Integration of Metabolism

1. Amino acid metabolism
2. Interconnection of pathways
3. Metabolic profile of organs
4. Food intake, starvation and obesity
5. Fuel choice during exercise
6. Ethanol alters energy metabolism
7. Hormonal regulation of metabolism
Metabolic Profile of Organs

- **Pancreas**
  - Secretes insulin and glucagon in response to changes in blood glucose concentration.

- **Liver**
  - Processes fats, carbohydrates, proteins from diet; synthesizes and distributes lipids, ketone bodies, and glucose for other tissues; converts excess nitrogen to urea.

- **Brain**
  - Transports ions to maintain membrane potential; integrates inputs from body and surroundings; sends signals to other organs.

- **Lymphatic system**
  - Carries lipids from intestine to liver.

- **Adipose tissue**
  - Synthesizes, stores, and mobilizes triacylglycerols.

- **Portal vein**
  - Carries nutrients from intestine to liver.

- **Small intestine**
  - Absorbs nutrients from the diet, moves them into blood or lymphatic system.

- **Skeletal muscle**
  - Uses ATP to do mechanical work.
1. Metabolic Profile of Brain

Glucose is fuel for human brain - consumes 120g/day - 60-70% of utilization of glucose

In starvation - ketone bodies can replace glucose
2. Metabolic Profile of Muscles

Major fuels are glucose, fatty acids, and ketone bodies
- has a large storage of glycogen -> about \( \frac{3}{4} \) of all glycogen stored in muscles
- glucose is preferred fuel for burst of activity -> production of lactate (anaerobe)
3. Metabolic Profile of Adipose tissue

Triacylglycerols are stored in adipose tissue -> enormous reservoir of metabolic fuel

-> needs glucose to synthesis TAG;

-> glucose level determines if fatty acids are released into blood
5. Metabolic Profile of the Liver
(Glucose)

Essential for providing fuel to brain, muscle, other organs

-> most compounds absorbed by diet pass through liver
-> regulates metabolites in blood
Metabolic Activities of the Liver

(Amino Acids)

- α-Ketoacids (derived from amino acid degradation)
- liver’s own fuel

\[ \text{Glucose} \rightarrow \text{Pyruvate} \rightarrow \text{Acetyl-CoA} \rightarrow \text{Citric acid cycle} \rightarrow \text{ATP} \]

\[ \alpha\text{-Ketoacids (derived from amino acid degradation)} \rightarrow \text{liver’s own fuel} \]
Metabolic Activities of the Liver
(Fatty Acids)
Food Intake, Starvation, and Obesity

Normal *Starved-Fed Cycle*:

1. Postabsorptive state -> after a meal
2. Early fasting state -> during the night
3. Refed state -> after breakfast

-> Major goal is to maintain blood-glucose level!
1. Postabsorptive state

Glucose + Amino acids -> transport from intestine to blood
Dietary lipids transported -> lymphatic system -> blood
Glucose stimulates -> secretion of insulin

Insulin:
-> signals fed state
-> stimulates storage of fuels and synthesis of proteins
-> high level -> glucose enters muscle + adipose tissue (synthesis of TAG)
-> stimulates glycogen synthesis in muscle + liver
-> suppresses gluconeogenesis by the liver
-> accelerates glycolysis in liver -> increases synthesis of fatty acids
-> accelerates uptake of blood glucose into liver -> glucose 6-phosphate more rapidly formed than level of blood glucose rises -> built up of glycogen stores
Postabsorptive State → after a Meal
2. Early Fasting State

Blood-glucose level drops after several hours after the meal -> decrease in insulin secretion -> rise in glucagon secretion

Low blood-glucose level -> stimulates glucagon secretion of α-cells of the pancreas

Glucagon:
- signals starved state
- mobilizes glycogen stores (break down)
- inhibits glycogen synthesis
- main target organ is liver
- inhibits fatty acid synthesis
- stimulates gluconeogenesis in liver
- large amount of glucose in liver released to blood stream -> maintain blood-glucose level

Muscle + Liver use fatty acids as fuel when blood-glucose level drops
Early Fasting State -> During the Night
3. Refed State

Fat is processed in same way as normal fed state

First -> Liver does not absorb glucose from blood (diet)

Liver still synthesizes glucose to refill liver’s glycogen stores

When liver has refilled glycogen stores + blood-glucose level still rises -> liver synthesizes fatty acids from excess glucose
Mobilization at Starvation

Also at not treated diabetes

1. Protein degradation yields glucogenic amino acids.
2. Urea is exported to the kidney and excreted in urine.
3. Citric acid cycle intermediates are diverted to gluconeogenesis.
4. Glucose is exported to the brain via the bloodstream.
5. Fatty acids (imported from adipose tissue) are oxidized as fuel, producing acetyl-CoA.
6. Lack of oxaloacetate prevents acetyl-CoA entry into the citric acid cycle; acetyl-CoA accumulates.
7. Acetyl-CoA accumulation favors ketone body synthesis.
8. Ketone bodies are exported via the bloodstream to the brain, which uses them as fuel.