Muscle Physiology

Lecture 2

Your body is responsible for so many different things and physiology is used to try to answer the questions about how the body functions and to come up with ways to prevent body failure. Within physiology is human performance, which asks specific questions about that body in order to try and maximize your body's capabilities to enhance your performance. Normally, there are 4 main categories of goals people have: physical appearance, athleticism/performance, health/longevity and injury therapy. To write exercise prescriptions to reach a goal, you need to use the fundamental principles of exercise physiology. These fundamentals include organ systems, homeostasis, control loops, and individuation. When training, it is important to remember not to overtrain and to be kind to your body. Remember, according to the Trainability Principle an untrained person will respond more rapidly than a very fit person and that different people require different types of exercise using methods such as FITT and Periodization.

License vs Certification: license is a permission to do something that would otherwise be forbidden, issued by gov. and is gov. privilege ; certification is someone's "stamp of approval", statement of qualification

- Every person who has ever lived has had a body, responsible for different activities
- Physiology addresses questions about how that body functions
- Bodies break down, we try to find ways to prevent and fix
- Human performance physiology is a new field of study, we understand training, nutrition, ways to maximize athletic performance
    - 4 categories of goals: physical appearance, athleticism/performance, health/longevity, injury therapy
- Fundamental principles of exercise physiology
    - ex) organ systems - way of organizing and classifying the body and its parts
        - Homeostasis - auto regulate internal environment
        - Control loops - positive and negative
        - Individuation - a body is not a body, differs between people/sex/age ; musculo - skeletal variations ; tissue integrity owing to history of injury, prior to training, illness or age ; functional differences (ROM) ; enzymatic composition ; hormonal balances ; metabolic conditions ; psychological differences such as goals, motivations or past associations ;
    - the positive injury theory - exercise is good for you because its bad for you

- Accommodations are immediate, quickly reversible changes such as the narrowing of your pupils in bright sunlight
- Adaption implies relatively permanent changes which develop slower and take longer to reverse, such as the O2 carrying capacity of your blood of alcohol tolerance

- Specificity of Adaptation: Wolff's Law *The Law of Bone Remodeling ;* Davis Law *Conservative Surgery*
- Overload/Adaptation Principle - training stresses have to exceed ones normal capacities for the body to adapt
- Steady state exercise - sustainable exercise in which energy supplied to the muscles keeps pace with energy demanded from them ; production and consumption/dissipation of sugar, heat, pH, etc ; owing to the body's homeostatic abilities to maintain internal physiology
- FITT - frequency, intensity, time, type
- Periodization - macrocycle (annual plan) , mesocycle (2-6 weeks), microcycle (a week's training program)
- Absolute vs Relative Intensity - relative % of max heart rate, % of max oxygen
- Dose Curve
- Trainability Principle - an untrained person will respond with rapid improvement
- overreaching/ overtraining (serious tissue of bone injury, insomnia, weight loss, impaired glucose regulation)

Lecture 3

So many different parts come together in order for your body to move and function including your skeletal muscles and joints. Each shape and length of the muscle also has a purpose. For example, a longer muscle has an increased among and speed of shortening while a thicker muscle has an increased force development. Your muscle can be divided into parts including the fascicles, fibers, myofibril, sarcomere and myofilaments. When these muscles get longer it is called sarcomerogenesis and when they get shorter it is called sarcomerolysis. In order for your muscles to contract and relax there has to be cross bridge cycling. Actin and myosin are the contractile components of this process. Some things that influence the force produced by these muscles include the total number of muscle fibers, amount of actin and myosin and how well the cross bridges are functioning.

Macrostructure - you have a bunch of skeletal muscles (>430 according to the book, probably >640)

- The purpose of skeletal muscles cross joints, move your bones around
- Shape: longer muscle - Increased amount of shortening and speed of shortening
    - Thicker muscle - increased force development

- all of your skeletal muscles are covered by an epimysium
    - inside that epimysium is a bunch of contractile proteins and a bunch of connective tissue
- epimysium (outer layer, surrounding whole muscle)
- perimysium (surrounding each fascicle)
- endomysium (surrounding individual fibers)

- Muscle anatomy
    - 1. Muscle
    - 2. Fascicles (bundles)
    - 3. Muscle fiber (cell)
    - 4. Myofibril
    - 5. Sarcomere
    - 6. Myofilament (actin, myosin)
- Sarcomere - sarx: flesh (generally muscle)
- Meros: portion or part
- Each individual sarcomere is approximately 2.2 to 3.3 micrometers in length
- Muscles get longer: sarcomerogenesis
- Muscles get shorter: sarcomerolysis

- Regulatory proteins
    - Tropomyosin
        - Stiffens the thin filament
        - Cover myosin binding sites
    - Troponin
        - 3 polypeptides
            - troponin T

- troponin I
- Troponin C

- Heavy chain - isoform affects function
    - Composed of tail region and globular head
    - Actin binding site
- Light chain - regulatory functions; stiffening of neck
- Tension comes from the mysiums a tiny bit, it comes from the connective tissue inside the fiber and it also comes from the contractile proteins but passive tension mostly comes from titin (largest known protein and third most abundant protein in muscle fiber)
- I - A - H band no myosin in I band, myosin in A band, H zone no actin
- Z discs compress in sliding filament theory
- ACTN3 has multiple alleles
    - Strong form (RR genotype)
    - Intermediate form (RX genotype)
    - Nonsense form (XX genotype)
- Cross bridge cycling
    - Actin and myosin are your contractile proteins
    - They are the “filaments” of “sliding filament theory”
    - Myosin is relatively thick tube: actin is relatively thin tube
    - Their interaction (binding of the two proteins) is muscle flexion
    - That binding is called “cross bridge”

- myosin has to be activated before it will do any binding
- if atp is connected to the myosin head or if ADP and phosphate are both connected to it, the bond between actin and myosin will be pretty weak
- if just adp is connected, actin and myosin will share a much stronger bond

- Cross bridge cycling
    - 1. There's a nerve impulse that reaches the muscle
    - 2. Calcium is released from the sarcoplasmic reticula
    - 3. That calcium binds to troponin which tugs the tropomyosin off of the myosin binding sites
    - 4. Myosin hydrolyzes an ATP molecule, which cocks its head, and it binds to those newly exposed binding sites
    - 5. Myosin is still hanging onto its ADP and phosphate so the bond it has with actin is weak
    - 6. Myosin releases its Pi, which activates the strong conformation
    - 7. The myosin head releases its ADP and performs its power stroke which creates movement in the contractile apparatus
    - 8. A new ATP molecule binds to the myosin head, which switches its bond to the weak conformation
    - 9. The myosin head is released from the binding site on the actin
    - 10. Myosin hydrolyzes the ATP, re cocks its head and latches onto new binding site

A - band: alignment of myosin filaments
I - band: two adjacent sarcomeres that contain only actin filaments
Z - line: middle of I - band
H zone: center of sarcomere where only myosin is present

Factors that influence muscle force generation

- The total number of muscle fibers being activated determines strength
- How much actin and myosin are in each of those contributing fibers
- How well the individual actin myosin cross bridges are functioning

- 1. Length tension relationship
- Force velocity relationship
- Muscle fiber types ½
- Motor unit recruitment

Lecture 4

You get your strength at the cellular level with the total number of muscle fibers contributing to each contraction, how much actin and myosin are in each fiber, and how well the individual actin/myosin cross bridges are functioning. You also have neural recruitment and motor activation. Muscle recruitment starts as an electrical event in the motor cortex which is the place where your nerve impulses for voluntary muscle contraction. You also have a primary and premotor cortex. The primary motor cortex is what controls the execution of movement and the premotor cortex is involved in support of motor control, sensory and spatial guidance of movement and probably some preparation to move functions. There Is also the Supplementary Motor Area which might be involved in a lot of movement planning and coordination of bilateral functioning and the Posterior Parietal Motor Cortex which has associative motor roles and transforms sensory information into motor commands. A motor unit is the motor nerve and all of the muscle fibers it innervates and activating it is based on voltage. These motor nerves travel by neuromuscular junctions.

The purpose of skeletal muscles (move your bones around)
The sheaths (epimysium, perimysium, and endomysium)
The structure (macro and micro)
You have different numbers of muscle fibers in different muscle groups
Each individual sarcomere is about 2.2 to 3.3 micrometers in length
Fibers font always run the length of the whole muscle
myofibrils gain sarcomeres: sarcomerogenesis
Myofibrils lose sarcomeres: sarcomerolysis
The # of sarcomeres in a myofibril adapts so that myofibril maintains optimal cross bridges between actin and myosin at a natural length

Where do you get your strength? At the cellular level, you produce it with actin-myosin bonds
1. total number of muscle fibers contributing to contraction
2. How much actin and myosin are in each fiber
3. How well the individual actin myosin cross bridges are functioning

Neural Recruitment/Motor Activation
You have upper and lower motor nerves. The lower motor nerves are activated by the upper nerves.
Muscle recruitment begins as an electrical event in the motor cortex, this is the place where your nerve impulses for voluntary muscle contraction

There's a premotor cortex and a primary motor cortex
Primary motor cortex: primary hunk of brain tissue that controls the execution of movement
Vladimir Betz was first person to characterize the cells
Betz cells: largest in CNS , they project out of the brain and send their axons down the spinal cord to the ventral horn

Betz cells are not the only cells in the primary motor cortex
(they account for about 10% of the cells that project into the spinal cord from the primary motor cortex)
They are a very distinctive feature of the primary motor cortex though
There isn't a single neuron for each individual muscle fiber
Motor control isn't that segregated
There's a lot of functional overlap; a system of integrated movements

Alpha motor nerve bodies live in the CNS, their axons extend out of the spine toward an extrafusal muscle; that impulse is carried within an alpha motor neuron in the spine, then exits through the ventral root

Premotor Cortex: involved in support of motor control
Sensory and spatial guidance of movement and probably some preparation to move functions
Supplementary Motor Area: might be involved in a lot of movement planning and coordination of bilateral functioning
Posterior Parietal Motor Cortex: has associative motor roles, seems to transform sensory information into motor commands

Motor unit: the motor nerve and all of the muscle fibers it innervates

- There are generally several hundred muscle fibers per motor unit
- All or none principle states that every single muscle fiber in a specific motor unit is activated maximally if activated at all

- If you're going to activate a motor nerve, its based on voltage
- A gradient (ionic balance) is maintained for several reasons
- Most important reason: immediate survival
- Cell membranes are a little bit permeable to ions, but very permeable to water
- Isotonic: normal cells
- Hypotonic: cells swell, burst
- Hypertonic: shriveled cells
- Since water follows ions, an appropriate ionic balance is to keep more sodium outside of the cell than inside
- Sodium potassium pump puts sodium out and pulls potassium inside cell, both moved against concentration gradient
- At resting potential, extracellular side is closed → depolarization: channel opens

- Myelin: spiral wrappings of tightly packed membranes
- Nodes of ranvier: action potential generation, high concentration of Na+ and K+ channels

- From a neural perspective, force of contraction is determined by the number of neurons recruited and by rate coding

- Rate coding is the frequency of achieving an action potential (duration of interspike intervals). Increase the load/stimulus and you'll increase the firing rate (number of action potentials in a given duration)

Neuromuscular Junction: the neuromuscular roadway is not a straight shot from the brain to the muscle, there are synaptic clefts

- These are spaces where the electrical signal has to cross a chemical synapse
- Upper motor nerves depolarize lower motor nerves using glutamate
- Lower motor nerves depolarize muscle fibers using acetylcholine
- Acetylcholine is stored in little sacs (vesicles)
- During action potential, calcium channels open and calcium enters
- Acetylcholine binds to postsynaptic cells (receptors) on the other side of the cleft
- acetylcholine Broken down by acetylcholinesterase

Lecture 5

Excitation contraction coupling involves electrical messages that depolarize the membrane of t tubules which then travel to dihydropyridine receptors. They then change their shape and link to ryanodine receptors that open and release calcium, binding to troponin c. This exposes the binding sites on the protein and can cause calcium induced calcium release. Your body also has the somatic nervous system that controls your skeletal muscle. This is where the voluntary control of your movements come from and where reflex arcs come from. A Reflex arc is a circuit that doesn't have to go all the way to the brain because it only goes as far as the spine. There are 5 components: Receptor, afferent nerve, integrator, different nerves and effector. The muscle sensors of the reflex arcs sense tension, sense length, and sense rate of change of length. A type of sensory receptor in skeletal muscle are muscle spindles. While muscle spindles notice length,the golgi tendon organ notices tension.

- Muscle sensors: sense tension, sense length, sense rate of change of length
- Muscle spindles are a type of sensory receptor in the skeletal muscle

Excitation Contraction Coupling

- The sarcolemma has invaginations called transverse tubules
- The electrical message depolarizes the membranes of those t tubules and it travels inside the sarcolemma
- The action potential reaches voltage dependent calcium channels in the t tubules called dihydropyridine receptors
- The dihydropyridine receptors changed their conformation (shape)
- A positive feedback loop, shape changed can initiate subsequent events
- The shape changing dihydropyridine receptors are linked to ryanodine receptors, which are connected to the sarcoplasmic reticula , so when it changed shape ryanodine receptors open which releases calcium and it binds to troponin c
- This causes binding sites on the protein to be exposed
- With ryanodine receptors, the efflux of calcium triggers the efflux of calcium
- Calcium induced calcium release

- The transverse tubules typically dive into the sarcolemma at the junctions of the A and I bands
- Depolarization causes the DHP to change conformation
- Ca2+ is released from the SR (DICR) which calcium induced calcium release
- Inactivation of contraction occurs when ca2+ is pumped back into the SR (requires a lot of ATP)
- As soon as the muscle is done with its contraction “sarcoplasmic reticulum calcium ATPases” begin pumping the calcium back into the reticula

Reflex Arcs

- The somatic nervous system controls your skeletal muscle, this is where the voluntary control of your movements come from and where reflex arcs come from
- Motor control impulses are carried to skeletal muscles from your ventral roots
- Sensory input impulses are carried from skeletal muscle to you dorsal roots
- Reflex arc is a circuit that doesn't have to go all the way to the brain, it only goes as far as the spine
- 5 components: 1. Receptor, 2. Afferent nerve 3. Integrator 4. Different nerves 5. Effector
- Muscle sensors: sense tension, sense length, sense rate of change of length
- Muscle spindles are a type of sensory receptor in the skeletal muscle

Golgi Tendon Organ

- Muscle spindles notice length, golgi tendon organ notices tension
- When the muscle attempts to tolerate a very heavy load, the GTO senses that load, sends an afferent signal to the spinal cord, activates an inhibitory interneuron and that hyperpolarizes (inhibits) the motor neuron that is producing force

Lecture 6

Two muscle fiber types are type 1, which are slow twitch, oxidative, red and normally reliable, and type 2 muscle fibers which are fast twitch, glycolytic and white. Type 2 muscle fibers are energy inefficnet and break down easily. The velocity of muscle shortening is affected by things like alpha motor nerve, myosin regulatory light chain isoform, myosin ATPase activity, sarcoplasmic reticulum concentration and enzymes for calcium release and reuptake. Alpha motor neurons have tickly myelinated axons which cause a fast conduction velocity. Type 1 muscle fibers are the main ones used everyday, and type 2 are used for hard activities such as sprinting. It is rare, but changing muscle fiber types surgically can be done. The more superficial in a muscle you are, the more type 2 muscles there are present.

Muscle Fiber Type: alpha motor neurons have thickly myelinated axons, meaning speedy conduction velocities (35 to 65 m/s)
Type 1: slow twitch, oxidative red

- Really reliable (like a school bus)

Type 2: fast twitch, glycolytic, white

- Super energy inefficient, breaks down easy (like a race car)

Skeletal muscle fibers vary morphologically and physiologically

- Myosin heavy chain: head and tail of myosin
- Myosin light chain: two per head, they bind heavy chains in neck to the tail
- Other factors affecting the contractile speed of muscle fibers include isoforms of the calcium reuptake and release proteins expressed and the density of the SR
- Fiber type distributions in human skeletal muscles are usually based on a sample of approximately 1000 fibers
- Other stuff affects the velocity of muscle shortening as well: alpha motor nerve innervation, myosin regulatory light chain isoform, myosin ATPase activity, sarcoplasmic reticulum concentration and enzymes for calcium release and reuptake
- Muscle fiber types can be changed surgically but it's rare
- The more superficial in a muscle you are the more type 2 you are

Lecture 7

Denny Brown and Pennybacker were the first to discover how motor units were controlled, with the Henneman's size principle, even though Henneman basically took credit. We know that the smallest, slowest muscles are recruited first in an activity and then fast, strong muscles are recruited next. This is comparable to type one muscle fibers being like a really light sleeper. They jump up at the slightest movement, just like how they are recruited first. Type 2 muscle fibers are like the deep, heavy sleepers. They are basically last case scenarios. The reason that this is a thing, is because of self preservation. Our bodies can't use everything at once or we won't have anything left to work with. One major example given in the lecture was if a person went shopping all day, or to Disneyland and walked around for hours and hours and hours. During this type of activity only type 1 low thresholds have been recruited and activated. To get the type 2 fibers involved you would then have to go sprint. It would still be possible, but you would be a lot slower because it would take longer for the type 2 fibers to become activated, because the type 1 fibers are fatigued and will take longer to reach them.

How are motor units controlled?

- Henneman's size principle
- Denny Brown and Pennybacker were first to discover this phenomenon
    - The smallest slowest muscles are recruited first and fastest strongest are recruited last, but end first

- Type 1 : leaping out of bed for slightest sound, type 2: sleeping through alarm
- self preservation is the reason why our body does these things

Higher threshold motor units have faster conduction velocities

Practical application: go shopping for like 6 hours and walk around, only type 1 low thresholds have been recruited and activated ; then do 100m sprint; you'll sprint slower because it now takes longer to get to the type 2 fibers because type 1 are fatigued

Recruitment is based on need, need is based on intensity, intensity involves a lot

Lecture 8

I am really bad at having a steady exercise routine and taking exercise seriously when I do it. I feel like based on the fact I rarely exercise I probably have way more Type 1 Fibers than I have Type 2, making them slower to activate when I do go to use them. I did not realize before how much more actually goes into performance and coaching. Most of the time in lower level athletics you are told to stand and cheer and encourage your teammates, but based on what we now know it may hurt your body's ability to perform at its true potential. I also did not realize that a player's ability to change and adapt mid performance had a name, or was the ability to inhibit. Reactive inhibition is seen a lot in sports and is seen less as a person ages. My goal is to start working on exercising more religiously and to be mindful of what I am doing in order to slow the loss of Type 2 muscle fibers as I age and decrease neuron sprouting of type 1 muscle fibers.

Peak force development rate is slower in the cold
Size principle is not based strictly on load

- Its based mostly on load, but those mechanoreceptors crunch a lot of data
- Amount of force
- Duration of tension
- Speed of contraction
- Angles, muscle length, etc

  Depending on the muscle and characteristics of the load, it may be possible to recruit nearly all of its motor units using a load that's just 30% of ones maximum strength, in other muscles it might require as much as 90% of one's maximum strength to achieve full recruitment

  Muscle accommodates demands in the safest, most efficient way possible
  What accounts for the initial improvements to strength training?
  - Neurotransmitters, agonist/antagonist recruitment activity, withdrawal of inhibition by GTO, rate coding, changes to motor cortex and descending neural tracts, better motor end plate connections, etc

If you lose the ability to inhibit, everything you do will be worse : for example a pitcher that needs to change its approach when a pitcher does “ reactive inhibition”

If you don't use type 2, when you age you can lose them

- Lose a lot of motor neurons when you age, and neuron sprouting happens, making more type 1 rather than type 2

Take your exercise seriously so inhibition and number of muscle fibers are high

Lecture 9

All living things make changes adapting to their environment based on the threats and stress they endure. Your body has to know how to respond and make changes so that we are better compatible with the environment. These changes include habituation (when you're exposed to something repeatedly and that familiarity diminishes your response), sensitization (developing the ability to tune and know exactly how to fix something), and accommodation (gradual tolerance). One idea that exists is general adaptation syndrome, where the body reacts to each stressor basically in the same way. Without stress causing adaptation your immune system and body can become weak. This idea reminds me of evolution, where everything just adapts in order to survive.

Specificity of Adaptation

Adaptation: biological things respond to their environments

- All living cells spend their loves making changes (however slight) to better tolerate their environments
- Every living thing respond to the threats and stresses they endure
- We're not tardigrades, human die from a lot of stuff
- We make changes to be more compatible to the environment , some of these changes are relatively permanent; others are relatively impermanent
- Toleration: you make do, think pain tolerance
- We make changes to be more compatible to the environment , some of these changes are relatively permanent; others are relatively impermanent: **habituation** - you're exposed to something repeatedly and that familiarity diminishes your response ex) living by train tracks and no longer hearing them
- Sensitization: develop ability to tune and know exactly how to fix something, musician and chef
- Accommodation: gradual tolerance, like getting to hot tub part by part , eyes change to light ; does not linger like habituation ; short term readily reversible
- adaptations , the adjustments are permanent - ish
- Julius Wolff publishes the law of bone remodeling
- Ligaments (or any other soft tissues) adapt to the forces stretching with lengthening response
- The immune system needs exposure to stress, without stress there will be weakness
- General adaptation syndrome: the body reacts to every source of stress (physical and emotional) in more or less the same way
- No matter what is causing you stress, physical or emotional you will enter into an alarm phase, which jolts your physiology into panic mode; you experience different amounts of panic, stress, alarm, whatever but really not different types
- While our biology reacts to every threat and source of stress very specifically, there is plenty of overlap in those reactions

Lecture 10

The biological purpose of life is self preservation and replication of genes. In order to do this your body has to endure both bad and good stress. Each cell and tissue can adapt to the stressor in order for it to meet the functional need. For example, orcas in captivity have deformities because of the mechanical variables applied to their tissues and cells. If your cells did not adapt, you would be threatened with death but adapting beyond the needs of the body may have the same results. This is because adaptation requires so much energy and the initial energy cost might not be the total energy cost which would result in a higher metabolic rate. Your body is resistant to change like this because then it will need more energy to survive. If generation after generation experiences the same stressor, then it becomes selective pressure driving genetic adaptation, also known as evolution. We are lucky because skeletal muscle is one of the most adaptable tissues.

Biological purposes of life: self preservation and replication of gene

Good vs Bad stress

- Every cell and tissue in your body adapts according to its exact functional need
- The breadth and depth of changes are based on how many (and which) body systems are being challenged by the exercise and how overwhelming
- Rates of orcas kept in captivity vs ocean dwelling orcas
    - In the wild you do see deformation, but not as much as in Sea Word: reasons may be because of unique mechanical stress (tons of swimming in counter clockwise circles) , surface swimming, dietary differences

- mechanical variables are applied to a tissue and your cells notice
- your body adapts accordingly to mechanical loads specifically
- your body documents every stress and writes their passage into its cells
- if a cell or tissue were to adapt shy of its needs, that would threaten survival, adapting beyond its needs may also be potentially life threatening
- adaptation requires a lot of energy, initial energy cost might not be the total energy cost , it's possible that the adaptations being made would result in a higher basal metabolic rate
- the body is resistant to change metabolism because then your body will need more energy to survive
- an organism responds to stress: if not lethal, we ignore it (or accommodate)
- if its significant, but infrequently experienced, it's likely that we will still merely accommodate until the stress passes
- if the stress is pronounces more frequently, we adapt tp tolerate it
- if that stress continues to affect us, generation after generation. Then it become selective pressure driving genetic adaptation ex) evolution
- skeletal muscle is one of the most adaptable tissues
- angular specificity - if you subject your tissues to the same anatomical position enough times your body will be able to tolerate it
- contact adaptation accounts for differences in pain, injuries, and recovery

Lecture 11

The history of minimalism begins with the idea behind the shoe. There was an idea that elite runners were setting records and enhancing performance when they were not wearing shoes. Being a minimalist in this aspect changes how your foot moves and the benefits of letting it behave mechanically. Maximalist shoes are ones with padding where your feet can no longer truly be responsible for balance and coordination or with the interaction you have with the environment. As time went on there were claims saying more injuries occurred with high end running shoes but other claims saying minimalist shoes were associated with more injury. This lecture really showed how quickly ideas can change when you look at both sides and how you should take each claim with a grain of salt. Each statement was true, but also wrong.

Minimalist - changes how they move, about letting the foot behave mechanically
Maximalist - padding, feet no longer responsible for balance and coordination , changing your interaction with the environment
The first shoes adidas vs puma
Specific loads and motor patterns = specific adaptations
Pronation - when the foot rolls inward while walking or jogging, skin is rotated inward and the leg moves toward the midline of the body.
If you wear shoes, specificity of adaptation is occurring

Lecture 12

Biomechanics is the mechanism through which components interact to create movement. By using biomechanics, sports performance as well as other areas of life can be enhanced. Biomechanists look at factors that can predict falls and jpw forces are sustained and distributed upon impact. By observing these things you can start to see how changing mechanics of items like knee braces, ice skates, and even diapers for toddlers can change how the person moves. For biomechanics you also have to look at levers which is a rigid bar that moves on a fixed point, moment arm which is perpendicular distance from an axis to the line of action of muscle force, muscle force which is the force generated by biochemical activity in the muscle, resistive force which is the force generated by something outside the body that opposes muscle force (gravity, friction) and torque which is moment of force, tendency for a force to produce a rotation and measured in foot pounds.

The ankle joint complex (two joints) is more complex
The talocrural joint is a true hinge joint that allows the motions of plantar flexion and dorsiflexion
The subtalar joint is not getting worked because we often walk on flat surface
Physiology and biomechanics share much of the same domain of exercise science
There are ways to have the mechanics of your movement evaluated ex) golf
Biomechanics can enter into sports and performance to enhance the sport, can also work with thinks like on keyboards, hiking poles, how to sit, lift with your legs instead of back
Biomechanists study factors that predict falls, and mechanical characteristics of safe landings and how forces are sustained and distributed upon impact
You can change mechanics of basically everything ex) knee brace, new ice skates, different type of pole for vaulting, different diaper for toddler learning to walk
Surgically lengthening hamstrings will change mechanics of cerebral palsy patients but it might diminish knee flexion, biomechanists can come up with solutions based on origins and insertions
The cardinal planes are three imaginary perpendicular reference planes that divide the body in half: transverse, frontal and sagittal
Anatomy - the study of components that make up the musculoskeletal machine
Biomechanics: the mechanisms through which these components interact to create movement
Statics- study of systems with motions that are constant, either not moving at all of moving at a constant velocity
Dynamics - study of systems that involve acceleration
Kinetics - causes of motion, it's the internal and external forces associated with motions
Kinematics - the motions themselves
Fleshy attachments, weaker than fibrous attachments
Muscle lever systems
Levers - a rigid bar that moves on a fixed point , force is applied to move a load, its a matter of leverage
Moment arm - perpendicular distance from an axis to the line of action of muscle force
Muscle force - the force generated by biochemical activity in the muscle
Resistive force - the force generated by something outside the body that opposes muscle force (gravity, friction)

Torque - moment of force, tendency for a force to produce a rotation , measured in foot pounds
Work: force x displacement x cosine of angle
Power: work/time
Strength is a component of power, for strength to become power the force you apply has to make something move
Origin: proximal insertion
Insertion: distal insertion
Agonist: prime mover
Antagonist: opposite
Synergist: indirect assister (stabilizer etc)
Variable resistance: longer moment arm (distance from the fulcrum to the load) means a heavier load

Lecture 13

There are 9 main biomechanical factors in human strength. These are neural recruitment, muscle cross sectional area which determines strength from the perspective of biological real estate, arrangement of muscle fibers (lots of architectural styles of muscle) muscle length (how stretched the sarcomere is affects the proportion of actin and myosin filaments that can interact), joint angle (different joint angles have different mechanical advantages; longer moment arm = more mechanical advantage amd longer moment arm (joint to the load) = less mechanical advantage; longer moment are (distance from the fulcrum to the load) means a heavier load), muscle contraction velocity (as the velocity of contraction increases, the force a muscle can exert decreases), strength to mass ratio (sprinting/jumping : ratio affects ability to accelerate body ; weight class sports: ratio helps determine relative success), body size (body mass reflects body size but body mass increases more rapidly than does functional muscle mass ; given constant body proportions, a smaller athlete has a higher strength to mass ratio), and physiological explanations (cross bridge cycling etc).

Testing strength and power: power has to be measured dynamically but strength can be measured isometric, isokinetic, isotonic

Biomechanical Factors in Human Strength

1. Neural Recruitment
2. Muscle cross sectional area: determines strength from the perspective of biological real estate
3. Arrangement of muscle fibers:lots of architectural styles of muscle ex) parallel (weaker, faster)l, circular, Pennate (stronger and slower)
4. Muscle length: how stretched the sarcomere is affects the proportion of actin and myosin filaments that can interact ; at rest actin and myosin are close. Facilitates cross bridge binding ; when stretched fewer actin and myosin are close so fewer potential cross bridge sites are available ; when contracted actin filaments overlap, number of available cross bridge sites are reduced
5. Joint angle ; different joint angles have different mechanical advantages; longer moment arm = more mechanical advantage ; Longer moment arm (joint to the load) = less mechanical advantage; longer moment are (distance from the fulcrum to the load) means a heavier load
6. Muscle contraction velocity - as the velocity of contraction increases, the force a muscle can exert decreases ; a fast movement corresponds to a low force output, a slow movement has a high force output ; as the load on the muscle is increased, the velocity of shortening is decreased
7. Strength to mass ratio - sprinting/jumping : ratio affects ability to accelerate body ; weight class sports: ratio helps determine relative success
8. Body size : body mass reflects body size but body mass increases more rapidly than does functional muscle mass ; given constant body proportions, a smaller athlete has a higher strength to mass ratio
9. Physiological explanations (cross bridge cycling etc)

Lecture 14

Before this lecture I never realized how things like posture and mechanics could change the loads that were being placed on your body. The way you exercise can have such a big impact on the results and the formation or prevention of injury. In this lecture it talks about how a lot of the time injuries on other body parts are a result of a weak core. Growing up and even now I have a lot of lower back pain. I've gone to the doctors for it and they sent me to physical therapy. They told me that it's because my core is so weak my back muscles are having to make up for it, resulting in the pain. I didn't understand how that even made sense until now. It makes sense because after ab exercises, my back will hurt so bad. I also never realized how injuring yourself can alter how you move and react in the future. Your body changes how it does things and you may even be hesitant to reinjure yourself. Injuring yourself can cause things like a change in neuromuscular recruitment patterns after injury owing to pain and fear of pain and reinjury which then predisposes athletes to a higher risk of re injury.

- Loads placed on the upper body are transmitted through the spine to the legs and the musculature in the back functions at a considerable mechanical disadvantage ; it produced much more force internally (frequently exceeding a factor of ten) than it generates externally ; thus your discs get compressed a lot
- When squatting, compressive forces are minimized when the back is either flat or in a slight lordotic curvature ; increasing intra abdominal pressure also reduces the need for the erector spinae to generate force to provide mechanical support, so intraabdominal pressure can reduce compressive forces on the discs, which can reduce your risk of injury
- A lot of injuries for different body parts can often be related back to a weaker core
- Weight lifting belts seem to work by increasing intra abdominal pressure which reduces spinal compression which reduces injury on spinal discs
- Should you lift with your legs? An argument that semi squat is better because the full squat doesn't eliminate compression, changing what's being compressed, biased article??
- The ratio of thoracic to lumbar compression force is posture dependent
- Flexion postures are associated with an appropriate doubling in lumbar compressive force but only small increases (or even decreases) in thoracic compression
- Secondary cellular death - There is an inflammatory response to skeletal muscle injury
- Interactions between the immune system and skeletal muscle may play a significant role in modulating the course of both the contusion injury and the subsequent muscle repair
- Once you're injured: recruitment characteristics change
    - ec) a tiny amount of swelling in one of the muscles can cause friction in corresponding/adjacent tissues
    - Most injuries are muscular and they often develop because of sport specific adaptations in motion and recruitment patterns

- specificity of adaptation: used tissues adapt, unused tissues do not
- the adapting tissues change to better tolerate the precise characteristics of the imposed strength

- each sport has its own mechanical and biological stresses, which condition bodies to exert force in different ways
-production of force is affected by a lot of variables
    - recruitments of skeletal muscle also affected by other variables (illness, temperature, etc)
- pain alters patterns of force production
- following injury the athletes mechanical and neural functioning are commonly reprogrammed, causing deviation in gross movement strategies
- Once you've experienced pain: conscious altering of muscular recruitment characteristics owing to the pain associated with activation of the affected tissue and unconscious, reflexive alteration in recruitment, which includes a delay in activation of the painful fibers, reduced magnitude of agonist recruitment, altered motor unit firing sequences in individual, whole muscles and sometimes different muscles being called upon entirely, including simultaneous contributions from different body segments
- not all voluntary contractions that are impaired: muscle spindles are centrally modulated in the presence of pain
- your underlying biomechanics may change when you experience an injury
- altered neural recruitment (kinetics) changes gross kinematics
- altered firing predisposes you to re injury

- 1. Neuromuscular recruitment patterns change after injury owing to pain and fear of pain and reinjury
- 2. Those altered firing patterns predispose athletes to a higher risk of re injury
- 3. Return to play testing batteries aren't considering neuromuscular phenomena; they're just testing gross movements

Lecture 15

Nociceptors are for when pain notifies you about possible threats and that triggers a protective response and when it goes for too long it can hypersensitive the nervous system so that otherwise innocuous movements now transmit messages of pain. There is also a gene mutation caused by mutation of the tropomyosin receptor kinase A gene, which codes for TrKA which mediates nerve growth factor, which is critical to the formation, function and survival of autonomic and sensory neurons and if you have it you can't feel pain. I feel like this is in a lot of movies and criminal shows where the crazy guy can't feel pain to make the shower scarier. Molecular mechanisms of nociception are stimulated by peptides, lipids, neurotransmitters, acidity, heat and pressure. These things either sensitize (lower the depolarization threshold of) the nociceptor or they just excite it. Under repeated injury they can increase in number.

If a patient is not currently feeling pain (or currently cold) total force output may return to somewhat normal values

- Extended nociceptor activity (pain sensation) can hypersensitive the nervous system so that otherwise innocuous movements now transmit messages of pain
- Nociceptors are for: pain notifies you about possible threats and that triggers a protective response , sometimes pain outlives its role as a threat alarm, and it continues to trigger a protective response
- If you cant feel pain you don't have afferent signals , when afferent fails to transmit nociceptor information
    - Gene mutation, caused by mutation of the tropomyosin receptor kinase A gene, which codes for TrKA which mediates nerve growth factor, which is critical to the formation, function and survival of autonomic and sensory neurons

Molecular mechanisms of nociception

- Stimulated by peptides, lipids, neurotransmitters, acidity, heat, pressure, etc
- These things either sensitize (lower the depolarization threshold of) the nociceptor or they just excite it

Under excessive inflammatory conditions or repeated injury, chemical receptors can be made more sensitive and can increase in number

More receptors = more binding = more triggering of the nerve , more responsive to the same concentration of chemicals

NMDA receptor permits the influx of sodium and calcium, the calcium can affect gene expression and interact with other proteins and receptors related to long term changes

Consistent firing turns on genes that create more receptors

Neuronal sensitization means there is an increased excitability of afferent neurons

- One cause may be pain signals get amplified

Allodynia: the nervous systems sensitization to pain; messages of pain are often transmitted in response to non painful stimuli

- Reorganization of spinal cord circuitry: mechanoreceptors can be reprogrammed to transmit messages of pain, silent nociceptors can be woken up

Lots of sensory fiber types

- Aa and Ab fibers are myelinated so messages travel very quickly
- They detect innocuous stimuli and typically don't contribute to pain, but their stimulation can reduce pain

Substances that are released during neural sensitization (substance P) can modify motor neuron excitability

- This can alter muscle recruitment patterns

- C fibers are unmyelinated and have slow nerve conduction velocity , they are second responder pain fibers, when they depolarize, what you feel is delayed, dull, diffuse pain

Lecture 16

There are different ways to classify injuries: acute which lasts about a week and is typically inflammatory ,subacute which is roughly the second week (begins 5-10 days after acute phase), chronic (or post acute) which is either in final stages of healing (4-6 weeks) or chronicity lasts long than a month and is not improving, and acute on chronic which is reinjury. After injury there are exercise strategies. During the inflammation phase you want to prevent disruption of new tissue and train uninjured extremities. During the repair phase you want to prevent atrophy and joint deterioration in the injured area and maintain muscular and cardiovascular function, and during the remodeling phase you want to begin adding more advanced, sport specific exercise and should be able to begin increasing velocity/speed of movement. Doing too much, too fast will just set you back. There are some clinical signs that will let you know you are injured like redness, pain, heat and swelling.

Justinus Kerner:sausage poison, myasthenia gravis - temporary paralysis, autoimmune disease

- Bacillus botulinus - type A blocks the release of acetylcholine from motor nerves

- just like we can deactivate and desensitize nerves, we can activate and hyper sensitize them

Indication: a valid reason to take medication, do a test, a procedure, etc

- Potassium sparing diuretics are indicated in the treatment of congestive heart failure

Contraindication: a reason not to do a test, take a medication, do a procedure , etc

- Massage is contraindicated in burn patients open, blistering wounds

Dislocation: complete displacement of the joint surfaces

Subluxation: partial displacement of the joint surfaces followed by relocation. This can affect ligaments, nerves, cartilage etc and can lead to instability, laxity

Sprain vs strain: ligament vs muscle/tendon

Exercise Strategies:

- During inflammation phase
    - Prevent disruption of new tissue
    - Train uninjured extremities (mirror neurons?)
- During repair phase
    - prevent atrophy and joint deterioration in injured area
    - maintain muscular and cardiovascular function
    - consider specificity of adaptation, improve neuromuscular control
- during remodeling phase
    - begin adding more advanced, sport specific exercise
    - able to begin increasing velocity/speed of movement

Injury → BLEED → Clot → repair → heal → function or dysfunction

The repair: following injury of musculoskeletal tissues

- Muscle, ligament, bone, tendon, articular structures

Macrotrauma - overwhelming force (more than the tissue can tolerate) force vector and body position determine which tissues are involved; probably bone, ligament and/or muscle tendon

microtrauma - there is gradual accumulation of micro insults

- Anabolism vs catabolism: catabolic signal predominates

Classifying injuries:

Acute - lasts about a week, typically inflammatory

Subacute - roughly the second week (begins 5-10 days after acute phase)

Chronic (or post acute) - either in final stages of healing (4-6 weeks) or chronicity lasts long than a month and is not improving

Acute on chronic - reinjury

1. You get injured:local tissue damage, cells have to migrate to ara, have to make a clot
   Internal clot = provisional matrix
   Provisional matrix = weal fibrin - fibronectin clot
   Fibrin is a fibrous protein involved in blood clots
   Fibronectin is a glycoprotein that binds to stuff

   Clinical signs: 1. Redness; increased blood flow
2. Pain: nociceptive inflammatory mediators
3. Heat: metabolic demand
4. Swelling: protein leakage, water follows
   may also observe a loss of function

After immune system does tidying, you begin laying collagen down

If you applied right amount of stress, and out down right kind of collagen you're healed

Lecture 17

You have a lot of blood and cells to help you heal. When you first get an injury your body reacts to try and start the healing process. The injury or stress on the tissue causes a disruption in the blood and lymphatic vessels. Platelets are the first responders, trying to form clots. The platelets can change shape and begin degranulation and secrete growth factors. The platelets and macrophages secrete cytokines, which are pro-inflammatory and the vascular endothelium starts to get "leaky". You swell because of this leakiness, because water follows. This leakiness also lets immune cells move into the area to start healing. The first cells that arrive are called neutrophils and they arrive by chemotaxis caused by the platelets and macrophages. They are directed by chemicals, attractants and repellents. Other causes of leakiness include complement proteins, kinin system, platelet activating factor, nitric oxide and serotonin

Pointed Ploughing Spade
Among the components of blood and lymph: fibrinogen, fibronectin, prothrombin
In the presence of calcium, prothrombin gets converted into thrombin (an enzyme)
When fibronectin is present, thrombin turns fibrinogen into fibrin
Platelets show up to form clots
Insoluble fibronectin is already hanging out in the extracellular matrix
Soluble fibronectin is a major component of blood plasma
When activated, platelets change shape and begin degranulation and secrete growth factors, cytokines, bradykinins, serotonin, histamine etc
All of this helps direct a bunch of cells and chemicals to a site of injury

- The first to arrive are neutrophils
  Cytokines in platelets regulate inflammation

Neutrophils migrate through the body by chemical gradients, migradition is called chemotaxis " to direct them based on chemicals - attractants and repellents
Vascular leakiness - the damage may start the leakiness but once pro inflammatory cytokines show up it gets more leaky

- Swollen because water follows leakiness

Leakiness is also caused by: complement proteins

- Complement phagocytic cells, helping them phagocytizing
- Kinin system
- Platelet activating factor
- Nitric oxide
- Serotonin

Cell membranes separate the inside and outside

Lecture 18

Before an injury is fully repaired, your body needs to clean the area. Neutrophils are bactericidal agents that help do this cleaning. The enzyme proteases also helps, but only lasts a couple of days before dying off. Following the neutrophils are the macrophages, which remove all of the other dead things. The severity of your injury determines how long the process takes. I think that it's cool that pus is just dead neutrophils. Every "gross" part of the body has a science reason behind it and if everyone knew the reasons I think people would be more accepting of others. There is such a thing as a good and bad healing environment. A good environment is a brief, robust inflammatory response, then a robust fibroblast presence with proper mechanical signaling so that the collagen aligns properly and a bad environment is when inflammation hangs around too long, impairing the arrival and action of the fibroblasts.

Before any repair, you need to clean

- Neutrophils are great cleaners : bactericidal agents, they go in and squirt superoxide and hydrogen peroxide all over the place killing everything
- Secrete proteases (enzyme that performs proteolysis) they only live for a couple of days, perform duties and then die
- Pus is dead neutrophils, plasma proteins and whatever else got stuck with it
- Macrophages follow the neutrophils, they eat up the garbage and other dead custodians
    - Severity of injury effects how long it takes

- while neutrophils and macrophages are cleaning they release proinflammatory cytokine
- a few days after initial injury, they secrete growth factors which help initiate the proliferation phase
- provisional matrix serves as chemostatic signal and provides worksite for the fibroblasts
- fibroblasts adhere to fibrin, but require the presence of fibronectin to do so; the cross linked provisional matrix is the perfect hub for fibroblasts to adhere and get to work (produce collagen
- fibroblasts are progenitor cells (not quite stem cells)

Osteoblasts are fibroblasts

Fibroblasts are defined by their ability to make collagen

- When they arrive, they attach to provisional matrix (fibrin)
- As fibrin gets removed a better matrix is formed by proteoglycans, glycoproteins and type 3 collagen
- Final phase : temp matrix is removed by extracellular and intracellular digestion
- The key for fast quality healing is a strong but brief inflammatory reaction, leaving inflammation in a tissue forever impairs the action of the fibroblasts
- Platelets → neutrophils → macrophages→ collagen 3 → fibroblasts → collagen 1
- Most disease is either an appropriate consequence of inappropriate stress of its failure of regulation
- Forming a big clot is a failure of regulation of endothelial factors, fibrin and platelets

Good vs Bad healing environment

Good - brief, robust inflammatory response, then a robust fibroblast presence with proper mechanical signaling so that the collagen aligns properly
Bad - inflammation hanging around too long, impairing the arrival and action of the fibroblasts
What do you need to heal?

1. Cells
2. Blood, cells have to be able to migrate to wound
3. And you need the tissue to be touching
4. Once you've gotten all cells there they need to adhere to wound in order to do remodeling, mechanical stress

Lecture 19

For the pump, metabolism is what determines blood flow. It works like this: When a muscle fiber contracts, it is a metabolic activity. Approximately one second after the initiation of exercise, there is an increase in blood flow in that fiber's direction. The substrates and products of that metabolism include numerous vasoactive molecules. They diffuse into the blood, which provides information about the internal metabolism of that cell. That informs the circulatory system to provide more blood (more metabolic substrates) the bulk of this delivery is by vasodilation. Using the size principle, you can recruit your motor units in a specific order, that means some fibers will activate while others will be inactive. The fibers in a single motor unit are distributed throughout the muscle. The muscle cells then receive their nutrition by capillaries and you are unable to adjust their volume. Muscle fibers tend to be longer than the capillaries supplying them, so they have multiple suppliers.

Functional hyperemia or reactive hyperemia
NAD reduced to NADH, which is an electron donating compound NADH excess indicates more reliance on anaerobic metabolism
Different presentations of hyperemia based on different durations of occlusion “hyperemia is caused by” assumes (probably falsely) that all presentations are similarly caused
Vasodilation is how the muscle gets more and more blood flow
Metabolism drives blood flow
How do you send more blood through capillary beds? The increase in oxygen delivery to a working skeletal muscle fiber is achieved by an increase in RBC flux through capillaries that supply the individual, active skeletal muscle fibers , metabolism detours blood to where there is the most effective use
The pump: metabolism is what determines blood flow

- When a muscle fiber contracts, it is a metabolic activity, approximately one second after the initiation of exercise, there is an increase in blood flow in that fibers direction
- The substrates and products of that metabolism include numerous vasoactive molecules. They diffuse into the blood, which provides information about the internal metabolism of that cell
- That informs the circulatory system to provide more blood (more metabolic substrates) the bulk of this delivery is by vasodilation
- size principle ensures that you recruit your motor units in a specific order, that means some fibers will activate while others will be inactive
- The fibers in a single motor unit are distributed throughout the muscle, no =t grouped together in neighborly cul de sacs
- Those well scattered muscle cells receive their nutrition by capillaries and capillaries font have smooth muscles so they are unable to adjust their volume, diameter adjustments must be made upstream
- Muscle fibers tend to be longer than the capillaries supplying them, so they have multiple suppliers

Lecture 20

Recap of all of the previous lectures. The ones I found most interesting were definitely the minimalist/maximalist, process of healing and biomechanics. I think that those ones are easier to understand and remember than mTOR and I find the actual science behind muscles boring. These past lectures have also taught us how we need to choose what articles and "facts" we believe wisely, because many are biased and full of opinion. Sometimes there isn't one clear answer but a "best" answer. I also think that knowing biomechanics allows you to better adapt and modify things if some people are incapable of doing an activity, like if someone was injured or disabled.

Lecture 21

Hormones play such an important role in our body. The endocrine system is a system of glands that secrete different types of messenger molecules into blood generally to regulate cells, tissues, organs and systems. The endocrine system includes pituitary, thyroid, adrenal, gonad, and pancreas. There is an interaction between the nervous system and the endocrine system called neuroendocrinology. The message is transmitted using a chemical messenger. These chemical messengers, or hormones, are synthesized, stored and released into the blood by endocrine glands. The hypothalamus is considered the link between the endocrine system and nervous system. Beneath the hypothalamus in rank is the pituitary gland. The pituitary regulates stress, blood pressure, growth, and reproduction. Other hormones include polypeptide hormones that target receptors that are integrated into cell membranes and initiates a signal transduction pathway, steroid hormones that interact directly with the regulatory elements of the DNA and eicosanoids.

Endocrine system: pituitary, thyroid, adrenal, gonad, pancreas

- Its a system of glands that secrete different types of messenger molecules into blood generally into blood to regulate cells, tissues, organs, systems

Neuroendocrinology - interaction between nervous system and endocrine system
A chemical messenger is a compound that transmits a message
Hormones: long ish range communicators ; chemical messengers or signal molecules that are synthesized, stored, and released into the blood by endocrine glands
Neurotransmitters - communication to adjacent cells
System of glands that secrete different types of messenger molecules
They enter the bloodstream. Travel around, eventually bind and regulate stuff
Neural signal from the brain are connected to remote glands throughout the body and the hormones regulate cells and tissues all over the place
The hypothalamus is considered the link between the endocrine system and nervous system

- Vasopressin ; antidiuretic hormone
- Corticotropin releasing hormone
- Growth hormone releasing hormone
- Gonadotropin releasing hormone
- Thyrotropin releasing hormone
- Prolactin releasing hormone
- Oxytocin

Hypothalamic effects are often routed elsewhere
The pituitary regulates: stress, blood pressure, growth, reproduction

- Releases growth hormone, thyroid stimulation, prolactin

Hypothalamus - links NS to endocrine system
Pituitary gland - growth hormone, vasopressin
Thyroid - thyroxine
Parathyroid: PTH

Adrenal glands - cortisol, epinephrine
Pancreas - insulin, glucagon
testes/ovaries - testosterone, estrogen

Each hormone is a signaling molecule produced by a gland, get transported in the circulation to a distant tissue or organ and influence behavior of that tissue by interacting with its cells

Polypeptide hormones: target receptors that are integrated into cell membranes, initiates a signal transduction pathway
Steroid hormones - interact directly with the regulatory elements of the DNA
Eicosanoids - hormones, chemical influence of cell signally

Lecture 22

The hypothalamus to anterior pituitary is connected by blood vessels, a capillary network called the hypophyseal portal system and lives in the infundibulum. The hypothalamus to posterior pituitary is connected by nerves and axons with cell bodies in the hypothalamus. The posterior pituitary does not produce hormones, it just stores and secretes HP adrenal, thyroid, gonadal and liver. This lecture also talked about autocrine secretion and paracrine secretion. Autocrine is when cells release hormones by itself for itself and the hormone never exits the tissue that produced it. Paracrine secretion is when the hormone gets released, acts with adjacent cells and does not need to enter circulation to get there. The binding proteins carry the hormones through the circulation.

Hypothalamus Pituitary whatever axes

Hypothalamus to anterior pituitary: connected by blood vessels, a capillary network (called the hypophyseal portal system) lives in the infundibulum. Hypothalamic hormones that instruct the anterior pituitary make the journey without having to enter systemic circulation

Hypothalamus to posterior pituitary : connected by nerves, axons with cell bodies in the hypothalamus descend through the infundibulum and the terminals are in the posterior pituitary. The posterior pituitary does not produce hormones, it just stores and secretes

HP adrenal

HP thyroid

HP gonadal

HP liver

Peptide: made in cells from amino acids,water soluble, usually act through second messenger on cell surface, fast initiation, temporary action

Steroid: made from cholesterol, fat soluble, adrenal cortex, testes, ovaries, nuclear or cytosolic receptors, slow initiation, long action

The signal from a hormone only affects cells that express a specific receptor, one that is specific to that exact hormone

Steroid hormones are synthesized from cholesterol and are fat soluble

Autocrine secretion: cell releases hormone by itself for itself, the hormone never exits the tissue that produced it

Paracrine secretion: hormone gets released, acts with adjacent cells, does not need to enter circulation to get there

Binding proteins: carry hormones through circulation, prolonging the half life of the hormone sutherland s discovery cAMPs role in glycogen regulation

Perilipin is the cat protein on the lipid droplet, which in its base state, protects that droplet from lipolysis

- Regulated by growth hormone, insulin, glucagon, cortisol

Lecture 23

The hormone classifications are polypeptide hormones that target receptors that are integrated into cell membranes, this initiates a signal transduction pathway, steroid hormones that interact directly with the regulatory elements of the DNA and eicosanoids. In 1849 the study of endocrinology began and found that the hypothalamus regulates X. A peptide is made in cells from amino acids (just like all peptides/proteins) are water soluble (so they cant diffuse across sarcolemma),usually act through a second messenger on the cell surface and are fast initiation with temporary action. A steroid is made from cholesterol, is fat soluble (so they can diffuse across sarcolemma), includes adrenal cortex, testes, ovaries, has nuclear or cytosolic receptors and is slow initiation, long action.

- - Hormone Classifications
- - 1849 the study of endocrinology began
- - The hypothalamus regulates X
- Hypothalamic - Pituitary - Whatever Axes:
- - Hypothalamus to anterior pituitary: connected by blood vessels. A capillary network (called the hypophyseal portal system) lives in the infundibulum. Hypothalamic hormones that instruct the anterior pituitary make the journey without having to enter systemic circulation

- Hypothalamus to posterior pituitary: connected by nerves. Axons with cell bodies in the hypothalamus descend through the infundibulum (called the hypothalamic - hypophyseal tract) and the terminals are in the posterior pituitary. The posterior pituitary does not produce hormones; it just stores and secretes

-
- - HP Adrenal : corticotropin - releasing hormone, adrenocorticotropic hormone
- - HP Thyroid : thyrotropin releasing hormone , thyroid stimulating hormone
- -HP Gonadal : gonadotropin releasing hormone, luteinizing hormone and follicle stimulation hormone
- - HP Liver : growth hormone - releasing hormone or somatostatin, growth hormone
-
- - chemical messenger: compound that transmits a message
- - Hormones are long range communication
- - neurotransmitters are communication to adjacent cells
-
- Hormones are: chemical messengers or signal molecules that are synthesized, stored and released into the blood by endocrine glands - body structures specialized for this function - and certain other cells
- Polypeptide hormones - target receptors that are integrated into cell membranes, this initiates a signal transduction pathway
  Steroid hormones - interact directly with the regulatory elements of the DNA
- Eicosanoids
- Peptide

- - made in cells from amino acids (just like all peptides/proteins)
- - water soluble (so they cant diffuse across sarcolemma)
- - usually act through second messenger on cell surface
- - fast initiation, temporary action
-
- Steroid
-
- - made from cholesterol
- - fat soluble (so they can diffuse across sarcolemma)
- - adrenal cortex, testes, ovaries
- - nuclear or cytosolic receptors
- - slow initiation, long action
- (different types based on different types of receptors they bind to)

most hormones come from glands, get shuttled around in circulation, and exert some physiological effect on a distant bunch of cells (a tissue of an organ)

- the signal from a hormone and the consequence of that signal only affects cells that express a specific receptor, one that is specific to that exact hormone
- otherwise, they would affect every (or at least any) cell in the body
- steroid hormones are synthesized from cholesterol and are fat soluble
- Autocrine secretion: cell releases a hormone by itself, for itself. the hormone never exits the tissue that produced it
- Paracrine secretion: hormone gets released, acts with adjacent cells, doesn't need to enter circulation to get there
- binding proteins: these carry hormones through circulation, prolonging the half life of the hormone. major role in endocrine function
- Carl Cori discovered and outlined glycogen catabolism/anabolism (the Cori cycle)
- Lipolysis is regulated by growth hormone, catecholamine, insulin, glucagon, cortisol, TNF

Lecture 24

Cellular signaling cascade was Sutherlands discovery. The steps include insulin binding to its receptor, PI3K getting activated, downstream of PI3K PKB gets activated, PI3K and PKB activate PDE, and PDE breaks down cAMP meaning PKA does not get activated, so it does not phosphorylate anything , so lipolysis doesn't happen. Binding proteins also have many functions, They are for storage and fight degradation, extend half life, modulate hormone activity, and increase solubility in the blood. One hormone is the growth hormone. This hormone preserves glycogen stores, increases lipolysis and use of fatty acids, decreases amino acid degradation, increases amino acid transport across cell membranes, increases protein synthesis (and muscle mass), increases collagen synthesis, and enhances immune cell function.

Autocrine - VEGF, MGF, immune chemicals
Paracrine - fibroblast growth factor, transforming growth factor, clotting factors, myostatin
Endocrine - insulin , glucagon, leptin, ghrelin, testosterone, estrogen, GH, IGF-1, myostatin

Cellular Signaling Cascades - sutherlands discovery: cAMPs role in glycogen regulation
Lipolysis is regulated by: epinephrine, glucagon, atrial natriuretic peptide, growth hormone, cortisol, tumor necrosis factor, insulin

Steps:

1. Insulin binds to its receptor
2. PI3K gets activated
3. Downstream of PI3K PKB gets activated
4. PI3K and PKB activate PDE
5. PDE breaks down cAMP
   So, PKA does not get activated, so it does not phosphorylate anything , so lipolysis doesn't happen

   Functions of binding proteins:
   1. Storage, fight degradation
   2. Extend half life
   3. Inactive from
   4. Modulate hormone activity
   5. Increase solubility in the blood

A muscle cell has a bunch of nuclei, each nucleus controls a nuclear domain, nuclear domain: a region of the muscle protein

Follistatin - glycoprotein (binding protein) that binds to TGF-B proteins (transforming growth factor)

Myostatin is myokine (little protein) produced by muscle cells that acts locally

IGF - 1 : hormone that is similar to insulin in molecule structure and function

Endocrine: produced in liver
Autocrine/Paracrine: produced by muscle cells

IGF production in the liver is stimulated by growth hormone release from the anterior pituitary, released 8-29 hours after stimulus
98% of IGF-1 circu;ation is bound to 1 of 6 binding proteins

Androgens - steroid hormones that bind to androgen receptors ex) testosterone, dihydrotest

- These are synthesized from cholesterol and are fat soluble, so they passively diffuse across the sarcolemma of a muscle fiber
- They bind with their receptors to form a hormone-receptor complex
- The H-RC gains access to the genetic material in the cell's nucleus and inl=fluences transcriptional units that code for protein synthesis

Growth hormone: has half life of 30 minutes
Most HGH is released during deep sleep, daytime levels are low
The effects of food and exercise vary depending on the food and exercise
Serum levels are typically higher in women than they are in men, depending on phase of menstrual cycle

GH does a lot:

- Preservation of glycogen stores
- Increase lipolysis and use of fatty acids
- Decreased amino acid degradation
- Increase amino acid transport across cell membranes
- Increase protein synthesis (and muscle mass)
- Increase collagen synthesis
- Cartilage growth, bone growth
- Enhance immune cell function

The hypothalamus releases thyrotropin-releasing hormone
The pituitary gland releases thyroid stimulating hormone

Lecture 25

One major debate called the Goldman Dilemma is whether or not it is fair for the use of steroids. I think that it's absolutely insane that over 50% of people said that they would choose a gold medal even if that meant death in 5 years. It reminds me of how that track runner chose to smoke weed knowing it could ruin her Olympic career if she failed the drug test. I think that the use of mechanical aids could be a worse disadvantage than physiological aids in sports because even when you take steroids you still have to work and know how to play but more money and better equipment can turn things in your favor quickly. I also thought it was interesting that positive self talk can improve your performance. I took sports psychology once and did not realize how bad your mind can play tricks on you and negatively influence your performance.

The Goldman Dilemma - goldman asked elite athletes if they would take a drug that guaranteed them a gold medal, but death in 5 years and >50% said yes

Three classes of ergogenic aid:
Mechanical aids - better cleats, pre bent fiberglass vaulting pole
Psychological aids - positive self talk, hypnosis, cheering music
Physiological aids - tylenol, steroids, creatine, water , vitamins

Arguments against steroids: steroids aren't natural, make sports unfair, cause health problems

Lecture 26

When I was in Oregon, my friend got into the bikini competitions and her "trainer" took a needle and said steroids were the only drug we should ever do. Her chest and back were covered in acne, and her voice was a lot deeper than the average females, I think because of the testosterone. I don't really care if someone takes them or not, because it

does not affect me at all, but I do like the idea that there are different competitions for natural and unnatural bodybuilders. Whether or not steroids have a massive effect, I still think it evens out the playing field even more and I think it's more impressive to see someone that big without the use of steroids. The statement that tylenol causes more liver damage than steroids do is also kind of scary because I know people who pop that like crazy. Do you have to take a whole lot or is it fairly easy to ruin your liver with tylenol? (LOL I didn't realize how much my thoughts on them matched up to the arguments against them)

Anabolic Steroids
Animal models:
Myosatellite cells: multipotent progenitor cells that can donate myonuclei to skeletal muscle fibers
How does testosterone work?

- Physiological level: they change the expression of your genes
- Increase myonuclei
- Muscle cells, like cancer cells, are huge with huge biological domains, these domains can't be governed by only one nucleus, you need multiple nuclei (full of DNA)
- Androgens increase the number of myonuclei and the possibility of protein accretion through a larger domain
- Must bind to androgen receptors
- Must have enough androgen receptors , otherwise you have to come up with ways of disposing it
- Without activation of the motor unit there's no adaption, just disposal
- Primary androgen interacting with skeletal muscle tissue is testosterone
- Androgens are a set of chemicals that can produce great effects and side effects
- Can be abused

- Oral steroids: portal circulation
- IM steroids: systemic circulation
  "Just remember tylenol is worse" for your liver, contradicting the argument that steroids need to be band because they are bad for your liver

  Left ventricular hypertrophy
    - Steroid use associates with a slight thickening of the wall
    - This would be bad but you'd have to do A LOT of drugs, and if you adjust for whole body muscle mass the heart isn't much bigger

Lecture 27

A major argument against steroids is that it will create an unlevel playing field, however it is already unfair based on aspects like genetics and money alone. Since the beginning of sports, it has never been a fair playing field or truly clean and if sports were like that less people would watch them because they would be less entertaining. Just like how bigger bodybuilding competitions can charge more, because the way these people who use steroids and other aids look is so much more interesting. If you say that steroids improve performance and should be banned then should weight rooms, supplements and coaching also be banned because they will also vary depending on team and person? Another argument is that there are rules to follow, but athletes already break rules in sports like fouling. It is also said that they are unnatural, but food we consume is also unnatural like inorganic GMOs.

9 arguments against steroids:

1. The athletes health
2. Unnecessary risk for harm, undue social coercion
3. Steroids are unfair
4. Steroids strip the soul from the sport
5. Natural vs. unnatural
6. Rules
7. Harm to other people
8. They don't work anyways
9. ??

The unnecessary risk for harm and the social coercion that facilitates it:

- Because some people are breaking the law and doing steroids, in order to compete at that level, you now need to do steroids too. You get coerced into it because there's no other way to keep up, and this puts you at an undue risk for harm
- Steroids are probably necessary to be able to compete at professional level
- From a legal perspective, social coercion does not work
- Trust science. “Who is making the argument that because football injures more athletes than steroids, football should be more illegal than steroids?”
- No one is forced to participate if they don't want to

- Level playing field, but in reality there is already no level playing field (money, genetics)

- Steroids strip the spirit of the sports
- If we eliminated doping, sports would be in the purest form ; but in history its never been truly clean
- When a sport is no longer entertaining, it ceases to exist
- Steroids don't change the sport itself, just potentially improve the athleticism of the participants
- Other ways to improve performance: weight rooms, supplements/nutrition, coaching

- Another argument is rules, but illegal acts include fouling, double dribbling, etc
- Natural vs unnatural: no even most food is natural, inorganic, GMO
- I DIDN'T KNOW BLOOD DOPING WAS EVEN A THING WHAT THE HECK

9. People think steroid users are getting something for nothing, but if you take them and do not exercise, very little happens
    - They do not create muscle, but allow you to train harder

Lecture 28

Enzymes are the main players in metabolism and cell signaling cascades and controlling these enzymes to facilitate or inhibit their activity can have a downstream metabolic implication like allosteric control, competitive inhibition, noncompetitive inhibition, uncompetitive inhibition, mixed inhibition, suicide inhibition, accumulation of product and phosphorylation. If you have a lot of ATP, it binds to an allosteric site, changes shape and shuts down glycolysis. In competitive inhibition, the substrate and inhibitor both compete for the same place, in noncompetitive inhibition changes the actual effect, in uncompetitive inhibition it only binds to the enzyme after the enzyme has bound to the substrate, in suicide inhibition the enzyme initiates catalysis (after binding to the inhibitor) that inhibitor gets modified in a way that irreversibly inhibits the enzyme and in phosphorylation a phosphate is added to a protein, which affects the activity of that protein

Enzymes: primary players in metabolism and cell signaling cascades
What we know: 1. Metabolism is the sum of your chemical reactions
2. Those reactions are catalyzed by enzymes

Catalysis is lowering the price (activation energy)
Enzymes do not get used up in the process
Enzyme + substrate ; enzymes are like sockets

When they bind, creating that enzyme and substrate complex, there are a variety of different consequences
Each consequence has a unique effect on your metabolism
There are plenty of ways to control the enzymes themselves, to facilitate or inhibit their activity
And any facilitation of inhibition of an enzyme will have downstream metabolic implications as well

1. Allosteric control
   Allosteric deactivation = negative modulation
   Allosteric activation = positive modulation

If you have a lot of ATP it binds to allosteric site, changed shape and shuts down glycolysis

2. Competitive inhibition
   Substrate and inhibitor both compete for same place
3. Non competitive inhibition
   Binds to an allosteric site, but no change in substrate affinity ; changes actual effect
4. Uncompetitive inhibition
   Potentiated by the substrate, only binds to the enzyme after the enzyme has bound to substrate
5. Mixed inhibition

Basically same as noncompetitive, but inhibitor does have preference if enzyme is free or complex

6. Suicide inhibition
   The inhibitors are substrates that are derived from the enzymes normal substrate
   When the enzyme initiates catalysis (after binding to the inhibitor) that inhibitor gets modified in a way that irreversibly inhibits the enzyme
7. Accumulation of product
8. Phosphorylation (toggling of active/inactive forms)
   A phosphate is added to a protein, which affects the activity of that protein
   Glycogen phosphorylase has an active form and an inactive form
   - Phosphorylate it and it turns on

   Phosphorylation activates glycogen phosphorylase
   Phosphorylation deactivated glycogen synthase

Lecture 29

Muscle metabolism is the idea that muscles are constantly changing in size to meet the standards of their environment and is based on protein turnover. Protein turnover is the balance of synthesis and degradation. Exercise is good for us, but it threatens our body and causes it to adapt. Hypertrophy makes our body more suitable for a higher stress load. Most of these lectures are all about how enzymes, muscles, tissues and everything else changes and adapts depending on what we do to it. The hardest thing for me to understand out of all of these lectures is mTOR. mTOR is a critical regulator of protein turnover and a major hub in cells that regulate growth. There are two mTOR complexes, raptor is complex 1 and rictor is complex 2.

1. What is hypertrophy?
   Muscle metabolism: muscles are constantly changing in size, they grow and shrink to meet the demands of their environments. Muscle metabolism is based on protein turnover
   Protein turnover - the balance of synthesis and degradation
   Hypertrophy - synthesis outpaces degradation

2. Why does hypertrophy happen?
   Exercise is good for us because its bad for us; it threatens us and our body adapts to it;

3. How does it happen? It makes your body more suitable for a higher stress load

4. mTOR (mostly complex 1)
5. Combining mTOR and everything else we've learned (Henneman)

   Reception → transduction → response

   Narrative version of insulins activation of PDE
   - Insulin binds to its receptor
   - Some stuff happens, then PI3K gets activated
   - Some stuff happens, then PKB gets activated
   - PKB phosphorylates PDE
   - PDE converts cAMP to AMP
   - Thus PKA does not get activated
   - So HSL and perilipin do not hey phosphorylated
   - Lipolysis doesn't happen

Glucose transporter 4, transports glucose into the cell

Why are signaling cascades important? We need info to be relayed into our cells
Transcription / Translation

What is mTOR? A critical regulator of protein turnover, major hub in cells that regulate growth
There are two mTOR complexes
Ractor is complex 1, Rictor is complex 2

Lecture 30

mTOR has two complexes, complex 1 which grows and divides and complex 2 which is the breath of metabolism (heart/liver, survival). A complex is how a bunch of proteins travel together all in the same household. Complex 1 is raptor, the most critical regulator of skeletal muscle metabolism and has multiple phosphorylation sites. Complex 2 is rictor and promotes stress responses for survival.

A bunch of proteins travel together in a complex, different proteins all in the same "household"
Complex 2 the 'breath of metabolism", heart/liver stuff, survival
Complex 1 grow and divide

mTOR
Complex 1: mTOR enzyme, raptor (regulatory associated protein of target of rapamycin),MLST8 (mammalian lethal with SEC13 protein 8)

- The most critical regulator of skeletal muscle metabolism (protein synthesis and degradation)
- Multiple phosphorylation sites
- Rheb promotes raptor phosphorylation in a positive way
  Summary of regulatory associated protein of target of rapamycin
  - Scaffolding protein responsible for the recruitment of mTPRS phosphorylation targets
  - Multiple phosphorylation sites: can be activated or inhibited by phosphorylation
  - Rheb promotes phosphorylation (by other stuff) of at least six sites on raptor
  - AMPK phosphorylates raptor negatively (in two spots)
  - MAPK phosphorylates raptor positively

- deptor - an inhibitory protein that gets phosphorylated by mTORC1 which relieves it of its inhibitory duties

Complex 2: mTOR enzyme, rictor (rapamycin - insensitive companion of target of rapamycin), MLST 8 (mammalian lethal with SEC13 protein 8), MSIN1 (mammalian stress activated protein kinase interacting protein 1)

- More about promoting stress responses necessary for cell survival

- mTORC2 regulates: protein translation, organization of actin cytoskeletons, ion transport, and metabolism
- mTORC2 phosphorylates: PKB, SGK and PKCa

Different things affect mTOR
mTOR phosphorylates p70s6k and 4E-BP1
That promotes more (and more efficient) translation
That's hypertrophy
Translational capacity = number of ribosomes
Translational efficiency = rate of mRNA translation

Lecture 31

mTOR looks and is a lot but I know that there are some things that can turn it on and induce hypertrophy like immune/chemical and mechanical tension. If you exercise a bunch of arachidonic acid is released which will help you grow. During our lives we will all get injured at one point or another and it is important to know how your body will respond in the presence of tissue damage. When your body detects damage, neutrophils, macrophages and cytokines are all released and sent to help. One important protein released is interleukin 15. This protein changes the behavior of other cells and is released in numbers proportionate to the amount of damage seen. Another way the body helps itself is when your mechanoreceptors sense the weight of the load, the duration of tension, speed of contraction, positions, angels and everything else quantifiable. What is senses gets converted into chemical and electrical signals that trigger the cascades that result in protein synthesis

The mTOR signaling at a glance looks like an amusement park map
What are things that turn on mTOR? And induce hypertrophy

- immune/chemicals
    - Go exercise, you'll release a bunch of arachidonic acid
    - Arachidonic acid is a substrate for COX, so you synthesize a bunch of prostaglandins
    - Prostaglandins signal the MEK-ERK pathway
    - You grow

    - In the presence of tissue damage, the body responds with immune and inflammatory cells (neutrophils, macrophages, cytokines)
    - Interleukin - 15 (a cytokine)(small protein that signals stuff, changed behavior of other cells) is released in abundance during tissue damage (proportionate to the amount of damage)
    - Appears to promote protein synthesis and inhibit protein degradation
    - Interferon y (cytokine that interferes with viral replication)
    - Myostatin : myokine (muscle made cytokine) that's mostly autocrine, member of the TGF B subfamily

    - inflammatory / immune activation of cell surface receptors; prostaglandins, interleukins 2 and 15, interferon y, reactive oxygen species, wnt proteins, TNFa, myostatin (negative regulator), works through MAPK and PI3K
- Mechanical tension
    - Your mechanoreceptors are sensing the weight of the load, the duration of tension, speed of contraction, positions, angels and everything else quantifiable
    - That info (characteristics of the load) gets converted into chemical and electrical signals that trigger the cascades that result in protein synthesis
    - Structural proteins called mechanoreceptors do detecting and collect information about whatever activity you're doing

- Structural and organizational proteins have regulatory functions
- TITIN (intracellular load), integrins (extracellular load) , cadherins (intercellular)
- Titin is partly responsible for the passive elasticity of muscle
    - Functions of titin
        - Longitudinal axis stabilizers of myosin
        - Template organizer for myosin assembly
        - Provides elasticity of sarcomere
        - Mechanotransduction

- integrins and cadherins = transmembrane proteins : if you have a multicellular structure, you have cell adhesion molecules

- Endocrine system
- Nutrition

Lecture 32

Testosterone and estrogen are able to enhance myosin and actin binding processes due to modulations in calcium mobilization, resulting in a greater force and or velocity. Testosterones primary effects are steroidal/genomic, secondary effects are non genomic, regulates anabolic cell signaling cascades, activates both PKB and MAPK and inhibits LKB1. Estrogen's primary effects are steroidal/genomic , secondary effects are non genomic , phosphorylates (deactivates) tuberin, and it promotes LKB1 and AMPk. The rapid activation of protein synthesis and the growth hormone requires signaling through mTOR. This can be activated by immune/chemicals, mechanical tension, the endocrine system, and nutrition. Amino acid signaling is really important for mTOR signaling.

Testosterone - primary effects are steroidal/genomic, secondary effects are non genomic, regulates anabolic cell signaling cascades , activates both PKB and MAPK , inhibits LKB1
Estrogen - primary effects are steroidal/genomic , secondary effects are non genomic , phosphorylates (deactivates) tuberin , promotes LKB1 and AMPk

The rapid activation of protein synthesis by growth hormone requires signaling through mTOR

mTOR can be activated by endocrine system: insulin - PI3K testosterone- Ca2+ dependent MAPK activation, increased IGF signaling, inhibition of LKB1 thyroid hormone- PI3k hGH/IGH - PI3K, MAPK, JAK-STAT estrogen- inhibition of tuberin, promotion of rheb, promotion of LKB1 and AMPK

Can be activated by

- immune/chemicals - as tissues are damaged/broken down, they release chemicals. Those chemicals can initiate hypertrophic cell signaling
- Mechanical tension - mechanical signals are created when a muscle resists a load, these signals are converted to chemicals, this is called mechanotransduction and it can initiate hypertrophic cell signaling
- Endocrine system - depending on your exercise stress, several hormones can be secreted, which affect protein turnover in different ways
- Nutrition - fats: lipids have stimulatory roles, diets rich in cholesterol elicit elevations in circulating steroid hormones, androgens and estrogens have secondary effects on mTOR signaling ; carbohydrates: glycogen can bind (inhibitory) to beta subunits on AMOK, carbohydrate ingestion increases blood glucose , insulin response stimulates PI3K ; proteins: the cell is capable of recognizing intracellular amino acids, leucine is the most significant and lysine/arginine are important

Amino acid sensing is important for mTOR signaling
Within the cytosol amino acid detection and mTOR activation involves a quadruple negative

Lecture 33

Many enzymes influence athletic performance via mTOR. Some enzymes like mitochondrial enzymes. Glycolytic enzymes and those involved in fatty acid metabolism also enhance endurance metabolism. For enzymatic adaptation for strength and hypertrophy you have to reduce the supply of those endurance enhancing enzymes. One enzyme, AMPK, is very important in conditions of cellular energy deficit and its ability to inhibit metabolic pathways that consume energy. When you add ATP and it binds to AMPK, ATP hydrolysis and adenylate kinase reaction are inhibited. When AMPK is activated, it switches its pathways that produce ATP and inhibits pathways that consume ATP. mTOR is turned on by need, nutrition and assumption of nutrition.

mTOR is an enzyme (kinase), lots of enzymes influence athletic performance, many of those lots do so via mTOR

Enzymes that enhance endurance metabolism:

- Mitochondrial enzymes
- Glycolytic enzymes
- Those involved in fatty acid metabolism

Enzymatic adaptations for strength and hypertrophy

- This is about attenuating the activity (or reducing the supply) of those endurance enhancing (and simultaneously catabolic) enzyme
- ex) AMPK helps regulate the energy status of your muscles during distance running and soccer and every other endurance sport , seems to phosphorylate mTOR directly which seems to impair mTOR signaling
- AMPK is considered as a key enzyme in conditions of cellular energy deficit and is able to inhibit metabolic pathways that consume energy and reciprocally to increase mechanisms that produce energy
- AMP activated protein kinase - in normal conditions you don't have a lot of AM so AMPK is inactive, get it from exercising
- AMP binds to AMPK, that promotes it, when ATP binds to AMPK, that inhibits it
    1. ATP hydrolysis
    2. Adenylate kinase reaction
    3. ATP and AMP compete for binding on y subunits on AMPK, ATP inhibits a phosphorylation, AMP promotes it
    4. Binding of first AMP on y enhances binding of a second
    5. With two AMPs bound, an upstream kinase activates AMPK by phosphorylating the a subunit

Once AMPK is activated, it switches on pathways that produce ATP and inhibits pathways that consume ATP

- As an energy sensor, its pivot point for whole body energy balance
- Might stop mTOR because “you are ramping up the electric bill” , you're using too much energy
- AMPK in the hypothalamus : if something is inhibiting food intake, its inhibiting AMPK; if something is stimulating intake, that thing is stimulating AMPK

mTOR is turned on by need, nutrition and assumption of nutrition.

Lecture 34

There are many applications of AMPK including healing, eccentric loading, speed of contraction, size principle, blood flow restriction, aerobics + anaerobics, and specificity of adaptation. The enzyme AMPK has a lot of metabolic functions. These include turning on atrophy. It can also help increase lifespan, cardiovascular health and cancer. Having it early enhances recovery while having it late may inhibit it. Some mechanical stimuli activate PKB-mTOR-P70S6K.Workloads that involve a low load and high duration don't but workloads that involve a high load and short duration do. Blood flow also affects mTOR. Blood flow restriction like lower intensity combined with occluded blood flow induces mTOR signaling disproportionately greater than the load but the strength adaptation is lower than that expected by the amount of hypertrophy.

Applications: healing, eccentric loading , speed of contraction , size principle , blood flow restriction, aerobics + anaerobics , specificity of adaptation , the food you eat
AMPK has a lot of metabolic functions
Turns on atrophy
Helps increase lifespan, cardiovascular, cancer
AMPK and insulin regulate glucose differently
AMPK - angiogenesis = early restoration of blood, access to nutrients in diabetic patients, depending on the nature and location you might induce apoptosis
Early - enhance late -inhibit
Eccentric loading
Slow eccentric stress may generate more MGF than fast eccentric stress
Size principle - mechanotransduction belongs to the fibers that were activated, passive fibers aren't really participating in the sensation of and response to the application of mechanical loads
Some mechanical stimuli activate PKB-mTOR-P70S6K
Workloads that involve a low load and high duration don't
Workloads that involve a high load and short duration do
Blood flow restriction - lower intensity combined with occluded blood flow induces mTOR signalling disproportionately greater than the load ; specificity of adaptation though, the strength adaption is lower than that expected by the amount of hypertrophy
Alfredson protocol - if all you do is stretch, this signal probably gets filtered out, if there's an increase in tension at the same time, the signal seems to be amplified

Lecture 35

Magic sauce, filling up on pills

Trained males who took a supplement of leucine experienced muscle protein synthesis 33% higher than those who did not take it. Other supplements such as HMB stimulate protein synthesis and preserve muscle mass. HMB also might show greater improvements for an untrained person when they start working out. Arachidonic acid is another supplement that is used, which has been shown to make you sore but also leads to improvements in strength after taking it. The supplement phosphatidic acid is another one that enhances mTOR and strength. For endurance, AMPK catabolic supplements are helpful. In order to improve your performance, realize that all enzymes are trainable through behavior nutrition, supplements and drugs. You also need to identify what conditions maximize the chemical mechanical and endocrine responses in the body. You can do heavy lifting using a large range of muscle groups in order to maximize the activation (chemical, mechanical, hormonal, nutritional).

Hypertrophy is protein translations that happen to optimize your tissues to the stresses that they face by mTOR.

AMPK is responsible enzyme for stiff arm mTOR

B carbohydrates bind

To eliminate amp you use amp deaminase

Lecture 36

Your nervous system is responsible for detecting, transmitting and evaluating the environment you live in in order to identify mechanical, thermal and chemical threats. Cellular mechanisms of muscle burning and fatigue. When your nociceptors sense pH, and too many H+ ions are detected the nerves transmit a warning signal which may cause muscle pain. The high number of protons is what causes the burning sensation you feel, even those lactic acid from anaerobic metabolism is what is blamed. Fatigue does not equal fatigue because there are always differences. These things include pH, ATP:ADP ratio, phosphate, magnesium, reactive oxygen species, local inflammation, structural damage to tissues, generation of heat, carbohydrate availability, tryptophan and serotonin, central fatigue. Intense exercise can also cause it because the rate at which ATP is resynthesized is not as fast as the rate it can be used.

- You have a nervous system with nerves whose job is to detect and transmit, constantly evaluating the environment in which they live in
- Nerves are very vigilant, they don't like silence but looking for mechanical, thermal, chemical threats
- Looks at external and internal environment
- Your body might make automatic changes
- Purpose of any nerve sensing information is to maintain homeostasis
- Nociceptors sense pH
- When too many protons are sensed, the nerve transmits a warning signal
- If something hurts people change their behaviors
- pH isn't the only thing that causes muscle pain , when ur pH changes your nerve senses it and thats what causes the burning sensation, anaerobic metabolism is what gets blames (lactic acid)
- Steps that release and consume hydrogen ions: 1. Hexokinase 3. Phosphofructokinase 6. Glyceraldehyde 3- phosphate dehydrogenase
- Glycolysis (beginning from glucose) yields no protons at all
- Glycolysis (beginning from glycogen) consumes one proton
- Once glycolysis is over, there are two possible fates for the pyruvate
- If it gets converted to lactate, you consume 2 more H+ ions (1 per reaction)
- If it gets converted to acetyl CoA a H+ and Co2 ion with each pyruvate are made
- At the end of TCA cycle you have 2 carbon dioxides + 1 for pyruvate and 3 H+ ion
- A pyruvate navigating the TCA cycle is responsible for 7 H+ ions
- The largest source of metabolic byproducts is ATP hydrolysis
- Fatigue does not equal fatigue
- At the cellular level, lots of stuff causes it : pH, ATP: ADP ratio, phosphate, magnesium, reactive oxygen species, local inflammation, structural damage to tissues, generation of heat, carbohydrate availability, tryptophan and serotonin, central fatigue
- Causes: how much calcium gets released from the sarcoplasmic reticulum
    - How sensitive the muscle is to that calcium, enabling cross bridge formation
    - How much force the actual cross bridges are capable of generating
    - Central fatigue

- intense exercise can increase your rate of energy use by a lot, ATP hydrolysis happens fast enough to support that , the rate at which ATP can be resynthesized isn't as fast and it can be overwhelmed
- you need ATP to go through cross bridge cycle

ATP: ADP ratio and fatigue

1. Cross bridge cycle needs ATP
2. Sodium potassium pumps have ATPases
3. The time course of cross bridge cycling might be affected by elevated levels of ADP because of greater likelihood of strong bond site
4. ADP can outcompete ATP
5. Cerebral uptake of ammonia might influence neurotransmitter function and incite some degree of central fatigue

Lecture 37

Muscle fatigue is thought to be caused by several things, but each should be taken with a grain of salt. These things are ATP: ADP ratio, hydrogen ions, which we know result in burning but not necessarily fatigue, phosphate, magnesium, reactive oxygen species, local inflammation, generation of heat, structural damage to tissues, carbohydrate availability, tryptophan and serotonin, and central fatigue. I think the one that makes the most sense is the structural damage to tissue. Obviously, if there is structural damage there will be problems such as inflammation and pain which will lead to fatigue. I also think that another good one is heat. Everyone gets hot and tired in the summer, but there are reasons behind fatigue from heat like your enzymes no longer being able to function and a change in blood distribution. I know that there are different workouts you do like Hot Yoga and Hot Pilates that you do in a heated room, so what is the heat cut off point from there it goes from beneficial to harmful?

pH and lactate are two different things, lactate is good and does not contribute to acidosis, it helps delay the buildup of protons

- It is possible that the generation of protons might contribute to muscle fatigue
- In the presence of elevated proton concentrations
- ; sarcoplasmic reticulum/calcium kinetic can be affected , the contractile unit itself can be obstructed, which could potentially weaken the cross bridge activity

- The buildup of H+ lowers the pH interfering with the SR Ca2+ release, and cross bridge cycling and resulting in impaired muscle
- Protons have a stronger inhibitory effect on the SR Ca2+ pump than they are suggested to have on troponin C
- Muscles contractions are an electrical event, to contract the cell must depolarize