CHAPTER VI

PHYSIOLOGY OF MUSCLES

Histology of muscles—*Vide* pages 52–65.

Composition of skeletal muscles

Water—75%.
Solid—25%

I. **Proteins**—20%. **Actin** and **myosin** form about half the total muscle protein. Myosin, actin and their complex **actomyosin, tropomyosin A** (*purified*) and **B** (*native* or *Bailey's tropomyosin* or *metin*), **troponin, α-actinin, β-actinin** and *M-band filament* (nature of the latter protein is not known) have been isolated. Proteolytic enzymes break myosin into *light meromyosin* (straight helical body portion) and *heavy meromyosin* (head portion). This heavy meromyosin can again be divided into *heavy meromyosin subfragment II* (neck portion) and *heavy meromyosin subfragment I* (proper head portion) that contains the ATP-*ase* activity of the myosin. Actin may be of **G-actin** or **F-actin** form. Actin also contains **tropomyosin** and **troponin.** *Actomyosin is a complex of three myosin and one actin.* Tropomyosin B (native) contains tropomyosin A and troponin. Tropomyosin and α-actinin are found at the Z-disc. **Myogen** is a protein of albumin nature and can be differentiated as **myosin A** and **B.** Enzymatic property is attributed to myosin A fraction. **Myoalbumin** is another protein found in sarcoplasm. **Myoglobin** is a conjugated protein and also named as *muscle haemoglobin.* Though it is functionally similar, still it differs from blood haemoglobin by molecular weight, isoelectric pH and absorption bands. The iron content is same in both cases. Several other proteins over and above the names already mentioned, are obtained in muscles in small amounts which are **component-C, delta protein, metamyosin, contractin, X-protein** and **Y-protein.** Little is known regarding their nature, properties and functions.

II. **Fats**—0·2% including cholesterol, lecithin and neutral fat.

III. **Carbohydrates**—1·0%. (*a*) Glycogen—0·5–1·0%. (*b*) Hexose phosphate—0·05%.

IV. **Inorganic salts**—1·0–1·5%. Contains potassium phosphate mainly, (K about 0·3%) and also traces of Ca (0·007%), Na (0·06%), Mg (0·02%). Fe, Cl (0·04%) and sulphate. Phosphates remain in various forms (P—0·2%). The ratio between Na : K is 1 : 5.

V. **Extractives**—A. NON-NITROGENOUS:

1. **Lactic acid**—0·02% in fresh resting muscle.
2. **Inositol** (muscle sugar, hexahydroxycyclohexane)—0·25%.

B. NITROGENOUS: 1. Adenosine triphosphate **(ATP)**—0·25%. Adenosine diphosphate **(ADP)**. Adenylic acid—also called Adenosine monophosphate **(AMP)**—0·15%.

2. **Creatine phosphate** ($CrPO_4$)—phosphocreatine or phosphagen —0·5%. (Creatine 0·35%).

[These phosphoric acid compounds—(1) and (2) act as coenzymes by working alternately as donors and acceptors of phosphoric acid. They form an essential part in the processes of phosphorylation involved in the chemical reactions underlying muscular contraction.]

3. **Xanthine, Hypoxanthine** and **Inosinic acid**—derived from adenylic acid of the tissues and the nucleoprotein of the nuclei.

4. **Carnosine**—0·3%. It is a dipeptide (β-alanyl histidine). In some animals its methyl derivative is found and is called **anserine.**

VI. **Pigments** (Porphyrin derivatives)—

1. **Myoglobin** (Myohaemoglobin or Myochrome)—It is an iron-containing chromoprotein found in red muscles and is already discussed under 'protein'.

2. **Cytochrome** (Myohaematin) It is an iron-porphyrin pigment, found in three forms—a, b, c.

3. Flavines and others.

VII. **Enzymes** and **Coenzymes:** 1. Enzymes and coenzymes of the glycolytic cycle.

2. Those that break down and re-synthesise ATP and phosphagen.

3. Enzymes of the citric acid cycle, that finally oxidise pyruvic acid into CO_2 and H_2O.

4. Other enzymes like deaminase, etc.

Composition of Plain and Cardiac muscles. Their composition differs from that of the skeletal muscle in the following respects. Both contain (1) less proteins, (2) less ATP, phosphagen and other phosphates, (3) less carnosine, (4) less glycogen. But both contain more (*a*) Na (Na : K = 1 : 2) and (*b*) nucleoprotein. Cardiac muscle contains more *phospholipids* and cholesterol than either plain muscle or skeletal muscle.

PROPERTIES OF SKELETAL MUSCLES

Skeletal muscle shows the following properties: (I) **excitability** and **contractility,** (II) **refractory period,** (III) **tonicity,** (IV) **conductivity,** (V) **extensibility** and **elasticity.**

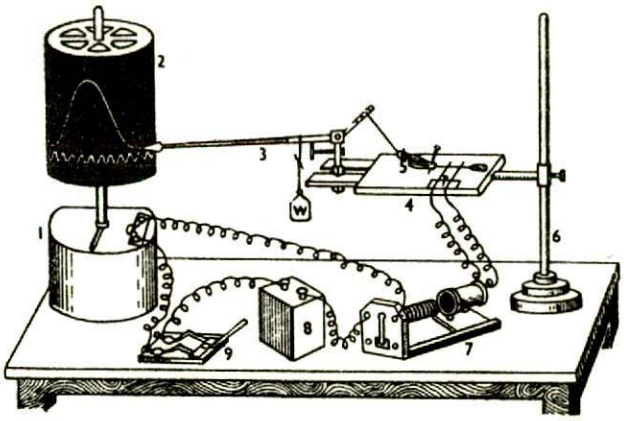


FIG. 115. Diagram shows the experimental set-up for the demonstration of simple muscle curve.

1—Motor. 2—Drum showing the curve. 3—Writing lever. 4—Myograph board. 5—Muscle and nerve with stimulating electrode. 6—Myograph stand. 7—Induction coil. 8—Battery. 9—Mercury key.

I. Excitability and Contractility. With an adequate stimulus, muscles are excitable. The stimulus may be *mechanical, thermal, chemical* or

electrical. For facilities of accurate adjustment, electrical stimulus is used in laboratory experiments.

When excited, the muscle contracts. This is immediately followed by relaxation. A single induction shock will produce a single contraction (twitch). The record of this on a moving drum (FIG. 115) will produce a curve, called the *simple muscle curve* (FIG. 116). But if the stimulus be strong, it may cause stronger contraction.

The **simple muscle curve** (FIG. 116), as obtained with a frog's gastrocnemius, has a total duration of about 0·1 second. It consists of three parts: (1) **Latent period** (0·01 second). It is the interval between the application of stimulus and the beginning of contraction. Latent period is due to time taken (*i*) for propagation of impulse from the point of stimulation to the neuromuscular junction and thence to the sarcolemma and (*ii*) for initiation of contraction. (2) **Period of contraction** (0·04 second), from beginning of the contraction up to the maximum contraction. (3) **Period of relaxation** (0·05 second), from the summit up to the original level.

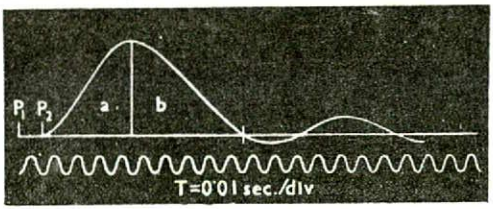


FIG. 116. Simple muscle curve (diagrammatic).
P_1—Point of stimulation. P_2—Beginning of contraction. P_1–P_2—Latent period.
a—Contraction phase. b—Relaxation phase.

The following factors affect **excitability** and **contractility** and therefore alter, in various ways, the nature of the simple muscle curve:

1. **Strength and duration of stimuli.** For stimulation to occur, two factors are necessary—a minimum strength and an adequate duration of the stimulus. Chronaxie, which includes both these factors, is the measure of excitability of a tissue (*vide* Chronaxie—pages 222–23).

2. **Effects of two successive stimuli** (FIG. 117). If the second stimulus is applied after sufficient intervals both first and second stimuli will cause contraction and two simple muscle curves will be recorded (FIG. 117, STAGE *a*). The second curve will be slightly higher than the first one due to the beneficial effect of contraction. If the second stimulus is applied in the relaxation period of the first, more or less two separate curves will be produced and the second curve will be higher (FIG. 117, STAGE *b*). If the second stimulus is applied within the contraction period of the first one the second curve will be superimposed on the first one with a higher height of contraction (FIG. 117, STAGE *c*). These are known as **summation of effects** (contraction). If the second stimulus is applied within the latent period but after refractory period of the first, then their effects are added together giving a simple muscle curve of larger height than either of them produced separately (FIG. 117, STAGE *d*). This effect is known as **summation of stimuli.** By using maximal or submaximal stimuli, these summated effects can be obtained. This is true for both

single muscle fibre or a whole muscle bulk. In case of submaximal stimuli, the summated effects are due to activation of more nerves and

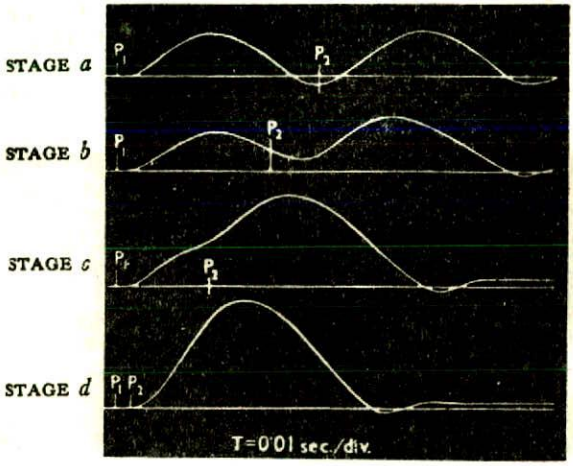


FIG. 117. Effects of two successive stimuli (diagrammatic).
P_1 & P_2—Points of stimulation.

STAGE *a*—The second stimulus is applied after sufficient intervals.
STAGE *b*—The second stimulus is applied in the relaxation period of the first.
STAGE *c*—The second stimulus is applied before the contraction of the first one is over.
STAGE *d*—The second stimulus is applied within the latent period of the first one.

muscle fibres, but in case of maximal stimuli, the greater response cannot be due to an increase in numbers of responding nerves and muscle fibres, but due to a difference in contractile mechanisms. It is claimed that these effects are due to beginning of second twitch before the active state for the first twitch is complete. That is the duration of the active state of the first response makes possible the augmentation of the second response. Thus this effect goes against the law of *all-or-none*.

3. **Effects of repetition of stimuli.** Following phenomena are observed:

(*a*) **Staircase phenomena.** When a freshly excised muscle is stimulated with a single induction shock of sufficient strength then a contraction of certain amplitude is recorded. If second stimulus of same strength is applied at an interval of about 1 second to the muscle after completion of the effect of first stimulus, then an increased amplitude of contraction is recorded. With a series of such stimuli (5 to 6 stimuli) but under the condition that each contraction is allowed to be completed before the next stimulus is applied, then a gradual increase in amplitude of contraction is obtained. This stair-like rise is called the **staircase (treppe) phenomenon.** Increased H^+ ion concentration and an increase of temperature within the muscle create a favourable condition for more work **(beneficial effect).** Hence, the contraction becomes stronger.

(*b*) **Clonus.** When repeated stimuli are applied, the type of response will vary according to frequency. When the frequency is such that each

successive stimulus falls within the period of relaxation of the previous curve, the record will show a series of wavy oscillations. This is called **clonus** or **incomplete tetanus** (FIG. 118, B–E).

(*c*) **Tetanus.** When the frequency is more, so that the stimuli fall within the latent period of the previous curve, the record traces a clear steady line, which rises at first abruptly and then gradually, till maximum contraction takes place. This is called **tetanus** (FIG. 118, F). Here the

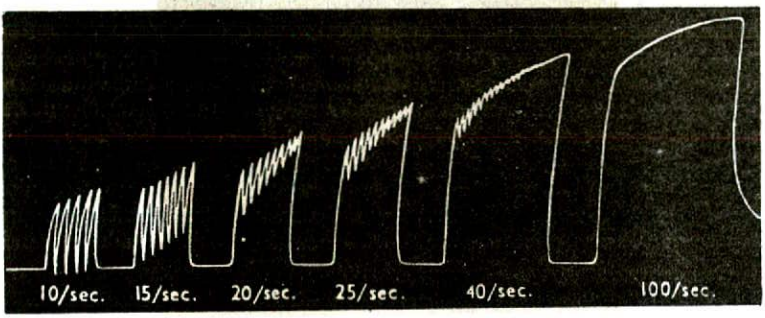


FIG. 118. Genesis of tetanus (diagrammatic).

fusion is complete and the muscle, instead of vibrating, exerts a steady pull. Due to summation, the height of tetanic contraction is usually higher than that of a single twitch. Frequency of stimulation, required for the induction of tetanus, varies with the nature of the muscle. In external eye muscle it is about 350/sec., in gastrocnemius muscle it is about 100/sec.

Clonus may be described as summation of successive contraction, whereas tetanus is summation of successive stimuli. The mechanical movement in response to voluntary stimuli is neither a twitch nor a tetanus (Lippold, 1957). During voluntary movement, the skeletal muscles are stimulated at low frequency, which is less than fusion frequency, and also asynchronously, so that the infrequent contraction of a large number of fibres give the appearance of a smooth response.

(*d*) **Fatigue.** When repeatedly stimulated, the muscle has lost its irritability, becomes gradually less excitable and ultimately ceases to respond. This phenomenon is called *fatigue* (FIGS. 119, 120 & 122). Muscular fatigue can be defined as the inability of the muscle to do further work. In the fatigue curve, all the periods are lengthened. The relaxation period is so much prolonged that the curve fails to reach the base line before the next stimulus arrives, thus leaving a **contraction remainder** (FIG. 119). The **causes of fatigue** might be due to (*i*) exhaustion of sources of energy of the muscle, (*ii*) accumulation of the end products of chemical reactions, such as lactic acid, carbon dioxide, ketone bodies and (*iii*) decrease of local synthesis of acetylcholine-like substances during prolonged exercise (Torda & Wolff, 1945). Oxygen is required for the removal of these substances and so for recovery. Fatigued muscle left in nitrogen does not recover. In studying fatigue in muscle *with circulation* and *without circulation*, the muscle gets

fatigue more earlier in case of the latter and does not recover on rest (FIG. 120, 1). But in case of muscle with circulation, fatigue comes later and the muscle recovers on rest (FIG. 120, 2). This shows that oxygen, which is supplied through blood circulation, is required for recovery of

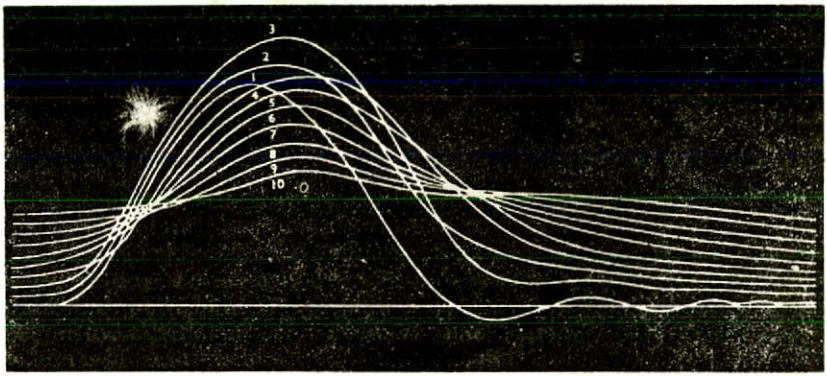


FIG. 119. Fatigue curve of a muscle in rapid moving drum (diagrammatic). The diagram indicates successive stages of the curve (beginning from 1). 2 and 3 are higher than 1 due to the beneficial effect of contraction. 10 shows the maximum development of contracture.

fatigue. The **seat of fatigue** lies in the muscle when it is directly stimulated. But when it is stimulated through the motor nerve, the seat of fatigue is in the neuromuscular junction. In physiological exercise, the *seat of fatigue* is neither in the muscle nor in the neuromuscular junction but at the synapses in the central nervous system (**central fatigue**). On comparison, it is seen that fatigue after voluntary work first appears in the synapses, then in the neuromuscular junctions and lastly in the muscle

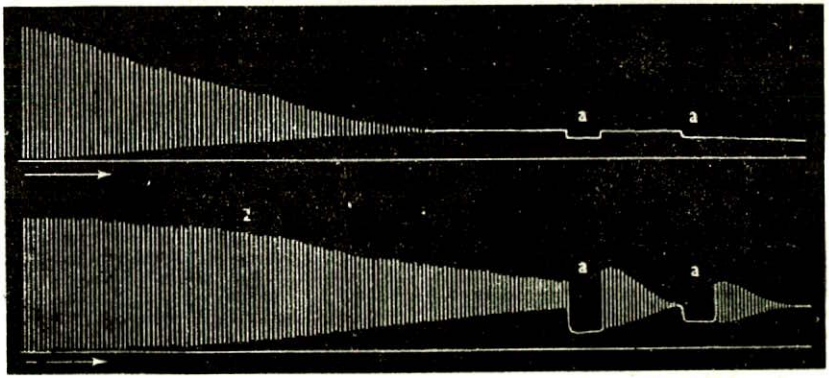


FIG. 120. Muscle fatigue in slow moving drum (diagrammatic). Diagram shows the effect of circulation on muscular fatigue. 1—without circulation. 2—with circulation. 'a' shows the effect of rest on recovery from fatigue. 2-a shows recovery from fatigue, whereas 1-a does not.

itself. In human subjects fatigue can be studied with the help of an instrument called **Ergograph** (FIG. 121).

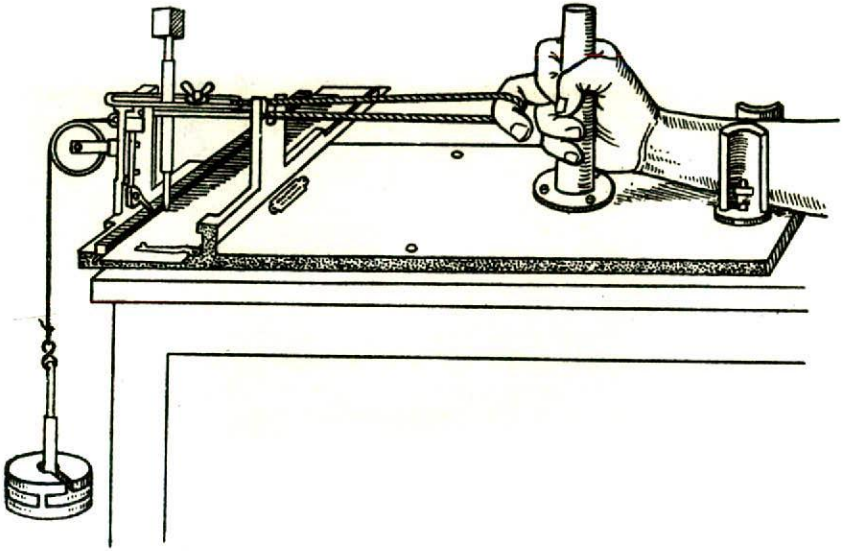


FIG. 121. Ergograph (diagrammatic).

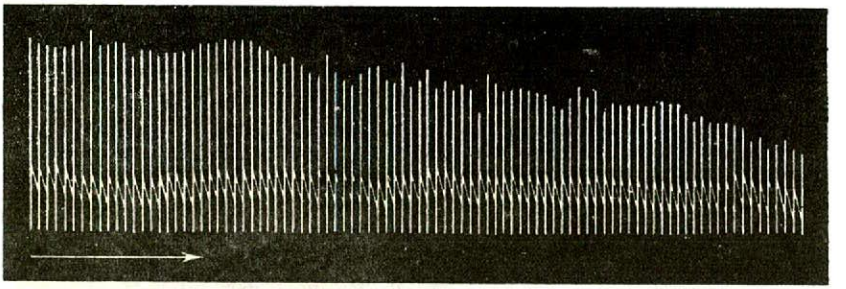


FIG. 122. Fatigue curve (diagrammatic) of the middle finger in the Ergograph.

Fatigue can be experimented by **noxious stimulation** at the foot of a spinal frog. If a reflex withdrawal of foot is obtained and by continuous stimulation the reflex contraction of the muscle is lost, the foot does not withdraw. At this stage if the flexor nerve is stimulated, then contraction of the muscle again occurs. This cessation of contraction is due to changes in the spinal cord. This can also be demonstrated in man by **protective mechanism.** When the arm or leg muscles of a subject are used to contract repeatedly with a weight attached to the part and he is unable to lift weight voluntarily, then electrical stimulation of the motor nerve through the skin produces a powerful contraction.

4. **All-or-none law.** It means that if a single muscle fibre contracts t all, it will contract to its maximum, provided the conditions remain onstant. If internal and external conditions are changed, the amount of ontraction will vary. This law holds good for a single muscle fibre and

does not apply for the whole muscle, which is composed of innumerable muscle fibres. Because, in the latter case, as the strength of the stimulus is increased, more and more muscle fibres will be affected and the degree of contraction will be raised (staircase phenomena) and a stage will be achieved when there will be no further rise (*all-or-none law* for whole muscle). But modern theory claims that the all-or-none law is applicable in case of development of the action potential but not for the activation of the contractile materials.

5. **Effects of temperature.** Moderate warmth (25°C.) increases and cold (5°C.) depresses both excitability and contractility. The former shortens and the latter lengthens all the periods of the muscle curve (Fig. 123). Temperature above 42°C. produces **heat rigor** due to coagulation of proteins present in the muscle.

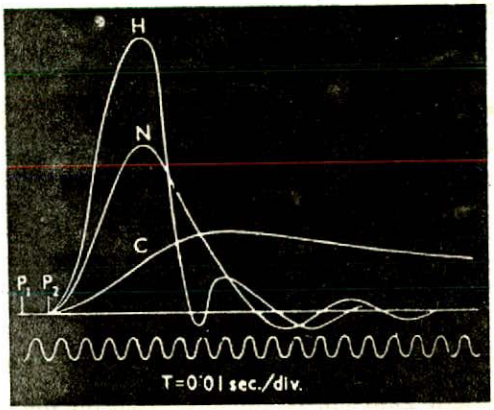


Fig. 123. Effects of temperature (diagrammatic).
P_1—Point of stimulation. P_2—Onset of contraction.
H—Effect of heat. N—Normal curve. C—Effect of cold.

6. **Effects of load.** Load lengthens the latent period but reduces the periods of contraction and relaxation. It also reduces the degree of contraction, i.e., the height of the curve (Fig. 124). The effect of load on the

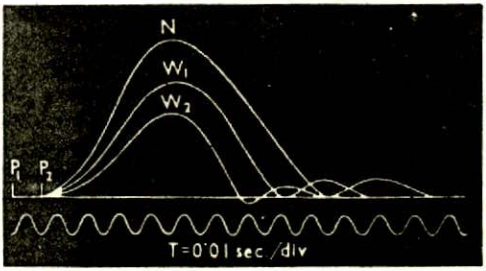


Fig. 124. Effects of load (diagrammatic).
P_1—Point of stimulation. P_2—Beginning of contraction. Uppermost curve (N)—*unloaded*. W_1 & W_2 curves due to applications of different graded loads.

work done by the muscle depends on the way in which the load is applied. If the weight is allowed to stretch the muscle prior to its contraction, the muscle is said to be *free-loaded* but if the lever is supported then the muscle is only stretched when the contraction begins, the muscle is said to be *after-loaded.* The mechanical efficiency in free-loaded muscle is higher than that in after-loaded muscle. This is mostly related with the increase in initial length of muscle fibres.

Work done by the muscle. The work done may be calculated by multiplying the weight with the actual height of the curve.

Actual height of contraction h in cm can be determined by dividing the observed height of contraction H in cm by the magnification of the lever (FIG. 125). The magnification of the lever can be determined by

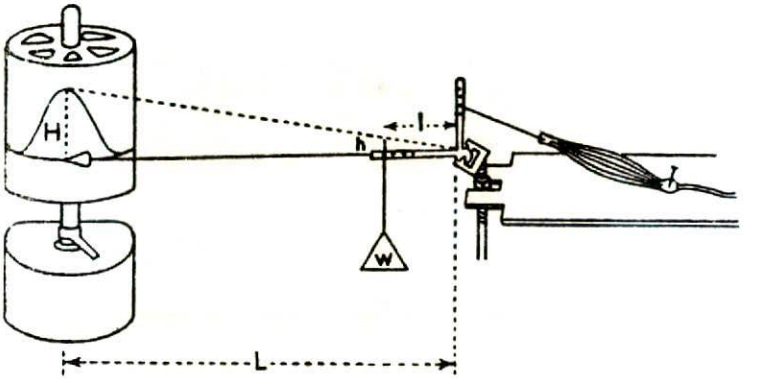


FIG. 125. Experimental set-up to calculate the work done by a single twitch.

dividing the length L in cm of the lever from the fulcrum to the tip of the lever, with the length l in cm from the fulcrum to the point of the lever from which the weight is lifted. So the magnification will be (L/l). Thus the calculation for actual height will be $h = H \div (L/l)$ or $(H \times l)/L$. If W is the weight in gms lifted then

$$\text{work done} = W \times \frac{H \times l}{L} \text{ gm cms}$$

$$= W \times \frac{H \times l}{L} \times 981 \text{ ergs.}$$

Work done by the muscle in free-loaded muscle within the physiological limits increases gradually with the increase of load but the same in after-loaded muscle does not follow linearly with the gradual increase of weight. The working efficiencies in such after-loaded muscle increase with a certain weight and then decreases gradually.

The chemical energy liberated during contraction is partly converted into mechanical energy which manifests itself as work. The term **mechanical efficiency** indicates what fraction of the total energy liberated is converted into work. In untrained men, the mechanical efficiency is 20%, in athletes, 25–30%. In isolated muscles, under optimum conditions, it may be as high as 40%.

It is seen that, the slower the speed of shortening, the greater is the amount of work done. But evidently, there is an optimum limit beyond which slowing the rate of contraction will reduce the work done.

7. **Effects of salts and ions.** (*a*) **Sodium salts** exert an excitatory effect. (*b*) **Calcium salts** have got role in initiation of contraction. Development of tension of the muscle is prevented if the Ca^{++} is not present in the medium. It is claimed that the Ca^{++} stimulates ATP-ase activity so that the association of actin and myosin in presence of ATP takes place promptly. Calcium ions and to a less extent Mg ions help the enzyme action of myosin. (*c*) **Potassium salts** reduce excitability and hasten fatigue. On stimulation, potassium ions escape from the interior of the muscle. It is believed that the excitability, contractility and electrical phenomenon of the muscle depend largely upon this migration of the potassium ions. The resting muscle membrane is permeable to potassium ion but not to sodium ion. (*d*) **Magnesium ion** is essential for the action of the enzyme *phosphorylase* which is very important for the phosphate transfer during muscular contraction. (*e*) Increased **H-ion** changes exert the same effect as excess potassium.

II. **Refractory period.** After stimulation there is a brief period during which the muscle is not excitable to a second stimulus. This period is called 'refractory period'. In the case of smooth muscles, refractory period is very short and falls within the latent period. In the skeletal muscles of frog, it is about 0·005 second, in the mammalian muscles it is about 0·002 second. Cold lengthens and heat shortens this period. During the first part of the refractory period, the muscle remains inexcitable to any strength of stimulus and is known as **absolute refractory period.** But in latter part of the refractory period the muscle may be excitable only with a stronger stimulus, and is known as **relative refractory period.** The absolute refractory period in skeletal muscle is shorter than that of in cardiac muscle and for this reason, the skeletal muscle can be tetanised or fatigued.

The earliest chemical change during muscular contraction is the breakdown of adenosine triphosphate (ATP). So long as the broken ATP is not re-synthesised in adequate amounts, the muscle cannot be excited. *Refractory period is that period during which this re-synthesis of broken ATP takes place.*

III. **Tonicity.** In the body the skeletal muscles always remain in a state of light tension. This is called **tone.** Tone of the skeletal muscle may be defined as the reflex sustained and partial contraction. In isolated muscle, tone is absent. If the motor nerve of the muscle is excised, tone is also lost. These experiments show that muscle tone is a *reflex process*, the centres being situated in the spinal cord. A muscle under 'tone' does not show fatigue. This is due to the fact that in tone production, the whole muscle is not contracting simultaneously. Only a few muscle fibres are contracting at a time. The muscle fibres contract in batches. When one batch is contracting, the other is relaxing. Hence, the whole muscle does not show any fatigue.

IV. **Conductivity.** After stimulation the wave of contraction starts at the point of stimulus and is propagated both ways along the muscle. In frog's muscles the rate of propagation is 3–4 metres per second. In warm-blooded animals 6–12 metres per second.

V. **Extensibility and Elasticity.** Muscle extends when stretched. When the tension is released, it goes back to its original length. But this

elastic return is a little slower. A rubber band is found to extend uniformly by increasing loads of equal weights upon it and returns quickly to the original position as soon as the weights are removed. But under the same conditions, muscle does not immediately come back to its original position. It takes a little longer time. This is called **extension remainder.**

Characteristics of Isotonic and Isometric Contraction. Contractions are of two types—**isotonic** and **isometric.** In *isotonic contraction* physical shortening of the muscle is allowed when one end of it is attached to a light weight which is lifted. This type of contraction has already been described and gives simple muscle curve. In *isometric contraction* physical shortening of the muscle is reduced to minimum by making it contract against a strong spring. The slight change in the spring is magnified by suitable instruments and is recorded. The curve of isometric contraction shows the following peculiarities: (1) The latent period is longer. (2) The period of contraction is longer and the tracing at first shows an upward concavity followed by an upward convexity up to the summit. (3) Relaxation period is more gradual and the curve shows a gentle slope with a slight upward concavity. The rise of tension is abrupt and commences very early. The amount of tension is also much higher than in isotonic contraction. Other things remaining constant the tension developed in the muscle fibres is directly proportional to the initial length of the fibre. The evolution of heat is also much more than in isotonic contraction.

Nature of Voluntary Contraction. Voluntary contraction differs from simple muscle twitch in two respects. First, it lasts much longer and secondly, the degree of contraction can be finely adjusted at will. The *voluntary contraction is neither a simple muscle twitch nor a tetanus* (p. 210). The rate of discharge is slow and less than fusion frequency and the number of cells discharging may vary in number and consequently the muscle fibres affected will vary. The cells do not all discharge at the same time. But they work in 'batches'. While one group is discharging the other group is resting. For this reason, the muscle fibres of all the motor units are not in the same state at the same time. They are at different phases of contraction and relaxation. Their algebraic sum gives a smooth, steady pull. The accurate gradation in the strength of contraction is due to the involvement of varying number of anterior horn cells.

Contracture. Under certain conditions skeletal muscles show a peculiar type of persistent contraction. This is called **contracture.** It differs from tetanus or any other forms of physiological contraction in two ways. First, in contracture only a part of the muscle may be involved, while the rest of the muscle remains relaxed. Secondly, the contractile process is not propagated along the muscle fibre and also no action potentials are seen with it. Contracture may be found under various conditions, such as (1) by strong, prolonged or multiple stimuli, (2) in fatigue, (3) in certain pathological states of the body.

PROPERTIES OF PLAIN (SMOOTH) MUSCLES

Broadly speaking, properties of the plain (smooth) muscles are same as those of the skeletal muscles, with the following differences: (1) **Excitability** and **Contractility**—Plain muscle is less excitable. Contraction is slow, and worm-like. All the periods are longer. The latent period varies from 0·2–2·0 seconds, period of contraction from 0·5 to several seconds, the period of relaxation is proportionately longer than that of contraction. The **refractory period** is also much longer. One more peculiarity is that, a particular stimulus (electrical or mechanical) may cause either contraction or relaxation. If

the muscle is relaxed, the stimulus will cause contraction; but if it is already contracted, the stimulus will relax the muscle. The effect of temperature is also different. Moderate warming causes relaxation and cooling contraction. (2) **Rhythmicity**—It has automatic inherent rhythmicity. When slightly stretched most varieties of plain muscles will exhibit rhythmic contractions. These contractions are independent of all nerves and are purely myogenic. The 'stretch' acts as a stimulus causing the relaxed muscle to contract and the contracted muscle to relax. In this way as long as the 'stretch' is maintained, the alternate rhythmic contraction and relaxation will continue. (3) **Conductivity**—The wave of contraction is propagated along the muscle fibre but the rate of propagation is much slower. *One peculiarity is that in the plain muscle the stimulus travels from fibre to fibre through the nexus and the wave of contraction is propagated through the whole muscle sheet.* The electric changes during contraction are also peculiar because, two negative potential changes are found to accompany each contraction. (4) **Tonicity**—Plain muscles remain in a state of light tension.

Factors affecting the activity of plain muscle. (1) **Temperature**—Heat diminishes both excitability and tonus. Cold, on the other hand, increases tonus. (2) **Salt balance**—The activity of the smooth muscle is modified by K : Ca ratio. Ca^{++} influences the Na^{+} permeability mechanism and increases the rate of rise of spike. K^{+} also increases the tone of the smooth muscle. (3) **pH**—Increase in pH lifts tonus and rhythmic activity, decrease in it produces quiescence and relaxation. (4) **Previous state of activity**—A stimulus which generally causes contraction, will induce relaxation in a smooth muscle if it is already in a state of high tonus. (5) **Hormones**—The secretion of ductless glands has profound influence over the activity of plain muscle. Contraction of uterus on stimulation is dependent on the state of oestrus of the organ. Acetylcholine stimulates and adrenaline depresses the tone of muscle. Posterior pituitary extract also increases tonic contraction of the uterine and intestinal muscles.

PROPERTIES OF CARDIAC MUSCLES—*Vide* Cardio-vascular System.

CHANGES DURING MUSCULAR CONTRACTION

The following changes are found to accompany muscular contraction: (I) **mechanical changes,** (II) **chemical changes,** (III) **thermal changes,** (IV) **electrical changes.**

I. **Mechanical changes.** During contraction, the muscle fibre shortens in length, increases in thickness, but the total volume remains same (or slightly increases). The muscular contraction may be isometric when the length of the muscle fibres remains constant but the tension increases, or isotonic when the muscle becomes shorter and thicker.

II. **Chemical changes.** Following chemical changes take place during contraction in the **anaerobic** and **aerobic phases.**

Glycolysis and Oxidative breakdown. This process involves many separate enzymes and different intermediates. The end products are pyruvic or lactic acid. The first step in the liberation of energy for contraction is the breakdown of glycogen in the muscle fibre. The glycogen reacts with inorganic phosphate (P_i) and splits up into glucose-1-phosphate (**Cori ester**) with the help of *phosphorylase*. Muscle phosphorylase contains pyridoxal phosphate as a cofactor. The process of uptake of the phosphate and its cleavage into glucose phosphate is called *phosphorolysis*. Glucose-1-phosphate is converted into glucose-6-phosphate. Glucose-6-phosphate is changed into fructose-6-phosphate, then into fructose-1, 6-diphosphate and into two triose phosphates. The triose phosphate is finally converted into pyruvic acid (Fig. 126). "*The details of the pathway and the different enzymes concerned are described fully in chapter on Carbohydrate Metabolism.*"

Pyruvic acid is reduced to lactic acid by reduced nicotinamide adenine dinucleotide (NAD.2H) [previously called reduced coenzyme-I or $DPNH_2$] and lactic dehydrogenase in the absence of oxygen. Out of the

total quantity of the lactic acid formed under anaerobic conditions *one-fifth* of it is oxidised to CO_2 and H_2O, and *four-fifths* are re-synthesised into glycogen in the liver. In the presence of oxygen the pyruvic acid is oxidised through a series of steps known as the Krebs tricarboxylic acid (TCA) cycle. In this cycle one molecule of pyruvic acid loses one molecule of CO_2 and is converted into **active acetate** (Acetyl coenzyme-A). The active acetate is metabolised through a series of reactions known as citric acid cycle (*described under Carbohydrate Metabolism*). Each molecule of pyruvic acid at each turn of the cycle liberates three molecules of CO_2 and two molecules of water.

There is net production of 39 ATP per one hexose unit of glycogen metabolised. But per oxidation of one molecule of glucose into CO_2 and water 38 ATP are produced. In anaerobic condition only 2 ATP are produced per molecule of glucose metabolised and 3 ATP are produced per hexose unit of glycogen metabolised under such condition.

Energy for muscular contraction is thus provided as ATP from (*a*) anaerobic glycolysis leading to breakdown of glycogen and glucose to pyruvic and lactic acids, (*b*) oxidation of lactic acid to pyruvic acid and further oxidation of pyruvic acid in TCA cycle *via* acetyl CoA into H_2O and CO_2, (*c*) fatty acid oxidation through β-oxidation and through TCA cycle also provides some amount of ATP as muscle energy, (*d*) during muscular activity creatine phosphate also maintains the ATP level of the muscle.

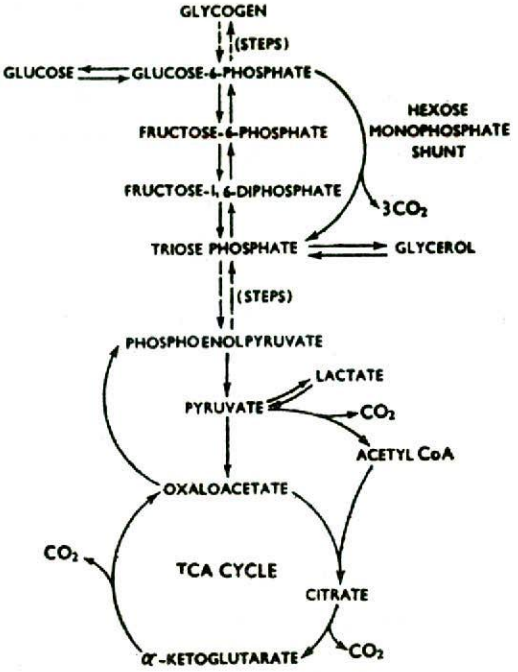


FIG. 126. Diagrammatic representation of glycolysis and oxidative breakdown in brief.

Role of Creatine Phosphate or Phosphagen and Adenosine Triphosphate (ATP). Creatine phosphate ($CrPO_4$) plays an essential role in the muscular contraction. The role of carbohydrate metabolism is to provide energy for the re-synthesis of creatine phosphate. The breakdown process of creatine phosphate involves the re-synthesis of ATP. Creatine phosphate reacts with ADP and as a result of which creatine phosphate loses its phosphate radical and ATP is formed. ATP is again broken down by adenosine triphosphatase (ATP-ase) to form ADP and inorganic phosphate. The breakdown of ATP precedes that of creatine phosphate. ATP is composed of adenine, *d*-ribose and 3-molecules of orthophosphate. The

energy-rich* phosphate bonds are contained in creatine phosphate and ATP, and this bond is indicated by a symbol '~' in their formulae. The terminal phosphate group which is split off from ATP or the phosphate bond energy may be transferred to other compound, e.g., in the conversion of fructose-6-phosphate into fructose-1, 6-diphosphate and ADP is formed.

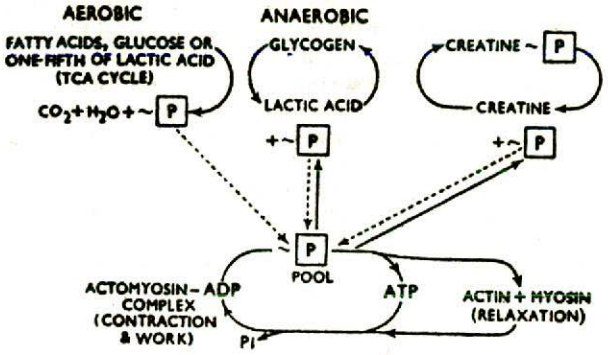


FIG. 127. Diagrammatic representation of the chemical reactions during muscular contraction.

The re-synthesis of creatine phosphate takes place with the help of phosphate released from ATP in a reversible reaction. As a result of transference of phosphate, ATP changes into ADP. Creatine phosphate also serves as a reserve source of phosphate bond energy for rapid re-synthesis of ATP in case of muscle poisoned with the iodo-acetic acid. In the iodo-acetate poisoned muscle the carbohydrate breakdown is inhibited but re-synthesis of ATP can take place for a considerable period with the help of creatine phosphate.

The **sequence of events may be summarised** in the following order: (1) ATP breaks down into ADP and there is release of phosphate and energy. Actin and myosin are the contractile substances. ATP helps in the shortening of actomyosin threads. (2) Creatine phosphate breaks down and the phosphate with its energy is transferred to ADP and forms ATP. The creatine phosphate store is thus a constant supplier of ATP. (3) Glycogen of the muscle breaks down in a series of stages and releases energy-rich phosphate bond in the intermediate stages which in turn help in the re-synthesis of ATP and also of re-synthesis of creatine phosphate. Under **anaerobic conditions** glycogen breakdown occurs as far as pyruvic acid, which again takes up hydrogen from NAD.2H and changes into lactic acid. A dehydrogenase catalyses this reaction which is reversible. Muscle glycogen is formed from this lactate by a process known as Cori cycle (described later). Under **aerobic conditions** lactic acid is also produced. It diffuses

* There are two types of phosphate bonds—**high-energy** bond (indicated by the sign ~) and **low-energy** bond. A high-energy bond when split up releases about 10,000–12,000 cal/gm/mol., whereas a low-energy bond liberates only 2,000 cal/gm/mol. ATP contains *two* high-energy and *one* low-energy phosphate bonds (**ATP=A—P~P~P**) and phosphagen contains *one* high-energy phosphate bond (**Cr~P**). It is believed that energy released from the high-energy bonds is not wasted as heat, etc., but is utilised for work and other cellular processes.

out into the circulation and other body fluids. It is re-oxidised into the pyruvic acid mainly in the liver and enter the citric acid cycle or may be transformed into glycogen.

Muscular contraction and its relationship with the breakdown of ATP. The **mechanism of muscular contraction** begins into the breakdown of ATP. The contraction takes place due to release of phosphate bond energy from ATP. When the muscle is stimulated the impulse travelling over the fibre is associated with an increase in sodium and calcium permeability of the membrane. As a result, inflow of sodium ions to the inside of the muscle fibre is accompanied by a slight inflow of calcium ions at the same time. The calcium ions then stimulates adenosine triphosphatase (ATP-ase) which helps in the release of energy from ATP surrounding the muscle filaments. The energy produces momentarily an electrostatic charge between the actin and myosin filaments which in turn pulls the actin filaments into the spaces between the myosin filaments. ATP-ase remains in an activated state so long calcium ions are present inside the muscle fibre. Surrounding the filaments and sarcoplasmic reticulum there is another substance known as *relaxing substance* which binds calcium ions within a fraction of a second after they enter the interior of the fibre so that the calcium is changed into unionised form. As a result of inactivation of calcium ions in the interior of the muscle fibre no more energy is released from adenosine triphosphate. The electrostatic charges between the actin and myosin filaments disappear, thus allowing the muscle to relax.

Utilisation of other fuels during muscular contraction. It is possible that skeletal muscle also utilises ketone bodies and free fatty acids for the re-synthesis of ATP. This is particularly applicable in the case of flight muscles of migratory birds, where glycogen store is not sufficient to supply energy for a long period of muscular contraction.

Cardiac muscle *is similar to the above flight muscle, biochemically, and consumes ketone bodies and free fatty acids in harmony with them for continued activity.*

Changes in H-ion concentration. The normal reaction of muscle is slightly on the alkaline side (pH 7·3). During muscular activity both acid and alkaline products are formed. These compounds try to neutralise each other and thereby prevent any serious change of reaction. Besides this, the muscles possess an efficient buffer system in the form of muscle proteins, their Na- and K-salts, the inorganic phosphates, the bicarbonates, etc., all of which help to prevent marked change of muscle pH. But in spite of this, in the initial stages the reactions become more alkaline due to the liberation of free creatine (which is strongly alkaline). In prolonged activity, specially under inadequate oxygen supply, the reaction becomes distinctly acid (pH about 6·0) due to accumulation of lactic acid.

Other chemical changes. In the resting muscle the R.Q. varies from 0·85 to 0·90, showing that the resting metabolism involves the oxidation of certain non-carbohydrate foodstuff. Hill, by determining the osmotic pressure of the muscle under various conditions, has proved that, unknown reactions of considerable magnitude other than carbohydrate oxidation, take place. It has also been shown that glycerol, ketones, etc., may join the path of glycogen metabolism and undergo a process of oxidation. Moreover, little is known about the changes seen in the nitrogenous constituents of muscles, such as carnosine, inositol, free creatine, etc. All these indicate that muscles utilise not only carbohydrates but other substances as well.

Oxygen utilisation and CO_2 production. The broad facts about this are as follows: (*a*) The resting muscle uses O_2 and liberates CO_2, the R.Q. being 0·85–0·90. (*b*) O_2 is not required for contraction and lactic acid formation. The muscle maintains its irritability and contractility for a good length of time even under complete anaerobic conditions. (*c*) Oxygen is essential during recovery process when lactic acid burns and glycogen is re-synthesised. The R.Q. of this period is unity.

Cori cycle. In the living body under normal conditions, the oxygen supply to the muscles is so efficient that slight or moderate exercise does not produce lactic acid accumulation. Because due to ready oxygen supply, lactic acid quickly disappears. But in heavy exercise, the oxygen supply becomes inadequate, excess of lactic acid accumulates in the muscle fibres and diffuses out into the blood stream. A considerable amount of this blood lactate is utilised by the heart and small amounts by other tissues. A little portion of it may re-enter the muscle to form glycogen. But the major part of the blood lactate is taken up by the liver and is converted into glycogen. *Liver can prepare glycogen from lactic acid more quickly than it is done by the muscles.* This liver glycogen is converted into glucose, which enters blood stream, and then into the depleted muscles and is converted into glycogen. *The muscle can form glycogen more readily from glucose than it is done by the liver.* In this way the muscle gains back its depleted glycogen store. Liver and muscle help each other to organise a bigger cycle through which lactic acid moves. This cycle is as follows: Muscle glycogen→ Muscle lactic acid→ Blood lactate→ Liver glycogen⇌ Blood glucose→ Muscle glycogen. This cycle is called the **Cori cycle** (FIG. 128).

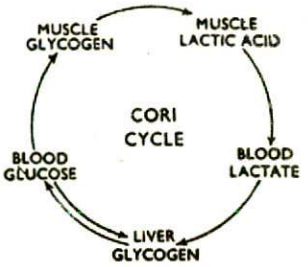


FIG. 128. Cyclic relationship of lactic acid and glycogen.

III. **Thermal changes.** During muscular contraction, heat is produced in the muscle, which has been measured with the help of an instrument called **Thermopile.** Heat is produced in two stages: (*a*) **initial heat,** which occurs at the onset of contraction, (*b*) **recovery heat** or **delayed heat,** which occurs, following the contraction. The initial heat is the rapid outburst of heat, whereas the recovery heat is slow and prolonged production of heat. The recovery heat is equal to the total energy set free during muscular contraction. In the recovery process the chemical changes, which is responsible for the initial liberation of energy, are reversed. A. V. Hill had shown that the heat produced in a single twitch of a frog's muscle may be divided into three stages: (*a*) *The heat of activation*—The heat of activation occurs immediately after stimulation and diminishes while the contraction proceeds. The heat production occurs about ten milliseconds after stimulation. (*b*) *The heat of shortening*—This is the second stage of heat liberation and depends upon the amount of shortening—ax, where x denotes the amount of shortening and a is the constant (multiplication of constant and variable). (*c*) *Recovery heat*—There is slow production of heat during recovery process in the presence of oxygen. The heat of shortening begins later. There is no heat of relaxation.

IV. **Electrical changes.** Instruments used for the purpose are *capillary electrometer, Einthoven's string galvanometer* or *cathode ray oscillograph.* The electrical changes are of the same nature as seen in the nerve. The cut surface or the stimulated spot is negative to the rest of the muscle fibre. When the injured and the uninjured areas are connected, current of injury will be found. By repeating the same experiments as in nerves **current of action** with *diphasic variation* and **current of injury** with *monophasic variation* can be found. Mechanical contraction starts when the electrical change attains its maximum, which takes place very early during the latent period. The **action potential** as well as the wave of mechanical contraction are propagated at the same rate (3–4 metres per second). Under no condition the electrical wave (*excitation process*) can be propagated without the accompanying wave of contraction. Hence, the electrical wave can be regarded as the index of the contraction wave. Cold slows and warmth hastens both these waves.

For further details *vide* '*Electrical Phenomena in Nerve Fibres*' under *Nervous System.*

Electromyography. Electromyography is a study of the action potential in human skeletal muscle. As a part of the electrical currents generated is transmitted to the outer surface of the body. The changes in action potential can be studied by either putting electrodes at the surface of active muscle area or inserting them directly into the muscle concerned. The potential can be recorded by cathode ray oscillograph. The study has a great clinical value in the diagnosis of different types of neuromuscular functional impairment in which either the rate or rhythm of nerve impulse is influenced.

Chronaxie and Rheobase

The excitability of different tissues varies widely. Some tissues are highly excitable whereas others are dull. While considering the excitability of a tissue two factors are to be considered: (*a*) the strength of the current used, and (*b*) the duration of the current flowing through the tissue. These two factors bear an inverse relation. The stronger the current the lesser will be the duration required. But there is a limit. Two standards have been established to measure the excitability of various tissues. [Instruments used —Lapicque's liquid potentiometer or Keith Lucas's spring rheotome.] The strength standard (*intensity threshold*) is called rheobase. The duration standard (*time characteristic*) is called by Lapicque as Chronaxie. **Rheobase** *is defined as the minimal galvanic current which when allowed to flow indefinitely will excite a tissue.* **Chronaxie** *is defined as the shortest duration of stimulus required to excite a tissue by a current strength equal to twice of Rheobase voltage.* Chronaxie of a tissue is a definite measure of its excitability. *A less excitable tissue has a longer chronaxie, whereas a more excitable tissue has a shorter one.* The speed of activity of tissue and its chronaxie bear a direct relation. A tissue, having shorter chronaxie, has shorter period of action, shorter refractory period and a quicker rate of propagation. Sluggish tissues, such as some form of plain muscle, have longer chronaxies. Owing to this, they fail to be excited by Faradic stimulation (*induction shock*), because the duration of the current here is very short. Chronaxies of the various tissues are as follows: (1) The tissues of the new-born child possess chronaxies which are ten times longer than those of adults. This explains the slower movements of infants.

(2) Tissue of cold-blooded animals generally possesses longer chronaxies (i.e., they are more sluggish) than those of warm-blooded types. (3) Muscles—(*a*) the chronaxies of the skeletal muscles are shorter than those of plain and cardiac. Flexor muscles have shorter chronaxies than extensors. The pale muscle fibres (more active) have shorter chronaxies than the red muscles (sluggish). Fatigue lengthens and adrenaline shortens the chronaxie of skeletal muscles. Similarly, cold lengthens and warm shortens it. A degenerating muscle has longer chronaxie; that is why it fails to be excited by Faradic stimulation in the early stage of reaction of degeneration. (*b*) Chronaxie of the plain muscle is longer than that of the skeletal muscle. Vagal stimulation shortens and sympathetic stimulation lengthens the chronaxie of the plain muscles of the stomach. Stretching diminishes their chronaxies and increases excitability. (*c*) Cardiac muscle—the chronaxies of ventricular and atrial muscles are same but that of the junctional tissues is three times longer. Stimulation of vagus, stretching, cold, and inhibitory drugs like acetylcholine shortens the chronaxie. Warmth, sympathetic stimulation and accelerator drugs like atropine, adrenaline, etc., lengthen chronaxie. (4) Nerves—the chronaxie of the autonomic nerves is more than that of the somatic nerves. Nerve fibres of larger diameter (which conduct more rapidly), have shorter chronaxies than thinner ones (having less conductivity). The chronaxies of the corresponding sensory and motor nerves are about the same. In a degenerating nerve the chronaxie becomes longer. [The chronaxies of certain frog's tissues are as follows: Skeletal muscles—0·3–0·9 millisecond, Ventricles—3·5 milliseconds, Stomach—30–100 milliseconds, Pigment cells of the skin—11,000–15,000 milliseconds.]

Rigor mortis

Rigor mortis is a state of rigidity that develops in the muscles after death. Isolated muscles also develop rigor mortis. While in this condition the muscle (1) *loses its excitability*, (2) *shortens in length*, (3) *increases in thickness*, (4) *becomes viscous and loses translucency*, (5) *becomes distinctly acid* (pH 5·8), (6) *gradually becomes stiff*, (7) *glycogen disappears*, and (8) *the muscles give off carbonic acid*. Severe muscular exercise immediately before death hastens the onset of rigor mortis. This is found in soldiers killed in action and also in hunted animals. The time of onset is not the same in all muscles. On the average, rigor mortis starts in the second hour and is completed in three hours after death. The muscles of the body are involved in the following order—lower jaw, face, neck, thorax, abdomen, upper extremities and lastly the lower extremities. Rigor mortis disappears 24 to 36 hours after death due to autolysis. The disappearance also follows the same order. Caffeine, arsenate, chloroform vapour, increased temperature and acidity hasten rigor mortis. Rigor mortis is a state of permanent irreversible contraction and is associated with deficiency of ATP causing establishment of permanent link between actin and myosin. This deficiency of ATP fails to bring about dissociation of actomyosin to actin and myosin. It is postulated that during activity creatine phosphate level is associated with the ATP level of the muscle. The creatine phosphate is the high-energy resource of the muscle and its level is again dependent upon the ATP. $CrPO_4 + ADP \rightleftharpoons$ creatine + ATP. When ATP falls to 85% and creatine phosphate to 30% of its initial value, the symptoms of rigor mortis begin to appear when the ATP level falls to 15% of its value.

CHARACTERISTICS OF SKELETAL, SMOOTH AND CARDIAC MUSCLES

Characteristics	Skeletal	Smooth	Cardiac
Histology			
1. Size and shape	Cylindrical; 1–40 mm long, 10 to 100 μ in diameter.	Elongated, fusiform, length 0·2 mm (aver.), width—6 μ (central portion).	Short cylindrical, rectangular in longitudinal section, polyhedral in transverse section.
2. Striations	Transverse, longitudinal.	Longitudinal (special preparation).	Both longitudinal and transverse.
3. Sarcolemma	Present and complete.	Present and complete.	Present and complete.
4. Nucleus	Multiple, just under the sarcolemma.	Single, at the centre with distinct nucleoli.	Single and central.
5. Sarcotubular system	Present, T-systems are at junctions of A–I band (in mammals). Terminal cisternae is prominent.	Present, but not so characterised.	Present, but without terminal cisternae. T-system is more prominent and present at Z-line (in mammals).
6. Branch	Nil.	Nil.	Multiple branches. In all directions—three-dimensional network without cytoplasmic continuity (false syncytial appearance).
7. Cell-to-cell conduction	Nil.	Through nexus.	Through specialised areas of intercalated disc.
Properties			
1. Rhythmicity	Nil.	Present.	Present and characteristic.
2. Conductivity	Very fast.	Slower.	Slower, different in different parts.
All-or-none law	True for single fibre.	True for single fibre.	True for the whole heart, because of functional syncytium.
3. Contractility	Simple muscle curve with characteristic features.	Slow and worm-like. All periods of the curve longer.	Characteristic muscle curve. Contraction, longer than relaxation.
4. Refractory period	Short—within latent period.	Longer than smooth.	Longest, whole contraction period is absolute refractory.
(*a*) Tetanus	Possible.	Not so.	Impossible.
(*b*) Fatigue	Possible.	Possible. difficult to demonstrate.	None. Long refractory period ensures recovery.
5. Tonicity	Tone depends on nerves.	Independent of nerve.	Independent of nerve.

CHARACTERISTICS OF SKELETAL, SMOOTH AND CARDIAC MUSCLES (*Contd.*)

Characteristics	Skeletal	Smooth	Cardiac
Composition			
1. Protein	Maximum.	Less.	Less.
2. Glycogen	Less.	More.	More.
3. ATP and Phosphagen	Present.	Present.	Present.
4. Carnosine	Maximum.	Less.	Less.
5. Fats	Mostly neutral fats.	Mostly neutral fats.	More phosphatids and cholesterol than in others.
6. Inorganic	Na/K—1/5. Ca^{++}.	About same.	Na/K—1/2, i.e., more Na. Ca^{++}.
Action of Ions			
1. Sodium	Excitation.	Probably same.	Initiates and maintains heart beat.
2. Calcium	Presents mostly in sarcoplasmic reticulum and stimulates ATP-*ase* activity during muscular contraction.	Same as skeletal.	Increases strength of contraction and duration of systole.
3. Potassium	Reduces excitability and hastens fatigue.	Probably same.	Inhibits contraction and produces relaxation.
Metabolism			
1. Carbohydrates			
(*a*) Lactic acid	Oxidised less easily than glucose and often incomplete.	Oxidised less easily than glucose and often incomplete.	Completely and more readily than glucose.
(*b*) Glycogen	Reduced in Starvation and Diabetes Mellitus.	Reduced in Starvation and Diabetes Mellitus.	Increased.
2. Blood supply and O_2 consumption	Moderate.	Less.	High.
Distribution	Skeletal.	Hollow viscera, capsules, skin, etc.	Only in heart.
Control	Under the *will*, so voluntary.	Not so, involuntary	Not so, involuntary.
Nerve Supply	Somatic with special nerve endings.	Autonomic with ganglia and free nerve terminals.	Same as in involuntary.