Chapter 10.5

Muscle Energy and Metabolism

How ATP is created for a skeletal muscle fiber?

Muscle "Energy" Metabolism

- The amounty of ATP needed is proportional to the level of skeletal muscle activity.
- You will need to deliver nutrients (e.g. glucose and oxygen) to the skeletal muscle so it can make ATP.
- When in a resting state, the heart and lungs work together to provide the appropriate amount of glucose and oxygen to meet the resting muscle energy requirements.
- If you start to walk then the muscle requires more energy for the increase in activity and the heart-lung function will increase (more heart beats per min and a faster respiratory rate).
- If you start to walk then you need to further increse heart rate and respiratory rate to meet the energy requirements of the skeletal muscles.
- We will review events which occur when you run a race!

Muscle “Energy” Metabolism

- We need ATP to preload myosin heads with energy // cock the myosin head
- After a contraction cycle we need more ATP to break the myosin-actin cross bridges /// this breaks one myosin-actin cross bridge as another crossbridge power-stroke occurs (if muscle is still contracting)
- If the muscle is relaxing then more ATP is required to pump calcium back into the sarcoplasmic reticulum ///
- So ATP is constantly being made
- ATP is not stored
- ATP is immediately consumed

Muscle “Energy” Metabolism

- *Ability to make small amount of ATP via glycolsis depends on availability of a reduced organic molecule (e.g. glucose)*

- *Ability to make large amounts of ATP depends on availability of a reduced organic molecule <u>(e.g. pyruvic acid from splitting glucose and/or acetyl groups produced by beta-oxidation of fatty acids)</u> plus the presence of oxygen*

  – Glycolysis vs Kreb's Cycle + Electron Transport System (note: Kreb's Cycle also called the citric acid cycle)

    - Glcolysis enzymes are in cytosol // anaerobic

    - KC-ETS enzymes are inside mitochondria // areobic

Muscle Metabolism

- Two main pathways for ATP synthesis
  - First metabolic pathway = anaerobic fermentation (glycolysis)
    - enables cells to produce ATP in the absence of oxygen / takes place in cytoplasm
    - yields little ATP // but immediately available
    - by product is toxic lactic acid /// believed to be factor in muscle fatigue

Muscle Metabolism

– Second metabolic pathway: aerobic respiration (Krebs Cycle also called Citrus Acid Cycle with ETS)

- takes place in the mitochondria
- requires oxygen
- produces much more ATP   // glycolysis = 2 vs Kreb's Cycle = 36 to 38
- toxic end product = CO_2
- produces H+ (acid) but use oxygen to make water with H+ (called metabolic water)
- reduces FAD and NAD / these reduced co-enzymes are then oxidized via electron transport system /// reduced co-enzymes transfer protons and electrons to ETS which produces most of the ATP using ATP Synthetase /// two ADP are directly phosphorlated within mitochondria during each "Krebs Cycle"
- Requires a continual supply of oxygen and glucose

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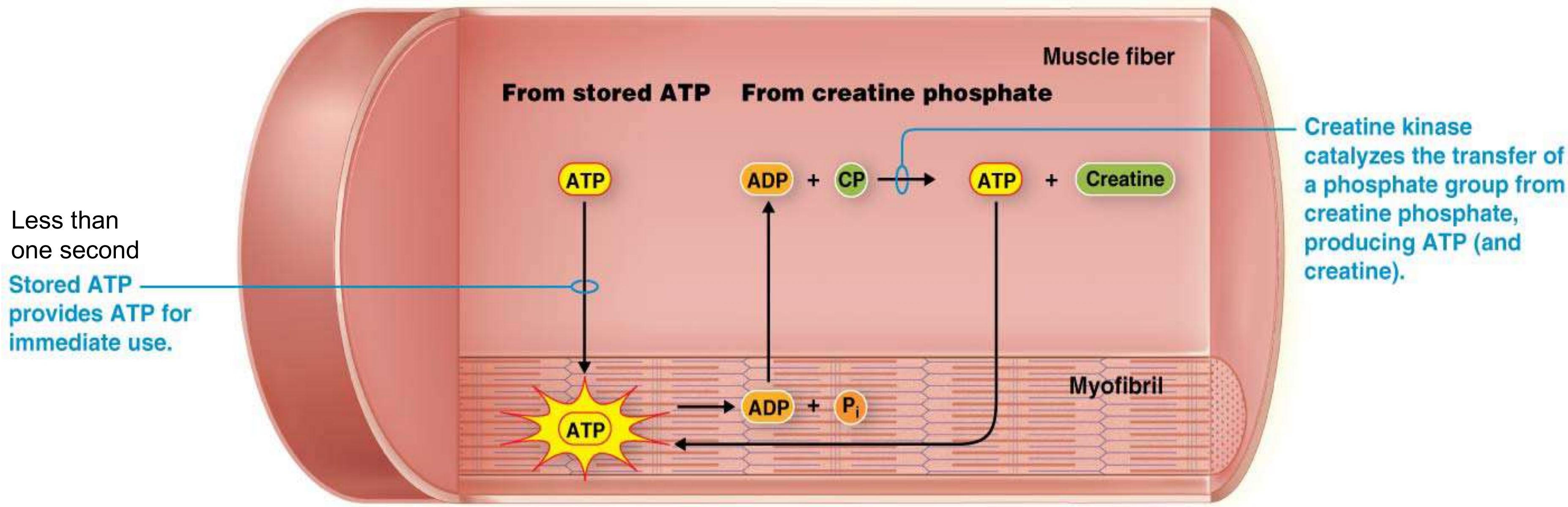
Key Idea: The level of activity (how fast the muscle fiber uses glucose and oxygen) determines the physiologic state of the muscle fibers. To support a high level of muscle contractions you need to increase the blood supply (delivery of glucose and oxygen) to the muscle fiber.

As you move from a resting state to an active state, there is a “ramping-up process” so the cardiovascular and respiratory systems may increase their functions to meet the demands of the now more active muscle organ. This will take several seconds and depends upon the fitness of the individual.

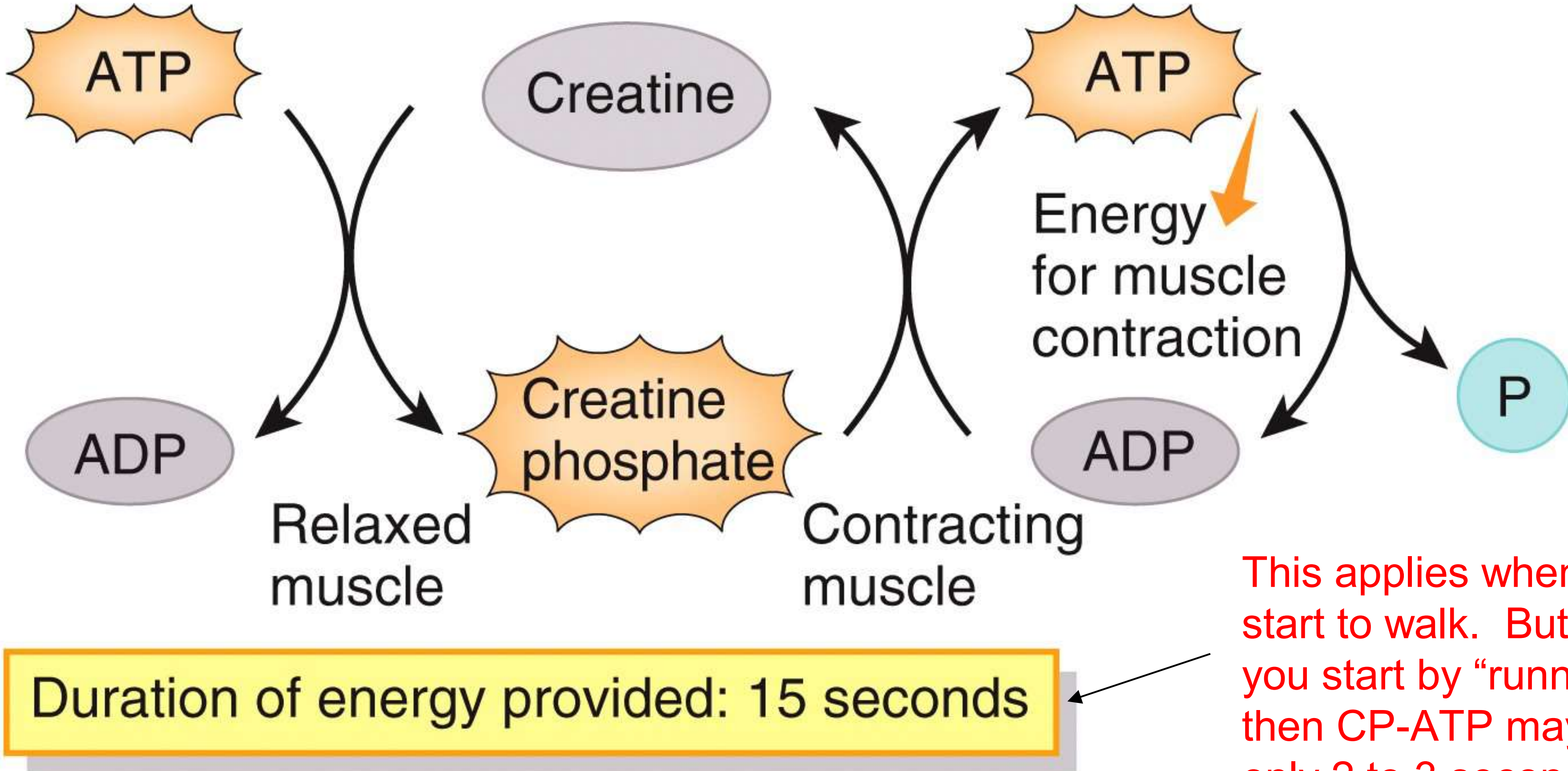
Therefore, the muscle fiber must have a mechanism to “bridge” the muscle's energy requirement from a resting state to an active state. This dynamic transition will occur between the resting state to walking to running.

Sources of energy for muscle fibers.



(a) Immediate energy sources

ATP is always being made within cytosol but when you start to exercise this small amount of ATP is consumed within a second. ADP can be "re-energized" by borrowing a phosphate from creatine phosphate (i.e. like getting a jump start to a battery). /// We may use the energy of excess ATP to energize creatine and at a later time use creatine phosphate to energize ADP!

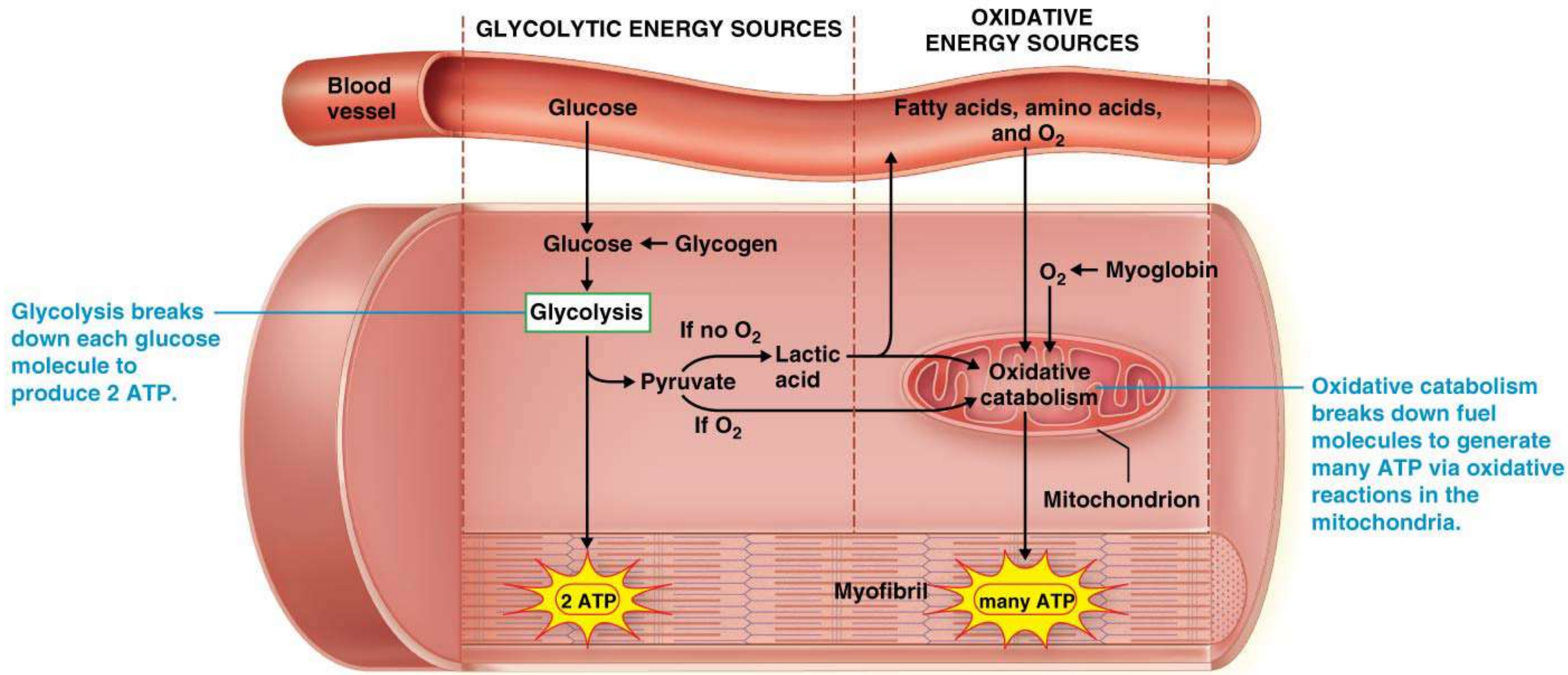


This applies when you start to walk. But if you start by “running” then CP-ATP may last only 2 to 3 seconds

(a) ATP from creatine phosphate

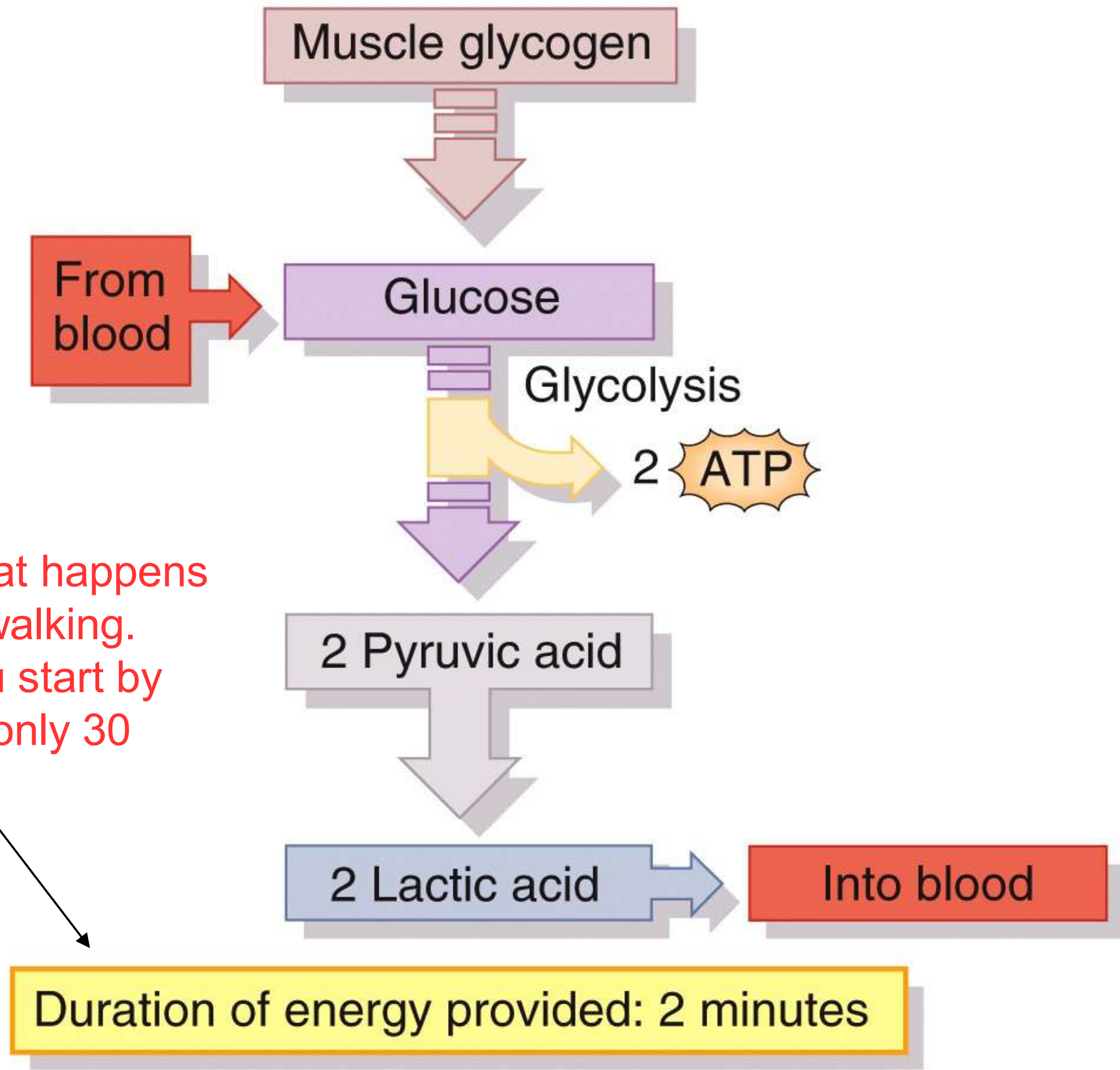
Myoglobin is a muscle fiber cytoplasmic protein. // Like hemoglobin, myoglobin binds and stores oxygen and may release oxygen so mitochondria can use this myoglobin's oxygen to produce limited amount of ATP. This is only enough to support Krebs Cycle for one second. Now the creatine phosphate (phosphogen system) may supplement ATP production after myoglobin is depleted of oxygen .

Sources of energy for muscle fibers.



(b) Glycolytic and oxidative energy sources

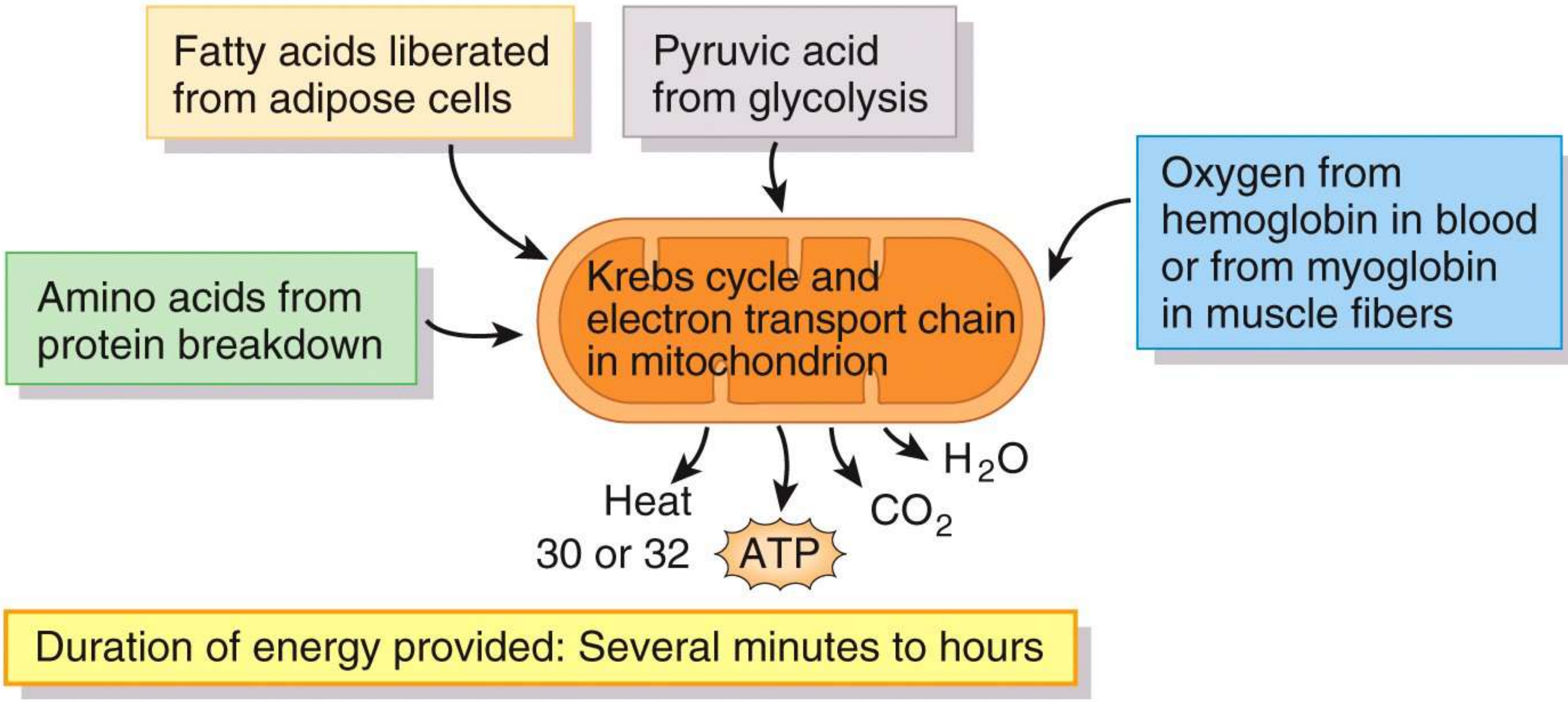
Muscle fibers store a small amount of oxygen bound to myoglobin. So at the start of exercise, oxidative catabolism starts but the stored oxygen is depleted in a second and more oxygen from lungs must be delivered. This process takes time. How is ATP produced during this “period”?



(b) ATP from anaerobic glycolysis

This shows what happens when you are walking. However, if you start by "running" then only 30 seconds +/-

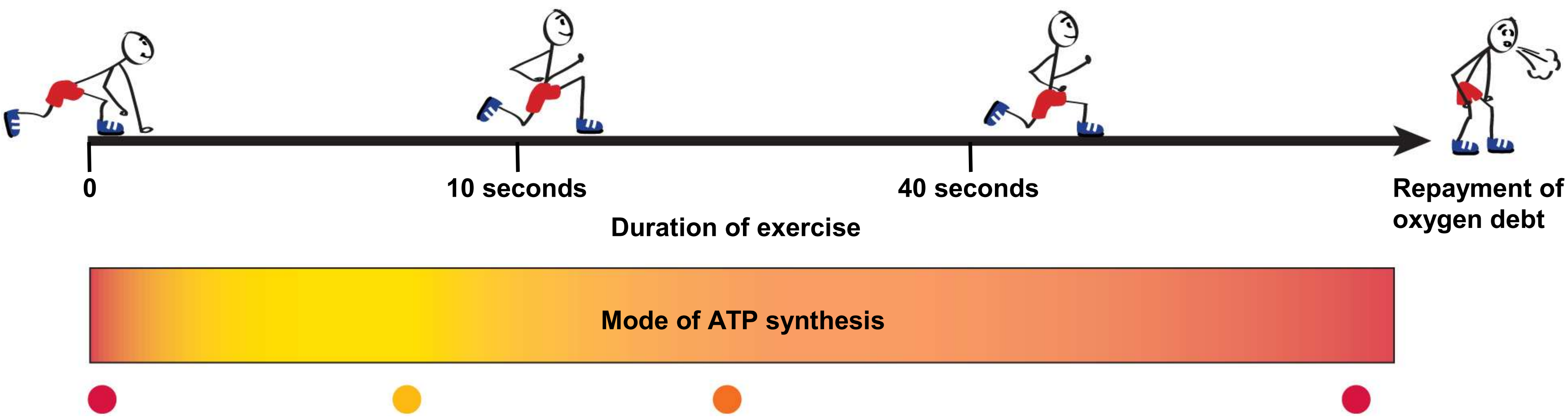
Different types of reduced molecles are modified so they may enter the Kreb's cycle at different entry points.   This allows for alternative fuel sources when glucose is not available.



(c) ATP from aerobic respiration

Note: How is skeletal muscle ATP managed if you want to run a long race? The next slides will outline the steps.

Modes of ATP Synthesis During Extreme Exercise



Cytosol ATP plus aerobic respiration using oxygen from Myoglobin. // < 1 sec

Phosphagen system // another couple of sec.

Catabolize cytoplasmic glycogen–lactic acid system // (anaerobic fermentation) // 30 sec

Aerobic respiration now possible due to cardiopulmonary function // reached after 40 sec

After race post exercise oxygen consumption remains hisgh so the ATP “borrowed” at the start of race may now be replaced.

At rest we oxidize fatty acids to supply energy for our skeletal muscles (note: our brains continue to oxidize glucose / brain cells and RBCs only ferment glucose)

As level of activity increases, skeletal muscles will shift from fat to glucose as an energy source.

Only after glucose reserves are exhausted will we shift back to fat metabolism

Immediate Energy Needs

- During short, intense exercise like a 100 m dash
- Skeletal muscles start to contract before blood supply to muscle organ increases to meet metabolic needs (e.g. blood brings oxygen, glucose, and removes waste products)
- Skeletal muscles contain only limited amount of myoglobin /// this stores small amount of oxygen inside muscle fibers
  - Maybe used to accommodate some aerobic respiration – 1 second or less
  - Myoglobin’s oxygen rapidly depleted

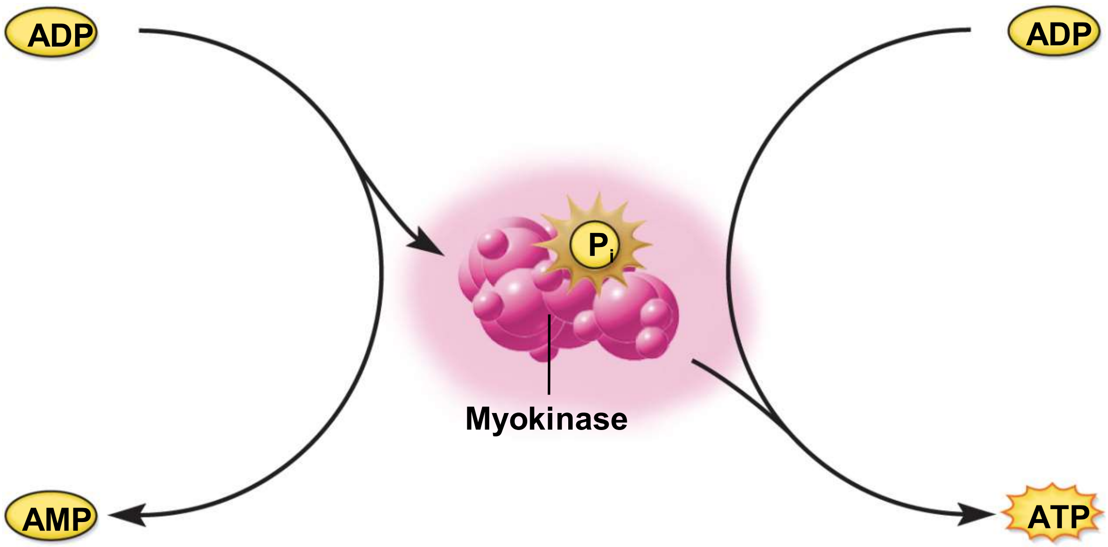
Immediate Energy Needs

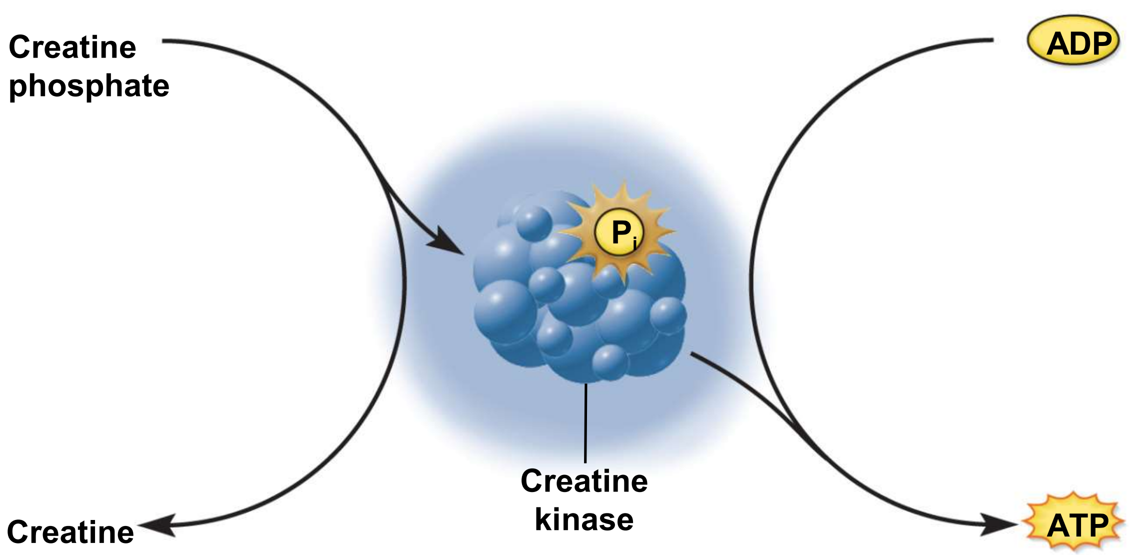
- After myoglobin gone / muscles meets ATP demand by borrowing phosphate groups (P_i) from other molecules and transferring the P_i to ADP (makes ATP!) = Phosphogen System
  - two enzyme systems control these phosphate transfers
    - <u>myokinase</u> – transfers P_i from one ADP to another converting the latter to ATP
    - <u>creatine kinase</u> – obtains P_i from a phosphate-storage molecule creatine phosphate (CP)
    - fast-acting system that helps maintain the ATP level while other ATP-generating mechanisms are being activated

Immediate Energy Needs

- Phosphagen system
  - provides nearly all energy used for short bursts of intense activity (after myoglobin depleted)
    - <u>one minute of brisk walking</u>
    - <u>6 seconds of sprinting or fast swimming</u>
    - important in activities that require brief but maximum effort // football, baseball, and weight lifting

Immediate Energy Needs





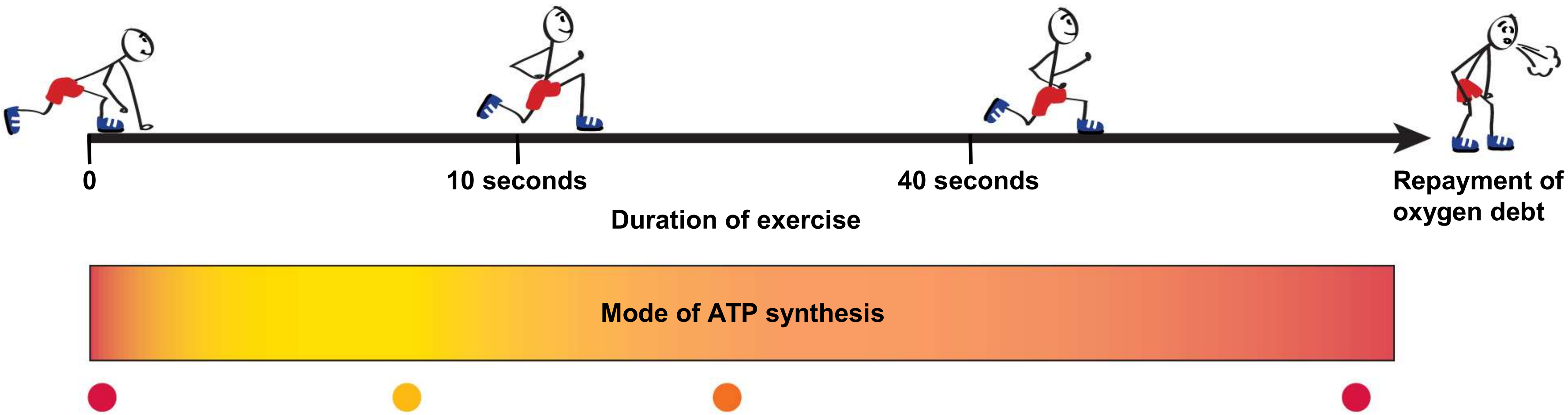
Short-Term Energy Needs

- as the phosphagen system is exhausted
- muscles shift to anaerobic fermentation
  - muscles obtain glucose from blood or muscle fiber's stored glycogen deposits
  - in the absence of oxygen
    - glycolysis can generate a net gain of 2 ATP for every glucose molecule consumed
  - converts glucose to lactic acid / L.A. leaves cell and transported to liver

Short-Term Energy Needs

- Glycogen (glucose) lactic acid system // the pathway from glycogen to lactic acid
- Produces enough ATP for 30 – 40 seconds of maximum activity
- Downside of anarobic fermentation is production of lactic acid!

Long-Term Energy Needs

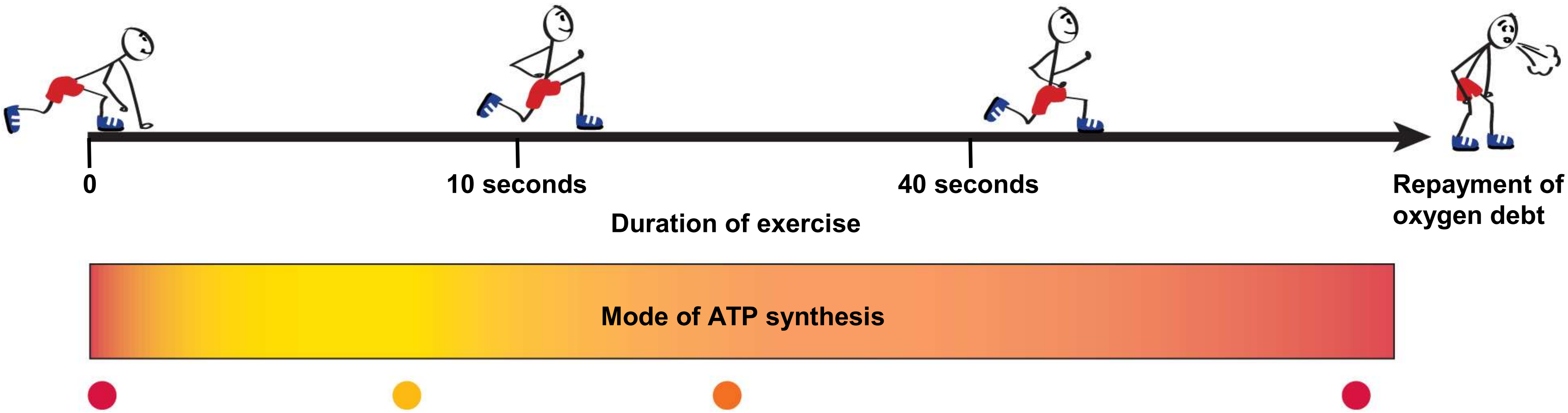


- After 40 seconds or so
  - respiratory and cardiovascular systems "catches up" to demands of skeletal muscles
  - now cardiorespiratory system able to deliver enough oxygen to meet the muscle's oxygen requirement for aerobic respiration /// mitochondria able to make enough ATP to sustain muscle contrations.

Long-Term Energy Needs

- Aerobic respiration produces 36-38 ATP per glucose
  - efficient means of meeting the ATP demands of prolonged exercise
  - one's rate of oxygen consumption rises for 3 to 4 minutes and levels off to a steady state in which aerobic ATP production keeps pace with demand
  - little lactic acid accumulates under steady state conditions
  - *depletion of glycogen and blood glucose, together with the loss of fluid and electrolytes through sweating, set limits on endurance and performance even when lactic acid does not*

Modes of ATP Synthesis During Extreme Exercise



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Runners experience this shift and call it "hitting the wall"

What is Oxygen Debt?

- Why does heavy breathing continues after strenuous exercise?
  - excess post-exercise oxygen consumption (EPOC) – the difference between the resting rate of oxygen consumption and the elevated rate following exercise.
  - typically about 11 liters extra is needed after strenuous exercise
  - oxygen debt occurs because we need to replace the ATP consumed to restore myoglobin and replenish CP

Oxygen Debt

- Oxygen need in excess of current muscle activity for the following reasons:
  - **replace oxygen to the myoglobin //** depleted in the first minute of exercise
    - oxygen bound to myoglobin and blood hemoglobin
    - oxygen dissolved in blood plasma and other extracellular fluid
    - oxygen in the air in the lungs
  - **replenishing the phosphagen system**
    - Synthesize extra ATP to replace phosphate “borrowed” from creatine-phosphate at the start of the race

Oxygen Debt

- Furthermore, additional oxygen needed for
- **Metabolize lactic acid**
    - 80% of lactic acid produced by muscles enter bloodstream
    - much of this lactic acid ends up in liver
    - converted back to pyruvic acid in the kidneys, cardiac muscle, and especially the liver
    - liver converts most of the pyruvic acid back to glucose to replenish the glycogen stored in the skeletal muscles or liver.
    - This requires ATP and explains continued demand for oxygen even after strenuous exercise stops!
  - **Serving the elevated metabolic rate**
    - occurs while the body temperature remains elevated by exercise and consumes more oxygen

Endurance

- Endurance – the ability to maintain high-intensity exercise for more than 4 to 5 minutes
  - determined in large part by one's maximum oxygen uptake (VO_2max)
  - maximum oxygen uptake – the point at which the rate of oxygen consumption reaches a plateau and does not increase further with an added workload
    - proportional to body size
    - peaks at around age 20
    - usually greater in males than females
    - can be twice as great in trained endurance athletes as in untrained person
    - May result in twice the ATP production

Muscle Fatigue

- Characterized by progressive weakness and loss of contractility from prolonged use of the muscles
  - To experience muscle fatigue try this:
    - repeated squeezing of rubber ball
    - rapidly opening and closing your hand as if making a fist (one minute)
    - holding text book out level to the floor

Fatigue

- Causes of muscle fatigue
  - ATP synthesis declines as glycogen is consumed
  - ATP shortage slows down the Na^+ - K^+ pumps
    - compromises their ability to maintain the resting membrane potential and excitability of the muscle fibers
  - Lactic acid lowers pH of sarcoplasm
    - inhibits enzymes involved in contraction, ATP synthesis, and other aspects of muscle function

Fatigue

- Causes of muscle fatigue (cont)
  - release of K^+ with each action potential causes the accumulation of extracellular K^+ /// hyperpolarizes the cell and makes the muscle fiber less excitable
  - motor nerve fibers use up their Ach /// less capable of stimulating muscle fibers – junctional fatigue
  - central nervous system, where all motor commands originate, fatigues by unknown processes, so there is less signal output to the skeletal muscles

Beating Muscle Fatigue

- Taking **oral creatine** increases level of creatine phosphate in muscle tissue and increases speed of ATP regeneration
  - useful in burst type exercises – weight-lifting
  - risks are not well known
    - muscle cramping, electrolyte imbalances, dehydration, water retention, stroke
    - kidney disease from overloading kidney with metabolite creatinine

Beating Muscle Fatigue

- carbohydrate loading – a form of dietary regimen
  - Loads maximum amount of glycogen into muscle cells
  - extra glycogen is hydrophilic and adds 2.7 g water/ g glycogen
    - athletes feel sense of heaviness outweighs benefits of extra available glycogen