REVIEW OF LITERATURE
CHAPTER 2

REVIEW OF LITERATURE

2.1 Neurological system

All of our body systems work in conjunction with each other and none are capable of working in isolation. The nervous system controls and coordinates the functioning of all other systems in response to our surroundings. Each stimulus or change in our environment is detected by our senses and messages are interpreted by the brain that in turn, sends directions to the various organs to respond and adapt according to the external conditions which affect our body. The function of the Neurological System is to transmit and receive a constant series of messages via electrical impulses to and from the control centre situated in the brain. These messages are either those receiving "information" from various body tissues via the sensory nerves or those initiating the function of other tissues such as organs, muscles, etc (Kimura, 1986).

2.2 Division of Nervous system

The nervous system is divided into the central nervous system (CNS) that includes the brain and spinal cord, and the peripheral nervous system (PNS) comprising cranial nerves and spinal nerves. The PNS includes nerves emerging from the brain (cranial nerves) and nerves emerging from the spinal cord (spinal nerves). These nerves are divided into sensory nerves that conduct messages from various parts of the body to the CNS, whilst motor nerves conduct impulses from the CNS to muscles and glands. The PNS is
further divided into the Somatic Nervous System (SNS) and Autonomic Nervous System (ANS), depending on the area of the body these messages are transmitted to and from. The SNS consists of sensory neurons from the head, body wall, extremities, and motor neurons to skeletal muscle. The motor responses are under conscious control and therefore the SNS is voluntary. Certain peripheral nerves perform specialized functions and form the autonomic nervous system; they control various activities that occur automatically or involuntarily such as the contraction of smooth muscle in the walls of the digestive system. The autonomic system is further divided into the sympathetic and parasympathetic systems. These two systems provide nerve stimuli to the same organs throughout the body, but bring about different effects. The Sympathetic Nervous System helps prepare the body for "fight or flight" and create conditions in the tissues for physical activity. It is stimulated by strong emotions such as anger and excitement and will therefore speed up heart rate, increase the activity of sweat glands, adrenal glands, and decrease those of the digestive system. It also produces rapid redistribution of blood between the skin and skeletal muscles. Conversely, the Parasympathetic Nervous System slows down the body and helps prepare for a more relaxed state, ready for digestion and sleep. It will therefore increase peristalsis of the alimentary canal, slow down the heart rate, and constrict the bronchioles in the lungs. The balance between these two systems is controlled to create a state of homeostasis that is where the internal stability of the bodily systems is maintained in response to the external environment (Binnie et al., 2004).
2.3 Structure & function of the peripheral nervous system

A basic knowledge of the anatomy of the peripheral nervous system is essential to understanding its physiology and pathophysiology. A brief review of the structure of peripheral nerve and its connections therefore follows, but more detailed accounts can be found in Landon (1976), Dyck et al. (1984), Sunderland (1991) and Thomas et al. (1991).

2.3.1 Anatomy of the Nerve Fibers

The nerve fibers (axons) are contained in the fascicles, surrounded by the endoneurium and processes of the Schwann cells. Nerve fiber diameters vary from 20 mm down to under 1.5μm. Fiber diameter diminishes as the nerve proceeds distally and also is variable from point to point along its course. The larger fibers are myelinated, whereas the smallest fibers are embedded in the Schwann cell walls. When viewed longitudinally, myelinated fibers have indentations in the myelin (nodes of Ranvier), which are the borders between adjacent Schwann cells. The axon is exposed in this area for a very short distance, but the exposed area is most critical for propagation of a nerve impulse. Schwann cell nuclei and cell bodies cover the myelin and, in turn, are covered by endoneurium. The axon is narrowed at the nodes and occasionally at other areas, such as under Schwann cell nuclei or other intracellular material within the Schwann cell. Unmyelinated fibers do not show the nodal pattern and are invested by Schwann cell processes. One Schwann cell may incorporate one or more small nerve fibers within its endoneurial tube (Gamble & Eames, 1964). Axons may branch along the course of the nerve, usually distally. This allows one neuron to innervate
widely separated regions. Axon reflexes, such as the triple flare response, may be explained by such branching, as might referred pain, though there is also evidence that referred pain may be a more central phenomenon. Nerve fibers lie very loosely within the fascicle. This allows some movement within the fascicle but also allows the nerve trunk to be moved or stretched without stretching the axons significantly. The connective tissue structures also tend to be lax, allowing much of the same protection against stretch injury.

2.3.2 Formation of peripheral nerves

Peripheral nerves comprise efferent and afferent fibres which connect the central nervous system to actuators and receptors. The efferent fibres leave the spinal cord via the anterior roots to innervate muscle and the afferent fibres, conveying impulses from receptors, enter the spinal cord from dorsal root ganglia via the posterior roots. Peripheral nerves also contain fibres of the autonomic nervous system.

Anterior and poster spinal roots fuse just inside the spinal canal to form a spinal nerve. A spinal nerve enters an intervertebral exit foramen and then, a little way out from the vertebral column, splits into a large anterior and smaller posterior primary ramus. At thoracic levels the posterior rami innervate paraspinal muscles and the anterior rami form intercostal nerves. At cervical and lumbosacral levels the anterior rami constitute the origins of the corresponding plexuses. Peripheral nerves arise distally from further divisions of these plexuses (Fowler et al., 1972).
2.3.3 Composition of peripheral nerve

Peripheral nerves are made up of multiple fascicles each consisting of a bundle of nerve fibres bound by connective tissue. The number of fascicles in a nerve is very variable. Sunderland (1979), showed that the structure of a peripheral nerve constantly changes throughout its length because the fascicles repeatedly divide and unite in complex elongated plexuses. Thus in four specimens examined at many different levels, the number of fascicles in the medial popliteal (tibial) nerve ranged from 11 to 93. A study of the sural nerve at the ankle in 27 post-mortem specimens showed that it usually contains between five and 10 fascicles (Jacobs and Love, 1985). In general, the size and number of fascicles is inversely related at any level. The fascicles are also smaller and more numerous where a nerve crosses a joint. Fascicles are loosely bound together by a connective tissue - the epineurium. This is mostly made up of longitudinally arranged collagen fibres, their loose attachment ensuring that fascicles are mobile to accommodate limb movement. The amount of collagen is greater at levels where nerves cross joints, and in peripheral nerves subject to pressure, such as the sciatic nerve in the thigh, the epineurium also contains fat (Sunderland, 1965). A rich anastomosing plexus of blood vessels in the epineurium is formed by longitudinal, spiral and axial vessels which renders the nerve highly resistant to ischaemia (Lundborg, 1970). Although acute emboli in major vessels can cause limb ischaemia and paralysis and loss of function within minutes, peripheral nerves can withstand several hours of partial ischaemia before undergoing changes of structural damage. The anastomotic transperineurial
circulation on the surface of rat sciatic nerve (Powell and Myers, 1986). Diffuse small vessel disease is however a potent cause of vasculitic neuropathy. Surrounding each fascicle is the perineurium. This is made up to laminated layers of flat polygonal cells bound by tight junctions to form a continuous ensheathing membrane. The perineurium presents an effective diffusion barrier which allows regulation of a separate intrafascicular milieu (Thomas and Olsson, 1984). The perineurium also contributes to the tensile strength of peripheral nerve so that the spinal roots, which lack perineurium, have the least resistance to stretch (Sunderland and Bradley, 1961). This factor becomes important in understanding severe brachial plexus injuries and is the cause for root avulsion from the spinal cord in many of these injuries. The perineurium extends distally, dividing to cover individual fibres and becoming continuous with the capsules of muscle spindles and sensory receptor end-organs. In motor nerves the perineurium surrounds the terminal portions of the nerve ending, but does not fuse with muscle connective tissues (Haller & Low, 1971). The minute gap of a few microns is a point at which toxins such as botulinum can gain access to the neuromuscular junction and thus to the endoneurial compartment.

The connective tissue within fascicles is known as the endoneurium and in normal nerve this has a sparse cellular content and occasional elastin fibre. The principle connective tissue component is collagen and very uniforms small diameter collagen fibres are arranged longitudinally in parallel with the nerve fibres. A marked proliferation of the endoneurial cells may occur in diseases of the peripheral nerve.
Contained within the fascicles are the individual nerve fibres. These have different diameters roughly according to function. A portion of human sural nerve stained so that myelin shows up black. In sensory nerve the unmyelinated fibres are three to four times more numerous than the myelinated fibres, although in motor nerves the ratio is 1:1. Each afferent or efferent peripheral nerve fibre has a central neuron which lies, respectively, in the dorsal root sensory ganglion or the anterior horn of the spinal cord, and projecting from the neuronal body – a long cytoplasmic process, the axon. Unmyelinated axons lie assembled within accesses of supporting cells. Myelinated axons are surrounded throughout their length by continuous cords of Schwann cells which wrap around the axon and enclose it in multiple lamellae of myelin. The limits of adjacent Schwann cell territories form gaps in the myelination: the nodes of Ranvier (Ross & Reith, 1967). The collagen fibers observed in the endoneurium tend to be longitudinal and often are closely apposed to the Schwann cells. This close relationship of endoneurium and Schwann cells helps form the tube through which regenerating nerve may pass following nerve injury (Gamble & Eames, 1964). These connective tissue structures serve to support and protect the underlying nerve tissue. They provide resistance to stretching, have some elastic properties, provide protection from penetration, and help dissipate compressive forces on the nerve (Haller & Low, 1971). A nerve may, therefore, be stretched without impairment of axon integrity. Tolerance to stretching may vary, in part due to nerves tested, relationship to points of entrapment, and the condition of nerves studied. Generally, the nerves may be stretched up to about 25% to 30% before the axon is damaged.
Ultrastructural studies of paranodal and nodal regions have shown these to possess considerable structural complexity (Landon and Williams, 1963). As the axon approaches the nodal region, it and its ensheathing myelin assume a crenated outline, but the surface grooves so formed are filled by mitochondria-rich cytoplasm of the surrounding Schwann cell to give a smooth outline to the paranodal region. In the nodal gap which is free from myelin, there is a complex external arrangement of microvilli embedded in an amorphous substance which has high cation-binding properties. The role of the paranodal and nodal apparatus is important in the ionic transfers of salutatory conducting action potentials.

Although myelinated fibres are so often schematically represented as series of short, fat, sausage-like segments, in reality the internodal distances are long in comparison to the fiber’s diameter. The relationship between diameter and internodal length is linear. The slope of the line of internodal length against diameter changes with growth and elongation of the limb (Fowler et al., 1972).

2.3.3.1 Afferent fibres

The afferent fibres in peripheral nerves transmit impulses generated by receptors in bone, tendons, muscles, joints and the skin. The process whereby a particular sensation is perceived remains the subject of controversy, polarized by the ‘theory of specificity’ and the alternative ‘pattern theory’ – see Wall and McMahon (1985) for a review. However, many of the peripheral mechanisms of cutaneous sensation are now better
understood as a result of human microneuronography experiments (Vallbo et al., 1979 and Hagbarth, 2002).

**2.3.3.2 The motor unit**

The concept of a motor unit was expounded by Sherrington in 1930. A motor unit was defined as the anterior horn cell, peripheral nerve and muscle fibres innervated by that motor axon, one motor axon connecting too many muscle fibres. The muscle fibres of a unit are distributed throughout the muscle in such a way that two muscle fibres belonging to the same motor unit are rarely adjacent to one another.

**2.3.4 Blood Supply of Nerves**

The blood supply of a nerve trunk consists of a network of longitudinally oriented arteries within the epineurium and over the nerve sheath. These arteries periodically receive branches from arteries in the surrounding tissues, forming an arborisation similar to that observed in the mesentery of the bowel. If one of these nutrient arteries is damaged, as happens in surgical mobilization of the nerve, there is still an adequate blood supply in the nerve through these longitudinal anastomoses. Mobilization of a nerve up to 12 cm has not shown significant impairment of circulation. Some interconnections between the longitudinal arteries then branch to deeper structures, pierce the perineurium in an oblique manner and enter the endoneurial space. The capillaries in the endoneurium have tight junctions and form the blood-nerve barrier similar to the type of barrier seen within the brain (Haller & Low, 1971). This blood-nerve barrier is of importance in some of the metabolic neuropathies, and the breakdown of this barrier in nerve injuries
may be of some importance during repair. Although the basic metabolic support of an axon comes from the cell body, there is considerable evidence that the endoneurial blood supply is very important to maintain axonal function. In clinical situations where the blood supply to a nerve has been restricted, symptoms have occurred (MacDougall et al., 1985).

2.3.5 The Schwann cell

The Schwann cells have an intimate relationship with the axons (Ross & Reith 1967). They probably have a trophic effect on the axons, help nourish the axon, and help form the "tube" through which the axon travels. The origin of these cells is disputed, but most feel that they migrate from the neural crests along with the axons. The Schwann cells are the source of the myelin in peripheral nerves, analogous with the oligodendroglial cells of the central nervous system. Myelinated axons are invested in myelin by a spiralling of a Schwann cell process about them. Nonmyelinated fibers lie embedded within a Schwann cell. Often such a cell may be surrounding several such axons. With axonal death, myelin is destroyed, but the Schwann cells survive and frequently increase in numbers. If the axon regenerates, the Schwann cell reinvests the axon, and forms myelin if needed (Seals & Victor, 1991).

2.4 Physiology of Nerve fibers (axons)

Transmission of a nerve action potential is dependent on the integrity of the axonal membrane. Damage to this membrane will interfere with normal neural function. In the steady state, this membrane has a transmembrane electrical potential of about -70 to -90 mV with the inside of
the axon being negative. The reason for this potential difference lies in both the structure of the membrane and the distribution of the solutes in the intracellular and extracellular spaces. The cell membrane is composed of a double layer of phospholipids with protein molecules scattered over the surface but also forming transmembrane channels for ions to cross the membrane. The membrane acts as a semipermeable membrane that allows some molecules to cross it while restricting others. Nerve membrane is quite permeable to K+ ions, Cl- ions, and less so to Na+ and other larger ions. Intracellular K+ concentration is markedly higher than that found outside the cell. If the K+ were free to diffuse across the membrane, there would be an efflux of the ion. The high extracellular Na+ would tend to try to get into the cell, where Na+ is low (Guyton, 1991). The membrane is less permeable to this ion, so less of a flow is present. The negative potential resists these flows and maintains the stability of the membrane. Other ions also participate in various gradients across the membrane and add their electrotonic forces to the equation, producing the final resting membrane potential. The transmembrane potential of K+ is very close to the actual resting membrane potential. In addition, an energy-dependent Na+-K+ "pump" moves Na+ ions out of the cell and K+ into the cell maintaining the relative concentrations within the cell. When a chemical or electrical stimulus is applied to this system, a series of events occurs that terminates in the generation of a nerve action potential. Such a stimulus needs to reverse (or depolarize) the negative polarization of the membrane in order to develop the action potential. When a critical level of depolarization is reached, there is a sudden reversal of polarity of the membrane to about +30 to +40 mV and an action potential is formed. Each time
that threshold is exceeded; the same amplitude of reversal occurs (the "all or none response"). Associated with this event is a sudden, brief change in membrane permeability of Na⁺ that flows into the cell. About 1 millisecond later, a similar but longer duration change occurs in the K⁺ permeability, which acts to end the action potential and repolarizes the membrane. During these brief periods of increased permeability, very few Na⁺ ions actually enter the cell, but the Na⁺-K⁺ pump will work to remove those few ions from the internal milieu (Guyton, 1991). When the action potential is generated, a current flows into the active areas of the membrane of the axon from the extracellular space. This flow then goes down the axon and exits the axon across the normal surrounding areas of the membrane into the extracellular space, completing the circuit. If the electrical changes in these normal regions exceed the threshold levels, then a new action potential is generated and the action potential is propagated down the axons by way of these local circuits. In unmyelinated fibers this process is relatively slow; however, the addition of myelin speeds up this process considerably. With the insulation provided by the myelin sheath not allowing the exit of electrical current except where it is absent (nodes of Ranvier), the flow of electrical current leaves the axon at some distance from the action potential (one to three nodes away). A new action potential is thus generated much farther down the nerve, allowing it to propagate down the nerve at a much faster rate (saltatory conduction). The longer the internode distance, the more rapidly the axon will conduct the action potential. It should be noted that the metabolism in an axon is greater in the nodal regions. Mitochondria are grouped in these regions, providing for the energy needed to sustain the Na⁺-K⁺ pump. The propagation of an action
potential requires no energy, but maintenance of the resting membrane potential does. Axon metabolism, in part, depends on substances produced in the cell body, which are conveyed distally by axoplasmic flow. Both a slow and a fast transport system occur down the axons and, in addition, there seems to be a flow in the opposite direction. There are, probably some Schwann cells and endoneurium contributions to axon metabolism. Certainly, oxygen and carbon dioxide gaseous exchange occurs in the nodal areas, as vascular occlusion of the vasa nervorum will cause malfunction of the axon (Guyton, 1991).

2.5 Neuromuscular junction structure & mechanisms of neuromuscular transmission

In the neuromuscular end-plate region of human skeletal muscle, a Schwann cell can be seen surrounding the circular profile of the motor axon terminal which is embedded in a raised area of the muscle surface, the ‘sole plate’. Within the terminal part of the nerve the acetylcholine-containing vesicles. On invasion of the presynaptic nerve by a depolarizing potential, the contents of a proportion of these vesicles is released into the neuromuscular cleft and the acetylcholine activates receptors on the muscle surface.

The Electrochemical processes of neuromuscular transmission i.e. acetylcholine receptors are located in the postsynaptic surface which extend from the top, one-third of the way down the postsynaptic clefts. Beneath the clefts the myofilaments are grouped into geometrical groups, the myofibrils (Edstrom and Grimby, 1986).
2.5.1 Physiology of nerve conduction

An account of the generation of action potentials has been given in 2.4. Here, those biophysical properties of neurons which relate particularly to conduction velocity are covered in brief.

2.5.1.1 Cable properties of axons

An unmyelinated nerve fibre axon consists of a phospholipid membrane enveloping a very long cylinder of amorphous gel matrix. The cytoplasmic include filamentous structures, organelles, proteins and electrolytes which together have a viscosity five times that of water. The electrical conductivity of his central gel is poor compared, for example, with copper. A current injected at one pint of the axon will travel less than 1 mm along the axon before becoming dissipated by the internal resistance of the axon cytoplasm and by radial current flow leaking out through the poorly insulated membrane. Membrane potential change decreases exponentially, but exactly how far current will travel without attenuation is largely determined by the internal resistance of the axon, which is turn, depends on the fibre diameter: the larger the diameter the further a signal can travel.

Axon membrane has a biphospholipid structure which has the capacity to store electrical charge. A finite time is therefore required to charge this capacitor which results in a delay in the change of membrane potential following an applied current. The time taken for the membrane to charge is referred to as the ‘time constant’. A long time constant will mean that longer time is taken to depolarize the membrane and the spread of current is slower. Speed of conduction is therefore increased by a short membrane time constant.
Since conductance is the reciprocal of resistance, a high radial resistance of an axon, as results from myelination, decreases the time constant and thus increases conduction velocity (Waxman, 1980).

Although poor, the cable properties of axons are fundamental to the conduction of impulses because it is by a combination of cable conduction and the unique property of excitable cells to regenerate action potentials, boosting the waveform at regular intervals, that impulses are conducted over long distances. The power of action potential regeneration is a property of the membrane not of the internal cytoplasm.

2.5.2 Conduction of action potentials

2.5.2.1 Continuous conduction

Current injected into an excitable cell will produce a change in the membrane potential, but after a certain level of local depolarization an explosive change in membrane potential occurs, always of the same amplitude, irrespective of the triggering stimulus. This is an action potential. With the onset of an action potential there is a rapid local increase in Na+ conductance, due to an opening of voltage-gated sodium channels. The exact mechanism whereby this is brought about is complex, but the gating mechanism is voltage sensitive so that a small level of depolarization, such as is required to bring the membrane to threshold, results in a sudden opening of the Na+ channels. With influx of sodium, the membrane polarity is reversed, the inside of the axon becoming 40-50mV positive with respect to the outside. The action potential is terminated by an inactivation of sodium conductance, and an increase in K+ conductance. Post-excitation changes last some
milliseconds and during this period the membrane is inexcitable or in a
‘refractory’ phase.

An action potential is transmitted along the axon by the
regeneration of new action potentials at regular distances. The voltage changes
which occur along an axon transmitting an impulse are complicated, needing
to be described in terms of time as well as distance. However, in essence, the
gradient of spread of the depolarization wave and thus the speed of conduction
depend upon cable properties and therefore upon the axon’s diameter.
Invertebrates such as squid, which possess only unmyelinated neurons, have
developed fibres with diameters up to 1000µm to attain high conduction
velocities – these phenomenally large axons were of inestimable value to the
pioneering biophysicists working on the mechanisms of nerve conduction.
However, higher orders of life have evolved an alternative means of speeding
up nerve fibre conduction and, in humans, very few unmyelinated fibres are
found with diameters greater than 2µm (Ritchie and Rogart, 1977).

2.5.2.2 Saltatory Conduction

The cable properties of unmyelinated axons are poor both
because of the low conductivity of the central cytoplasm as well as the poor
insulating capacity of the axon membrane which allows radial dissipation of
current. The distance that current can travel by the cable properties of axons
before requiring boosting can be vastly increased by increasing the electrical
insulation of the axon. A covering around the axon of high resistance fatty
material, myelin, has this effect.
In fibres covered by myelin, conduction along the internal length of the axon is by cable properties, facilitated by the increased membrane resistance of this fatty material, thereby reducing radial current leakage. At regular intervals there are the nodes of Ranvier where the action potential is regenerated. Nodal regions have been shown to have much higher densities of sodium channels than other parts of the axon (Ritchie and Rogart, 1977), since in normal axons these are the only sites at which action potentials need be generated. The action potential therefore jumps from one node to the next by so-called ‘saltatory conduction’.

For both myelinated and unmyelinated fibres, conduction velocity is related to axon diameter, although the addition of myelin alters this relationship by several orders of magnitude. In myelinated fibres, the thickness of myelin as well as the length of myelinated segments is important determinants of conduction velocity (Ritchie and Rogart, 1977).

### 2.6 Neurophysiological aspects of exercise training

#### 2.6.1 Neural adaptation

Neural adaptation or sensory adaptation is a change over time in the responsiveness of the sensory system to a constant stimulus. It is usually experienced as a change in the stimulus. For example, if one rests one's hand on a table, one immediately feels the table's surface on one's skin. Within a few seconds, however, one ceases to feel the table's surface. The sensory neurons stimulated by the table's surface respond immediately, but then respond less and less until they may not respond at all; this is neural adaptation.
Failure of a muscle group to generate sufficient force to overcome an external force has several different aetiologies relating to neural activation. While strength capacity of an isolated muscle fibre is generally considered proportional to muscle cross sectional area (CSA) the increase of strength during the initial weeks of a training program are not always directly proportional to muscle hypertrophy (DeLisa et al., 1994). Ploutz and colleagues reported a 14% increase in strength accompanied by only a 5% increase in CSA. The term ‘neural adaptations’ is used to summarize these adaptations made by the nervous system in response to resistance training and have been extensively reviewed elsewhere. Briefly, much of the initial rapid progress experienced by an individual new to strength training generally relates to adaptations within the motor cortex that improve the coordination of agonist and synergist muscle groups. Fleck and Kreamer [1987] found a 20% decrease in antagonist coactivation in the first week of a resistance training program, a process referred to as reciprocal inhibition, by way of enhancing stimulation of the Ia inhibitory interneuron. There is also a parallel reduction in the activity of Renshaw cells and Ib inhibitory interneuron which reduces the amount of inhibition to the agonists and synergists (i.e. reduced recurrent and autogenic inhibition). Therefore, two key benefits of resistance training are the capacity to reduce inhibition to agonists and synergists, and increasing inhibition to antagonists. The traditional model of neural adaptations mainly describe their effects occurring in novice strength trained subjects before stabilizing after an initial 6-8 weeks (Pfeiffeer and Francis, 1986). Häkkinen and colleagues demonstrated in experienced weightlifters that training blocks of several months of lower intensity training results in reduced iEMG during
maximal voluntary contractions at the end of the training period, but periods of higher intensity training increased iEMG during maximal voluntary contractions. (Al-Seffar, 1990a) also concluded neural adaptations were present from EMG analysis in experienced track and field athletes after 16 weeks of a sport-specific resistance training program. These findings suggest that adaptation of the nervous system continues even after many months of resistance training. By inducing neural responses, fatigue and high intensity training may strengthen the neural adaptations, even in trained athletes. Training to the point of repetition failure may stimulate several neural mechanisms for promoting greater strength development over and above those already present in nonfailure training. Fatigue to the point of repetition failure has been indicated to maximize recruitment and the training stimulus to all muscle fibres. Fox et al. (1993) indicated that the extent of activation is related to strength development. He noted in individuals training one set to failure that each repetition increased the iEMG signal, and iEMG was highest between 80-100% of reps to failure. He concluded that the final repetitions to failure were critical for the training response given their high activation potential. The importance of high intensity and fatigue is likely related to the size principle, which dictates an assigned order of motor unit activation with low threshold motor units initially activated for their higher precision and lower force endurance properties. Additional motor units of higher threshold are recruited as increased force or velocity is required and fatigue increases (Burke et al., 1967). Since activating and overloading a high number of motor units is important to facilitate strength development training to repetition failure should maximize the number of active motor units and therefore the
magnitude of the adaptations made by these motor units (Borge et al., 1968). As a muscle approaches task failure more motor units are recruited but firing frequency begins to decline. Therefore, there is a potential for failure training to optimally develop strength by maximizing motor unit recruitment. Therefore, fatigue from heavy lifting is necessary to stimulate high threshold motor units not activated by lower intensity contractions. The capacity to activate and train high threshold motor units has particular relevance to team sport athletes who need to exert high levels of force, as it is these high threshold motor units that are capable of generating the highest amount of force and power. Since the highest threshold motor units are not activated until there is a high relative load or high levels of muscular fatigue, training with very high loads and fatigue should be useful in training the activation of these motor units. An additional advantage in training to the point of repetition failure relates to the stretch-shortening cycle (SCC). Previous research (Milner-Brown et al., 1973) has demonstrated four areas in the concentric phase of the bench press relating to increasing or decreasing power. During the concentric movement, the time-course of changes in power shows an initial spike before decreasing into a so-called “sticking point”, after which the power begins increasing again to the repetition’s peak power, before finally decreasing again to finish the concentric phase. While power production in the second (sticking point) phase would be dependent on voluntary activation of cross-bridge cycling of the active muscle groups, power production during the first phase involves both voluntary activation and the SCC given it is immediately preceded by the eccentric movement (Czekajewski et al., 1969). The SCC components are much more resilient against fatigue than voluntary
contractions as SCC components involve reflex and elastic components. Consequently, only when involuntary SCC components normally exerted during the first phase are no longer adequately compensating for the dramatic loss of power from voluntary cross-bridge cycling would there be insufficient power generated to push through the sticking point. Since stretch reflexes are trainable, developing these components over a longer training period (e.g. 6-8 weeks) may be a key component to improving the ability to generate sufficient power to continue through the sticking point, and therefore perform additional repetitions. Graph from (Hjorth and Wilson, 1973) depicting four different phases of high and low force during the bench press concentric movement.

Training to repetition failure may be beneficial in resistance training programs since exerting maximal efforts is a skill that must be learned; generating a maximal effort has high mental demands and training for full activation during resistance training is a mental skill required by athletes. An athlete well-practiced at exerting truly maximal efforts during resistance training may have a higher amount of supraspinal discharge. In a classic study investigating regulation of muscle force. He also found that muscle force could be maximized under a state of hypnosis, implicating the involvement of cognitive and mental skills in maximal efforts. Should such a characteristic be trainable, athletes on resistance training programs theoretically could train at higher intensities or higher volumes and attain greater physiological and performance benefits.
2.6.1.1 Rhythmic behaviors - short term adaptations

Short term neural adaptations occur in the body during rhythmic activities. One of the most common activities when these neural adaptations are constantly happening is walking (Pearson, 2000). As a person walks, the body constantly gathers information about the environment and the surroundings of the feet, and slightly adjusts the muscles in use according to the terrain. For example, walking uphill requires different muscles than walking on flat pavement. When the brain recognizes that the body is walking uphill, it makes neural adaptations that send more activity to muscles required for uphill walking. The rate of neural adaptation is affected by the area of the brain and by the similarity between sizes and shapes of previous stimuli (Verhoef et al., 2008). Adaptations in the inferior temporal gyrus are very dependent on previous stimuli being of similar size, and somewhat dependent on previous stimuli being of a similar shape. Adaptations in the Prefrontal Cortex are less dependent on previous stimuli being of similar size and shape.

2.6.1.2 Rhythmic behaviors - long term adaptations

Some rhythmic movements, such as respiratory movements, are essential for survival. Because these movements must be used over the course of the entire lifetime, it is important for them to function optimally. Neural adaptation has been observed in these movements in response to training or altered external conditions (Pearson, 2000). Animals have been shown to have reduced breathing rates in response to better fitness levels. Since breathing rates were not conscious changes made by the animal, it is presumed that neural adaptations occur for the body to maintain a slower breathing rate.
2.6.2 *Muscle strength training and its effects on the neuromuscular system*

Muscle strength training in various forms is one of the most common therapy methods in physical therapy, and it is commonly used to improve muscle performance and strength. Because strength training causes both neural and muscular changes and adaptation of the neuromuscular system, it may also change the movement patterns performed with the trained muscles and effect changes in coordination. Three main principles of training have been presented: 1) overload principle (Sale and Macdougall, 1981), 2) specificity principle (Behm & Sale 1993) and 3) reversibility principle (Clarke, 1973). According to the overload principle, “to increase their size or functional ability, muscle fibers must be taxed toward their present capacity to respond”, which means that there is a threshold point that must be exceeded before an adaptive response will occur (Sale & Mac Doughall, 1981). According to the specificity principle “training adaptations are specific to the cells and their structural and functional elements that are overloaded”, which means that the induced change is specific to the exercise stress, and that strength training, for example, increases strength rather than endurance (Behm & sale, 1993). The reversibility principle points out that “training-induced adaptations are transient”, which means that when the training is discontinued, the system adapts to the new and lower requirements (Clarke, 1973). There are several training and loading techniques which increase muscle strength. The most commonly used training techniques are isometric training, dynamic training, training with accommodation devices, plyometric training and neuromuscular electrical stimulation. The main principles of these techniques are that the muscle length is constant in isometric training and varies in
dynamic training. Training with accommodation devices provides an accommodating resistance, and one special type of this training is isokinetic training, i.e. movement in which the angular velocity is constant. Plyometric exercises train a specific movement pattern, the eccentric-concentric sequence of muscle activity, and in neuromuscular electrical stimulation muscles are activated by external electric shocks (Chu, 1992). The quantity of load used during training depends on the subject’s initial strength level and the main goal of training (i.e. whether the main goal is to increase maximal strength, endurance strength or speed strength), and the exact numerical load values must be defined individually.

2.6.2.1 Acute changes

One characteristic of the motor system is its adaptability to different levels of usage. The increase in core temperature achieved by a warm-up or muscular work improves the biomechanical performance of the motor system by increasing the dissociation of oxygen from hemoglobin and myoglobin, increasing metabolic reactions and muscle blood flow and enhancing the conduction velocity of action potentials (Katz & Sahlin, 1990). In addition, an increase in muscle temperature causes changes in muscle stiffness, defined as the slope of a force-length relationship. Muscular work disturbs the actin-myosin bonds that have developed and thereby reduces the passive stiffness of the muscles by moving the muscle groups through a complete range of motion (Gonya & Erricson, 1977). On the other hand, muscular work and strength training cause neuromuscular fatigue, which impairs some aspects of performance. Heavy muscular work performed with
continuous isometric (Smith, 1991), intense intermittent isometric (Garfinkel & Cafarelli, 1992) or dynamic (Giddings & Gonya, 1992) resistance decreases muscle strength temporarily in trained muscles. In addition, one strength training session decreases electromyographic (EMG) activity and shifts the shape of the force-time curve of trained muscles. Previous findings have suggested that these changes may be consequences of neuromuscular fatigue. Neuromuscular fatigue is not caused by impairment of a single process, and fatigue varies from one condition to another, depending on the amount of force, the muscles involved and the duration of activity. This phenomenon is called the task dependency of muscle fatigue (Clarke, 1973). Neuromuscular fatigue has been classified as central or peripheral and Ritchie (1977) defined the potential sites of neuromuscular fatigue as: 1) excitatory input to higher motor centres, 2) excitatory drive to lower motor 32 neurons, 3) motor neuron excitability, 4) neuromuscular transmission, 5) sarcolemma excitability, 6) excitation-contraction coupling, 7) contractile mechanisms, and 8) metabolic energy supply and metabolite accumulation. The neural drive to the muscles at the central level has been tested by comparing the force of fatigued muscles during a maximum voluntary contraction to the force which has been added via external electrical stimulation. These tests indicate that the neural drive to the muscle provided by the central nervous system is not always maximal, and that the decrease in central drive can be a factor which decreases the force output. There is some evidence that physical activity has some influence on nerve conduction velocity. Halar et al. (1985) showed in 20 subjects that the nerve conduction velocity of the sural nerve increased from 36.1±3.1 m/sec to 39.0±3.2 m/sec during 30 minutes of walking. However, they pointed out that
this influence is not the same for all types of exercise and that not all nerves may be affected in the same way. There are some studies which suggest that impairment of neuromuscular propagation (conversion of an axonal action potential into a sarcolemmal action potential) is one mechanism that may contribute to the decline in force during different tasks (Fuglevand et al., 1993). At the muscle level, fatigue may take place at the conversion of the action potential into a muscle fiber force (excitation-contraction coupling). Changes in the intracellular state decrease the amount of Ca2+ released (essential factor in muscle contraction) and the amount of Ca2+ returned to the sarcoplasmic reticulum (Guyton, 1991). In addition, products of energy metabolism and blood flow may decrease muscle force during muscle work. For example, intramuscular pressure during muscle work can compress blood vessels and occlude blood flow (Sjogaard et al. 1991). Intensive muscle work, especially with eccentric contractions, may cause muscle soreness, most commonly 24-48 hrs after the exercise. There is no full consensus as to the mechanism that causes muscle soreness, but several potential explanations have been presented. It is assumed it to be result from the process where the acto-myosin bond is broken mechanically (Ritchie & Rogart, 1977) presumed the main reason to be the loss of cellular calcium homeostasis, while (Smith,1991) assumed muscle soreness to be a consequence of an inflammatory response. (Landon & Williams, 1963) showed that neuromuscular fatigue did not affect unresisted fractionated reaction time components (premotor time + motor time = total reaction time), but increased all resisted total reaction times. Because the changes were manifested in the motor time component, he suggested that neuromuscular fatigue takes place in
the peripheral muscular component. MacLaren et al. (1989) investigated the effects of agonist and antagonist muscle fatigue on the performance of rapid, self-terminating arm movements. They found agonist muscle fatigue to be associated with a decrease in peak velocity and peak deceleration and antagonist muscle fatigue to be associated with a decrease in peak deceleration. They suggested that agonist muscle fatigue affects movement velocity more than antagonist muscle fatigue (Medbo et al., 1988).

2.6.2.2. Long term changes

It is well known that prolonged muscle strength training increases muscle strength in trained muscles. This effect has been perceived in children (Edstorm & Grimby, 1986), middle-aged subjects (MacDougall et al., 1980) and elderly people (Lorsson & Ansved, 1985). However, the increase of muscle strength is greatly training-specific and depends on the type, intensity and duration of muscle work, and the changes in measured muscle strength are greatest in the tasks and exercises that have been used during the exercise period. Strength training causes both neural and muscular changes and adaptation of the neuromuscular system. Neural adaptation predominates in the early phase of training (Stauber, 1989). It is presumed that the neural adaptation of muscles in the early phase of training is due to a more active recruitment of motor units and an increase of their firing rates upon maximum voluntary contraction. The recruitments of slow- (type I) and fasttwitch (type IIa,b) muscle fibers are in relation to the intensity of effort. For rapid, powerful movements, the fast-twitch fibers are activated (Edgerton 1976). The authors assumed the improvement of strength performance to be due to the
fact that the subjects can recruit more of type IIa, and especially type IIb, motor units during maximum contraction of the measured muscles, and that they can express their true strength capacity by increasing their capacity to recruit more type II motor units during rapid, powerful movements. This means that strength trained subjects can more fully activate their prime moving muscles in maximal voluntary contractions. However, there is intersubject variability in this ability, and some muscles are more difficult to activate than others. Untrained subjects may have difficulty both in recruiting all motor units and in gaining optimal firing rates of the activated units in certain muscles (Sale, 1987). Apart from the increased activation of the agonist muscle (prime movers in a task), neural adaptation may cause changes in the activation of synergist and antagonist muscles, which can be manifested as improved skill and coordination (Rutherford & Jones, 1986). The cocontraction of antagonist muscles may provide a stabilization factor during rapid contractions of agonist muscles. On the other hand, co-contractions of antagonist muscles may be a limit factor for full motor unit activation of agonist muscles. Muscle training may decrease the amount of co-contraction, offering a greater force in the direction of agonist muscle movement.

The greater motor unit activation achieved by muscle training may also increase the rate of force development, but this may be require explosive type of training (Edgerton et al., 1976). A good example of neural factor adaptations are the strength training studies of unilateral extremities. These studies have shown that strength also increases in the untrained extremity, but changes only take place in EMG values, not in muscle size.
This indicates that the “crosstraining” effect is a result of neural adaptation (Stauber, 1989). These findings lead to the conclusion that it is possible to increase strength without adaptation in the muscle, but not without adaptation in the nervous system (Clarke, 1973). When muscle strength training continues for over three or four weeks, the increase in strength is caused notably by the mechanisms that increase muscle size. The contribution of neural factors decreases over time, but they continue to play some role for at least eight weeks (Sale, 1987). The increase in muscle cross-sectional area and size is a consequence of hypertrophy, and implies an increase in the cross-sectional area of a single muscle fiber. It has been suggested that hypertrophy of muscle fibers is a consequence of a change in the ratio of protein synthesis to reduction, but this has not been clearly defined. It has been assumed, that this ratio depends on hormonal (testosterone, growth hormone, insulin), metabolic and mechanical (stretch, contraction) factors. However, the increase in cross-sectional area depends greatly on the subject’s initial strength level. With novice subjects, 6 weeks of isometric strength training increased the cross-sectional area of biceps brachii and brachioradialis by 5% and 8 weeks’ training increased the cross-section of quadriceps femoris by 15% (Garfinkel & Cafarelli, 1992), but not even 24 weeks’ strength training increased the cross-sectional area of the muscle fibers of biceps brachii in a group of experienced body builders. After all, most studies on muscle strength training have addressed the effect of training on muscle force and EMG changes (Hodes et al., 1948). The authors of previous studies have given very little attention to the effects of strength training on the other motor components of
the trained extremities, such as reaction time, speed of movements and coordination.

2.7 How to improve athletic performance by optimizing the functioning of nervous system

When a muscle becomes stronger in response to training, the gain in strength is usually attributed to an improvement in the size or quality of the muscle. The truth, however, is that strength upgrades can occur without any change in the muscle at all. Many upswings in strength are actually the result of alterations in the way the muscle is controlled by the nervous system. Specifically, the nervous system can do a better job of recruiting muscle fibres and collections of muscle cells (motor units) within the muscle during an athlete's sporting activity, thus producing more forceful movements. (Christensen & Galbo, 1983) The nervous system might also become more accomplished at stimulating 'synergists', i.e., muscles which aid the primary muscle in carrying out its assigned function. Importantly, the nervous system can also enhance its ability to inhibit 'antagonists', i.e., muscles which produce forces counter to the desired direction of movement; when this 'restraining order' is put in place, prime movers and synergists can create considerably stronger movements. However, bear in mind that those three key roles - activating, synergizing, and inhibiting - only scratch the surface of what the nervous system can do to improve strength. From a neural standpoint, strength is a function not only of how well the nervous system stimulates prime movers and synergists and inhibits antagonists - but of how long the nervous system chooses to sustain this stimulation and inhibition. Brief stimulations lasting
no more than a few milliseconds tend to produce modest movements, but a more continuous activation/inhibition of key muscles allows forces to be maintained for a longer period of time, thus permitting the muscles to carry out more total work. (Ginzel, 1977).

And don't forget that the nervous system may also become more highly reactive - and thus able to stimulate motor units more quickly. While this by itself does not upgrade force production, it allows forces to develop more rapidly i.e. it converts strength into power. To put it another way, if you are a strong Tour de France cyclist and your nerves learn to activate your leg muscles more quickly, you would have not only the strength to scale the various mountains along the Tour's route but also the power to climb those promontories quickly. If you are a competitive runner (or at least you run during your sporting activity), you would be able to move along at higher rates of speed. Finally, the nervous system can also learn to activate motor units in a way which will produce not only the desired level of strength and power for a particular sport but also the most energy-efficient production of strength and power. By 'dialling up' just the right motor units for a particular activity and 'calling' them at the correct time, the nervous system enhances coordination (skill and efficiency of movement), thus conserving energy and allowing competitive levels of effort to be carried out at a lower (and thus easier) percentage of 'max'. It matters not whether the 'max' refers to maximal aerobic capacity (VO2max), maximal running speed, max cycling speed, max rowing speed, top swimming speed, etc. - if the nervous system allows any effort
to be carried out at a lower percentage of maximal that effort will be easier to tolerate and sustain during workouts and competitions. All of these positive changes within the nervous system (spiked stimulation, synergy, inhibition, continuity, reactivity, and efficiency) can be called 'neural adaptations' to training. (Honet et al., 1968). As you can see, proper nervous-system activity is critically important for athletic success. The million-rupee question is: how should you structure your training programme in order to optimize the functioning of your nervous system?

Fortunately, scientific research provides a number of important clues. For example, in a key study carried out more than two decades ago, researchers simply trained the elbow-flexor muscles of their subjects (basically, the biceps brachii, brachialis, and brachioradialis muscles). An important aspect of this research was that each athlete strength-trained only one arm, with the other arm serving as a 'control'. At the end of the study, elbow-flexor strength in the athletes' trained arms had improved by about 35 per cent. As part of their research, the exercise scientists involved in this investigation placed electrodes on the athletes' arms directly over their elbow-flexor muscles, both at the beginning and end of the study. During elbow flexion, these electrodes detected and recorded electrical activity in the elbow flexors; each recording was quantified as an 'integrated electromyogram', or I EMG. By creating an I EMG before and after the training period, the scientists could uncover changes in the way the athletes' nervous systems were regulating the elbow flexors in response to the training. As you might expect, the I EMG for a particular muscle tends to increase in response to appropriate
strength training, and enhancements in I EMG are correlated with improvements in voluntary strength. A more expansive I EMG can mean that the nervous system is recruiting more muscle cells to carry out a specific activity. Interestingly enough, in this benchmark study the cross-sectional areas of the trained arms increased over the course of the investigation by almost 10 per cent, indicating that some of the observed gains in strength were due to increased muscle volume. To put it simply, individual muscle cells within the elbow flexors got bigger, and as they grew in size they were able to create more force. However, a significant portion of the strength gain was caused by neural adaptation (Sale, 1987). Activation level (I EMG) increased by more than 10 per cent over the course of the study, indicating that the nervous system was doing a better job of recruiting the muscle fibres required for forceful elbow flexion.

But here's where things got really interesting: in the trained arm, the activation level (I EMG) linked with a particular quantity of force declined, and the amount of force associated with a particular activation level (I EMG) increased significantly (Burke, 1967). In other words, after training it took less nervous-system activity to create a specific force (since the individual muscle fibres were stronger, fewer needed to be recruited to generate a fixed amount of force), but for a given activation level (I EMG), greater force was automatically generated (since the nervous system was recruiting stronger individual muscle cells). As you might expect, it is possible to tease apart the changes in strength associated with differences in (1) activation level and (2) muscle size merely by plotting I EMG against force.
during the muscle activity of interest - before and after training. To understand how this is possible, you need to know that the relationship between force and I EMG tends to be linear, i.e., as force increases I EMG also expands in a straightforward and linear manner. However, as muscle size increases the slope of this line will be less steep, i.e., augmentations in I EMG will be smaller for each unit increase in force, since the new bulkiness of the muscle fibres means that the nervous system has to dial up fewer fibres to create a given level of strength. To put it another way, the (bigger) muscle is making it easier for the nervous system to generate force production (Roy et al., 1991).

Naturally, you would expect that - after appropriate training - a muscle or group of muscles would be able to create a new maximal ('peak') force, and that this new peak would be associated with a higher I EMG (bear in mind that even though less neural activation is required for a particular submaximal force, enhancements in peak force are usually the result not only of upgrades in muscle size but also upswings in the ability of the nervous system to stimulate the muscle fibres). Sometimes, though, the new peak force is created without any increase in muscle size - and is entirely the result of greater neural activation (neural adaptation). When that happens, the slope of the line linking increases in I EMG with upswings in force does not change (after all, the muscle cells have not improved their quality or quantity, so a given I EMG will not lead to improved force production - and all enhancements in strength are due to an upgraded activation level, or I EMG).

Amazingly enough, this is exactly what was observed in the untrained arm in this elbow-flexion research: Despite undergoing no training
at all, the untrained arm was more than 20-per cent stronger at the end of the study! The untrained elbow flexors had tacked on not even an ounce of new muscle tissue, but they were significantly stronger, because the nervous system had an improved ability to stimulate and control their activity. Basically, the nervous system had taken the pattern of muscle control it had developed to promote strength in the trained arm and was using it to bolster strength in the still-physically feeble, untrained arm. Now that is neural adaptation (Al-Seffar, 1990b).

Thus the nervous system plays a critically important role in the development of greater strength, and the nervous system can even learn patterns of muscle coordination and activation which can be utilized to boost strength in completely untrained muscles.

Another important study

This early, groundbreaking study demonstrated both the amazing adaptability of the nervous system and also its tremendous importance in the development of strength. An important corollary investigation completed in a different laboratory reaffirmed the notion that the nervous system is a key player in strength enhancement - and showed athletes how to develop training programmes which could optimally develop functional strength (unfortunately, this study and others like it have been almost completely ignored by the athletic community). In this second piece of research, athletes carried out eight weeks of barbell squat training and by doing so were able to increase peak barbell-squatting strength by more than 70 per cent. The Scandinavian scientists involved in this study had the presence
of mind to measure changes in strength during other activities involving the key muscles of the legs and learned that leg-press strength also increased during the eight-week period - but to a considerably smaller extent. Most notable, however, was the fact that knee-extension strength - measured during a seated exercise which involved straightening the legs against resistance - did not improve at all over the eight-week time frame, even though the key muscles involved in knee extension - the quadriceps - had been considerably strengthened by the barbell-squatting routines.

The key to this 'strange' finding was that the I EMG (neural activation) during knee extension did not improve at all over the course of eight weeks. Thus, even though the athletes' quadriceps muscles were 'stronger', their nervous systems had not improved their ability to activate the quads during knee extensions (indeed, there was some evidence that the nervous systems were less skilled at activating the quads during knee extensions after eight weeks, perhaps because they had poured their energies into learning how to control barbell squatting), and thus no upgrade in knee-extension strength was apparent. The fortified quads simply sat there like slabs of beef during knee extensions; the athletes' quads were bigger but were only able to exhibit improved strength during movements which were actually practised during training (barbell squats), or during movements (leg presses) which closely resembled the practised ones. Strength did not 'transfer' between dissimilar activities. (Roy et al. 1991). (i.e., from squatting to leg extensions)

To put it another way, you can beef up your muscles all you want, but you won't necessarily be stronger in your sport unless you have done the right thing i.e. focused on the necessary neural adaptations as well. The
key lessons are as follows: (1) the strength gained in one activity does not automatically transfer over to other activities. The transference in strength gets smaller (and may approach zero) as the activities become more dissimilar (2) in your training, you should focus on strengthening sport-specific movements, not individual muscles or muscle groups. If you fail to concentrate on movements, you are leaving the nervous system out, and gains in strength will not be optimized (3) If your sport involves running and you would like to run faster, you should try to avoid seated strengthening exercises, which isolate muscle groups, and 'two-leg' exercises, and instead focus on exercises in which strength is exerted in a coordinated fashion by one leg at a time, as is the case with actual running. One-leg squats are superior to two-leg squats, one-leg hops are better than two-leg jumps, high-bench step-ups are preferred over regular barbell squats, and so on (Costill, 1985).

2.8 Peripheral neuropathy

Peripheral neuropathy is damage to the nerves in the peripheral nervous system. Because there are so many types of peripheral neuropathies, they can affect anyone, at any age.

Peripheral neuropathy occurs when the peripheral nerves are damaged or destroyed. This may be caused by disease, injury, inherited disorders, metabolic disorders, growths that put pressure on nerves, poor nutrition, infection, or exposure to toxic substances such as mercury or lead. Some common causes include diabetes, Lyme disease, chronic alcoholism, kidney failure, the varicella-zoster virus that causes shingles, and a type of food poisoning called botulism. Leprosy is a common cause of peripheral
neuropathy worldwide. Polio and diphtheria can also cause peripheral neuropathy. Some better-known types of peripheral neuropathies include Charcot-Marie-Tooth disease, Guillain-Barre syndrome, carpal tunnel syndrome, and sciatica. In some cases, however, the cause is unknown.

The symptoms of peripheral neuropathy depend upon the cause and the location of the nerve damage. If sensory nerves are damaged, symptoms can include numbness and pain, usually in the hands, arms, legs, or feet; “pins and needles” sensations; and tingling or burning. Damage to motor nerves causes general muscle weakness. Over time, the muscles will shrink (atrophy). Symptoms can progress to complete paralysis. (Bostock, 1993)

The principle changes in nerve function are related to demyelination, axonal degeneration and conduction block. There are no absolute dividing lines between these situations; they show some overlap and also dynamic changes from one stage to another due to the interaction between Schwann cells and the axonal condition. In cases of demyelination, the conduction velocity is reduced. In cases of axonal degeneration, there may be normal velocity in the remaining axons, but a weaker muscle response is evoked. In cases of conduction block, no axonal degeneration occurs and therefore a normal response is obtained when stimulating distal to the lesion. When stimulation is performed proximal to the site of abnormality, a reduced number of axon conducts impulses, and a smaller than normal muscle response is obtained.
2.8.1 Polyneuropathy

Polyneuropathy may be expressed as axonal or demyelinating, sensory, motor or sensory-motor. The type of electrophysiological picture depends on the underlying cause. In a typical case of sensory-motor demyelinating polyneuropathy (diabetes mellitus) the following may be found; Abnormalities are more pronounced in the legs than in the arms. Sensory findings are often more abnormal than motor. Note that this may not always reflect a more severe sensory involvement, but may be due to the fact that sensory nerves are usually investigated in a more distal segment than the motor nerves. The conduction velocity (CV) is reduced relatively more than the amplitude drops. (Albers & Kelly, 1989)

2.8.2 Hereditary Motor Sensory Neuropathies

The hypertrophic (type I) and neuronal (type II) varieties of Charcot-Marie-Tooth disease are the most common forms of hereditary motor sensory neuropathy (HMSN). These usually show an autosomal dominant inheritance. The hypertrophic variety shows enlargement of the peripheral nerves, segmental demyelination and remyelination with onion-bulb formation, and axonal atrophy. A very slow nerve conduction velocity is a hallmark of the HMSN type I. Prolonged terminal latencies in the early stages indicates prominent distal slowing. Despite slowing the degree of temporal dispersion is limited, which indicates homogeneity of the pathologic process. Such uniformity helps in differentiating this entity from acute inflammatory polyneuropathy (Berciano et al., 1984).
In the neuronal variety of HMSN, patients have neither hypertrophic nerves nor prominent segmental demyelination. Electrophysiological studies reveal mild slowing of the nerve conduction velocities, and reduction in amplitude of the sensory and muscle action potentials [Kimura, 1989].

2.8.3 Mononeuropathy; lesion, entrapment (Carpal Tunnel Syndrome, CTS)

In cases of lesions and entrapment, e.g. across the elbow, the study of short segments (inching, centimetre) may be very important. In cases of local demyelination, a local slowing is seen. (Gilliatt, 1978) The site of a conduction block is revealed by short segment studies. In some instances needle stimulation may be helpful to localise the lesion or entrapment with precision. It should be noted that both proximal and distal stimulation is important to give the complete picture. Comparison between sides regarding CMAP amplitude and latency may also provide important information.

2.8.4 ALS (Amyotrophic lateral sclerosis)

In motor neuron disease, the motor and sensory nerve conduction velocities are normal in preserved axons. A slowing may be seen when severe atrophy has developed and the CMAP is distinctly reduced. The change in the CV is considered to be due to the random loss of axons with no preferential early involvement of large axons.

The sensory nerve conduction velocities and amplitudes are normal in MND (motor neuron disease). This is an important finding which helps to differentiate ALS from axonal neuropathies.
Since pure motor nerve neuropathies do occur and can produce the same nerve conduction findings as MND (motor neuron disease), the ultimate diagnosis will depend on the EMG findings and clinical presentation.

2.8.5 MMN (Multifocal Motor Neuropathy)

MMN is a disorder that also shows conduction block (Lewis & Sumner, 1982 and Parry, 1993), called Multifocal motor neuropathy (motor neuropathy with persistent multifocal conduction block), MMN. This disorder may be clinically similar to motor neuron disease. Therefore, in each patient with suspected motor neuron disease, AMPL DECAY must be studied in several motor nerves. Not only the usual segments in the forearm should be tested, but also the nerves should be stimulated at proximal sites in the axilla and the supraclavicular fossa of the ulnar nerve. Sensory nerves do not show conduction block. In many respects multifocal motor neuropathy is similar to Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) (Parry, 1993).

2.9 Peripheral nerve disorders in athletes

The cranial and thoracic nerves generally do not involve themselves in plexus formation and can be traced from the skull or the spine to their destinations. The roots, plexuses and peripheral nerves branch at various levels, sending fibers to specific muscles along their course and receiving sensory fibers from sensory endings in the skin, muscle, and viscera. These branches generally follow a fairly consistent pattern on joining the nerve trunk. This pattern of branching has been helpful to clinicians assessing nerve function following injury and is one of the anatomic bases for electromyographic evaluation of nerve injuries. The long course of the
 peripheral nerves makes them susceptible to damage from movements of the limbs. Areas of greater susceptibility exist in most peripheral nerves, and these areas of entrapment are well known clinically but will be enumerated here. In the upper extremity, the median nerve is entrapped as it traverses the wrist underneath the transverse carpal ligament (Thomas et al., 1991). Less known but equally damaging is compression of the nerve at the ligament of Struthers at the distal extent of the humerus. The anterior interosseous branch may be caught in the pronator teres or in the fascia of the flexor muscles in the forearm. The ulnar nerve may be entrapped at the cubital tunnel or in the groove in the elbow, where it is also susceptible to trauma. Another area of entrapment is found at the wrist in Guyon's canal. The radial nerve is most susceptible to injury in the spiral groove of the humerus, where it is in close apposition to the bone. It also may be bound down as it makes a sharply angled dive to become the posterior interosseous nerve just below the elbow. In the lower extremity, the peroneal nerve lies very close to the head of the fibula in a superficial position, allowing it to be traumatized quite easily. It also is bound with fibrous tissue to some extent at this point. The nerve also is bound at the ankle. This is probably of little clinical importance, however. The posterior tibial nerve enters the arch of the foot through the tarsal canal, made up of ligaments of the arch and underlying bone, and is subject to trauma in this region. The sciatic nerve can be fixed in the sciatic notch, especially with marked flexion of the hips when squatting (hunkering). The sciatic nerve also pierces the piriformis muscle in a significant number of persons and may be compressed at that point. The femoral nerve is most susceptible as it enters the femoral triangle in the groin area (Thomas & Olsson, 1984).
2.10 Peripheral nerve injuries in athletes

Gowers in 1892 described a radial nerve injury in a patient “throwing a stone with energy”. Forceful muscular effort resulted in a humerus fracture with a radial nerve injury. Since this early report, sports have taken on a larger role in our lives. With increased athletic participation, there has been a rise in sports-related injuries.

2.10.1 Baseball and Throwing Sports

Nerve injuries to the throwing arm are caused by the extreme stresses generated across joints during the throwing motion. These stresses are greatest at the shoulder and elbow. Analysis of the throwing motion is important to understanding the mechanisms of injury (McLeod, 1985).

2.10.1.1 Ulnar Neuropathy

Recurrent valgus stress on the elbow during the throwing motion results in ligamentous inflammation and joint laxity (Conway et al., 1992). Increased joint mobility allows recurrent stretch, compression and subluxation of the ulnar nerve. Intermittent and persistent symptoms and signs appear, such as elbow pain, numbness and tingling in the ulnar digits, and weakness of ulnar innervated muscles. The syndrome occurs in adults and in adolescents in what is termed, “The Little Leaguer’s Elbow” (Jobe & Nuber, 1986 and Pappas, 1982). Early evaluation by a sport-physician is important to management. Electrophysiologic evaluation, electromyography and nerve conduction studies, may reveal conduction delay across the elbow and denervation of ulnar muscles. Some athletes respond to rest while others
require repair of the ligament with submuscular or subcutaneous transposition of the nerve (Andrews & Timmerman, 1995).

2.10.1.2 Suprascapular Neuropathy

Stress across the shoulder is greatest during the acceleration and deceleration phases. A commonly observed syndrome in throwing athletes, such as volleyball players, baseball players, and javelin throwers, is the suprascapular neuropathy (Ringel et al., 1990). As the nerve courses over the scapula to innervate the supraspinatus and infraspinatus, 2 sites of compression and stretch are the suprascapular notch and the spinoglenoid ligament. Athletes complain of pain and exhibit weakness of abduction and external rotation of the shoulder. Nerve conduction studies may reveal delay across the points of entrapment. Electromyography demonstrates denervation and axonal loss depending on the severity of the injury. Additional imaging is required to identify cysts or ganglia in the spinoglenoid region (McClusky et al., 1999). The athlete should be removed from competition. Therapy is directed at maintaining range of motion and strengthening shoulder abductor and external rotator muscles. In some instances, the nerve may be surgically explored and released to diminish pain and improve strength.

2.10.2 Football

The 5th through the 8th cervical roots exit the spinal canal to form the trunks and cords of the brachial plexus before dividing into the nerves of the arm. The plexus lies in close proximity to the shoulder, the 1st rib, and clavicle. Sudden depression of the shoulder with contra lateral
distension of the head places compressive and traction forces on the nerves of
the plexus, the cervical roots and even the spinal cord.

Following a collision or tackle, the “stinger or burner” describes the burning and tingling experienced by the player from the shoulder
to the hand. Weakness of the shoulder may accompany sensory symptoms. In
most cases, the symptoms and signs are brief, lasting seconds to minutes. The
anatomic origin of the symptoms is debated. The athlete with persistent motor
or sensory findings should not compete. Recurrent trauma with progressive
symptoms likewise limits return to play. Persistent weakness and sensory loss
require electromyographic and radiographic evaluation of the cervical spine
and brachial plexus (Meyer et al., 1994; Markey et al., 1993 and McLeod,
1985).

2.10.3 Running

Long-distance runners do not develop peripheral neuropathy as
a result of running. They frequently experience transient paresthesias
associated with minor injuries to the feet and toes (Dyck et al., 1987). Runners
and dancers complain of deep burning, lancinating pain of the toes due to
recurrent microtrauma to the interdigital nerves resulting in web space
neuroma formation. Deep pain and numbness on the sole of the foot provoked
by running or jogging raises the possibility of focal entrapment or trauma to
the medial plantar cutaneous branch of the distal posterior tibial nerve at the
ankle. This is called the tarsal tunnel syndrome. Lateral and calcaneal
branches may also be involved. The electrophysiologic features of these
syndromes include distal latency prolongation and denervation of intrinsic foot
muscles. Treatments include rest, orthotics, local injection, and in some instances surgery (Schon & Baster, 1990).

Upper extremity peripheral nerve syndromes may be seen in runners. We observed a distal median neuropathy at the wrist in an athlete competing in an Ultra Marathon in New York City’s Shea Stadium. Ice taped to his wrists to promote cooling during the race caused distal median paresthesias. Symptoms resolved over 6 weeks. Electrophysiologic studies were not performed.

2.10.4 Cycling

Mechanical compression and ischemia also cause neuropathies in bicyclists. Numbness and weakness of the hands common in cyclists are due to handlebar compression of ulnar nerve at Guyon’s canal (hypothenar aspect of the palm) or the median nerve at the carpal tunnel (Rettig, 1990). Nerve conduction studies demonstrate conduction delays across these regions of compression or may be entirely normal (Jackson, 1989). Pudendal and genitofemoral neuropathies are caused by compression on the bicycle seat (Mellion, 1991). Symptoms fortunately remit with technical adjustments, such as specialized gloves, padded handlebars, and alteration of hand and trunk positions.

Lorei & Hershman (1993) reported that in the shoulder, spinal accessory nerve injury is caused by a blow to the neck and results in trapezius paralysis with sparing of the sternocleidomastoid muscle. Scapular winging results from paralysis of the serratus anterior because of long thoracic nerve palsy. A lesion of the suprascapular nerve may mimic a rotator cuff tear with
pain a weakness of the rotator cuff. Axillary nerve injury often follows anterior shoulder dislocation. In the elbow region, musculocutaneous nerve palsy is seen in weightlifters with weakness of the elbow flexors and dysesthesias of the lateral forearm. Pronator syndrome is a median nerve lesion occurring in the proximal forearm which is diagnosed by several provocative manoeuvres. Posterior interosseous nerve entrapment is common among tennis players and occurs at the Arcade of Froshe—it results in weakness of the wrist and metacarpophalangeal extensors. Ulnar neuritis at the elbow is common amongst baseball pitchers. Carpal tunnel syndrome is a common neuropathy seen in sport and is caused by median nerve compression in the carpal tunnel (Gilliatt, 1978). Paralysis of the ulnar nerve at the wrist is seen among bicyclists resulting in weakness of grip and numbness of the ulnar 1.5 digits. Thigh injuries include lateral femoral cutaneous nerve palsy resulting in loss of sensation over the anterior thigh without power deficit. Femoral nerve injury occurs secondary to an iliopsoas haematoma from high energy sports. A lesion of the sciatic nerve may indicate a concomitant dislocated hip. Common peroneal nerve injury may be due to a direct blow or a traction injury and results in a foot drop and numbness of the dorsum of the foot. Deep and superficial peroneal nerve palsies could be secondary to an exertional compartment syndrome. Tarsal tunnel syndrome is a compressive lesion of the posterior tibial nerve caused by repetitive dorsiflexion of the ankle—it is common among runners and mountain climbers (Lorei & Hershman, 1993).

Peripheral nerve injury is one of the serious complications of athletic injuries; however, they have rarely been reported. According to the
In a study by Takazawa et al., there were only 28 cases of peripheral nerve injury among 9,550 cases of sports injuries which had been treated in the previous 5 years at the clinic of the Japanese Athletic Association. The authors have encountered 1,167 cases of peripheral nerve injury during the past 18 years. Sixty-six of these cases were related to sports (5.7%). The nerves most frequently involved were: brachial plexus, radial nerve, ulnar, peroneal, and axillary nerves (in their order of frequency). The most common causes of such injuries were mountain climbing, gymnastics, and baseball. More often, peripheral nerve injury seemed to be caused by continuous compression and repeated trauma to the involved nerve. Usually it appeared as an entrapment neuropathy and the symptoms could be improved by conservative treatment. Some of the cases were complicated by fractures and surgical exploration became necessary. Results of treatment produced excellent to good improvement in 87.9% of the cases. With regard to compartment syndrome, the authors stress the importance of early and precise diagnosis and a fasciotomy (Hirasawa & Sakakida, 1983).

Norkus & Meyers (1994) reported that ulnar nerve entrapment is the second most common compressive neuropathy in the upper extremity in the throwing sport athlete because of its anatomy and superficial location.

McCrory et al. (2002) reported that exercise-related leg pain is a common and yet difficult management problem in sports medicine. There are many common causes of such symptoms including stress fractures and muscle compartment syndromes. There are also a number of less common but important conditions including popliteal artery entrapment and nerve...
entrapment syndromes. Even for an astute clinician, distinction between the different medical causes may be difficult given that many of their presenting features overlap. This review highlights the common clinical presentations and raises a regional approach to the diagnosis of the neurogenic symptoms. In part, this overlapping presentation of different pathological conditions may be due to a common aetiological basis of many of these conditions namely, fascial dysfunction. The same fascial restriction that predisposes to muscle compartment syndromes may also envelop the neurovascular structures within the leg resulting in either ischaemic or neurogenic symptoms. For many athletes with chronic exercise-related leg pain, combinations of such problems often coexist suggesting a more widespread fascial pathology. In our clinical experience, we often label such patients as ‘fasciopath’s; however, the precise pathophysiological basis of this fascial problem remains to be elucidated. This review discusses the various nerve entrapment syndromes in the lower limb that may result in exercise-related leg pain in the sporting context. The anatomy, clinical presentation, investigation, medical management and surgical treatment are discussed at length for each of the syndromes. It is clear from clinical experience that the outcome of surgical management of such syndromes fares much better where a clear dermatomal pain distribution is present or where focal weakness and/or sensory symptoms appropriate for the nerve are present. In many situations, however, nonspecific leg pain or vague nonlocalising sensory symptoms are present and in such situations, alternative diagnoses must be considered and investigated appropriately. As mentioned above, many different pathologies may coexist in the lower limb and may be a
source of confusion for the clinician or alternatively may be the reason for poor treatment outcomes.

Thierry et al. (2000) retrospectively analyzed the charts of 13 athletes (18 limbs) who had sural nerve entrapment localized in the passage of the nerve through the superficial sural aponeurosis. There were 11 men and 2 women (average age, 43 years; range, 31 to 59). All patients reported chronic calf pain that was exacerbated during physical exertion. Delay to diagnosis averaged 9 months (range, 5 to 24). Tenderness in the calf was identified along the course of the sural nerve in all cases. In 10 patients (15 limbs) electrodiagnostic testing before surgery was positive. After failure of nonoperative treatment, surgery was conducted under local anesthesia. Neurolysis was performed by incising the superficial sural aponeurosis and the fibrous band in it through which the nerve passes. The results of the operation were evaluated in terms of residual symptoms, ability to return to the former sport, and degree of patient satisfaction. A final follow-up examination was performed an average of 14 months (range, 6 to 30) after the operation. The final result was excellent in 9 limbs (2 bilateral), good in 8 limbs (2 bilateral), and fair in 1 case. The differential diagnosis of sural nerve entrapment in athletes is discussed. Increase in sural muscle mass or development of local fibrous scar tissue compromised the sural nerve in its course through the unyielding and inextensible superficial sural aponeurosis.

2.11 Clinical Electrodiagnosis

Electrodiagnostic tests are an extension of the bedside clinical evaluation of the peripheral nervous system. They add objective data about the
function of the peripheral nerve and should provide accurate neurologic information if a nerve is damaged. These tests are useful when minor changes are unable to be identified clinically or when the functions presented are in locations that are difficult to examine clinically. They shed light on pathophysiologic mechanisms that otherwise would be difficult to delineate at the bedside (e.g. differentiating neuropopraxia from a more severe injury to the axon, or delineating sensory nerve root involvement from a plexus injury).

Clinical electrophysiologists have to be well versed in neuroanatomy, topographic anatomy, and nerve physiology to make meaningful assessments of nerve function (Fraser & Olney 1992). The procedures require discrete placements of the recording electrodes/or needles, and stimulating probes to be accurate. In addition, knowledge of the disease processes affecting peripheral nerves is of great importance to the examiner in order for him or her to interpret the test findings in the proper context of the nerve dysfunction.

Clinical electrophysiologic testing of the peripheral nervous system can be divided into two broad categories: (1) nerve conduction studies with their related studies, somatosensory evoked responses, and long latency reflexes (H-reflex, F wave); and (2) electromyography (EMG) (Kaeser, 1970).

### 2.12 Nerve Conduction Studies

The function of the peripheral nerve is to transmit an electrical impulse from one point to another. The electrical stimulus normally comes from the nerve cell body or from receptor structures. In nerve conduction studies, however, the nerve is stimulated by an external electrical source. When the nerve is near the surface of the body, skin electrodes may deliver the
shock. Deeper nerves require needle electrodes. With nerves exposed at surgery, stimulating electrodes may be applied directly to the nerves. Stimulation is made with supermaximal shocks to make sure that all nerve fibers are stimulated and that a maximal response is obtained. Less than maximal stimulation may give spurious results. Recording electrodes may also be surface, needle, or directly applied types. They may be placed over muscle to record the evoked muscle action potential, or they may be applied directly over a nerve to record a nerve action potential. In sensory nerves, the potential is purely a sensory nerve action potential (SNAP), but over a nerve trunk, elements of both motor and sensory nerve action potentials are present (mixed nerve action potential). Conduction velocities measure the fastest conducting fibers of the nerve. Motor nerve conduction studies are done by stimulating the nerve at two or more points along the course of the nerve and measuring the evoked motor responses from an appropriate muscle. If the nerve length can be measured between the stimulus sites, conduction velocities can be calculated (Gilliatt, 1971). Various segments along the nerve may be tested, allowing for greater precision in identifying an area of dysfunction. Motor nerve conduction velocities vary from nerve to nerve but generally are comparable from side to side; therefore, it is most helpful to have information from the "normal" nerve on the opposite side to compare with the target nerve being evaluated. Exact normal velocities expressed in meters per second vary somewhat from lab to lab but generally are similar. Sensory nerve conduction studies may be performed in two ways. A stimulus may be applied distally to a pure sensory nerve and recorded proximally (orthodromic) or to a nerve trunk and recorded distally off of the pure sensory branch (antidromic). Both
methods achieve comparable results, though antidromic stimulation may elicit motor responses that may obscure the smaller sensory response (Cohn et al., 1990). Like motor conduction studies, comparison with the other side is often helpful. Conduction velocities are only part of the information that can be obtained from the test. The amplitude of the response, whether motor or sensory, is a reflection of the numbers of axons that are conducting an impulse (Chodoroff 1985). Low amplitude responses suggest problems with or loss of axons between the nerve cell body and the site of recording. The presence of normal sensory nerve action potentials in the presence of severe sensory loss points to a lesion proximal to the dorsal root ganglion, suggesting an avulsion of a nerve root. Somatosensory evoked potentials (SEPs) are most helpful in evaluating the proximal segments of a peripheral nerve that normally are inaccessible to conventional nerve conduction studies. A stimulus is usually applied to a nerve peripherally, and recordings of potentials are made from proximal nerve sites, areas of entry into the spinal cord, sites on the spinal cord, and more proximal areas within the brain. SEPs, therefore, allow evaluation of the entire sensory system (Buchthal & Resenfalk 1966 a). Proximal nerve segments, therefore, can be compared with the more peripheral segments. SEPs should be performed unilaterally and also simultaneously for comparison between the two sides. The H-reflex, first described by Hoffmann is the electrical evocation of the spinal monosynaptic reflex. It therefore allows for the assessment of both proximal sensory and proximal motor nerve pathways. It is best elicited from the calf muscles but also is seen in the flexor carpi radialis. The stimulus in the leg is applied to the posterior tibial nerve, allowing evaluation of conduction in the sciatic nerve and in the SI root (Ma &
Liveson 1983). In the arm, the median nerve, the lateral cord and upper trunk of the brachial plexus, along with the C6 and C7 root, may be assessed with the H-reflex. F waves measure the motor conductions along the proximal portions of the nerve. The stimulus impulse travels toward the cord in the motor axon (antidromic). Upon reaching the motor neuron in the anterior horn, it reverses itself and goes peripherally along the same axon to the muscle (orthodromic). Unlike the H-reflex, which can be elicited only in a few nerves ((Kaeser, 1970), the F wave response may be obtained from any accessible motor nerve.

The reported normal values of median Motor Nerve Conduction Velocity (MNCV) 58.52 ± 3.76 m/s (Misra and Kalita, 2004); ulnar MNCV below elbow was 58.7 ± 5.1 m/s (Kimura 1986) and above elbow 61.0 ± 5.5 m/s (Kimura 1986); Sensory Nerve Conduction Velocity (SNCV) of median nerve (digit to wrist) was 56.2 ± 5.8 m/s (Kimura, 1986) and SNCV of ulnar nerve was 54.17 ± 6.10 m/s (Misra and Kalita, 2004). In case of lower extremity, the normal values of MNCV for CPN below knee segment 48.3 ± 3.9 m/s (Sourkes and Stewart 1991); above knee segment 52.0 ± 6.2 m/s (Sourkes and Stewart 1991); for PTN 48.3 ± 4.5 m/s (Ma and Liveson 1983) and SNCV for sural was 50.9 ± 5.4 m/s (Misra and Kalita, 2004). Nerve conduction studies may be affected by numerous factors.

### 2.13 Determinants of Nerve Conduction Velocity

Nerve conduction velocities are faster in larger nerves and those nerves that are myelinated (Campbell et al., 1980). They tend to be faster in the proximal segments than distally. Higher temperatures may
increase conduction velocities. This, in part, may account for the above observation. Conversely, cool temperatures slow conductions, giving the impression that nerve conduction velocities are slower in winter time when the extremities tend to be colder. Constant temperature conditions in the examining room minimize these effects. Age affects conduction velocities, with infant velocities being low and speeding up to adult levels at about 3 years of age. Ischemia within a limb also may slow conduction. The greatest slowing in conduction velocities occurs with demyelination or compression of the nerve, or both. Neuropraxia and nerve lacerations abolish nerve conduction across the lesion; however, after a neuropraxic lesion, the distal segment remains excitable and conduction remains normal. After a transection, the distal nerve may remain excitable for 4-7 days after the injury and then stop functioning.

2.13.1 Relationship between fibre diameter and conduction velocity

From previous considerations it is clear that, within the class of either myelinated or unmyelinated fibres, diameter is the major determinant of conduction velocity. This relationship was predicted from theoretical considerations (Rushton, 1951) and has been confirmed by experimental observations. A linear proportionality was calculated for myelinated fibres, whereas for unmyelinated fibres the velocity calculated to be proportional to the square root of the diameter.

Since diameter is also a major determinant of internodal length and myelin thickness, it has been difficult to establish experimentally the contribution of diameter alone. Computer modeling of conduction in nerve has
permitted examination of the problem by altering one parameter, such as diameter, while holding others constant (Waxman, 1980). Such studies have shown a slightly different relationship between conduction velocity and diameter than was first thought, particularly for smaller diameter fibres (i.e. less than 2µm). Originally it was thought that, in very thin axons, conduction in myelinated fibres would be slower than in unmyelinated fibres and interesting few myelinated axons of less than 2µm diameter are found in mammalian peripheral nerve (Ochoa and Mair, 1969). Computer modeling, however, has shown that myelinated fibres would conduct faster than unmyelinated fibres, even down to a diameter of 0.3µm, and such small-diameter myelinated fibres do exist in the vertebrate central nervous system (Waxman, 1980).

2.13.2 Relationship between axon diameter and myelin thickness

Also predicted from theoretical consideration was the optimal thickness of myelination (Rushton, 1951). If, in a theoretical model of a fibre of fixed external diameter, the myelin thickness is increased this will be at the expense of the internal diameter of the axon, and the advantage to conduction velocity from the increased radial resistance will be offset by the increase in axial resistance. Rushton predicted an optimal value of 0.6 for the ‘g’ ratio and subsequent computer modeling experiments confirmed the value for this relationship (Waxman, 1980):

\[
g \text{ ratio} = \frac{\text{Axon diameter (d)}}{\text{Total fibre diameter (D)}}
\]
However, measurements on mammalian fibres consistently yield a higher value of between 0.7 and 0.8, the value being at its highest in the largest and smallest diameter fibres (Jacobs and Love, 1985).

2.13.3 Relationship between diameter and internodal length

Axon diameter, the major determinant of the distance membrane potential changes can be transmitted by cable properties, is therefore the determining factor of the distance between nodes. Studies of internodal length plotted against diameter show that the relationship is linear for the whole range of fibre diameters in a peripheral nerve, although this relationship does not apply in the nerve roots. With growth of a part, the ratio of internodal length to diameter changes, so that for fibres from the facial nerve it is much less than for those from the ulnar or peroneal nerves (Vizoso, 1950).

With the onset of senescence, at around 60 years in man, the sural nerve shows considerable variability in internodal length because nodes have demyelinated and remyelinated in shorter segments as part of the ‘neuropathy of ageing’.

2.13.4 Fibre diameters in human nerve

A relationship between fibre diameter and conduction velocity was first proposed by Gasser and Erlanger (1927) as the explanation for the observation that the shape of a compound nerve action potential changes with increasing distance between the stimulating and recording electrodes. The various peaks of the compound nerve action potentials were labelled.
The \( \alpha/\beta \) peak is made up of heavily myelinated fibres, which in man have diameters between 7 and 15\( \mu \)m and conduction velocities of 35-70m/s. If sensory, these fibres terminate in sensory endings which respond to stimuli of light touch and vibration. If motor, fibres of this diameter would be alpha motor neuron fibres, the motor innervators of skeletal motor units.

The \( \alpha \) peak is made up of smaller diameter myelinated fibres with consequently thinner myelin covering. This class of fibres has diameters from 2 to 6\( \mu \)m and conduction velocities of 5-30m/s. In human sensory nerve, such fibres convey some types of mechanical stimuli, pain and sensations of cooling. In motor nerve, the innervation of the muscle spindles, the gamma efferents, would be of this size.

The C peak is made up of unmyelinated fibres and is of lower amplitude only because unmyelinated fibres generate lower external depolarizing current, not because there are fewer such fibres. In fact, the converse is true for sensory nerves: in human sural nerve the number of unmyelinated relative to myelinated fibres is about 3.7:1 (Ochoa and Mair, 1969). In the distal limb primate nerve, the majority of fibres in this group convey sensations of pain, although warming is also transmitted by them. These fibres conduct at rates of between 0.4 and 2m/s. Autonomic fibres are also unmyelinated, and on light microscopy unmyelinated afferents and sympathetic efferents are indistinguishable (Ochoa and Mair, 1969), although with electron microscopy the latter can be seen to contain dense-core catecholamine-containing vesicles.
2.14 Variables Influencing Nerve Conduction Velocity

2.14.1 Age

Conduction velocity is age dependent. Full term infants have conduction velocities, which are approximately half of that seen in adults. Conduction velocities rapidly increase from the values recorded in infants to near adult values at around 3-5 years of age. Furthermore pre-term infants have slower values at around 14-28 m/s. In the teens conduction velocities are almost the same as those of adult values (Lang et al., 1985; Rosenfalck and Rosenfalck, 1975; Gamstorp and Shelburne, 1965). After the second to fourth decade, conduction velocities start to decrease very slowly. CV decrease by 0.5-1.8 m/s for each decade (Buchthal & Rosenfalck, 1966a; Buchthal & Rosenfalck 1966 b).

2.14.2 Length of segment and height

Longer nerves generally conduct more slowly than shorter nerves (Campbell et al. 1981). It has been shown that there is a good correlation between CV and estimated axonal length in the peroneal and sural nerves, but not in the motor or sensory fibers of the median nerve. Based on a good correlation between the height of the patient and the length of the nerve, the CV in lower limbs decreases by 2-3 m/s for 10 cm increase in height (Falck and Stålberg, 1995). Nerve impulses propagate faster in the proximal than in the distal nerve segments (Gilliatt and Thomas, 1960).

2.14.3 Gender

It has been reported that CV is slower in women than that in men (Stetson et al., 1992; LaFratta and Smith, 1964), but the correlation is
complex since gender and height are not independent of each other (Falck and Stålberg, 1995). In our routine, we use the same reference values for women and men.

### 2.14.4 Temperature

The temperature affects the conduction velocity (CV), both locally at the recording site and generally along the nerve. Locally the amplitude increases as the temperature in the recording site decreases. The amplitude increases by 1.7% per degree Celsius (Lopate et al., 1997).

The temperature also affects the conduction along the nerve segment. The conduction velocity (CV) decreases as it cools with a factor ranging from 1.2 to 2.4 m/s per degree Celsius. This varies for different nerve (Dioszeghy and Stålberg, 1992). This will reduce the amplitude. These two effects of the temperature on the amplitude neutralize each other. In order to standardize CV and amplitude measurements, it is recommended to keep the skin temperature at above 29° C for the dorsum of the hand and 27° C for the dorsum of the foot (Falck and Stålberg, 1995).

### 2.14.5 Stimulating systems

Failures of the stimulating systems may results in absent or unexpected responses this may be due to the submaximally stimulation of the nerve or the applied current may not reach the intended target or the stimulator may be pressed firmly to the target nerve. Cooper et al., 1980) A submaximal current may result in misdiagnosis of conduction block if larger amplitude is obtained on distal stimulation. An important source of failure of stimulating
system is shunting of current between anode and cathode either by sweat or formation of bridge by conducting jelly.

### 2.14.6 Recording Systems

Faulty connection in the recording system may result in the errors include (1) breaks in electrode wire (2) connection to wrong preamplifier and (3) incorrect oscilloscope settings of gain, sweep and filter. With partial damage to cable, stimulus induced twitches cause movement related potentials, which may be mistaken for CMAP. An early positivity preceeding the peak CMAP suggests erroneous positioning of the active electrode. Relocation the active electrodes close to the end plate region eliminates this positivity. Similar possibility may also happen because of volume conduction or stimulation of other muscle due to anomalous innervations or unintended stimulation of adjoining nerves (Gilliatt *et al.*, 1965). The recorded potential is also distorted if the reference electrode is located in an active rather than a remote region in relation to muscle action potential.

### 2.14.7 Inadvertent stimulation of unintended nerves

Spread of stimulating current to an adjoining nerve or root not under study is common and failure to identify it results in errors in latency measurement (Gassel, 1964).

### 2.14.8 Anomalous cross over between the nerves

Anomalous innervations of muscle can also result in errors of amplitude measurement.