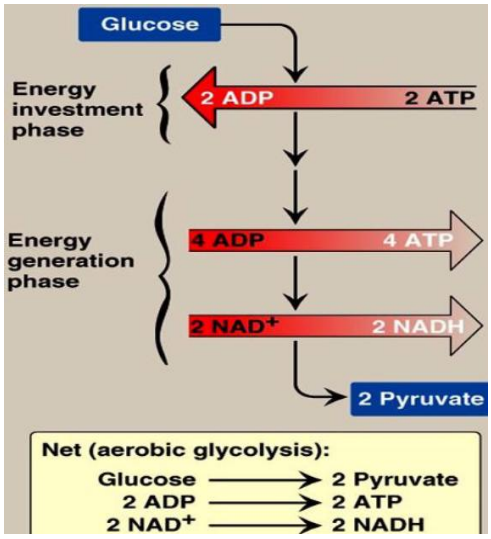
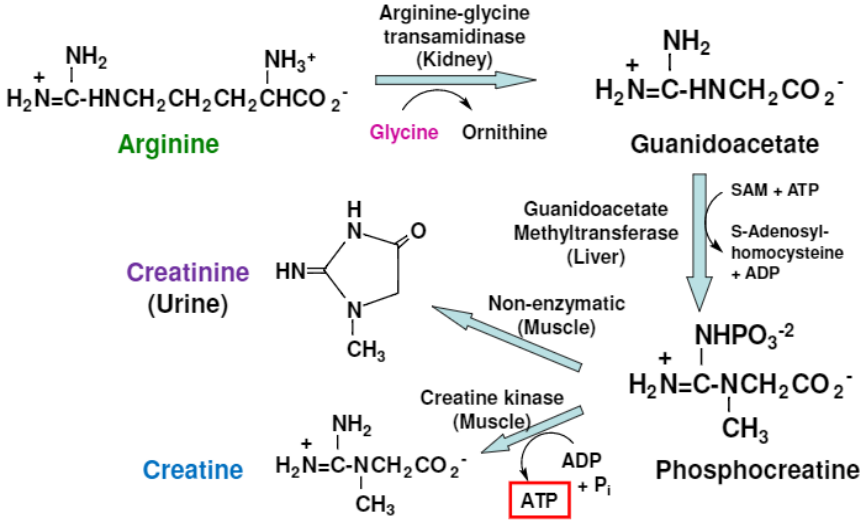
Unit I – Problem 5 – Biochemistry: Creatine Metabolism, High Energy Phosphates and Muscle's Energy Supply

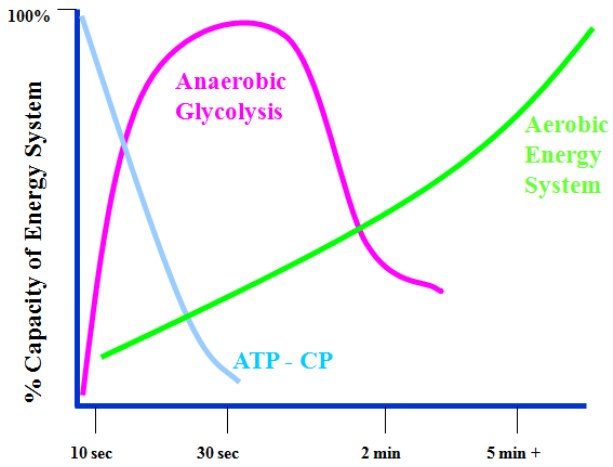
- **Muscles:**
  - They represent the largest organ in the body.
  - **In relation to total body weight, muscles account for:**
    - ✓ 25% at birth.
    - ✓ > 40% in young adults.
    - ✓ < 30% in old adults.
  - A muscle is the major biochemical transducer which converts chemical energy into mechanical energy.
  - Muscles have constant supply of chemical energy in the form of ATP and creatine phosphate.
  - **The sarcoplasm of muscle cells contains:**
    - ✓ Glycogen.
    - ✓ Glycogenolysis enzymes except (glucose-6-phosphatase).
    - ✓ Glycolytic enzymes.
    - ✓ ATP.
    - ✓ Creatine phosphate.
- **The source of ATP for contraction/relaxation cycles:**
  - **Creatine phosphate.**
  - **2 ADP by adenylyl kinase.**
  - **Glycolysis**: using blood glucose or muscle glycogen.
  - **Respiratory chain**: NADH, FADH
- **Fuel usage:**
  - **Light exercise (such as walking):**
    - ✓ ATP consumption makes ADP available for new ATP synthesis.
    - ✓ The presence of ADP stimulates the movement of H^+ into the mitochondria; this, in turn, reduces the proton gradient and stimulates electron transport.
    - ✓ NAD^+ becomes available; fatty acids and glucose are oxidized.
- **Sources of ATP (in the presence of oxygen):**
  - Under aerobic conditions, ATP is produced mainly by oxidative phosphorylation (respiratory chain), substrate sources are:
    - ✓ Glucose.
    - ✓ Fatty acids.
  - The oxygen is stored in myoglobin (in red muscles).
  - The amount of ATP at one time in the muscles is sufficient for only 1-2 seconds of activity (contraction/relaxation) thus it should be provided continuously.
- **Glucose from glycogen:**
  - Muscles contain large quantity of glycogen packed in granules in the sarcoplasm.
  - The release of glucose from glycogen is catalyzed by the enzyme glycogen phosphorylase-a.
  - Phosphorylase-a is produced from phosphorylase-b by the action of phosphorylase-b kinase (adding phosphate).
  - The phosphorylase-a production is stimulated by:
    - ✓ Calcium.
    - ✓ Epinephrine.
    - ✓ AMP.
  - The calcium activates phosphorylase-b kinase by phosphorylation
  - Energy yield from glycolysis (see the image in next page).



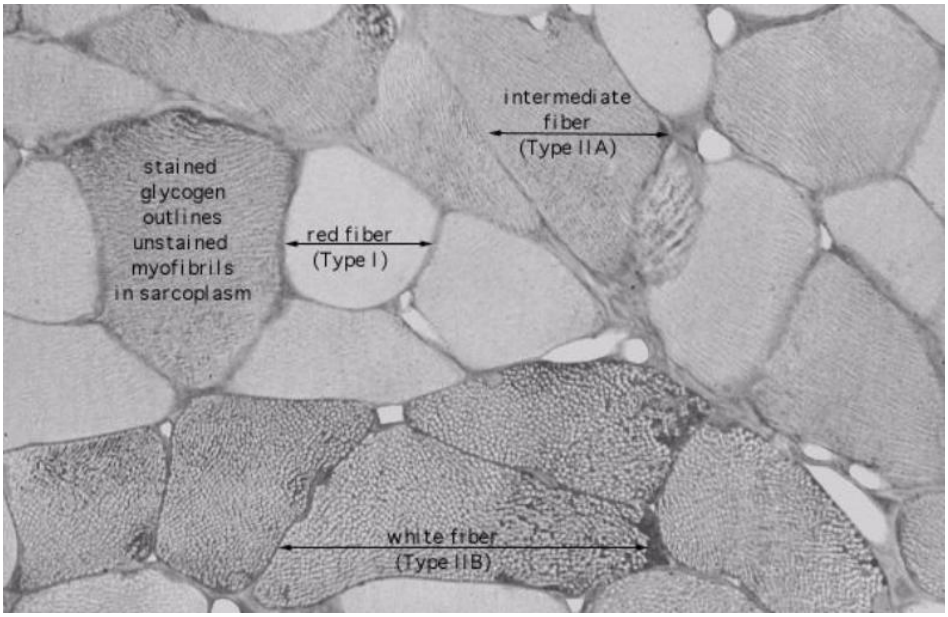
- **Creatine phosphate:**
  - It is the major energy reserve in muscles.
  - It provides the high energy phosphate to ADP to regenerate ATP.
  - It is formed by phosphorylation of creatine by creatine kinase (CK) enzyme using ATP as a source of phosphate when a muscle is at rest.
  - (CK) is of clinical use, it is elevated in acute and chronic muscle diseases.



- **ATP metabolites:**
  - Adenylyl kinase enzyme uses two ADP molecules to produce ATP and AMP.
  - AMP determined by AMP deaminase to form IMP and ammonia (muscle is a source of ammonia).
  - Or AMP dephosphorylated to give adenosine (vasodilator) which increase the blood supply to muscles.
- **Energy transfer systems and exercise:**



- **Types of muscle fibers:**
  - **Skeletal muscles contain two types of fibers:**
    - ✓ Red (type-I): slow-twitch, oxidative fibers.
      - ❖ They are red because of being rich in myoglobin and mitochondria, metabolism is aerobic and they maintain sustained contraction.
    - ✓ White (type-II): fast-twitch, glycolytic fibers.
      - ❖ They are white because they lack myoglobin; few mitochondria; energy is produced from aerobic glycolysis; short duration of contraction.



- **Energy for exercise:**
  - For the first 5-6 seconds of muscle power, the chemical energy that fuels muscular activities is ATP.
  - The next 10-15 seconds of muscle power can be provided through the body's use of the phosphagen system.
  - For longer and more intense periods of physical activity, the body must rely on breakdown of glucose to produce ATP.
  - The glycogen lactic acid system, through its anaerobic breakdown of glucose, provides approximately 30-40 seconds more of maximal muscle activity.
  - Each glucose molecule is split into two pyruvate molecules, and energy is released as 2 ATP molecules (net).
  - Some pyruvate is reduced to lactate, which if allowed to accumulate in muscle, will result in muscle fatigue.
  - At this point, the aerobic system must become active.