Physiology #4

مجموعة التفريغ السريع

MSS

Subject: *Types of Muscle fibers*

Done by: *See last page*

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Date: *Thursday, September 26, 2013*

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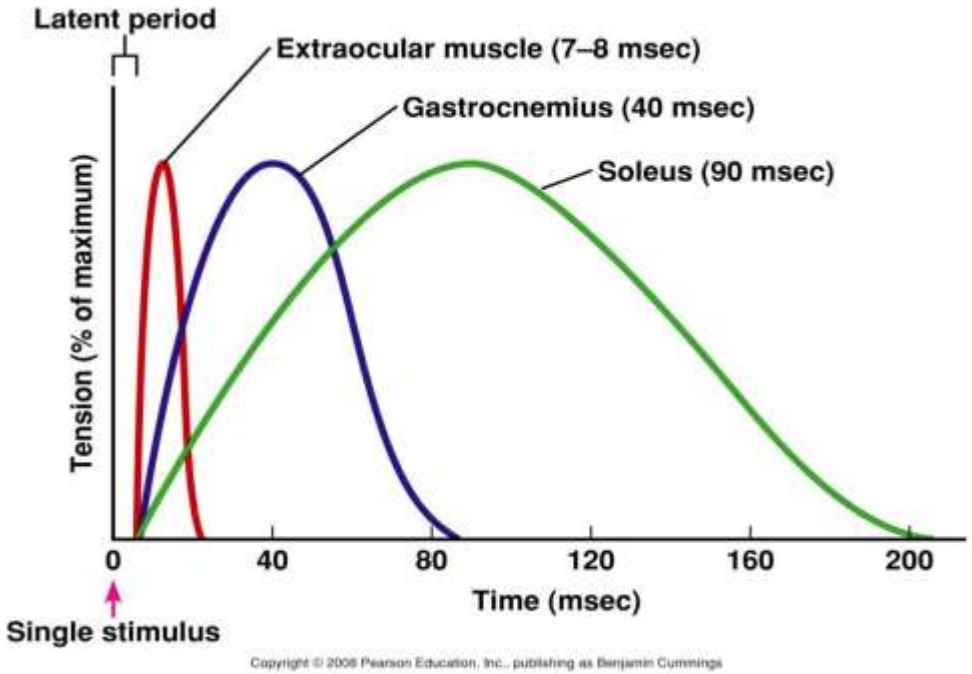
We talk about the mechanism of skeletal muscle contraction and the molecular characteristic of skeletal muscle contraction. Today we will talk about the **fiber types and muscle energetics**. The same setup that we show you the last time, which we use it to record the muscle twitch or muscle contraction, if we take different muscles, we get different twitches.



Here three different muscles with three different shapes of twitches:

They are all the same active force; they differ in their velocity of shortening

I. Extraocular muscle : it is short twitch, has short duration, "high velocity".
II. Gastrocnemius: it is intermediate, has intermediate duration with "intermediate velocity".
III. Soleus: it is longer, has long duration and "low velocity".

The difference is in the time and so the velocity of contraction, ability to contract "their rate in contraction ".

* Rate of shortening in a muscle fiber (sarcomere) depends directly on the turnover rate of the cross-bridges" the rate by which those bridges are formed".

- Each cross-bridge cycle slides the thin filament about 10 nm past the thick filament.
- Rapid cross-bridge cycling means that the thin filament slides the thick filament more quickly.
- Thus, the velocity of shortening the muscle (each single sarcomere), depends on the turnover rate of the cross-bridges.

*The turnover rate of the cross-bridges depends on the ATPase activity of myosin, which depends on the myosin isoforms. (The higher the ATPase activity the faster the turnover rate we get, the faster the velocity of contraction).

* We have different ATPase activity because we have different myosin isoform that result from having different genetics make up that we cannot change it!

- ❖ Myosin isoforms are encoded by separate genes, in the adult there are two basic varieties:

- Slow myosin (slow ATPase activity) – slow fibers.

- Fast myosin (fast ATPase activity) - fast fibers.

- ❖ Myosin isoforms stain differently in histological sections.
- ❖ Myosin staining is one basis for fiber classification.

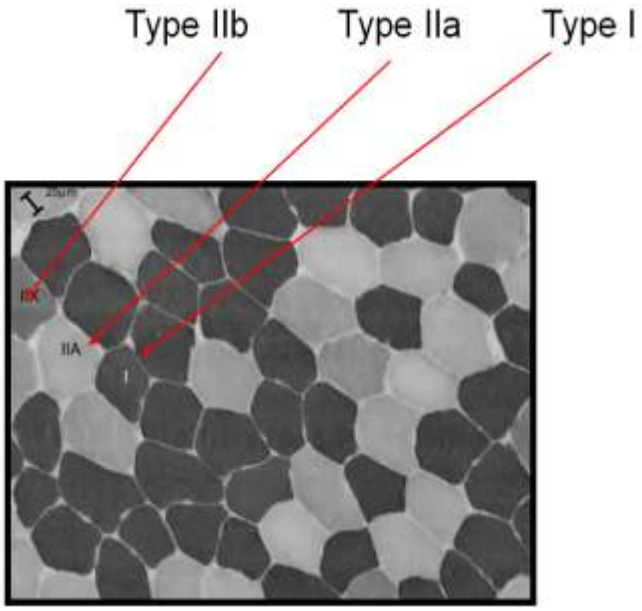
Fiber classification:

I. Brook classification of muscle fiber:

- Type I (Slow fibers) appear dark.
- Type II (Fast fibers) appear light.

*Fiber types characterized using ATPase histochemistry.

** Note: single muscle contains all isoforms with different ratios.



II. Muscles can be classified based on their metabolic properties (Peter and coworker):

1. Slow oxidative (SO) fiber: can sustain longer duration exercise with moderate intensity.
2. Fast glycolytic (FG): can sustain high intensity for short duration like lifting loud for two to 3 times at most.
3. Fast oxidative-glycolytic (FOG): can sustain longer duration to some extent high intensity exercise.

These types in this classification does not 100% correlate with the last classification, its different criteria for classification.

We sub classify type II to a and b to differentiate between the two subtypes of myosin .
**typeII A stains light .*
***type II B stains intermediate .*

In general:

*Red fibers, which "used for longer duration and moderate intensity like running a marathon" contains:

-A lot of mitochondria

-A lot of myoglobin

-Have large oxidative capacity

-They are slower and fatigue resistant

III.Burke classified muscle fiber based of their mechanical properties into:

1. Slow (S)
2. Fast fatigue resistant (FR)
3. Fast intermediate (FI)
4. Fast fatigable (FF)

*Whole muscles in the body are mixtures of muscle fiber types, determined by our genes “the rate

Ion “

**Single muscle can be predominantly one type or another.

For example, Extraocular muscle predominantly is fast twitch fiber, Gastrocnemius is fast oxidative glycolytic fiber, and Soleus is slow muscle fiber.

*** Depending on the function of the muscle:

1. Extra ocular muscle needs rapid action to fix the eye on specific object.
2. Gastrocnemius: needs fast and sustain action like running and jumping.
3. Soleus: needs longer duration like maintaining the body against the gravity.

-The ratio of a given muscle fiber types in a specific muscle vary between individuals also determined by our genetics.

Muscle fiber types differ also in the isoforms of many different proteins for example:

We have many cofactors protein, many contractile proteins of which differ from one muscle fiber to another.

For example, Fast twitch fiber contains SERCA1a “isoform of calcium pump that return calcium to the endoplasmic reticulum storages” & TnC2 “troponin C isoform “while slow twitch fiber contains SERCA2a & TnC1 so they have different kinetics.

Like the turnover rate, or the rate by which the calcium bind to troponin C slower than the b ending in the fast fibers.

Muscle fiber types also differ in the relative amount of organelles:

1. Mitochondria
2. SR volume
3. SR calcium pump

Higher in the fast twitch fibers

4. Myoglobin

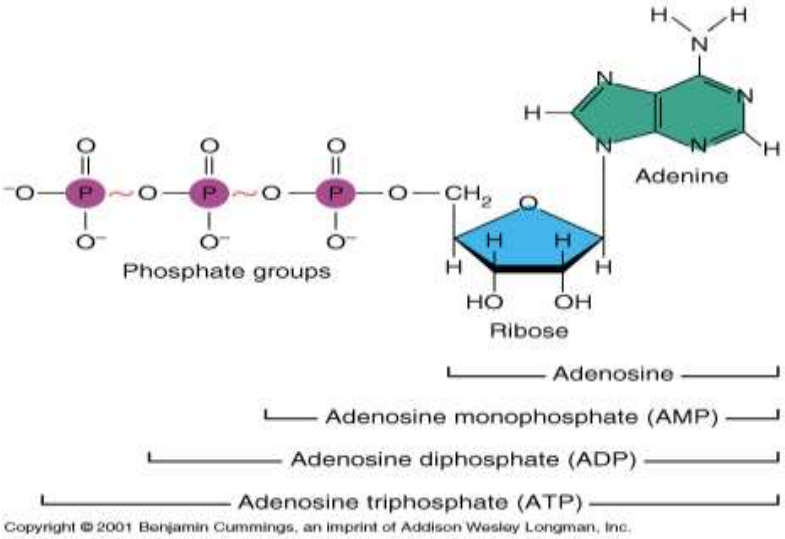
Muscle fibers also differ in the relative amount of organelles

1- Mitochondria and myoglobin : are higher in red muscle fibers
2- SR volume and SR calcium pump : are higher in the fast twitch muscle fibers

The source of energy that makes the mechanical work in muscle contraction (the cross-bridges formation) is the hydrolysis of ATP

The structure of ATP:

1- The adenosine moiety.
2- the ribose
3- Three phosphate groups (alpha, Bata, gamma). The breakdown of these bonds releases high amount of energy, about 57KJ per one bond of phosphate.



$$ATP \xrightarrow{H_2O} ADP + P_i + Energy$$

ATP is also needed for other reactions in the muscle fiber:

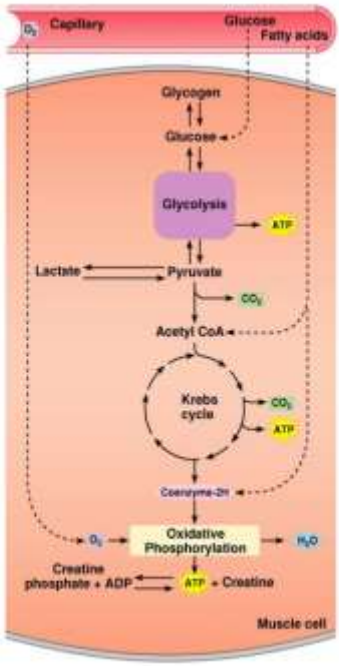
1- Calcium reuptake into the SR
2- Sodium-Potassium ATPase to maintain the ionic composition of the two sides of the cell membrane : to maintain the plasma membrane potential
3- Other functions of the cell such as protein expression

Note that during heavy activity, cross-bridges formation is the main drain on ATP stores in muscle cell, and the ATPase activity of the myosin head is the main cause for the depletion of ATP in the myoplasm.

Rate and amount of ATP consumption varies with the intensity and duration of the exercise, as you can expect in moderate exercise ATP consumption rate will be lower, and during high intensity, exercise the rate and amount of ATP will be higher.

You have to know that during any time there is fast consumption of ATP, but what is the difference between high and low intensity exercise.

In long duration exercise with moderate intensity, we have a long rest period to regenerate ATP in the myoplasm, but during intense exercise for longer duration, there is no rest period, so there will be depletion of ATP (energy source).

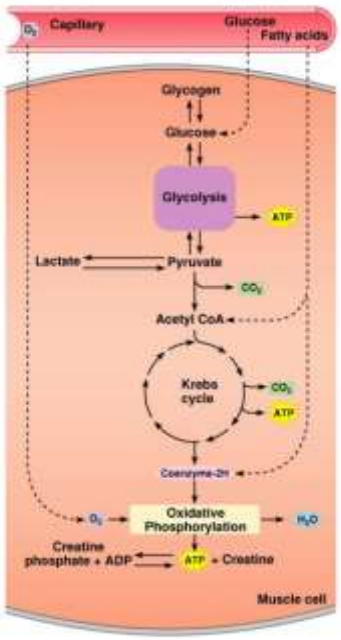


The sources for ATP regeneration:

1- Cytoplasmic ATP (5 mm) can support full contraction for about 1-2 second at most.
2- Creatine phosphate(CP) regenerates ATP fastest to its normal cytoplasmic concentration , this source of energy supports maximal muscle contraction for another 5 to 8 seconds

CP + ADP = ATP + Creatine

All kinds of exercises use the rest ATP in the cytoplasm and depends on creatine phosphate
3- Glycolysis (glucose metabolism) rapid but low capacity supply of ATP for fast twitch fibers



1 glucose …. 2 ATP

- For sure, it will use creatine phosphate but the main source of ATP during intense exercise is glycolysis.
- Glycolysis is an anaerobic metabolism

4- 4. Oxidative phosphorylation: slower but high capacity source of ATP: Electron transport chain
One glucose…30 ATP

- Oxygen is the last electron receptor in oxidative phosphorylation, so it is an aerobic metabolism.
- This is the main energy source in long duration moderate intensity exercise

Fuel sources

1- Carbohydrates
2- Fat
3- Proteins

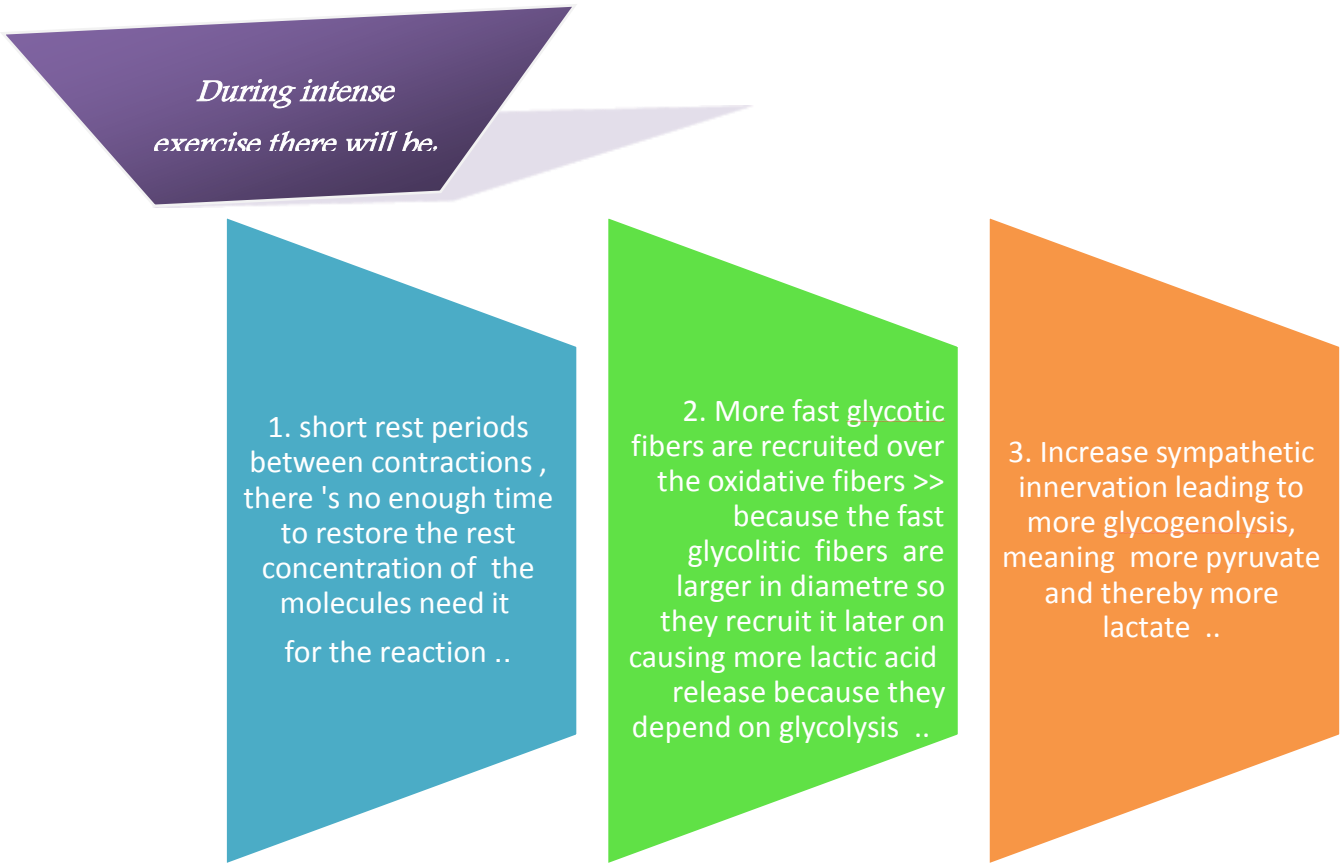
1- Carbohydrates

Stored as Glycogen which is mobilized by glycogenolysis; rapid muscle activity utilizes Glycogenolysis, resorted during rest.

Glycolysis the source of glucose from either glycogen or blood, **Glucose is converted into… ATP, pyruvate and NADH** (anaerobic metabolism) , **Mitochondria generates NAD+ in order for glycolysis to continue or Lactic dehydrogenase converts pyruvate into lactic acid and generates NAD+ during rapid bursts of glycolysis** , so during high intensity exercise miss-match between the ability of muscle cell mitochondria to regenerate NAD^+ and the utilization of glucose , this will lead to more production of lactate .

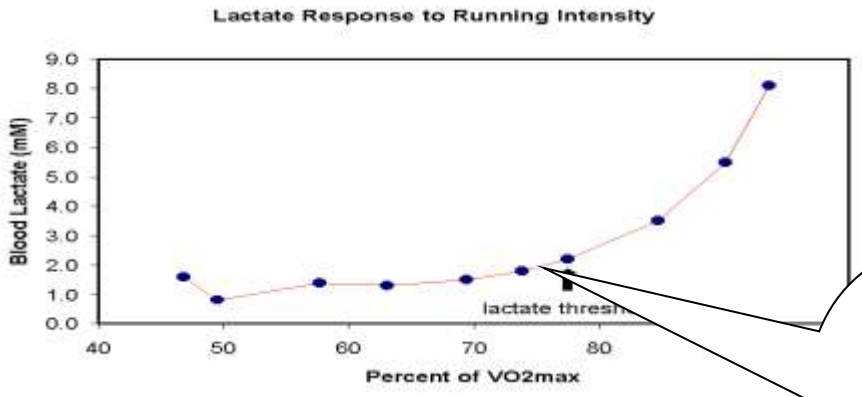
You may think that lactate is produced under anaerobic conditions, but it can take a place when the muscle is fully oxygenated because of high burst of exercise and the formation of NADH is very rapid and we need to replenish the cytoplasmic concentration of NAD^+, this will shift to formation of lactic acid by lactic dehydrogenase, this is called the lactate threshold.

Lactate threshold: Is the intensity of exercise at which the body will Accumulate lactic acid.



💣 Thus, During intense Exercise there is more lactic acid production in the muscle even if it is fully oxygenated >> bcz there is a mismatch between the ability of the muscle to produce *ATP* & the need for *ATP* & the ability for the muscle cell to buffer *lactic acid* which cause "Muscle fatigue" ☹☹☹☹

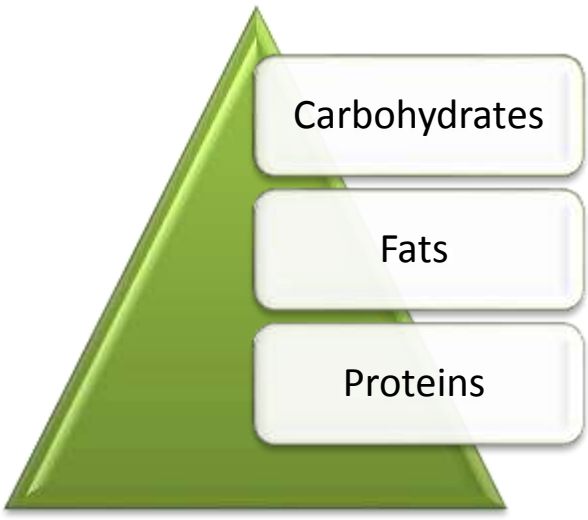
Lactic acid can be buffered in the mitochondria & through Cori cycle **" in which lactic acid go to the blood then to the liver to be converted into pyruvate and then to glucose " & in the same muscle fiber we have oxidative fibers and glycolytic fibers so it'll diffuse from the glycolytic to oxidative fibers and there will be oxidative there to pyruvate ,, so** During intense Exercise the lactic acid production **will exceeds its buffering and this will decrease the muscle pH >>which will affect the actomycin and this is the intensity of exercise > then at specific level there will be up rise to lactate in the blood …**



Lactate threshold:

The intensity of exercise at which lactate starts to accummlate in muscle or blood ..

Fuel sources:



☺ Fuel type vary with the type, intensity & duration of exercise...

☺ At rest, we mainly depend on three fatty acids from fats & if we do exercise, we take 50% fats + 50% glycolysis "Carbohydrates" bcz we need more ATP and glycolysis is the fast way & at intense exercise we depend only at glycolysis bcz fats "free fatty acids depend on oxidative phosphorylation & protein during starvation ...

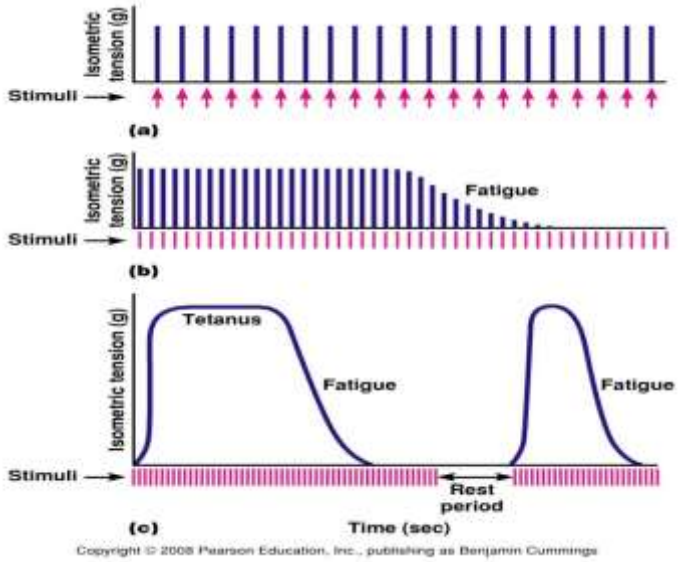
Muscle fatigue ^_^

Muscle fatigue is a reduction in developed force resulting from previous muscle activity :D

- maximal force that can be generated from resting muscle, any decrease of this maximal force is called fatigue. Maximal force can be sustained only very short time (only once)...

Metabolic fatigue is a reduction in submaximal force after prolonged repetitive stimulation :')

- usually exercise is done at submaximal force from many repetition, then we become tired and be unable to do this submaximal force ... "depletion of glycogen stores " > the cause of it ..



Fatigue in maximum sustained contraction is not in the brain in humans > which means that the fatigue in the muscle itself like an isolated muscle and you develop the maximal force then you stimulate it with an extracellular stimulator there will be no increase in force bcz it's not in the neuromuscular junction it's inside the muscle …

Pi and H+ in muscle interfere with force development by ***actomyosin ATPase***

- During fast twitch muscle use PC and glycolysis for ATP generation, PC accumulates Pi and Glycolysis accumulates lactic acid. The pH of and exercising muscle falls to pH 6.0 …

- Both Pi and pH reduce developed force at the level of cross-bridges formation, which is perceived as **fatigue**.

- Fatigue at submaximal force can be postponed by glycogen super compensations (***carbohydrate loading***) for ex.:
you can like make exercise for 4o minutes and then eat for 2 hours of high carbohydrates diet you used more glycogen in the muscle fiber and thereby you can postpone fatigue "you can sustain your exercise for longer time " & we can use this with athletes in preparing to marathon running by increasing glycogen store in their muscles ☺ …

Exercise increases glucose transporter (GLUT4) in the muscle sarcolemma, this is same transporter that insulin increase in sarcolemma to reduce the blood glucose. Therefore, if a diabetic patient starts to exercise he can cut back on his insulin. WHY? Because it is an additive effect, and if he exercise and take insulin, there may be a phase like hypoglycemic shock.

Blood glucose can be reduced by:

1) Exercise

2) Insulin.

Both of them can increase the number of glucose transporter, there are different isoforms of glucose transporter, like the one in muscle sarcolemma which is called (GLUT4), and this will reduce the blood glucose, so diabetic patient can decrease their blood glucose by exercising .

Resistant training which means "shortening your muscle against an after load" will hypertrophies the muscle means increase the muscle size (not number) .

*increasing the number called hyperplasia.

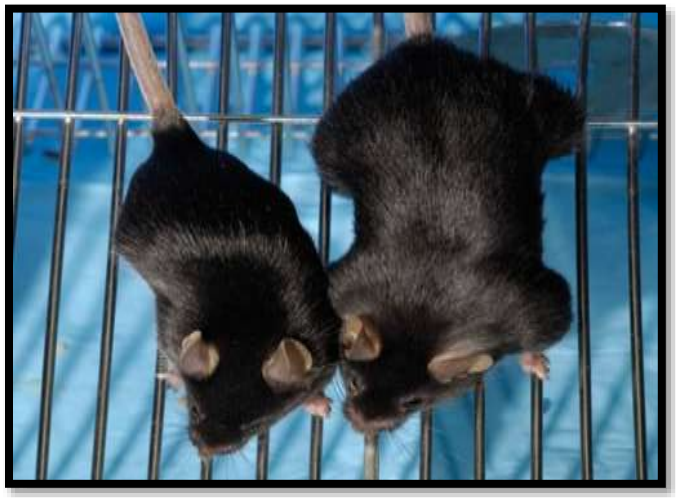
There are many signals for hypertrophy but you have to know these:

1) Increase in the size of the cell.
2) Increase in the number of the microfilaments
3) Increase in the contractile protein
4) Increase in the myoplasm
5) Increase in the sarcoplasmic reticulum
6) There might be SMALL increase in the number.

Hypertrophy takes place through recruitment of satellite cells, with specific signaling by induction of "satellite cells" which are the stem cells in muscle cells. Signals that control muscle mass can be:

1) Stretch… exercise is kind of stretch
2) Hypoxia
3) Androgen
4) Glucocorticoids
5) CA++
6) Protein called Myostatin, which is a negative regulator, which reduces all these signals that produce hypertrophy.

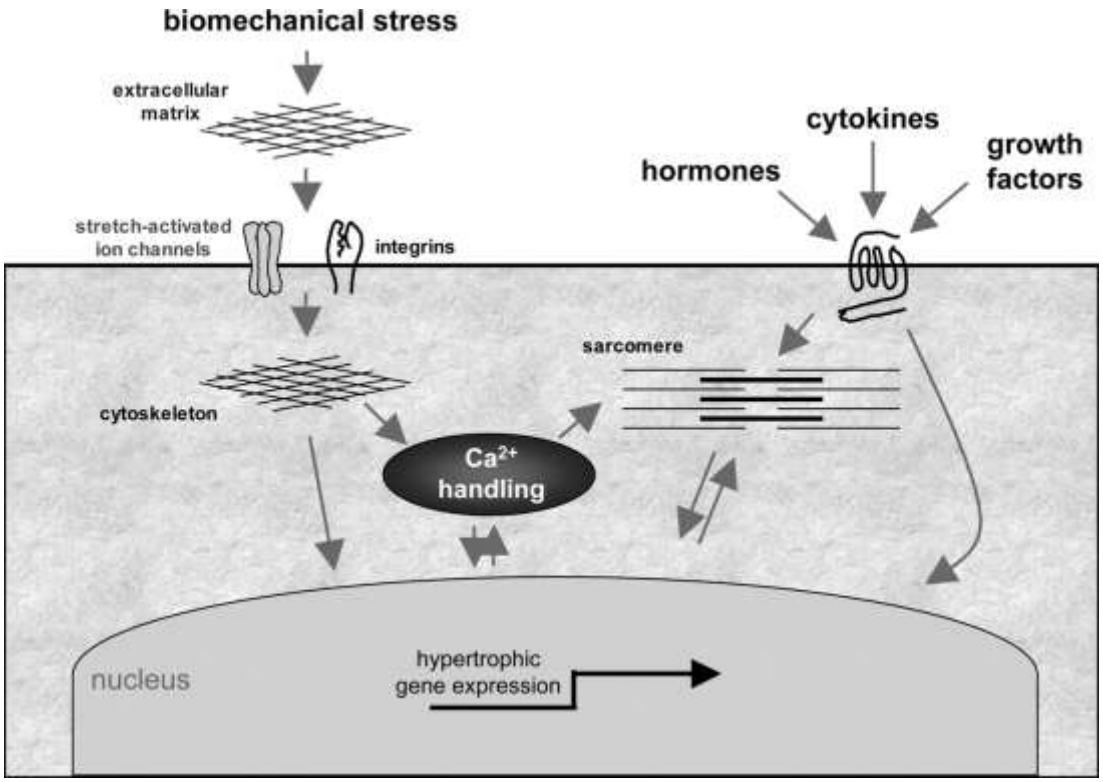
All these cause hypertrophy but Myostatin reduce the muscle mass. Therefore, if you knock out myostatin in a mouse or any animal you will produce hypertrophy in the animal's all muscles.



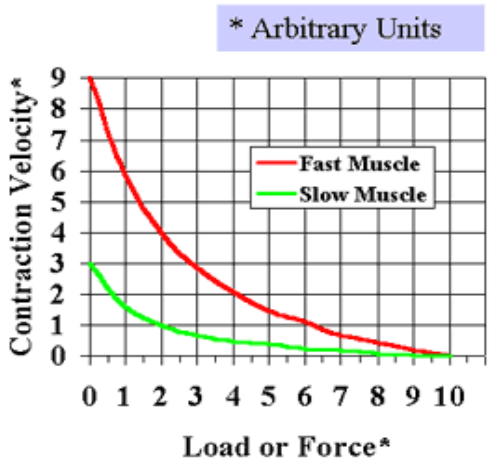
The mouse to the right does not have myostatin gene, the gene is deleted. Myostatin plays two roles:

1) Increase the body /muscle mass “hypertrophy”.
2) Reduce the fat in the body.

In the picture below molecular mechanism for the hypertrophy. It shows the signals, which will produce intracellular signaling that will play role in protein expression and increasing the proteins necessary for hypertrophic cells.



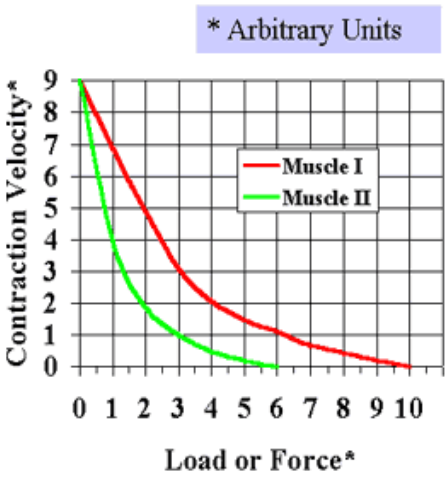
Exercise and force velocity relationship



In this figure fast, twitch muscle and slow twitch muscle, max velocity on Y-axis and the max isometric force on X-axis. Notice, at zero velocity we have the max isometric force.

These are hypothetical muscles

The difference is in the velocity of contaction, but the max developed force is the same. Between the two extreme points every where the fast twich muscle is faster to contract against any after load.



These two muscles has the same muscle fiber so they have the same initial velocity but different isometric force. Meaning that a slow muscle can contract as rapidly as fast muscle, how this? If you increase cross sectional area of a muscle by resistant training you will increase both the velocity and isometric force.

Notes:

*by exercising you don't change a muscle's fiber type, you only change the cross sectional area of it.

* you can do that for animals by dealing with genes but not for humans .

* its very minimal change done by exercise, it needs very long time of adaptation and doing high intencity exercise to increase the fast twitch fiber's cross sectional area.

* if you are a marathon runner you will increase the slow muscle fiber but this is a very minimal change in the muscle cross sectional area .

Muscle Atrophy

Is the decrease of the muscle size, the opposite of hypertrophy, this can happen if you reduce the innervation of the muscle for one month for example, and this will reduce the muscle activity, if you don't regenerate this muscle quickly this situation will persist for ever , and this will decrease all the parameters of contaction because there will be increase in fat and fibrosis in the slight body mass.

Steroid Hormones They causes hyper trophythe

same as growth hormones the testerone because the testeron enhanse synthesis of contractile protein and enlargement of the skeletal muscle causing hyper trophy .

thyroid hormone elevate the rate of energy consumption even in resting and activating state.

Epinephrine stimulate the metabolism rate and the sympathetic innervations increase the glycolysis.

Doctor said that the lectures with his talk are enough for the exam, and he has handout, which covers every things he discussed in the lectures.

The end

Done by :

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Notes :