Section 1: Overview Metabolism

Fuel Metabolism Overview
(Chapter 1)

Student Learning Outcomes:
• To explain briefly an overview of human metabolism:
• To explain the differences in the fed vs. fasting states in terms of fuel utilization
• To describe examples of medical problems that arise from improper metabolism

Essential metabolic requirements:
• synthesize compounds not supplied by diet
• protect internal environment from toxins & changing external environment

4 general metabolic routes for dietary components

Metabolism overview

Anabolic pathways:
Biosynthetic
Include fuel storage

Catabolic pathways:
Breakdown macromolecules
Fuel oxidation

Specialized tissues:
Liver - biosynthesis
Adipose tissue - storage
Transport, hormone signaling
Chapt. I. Metabolic fuel & dietary components

**Diet requirements:**
- fuels to drive body functions
- essential amino acids, vitamins, minerals, water

**Dietary fuel:**
- carbohydrates
- fats
- proteins

Excess fuel stored in liver, muscle, adipose tissue

---

I. Dietary fuels provide energy as ATP

**Oxidation of fuels is extraction of electrons**
- extraction of electrons: glycolysis, TCA cycle
- transfer of electrons to O₂ (electron transport chain)
- generates ATP
- products are H₂O, CO₂
- respiration

**Major fuels:** carbohydrates, proteins, fats
| Table 1.2   Calorie content of Fuels |
|------------|----------------------------------|
| 1 ‘Calorie’ = 1 kilocalorie          |
| energy to raise 1 L of water by 1 °C |
| **Calorie content of Fuels kcal/g**  |
| Carbohydrate  4                      |
| Fat          9                        |
| Protein      4                        |
| Alcohol      7                        |

Carbohydrates

**Typical carbohydrates**: (CH₂O)ₙ
Already partially oxidized:
Starch, Glycogen (polymers); Glucose (monomer)

![Chemical structure of carbohydrates](image)

Proteins

**Proteins are linear chains of amino acids**

![Chemical structure of proteins](image)

Fig. 1.4 Amino acids have amino group, carboxyl group;
R = different side chains
Fats are triacylglycerol lipids

Fats:
Triglycerides

Triacylglycerol lipids:
Glycerol joined to 3 fatty acids

Saturated (C-C)
Unsaturated (C=C)

Give more energy when oxidized,
(more reduced)

II. Fuel Stores

Table 1.2 Fuel composition after overnight fast
* "typical human" is 70-kg man (154 lbs)

<table>
<thead>
<tr>
<th>Fuel</th>
<th>Amount (kg)</th>
<th>% stored calories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycogen muscle</td>
<td>0.15</td>
<td>0.4</td>
</tr>
<tr>
<td>Glycogen liver</td>
<td>0.8</td>
<td>0.2</td>
</tr>
<tr>
<td>Protein</td>
<td>6.0</td>
<td>14.4</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>15</td>
<td>85.</td>
</tr>
</tbody>
</table>

Fat in adipose tissue is efficient Fuel storage:
more calories/g; not much water in adipose tissue

III. Calculate daily energy expenditure

Balance fuel intake with energy expenditure to avoid weight gain

Daily energy expenditure:
• Energy for basal (or resting) metabolic rate (BMR)
  • Table 1.4 for calculations based on age, sex
• Energy for physical activity:
  • ~ 30% of BMR if sedentary,
  • ~ 70% BMR if 2 hrs exercise
• Energy to process food intake
  • diet-induced thermogenesis (<10% BMR)
Maintain Healthy Body Weight

Body Mass Index (BMI):
tool to estimate whether ideal body weight:

\[
\text{weight/height}^2 \text{ (kg/m}^2\text{)} = \left[\frac{\text{lbs}}{\text{in}^2}\right] 
\]

Overweight is defined as >20% of ideal weight:

<table>
<thead>
<tr>
<th>BMI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Healthy</td>
<td>18.5 - 25</td>
</tr>
<tr>
<td>Overweight</td>
<td>25 – 30</td>
</tr>
<tr>
<td>Obese</td>
<td>&gt;30</td>
</tr>
</tbody>
</table>

Fuel intake vs. energy expenditure

Increasing obesity in the United States
Plumped-up Colo. Still the least obese:
(Denver Post article 7/8/2011):

<table>
<thead>
<tr>
<th>Year</th>
<th>Obesity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988-1990</td>
<td>6.9 %</td>
</tr>
<tr>
<td>1993-1995</td>
<td>10.78%</td>
</tr>
<tr>
<td>1998-2000</td>
<td>14.5%</td>
</tr>
<tr>
<td>2008-2010</td>
<td>19.8%</td>
</tr>
</tbody>
</table>

IV. Dietary requirements

RDA = Recommended Dietary Allowance

Carbohydrates

Essential Fatty Acids – ex. Docosahexaenoic acid

Protein total ~ 50-60g total
9 essential aa: lys, ile, leu, thr, val, trp, phe, met, his

Nitrogen balance - need sufficient protein

Vitamins – organic molecules (coenzymes, hormones)

Minerals – electrolytes (Na+, K+, Cl), Ca++, P, Mg, Fe, S, and trace elements (I, Cu, Zn...)
Elements found in Biological systems

Elements found in Biological Systems:
More abundant elements darkly shaded;
Trace elements lightly shaded.
(Only subset of Periodic table).

Dietary guidelines – the old pyramid

Healthy eating

Dietary guidelines: then came the USDA pyramid

Healthy eating revised
Dietary guidelines: the new USDA plate

Healthy eating
Newest version

As interpreted by Mike Keefe, cartoonist

Summary key concepts

Key concepts:

- Fuel is provided as carbohydrates, fats, proteins
- Energy from fuel is oxidized to CO$_2$ and H$_2$O
- Unused fuel stored is as fat or glycogen (carb)
- Weight gain or loss: balance intake, expenditure
- RMR: energy to maintain nonexercise body functions
- BMI: rough measure to determine ideal weight
- Diets must provide nutrients, vitamins, minerals, essential fatty acids, amino acids
### Chapter 1 Review questions

**Review questions:**
- Diagram structures of carbohydrate, fat and protein
- What are some essential amino acids?
- What are examples of vitamin deficiencies?
- Calculate calories consumed by:
  - Ann O’Rexia: 120 g carb, 20 g protein, 20 g fat
  - Ivan Applebod: 490 carb, 100 g protein, 60 g fat and 30 g alcohol

### Chapter 1 review question

**Review question:**
The caloric content per gram of fuel is best represented by which one of the following:

a. It is higher for carbohydrates than for triacylglycerols
b. It is higher for protein than for fat
c. It is proportionate to the amount of oxygen in a fuel
d. It is the amount of energy that can be obtained from oxidation of the fuel
e. It is higher for children than for adults

### Clinical comments on patients

- **Ann O’Rexia:** 99 lbs (67” tall); early anorexia nervosa: very low calorie intake
- **Ivan Applebod:** 264 lbs (70” tall); obese: risk of atherosclerotic vascular, hypertension,
- **Otto Shape:** 187 lbs (70” tall); overweight: should watch calories, exercise
- **Percy Veere:** 125 lbs (71” tall); underweight, malnourished, depression after wife died
Chapter 2. Fed or Absorptive state:

Fed or absorptive state

Student learning outcomes:
• Explain the process of digestion and absorption of macromolecules
• Explain changes in hormones insulin and glucagon after a meal
• Describe fate of glucose after a meal
• Describe fate of lipids or amino acids after a meal

2. The Fed or Absorptive State

Carbohydrates, lipids and proteins are ingested, digested & absorbed:

Major fates of fuels in fed state:
• Oxidized for energy
• Stored
• Used for biosynthesis

Fig. 2.1 Fed state

The fed state: fate of carbohydrates, proteins, fats

Fig. 2.2
Digestion and absorption:

- Carbohydrates and proteins converted to monomers
- Fats are emulsified by bile, digested to fatty acids and monoacylglycerols, form micelles; packaged with proteins, cholesterol, phospholipids

Changes in hormone levels after meal:
High carbohydrate ->
- **Insulin** increases -> glucose is available to be used, and stored
- **Glucacon** decreases -> so not generate glucose from the stores

Fate of glucose after meal: conversion in liver
Glycogen and triacylglycerols (TG) are made in liver
Triacylglycerols are stored in adipose tissue

Fate of glucose other tissues

**Muscle:**
- Stores glycogen for use in exercising muscle

**Brain:**
- Glucose is main fuel

**Red blood cells:**
- Glucose is only fuel (no mitochondria)
IV Fate of lipoproteins, amino acids

Lipoproteins (Chylomicrons & VLDL) transport triacylglycerols and cholesterol to adipose tissue. Amino acids are used in liver for serum proteins, N-containing compounds.

Fig. 2.2

Summary of key concepts

Key concepts:
- During meal, ingest carbohydrate, lipids, proteins
- Endocrine hormones insulin & glucagon regulate fuel storage, retrieval
- Major carbohydrate in blood is glucose: blood glucose levels regulate insulin, glucagon levels
- Glucose used as fuel, and precursor for storage via glycogen or triacylglycerol
- Insulin stimulates uptake of glucose into adipose and muscle tissue for storage
- Adipose tissue - storage site for triacylglycerol

Review questions chapt. 2

Review question

During digestion of a mixed meal, which of the following is most likely to occur?
- a. starch and other polysaccharides are transported to the liver
- b. proteins are converted to dipeptides, which enter the blood
- c. dietary triacylglycerols are transported in the portal vein to the liver
- d. monosaccharides are transported to adipose tissue via the lymphatic system
- e. glucose levels increase in the blood
More Clinical comments on patients

**Ivan Applebod:** 270 lbs (70” tall); obese: type 2 diabetes mellitus (insulin-resistant): hyperglycemia: fasting 162 mg/dL (80-100 normal) hyperlipidemia (cholesterol 315 mg/dL (<200 normal)) triacylglycerol 250 mg/dL (60-160 normal)

**Otto Shape:** 187 lbs (70” tall); overweight: watch calories, exercise

Chapter 3 Fasting:

**Fasting:** 2-4 hours after meal; starvation

**Student learning outcomes:**
- Explain process 2-4 hours after meal;
- Explain role of blood glucose, insulin and glucagon and role of liver, adipose tissue
- Explain fuel requirements of different tissues
- Describe processes occurring in starvation

3. Fasting: 2-4 hours after meal

Fasting: blood glucose levels drop; liver degrades glycogen stores (glycogenolysis)

Fig. 3.1 basal state = 12 hrs after meal
3. Fasting: 2-4 hours after meal

**Gluconeogenesis**: Liver makes new glucose from precursors lactate, glycerol, amino acids

![Fig. 3.1 basal state = 12 hrs after meal](image)

**Fasting: role of adipose tissue**

**In Adipose tissue:**
- **Lipolysis**: lysis of triacylglycerols
  \[\text{fatty acids} \rightarrow \text{fatty acids, a major fuel for many tissues} \rightarrow \text{Ac-CoA};\]
- Only the glycerol is used for gluconeogenesis in liver
- Liver also makes ketone bodies (fuel for other tissues)

**Proteolysis of muscle protein**
- Provides amino acids

![Fig. 3.2 ketone bodies](image)

**Table 3.1 Metabolic capacities of various tissues**

<table>
<thead>
<tr>
<th>Process</th>
<th>Liver</th>
<th>Adipose Tissue</th>
<th>Kidney Cortex</th>
<th>Muscle</th>
<th>Brain</th>
<th>Red Blood Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCA cycle (ketone body = CO2 + H2O)</td>
<td>+++++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Oxidation of fatty acids</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketone body formation</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketone body utilization</td>
<td>--</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Complete respiration</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyruvate + glucose (glycolysis)</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Lactate production (glucose = lactate)</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Glucose oxidation</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Glucose metabolism (glycolysis and oxidation)</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Glucose deamination (glycolysis, amino acids, glycolysis)</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Glucose oxidation</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Proline transamination (glycine)</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Serine transamination (glycine)</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Table 3.1 Metabolic Capacities of Various Tissues</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
II Prolonged fasting: starved state

Conserve muscle protein (oxidize fatty acids).
Liver makes ketone bodies, which brain can use, so less glucose needed.

Fig. 3. Starved state:
Red increased;
Dotted line decreased

Changes in fuels in blood in prolonged fast

Muscle decreases use of ketone bodies (uses fatty acids)
Liver makes ketone bodies from fatty acids
Brain can use ketone bodies, so less need for glucose
Red blood cells need glucose
But less protein degradation to supply aa to make glucose

Fig. 3.4 plasma levels during starvation

Changes in urea excretion during fasting

Urea concentrations decrease with increased starvation:
Muscle protein breakdown is ‘spared’ as tissues use ketone bodies & fatty acids instead of glucose

Death by starvation: when loss of ~ 40% body weight
(30-50% body protein, 70 to 98% fat stores)
~ BMI 13 men, 11 women

Fig. 3.5
Summary of fasting

Key concepts:
- Blood glucose levels drop -> glucagon is released
- Glucagon signals liver to hydrolyze stored carbohydrate to release glucose in blood (brain, rbc)
- After 3 days fasting, liver releases ketone bodies (from fat oxidation) as alternative fuel to brain; gluconeogenesis provides glucose to rbc and brain
- Glucagon signals fat cells to degrade triacylglycerols -> fatty acids for energy, glycerol for gluconeogenesis
- Liver uses lactate (from rbc) and aa (muscle protein degradation) and glycerol to make glucose

3. Review questions

Review question:
In a well-nourished individual, as the length of fasting increases from overnight to 1 week, which of the following is most likely to occur?

a. Blood glucose levels decrease by ~ 50%
b. Red blood cells switch to using ketone bodies
c. Muscles decrease their use of ketone bodies, which increase in the blood
d. The brain begins to use fatty acids as a major fuel
e. Adipose tissue triacylglycerols are nearly depleted.

Clinical comments on patients

Ann O'Rexia: now 85 lbs (67" tall); BMI 13.3; anorexia nervosa: malnourished
blood glucose 65 mg/dL (normal 80-100)
serum ketones 4200 uM (normal 70)

Percy Veere: 125 lbs (71" tall); BMI 17.5
underweight, malnourished, depression after wife died; protein, iron, vitamin deficiencies
serum albumin and transferrin low (protein malnutrition)
serum ketones 110 uM (normal 70); has fat stores