MUSCLES

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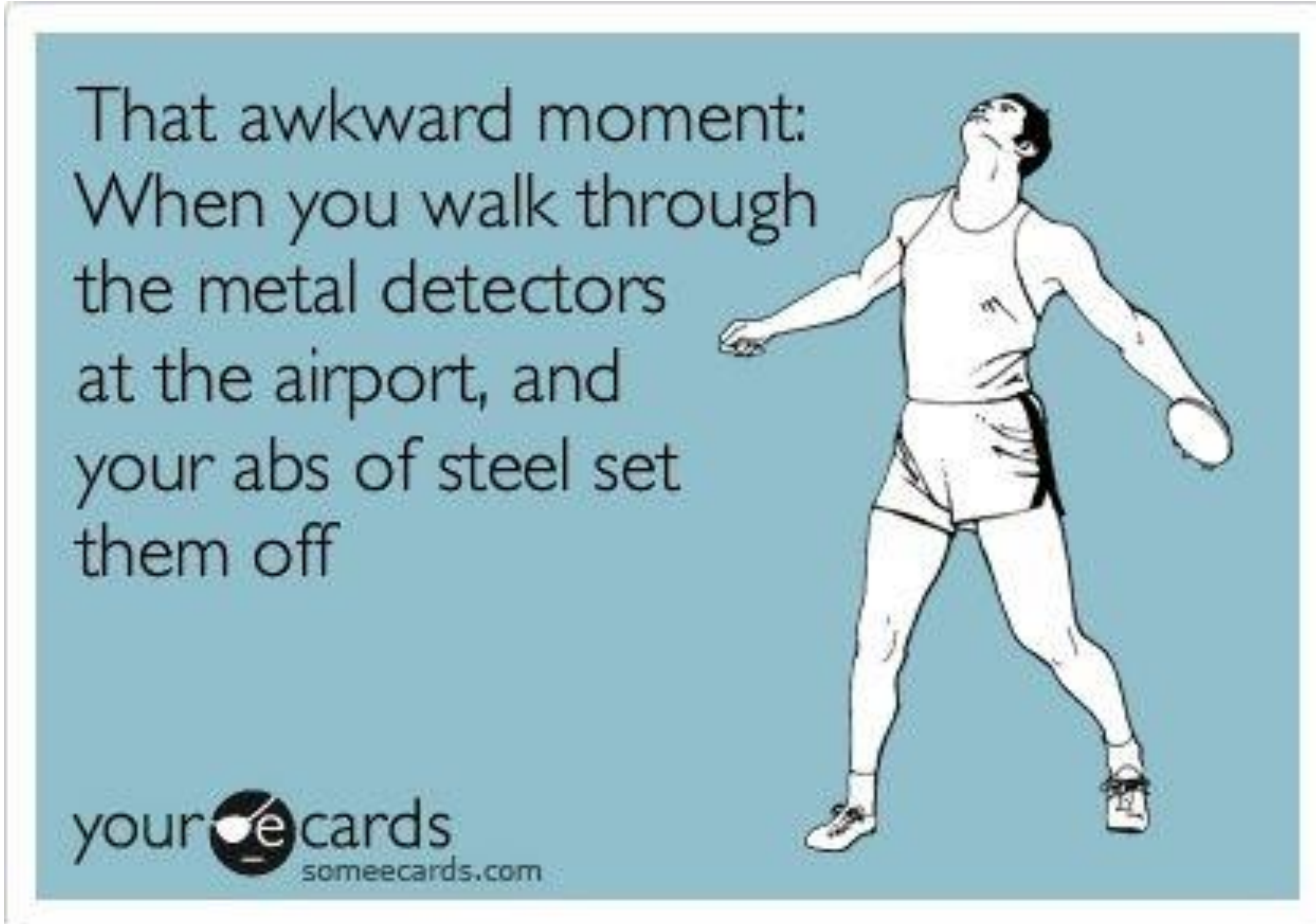
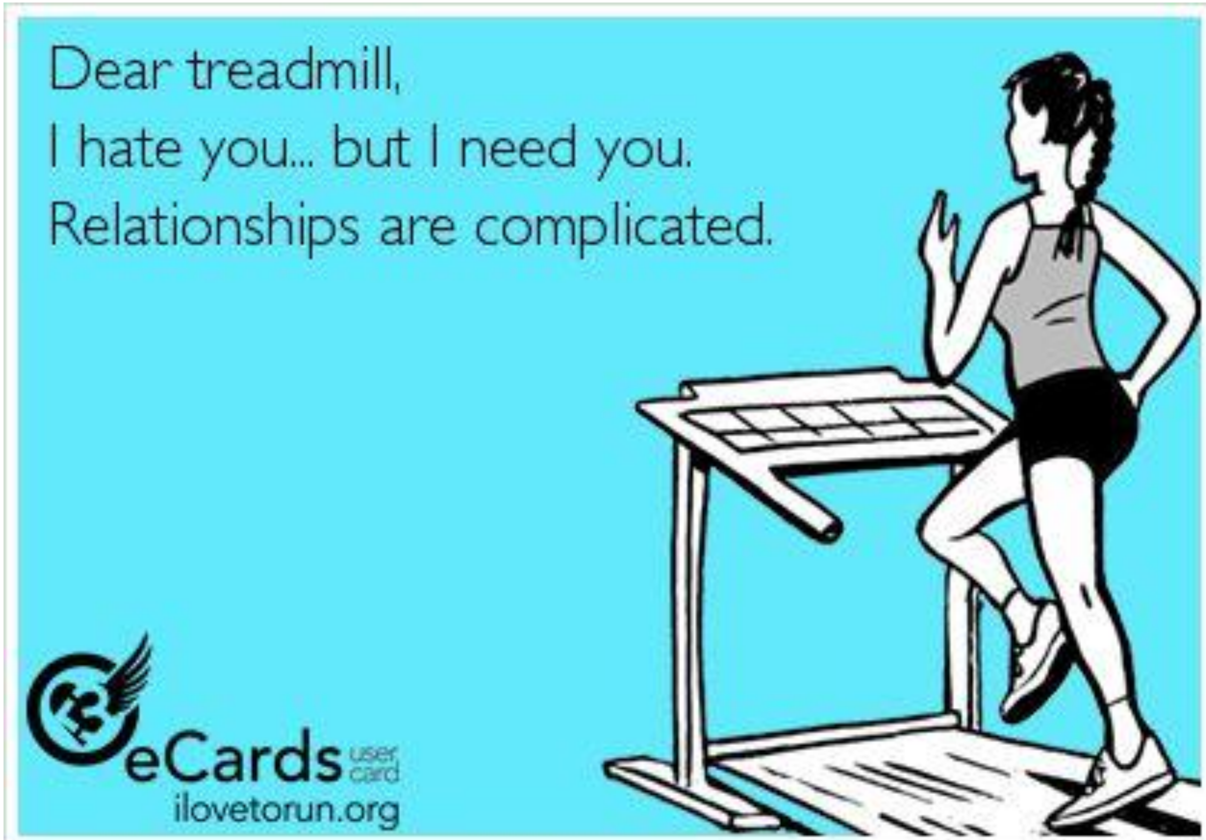

That awkward moment:
When you walk through
the metal detectors
at the airport, and
your abs of steel set
them off
your ecards
someecards.com


Dear treadmill,
I hate you... but I need you.
Relationships are complicated.
eCards user card
ilovetorun.org

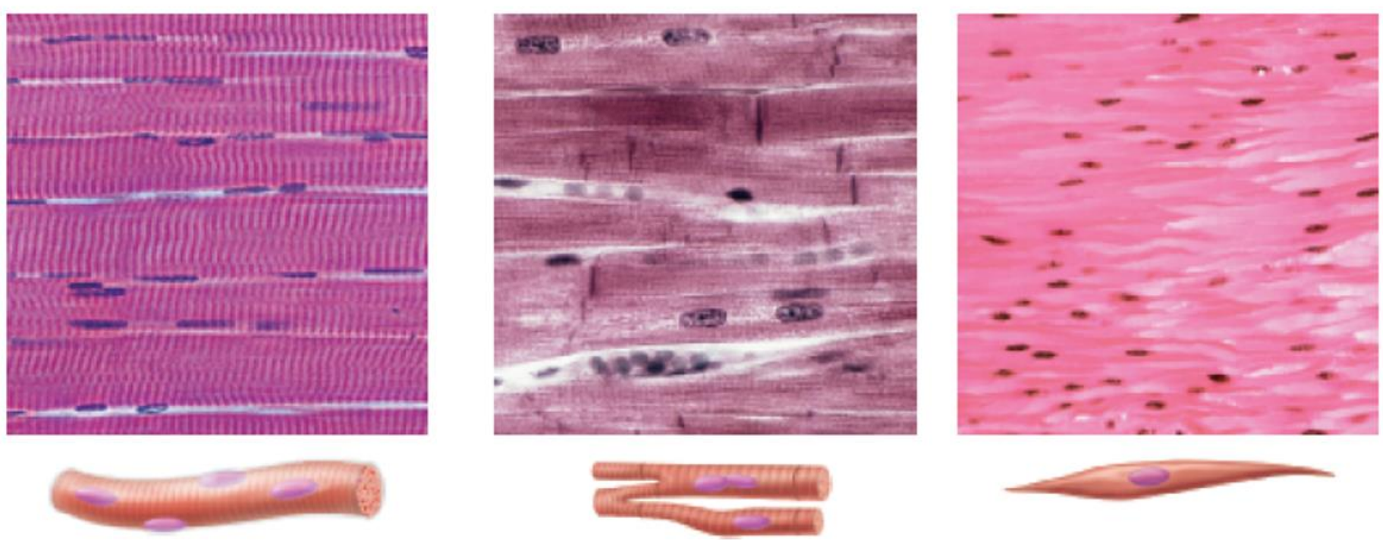
Muscle Tissue

- Three types:

1. Skeletal
   - Voluntary muscle, striated with many nuclei
   - Found in limbs, trunk of body, jaws, face, eyes, etc
2. Cardiac
   - Makes up the myocardium, striated
   - Involuntary (controlled by autonomic nervous system)
3. Smooth
   - Found in digestive tract, bladder, ducts, arteries, veins to regulate internal processes
   - Involuntary (under the control Autonomic Nervous System)

Muscle type	Structural elements	Function	Location
Skeletal	Long cylindrical fiber, striated, many peripherally located nuclei	Voluntary movement, produces heat, protects organs	Attached to bones and around entry & exit sites of body (e.g., mouth, anus)
Cardiac	Short, branched, striated, single central nucleus	Contracts to pump blood	Heart
Smooth	Short, spindle-shaped, no evident striation, single nucleus in each fiber	Involuntary movement, moves food, involuntary control of respiration, moves secretions, regulates flow of blood in arteries by contraction	Walls of major organs and passageways

Skeletal	Cardiac	Smooth

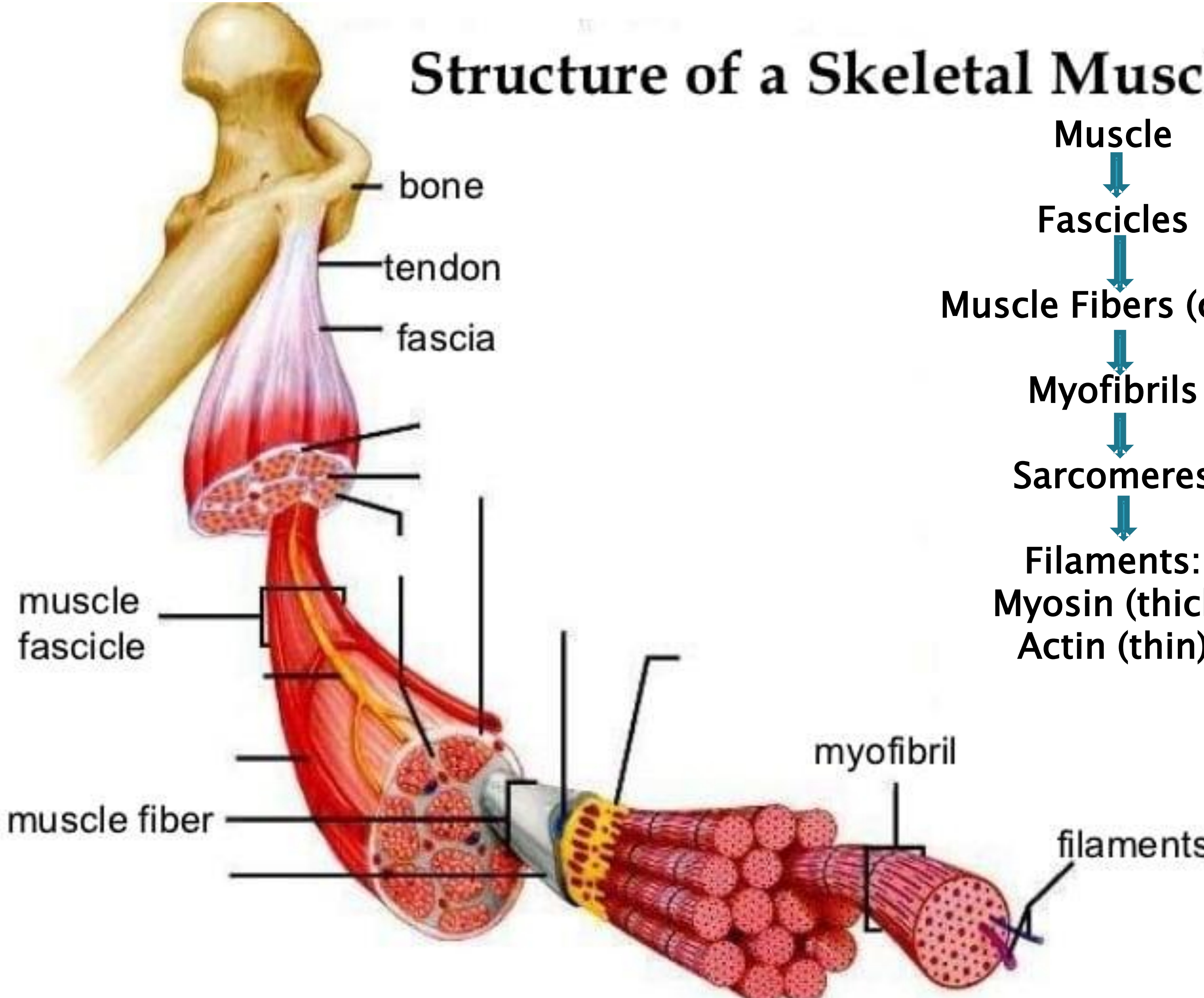


Skeletal	Cardiac	Smooth
Single, very long cylindrical, multinucleate cells with obvious striations	Branching chains of cells; uni- or binucleate; striations	Single, fusiform, uninucleate; no striations

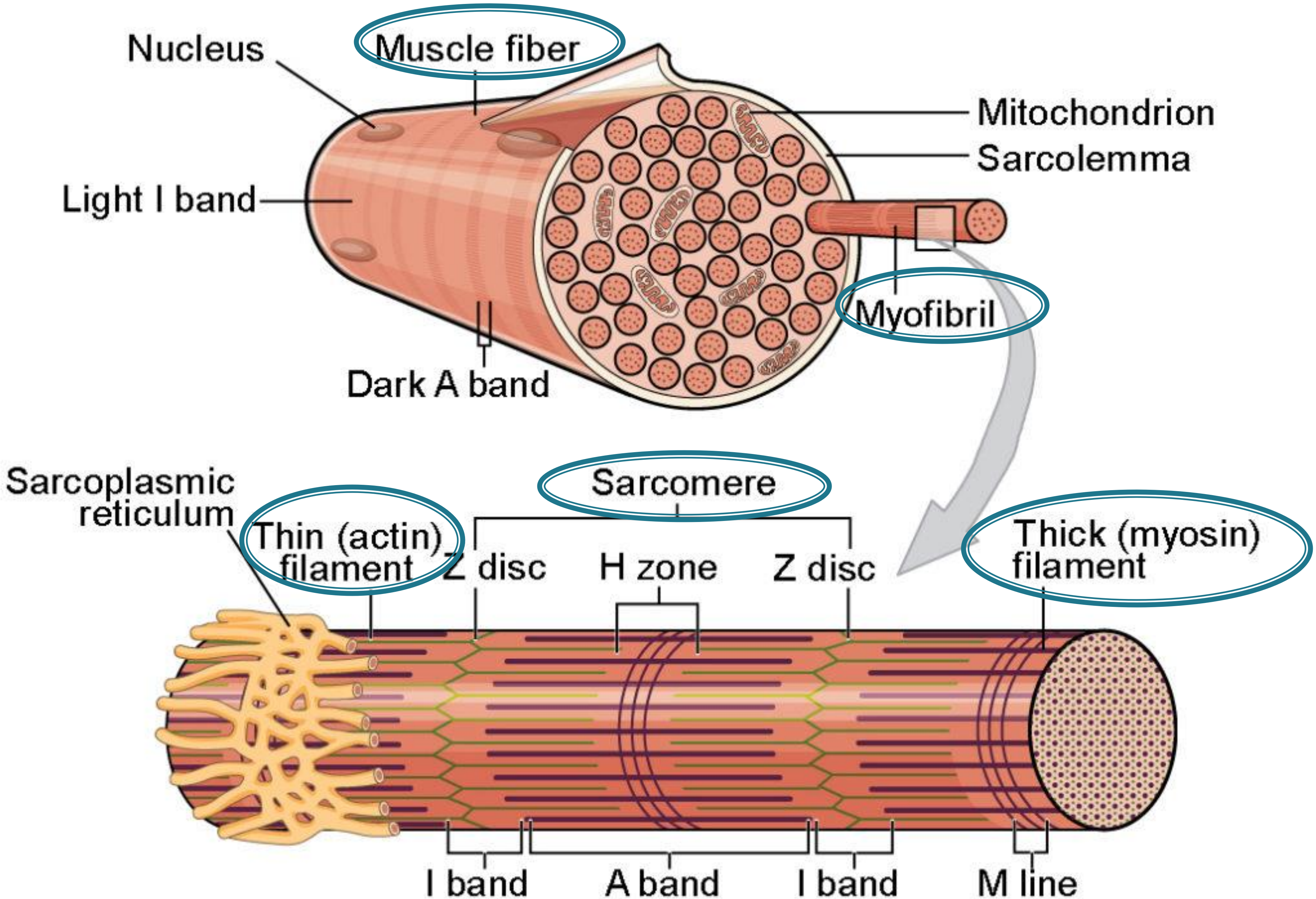
Organization of Skeletal Muscles

- *Skeletal muscles* consist of tightly packaged *muscular bundles* (fascicles) surrounded by connective tissue (perimysium)
- Each bundle contains multiple *muscle fibres*, which are formed when individual muscle cells fuse together
- Muscle fibres contain tubular *myofibrils* that run the length of the fibre and are responsible for muscular contraction
- The myofibrils can be divided into repeating sections called *sarcomeres*, each of which represent a single contractile unit

Structure of a Skeletal Muscle



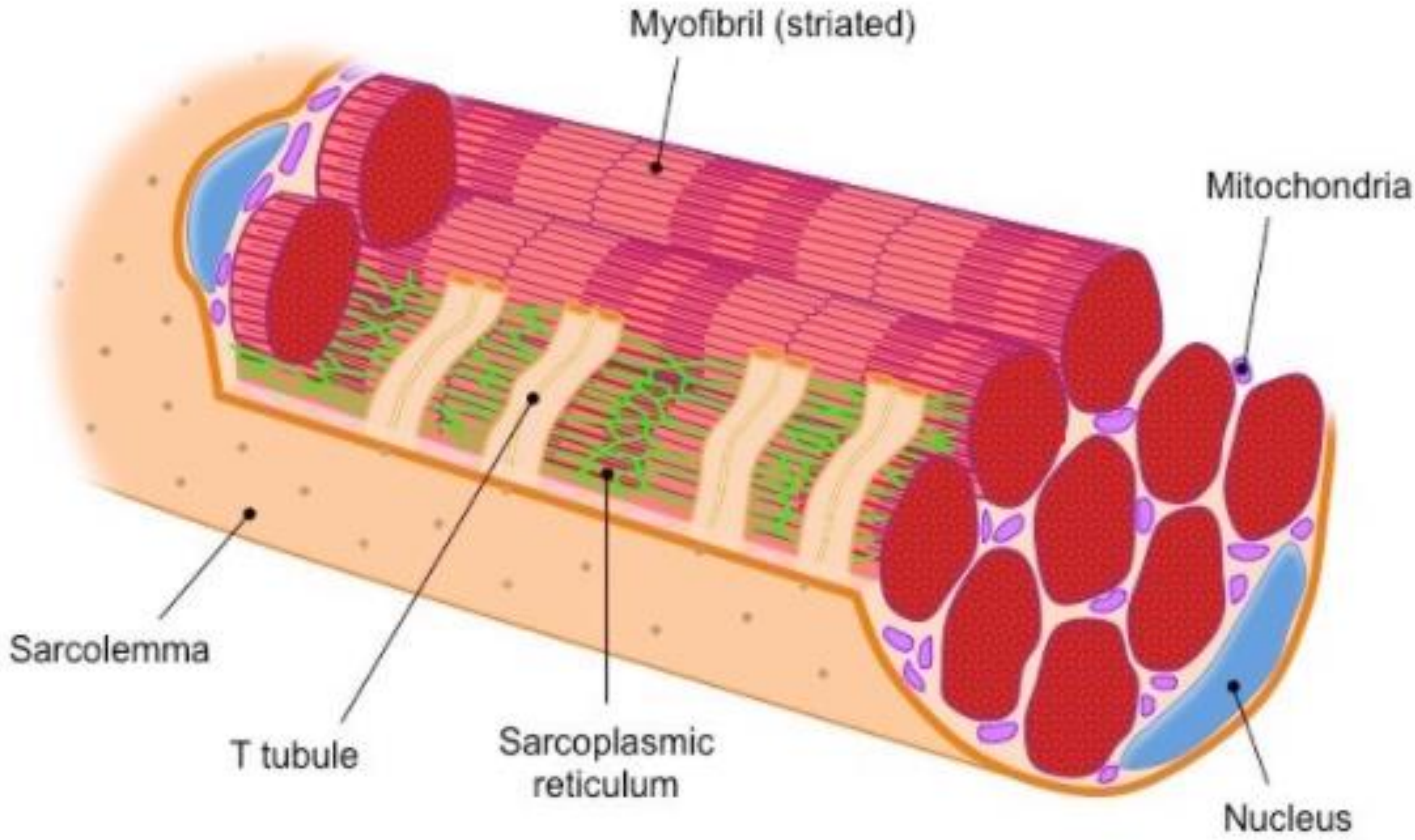
Muscle
↓
Fascicles
↓
Muscle Fibers (cells)
↓
Myofibrils
↓
Sarcomeres
↓
Filaments:
Myosin (thick)
Actin (thin)


Nucleus
Muscle fiber
Mitochondrion
Sarcolemma
Light I band
Myofibril
Dark A band
Sarcoplasmic reticulum
Thin (actin) filament
Sarcomere
Z disc
H zone
Z disc
Thick (myosin) filament
I band
A band
I band
M line

Muscle Fiber Structure

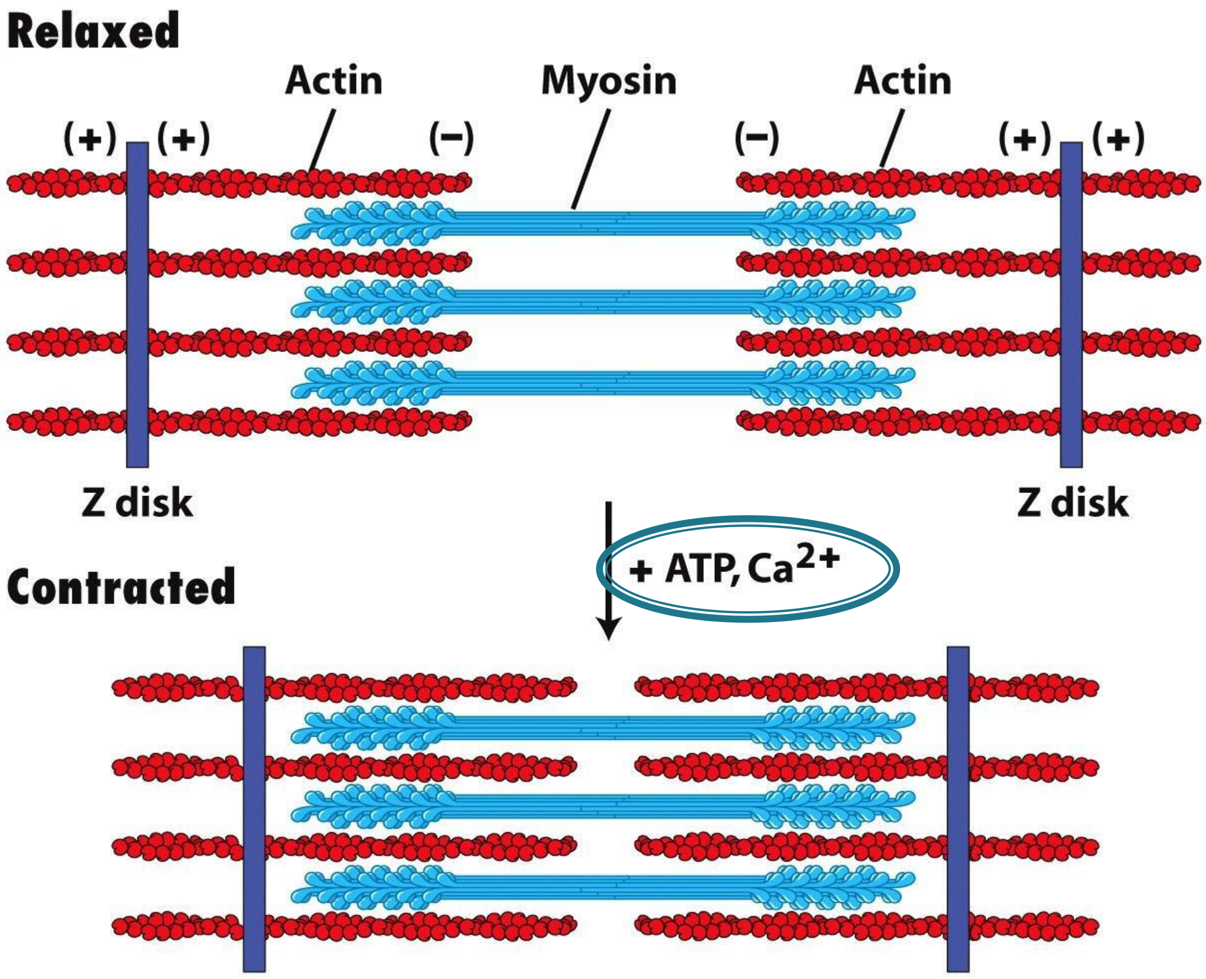
Each individual muscle fiber has the following specialized features designed to facilitate muscle contraction:

- They have many nuclei (fibers form from the fusion of individual muscle cells)
- They have a large number of mitochondria (muscle contraction requires ATP hydrolysis)
- They have a specialized endoplasmic reticulum (system of sac-like membranes) where calcium ions are stored
- They contain tubular myofibrils made up of two different myofilaments – **thin filament (actin**) and **thick filament (myosin)**
- The continuous membrane (**sarcolemma)** surrounding the muscle fiber contains **T tubules** through which electrical impulses are transmitted

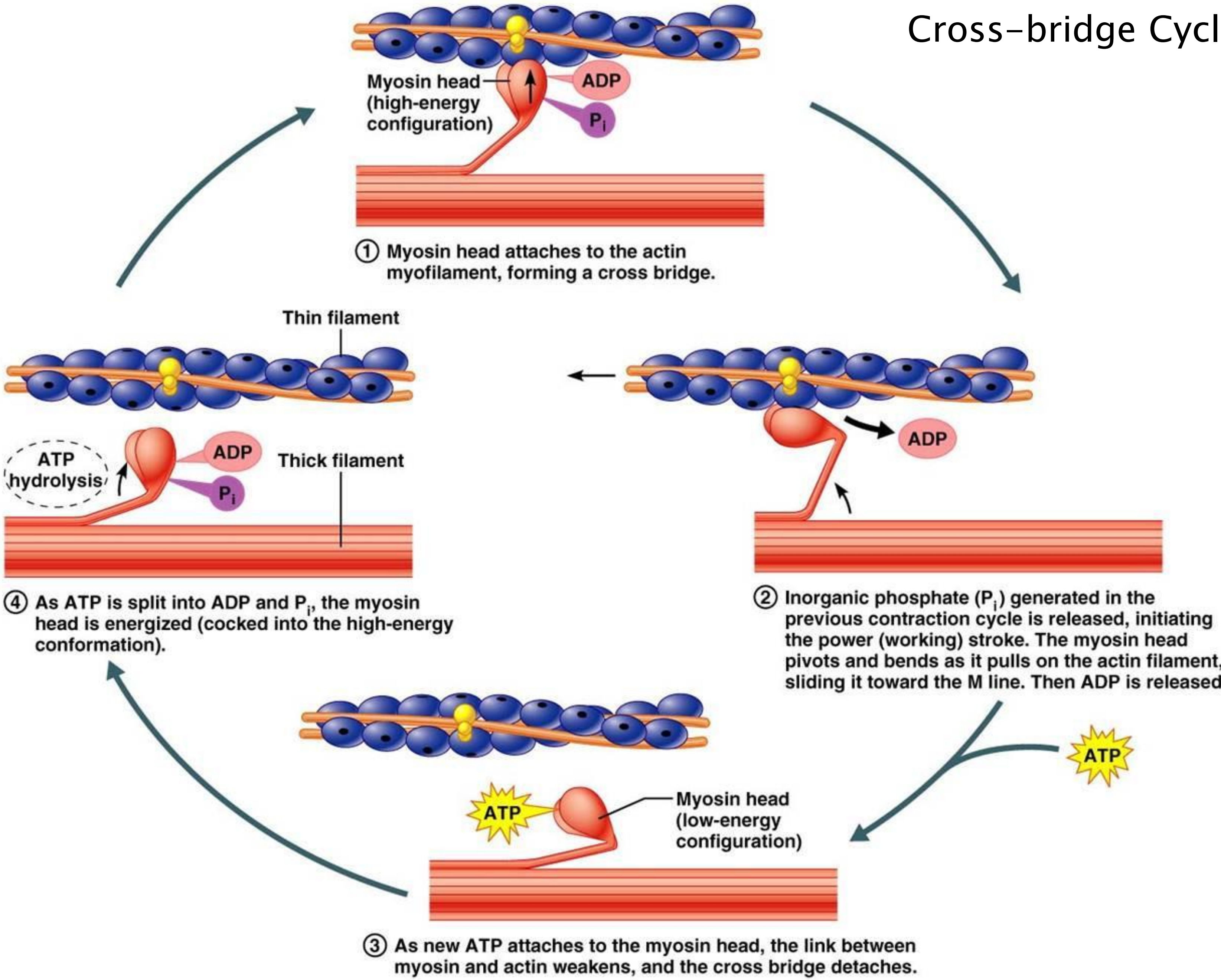

Myofibril (striated)
Mitochondria
Sarcolemma
T tubule
Sarcoplasmic
reticulum
Nucleus

Mechanism of Contraction

- Myosin filaments pull actin filaments inwards towards the center of sarcomere
- Sarcomere shortens as well as length of muscle fiber



Cross-bridge Cycle



- Actin (thin filament) – A globular protein that links into chains. Two chains twist helically forming microfilaments.
- Myosin (thick filament) – A protein filament that interacts with actin filaments to cause cell contraction. Myosin globular heads contain Actin Binding Sites and ATP Binding Sites.
- Tropomyosin – A protein of the thin filament that winds around actin whose function is to block the actin/myosin binding sites.

Muscle Contraction Physiology

1. An action potential in a motor neuron causes acetylcholine to release in the synaptic cleft.
2. Acetylcholine binds with receptors on the cell membrane on the muscle fiber, opening -Na+ and Ca2+ channels.
3. Calcium is released from the terminal cisternae into the muscle fiber.
4. Calcium binds to troponin
5. Troponin shifts tropomyosin, which was blocking the active site on the actin.
6. Myosin heads attach to actin by breaking down ATP to ADP and a phosphate via Myosin-ATPase

7. The Myosin head forms a ‘cross-bridge’ on the active site of the actin filament.
8. The cross bridge pulls actin, which slides over the myosin – known as the ‘Power Stroke.’
9. The release of ADP completes the cross-bridge movement and ATP attaches to myosin, breaking the actin-myosin crossbridge.
10. Every time ATP is split into ADP + P, the myosin head ‘cocks’ into place to form another cross bridge with actin.

- This entire process shortens the sarcomere, which is functional unit of a muscle cell.

Calcium

- Ca is required for muscle contraction/relaxation
- Ca functions like a key which allows for the uncoupling of actin/myosin
- Sufficient Ca is required for full muscle relaxation
- Cramping occurs with mineral deficiencies – usually Ca and Mg but also K

Muscle Movement

- Muscles require regular use in order to avoid atrophy.
- When activity exceeds one's fitness level, soreness occurs caused by microscopic tears and micro-hemorrhaging in the muscle – this is normal.
- In a healthy person, exercise produces some tissue breakdown as sore muscles and inflammation. As the tissue heals, it becomes a little stronger, often bigger, and a little more resilient than before.

Muscle Regeneration

- Skeletal muscle
  - When skeletal muscles are damaged, satellite cells are stimulated to divide. After dividing, the cells fuse with existing muscle fibers to regenerate and repair the damaged fibers
- Cardiac muscle
  - When cardiac muscle cells die, they are not replaced
- Smooth muscle
  - Smooth cells have the greatest capacity to regenerate by dividing and increasing in number.

Recovery and Rebuilding

- Successful recovery and rebuilding depends on
  - Adequate rest
  - Sufficient nutrients
  - Good blood flow
  - Lymph drainage from the region
  - Healthy hormonal and immune systems
  - Healthy nerve function
  - Balanced sympathetic/parasympathetic nervous systems

Muscle Healing Nutrients

- Cytozyme-H – heart glandular for healing heart and skeletal muscles. Prime supplement for any muscular tissue damage.
- Gammanol Forte with FRAC – Promotes growth and repair through IGF
- Bio-Anabolic Pack – Broad-spectrum formula for lean body mass, muscle, bone and cartilage healing
- CoQ-Zyme 100 Plus – supports energy metabolism

Muscle Healing Nutrients

- Bio-3B-G – B vitamins for Krebs cycle support, energy metabolism, and reduction of lactic acid buildup
- Amino Sport – Ensures sufficient amino acids for anabolic and energy metabolism, stimulation of endogenous growth hormone, and tissue repair
- Whey Protein Isolate – High-quality protein powder for muscle health, energy production, and promotion of growth and repair

Muscle Metabolism: Energy

- Muscular activity accounts for much of the body's energy consumption.
- ATP is used for:
  - Contractile process
  - Restoration of intracellular Ca levels
  - Maintenance of ion gradients
- Muscles keep a reserve of carbohydrate in the form of glycogen, which is ready fuel for both aerobic and anaerobic metabolism.
- Decreased ATP availability or inhibition of any associated enzyme will cause a decrease in muscle force production.

ATP

- The amount of ATP in skeletal muscle is only sufficient for a few seconds, so ATP must be constantly renewed
- Energy systems for muscle contraction:
  - Creatine phosphate shuttle
  - Anaerobic glycolysis (using blood glucose or muscle glycogen)
  - Aerobic metabolism via oxidative phosphorylation
  - A reaction catalyzed by adenylate kinase

Metabolism – 3 ways to produce ATP

1. Muscles conserve energy in the form of creatine phosphate (phosphocreatine)
   - Creatine is made from arginine and glycine

2. In Anaerobic Metabolism, glucose is metabolized through glycolysis producing 2 ATP molecules and 2 lactic acid molecules.

3. In Aerobic Metabolism, pyruvate formed from glycolysis is carried into mitochondria with the help of thiamin to be metabolized through the Kreb's Cycle

Creatinine

- Creatine phosphate is unstable and spontaneously cycles to form **creatinine**, which is excreted in the urine
- The spontaneous production of creatinine occurs at a constant rate and is proportional to body muscle mass
- The amount of creatinine excreted each day is constant and can be used as an indicator of the excretory function of the kidneys

Muscle at rest

$$\text{ATP from metabolism} + \text{creatine} \xrightarrow[\text{kinase}]{\text{creatine}} \text{ADP} + \text{phosphocreatine}$$

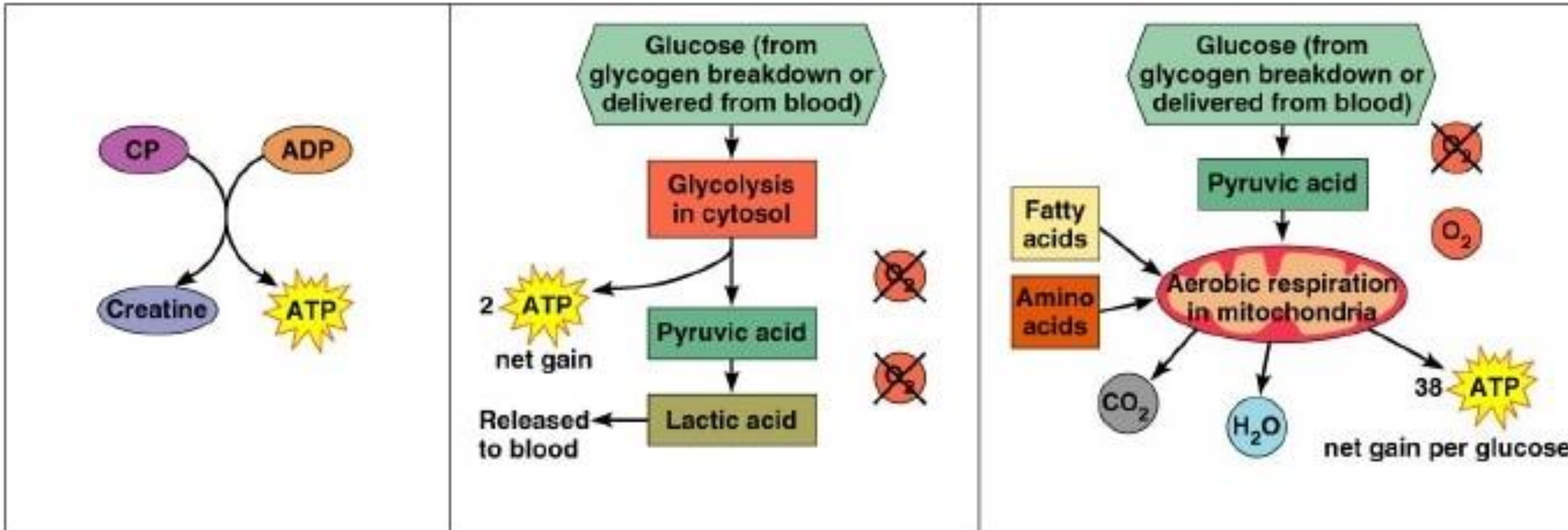
Working muscle

$$\text{Phosphocreatine} + \text{ADP} \xrightarrow[\text{kinase}]{\text{creatine}} \text{Creatine} + \text{ATP}$$

needed for

- Myosin ATPase (contraction)
- Ca^{2+}-ATPase (relaxation)
- Na^{+}-K^{+} ATPase (restores ions that cross cell membrane during action potential to their original compartments)

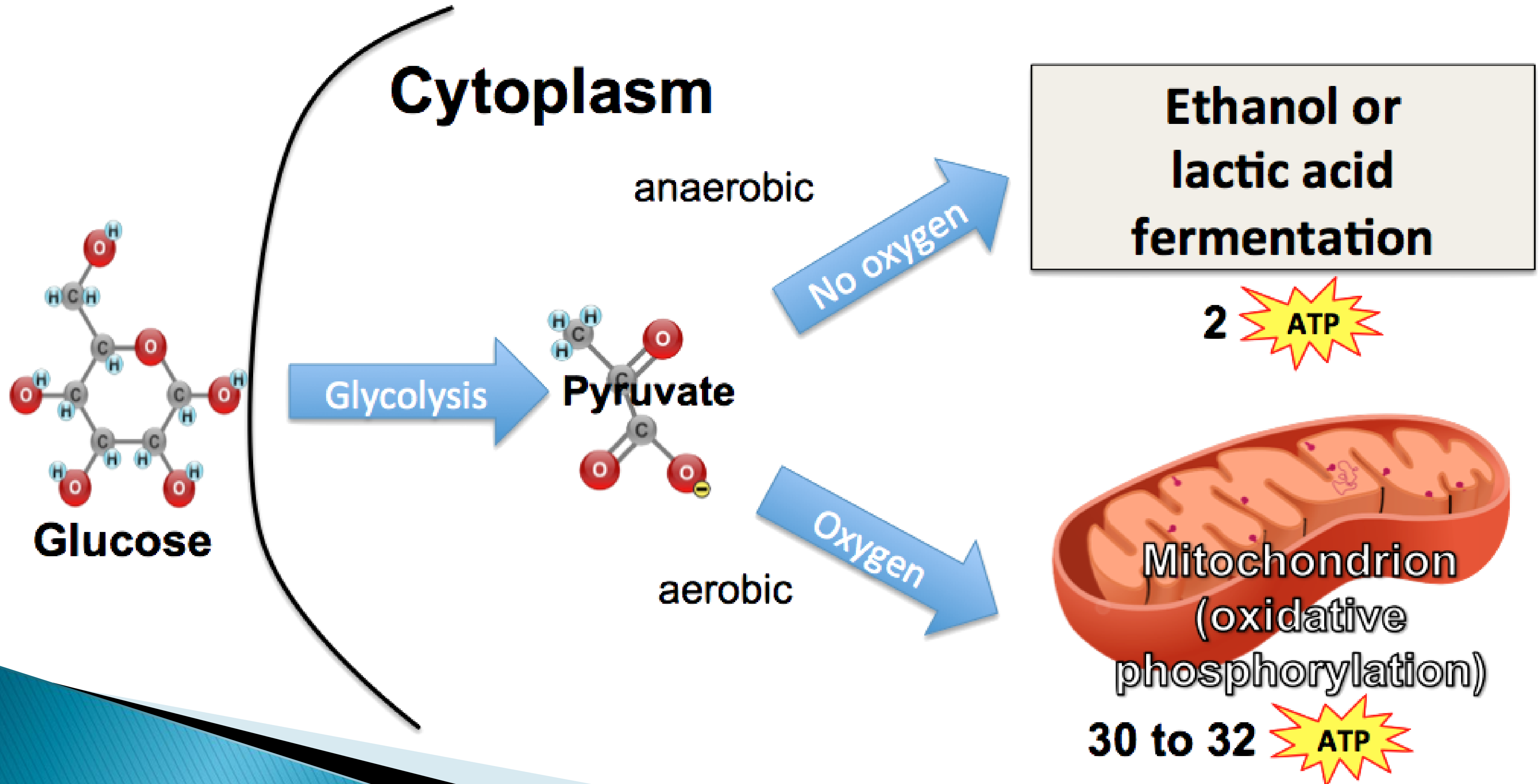
Muscle Metabolism: Energy for Contraction



(a) Direct phosphorylation [coupled reaction of creatine phosphate (CP) and ADP]	**(b) Anaerobic mechanism (glycolysis and lactic acid formation)**	**(c) Aerobic mechanism (aerobic cellular respiration)**
Energy source: CP	Energy source: glucose	Energy source: glucose; pyruvic acid; free fatty acids from adipose tissue; amino acids from protein catabolism
Oxygen use: None Products: 1 ATP per CP, creatine Duration of energy provision: 15 s.	Oxygen use: None Products: 2 ATP per glucose, lactic acid Duration of energy provision: 30–60 s.	Oxygen use: Required Products: 38 ATP per glucose, CO_2, H_2O Duration of energy provision: Hours

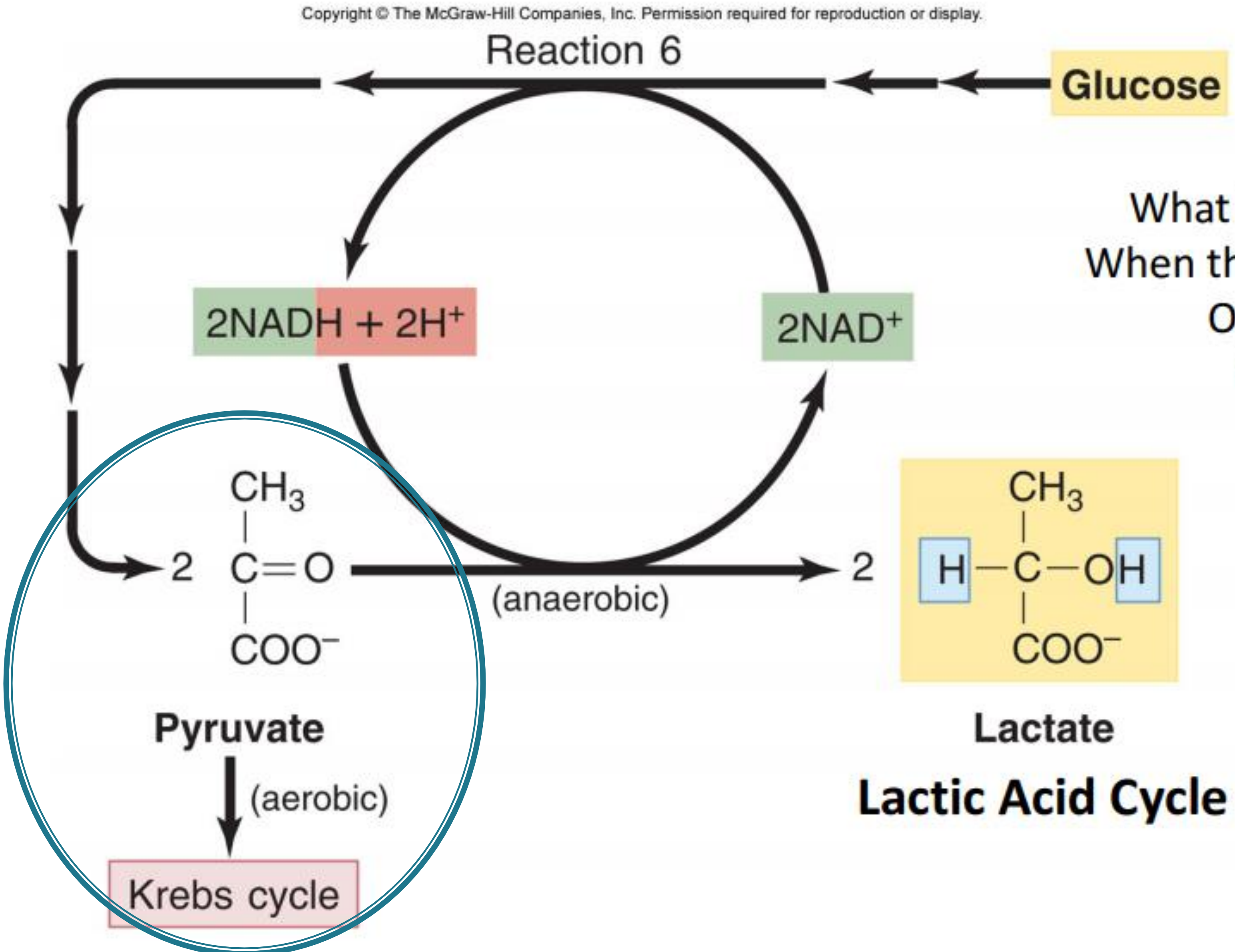
Metabolism: Aerobic / Anaerobic

- Carbohydrates or sugars are processed through glycolysis into the 3 carbon pyruvate



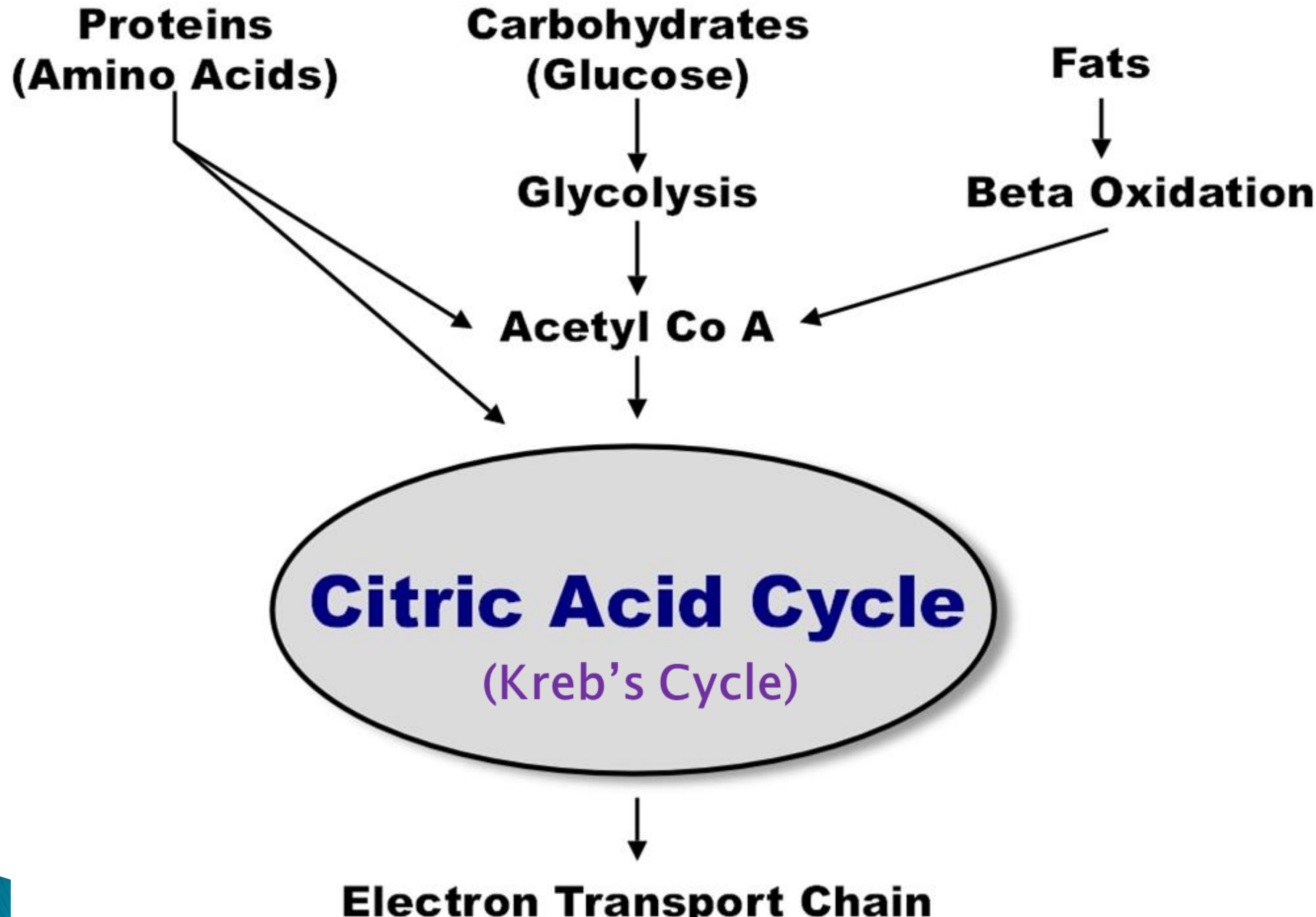
Fate of Pyruvate

Aerobic - Anaerobic



What Happens When the Cell Runs Out of O_2?

Lactic Acid Cycle


Proteins
(Amino Acids)
Carbohydrates
(Glucose)
Fats
Glycolysis
Beta Oxidation
Acetyl Co A
Citric Acid Cycle
(Kreb's Cycle)
Electron Transport Chain

- In Aerobic respiration pyruvate is delivered into the CAC cycle, after a carbon is removed to form acetyl-Co-A.
- Acetyl-Co-A is made from pantothenic acid (B5)
- Energy is liberated during the CAC cycle by the transfer of a hydrogen ion to the carrier molecules:
  - NAD (**nicotinamide** adenine dinucleotide **B3,**) and
  - FAD (**Flavin** adenine dinucleotide, **B2**)
  - Which then become NADH+ and FADH+
- These co-enzymes are then utilized by **the inner membrane of the mitochondria,** the electron transport chain, where the H+ is used to “push” a phosphate on to the ADP (adenosine diphosphate) molecule producing a high energy ATP or adenosine triphosphate

Aerobic and Anaerobic Respiration

Summary of Cellular Respiration (Aerobic Respiration)

Process	What Happens?	What's Made?
Glycolysis	glucose breaks down into pyruvic acid	2 ATP 2 NADH
Krebs Cycle	pyruvic acid is broken down into carbon dioxide	2 ATP 8 NADH 2 $FADH_2$
Electron Transport Chain	ATP is formed from the transport of high-energy electrons	34 ATP

All these transfers of energy from the Citric Acid Cycle (CAC) and Electron Transfer Chain (ETC) occur in the inner membrane of the mitochondrion…

- Mitochondrial Mitophagy –Targeted destruction of dysfunctional mitochondria … think of it apoptosis or “Only the strong survive”
- Insufficient mitochondrial Mitophagy promotes oxidative and inflammatory injury
- Excess Mitophagy leads to insufficient production of ATP and causes cell death and resultant tissue/ organism failure

26 ways to enhance Mitochondrial Function

Functional Inflammology, Alex Vasquez DC, ND,DO., ICHNFM.Org p. 485-500

1. Carbohydrate restriction/ Avoidance, fasting, ketogenic diet:

2. Exercise

3. Five -part supplemented Paleo-Mediterranean Diet: plant based protein adequate organic diet supplements with Vitamins, Minerals, Fatty Acids, and Probiotics (see below)

4. Coenzyme -Q10: (CoQ100 plus 1-2 per day)

5. Vitamin E: as in mixed tocopherols with gamma-tocopherol (High Gamma E 400 -1600 i.u.)

6. Lipoic acid: 100-400 mg tid-qid

7. L-Carnitine and Acetyl L-Carnitine :(2-4 grams per day)

8. Biotin: 2-10 grams per day

9. Magnesium: 600 mg/day or bowel tolerance (Mg-zyme h.s)

10. Medium Chain Triglycerides: (MCT's 1-2 tbsps. Diarrhea is sign of too much)

11. Resveratrol: 250 mg/d or more (ReveraSirt-HP)

12. DHA (docosahexaenoic acid) from fish oil or blue green algae 500-2000 mg or more (Optimal EFA's or EFA Sirt Supreme)

13. Optimization of iron status: Avoiding Iron deficiency while also avoiding iron overload.

14. N-Acetyl-Cysteine: (NAC) 600 mg bid up to 1500 mg tid
15. General Antioxidant support: ProMultiplus or VasculoSirt 2-3 tid
16. General Anti-Inflammatory Support : Vitamin D, low carb diets, multivitamin mineral support are examples
17. High salicylate diet and or low dose aspirin to provide salicylate for ionophore alleviation of mitochondrial hyperpolarization- hypothesis
18. Alkalinization acid-base balance , pH: retention of minerals K, Ca, Mg, increases intracellular uptake of Mg, increased excretion of toxins and xenobiotics, < serum cortisol, > bone health markers > endorphins

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19. Melatonin support, including sleep, 5HTP, dietary tryptophan such as whey protein isolate

20. Phospholipid replacement therapy: Phosphatidyl Choline or Phosphatidyl Serine

21. Oxygen, deep breathing, exercise, hyperbaric oxygen

22. Ginko Biloba

23. Detoxification, avoidance of toxins (xenobiotics) that impair mitochondrial function… round up… etc.

24. Eradication of gastrointestinal dysbiosis and small intestinal bacterial overgrowth:

Dysbiotic bacteria in the intestines impair systemic mitochondrial function via gut-to- system absorption of D-lactic acid, hydrogen sulfite, and endotoxins/Lipopolysaccarides (LPS)

Chronic Fatigue, Fibromyalgia, migraine headaches are a few of the examples of clinical success by addressing the above.

25. Eradication/Suppression of any persistent “internal” infection

26. Avoidance of dietary sulfite, eradication of H2S – producing dysbiosis and or chelation /detoxification of sulfite and H2S with hydroxocobalamin (B12 2000 Lozenges)

Fat combustion

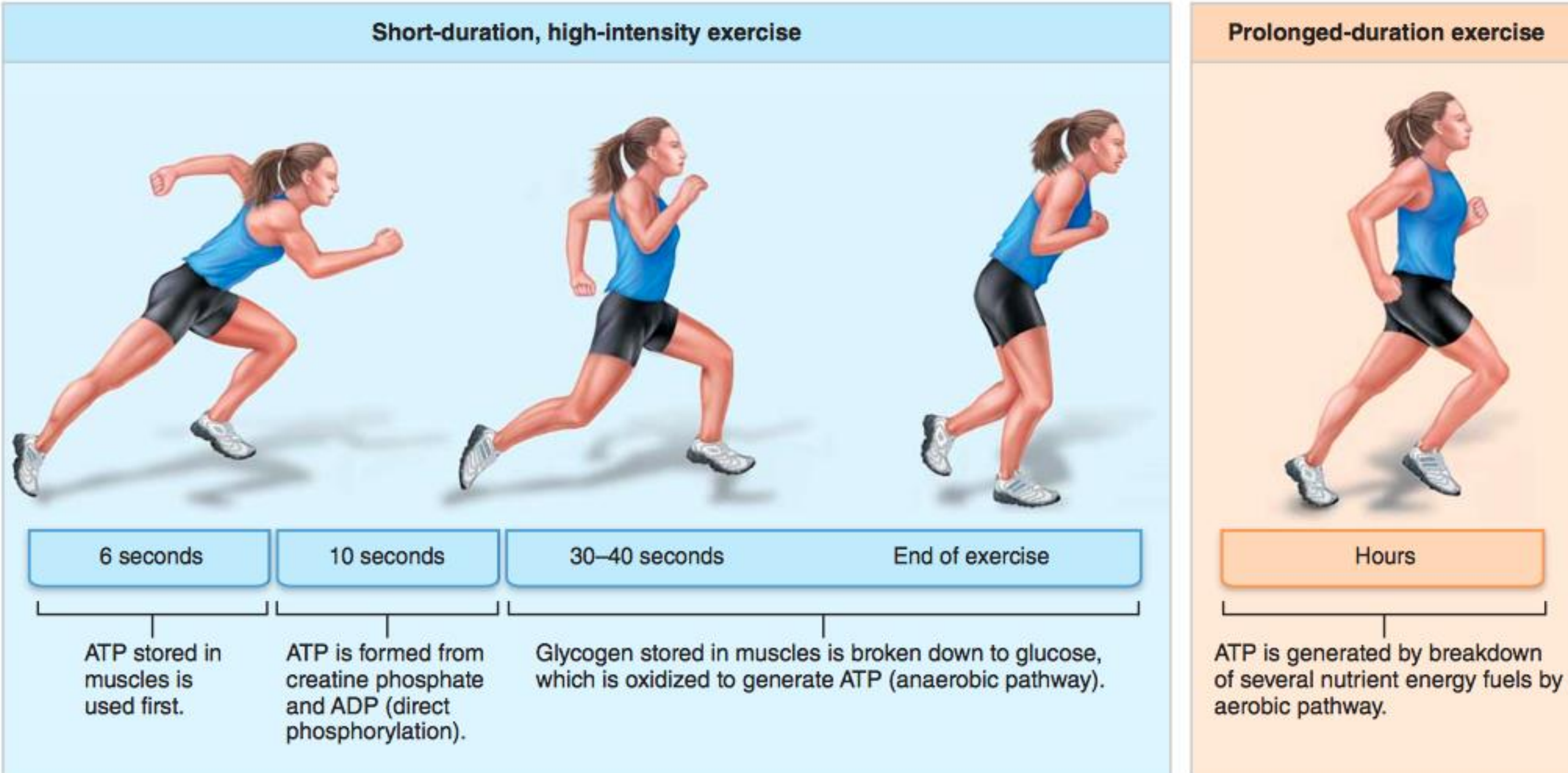
- Muscle cells also contain storage fat, which can be used during aerobic metabolism. It takes longer to engage this process –at about 20 minutes of sustained exercise, but it produces significantly more energy
- When fat begins to burn, there is a surge of endorphins released.
- On the other hand, “hitting the wall” occurs when enzyme systems are depleted and cannot extract energy from fuels. At this point one must stop or risk serious complications.

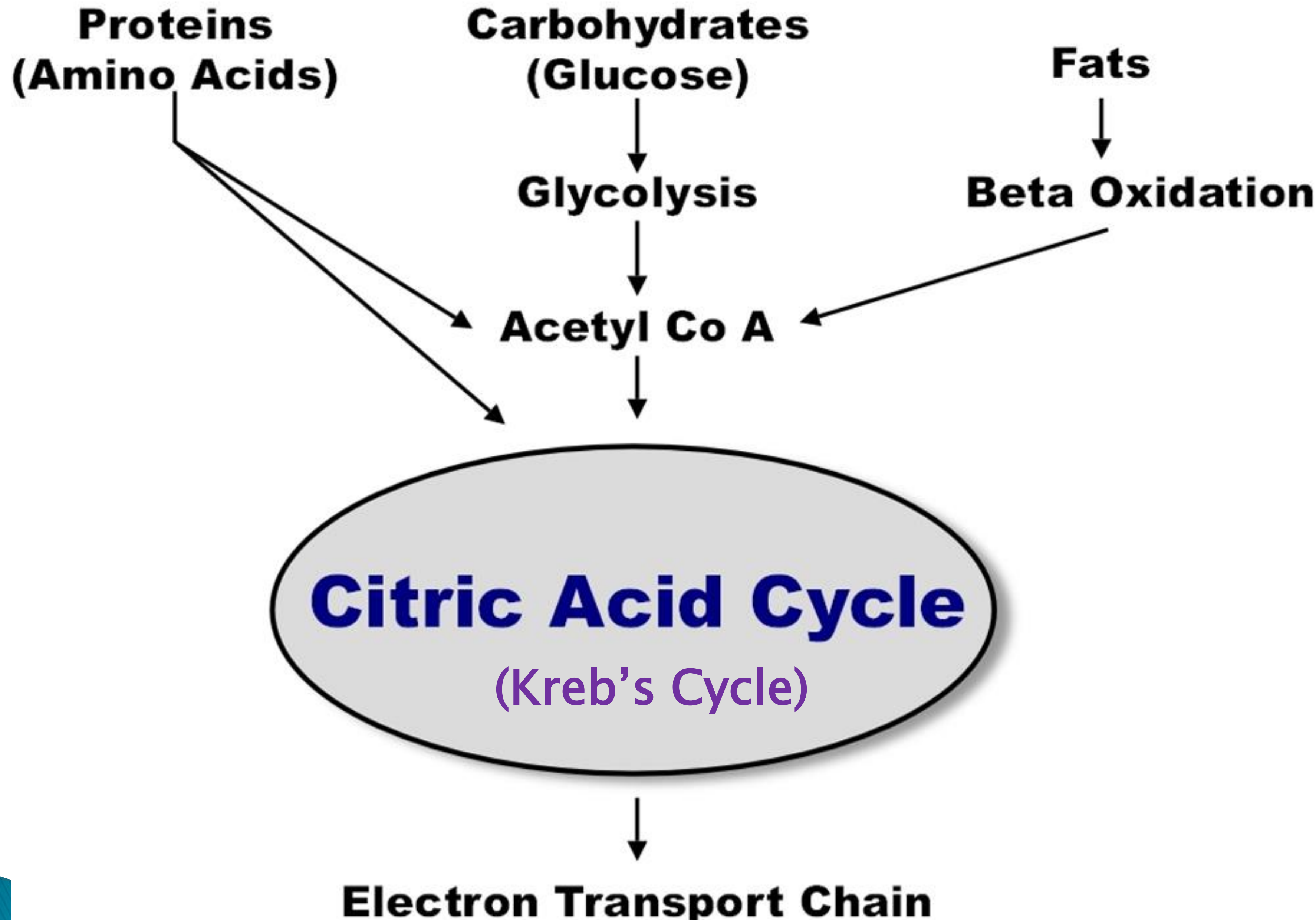
Fats

- Fats are broken down into acetyl –CoA through a process called beta oxidation.
- Assure proper fat digestion is taking place.. Fat is a major source of energy and needed for enzymes, antibodies, hormones and cell membrane transport..
- Dr. Goodheart taught:
  # 1 deficiency Water
  # 2 deficiency   EFA's

Nutrients to support energy from fats

- L-Carnitine
  - Vegans/Vegetarians benefit from l-carnitine
  - Heavy meat eaters who take l-carnitine have increased inflammation
- B2 (Riboflavin)
  - Bio-GGG-B – portion of B vitamins particularly useful for supporting fat metabolism, skin and nerve health, and parasympathetic functioning
  - Bio-B Complex – higher doses of all B vitamins
  - Bio-B 100 – balanced profile of B vitamins, B&G cofactors
- B3 (Niacin)
- B5 (Pantothenic Acid)
- Coconut oil – SCFAs stimulate fat metabolism

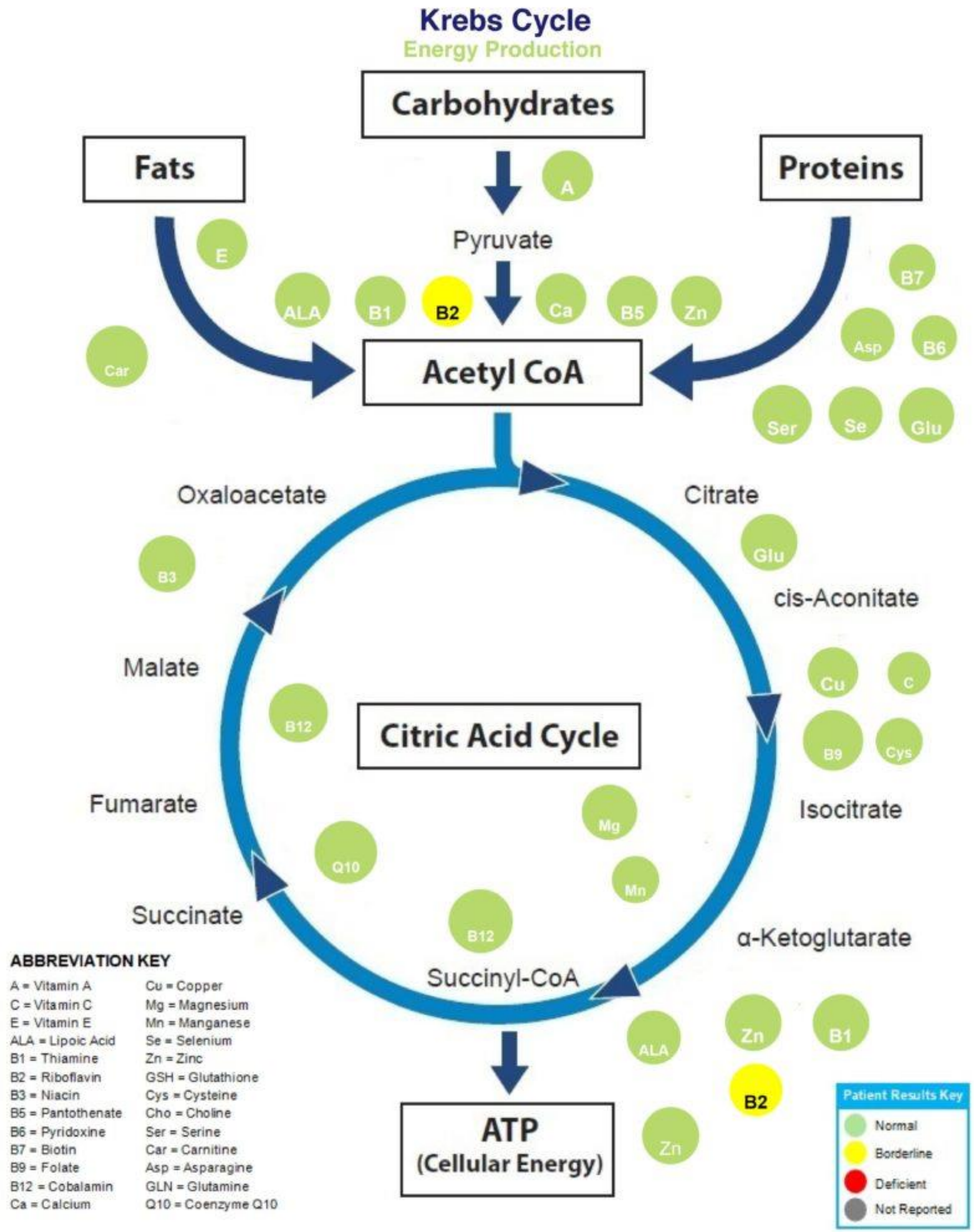

Short-duration, high-intensity exercise
Prolonged-duration exercise
6 seconds
10 seconds
30–40 seconds
End of exercise
Hours
ATP stored in muscles is used first.
ATP is formed from creatine phosphate and ADP (direct phosphorylation).
Glycogen stored in muscles is broken down to glucose, which is oxidized to generate ATP (anaerobic pathway).
ATP is generated by breakdown of several nutrient energy fuels by aerobic pathway.


Proteins
(Amino Acids)
Carbohydrates
(Glucose)
Fats
Glycolysis
Beta Oxidation
Acetyl Co A
Citric Acid Cycle
(Kreb's Cycle)
Electron Transport Chain

Energy Metabolism

- Proteins are broken into Amino Acids and utilized at various points in the Citric Acid or Krebs Cycle

- Assure adequate protein digestion is taking place, i.e. HCL


Krebs Cycle
Energy Production
Carbohydrates
Fats
Proteins
A
Pyruvate
E
ALA
B1
B2
Ca
B5
Zn
B7
Asp
B6
Car
Acetyl CoA
Ser
Se
Glu
Oxaloacetate
Citrate
Glu
B3
cis-Aconitate
Malate
Cu
C
B12
Citric Acid Cycle
B9
Cys
Fumarate
Mg
Isocitrate
Q10
Mn
Succinate
B12
α-Ketoglutarate
Succinyl-CoA
ALA
Zn
B1
B2
ATP
(Cellular Energy)
Zn
ABBREVIATION KEY
A = Vitamin A
C = Vitamin C
E = Vitamin E
ALA = Lipoic Acid
B1 = Thiamine
B2 = Riboflavin
B3 = Niacin
B5 = Pantothenate
B6 = Pyridoxine
B7 = Biotin
B9 = Folate
B12 = Cobalamin
Ca = Calcium
Cu = Copper
Mg = Magnesium
Mn = Manganese
Se = Selenium
Zn = Zinc
GSH = Glutathione
Cys = Cysteine
Cho = Choline
Ser = Serine
Car = Carnitine
Asp = Asparagine
GLN = Glutamine
Q10 = Coenzyme Q10
Patient Results Key
Normal
Borderline
Deficient
Not Reported

Citric Acid Cycle Nutrients

B vitamins are crucial for entry of pyruvate into the Krebs Cycle

- B1 “B” (Thiamine) – Bio-3BG
- B2 “G”(Riboflavin) – Bio-GGG-B
- B3 (Niacinamide) – Niacin 100
- Pantothenic acid – Bio B Compex, Bio-B100
- B6 (Pyridoxine) – B6 phosphate, Bio-GGG-B
- Manganese – Mn-zyme
- Lipoic Acid
- Biotin
- Magnesium – Mg-Zyme or Mg-Orotate 500
- Phosphorus – Super Phosphozyme

Electron Transport Chain Nutrients

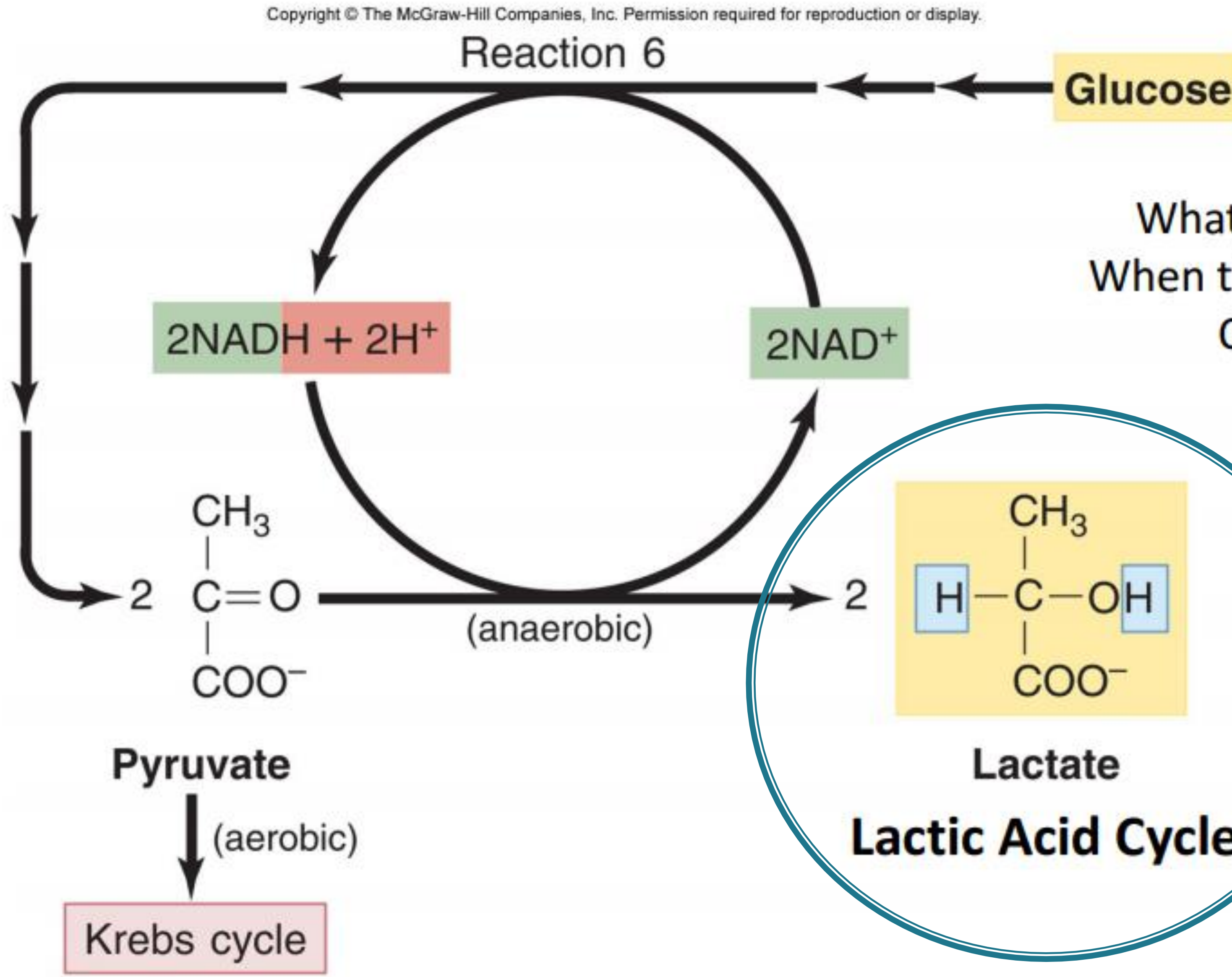
- Coenzyme Q10 (CoQ-Zyme 100 plus)
  - Key enzyme in oxidative reactions in mitochondrial membranes which generate ATP
  - Declines with age and with oxidative damage
- Iron (Fe-Zyme)
  - Critical mineral metabolite and oxidizer for energy metabolism
- Copper
- Phosphorus (Super Phosphozyme)
  - key constituent of the ATP molecule

Energy Metabolism: The Big Picture

- Numerous enzymes, vitamins, minerals and their cofactors are involved in the energy extraction process.
- ATP is the energy currency of the body, created in the mitochondria and utilized throughout the body enzymatically wherever energy is required.
- When we give a high quality Bio-Available multiple vitamin mineral (ProMultiPlus or VasculoSirt), use fatty acid therapy (Optimal EFA's), heal the gut (BioDoph 7 plus), take Vitamin D to quench genetic inflammation, we are building our patients' infrastructure, in a sense pruning the energy factories (mitochondria) in our cells.
- These are not casual recommendations!!!!!

Fate of Pyruvate

Aerobic - Anaerobic



What Happens When the Cell Runs Out of O_2?

Lactic Acid Cycle

Lactic Acid Pathway in Humans

- Some tissues better adapt to anaerobic conditions
- RBCs do not contain mitochondria and only use the lactic acid pathway
- When ratio of oxygen supply to oxygen need falls below critical level, muscles can metabolize glucose anaerobically through glycolysis, in which only 2 ATP molecules and 2 lactic acid molecules are produced

Lactic Acid pathway cont.

- *Oxygen debt*: The amount of energy required to return blood glucose levels back to normal and to replace glycogen reserves in muscle and liver
  - Skeletal muscle
    - Normal daily occurrence
    - Does not harm muscle tissue
  - Cardiac Muscle
    - Cardiac muscle normally respires aerobically
    - Myocardial ischemia (restriction of blood supply) occurs under anaerobic conditions

- Lactate buildup causes pH to fall and pain & muscle fatigue
- When activity returns to normal and oxygen becomes available, lactate is converted back to pyruvate to enter the Krebs Cycle

HOPE MOLECULES

- **Skeletal muscle as an endocrine organ: PGC-1α, myokines and exercise**
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4657151/
- Myokines are power-packed molecules that are released by your muscles when you follow a protocol. They act like micro-messengers, sending signals to other parts of your body to directly assist them to become stronger and healthier.
- Myokines are often called "Hope Molecule™" because they offer so many benefits for human health and muscle development. By putting your body through physical related protocols, you can help your body produce more myokines, which can help you feel better and get stronger over time.

HOPE MOLECULES

- Muscles work hard and need extra nutrients and oxygen to keep going. Myokines help deliver these nutrients and oxygen to your muscles, which help them grow and get stronger.

- Myokines also perform other important functions. They help reduce inflammation.

Muscle–bone crosstalk by organokines – the new “hope molecules”

- Organ crosstalk, the unique and sophisticated method of cell-cell and organ-to-organ communication, is essential for maintaining multiple physiologic functions and regulating metabolic pathways. It is now recognized that, apart from receiving endocrine signals through growth hormones, growth factors, and the like, muscles, bone, and other tissues can secrete biochemical signals by their cells facilitating the metabolism of its tissues and the whole body.
- These molecules are known as “organokines” in general and depending on their tissue of origin, they are named adipokines, hepatokines, batokines, osteokines, and myokines. Research data reveals that the organokines are essential for maintaining whole-body metabolism through autocrine, paracrine, and endocrine pathways and can be used as valuable biomarkers for monitoring various organs’ physiologic and metabolic responses to mechanical loading.
- https://www.jwfo.org/article/S2212-4438(22)00013-3/abstract