Physiology of Muscle Tissue

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2nd year

Lecture 2

Learning Objectives

- Explain behavior of skeletal muscle fibers
- Explain behavior of whole muscles
- Clarify muscle metabolism
- Explain features of cardiac and smooth muscles

Aim of this lecture

- By the end of this lecture, students should be able to clarify muscle tissue behavior and metabolism and to differentiate between types of muscle tissue.

Length-Tension Relationship

- Length – Tension Relationship - the amount of tension generated by a muscle and the force of contraction depends on how stretched or contracted it was before it was stimulated

- if overly contracted at rest, a weak contraction results
  - thick filaments too close to Z discs and can't slide

- if too stretched before stimulated, a weak contraction results
  - little overlap of thin and thick does not allow for very many cross bridges to form

- optimum resting length produces greatest force when muscle contracts
  - muscle tone – central nervous system continually monitors and adjusts the length of the resting muscle, and maintains a state of partial contraction called muscle tone
  - maintains optimum length and makes the muscles ideally ready for action

Length-Tension Relationship

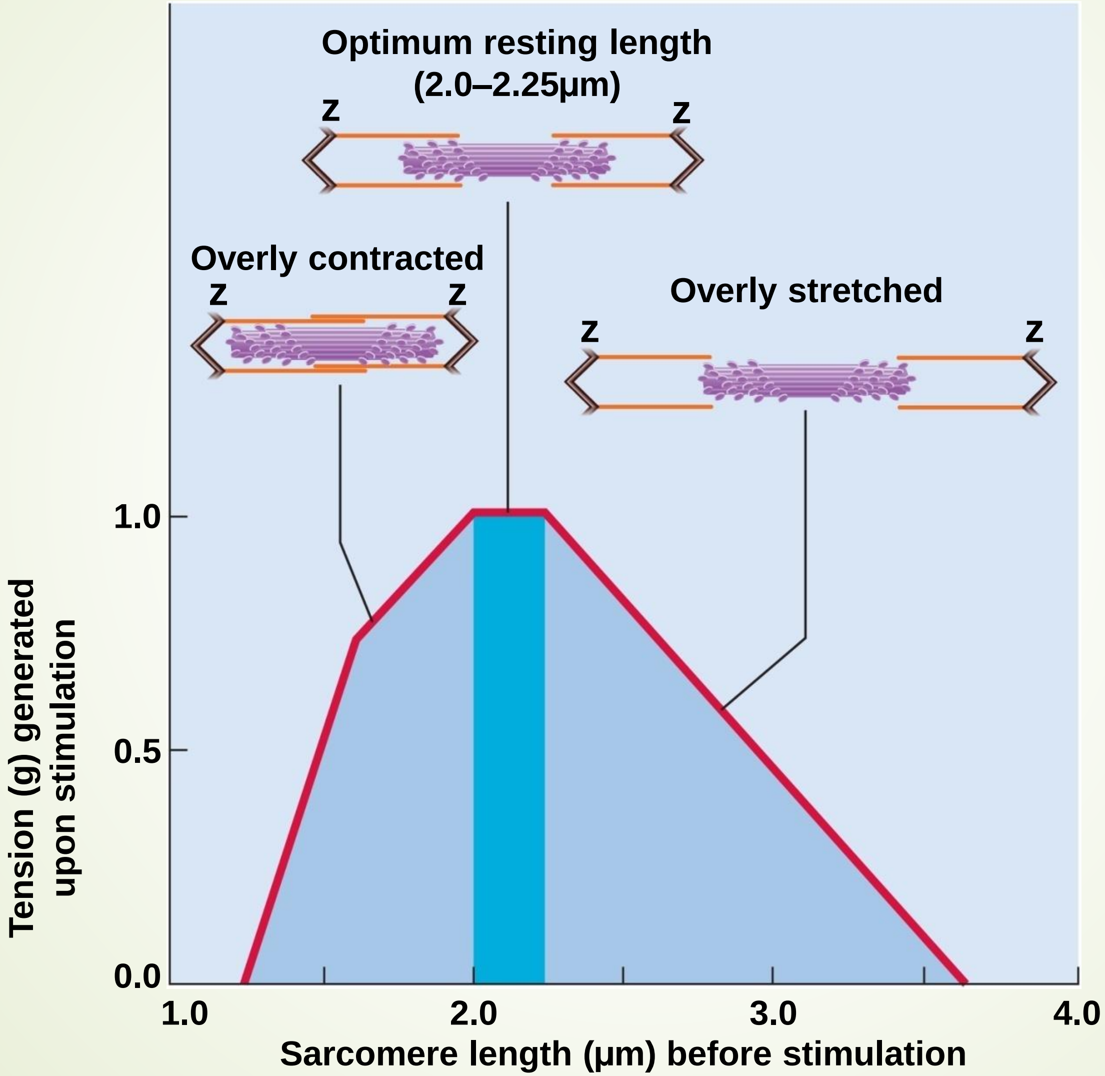

Figure 11.12

Behavior of Whole Muscles

- the response of a muscle to weak electrical stimulus seen in frog gastrocnemius - sciatic nerve preparation
- myogram – a chart of the timing and strength of a muscle's contraction
- weak, subthreshold electrical stimulus causes no contraction
- threshold - the minimum voltage necessary to generate an action potential in the muscle fiber and produce a contraction
  - twitch – a quick cycle of contraction when stimulus is at threshold or higher

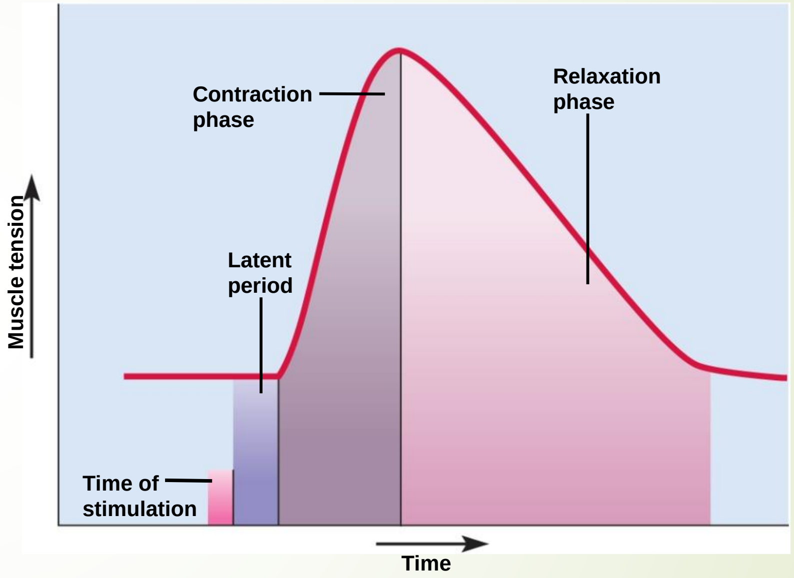

Figure 11.13

Phases of a Twitch Contraction

- latent period - 2 msec delay between the onset of stimulus and onset of twitch response
  - time required for excitation, excitation-contraction coupling and tensing of elastic components of the muscle
  - internal tension – force generated during latent period and no shortening of the muscle occurs
- contraction phase – phase in which filaments slide and the muscle shortens
  - once elastic components are taut, muscle begins to produce external tension – in muscle that moves a load
  - short-lived phase
- relaxation phase - SR quickly reabsorbs Ca^{+2}, myosin releases the thin filaments and tension declines
  - muscle returns to resting length
  - entire twitch lasts from 7 to 100 msec

Contraction Strength of Twitches

- at subthreshold stimulus – no contraction at all
- at threshold intensity and above - a twitch is produced
  - twitches caused by increased voltage are no stronger than those at threshold
- not exactly true that muscle fiber obeys an all-or-none law -contracting to its maximum or not at all
  - electrical excitation of a muscle follows all-or-none law
  - not true that muscle fibers follow the all or none law
  - twitches vary in strength depending upon:
    - stimulus frequency - stimuli arriving closer together produce stronger twitches
    - concentration of Ca^{+2} in sarcoplasm can vary the frequency
    - how stretched muscle was before it was stimulated
    - temperature of the muscles – warmed-up muscle contracts more strongly – enzymes work more quickly
    - lower than normal pH of sarcoplasm weakens the contraction - fatigue
    - state of hydration of muscle affects overlap of thick & thin filaments
- muscles need to be able to contract with variable strengths for different tasks

Recruitment and Stimulus Intensity

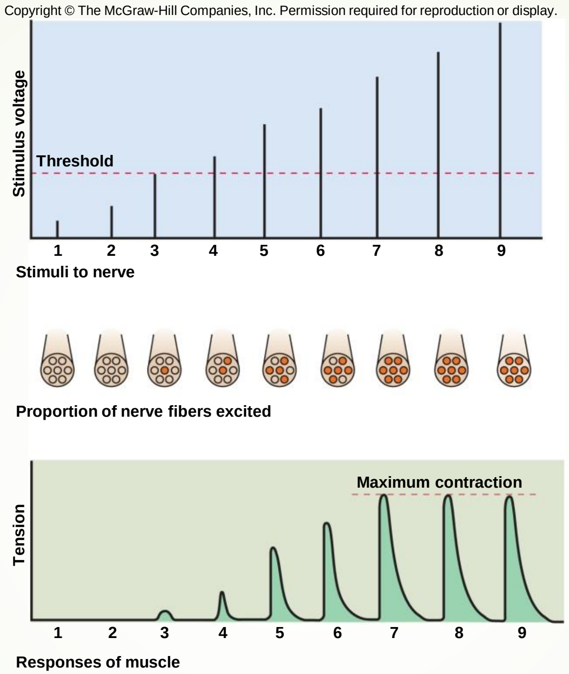

Figure 11.14

- stimulating the nerve with higher and higher voltages produces stronger contractions
  - higher voltages excite more and more nerve fibers in the motor nerve which stimulates more and more motor units to contract
- recruitment or multiple motor unit (MMU) summation – the process of bringing more motor units into play

Twitch Strength & Stimulus Frequency

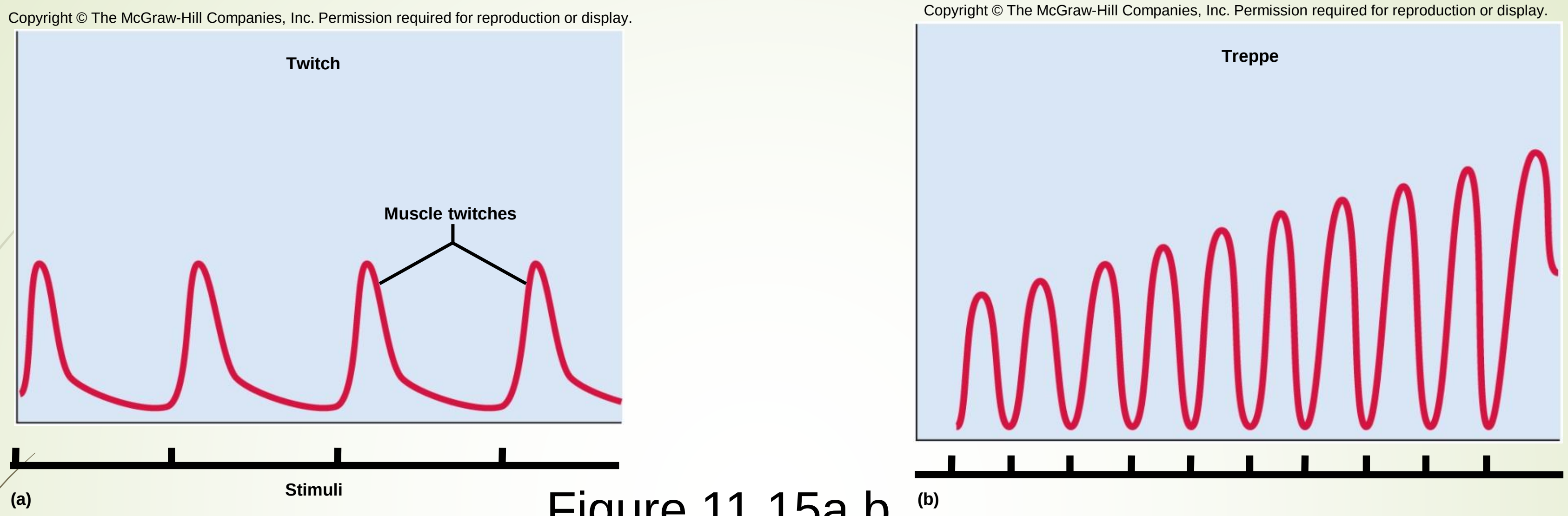

Figure 11.15a,b

- when stimulus intensity (voltage) remains constant twitch strength can vary with the stimulus frequency
- up to 10 stimuli per second
  - each stimulus produces identical twitches and full recovery between twitches
- 10-20 stimuli per second produces treppe (staircase) phenomenon
  - muscle still recovers fully between twitches, but each twitch develops more tension than the one before
  - stimuli arrive so rapidly that the SR does not have time between stimuli to completely reabsorb all of the Ca^{+2} it released
  - Ca^{+2} concentration in the cytosol rises higher and higher with each stimulus causing subsequent twitches to be stronger
  - heat released by each twitch cause muscle enzymes such as myosin ATPase to work more efficiently and produce stronger twitches as muscle warms up

Incomplete and Complete Tetanus

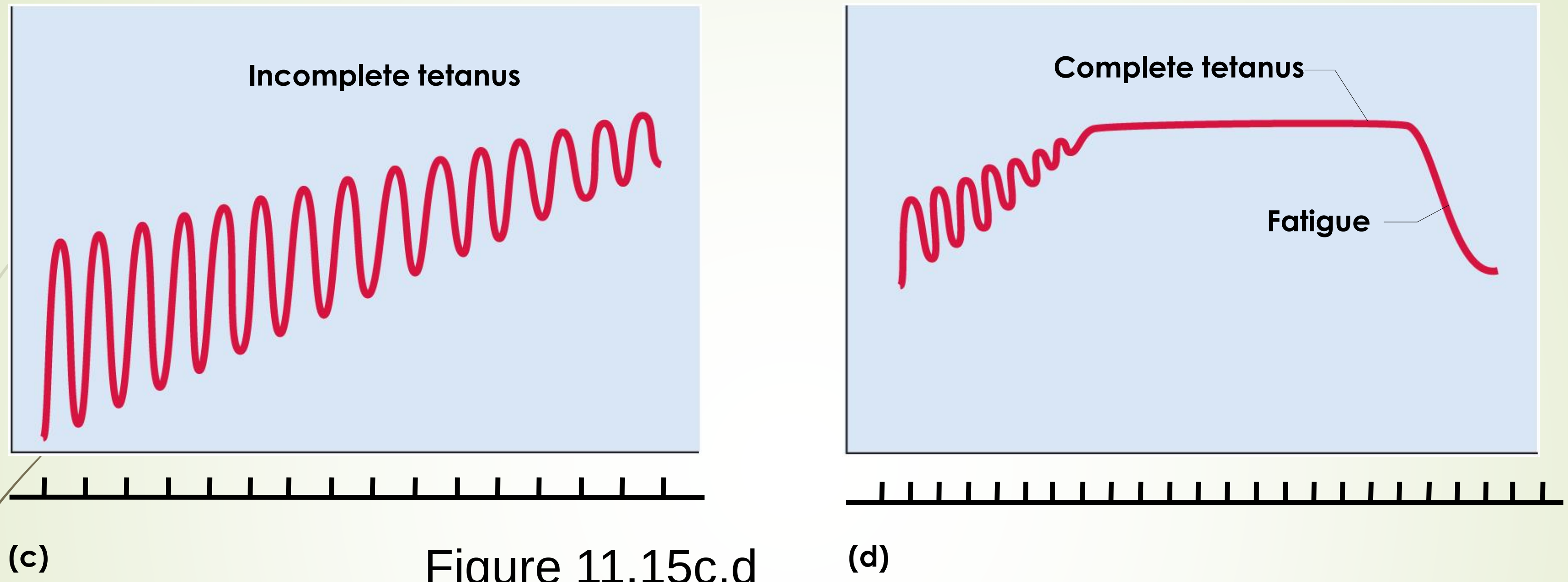

Figure 11.15c,d

- 20-40 stimuli per second produces incomplete tetanus
  - each new stimulus arrives before the previous twitch is over
  - new twitch "rides piggy-back" on the previous one generating higher tension
  - temporal summation – results from two stimuli arriving close together
  - wave summation – results from one wave of contraction added to another
  - each twitch reaches a higher level of tension than the one before
  - muscle relaxes only partially between stimuli
  - produces a state of sustained fluttering contraction called incomplete tetanus

Incomplete and Complete Tetanus

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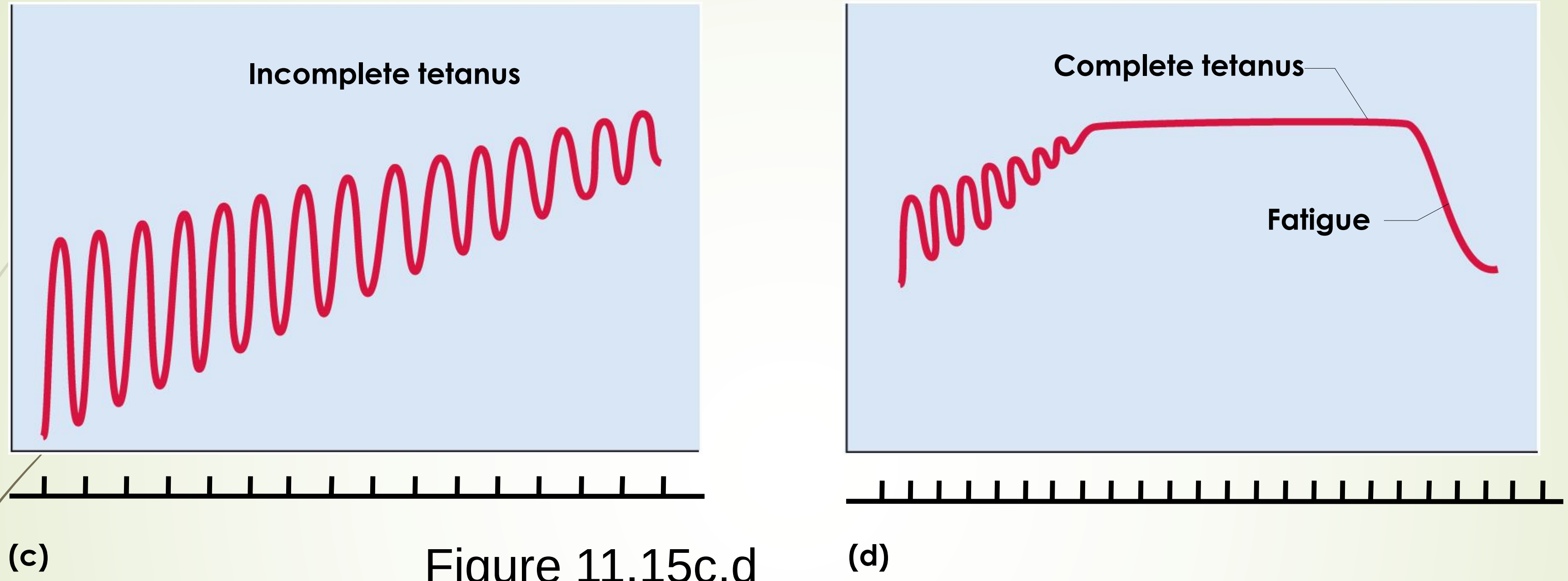
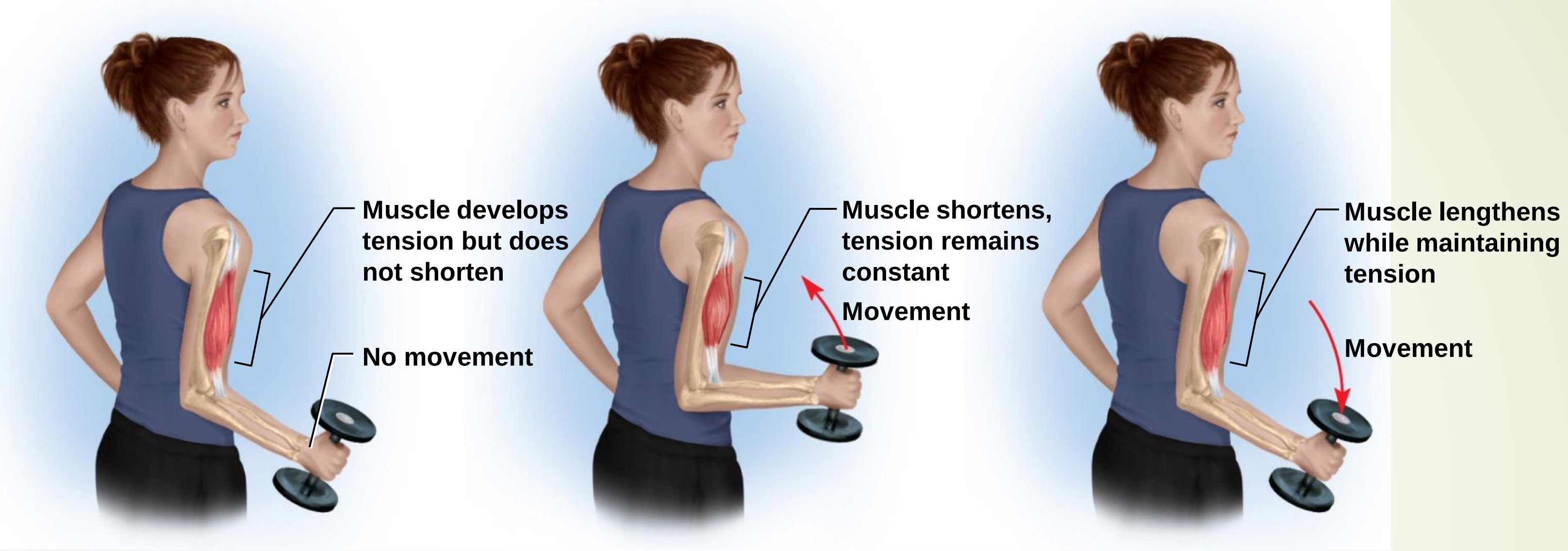


Figure 11.15c,d

- 40-50 stimuli per second produces complete tetanus
  - muscle has no time to relax at all between stimuli
  - twitches fuse to a smooth, prolonged contraction called complete tetanus
  - a muscle in complete tetanus produces about four times the tension as a single twitch
  - rarely occurs in the body, which rarely exceeds 25 stimuli per second
  - smoothness of muscle contractions is because motor units function asynchronously
    - when one motor unit relaxes, another contracts and takes over so the muscle does not lose tension

Isometric and Isotonic Contractions



(a) Isometric contraction (b) Isotonic concentric contraction (c) Isotonic eccentric contraction

Figure 11.16

- isometric muscle contraction
  - muscle is producing internal tension while an external resistance causes it to stay the same length or become longer
  - can be a prelude to movement when tension is absorbed by elastic component of muscle
  - important in postural muscle function and antagonistic muscle joint stabilization
- isotonic muscle contraction
  - muscle changes in length with no change in tension
  - concentric contraction – muscle shortens while maintains tension
  - eccentric contraction – muscle lengthens as it maintains tension

Isometric and Isotonic Phases of Contraction

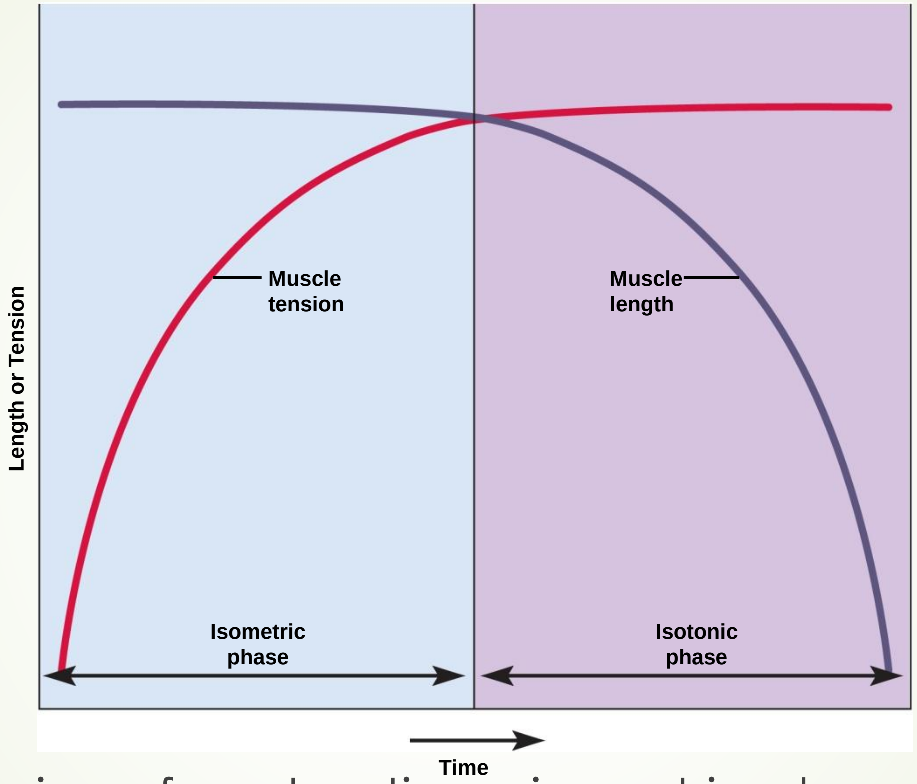


Figure 11.17

- at the beginning of contraction – isometric phase
  - muscle tension rises but muscle does not shorten
- when tension overcomes resistance of the load
  - tension levels off
- muscle begins to shorten and move the load – isotonic phase

Muscle Metabolism

- all muscle contraction depends on ATP
- ATP supply depends on availability of:
  - oxygen
  - organic energy sources such as glucose and fatty acids
- two main pathways of ATP synthesis
  - anaerobic fermentation
    - enables cells to produce ATP in the absence of oxygen
    - yields little ATP and toxic lactic acid, a major factor in muscle fatigue
  - aerobic respiration
    - produces far more ATP
    - less toxic end products (CO_2 and water)
    - requires a continual supply of oxygen

Modes of ATP Synthesis During Exercise

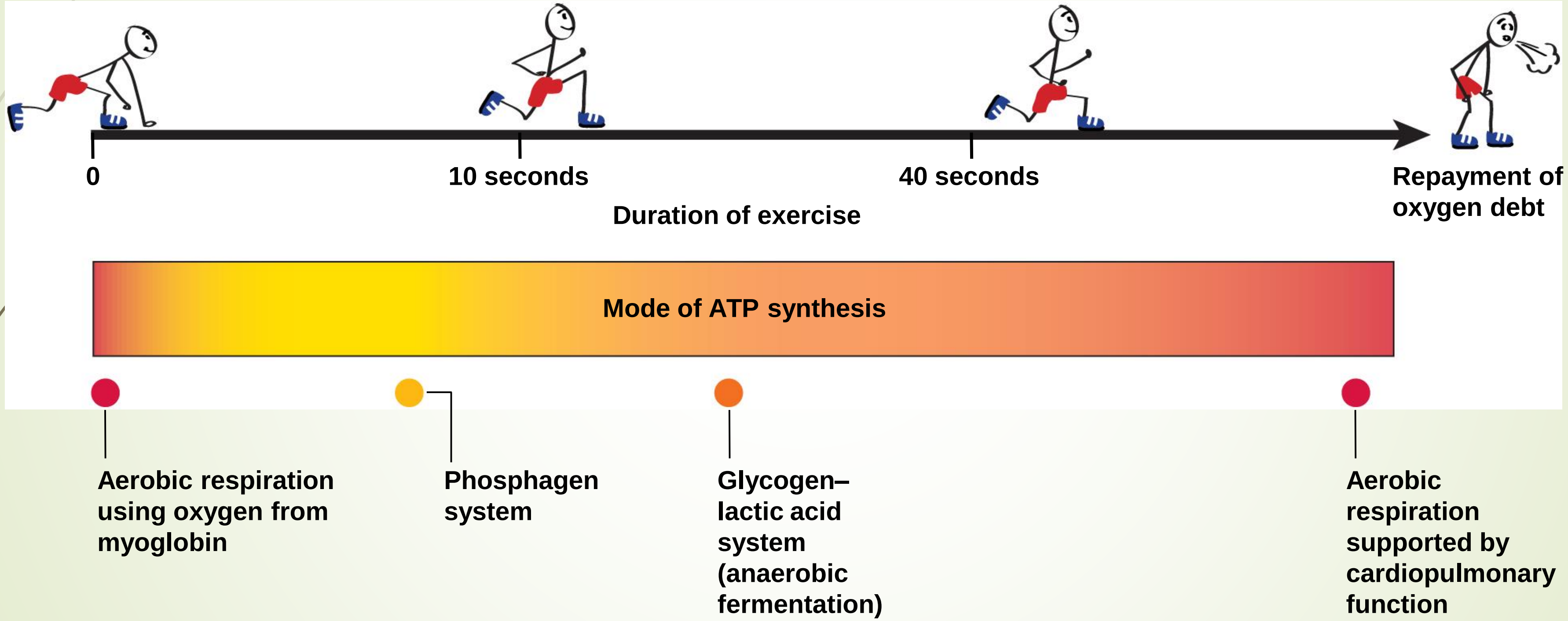


Figure 11.18

Immediate Energy Needs

- short, intense exercise (100 m dash)
  - oxygen need is briefly supplied by myoglobin for a limited amount of aerobic respiration at onset – rapidly depleted
  - muscles meet most of ATP demand by borrowing phosphate groups (P_i) from other molecules and transferring them to ADP
- two enzyme systems control these phosphate transfers
  - myokinase – transfers P_i from one ADP to another converting the latter to ATP
  - creatine kinase – obtains P_i from a phosphate-storage molecule creatine phosphate (CP)
    - fast-acting system that helps maintain the ATP level while other ATP-generating mechanisms are being activated
- phosphagen system – ATP and CP collectively
  - provides nearly all energy used for short bursts of intense activity
    - one minute of brisk walking
    - 6 seconds of sprinting or fast swimming
    - important in activities requiring brief but maximum effort
      - football, baseball, and weight lifting

Immediate Energy Needs

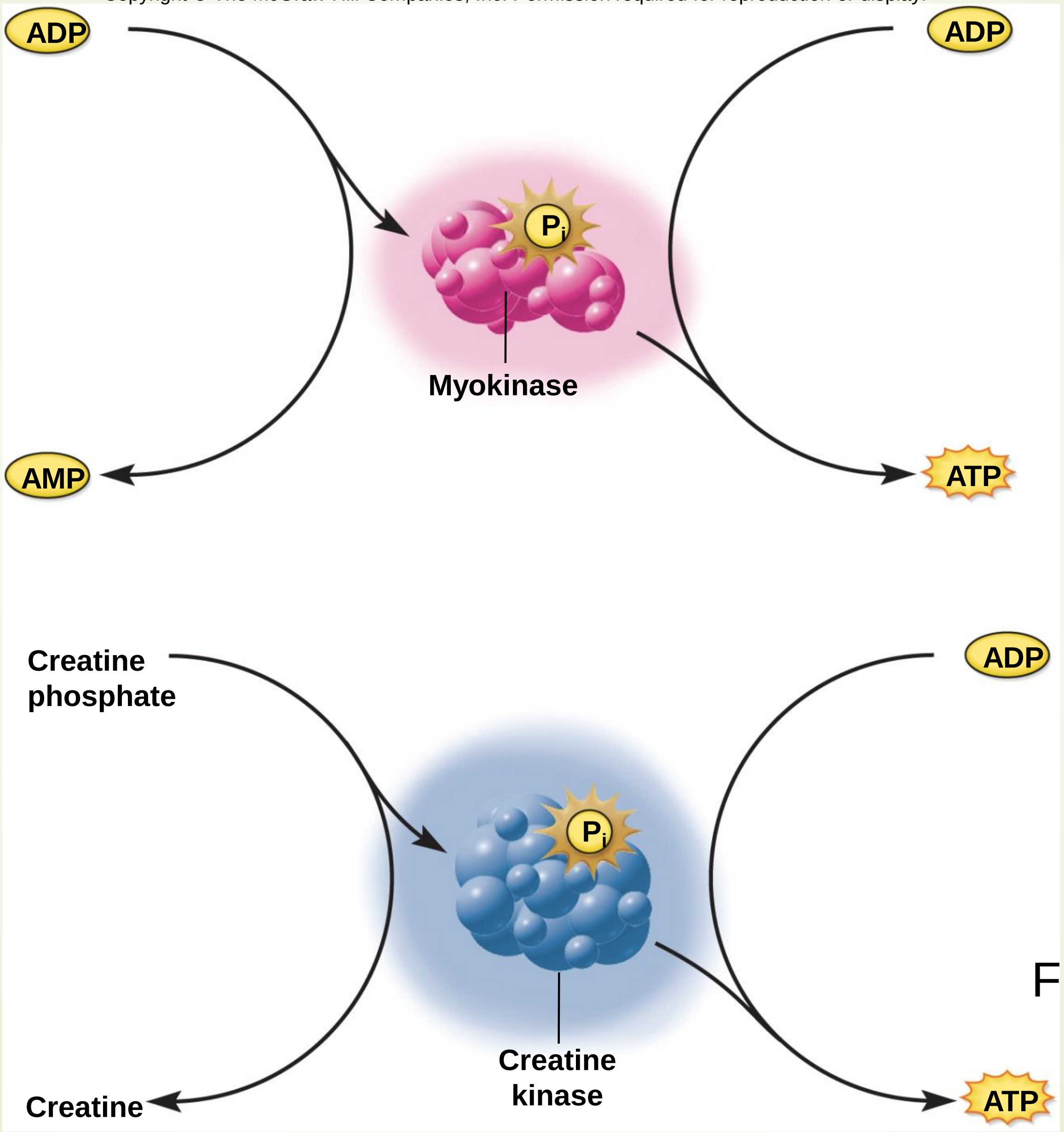


Figure 11.19

Short-Term Energy Needs

- as the phosphagen system is exhausted
- muscles shift to anaerobic fermentation
  - muscles obtain glucose from blood and their own stored glycogen
  - in the absence of oxygen, glycolysis can generate a net gain of 2 ATP for every glucose molecule consumed
  - converts glucose to lactic acid
- glycogen-lactic acid system – the pathway from glycogen to lactic acid
- produces enough ATP for 30 – 40 seconds of maximum activity

Long-Term Energy Needs

- after 40 seconds or so, the respiratory and cardiovascular systems “catch up” and deliver oxygen to the muscles fast enough for aerobic respiration to meet most of the ATP demands
- aerobic respiration produces 36 ATP per glucose
  - efficient means of meeting the ATP demands of prolonged exercise
  - one’s rate of oxygen consumption rises for 3 to 4 minutes and levels off to a steady state in which aerobic ATP production keeps pace with demand
  - little lactic acid accumulates under steady state conditions
  - depletion of glycogen and blood glucose, together with the loss of fluid and electrolytes through sweating, set limits on endurance and performance even when lactic acid does not

Fatigue

- muscle fatigue - progressive weakness and loss of contractility from prolonged use of the muscles
  - repeated squeezing of rubber ball
  - holding text book out level to the floor

- causes of muscle fatigue
  - ATP synthesis declines as glycogen is consumed
  - ATP shortage slows down the Na^+ - K^+ pumps
    - compromises their ability to maintain the resting membrane potential and excitability of the muscle fibers
  - lactic acid lowers pH of sarcoplasm
    - inhibits enzymes involved in contraction, ATP synthesis, and other aspects of muscle function
  - release of K^+ with each action potential causes the accumulation of extracellular K^+
    - hyperpolarizes the cell and makes the muscle fiber less excitable
  - motor nerve fibers use up their ACh
    - less capable of stimulating muscle fibers – junctional fatigue
  - central nervous system, where all motor commands originate, fatigues by unknown processes, so there is less signal output to the skeletal muscles

Endurance

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

Oxygen Debt

- heavy breathing continues after strenuous exercise
  - excess post-exercise oxygen consumption (EPOC) – the difference between the resting rate of oxygen consumption and the elevated rate following exercise.
  - typically about 11 liters extra is needed after strenuous exercise
  - repaying the oxygen debt
- needed for the following purposes:
  - replace oxygen reserves depleted in the first minute of exercise
    - oxygen bound to myoglobin and blood hemoglobin, oxygen dissolved in blood plasma and other extracellular fluid, and oxygen in the air in the lungs
  - replenishing the phosphagen system
    - synthesizing ATP and using some of it to donate the phosphate groups back to creatine until resting levels of ATP and CP are restored
  - oxidizing lactic acid
    - 80% of lactic acid produced by muscles enter bloodstream
    - reconverted to pyruvic acid in the kidneys, cardiac muscle, and especially the liver
    - liver converts most of the pyruvic acid back to glucose to replenish the glycogen stores of the muscle.
  - serving the elevated metabolic rate
    - occurs while the body temperature remains elevated by exercise and consumes more oxygen

Beating Muscle Fatigue

- Taking oral creatine increases level of creatine phosphate in muscle tissue and increases speed of ATP regeneration
  - useful in burst type exercises – weight-lifting
  - risks are not well known
    - muscle cramping, electrolyte imbalances, dehydration, water retention, stroke
    - kidney disease from overloading kidney with metabolite creatinine
- carbohydrate loading – dietary regimen
  - packs extra glycogen into muscle cells
  - extra glycogen is hydrophilic and adds 2.7 g water/ g glycogen
    - athletes feel sense of heaviness outweighs benefits of extra available glycogen

Physiological Classes of Muscle Fibers

- slow oxidative (SO), slow-twitch, red, or type I fibers
  - abundant mitochondria, myoglobin and capillaries - deep red color
    - adapted for aerobic respiration and fatigue resistance
      - relative long twitch lasting about 100 msec
      - soleus of calf and postural muscles of the back
- fast glycolytic (FG), fast-twitch, white, or type II fibers
  - fibers are well adapted for quick responses, but not for fatigue resistance
  - rich in enzymes of phosphagen and glycogen-lactic acid systems generate lactic acid causing fatigue
  - poor in mitochondria, myoglobin, and blood capillaries which gives pale appearance
    - SR releases & reabsorbs Ca^{+2} quickly so contractions are quicker

      (7.5 msec/twitch)
      - extrinsic eye muscles, gastrocnemius and biceps brachii
- ratio of different fiber types have genetic predisposition – born sprinter
  - muscles differ in fiber types - gastrocnemius is predominantly FG for quick movements (jumping)
  - soleus is predominantly SO used for endurance (jogging)

FG and SO Muscle Fibers

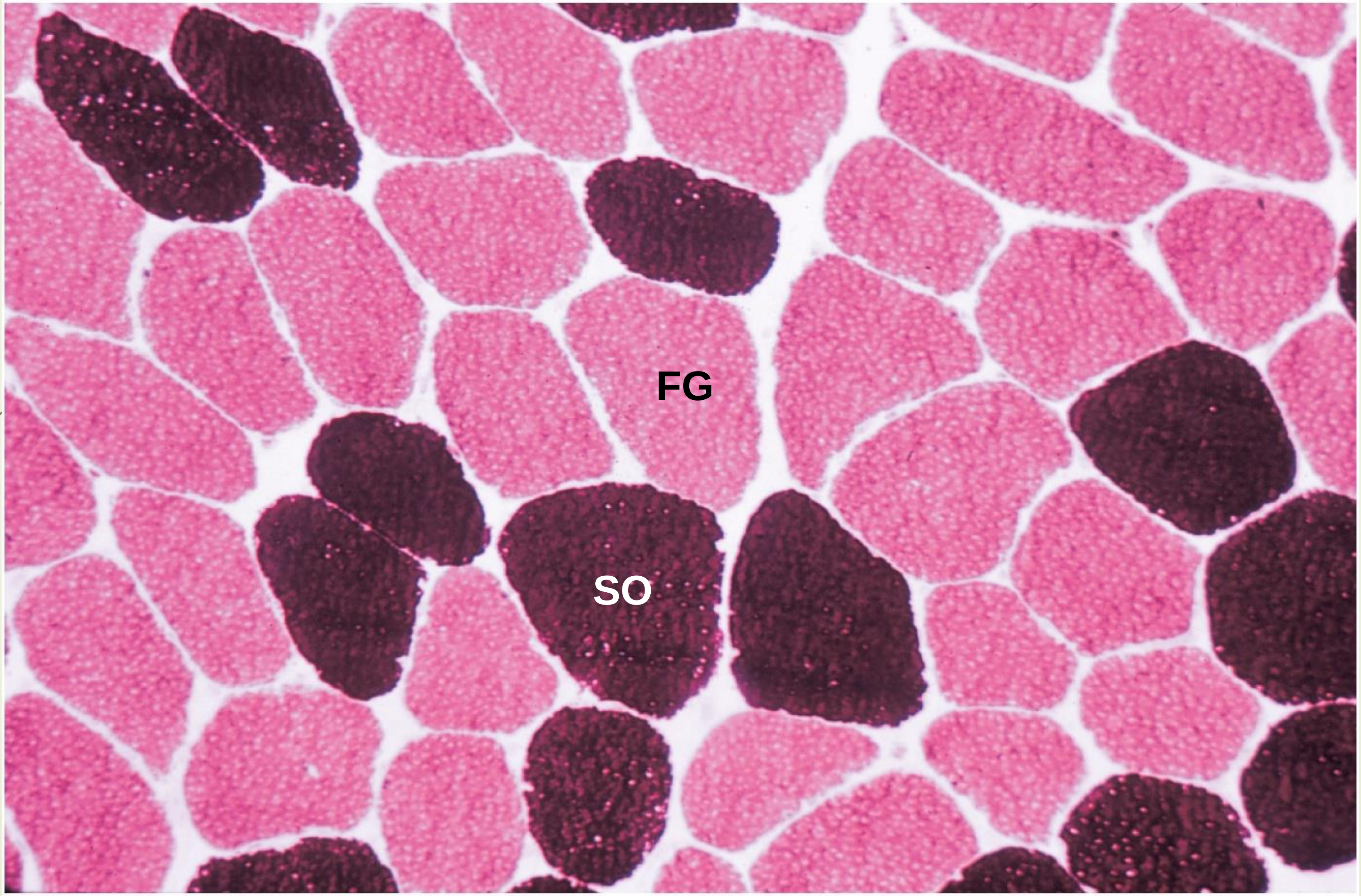


Figure 11.20

Strength and Conditioning

- muscles can generate more tension than the bones and tendons can withstand
- muscular strength depends on:
  - primarily on muscle size
    - a muscle can exert a tension of 3 or 4 kg / cm^2 of cross-sectional area
  - fascicle arrangement
    - pennate are stronger than parallel, and parallel stronger than circular
  - size of motor units
    - larger the motor unit the stronger the contraction
  - multiple motor unit summation – recruitment
    - when stronger contraction is required, the nervous system activates more motor units
  - temporal summation
    - nerve impulses usually arrive at a muscle in a series of closely spaced action potentials
    - the greater the frequency of stimulation, the more strongly a muscle contracts
  - length – tension relationship
    - a muscle resting at optimal length is prepared to contract more forcefully than a muscle that is excessively contracted or stretched
  - fatigue
    - fatigued muscles contract more weakly than rested muscles

Strength and Conditioning

- resistance training (weight lifting)
  - contraction of a muscles against a load that resist movement
  - a few minutes of resistance exercise a few times a week is enough to stimulate muscle growth
  - growth is from cellular enlargement
  - muscle fibers synthesize more myofilaments and myofibrils and grow thicker
- endurance training (aerobic exercise)
  - improves fatigue resistant muscles
  - slow twitch fibers produce more mitochondria, glycogen, and acquire a greater density of blood capillaries
  - improves skeletal strength
  - increases the red blood cell count and oxygen transport capacity of the blood
  - enhances the function of the cardiovascular, respiratory, and nervous systems

Cardiac Muscle

- limited to the heart where it functions to pump blood
- required properties of cardiac muscle
  - contraction with regular rhythm
  - muscle cells of each chamber must contract in unison
  - contractions must last long enough to expel blood
  - must work in sleep or wakefulness, with out fail, and without conscious attention
  - must be highly resistant to fatigue

Cardiac Muscle

- characteristics of cardiac muscle cells
  - striated like skeletal muscle, but myocytes (cardiocytes) are shorter and thicker
  - each myocyte is joined to several others at the uneven, notched linkages – intercalated discs
    - appear as thick dark lines in stained tissue sections
    - electrical gap junctions allow each myocyte to directly stimulate its neighbors
    - mechanical junctions that keep the myocytes from pulling apart
  - sarcoplasmic reticulum less developed, but T tubules are larger and admit supplemental Ca^{2+} from the extracellular fluid
  - damaged cardiac muscle cells repair by fibrosis
    - a little mitosis observed following heart attacks
    - not in significant amounts to regenerate functional muscle

Cardiac Muscle

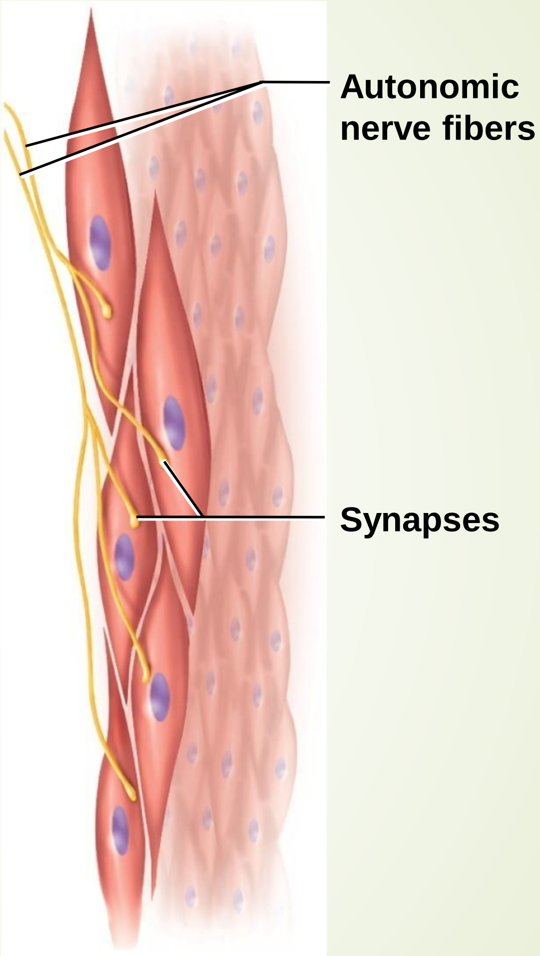
- can contract without need for nervous stimulation
  - contains a built-in pacemaker that rhythmically sets off a wave of electrical excitation
  - wave travels through the muscle and triggers contraction of heart chambers
  - autorhythmic – because of its ability to contract rhythmically and independently
- autonomic nervous system does send nerve fibers to the heart
  - can increase or decrease heart rate and contraction strength
- very slow twitches - does not exhibit quick twitches like skeletal muscle
  - maintains tension for about 200 to 250 msec
  - gives the heart time to expel blood
- uses aerobic respiration almost exclusively
  - rich in myoglobin and glycogen
  - has especially large mitochondria
    - 25% of volume of cardiac muscle cell
    - 2% of skeletal muscle cell with smaller mitochondria
- very adaptable with respect to fuel used
- very vulnerable to interruptions of oxygen supply
- highly fatigue resistant

Smooth Muscle

- composed of myocytes that have a fusiform shape
- there is only one nucleus, located near the middle of the cell
- no visible striations
  - reason for the name ‘smooth muscle’
  - thick and thin filaments are present, but not aligned with each other
- z discs are absent and replaced by dense bodies
  - well ordered array of protein masses in cytoplasm
  - protein plaques on the inner face of the plasma membrane
- cytoplasm contains extensive cytoskeleton of intermediate filament
  - attach to the membrane plaques and dense bodies
  - provide mechanical linkages between the thin myofilaments and the plasma membrane
- sarcoplasmic reticulum is scanty and there are no T tubules
- Ca^{2+} needed for muscle contraction comes from the ECF by way of Ca^{2+} channels in the sarcolemma
- some smooth muscles lack nerve supply, while others receive autonomic fibers, not somatic motor fibers as in skeletal muscle
- capable of mitosis and hyperplasia
- injured smooth muscle regenerates well

2 Types of Smooth Muscle

- multiunit smooth muscle
  - occurs in some of the largest arteries and pulmonary air passages, in piloerector muscles of hair follicle, and in the iris of the eye
  - autonomic innervation similar to skeletal muscle
    - terminal branches of a nerve fiber synapse with individual myocytes and form a motor unit
    - each motor unit contracts independently of the others

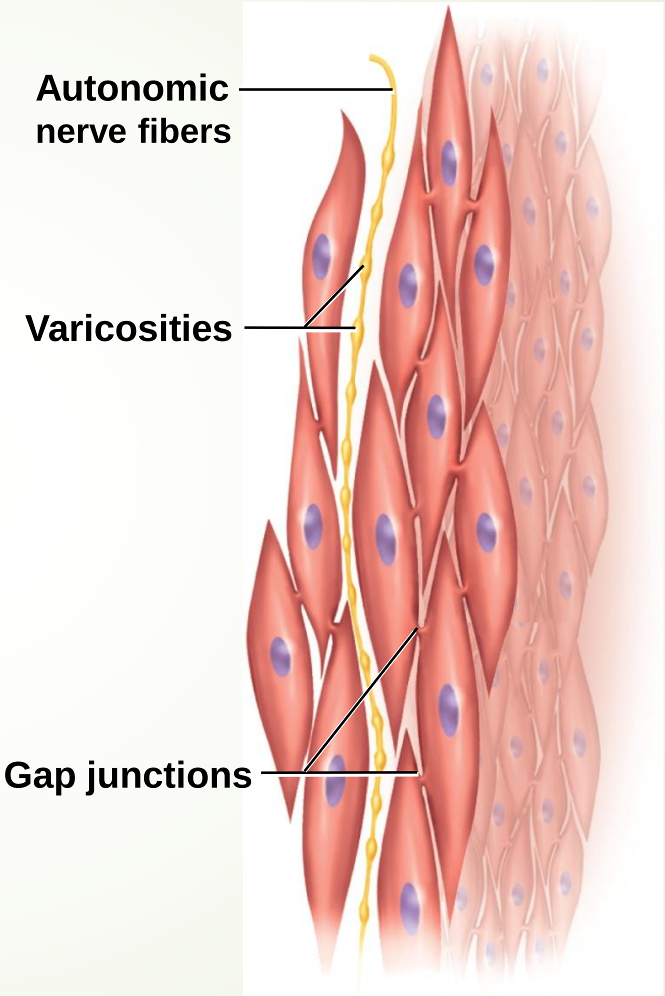


(a) Multiunit smooth muscle

Figure 11.21a

2 Types of Smooth Muscle

- single-unit smooth muscle
  - more widespread
  - occurs in most blood vessels, in the digestive, respiratory, urinary, and reproductive tracts – also called visceral muscle
    - often in two layers
      - inner circular
      - outer longitudinal
  - myocytes of this cell type are electrically coupled to each other by gap junctions
  - they directly stimulate each other and a large number of cells contract as a single unit



(b) Single-unit smooth muscle

Figure 11.21b

Layers of Visceral Muscle

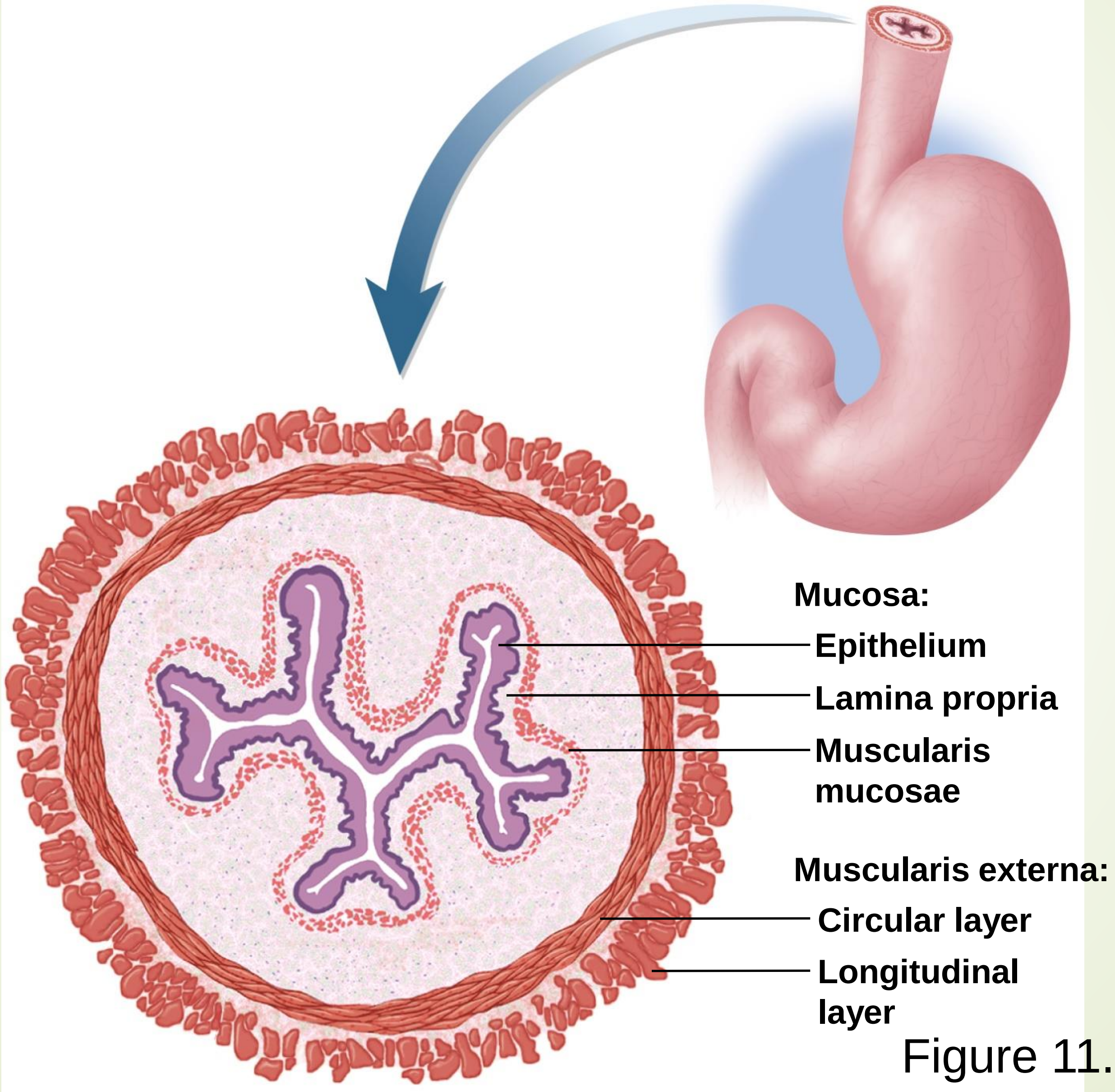


Figure 11.22

Stimulation of Smooth Muscle

- smooth muscle is involuntary and can contract without nervous stimulation
  - can contract in response to chemical stimuli
    - hormones, carbon dioxide, low pH, and oxygen deficiency
    - in response to stretch
    - single unit smooth muscle in stomach and intestines has pacemaker cells that set off waves of contraction throughout the entire layer of muscle
- most smooth muscle is innervated by autonomic nerve fibers
  - can trigger and modify contractions
  - stimulate smooth muscle with either acetylcholine or norepinephrine
  - can have contrasting effects
    - relax the smooth muscle of arteries
    - contract smooth muscles of the bronchioles
- in single unit smooth, each autonomic nerve fibers has up to 20,000 beadlike swelling called varicosities
  - each contains synaptic vesicles and a few mitochondria
  - nerve fiber passes amid several myocytes and stimulates all of them at once when it releases its neurotransmitter
    - no motor end plates, but receptors scattered throughout the surface – diffuse junctions – no one-to-one relationship between nerve fiber and myocyte

Stimulation of Smooth Muscle

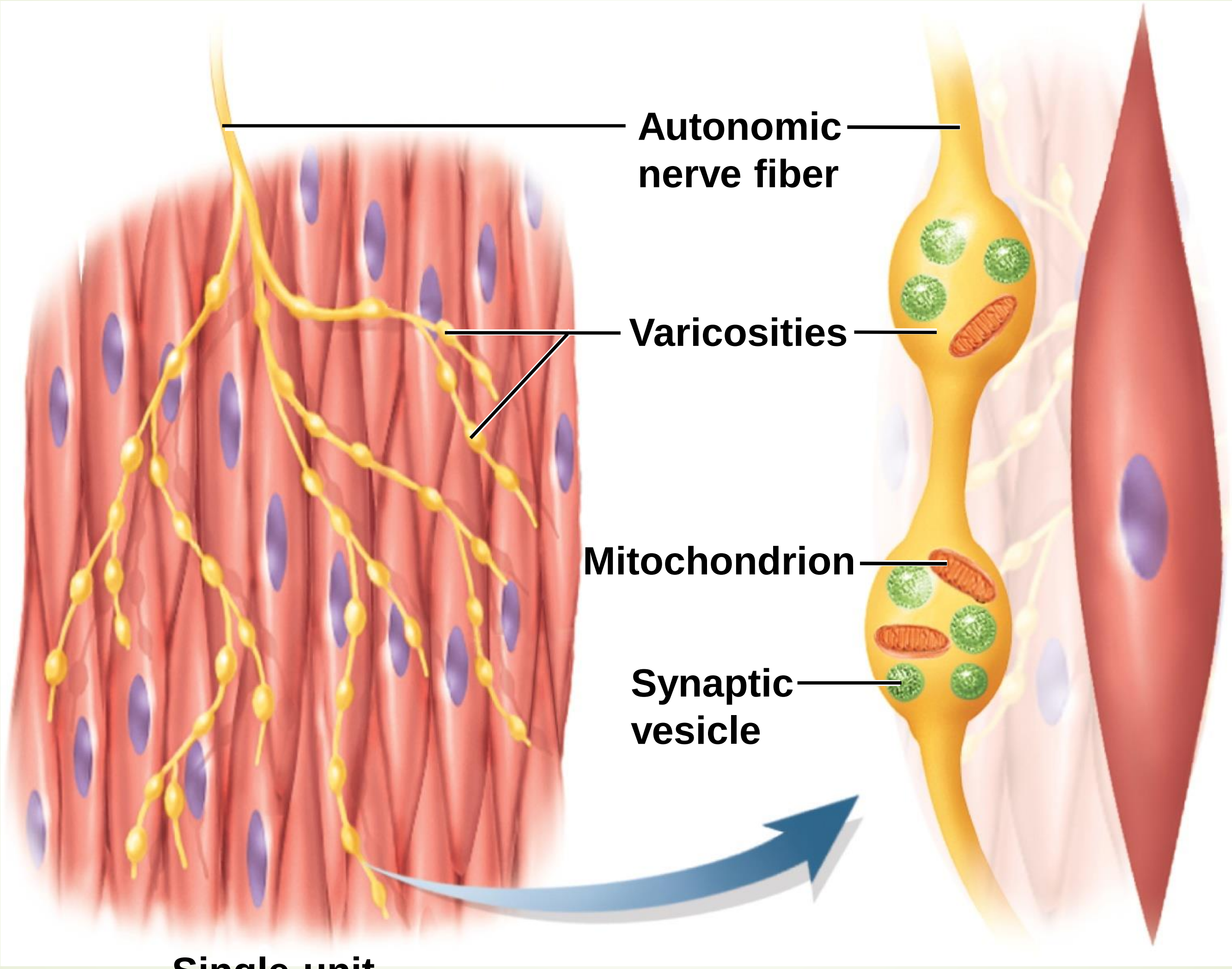


Figure 11.23

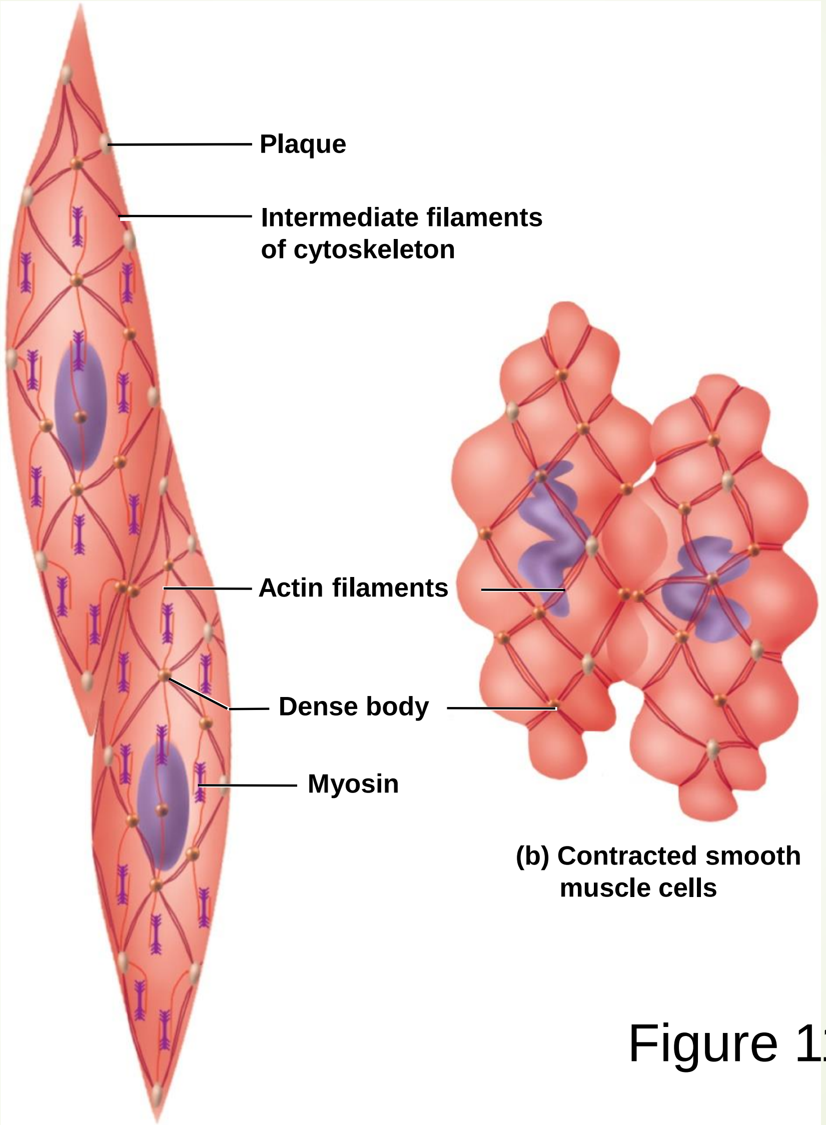
Contraction and Relaxation

- contraction is triggered by Ca^{+2}, energized by ATP, and achieved by sliding thin past thick filaments
- contraction begins in response to Ca^{+2} that enters the cell from ECF, a little internally from sarcoplasmic reticulum
  - voltage, ligand, and mechanically-gated (stretching) Ca^{+2} channels open to allow Ca^{+2} to enter cell
- calcium binds to calmodulin on thick filaments
  - activates myosin light-chain kinase – adds phosphate to regulatory protein on myosin head
  - and myosin ATPase, hydrolyzing ATP
    - enables myosin similar power and recovery strokes like skeletal muscle
  - thick filaments pull on thin ones, thin ones pull on dense bodies and membrane plaques
  - force is transferred to plasma membrane and entire cell shortens
  - puckers and twists like someone wringing out a wet towel

Contraction and Relaxation

- contraction and relaxation very slow in comparison to skeletal muscle
  - latent period in skeletal 2 msec, smooth muscle 50 - 100 msec
  - tension peaks at about 500 msec (0.5 sec)
  - declines over a period of 1 – 2 seconds
  - slows myosin ATPase enzyme and slow pumps that remove Ca^{+2}
  - Ca^{+2} binds to calmodulin instead of troponin
    - activates kinases and ATPases that hydrolyze ATP
- latch-bridge mechanism is resistant to fatigue
  - heads of myosin molecules do not detach from actin immediately
  - do not consume any more ATP
  - maintains tetanus tonic contraction (smooth muscle tone)
    - arteries – vasomotor tone   intestinal tone
  - makes most of its ATP aerobically

Contraction of Smooth Muscle



(b) Contracted smooth muscle cells

Figure 11.24

(a) Relaxed smooth muscle cells

Stretching Smooth Muscle

- stretch can open mechanically-gated calcium channels in the sarcolemma causing contraction
  - peristalsis – waves of contraction brought about by food distending the esophagus or feces distending the colon
    - propels contents along the organ
- stress-relaxation response (receptive relaxation) - helps hollow organs gradually fill (urinary bladder)
  - when stretched, tissue briefly contracts then relaxes – helps prevent emptying while filling

Contraction and Stretching

- skeletal muscle cannot contract forcefully if overstretched
- smooth muscle contracts forcefully even when greatly stretched
  - allows hollow organs such as the stomach and bladder to fill and then expel their contents efficiently
- smooth muscle can be anywhere from half to twice its resting length and still contract powerfully
- three reasons:
  - there are no z discs, so thick filaments cannot butt against them and stop contraction
  - since the thick and thin filaments are not arranged in orderly sarcomeres, stretching does not cause a situation where there is too little overlap for cross-bridges to form
  - the thick filaments of smooth muscle have myosin heads along their entire length, so cross-bridges can form anywhere
- plasticity – the ability to adjust its tension to the degree of stretch
  - a hollow organ such as the bladder can be greatly stretched yet not become flabby when it is empty