotein delivers cholesterol to body cells?
  - Chylomicron
  - VLDL
  - LDL
  - HDL

**Question 2**

- Name the 3 pathways (series of reactions) that produce ATP during the complete oxidation of glucose.
- What is gluconeogenesis and why is it important?

**Protein metabolism**

- Dietary protein
  - Amino acids
  - Excess aa are converted into glucose (gluconeogenesis), triglycerides (lipogenesis).
  - New proteins for growth & tissue repair.
  - Oxidized to produce ATP.

**Protein catabolism**

- Proteins from worn out cells are broken down into amino acids.
- Before entering Krebs cycle the amino group must be removed – deamination.
- Produces ammonia, NH₃.
- Liver cells convert NH₃ to urea, excreted in urine.
Protein synthesis

- Carried out in almost every cell in the body
- 20 amino acids in the human body
  - Nonessential amino acids can be synthesized in the body by transamination
  - Transfer of amino group from an amino acid to a keto acid
  - 10 are “essential” amino acids
  - Must be present in the diet because body can’t synthesize them in adequate amounts

Key molecules in metabolism

- 3 molecules play key roles in metabolism
  - Glucose-6-phosphate
  - Pyruvic acid
  - Acetyl CoA
  - Stand at metabolic crossroads

Key molecules in metabolism

- Glucose-6-phosphate (G-6-P)
  - Made shortly after glucose enters body cell
  - 4 fates
    - Synthesis of glycogen
    - Conversion to pyruvate via glycolysis
    - Make ribose-5-phosphate for synthesis of RNA and DNA
    - Release of glucose into bloodstream

Key molecules in metabolism

- Acetyl Coenzyme A
  - Acetyl CoA is the entry into the Krebs cycle
  - When ATP is low and oxygen plentiful, most pyruvic acid goes to ATP production via Acetyl CoA
  - Can also be used to synthesize fatty acids, ketone bodies, and cholesterol

Metabolic adaptations

- Your metabolism depends on how recently you have eaten
  - Absorptive state
    - Ingested nutrients are entering the blood stream
    - Glucose readily available for ATP production
  - Post-absorptive state
    - Absorption of nutrients from GI tract is complete
    - Energy needs must be met by stored fuels
    - Maintaining steady blood glucose critical
      - Nervous system and red blood cells depend on glucose
Metabolism during the absorptive state

- Soon after a meal, nutrients enter blood
- Glucose, amino acids, and triglycerides in chylomicrons
- 2 metabolic hallmarks
  - Most body cells produce ATP by oxidizing glucose
  - Storage of excess fuel molecules in
    - Liver: glucose converted to glycogen, triglycerides
    - Liver: amino acids converted to carbohydrates, fats and proteins
    - Adipose tissue: dietary lipids are stored
    - Skeletal muscle cells: store glycogen

Absorbed glucose
- 50% → ATP via cellular respiration
- 40% is converted to triglycerides
- 10% is stored as glycogen

Dietary lipids
- Most are stored in adipose tissue
- Triglycerides synthesized in liver are packaged into VLDLs and transported to adipose tissue for storage

Metabolism during the absorptive state

- Absorbed amino acids
  - In liver, most amino acids enter the Krebs cycle → ATP
  - Some amino acids used for protein synthesis (e.g. plasma proteins)
  - In muscle and other tissues, amino acids used for protein synthesis

Metabolism during the absorptive state

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Regulation of metabolism – absorptive state

- Pancreatic beta cells release insulin
  - Promotes entry of glucose and amino acids into cells
  - Stimulates protein synthesis
  - Enhances triglyceride synthesis in liver and adipose tissue

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Metabolism during the post-absorptive state

- About 4 hours after the last meal absorption in small intestine nearly complete
- Blood glucose levels start to fall
- Main metabolic challenge: maintain normal blood glucose levels
  - Glucose production
    - Breakdown of liver glycogen, lipolysis, gluconeogenesis using lactic acid and/or amino acids
  - Glucose conservation
    - Oxidizing fatty acids and other fuel molecules → ATP

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Homeostasis of blood glucose concentration

- Especially important for the nervous system and red blood cells
- Nervous system
  - Uses glucose for ATP production because fatty acids can’t pass the blood-brain barrier
- Red blood cells
  - Derive all of their ATP from glycolysis of glucose because they lack mitochondria and thus lack the Krebs cycle and electron transport chain

Post-absorptive state: reactions that produce glucose

1. Breakdown of liver glycogen
2. Lipolysis: breakdown of triglycerides in adipose tissue → glycerol → glucose
3. Gluconeogenesis using lactic acid
4. Gluconeogenesis using amino acids

Postabsorptive state: producing ATP without glucose

- Oxidation of fatty acids via Krebs cycle and electron transport
  - Most cells
- Oxidation of lactic acid
  - Heart muscle
- Oxidation of amino acids
  - Hepatocytes
- Oxidation of ketone bodies
  - Hepatocytes
- Breakdown of muscle glycogen
  - Skeletal muscle

Regulation of metabolism – postabsorptive state

- As blood glucose declines, pancreas secretes glucagon
  - Glucagon increases release of glucose into blood by stimulating gluconeogenesis and glycogenolysis
- Sympathetic division of ANS releases norepinephrine and adrenal medulla releases epinephrine and norepinephrine
  - Stimulate lipolysis, glycogen breakdown

Test your understanding: Metabolism during starvation

- People can survive without food for 2 months if they drink enough water to prevent dehydration
- Glycogen stores are depleted within a few hours
- Where does the energy needed for survival come from?

When food is scarce, body protein and body fat are used to produce energy
Body Temperature Homeostasis

How do we maintain a constant core temp near 37°C?

Body temperature homeostasis

- Despite wide fluctuations in environmental temperatures, homeostatic mechanisms maintain normal range for internal body temperature
- Core temperature (37°C or 98.6°F) versus shell temperature (1-6°C lower)
- Heat produced by exercise, some hormones, sympathetic nervous system, fever, ingestion of food, younger age, etc.

Energy is lost as heat

- Heat released during cellular respiration is used to maintain our body temperature

What is BMR?

- Basal metabolism (BMR) - energy used to maintain the body’s basal or resting functions
- Breathing, blood circulation, maintaining body temp, etc
- Energy needed to digest and absorb food
- Energy used for physical activity

Factors affecting BMR

- Gender
- Lean body mass
- Height
- Age
- Thyroid hormone levels
- Stress, fever, illness
- Pregnancy and lactation

Thermoregulation

- If core temperature declines
  - Skin blood vessels constrict
  - Release of thyroid hormones, epinephrine and norepinephrine increases cellular metabolism
  - Shivering
- If core body temperature too high
  - Dilation of skin blood vessels
  - Decrease metabolic rate
  - Stimulate sweat glands