Metabolism

**Glycolysis**
- Glucose → Pyruvic acid
  - (4 ATP - 2 ATP used for activation energy)
  - Net +2 ATP by substrate-level phosphorylation

**Krebs cycle**
- 2 Acetyl CoA
- 6 NADH + H^+ → +2 ATP by substrate-level phosphorylation
- 2 FADH_2 → + about 34 ATP by oxidative phosphorylation

**Electron transport chain and oxidative phosphorylation**
- 10 NADH + H^+ × 3 ATP
- 2 FADH_2 × 2 ATP
- + about 34 ATP

**Net ATP yield**
- About 36 ATP per glucose

**Summary**
- Maximum ATP yield per glucose
Metabolism

- Glucose
- Anabolism/Catabolism
Metabolism

- Gluconeogenesis

Key:
- Gluconeogenesis (stimulated by cortisol and glucagon)
Metabolism

• Lipid Metabolism

  – Oxidation of Glycerol and Fatty Acids

    • Glycerol – converted to glyceraldehyde phosphate and enter glycolysis (obtain approximately 18 ATP)

  – Fatty Acids – Beta Oxidation

    • Fatty acids catabolized to 2 carbon molecules (acetic acid)
    • Acetic acid joins with CoA to form acetylCoA (where does this go?)
Metabolism

- Lipids
  - Lipase
  - Glycerol
  - Fatty acids
    - ATP
    - Coenzyme A
      - NAD^+
      - NADH + H^+
      - FAD
      - FADH_2
      - β Oxidation in the mitochondria
      - Cleavage enzyme snips off 2C fragments
  - Glycolysis
    - Glyceraldehyde phosphate
    - Pyruvic acid
  - Acetyl CoA
  - Krebs cycle
Metabolism

- Lipogenesis and Lipolysis – neutral fats are constantly being anabolized and catabolized
Metabolism

- Synthesis and Structural Materials
  - Phospholipids and cholesterol needed to build cell membranes
  - Phospholipids needed for myelin sheaths
  - Liver
    - Makes lipoproteins for transport of cholesterol and fats (more in a bit)
    - Produces the clotting factor, *tissue factor*
    - Produces cholesterol from acetylCoA and makes bile salts from it
    - Ovaries, testes, and adrenal gland use cholesterol to make their steroid hormones
Metabolism

- **Protein Metabolism**
  - Digestion produces free amino acids
  - Oxidation of Amino Acids – before they can be oxidized, amino acids must be deaminated
    - Transamination
    - Oxidative Deamination
    - Keto Acid Modification – two possible routes
      - Can be converted to metabolites such as pyruvic acid, CoA, α-ketoglutaric acid, and oxaloacetic acid (significance?)
      - Pyruvic acid produced can be used for gluconeogenesis
Metabolism

- Protein Synthesis

  - What are proteins used for in living things?
  
  - Regulated by hormones such as: growth hormone, thyroxine, sex hormones etc.
  
  - Via transamination reactions the liver can produce non-essential amino acids from essential amino acids
Metabolism

- Metabolic Role of the Liver – see Table 24.7 for an overall review
  - Cholesterol Metabolism and Regulation of Blood Cholesterol Levels
    - Cholesterol
      - Used for:
        » bile salts
        » steroid hormones
        » vitamin D synthesis
        » structural elements of cell membranes
      - 15% comes from diet; remaining 85% synthesized from acetyl CoA
      - Removed from the body in bile salts, feces
Metabolism

- Cholesterol Transport – needs to be associated with proteins to make them soluble; lipoproteins
  - Types of Lipoproteins the lower the density the greater the proportion of the molecule is made up of lipid
    » Very Low Density Lipoproteins (VLDLs)
      synthesized in the liver
      transport triglycerides to mostly fat cells; remaining components converted to LDLs
    » Low-Density Lipoproteins (LDLs)
      rich in cholesterol
      regulates cholesterol synthesis by peripheral cells
    » High-Density Lipoproteins (HDLs)
      rich in phospholipids and cholesterol
      carries cholesterol from periphery to the liver to be excreted from the body
Metabolism

• Clinical Aspects of Cholesterol
  - Blood levels should be <200 mg/dl
  - HDLs good cholesterol
    » 35 – 60 mg/dl ok
    » >60 can actually protect against heart disease
  - LDLs bad cholesterol - >160; lipoprotein “a” is especially bad, clogs arteries

• Factors Regulating Plasma Cholesterol Levels
  - Diet
    » Saturated fats stimulate production
    » Inhibit excretion
    » Unsaturated fats enhance excretion
    » Trans fatty acids even more harmful than saturated
    » Omega 3 fatty acids particularly helpful

      platelets less sticky
      antiarrhythmic effect
      lower blood pressure
Metabolism

- Other factors
  - Smoking (-)
  - Coffee drinking (-)
  - Stress (-)
  - Aerobic exercise (+)
Metabolism

• Nutrition – the taking in of food
  – Nutrients
    • Chemicals that are used by the body and consist of:
      – Carbohydrates
      – Lipids
      – Proteins
      – Vitamins
      – Minerals
      – Water
  • Essential Nutrients - cannot be synthesized by the body
Metabolism

- Kilocalorie
  - Proteins – 4/g
  - Carbohydrates – 4/g
  - Lipids – 9/g

- Carbohydrates
  - 125 – 175 g/day

- Lipids
  - No more than 30% of kcal/day
  - <= 300 mg/day cholesterol

- Proteins
  - 0.8 g /kg/day

- Vitamins
  - Many function as coenzymes
  - Most are not produced by the body
  - Classified as either fat-soluble or water-soluble
Metabolism

- Minerals important for:
  
  • Normal metabolism
  • Mechanical strength (bones and teeth)
  • Function as buffers
  • Involved in osmotic balance
Metabolism

- Metabolic States
  - Absorptive
    - Most body cells produce ATP by using glucose
    - Glucose transported to liver
      - Glycogen
      - Triglycerides
    - Lipids stored in adipose tissue
    - Amino Acids – converted in liver to carbohydrate, fats and proteins
    - Regulated by insulin
Metabolism

Increase in blood glucose levels

Stimulates

Beta cells of pancreatic islets

Increased levels of insulin in the blood

Targets tissue cells

Enhances

Active transport of amino acids into tissue cells

Facilitated diffusion of glucose into tissue cells

Protein synthesis

Cellular respiration

Enhances glucose conversion to:

- $CO_2 + H_2O + ATP$
- Fatty acids + glycerol
- Glycogen

Key:
- Initial stimulus
- Physiological response
- Result
Metabolism

- Postabsorptive State
  - Body attempts to maintain normal glucose levels
    - 70 – 110 mg/100 ml
    - Liver and muscle convert glycogen to glucose
    - Glycerol produce by hydrolyzing fats used to make glucose
    - Amino acids (gluconeogenesis)
  - Eventually all but nervous tissue switch to fatty acid metabolism
  - Regulated mostly by glucagon
Metabolism
Metabolism

Decrease in plasma glucose concentration (and rising levels of amino acids)

Stimulates

Alpha cells of pancreatic islets

Increase plasma levels of glucagon

Stimulates glycogenolysis and gluconeogenesis

Stimulates fat breakdown

Liver

Adipose tissue

Key:
- Increases, stimulates
- Reduces, inhibits
- Initial stimulus
- Physiological response
- Result

Increased levels of glucose (and insulin) in plasma

Increased levels of fatty acids in plasma

Fat used by tissue cells = glucose sparing

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Metabolism

- Metabolic Rate - energy expenditure per unit time – kcal/m$^2$/hr
  - measured by using oxygen consumption – three components

  - Basal Metabolic Rate (BMR) 60% of all metabolism, measured under particular conditions
    - Resting (no exercise for 30 – 60 min)
    - Awake
    - Room temperature
    - Fasting for at least 12 hours
    - Normal body temperature

  - Thermic Effect of Food – energy expenditure when digesting foods, 10%

  - Muscular Activity – only one we can reasonably control
Metabolism

- Body Temperature Regulation – balance between heat gain and heat loss
  - Heat produced during metabolism
  - Heat lost via
    - Radiation
    - Conduction
    - Convection
    - evaporation
Metabolism

**Heat production**

- Basal metabolism
- Muscular activity (shivering)
- Thyroxine and epinephrine (stimulating effects on metabolic rate)
- Temperature effect on cells

**Heat loss**

- Radiation
- Conduction/convection
- Evaporation
Metabolism

Skin blood vessels dilate: capillaries become flushed with warm blood; heat radiates from skin surface

Sweat glands activated: secrete perspiration, which is vaporized by body heat, helping to cool the body

Body temperature decreases: blood temperature declines and hypothalamus heat-loss center “shuts off”

Blood warmer than hypothalamic set point

Stimulus: Increased body temperature (e.g., when exercising or the climate is hot)

Activity: Heat-loss center in hypothalamus

Body temperature increases: blood temperature rises and hypothalamus heat-promoting center “shuts off”

Skin blood vessels constrict: blood is diverted from skin capillaries and withdrawn to deeper tissues; minimizes overall heat loss from skin surface

Blood cooler than hypothalamic set point

Stimulus: Decreased body temperature (e.g., due to cold environmental temperatures)

Activity: Heat-promoting center in hypothalamus

Skeletal muscles activated when more heat must be generated; shivering begins

Homeostasis = normal body temperature (35.6°C–37.8°C)
Metabolism

Review tables 24.2 and 24.3
Know in particular, the whether or not a vitamin is water or fat soluble, the importance of the mineral or vitamin in question, and sources of the particular nutrient