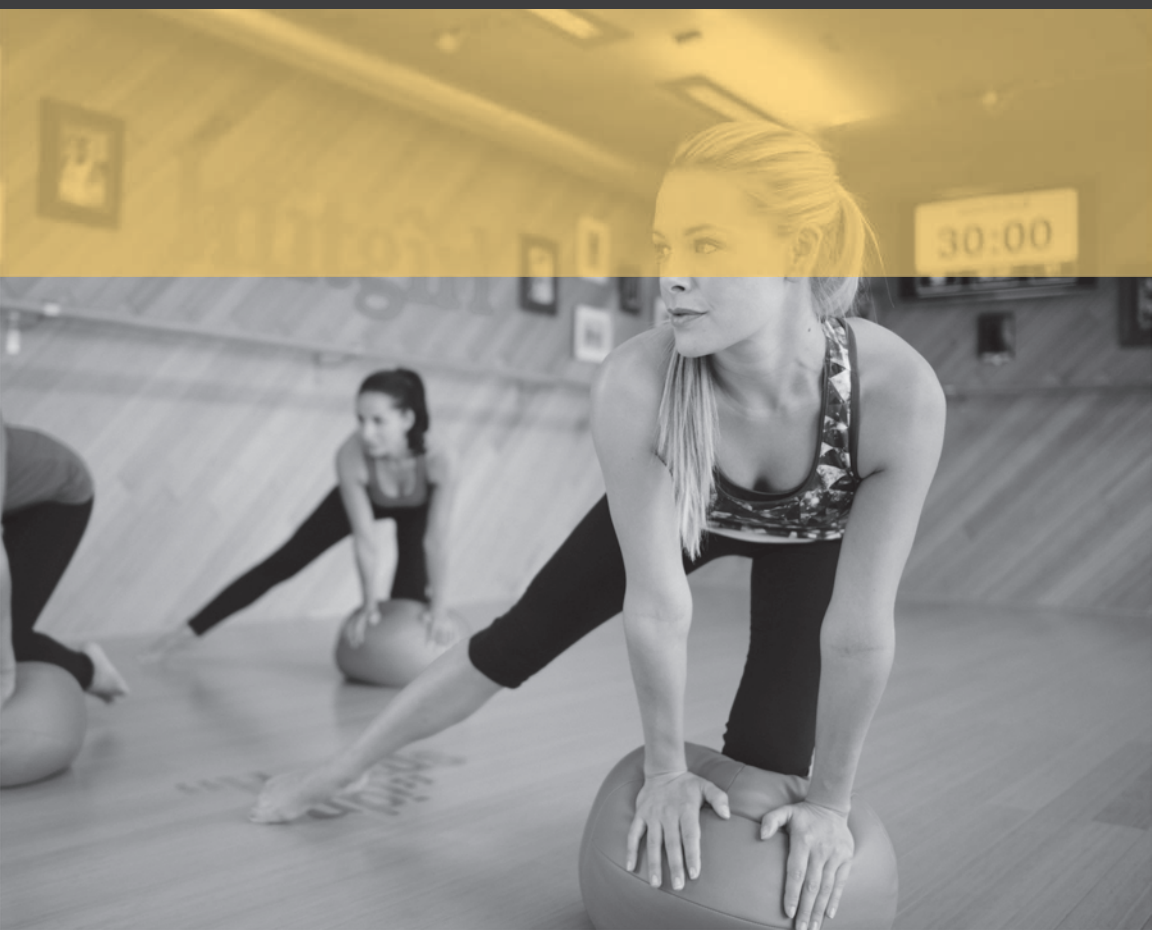
The Physiological Basis of Physical Education

Govind Bora



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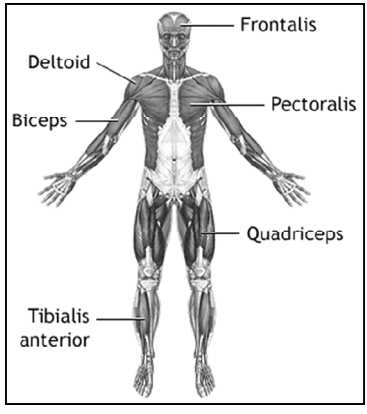
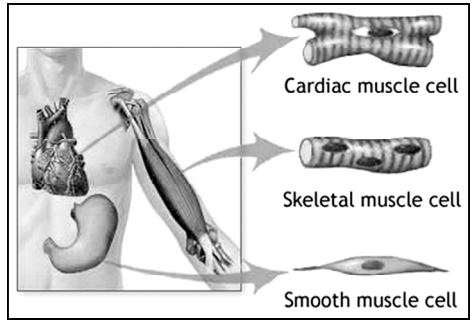
Understanding the Physiological Aspects of Physical Education

MUSCULAR SYSTEM

Over 600 skeletal muscles function for body movement through contraction and relaxation of voluntary, striated muscle fibres. These muscles are attached to bones, and are typically under conscious control for locomotion, facial expressions, posture, and other body movements. Muscles account for approximately 40 per cent of body weight. The metabolism that occurs in this large mass-produces heat essential for the maintenance of body temperature.





CARDIAC MUSCLE

Cardiac muscle is only in the heart and makes up the atria and ventricles (heart walls). Like skeletal muscle, cardiac muscle contains striated fibres. Cardiac muscle is called involuntary muscle because conscious thought does not control its contractions. Specialized cardiac muscle cells maintain a consistent heart rate.

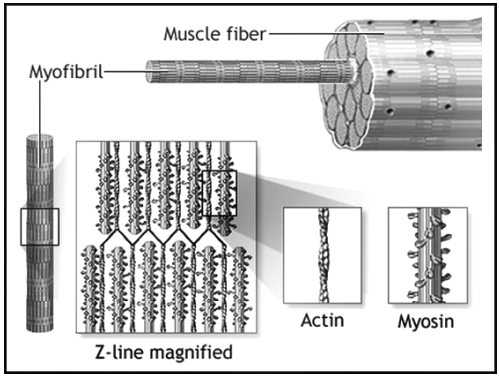
SMOOTH MUSCLE

Smooth muscle is throughout the body, including in visceral (internal) organs, blood vessels, and glands. Like cardiac muscle, smooth muscle is involuntary. Unlike skeletal and cardiac muscle, smooth muscle is non-striated (not banded). Smooth muscle, which is extensively within the walls of digestive tract organs, causes peristalsis (wave-like contractions) that aids in food digestion and transport. Except the heart, any action that the body performs without conscious thought is done by smooth muscle contractions. This includes diverse activities such as constricting (closing) the bronchioles (air passages) of the lungs or pupils of the eye or causing goosebumps in cold conditions.

SKELETAL MUSCLE

A skeletal muscle has regular, ordered groups of fascicles, muscle fibres, myofibrils, and myofilaments. Epimysium (thick connective tissue) binds groups of fascicles together. A fascicle

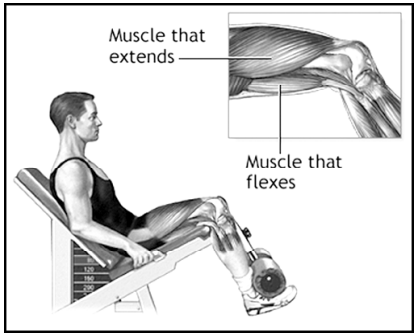
has muscle fibres; perimysium (connective tissue) envelops the fascicle. Endomysium (connective tissue) surrounds the muscle fibres. A muscle fibre divides into even smaller parts. Within each fibre are strands of myofibrils. These long cylindrical structures appear striped due to strands of tiny myofilaments. Myofilaments have two types of protein: actin (thin myofilaments) and myosin (thick myofilaments).



The actin and myosin myofilaments align evenly, producing dark and light bands on the myofibril. Each dark band depicts an area where the myofilaments overlap, causing the striated appearance of skeletal muscle. All dark and light bands of the myofilaments have names. At the Z-line, actin strands interweave.

The region between two Z-lines is a sarcomere, the functional unit of skeletal muscle. Muscle contraction occurs when overlapping actin and myosin myofilaments overlap further and shorten the muscle cell. The myofilaments keep their length.

The overlapping of myofilaments is the basis for the sliding filament theory of contraction. Skeletal muscle is a system of pairs that relax and contract to move a joint. For example, when front leg muscles contract, the knee extends (straightens) while back leg muscles relax. Conversely, to flex (bend) the knee, back leg muscles contract while front leg muscles relax. Some muscles are named for their ability to extend or flex a joint; for example, extensor carpiradialis longus muscle and flexor digitorum brevis muscle.



Tendons attach most skeletal muscles to bones. Tendons are strong sheets of connective tissue that are identical with ligaments. Tendons and ligaments differ in function only: tendons attach muscle to bone and ligaments attach bone to bone.

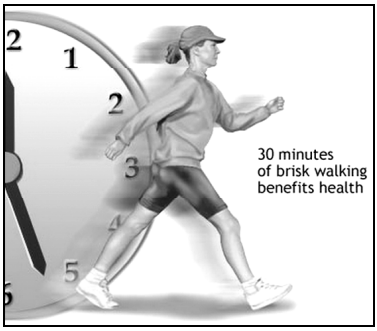
Physical exercise strengthens the attachment of tendons to bones. Skeletal muscles have muscle tone (remain partly contracted), which helps maintain body posture. Ongoing signals from the nervous system to the muscle cells help maintain tone and readiness for physical activity. Skeletal muscle aids in heat generation. During muscle contractions, muscle cells expend much energy, most of which is converted to heat. To prevent overheating, glands in the skin produce sweat to cool the skin; and, the body radiates heat from the blood and tissues through the skin. When the body is chilly, shivering causes quick muscle contractions that generate heat.

EFFECT OF EXERCISE ON THE MUSCULAR SYSTEM

Supply of Oxygen

Skeletal muscles have two types of muscle fibres: fast-twitch and slow-twitch. Anaerobic exercise uses fast-twitch fibres. Such exercise includes activities that are fleeting and require brief high-energy expenditure. Weightlifting, sprinting, and push-ups are examples of anaerobic exercise. Because all cells require oxygen to produce energy, anaerobic exercise depletes oxygen reserves in the muscle cells quickly. The result

is an oxygen debt. To repay the debt, humans breathe deeply and rapidly, which restores the oxygen level. Anaerobic exercise creates excess lactic acid (a waste product). By increasing oxygen intake, the liver cells can convert the excess lactic acid into glucose, the primary food molecule used in cellular metabolism.



Aerobic exercise uses slowtwitch muscle fibres. Such exercise includes activities that are prolonged and require constant energy. Long distance running and cycling are examples of aerobic exercise. In aerobic exercise, the muscle cell requires the same amount of oxygen that the body supplies. The oxygen debt is slashed and lactic acid is not formed.

Effects of Steady Exercise

Steady exercise is when sufficient oxygen can be breathed in to satisfy the needs of the muscles. Oxygen is required by the muscles to clear away waste products [lactic acid] which are formed during the contraction of muscle. During steady exercise the muscles use mostly fat for the creation of energy, but also glucose. As long as the glucose supplies last, the body can continue the exercise quite comfortably. However, when the glucose is all used then the body has to continue on fats alone.

The effect of this is a build up of acid in the blood stream, and heavy sweating resulting in dehydration. The body cannot continue due to a raising of temperature and the person has to stop. If he attempted to continue he would eventually collapse.

Effects of Intense Exercise

When the level of exercise reaches the stage where the amount of oxygen breathed in is insufficient to clear away the waste products formed by the muscle contractions, then an oxygen debt builds up. The waste products (mainly lactic acid) continue to build up causing pain in the muscles and breathlessness. Soon, the performer has to stop or at least slow down. The rate of breathing will stay very high until the oxygen debt has been paid off, *i.e.* the waste products have been cleared away.

THE CIRCULATORY SYSTEM

The Circulatory System is the main transportation and cooling system for the body. The Red Blood Cells act like billions of little UPS trucks carrying all sorts of packages that are needed by all the cells in the body. Instead of UPS, I'll call them RBC's. RBC's carry oxygen and nutrients to the cells. Every cell in the body requires oxygen to remain alive. Besides RBC's, there are also White Blood Cells moving in the circulatory system traffic. White Blood Cells are the paramedics, police and street cleaners of the circulatory system. Anytime we have a cold, a cut, or an infection the WBC's go to work.

The highway system of the Circulatory System consists off a lot of one way streets. The superhighways of the circulatory system are the veins and arteries. Veins are used to carry blood *to* the heart. Arteries carry blood *away* from the heart. Most of the time, blood in the veins is blood where most of the oxygen and nutrients have already been delivered to the cells. This blood is called deoxygenated and is very *dark* red. Most of the time blood in the arteries is loaded with oxygen and nutrients and the colour is very *bright* red. There is one artery that carries deoxygenated blood and there are some veins that carry oxygenated blood. To get to the bottom of this little mystery we need to talk about the Heart and Lungs.

TYPES OF CIRCULATORY SYSTEMS

Living things must be capable of transporting nutrients, wastes and gases to and from cells. Single-celled organisms use their cell surface as a point of exchange with the outside environment. Multicellular organisms have developed transport and circulatory systems to deliver oxygen and food to cells and remove carbon dioxide and metabolic wastes. Sponges are the simplest animals, yet even they have a transport system. Seawater is the medium of transport and is propelled in and out of the sponge by ciliary action. Simple animals, such as the hydra and planaria, lack specialized organs such as hearts and blood vessels, instead using their skin as an exchange point for materials. This, however, limits the size an animal can attain. To become larger, they need specialized organs and organ systems.

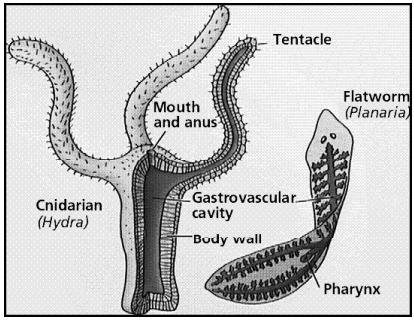


Fig. Structures that Serve some of the Functions of the Circulatory System in Animals that Lack the System

Multicellular animals do not have most of their cells in contact with the external environment and so have developed circulatory systems to transport nutrients, oxygen, carbon dioxide and metabolic wastes.

Components of the circulatory system include:

- *Blood*: A connective tissue of liquid plasma and cells
- *Heart*: A muscular pump to move the blood
- *Blood vessels*: Arteries, capillaries and veins that deliver blood to all tissues

There are several types of circulatory systems. The open circulatory system, examples of which are diagrammed in Figure below, is common to molluscs and arthropods. Open circulatory systems (evolved in insects, mollusks and other invertebrates) pump blood into a hemocoel with the blood diffusing back to the circulatory system between cells. Blood is pumped by a heart into the body cavities, where tissues are surrounded by the blood. The resulting blood flow is sluggish.

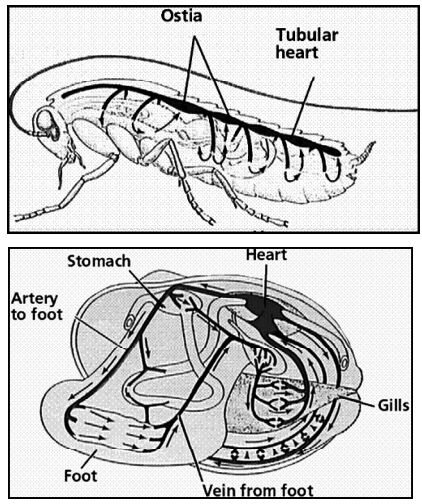


Fig. Circulatory Systems of an Insect (Top) and Mollusc (Middle).

Vertebrates, and a few invertebrates, have a closed circulatory system, shown in Figure. Closed circulatory systems (evolved in echinoderms and vertebrates) have the blood closed at all times within vessels of different size and wall thickness. In this type of system, blood is pumped by a heart through vessels, and does not normally fill body cavities. Blood flow is not sluggish. Hemoglobin causes vertebrate blood to turn red in the presence of oxygen; but more importantly hemoglobin molecules in blood cells transport oxygen. The human closed circulatory system is sometimes called the cardiovascular system. A secondary circulatory system, the lymphatic circulation, collects fluid and cells and returns them to the cardiovascular system.

VERTEBRATE CARDIOVASCULAR SYSTEM

The vertebrate cardiovascular system includes a heart, which is a muscular pump that contracts to propel blood out to the body through arteries, and a series of blood vessels. The upper chamber of the heart, the atrium is where the blood enters the heart. Passing through a valve, blood enters the lower chamber, the ventricle. Contraction of the ventricle forces blood from the heart through an artery. The heart muscle is composed of cardiac muscle cells. Arteries are blood vessels that carry blood away from heart. Arterial walls are able to expand and contract. Arteries have three layers of thick walls. Smooth muscle fibres contract, another layer of connective tissue is quite elastic, allowing the arteries to carry blood under high pressure. A diagram of arterial structure is shown in Figure below.

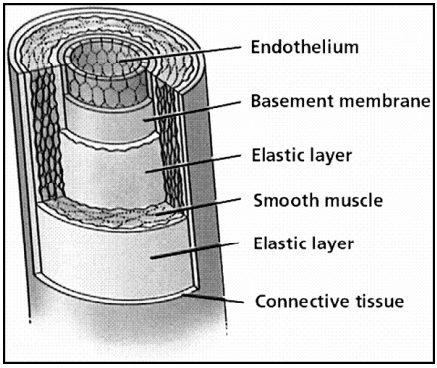


Fig. Structure of an Artery.

The aorta is the main artery leaving the heart. The pulmonary artery is the only artery that carries oxygen-poor blood. The pulmonary artery carries deoxygenated blood to the lungs. In the lungs, gas exchange occurs, carbon dioxide diffuses out, oxygen diffuses in. Arterioles are small arteries that connect larger arteries with capillaries. Small arterioles branch into collections of capillaries known as capillary beds, an exampe of one is shown in Figure below. Structure and blood flow through a vein. The above illustration is from.

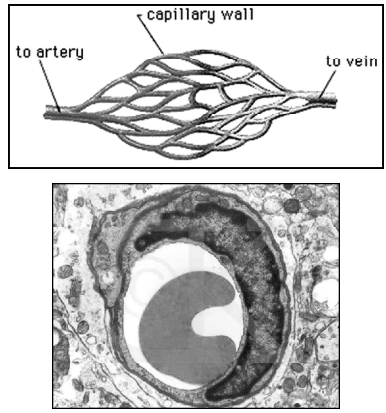


Fig. Capillary with Red Blood Cell.

Capillaries, shown in Figures, are thin-walled blood vessels in which gas exchange occurs. In the capillary, the wall is only one cell layer thick. Capillaries are concentrated into capillary beds. Some capillaries have small pores between the cells of the capillary wall, allowing materials to flow in and out of capillaries as well as the passage of white blood cells. Changes in blood pressure also occur in the various vessels of the circulatory system. Nutrients, wastes, and hormones are exchanged across the thin walls of capillaries. Capillaries are microscopic in size, although blushing is one manifestation of blood flow into capillaries. Control of blood flow into capillary beds is done by nerve-controlled sphincters.

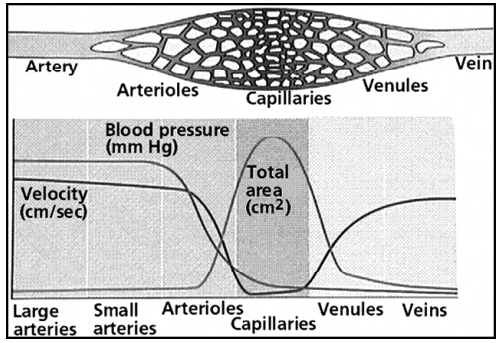


Fig. Changes in Blood Pressure, Velocity, and the Area of the Arteries, Capillaries, and Veins of the Circulatory System.

The circulatory system functions in the delivery of oxygen, nutrient molecules, and hormones and the removal of carbon dioxide, ammonia and other metabolic wastes. Capillaries are the points of exchange between the blood and surrounding tissues. Materials cross in and out of the capillaries by passing through or between the cells that line the capillary.

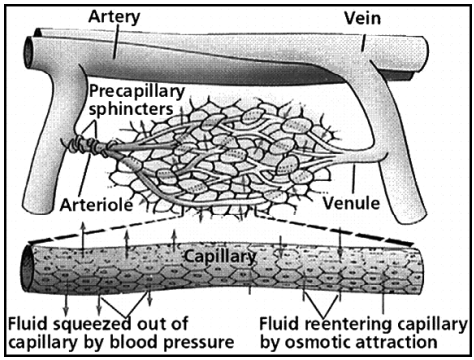


Fig. Capillary Structure, and Relationships of Capillaries to Arteries and Veins.

The extensive network of capillaries in the human body is estimated at between 50,000 and 60,000 miles long. Thoroughfare channels allow blood to bypass a capillary bed. These channels can open and close by the action of muscles that control blood flow through the channels.

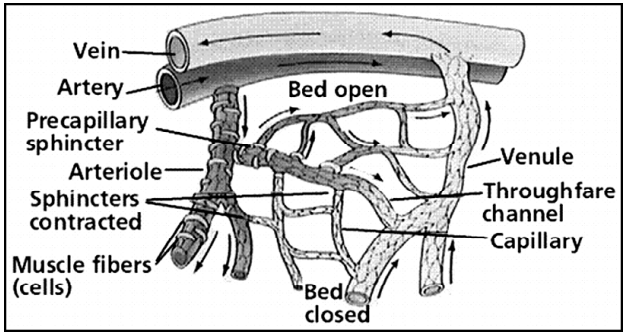


Fig. Capillary Beds and their Feeder Vessels.

Blood leaving the capillary beds flows into a progressively larger series of venules that in turn join to form veins. Veins

carry blood from capillaries to the heart. With the exception of the pulmonary veins, blood in veins is oxygen-poor. The pulmonary veins carry oxygenated blood from lungs back to the heart. Venules are smaller veins that gather blood from capillary beds into veins. Pressure in veins is low, so veins depend on nearby muscular contractions to move blood along. The veins have valves that prevent back-flow of blood.

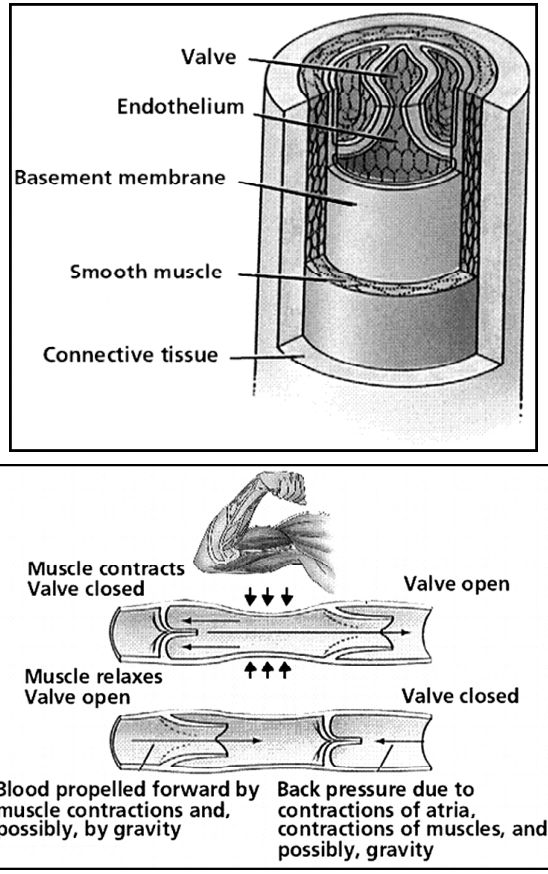


Fig. Structure of a Vein (Top) and the Actions of Muscles to Propel Blood through the Veins.

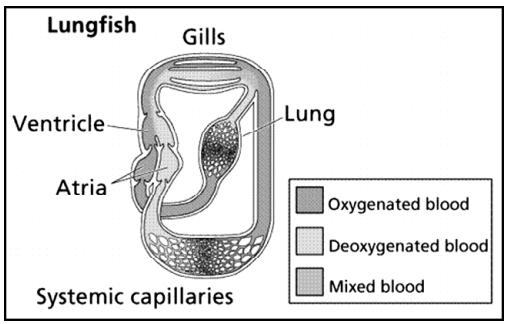
Ventricular contraction propels blood into arteries under great pressure. Blood pressure is measured in mm of mercury;

healthy young adults should have pressure of ventricular systole of 120mm, and 80 mm at ventricular diastole. Higher pressures (human 120/80 as compared to a 12/1 in lobsters) mean the volume of blood circulates faster (20 seconds in humans, 8 minutes in lobsters). As blood gets farther from the heart, the pressure likewise decreases. Each contraction of the ventricles sends pressure through the arteries. Elasticity of lungs helps keep pulmonary pressures low. Systemic pressure is sensed by receptors in the arteries and atria. Nerve messages from these sensors communicate conditions to the medulla in the brain. Signals from the medulla regulate blood pressure.

VERTEBRATE VASCULAR SYSTEM

Humans, birds, and mammals have a four-chambered heart that completely separates oxygen-rich and oxygen-depleted blood. Fish have a two-chambered heart in which a single-loop circulatory pattern takes blood from the heart to the gills and then to the body. Amphibians have a three-chambered heart with two atria and one ventricle.

A loop from the heart goes to the pulmonary capillary beds, where gas exchange occurs. Blood then is returned to the heart. Blood exiting the ventricle is diverted, some to the pulmonary circuit, some to systemic circuit. The disadvantage of the three-chambered heart is the mixing of oxygenated and deoxygenated blood. Some reptiles have partial separation of the ventricle. Other reptiles, plus, all birds and mammals, have a four-chambered heart, with complete separation of both systemic and pulmonary circuits.



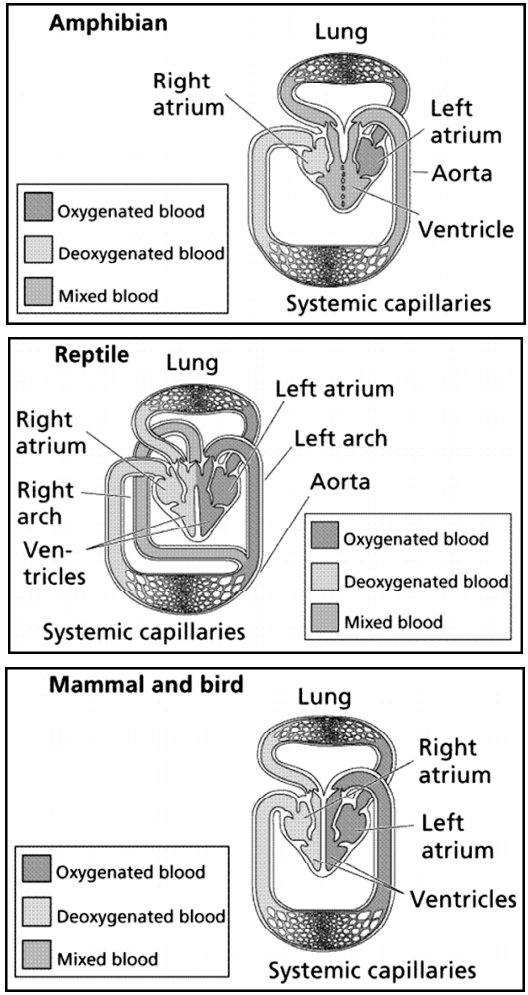


Fig. Circulatory Systems of Several Vertebrates Showing the progressive Evolution of the Four-chambered Heart and Pulmonary and Systemic Circulatory Circuits.

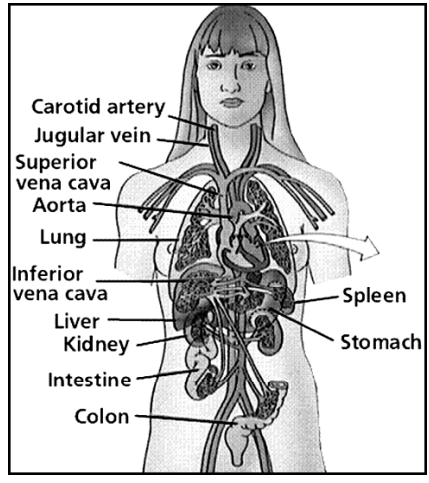
THE HEART

The heart is a muscular structure that contracts in a rhythmic pattern to pump blood. Hearts have a variety of forms: chambered hearts in mollusks and vertebrates, tubular

hearts of arthropods, and aortic arches of annelids. Accessory hearts are used by insects to boost or supplement the main heart's actions.

Fish, reptiles, and amphibians have lymph hearts that help pump lymph back into veins. The basic vertebrate heart, such as occurs in fish, has two chambers. An auricle is the chamber of the heart where blood is received from the body. A ventricle pumps the blood it gets through a valve from the auricle out to the gills through an artery. Amphibians have a three-chambered heart: two atria emptying into a single common ventricle. Some species have a partial separation of the ventricle to reduce the mixing of oxygenated (coming back from the lungs) and deoxygenated blood (coming in from the body). Two sided or two chambered hearts permit pumping at higher pressures and the addition of the pulmonary loop permits blood to go to the lungs at lower pressure yet still go to the systemic loop at higher pressures.

Establishment of the four-chambered heart, along with the pulmonary and systemic circuits, completely separates oxygenated from deoxygenated blood. This allows higher the metabolic rates needed by warm-blooded birds and mammals. The human heart is a two-sided, four-chambered structure with muscular walls. An atrioventricular (AV) valve separates each auricle from ventricle.



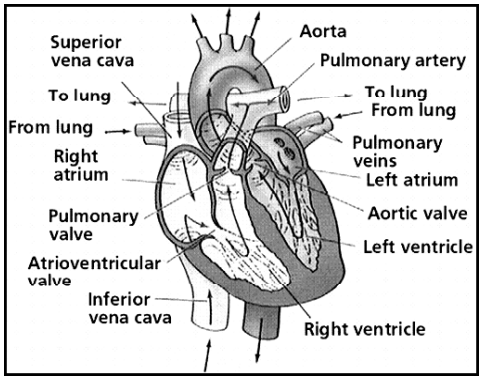


Fig. The Relationship of the Heart and Circulatory System to Major Visceral Organs. Below: the Structure of the Heart.

A semilunar (also known as arterial) valve separates each ventricle from its connecting artery. The heart beats or contracts approximately 70 times per minute. The human heart will undergo over 3 billion contraction cycles, during a normal lifetime. The cardiac cycle consists of two parts: systole (contraction of the heart muscle) and diastole (relaxation of the heart muscle). Atria contract while ventricles relax. The pulse is a wave of contraction transmitted along the arteries. Valves in the heart open and close during the cardiac cycle. Heart muscle contraction is due to the presence of nodal tissue in two regions of the heart. The SA node (sinoatrial node) initiates heartbeat. The AV node (atrioventricular node) causes ventricles to contract. The AV node is sometimes called the pacemaker since it keeps heartbeat regular. Heartbeat is also controlled by nerve messages originating from the autonomic nervous system.

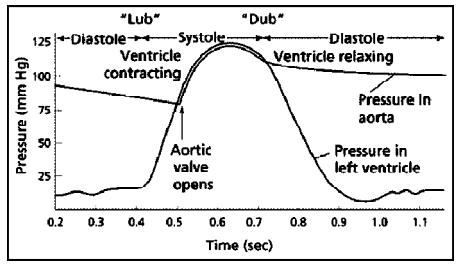
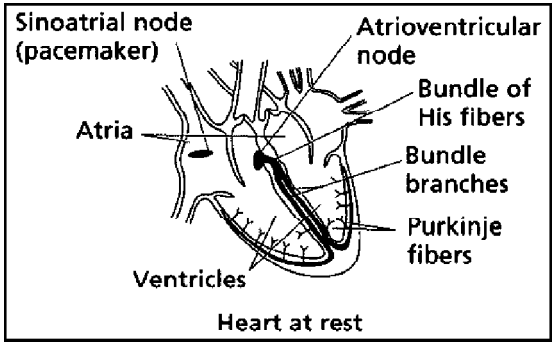


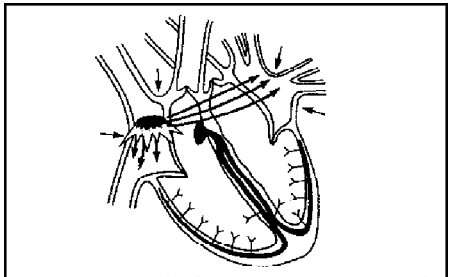
Fig. The Cardiac Cycle.

Blood flows through the heart from veins to atria to ventricles out by arteries. Heart valves limit flow to a single direction. One heartbeat, or cardiac cycle, includes atrial contraction and relaxation, ventricular contraction and relaxation, and a short pause. Normal cardiac cycles (at rest) take 0.8 seconds. Blood from the body flows into the vena cava, which empties into the right atrium. At the same time, oxygenated blood from the lungs flows from the pulmonary vein into the left atrium.

The muscles of both atria contract, forcing blood downward through each AV valve into each ventricle. Diastole is the filling of the ventricles with blood. Ventricular systole opens the SL valves, forcing blood out of the ventricles through the pulmonary artery or aorta. The sound of the heart contracting and the valves opening and closing produces a characteristic "lub-dub" sound. Lub is associated with closure of the AV valves, dub is the closing of the SL valves.



Heart at rest


Sinoatrial node fires, action potentials spread through atria which contract

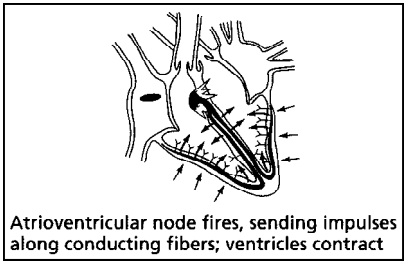


Fig. The Contraction of the Heart and the Action of the Nerve Nodes Located on the Heart.

Human heartbeats originate from the sinoatrial node (SA node) near the right atrium. Modified muscle cells contract, sending a signal to other muscle cells in the heart to contract. The signal spreads to the atrioventricular node (AV node). Signals carried from the AV node, slightly delayed, through bundle of His fibres and Purkinjie fibres cause the ventricles to contract simultaneously. Figure below illustrates several aspects of this.

Heartbeats are coordinated contractions of heart cardiac cells, shown in an animate GIF image in Figure below. When two or more of such cells are in proximity to each other their contractions synch up and they beat as one.

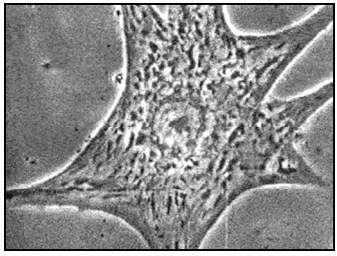


Fig. Animated GIF Image of a Single Human Heart Muscle Cell Beating.

An electrocardiogram (ECG) measures changes in electrical potential across the heart, and can detect the contraction pulses that pass over the surface of the heart. There are three slow, negative changes, known as P, R, and T as shown in Figure below. Positive deflections are the Q and S

waves. The P wave represents the contraction impulse of the atria, the T wave the ventricular contraction. ECGs are useful in diagnosing heart abnormalities.

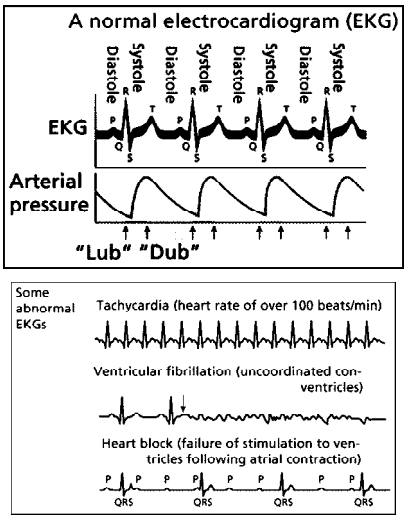


Fig. Normal Cardiac Pattern (Top) and some Abnormal Patterns (Bottom).

DISEASES OF THE HEART AND CARDIOVASCULAR SYSTEM

Cardiac muscle cells are serviced by a system of coronary arteries. During exercise the flow through these arteries is up to five times normal flow. Blocked flow in coronary arteries can result in death of heart muscle, leading to a heart attack. Blockage of coronary arteries, is usually the result of gradual buildup of lipids and cholesterol in the inner wall of the coronary artery. Occasional chest pain, angina pectoralis, can result during periods of stress or physical exertion. Angina indicates oxygen demands are greater than capacity to deliver it and that a heart attack may occur in the future. Heart muscle cells that die are not replaced since heart muscle cells do not divide. Heart disease and coronary artery disease are the leading causes of death in the United States.

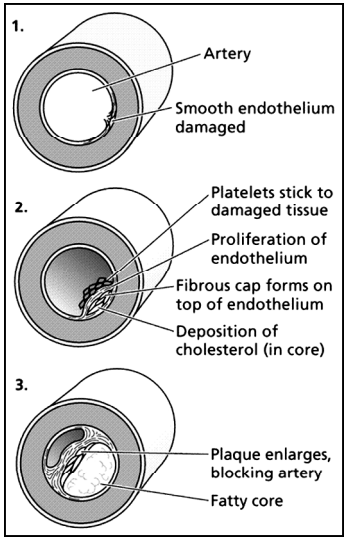


Fig. Development of Arterial Plaque

Hypertension, high blood pressure (the silent killer), occurs when blood pressure is consistently above 140/90. Causes in most cases are unknown, although stress, obesity, high salt intake, and smoking can add to a genetic predisposition. Luckily, when diagnosed, the condition is usually treatable with medicines and diet/exercise.

THE VASCULAR SYSTEM

Two main routes for circulation are the pulmonary (to and from the lungs) and the systemic (to and from the body). Pulmonary arteries carry blood from the heart to the lungs. In the lungs gas exchange occurs. Pulmonary veins carry blood from lungs to heart. The aorta is the main artery of systemic circuit.

The vena cavae are the main veins of the systemic circuit. Coronary arteries deliver oxygenated blood, food, etc. to the heart. Animals often have a portal system, which begins and ends in capillaries, such as between the digestive tract and the liver. Fish pump blood from the heart to their gills, where gas exchange occurs, and then on to the rest of the body. Mammals

pump blood to the lungs for gas exchange, then back to the heart for pumping out to the systemic circulation. Blood flows in only one direction.

BLOOD

Plasma is the liquid component of the blood. Mammalian blood consists of a liquid (plasma) and a number of cellular and cell fragment components. Plasma is about 60 per cent of a volume of blood; cells and fragments are 40 per cent. Plasma has 90 per cent water and 10 per cent dissolved materials including proteins, glucose, ions, hormones, and gases. It acts as a buffer, maintaining pH near 7.4. Plasma contains nutrients, wastes, salts, proteins, etc.

Proteins in the blood aid in transport of large molecules such as cholesterol. Red blood cells, also known as erythrocytes, are flattened, doubly concave cells about 7µm in diameter that carry oxygen associated in the cell's hemoglobin. Mature erythrocytes lack a nucleus. They are small, 4 to 6 million cells per cubic millimeter of blood, and have 200 million hemoglobin molecules per cell. Humans have a total of 25 trillion red blood cells (about 1/3 of all the cells in the body). Red blood cells are continuously manufactured in red marrow of long bones, ribs, skull, and vertebrae.

Life-span of an erythrocyte is only 120 days, after which they are destroyed in liver and spleen. Iron from hemoglobin is recovered and reused by red marrow. The liver degrades the heme units and secretes them as pigment in the bile, responsible for the colour of feces. Each second two million red blood cells are produced to replace those thus taken out of circulation. White blood cells, also known as leukocytes, are larger than erythrocytes, have a nucleus, and lack hemoglobin. They function in the cellular immune response. White blood cells (leukocytes) are less than 1 per cent of the blood's volume.

They are made from stem cells in bone marrow. There are five types of leukocytes, important components of the immune system. Neutrophils enter the tissue fluid by squeezing through

capillary walls and phagocytozing foreign substances. Macrophages release white blood cell growth factors, causing a population increase for white blood cells. Lymphocytes fight infection. T-cells attack cells containing viruses. B-cells produce antibodies. Antigen-antibody complexes are phagocytized by a macrophage. White blood cells can squeeze through pores in the capillaries and fight infectious diseases in interstitial areas.

Platelets result from cell fragmentation and are involved with clotting, as is shown by Figures. Platelets are cell fragments that bud off megakaryocytes in bone marrow. They carry chemicals essential to blood clotting. Platelets survive for 10 days before being removed by the liver and spleen. There are 150,000 to 300,000 platelets in each millilitre of blood. Platelets stick and adhere to tears in blood vessels; they also release clotting factors.

A hemophiliac's blood cannot clot. Providing correct proteins (clotting factors) has been a common method of treating hemophiliacs. It has also led to HIV transmission due to the use of transfusions and use of contaminated blood products.

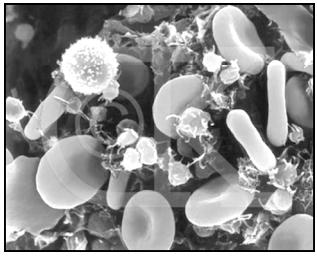
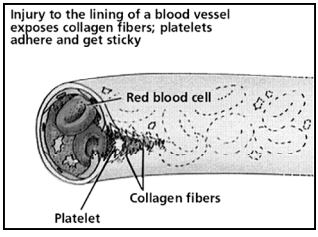


Fig. Human Red Blood Cells, Platelets and T-lymphocyte.



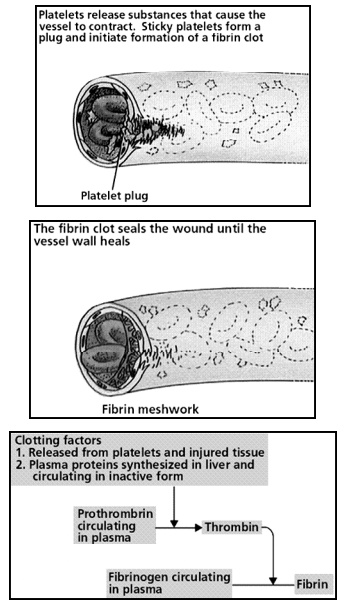


Fig. The Formation and Actions of Blood Clots

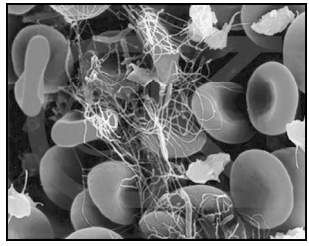


Fig. Blood Clot Formation

THE LYMPHATIC SYSTEM

Water and plasma are forced from the capillaries into intracellular spaces. This interstitial fluid transports materials between cells. Most of this fluid is collected in the capillaries of a secondary circulatory system, the lymphatic system. Fluid in this system is known as lymph. Lymph flows from small lymph capillaries into lymph vessels that are similar to veins in having valves that prevent backflow. Lymph vessels connect

to lymph nodes, lymph organs, or to the cardiovascular system at the thoracic duct and right lymphatic duct. Lymph nodes are small irregularly shaped masses through which lymph vessels flow. Clusters of nodes occur in the armpits, groin, and neck. Cells of the immune system line channels through the nodes and attack bacteria and viruses travelling in the lymph.

EXERCISE AFFECTS THE CIRCULATORY SYSTEM

Exercise helps improve the hearts health and can reverse some heart disease risk factors. The heart, when exercised, becomes stronger, so will pump more blood through the body. It can work at maximum level with less strain. When a person exercises daily the left ventricle of the heart increases in volume to help the demand of overload. A person who exercises often have slower resting pulse.

A study in 2003 showed that individuals that perform moderate intense exercise for 30 minutes on most days of the week have a 45 per cent lower risk of developing heart disease than non-active people. When worked the heart pumps blood quicker as the body is in demand for oxygenated blood. The heart rate should average 60 to 80 beats per minute in an healthy adult. The heart rate increases in direct proportion to the exercise intensity until the maximum heart rate is reached. After exercising the B.P.M (beats per minute) will return to normal resting rate.

The more you exercise the quicker it will recover. Aerobic capacity is the highest amount of oxygen consumed during maximal exercise. An aerobic capacity is based on how efficiently your body can deliver oxygen to your muscles. Regular exercise, long-term, will help increase your ability to take in, transport and use oxygen for exercise. You should exercise at an intensity (aerobic training zone) for a minimum of 20 minutes, three times a day. To work out roughly your aerobic training zone: Subtract your age from 220 (men), 226(women), which gives you your maximum heart rate.

Multiply the number by.5 (for the lower end of the target zone) and by.85 (for the upper end of the zone). When

exercising you become heavier and deeper breathing, this is because your body needs as much oxygen to supply the muscles with. If your out of breath, sweaty and can't talk, then you have pushed yourself over your aerobic zone. Once the heart rate slows your breathing will too as the body doesn't need as much oxygen.

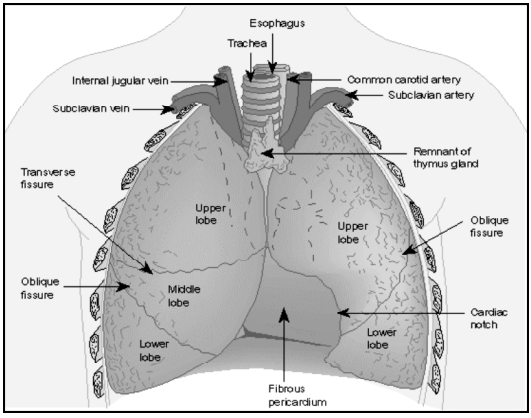
It can burn calories and increase metabolic rate. Both of these will help you lose weight, try exercising for longer periods and more frequently as well as decreasing your calorie intake.

There are many different ways of training to improve your cardiovascular system:

- Running, cycling,
- Walking,
- Jogging,
- Swimming,
- Rowing machines,
- Treadmills and stationary cycling.

Make sure that your exercise programme is frequent and right for you. And that warm- up and cool downs aren't forgotten.

RESPIRATORY SYSTEM



MECHANICS OF BREATHING

Inspiration

Inspiration is the active part of the breathing process, which is initiated by the respiratory control centre in medulla oblongata (Brain stem). Activation of medulla causes a contraction of the diaphragm and intercostal muscles leading to an expansion of thoracic cavity and a decrease in the pleural space pressure. The diaphragm is a dome-shaped structure that separates the thoracic and abdominal cavities and is the most important muscle of inspiration.

When it contracts, it moves downward and because it is attached to the lower ribs it also rotates the ribs towards the horizontal plane, and thereby further expands the chest cavity. In normal quite breathing the diaphragm moves downward about 1 cm but on forced inspiration/expiration total movement could be up to 10 cm. When it is paralysed it moves to the opposite direction (upwards) with inspiration, paradoxical movement. The external intercostal muscles connect adjacent ribs. When they contract the ribs are pulled upward and forward causing further increase in the volume of the thoracic cavity. As a result fresh air flows along the branching airways into the alveoli until the alveolar pressure equals to the pressure at the airway opening.

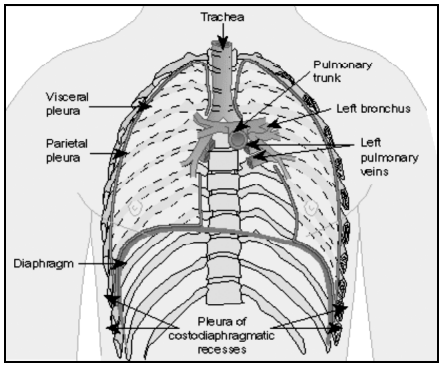
Expiration

Expiration is a passive event due to elastic recoil of the lungs. However, when a great deal of air has to be removed quickly, as in exercise, or when the airways narrow excessively during expiration, as in asthma, the internal intercostal muscles and the anterior abdominal muscles contract and accelerate expiration by raising pleural pressure.

Coupling of the Lungs and the Chest Wall

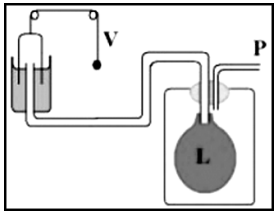
The lungs are not directly attached to the chest wall but

they change their volume and shape according to the changes in shape and volume of the thoracic cavity. Pleura covering the surfaces of the lungs (visceral) or the thoracic cavity (parietal) together with a thin (20μm) layer of liquid between them create a liquid coupling.



Pressure-volume Relationship

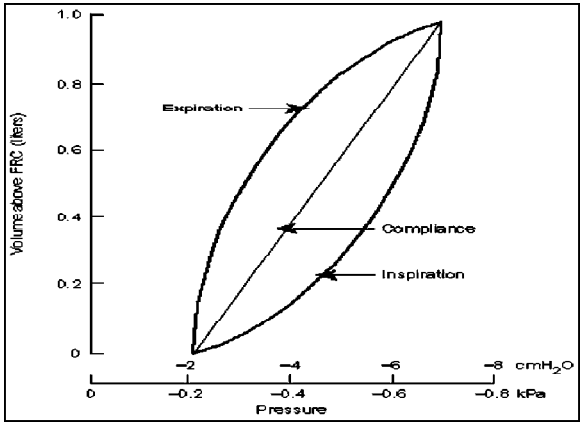
In the pulmonary physiology absolute pressure means atmospheric pressure (760 mm Hg at sea levels). The pressures and the pressure differences of the respiratory system are expressed as relative pressures to the atmospheric pressure. When it is said that alveolar pressure is zero, it means that alveolar pressure = atmospheric pressure.



If one excises animal lung and places it in a jar, one could measure the changes in volume with a spirometer through a cannula attached to the trachea. When the pressure inside the jar below atmospheric pressure, the lung expands and the change in its volume is measured and the pressurevolume curve is plotted. When there is no pressure distending the lung there is a small volume of gas in it.

As the pressure in the jar is gradually reduced, the volume of the lungs increases. This is initially a rapid event but after a certain pressure the changes become less evident. It means that the lung is stiffer when it is expanded and thereby, the pressure-volume curves during inflation and deflation are different = hysteresis.

Another important point is the volume at a given pressure during deflation is always larger than during inflation. Even when the pressure outside the lung is increased above the atmospheric pressure, very little further air is lost and the air is trapped in the alveoli. The volume of the air trapped in the lung is increased with age and in some respiratory diseases.



Compliance

The slope of the pressure-volume curve, the volume change per unit pressure is known as compliance. In normal expanding range (2-10 mm water) the lung is very dispensable, in other words it is very compliant. The compliance of the human lung is 0.15 L/cm H_2O. However, it gets stiffer (compliance smaller) as it is expanded above the normal range.

Compliance is reduced when:

- The pulmonary venous pressure is increased and the lung becomes engorged with blood

- There is alveolar oedema due to insufficiency of alveolar inflation
- *The lung remains unventilated for a while e.g.* atelectasis
- *Because of diseases causing fibrosis of the lung e.g.* chronic restrictive lung disease

On the contrary in chronic obstructive pulmonary disease (COPD, *e.g.* emphysema) the alveolar walls progressively degenerate, which increases the compliance. The lung compliance is changed according to the lung size: Obviously the compliance of a mouse lung is much smaller than a human lung. At the birth the lung compliance is the smallest and increased with age (until adulthood) due to increase in the size of the lungs. Specific compliance (compliance per unit of lung volume) could be calculated in order to correct this value for lung size.

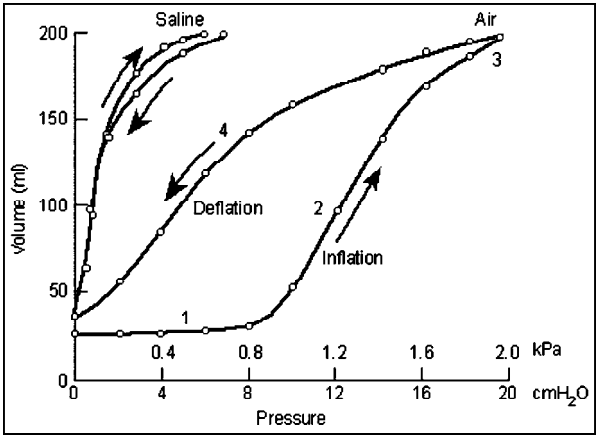
In asthma (hyperactive airway smooth muscle) the lung compliance is usually normal. The standard procedure for measuring compliance in humans is to determine the pressure-volume relationship during a passive expiration from total lung capacity.

If the lung deflates slowly, alveolar pressure is equal to atmospheric pressure, and pleural pressure is nearly same as the pressure in the oesophagus, which is usually measured with a thin-walled balloon attached via a plastic tube to a pressure-sensor.

Chest Wall Compliance

Changes in chest wall compliance are less common than changes in the lung compliance:

- Pathologic situations preventing the normal movement of the rib cage, such as, distortion of the spinal column
- Pathologic (cancer) or physiologic (pregnancy) reasons increasing the intra abdominal pressure
- Stiff chest, such as broken ribs



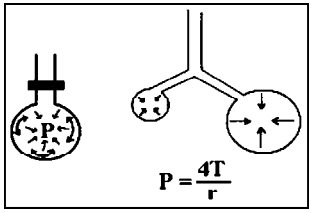
Surface Tension

A thin film of liquid lines the alveoli and the surface tension of this film is another important factor in the pressure-volume relationship of the lung. The surface tension arises because the attractive forces between adjacent molecules of the liquid are much stronger than those of between the liquid and the gas. As a result of that the liquid surface area becomes as small as possible. At the interface between the liquid and the alveolar gas, intermolecular forces in the liquid tend to cause the area of the lining to shrink (the alveoli tend to get smaller).

The surface tension contributes to the pressure-volume behaviour of the lungs because when the lungs are inflated with saline they have much larger compliance that when they are filled with air (because saline abolishes the surface tension). This behaviour can clearly be seen in a soap bubble, blown on the end of a tube. The surfaces of the bubble contract as much as possible and form the smallest possible surface area, a sphere. This generates a pressure predicted from Laplace's law:

$$\text{Pressure} = (4 \times \text{surface tension})/\text{radius}$$

The surface tension contributes a large part of the static recoil force of the lung (expiration). The surface tension changes with the surface area: The larger the area the smaller the surface tension gets.



The most important component of this liquid film is surfactant. It is produced by type 2 alveolar epithelial cells and its major constituent is dipalmitoyl phosphotidylcholine (DPPC), a phospholipid with detergent properties. The phospholipid DPPC is synthesised in the lung from fatty acids that are either extracted from the blood or are themselves synthesised in the lung.

Synthesis is fast and there is a rapid turnover of surfactant. If the blood flow to a region of lung is restricted due to an embolus the surfactant may be depleted in the effected area. Surfactant synthesis starts relatively late in foetal life and premature babies without adequate amount of surfactant develop respiratory distress which could be life threatening. What are the advantages of having surfactant and the low surface tension?

- It increases the compliance of the lung
- It reduces the work of expanding of the lung with each breath
- It stabilises the alveoli (thus the smaller alveoli do not collapse at the end-expiration)
- It keeps the alveoli dry (as the surface tension tends to collapse alveoli, it also tends to suck fluid into the alveolar space from capillaries)

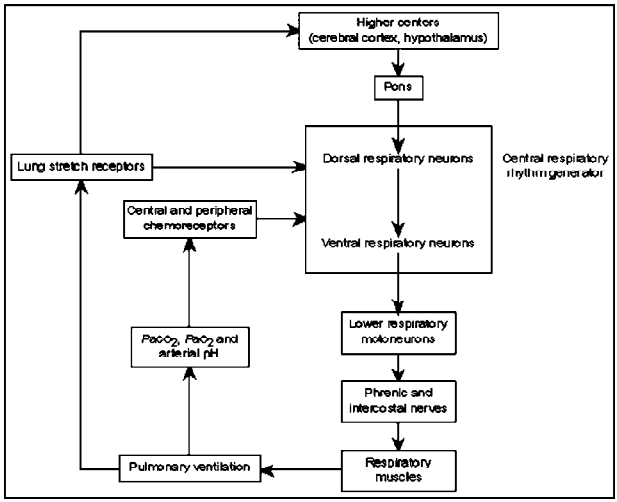
REGULATION AND CONTROL OF BREATHING

In order to maintain normal levels of partial oxygen and carbon dioxide pressure both the depth and rate of breathing are precisely regulated.

Basic elements of the respiratory control system are:

- Strategically placed sensors

- Central controller
- Respiratory muscles



Central Controller

Breathing is mainly controlled at the level of brainstem. The normal automatic and periodic nature of breathing is triggered and controlled by the respiratory centres located in the pons and medulla. These centres are not located in a special nucleus or a group of nuclei but they are rather poor defined collection of neurones.

Medullary Respiratory Centre

- Dorsal medullary respiratory neurones are associated with inspiration: It has been proposed that spontaneous intrinsic periodic firing of these neurones responsible for the basic rhythm of breathing. As a result, these neurones exhibit a cycle of activity that arises spontaneously every few seconds and establish the basic rhythm of the respiration. When the neurones are active their action potentials travel through reticulospinal tract in the

spinal cord and phrenic and intercostal nerves and finally stimulate the respiratory muscles.

- Ventral medullary respiratory neurones are associated with expiration. These neurones are silent during quite breathing because expiration is a passive event following an active inspiration. However, they are activated during forced expiration when the rate and the depth of the respiration is increased *e.g.* exercise. During heavy breathing increased activity of the inspiratory centre neurones activates the expiratory system. In turn, the increased activity of the expiratory system inhibits the inspiratory centre and stimulates muscles of expiration. The dorsal and ventral groups are bilaterally paired and there is cross communication between them. As a consequence they behave in synchrony and the respiratory movements are symmetric.

Apneustic Centre

It is located in the lower pons. Exact role of this centre in the normal breathing is not known. Lesions covering this area in the pons cause a pathologic respiratory rhythm with increased apnoea frequency. What is known is nerve impulses from the apneustic centre stimulate the inspiratory centre and without constant influence of this centre respiration becomes shallow and irregular.

Pneumotaxic Centre

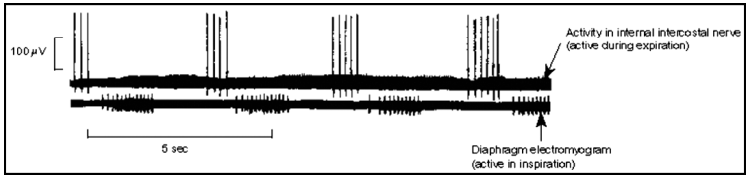
It is located in the upper pons. This centre is a group of neurones that have an inhibitory effect on the both inspiratory and apneustic centres. It is probably responsible for the termination of inspiration by inhibiting the activity of the dorsal medullar neurones. It primarily regulates the volume and secondarily the rate of the respiration. Because in the lesions of this area normal respiration is protected it is generally believed that upper pons is responsible for the fine-tuning of

the respiratory rhythm. Hypoactivation of this centre causes prolonged deep inspirations and brief, limited expirations by allowing the inspiration centre remain active longer than normal. Hyperactivation of this centre on the other hand results in shallow inspirations. The apneustic and pneumotaxic centres function in co-ordination in order to provide a rhythmic respiratory cycle: Activation of the inspiratory centre stimulates the muscles of inspiration and also the pneumotaxic centre. Then the pneumotaxic centre inhibits both the apneustic and the inspiratory centres resulting in initiation of expiration.

Spontaneous activity of the neurones in the inspiratory centre starts another similar cycle again. Breathing in some extent is also controlled consciously from higher brain centres. This control is required when we talk, cough and vomit. It is also possible voluntarily change the rate of the breathing. Hyperventilation can decrease blood partial carbon dioxide pressure (PCO_2) due to loss of CO_2 resulting in peripheral vasodilatation and decrease in blood pressure. One can also stop breathing voluntarily.

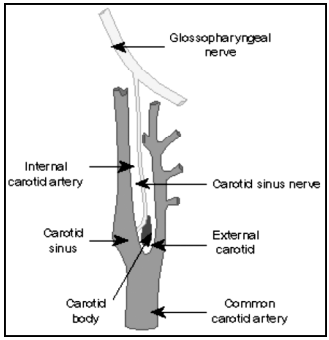
That results in an increase in arterial partial oxygen pressure (PO_2), which produces an urge to breathe. When eventually PCO_2 reaches the high enough level it overrides the conscious influences from the cortex and stimulates the inspiratory system.

If one holds his breath long enough to decrease PO_2 to a very low level one may loose his consciousness. In an unconscious person automatic control of the respiration takes over and the normal breathing resumes. Other parts of the brain (limbic system, hypothalamus) can also alter the breathing pattern *e.g.* affective states, strong emotions such as rage and fear. In addition, stimulation of touch, thermal and pain receptors can also stimulate the respiratory system.



Respiratory Muscles

Diaphragm, intercostal muscles and the other accessory respiratory muscles work in co-ordination for normal breathing under central controller. There is evidence suggesting that in premature new-born babies this co-ordination is not mature enough and this could be responsible for the sudden infant death syndrome.



Sensors

Mechanoreceptors

These receptors are placed in the walls of bronchi and bronchioles of the lung and the main function of these receptors is to prevent the overinflation of the lungs. Inflation of the lungs activates these receptors and activation of the stretch receptors in turn inhibits the neurones in inspiratory centre via vagus nerve. When the expiration starts activation of the stretch receptors gradually ceases allowing neurones in the inspiratory neurones become active again. This phenomenon is called Hering-Breuer Reflex. It is particularly important for infants. In adults it is functional only during exercise when the tidal volume is larger than normal.

Chemoreceptors

The respiratory system maintains concentrations of O_2, CO_2 and the pH of the body fluids within the normal range of

values. Any deviation from these values has a marked influence on the respiration. Chemoreceptors are specialised neurones activated by changes in O_2 or CO_2 levels in the blood and the brain tissue, respectively. They are involved in the regulation of respiration according to the changes in PO_2 and pH. O_2-sensitive chemoreceptors (Peripheral chemoreceptors) are located at the bifurcation of the carotid artery in the neck and the aortic arch.

They are small vascular sensory organs encapsulated with the connective tissue. They are connected to the respiratory centre in the medulla by glossopharingeal nerve (carotid body chemoreceptors) and the vagus nerve (aortic body). Central chemoreceptors are located bilaterally in the chemosensitive area of the medulla oblongata and exposed to the cerebrospinal fluid (CSF), local blood flow and local metabolism. They actually respond to changes in H^+ concentration in these compartments. When the blood partial PCO_2 is increased CO_2 diffuses into the CSF from cerebral vessels and liberates H^+. (When CO_2 combines with water forms carbonic acid and liberates H^+ and HCO_3^-).

$$CO_2 + H_2O \leftrightarrow H_2CO_3$$

$$H_2CO_3 \leftrightarrow HCO^-_3 + H^+$$

An increase in H^+ stimulates chemoreceptors resulting in hyperventilation which in turn reduces PCO_2 in the blood and therefore in the CSF. Cerebral vasodilatation always accompanies an increased PCO_2 and enhances the diffusion of CO_2 into the CSF. Because CSF has less protein than blood it has a much lower buffering capacity. As a result changes in pH for a given change in PCO_2 is always bigger than the change in blood.

CO_2 level is a major regulator of respiration. It is much more important than oxygen to maintain normal respiration. Even very small changes in carbon dioxide levels (5 mm Hg increase in PCO_2, hypercapnia) in the blood cause large increases in the rate and depth of respiration (100 per cent increase in ventilation). Hypocapnia, lower than normal PCO_2

level in the blood causes in periods in which respiratory movements do not occur. Effects of PO_2 (if the changes occur within the normal range) on respiration is very minor. A decrease in PO_2 is called hypoxia and only after 50 per cent decrease in PO_2 can produce significant changes in respiration. This is due to the nature of O_2-Hb saturation that at any PO_2 level above 80 mm Hg Hb is saturated with O_2.

Consequently only big changes in PO_2 produce symptoms otherwise it is compensated by O_2, which is bound with Hb. In stroke patients or physiologically at high altitude blood PO_2 level may drop considerably and activate peripheral chemoreceptors and activate stimulation. At high altitude because the ability of the lung to eliminate CO_2 is not affected, in response to increased respiration, blood PCO_2 is decreased. If PO_2 drops under certain level respiratory system does not respond and death will occur.

VENTILATION

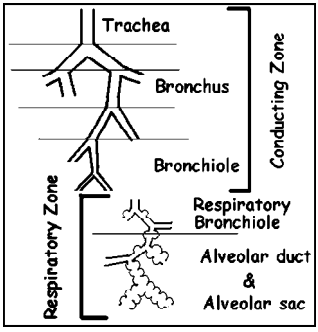
Airways and Airflow

Inhaled air passes through the conducting airways and eventually reaches the respiratory epithelium of the lungs. The conducting airways consist of a series of branching tubes which become narrower, shorter and more numerous as they penetrate deeper into the lung. The trachea divides into right and left main bronchi, which in turn divide into lobar, then segmental bronchi.

This process continues down to the terminal bronchioles, which are the smallest airways without alveoli. Since the conducting airways have no alveoli they do not take part in gas exchange but constitute the anatomical dead space. Its volume is about 150 ml but it varies because airways are not rigid; during inspiration, respiratory tubes are lengthened and dilated, especially in deep breathing. Since the airways serve as a barrier as well, harmful foreign material including most micro-organisms can not easily enter the lower respiratory

passages. The very first barrier starts at the vestibules of the nose, which contain hairs, and healthy, sticky mucus intercepting air-borne particles. Caught particles are then ejected by ciliated epithelium, which covers the entire upper respiratory tract.

Various factors can interfere with ciliary activity: for example nicotine and tar in tobacco smoking. Coughing occurs in response to chemical or mechanical irritation of nerve endings in the upper respiratory tract. The larynx and the bifurcation of the trachea are the most sensitive regions and any particles of foreign matter lodged in these regions are removed when a cough sends a rapid blast of air sweeping out the respiratory tree.

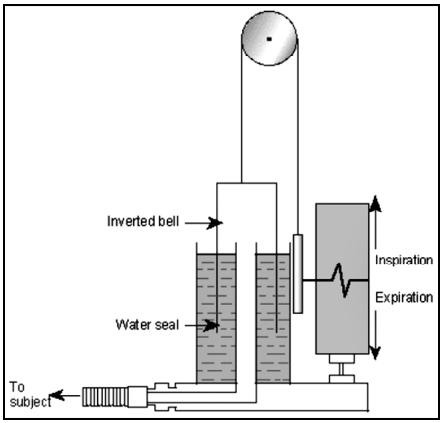


The alveolated region of the lung includes respiratory bronchioles (divided from terminal bronchioles and have only occasional alveoli on their walls) and alveolar ducts (completely lined with alveoli). This zone is called respiratory zone and the gas exchange occurs here. The distance from the terminal bronchiole to the distal alveous is only a few mm, but the respiratory zone makes up most of the lung, its volume being about 2.5 to 3 L. Blood is brought to the other side of the blood-gas barrier from the right heart by pulmonary arteries, which also form a series of branching tubes leading to the pulmonary capillaries and back to the pulmonary veins.

The capillaries lie in the walls of the alveoli and form a dense network that the blood continuously runs in the alveolar wall. At resting not all the capillaries are open but when the pressure rises (*e.g.* exercise) recruitment of the close capillaries

occurs. The diameter of a capillary segment is about 10μm, just large enough for a red blood cell. The pulmonary artery receives the whole output of the right heart, but resistance of pulmonary circuit is very low. This enables the high blood flow to the circuit.

LUNG VOLUMES AND PULMONARY FUNCTION TESTS



Pulmonary function can be examined by the spirometry technique. Spirometers are the traditional tools of the respiratory physiologists. The subject breathes into a closed system in which air is trapped (bell). As the subject breathes air movement into or out of the mouthpiece causes the bell to rise (inspiration) or fall (expiration). Corresponding movements of an attached pen register the change in volume on a rotating drum recorder.

From such a recording we could measure:

- *Tidal volume (TV)*: Volume of air inhaled or exhaled with each breath during normal breathing (0.5 L).
- *Inspiratory reserve volume (IRV)*: Maximal volume of air inhaled at the end of a normal inspiration (3 L).
- *Expiratory reserve volume (ERV)*: Maximal volume of air exhaled at the end of a tidal volume (1.2 L).
- *Inspiratory capacity (IC)*: Maximal volume of air inhaled after a normal expiration (3.6 L) (TV+IRV).

- *Functional Residual Capacity (FRC)*: The volume of gas that remains in the lung at the end of a passive expiration. (2-2.5 L or 40 per cent of the maximal lung volume) (ERV+RV).
- *Residual Volume (RV)*: The volume of gas remains in the lung after maximal expiration. (1-1.2 L).

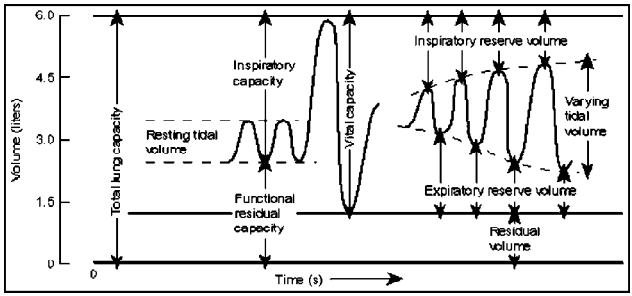


Fig. FRC and RV can not be Measured with an Ordinary Spirometer

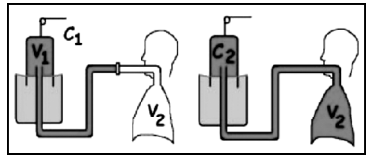
- *Total Lung Capacity (TLC)*: The maximal lung volume that can be achieved voluntarily. (5-6 L) (IRV+ERV+TV+RV).
- *Vital capacity (VC)*: The volume of air moved between TLC and RV. (4-5 L) (IRV+ERV+TV). Multiplying the tidal volume at rest by the number of breaths per minute gives the total minute volume (6 L/min). During exercise the tidal volume and the number of breaths per minute increase to produce a total minute volume as high as 100 to 200 L/min.

Measurements of Functional Residual Capacity (FRC) and Residual Volume (RV)

Helium Spirometry

In this technique a subject is connected to a spirometer filled with helium which is virtually insoluble in the blood. After some breathes the amount of helium in the lung and the spirometer reach equilibrium. Because there is no lost of gas

during the experiment the amount of helium before ($C_1 \times V_1$) and after the equilibrium ($C_2 \times [V_1 + V_2]$) is same.



$$V_1 = C_2 \times (V_1 + V_2)$$
$$V_2 = V_1 \times (C_1 - C_2) / C_2$$
$$V_2 = FRC$$

Another way of measuring FRC is with a body plethysmograph. It is a big airtight box in which the subject sits. At the end of a normal expiration, the mouthpiece is shut and the subject makes respiratory efforts. When the subject makes an inspiratory effort against a closed airway s/he slightly increases the volume of his/her lung, airway pressure decreases and the box pressure increases:

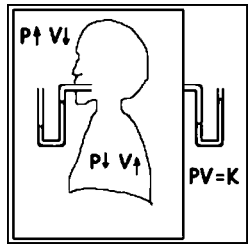
$$P_1 \times V_1 = P_2 \times (V_1 - \Delta V)$$

The pressure in the box before (P_1) and after (P_2) the respiratory efforts, V: Volume in the box before the respiratory efforts and DV can be measured. The Boyle's law can also be applied to the gas in the lung:

$$P_3 \times V_2 = P_4 \times (V_2 + \Delta V)$$
$$V_2 = FRC$$

$P_{3,4}$: Mouth pressures before (P_3) and after (P_4) the respiratory efforts. If the measurement is done following a forced expiration:

$$V_2 = RV$$



In contrast to the helium technique, which measures only the ventilated air, the body plethysmograph measures the total volume in the gas in the volume including the gas trapped in the airways (if there is any). Normally measurements with these techniques are similar. However, the difference is increased in the presence of lung diseases.

Total Ventilation

The total volume of the gas leaving the lung per unit time. If TV is 500 ml and there are approximately 15 breaths/min the total volume of the gas leaving the lung, total ventilation will be 500 × 15 = 7500 ml/min. It can be measured by having the subject breath through a valve that separates the inspired air from expired air and collecting the expired air.

Alveolar Ventilation

The volume of the gas reaching the respiratory zone of the airways. However, not all of the total ventilation volume reaches the alveoli. 150 ml of the TV (500 ml) is left behind in the airways, which does not contain alveoli, therefore does not contribute the diffusion (Anatomic death space). Thus, the volume of gas entering the respiratory zone, alveolar ventilation, is (500-150) × 15 = 5250 ml/min. The measurement of alveolar ventilation is more difficult. One way is to measure the volume of anatomic dead space and calculate the dead space ventilation. This then subtracted from the total ventilation.

Alveolar ventilation = Total ventilation – Anatomic death space ventilation

Anatomic dead space ventilation = Anatomic dead space volume × respiration frequency

- V_E: Total expiration volume
- V_T: Tidal volume
- V_D: Dead Space volume
- V_A: Volume of alveolar gas during tidal breathing

V: volume per unit time:

$$V_T = V_D + V_A$$

$$(V_T \times n) = (V_D \times n) + (V_A \times n)$$

- V: volume per unit time
- V_E: Expired total ventilation
- V_D: dead space ventilation
- V_A: alveolar ventilation

$$V_E = V_D + V_A$$
$$V_A = V_E - V_D$$

The disadvantage of this method is it is not very easy to determine dead space volume without a considerable error. Another way of measuring the alveolar ventilation is from concentration of CO_2 in expired air. Since the amount of CO_2 in the inspired air is negligible and no gas exchange occurs, we could assume that there is CO_2 in the anatomic dead space. Therefore CO_2 in the expired air comes from alveoli.

$$V_{CO_2} = V_A \times \%CO_2 / 100$$

V_{CO2} = the volume of CO_2 exhaled per unit time.

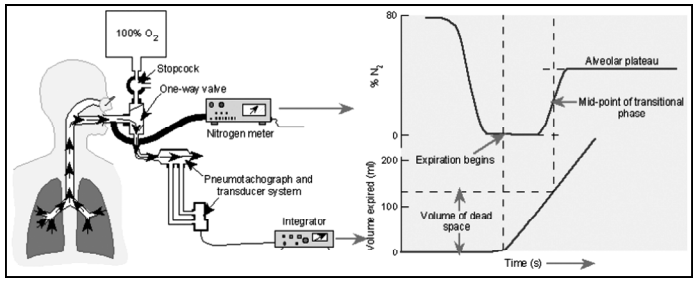
$$V_A = \left(V_{CO_2} \times 100\right) / \%\, CO_2$$

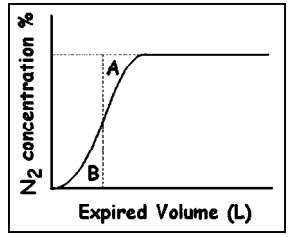
per cent CO_2 = Fractional CO_2 concentration = F_{CO2}

Anatomical Dead Space

Volume of the conducting airways. It is approximately 150 ml but its volume increases with large inspiration and depends on the size and the posture of the subject. Measurement of dead space: Fowler's method: The subject breaths pure oxygen through a valve box and a rapid nitrogen analyser samples and measures the nitrogen concentration in the expired air. After a single inspiration of pure oxygen (100 per cent) nitrogen concentration in the expired air is increased as the gas in the dead space is washed by pure oxygen. Nitrogen concentration quickly reaches a plateau level (alveolar plateau).

The dead space is found by plotting nitrogen concentration against the expired volume. The expired volume up to the vertical line drawn such that area A = area B represents the anatomical dead space volume.





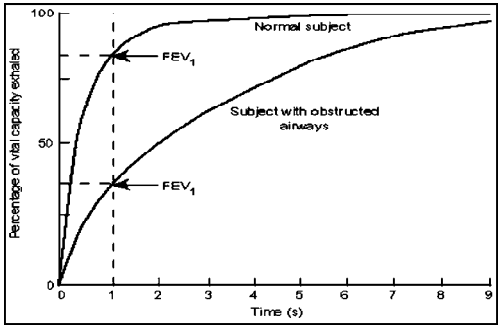
Pulmonary Function Tests

Pulmonary function tests are very useful tests to diagnose several lung diseases. The simplest but one of the most informative tests of lung function is a forced expiration.

Tests of Ventilatory Capacity

Forced Expiratory Volume (FEV)

It is the volume of gas exhaled in one second by a forced expiration following a full inspiration (FEV1). The total volume of the gas exhaled after a full inspiration represents the vital capacity. However, this value could be slightly smaller than the vital capacity measured with a slow (normal speed) expiration. Therefore, this value is called forced vital capacity (FVC). The normal ratio of the FEV1 is 80 per cent of FVC.



Forced Expiratory Flow (FEF25-75)

This measurement represents the expiratory flow rate over the middle half of the FVC (between 25 – 75 per cent). It is obtained by identifying the 25 per cent and 75 per cent volume points of FVC, measuring the time between these points and calculating the flow rate. Interpretation of tests of forced expiration: On the basis of the knowledge obtained from these functional tests, lung diseases can be classified as restrictive or obstructive. In restrictive lung diseases (such as pulmonary fibrosis), the vital capacity is reduced to below normal levels. However, the rate at which the vital capacity is forcefully exhaled is normal.

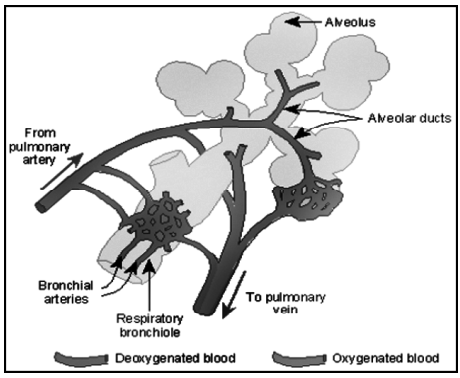
In obstructive lung disease (such as asthma, emphysema, bronchitis) the vital capacity is normal because lung tissue is not damage and its compliance is unchanged. In asthma the small airways (bronchioles) constrict, bronchoconstriction increases the resistance to airflow. Although the vital capacity is normal, the increased airway resistance makes expiration more difficult and takes longer time. Obstructive disorders are therefore diagnosed by tests that measure the rate of forced expiration, such as the FEV1 and FEF25-75. A significant decrease in these values suggests an obstructive lung disease.

DIFFUSION

Blood-gas Exchange

Oxygen and carbon dioxide move between air and blood

by simple diffusion: from an area of high to low partial pressure, as simple as water runs downhill. It is a passive process which means requires no energy. Fick's law of diffusion determines the amount of gas moves across the tissue is proportional to the area of the tissue but inversely proportional to its thickness. Because the blood-gas barrier in the lung is extremely thin and has a very large area (50-100 m2), it is well suited to its function.



How does the Lung Achieve such a large Surface Area of Blood-gas Barrier Inside the Limited Thoracic Cavity

This is achieved by wrapping the pulmonary capillaries around an enormous number of small air sacs, alveoli, and each about 1/3 mm in diameter. There are about 300 million alveoli in the human lung, creating 85 m2 surface area but having a volume of only 4L.

Calculations of Oxygen and Carbon Dioxide Partial Pressures

Dalton's Law

Total pressure of a gas mixture (in our case air) is equal to the sum of the pressures that each gas in the mixture would have independently (Partial Pressure of each gas).

$$P_{dry\,atmosphere} = PN_2 + PO_2 + PCO_2 = 760 mmHg$$

Since oxygen constitutes 21 per cent of the atmosphere, PO2 = 159 mm Hg. nitrogen 78 PN2 = 593 mmHg.

Inspired air also contains moisture and its amount may vary with temperature etc. However when the inspired air arrived the alveoli it is normally saturated with water vapour. Because the temperature in the lungs does not change significantly water vapour of the alveolar air could be considered constant (47 mm Hg).

$$P_{wet\,atmosphere} = PN_2 + PO_2 + PCO_2 + PH_2O = 760 mmHg$$

PO2 = 0.21 (760-47) = 150 mm Hg (oxygen partial pressure of the inspired air when it arrives alveoli, before the gas exchange).

Why are the Measurements of PO_2 and PCO_2 Important

The measurement of PO_2 of arterial blood is particularly important because it provides a good index of lung function. The actual amount of dissolved O_2 is a linear function of the PO_2: The higher PO_2 indicates that more O_2 is dissolved. Blood PO_2 measurements are not affected by the O_2 in red cells. A normal PO_2 in the inspired air together with low arterial PO_2 means that the gas exchange in the lungs is impaired.

In summary, the measurement of PO_2 is important for:

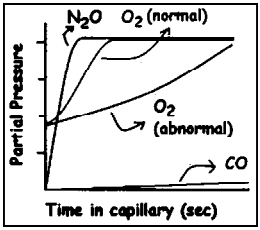
- Treating patients with pulmonary diseases
- Performing safe surgery (when anaesthesia is used)
- The care of premature babies with respiratory distress syndrome

	Inspired Air	**Alveolar Air**
H_2O	Variable	47 mm Hg
CO_2	0.3 mm Hg	40 mm Hg
O_2	159 mm Hg	105 mm Hg
N_2	601 mm Hg	568 mm Hg
Total Pressure	760 mm Hg	760 mm Hg

Diffusion and Perfusion Limitations

How does oxygen get into the circulation? To answer this

question we will first examine two extreme examples: If a subject breathes CO (carbon monoxide) because CO moves rapidly across the blood-gas barrier, the content of CO in red blood cells is increased. However, CO forms very tight bonds with Hb that even though large amount of CO is taken up by the red blood cells almost no increase in the CO partial pressure is observed. Therefore, the amount of CO that gets unto the blood is limited by the diffusion properties of the blood-gas barrier and not by the amount of blood available: diffusion limited.

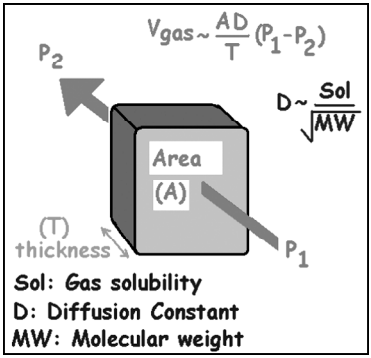


The other extreme example is nitrous oxide: Nitrous oxide diffuses across the barrier but forms no combination with Hb. As a result its partial pressure rises very rapidly. The amount of nitrous oxide taken up by blood depends on the amount of blood available: perfusion limited.

The time course of O_2 transfer is in between. It does bind to Hb but nothing like the avidity of CO. In normal conditions capillary PO_2 reaches that of alveolar gas when the red cell is about 1/3 of the way along the capillary. Thus, in normal, physiological condition oxygen transfer is perfusion limited. In pathological conditions, *e.g.* thickening of alveolar wall, there would be some diffusion limitations as well. PO_2 of the venous blood and the alveolar air is 40 and 100 mm Hg, respectively.

At the end of the capillary blood PO_2 reaches the same value with the alveolar air PO_2. During exercise the pulmonary blood flow is increased and the average travel time of a red blood cell in the capillary is shortened. However, in normal subjects still there would be no difference between the PO_2 of alveolar air and the blood at the end of the capillary. On the other hand if there is thickening of alveolar wall oxygen

transport would be impaired and measurable difference between alveolar gas and end-capillary blood PO_2 occurs.



The laws of diffusion state that:

$$V_{Gas} = A.D.(P_1 - P_2)$$

A: Area

D: Diffusion Constant

Because it is not possible to measure the area and the thickness in living subjects one can introduce DL, diffusing capacity of the lung.

$$V_{Gas} = D_L \bullet (P_1 - P_2)$$
$$D_L = V_{Gas} / (P_1 - P_2)$$

Because transfer of CO is entirely diffusion limited it is an ideal gas to use for diffusion capacity measurements.

$$D_L = V_{CO} / (P_1 - P_2)$$

Since CO in the capillary blood is negligible.

$$D_L = V_{CO} / (P_{ACO})$$

The Diffusing Capacity of the Lung for CO is the Volume of CO Transferred in mm per mm Hg of Alveolar Partial Pressure

Single breath method: A single inspiration of a dilute mixture of CO is made and the rate of disappearance of CO from the alveolar gas during a 10 sec breath hold is calculated.

Steady state method: A subject breathes low concentration of CO until steady state is reached. Then rate of disappearance of CO from alveolar gas is measured for a short period. The normal value is 25 ml/min/mm Hg. With exercise this value increases 2-3 times. Solubility of CO_2 is higher and it diffuses through tissue 20 times faster than oxygen. Therefore, carbon dioxide transfer is mainly perfusion limited.

PERFUSION

The main function of the pulmonary circulation is to bring systemic venous blood into contact with alveoli for gas exchange. It begins at the main pulmonary artery, which receives the mixed venous blood pumped by the right ventricle. This artery then branches successively like the system of airways. Each time the airway branches, the arterial tree branches that the two parallel each other.

The oxygenated blood is collected from the capillary bed by the pulmonary vein, which drains into the left atrium. In addition, pulmonary vessels protect the body from obstruction of important vessels in other organs such as renal or cerebral vessels. When air, fat or blood cloths enter the blood stream (*e.g.* during surgery or trauma) pulmonary vessels trap this emboli and endothelial cells release fibrinolytic substances that help dissolve thrombi.

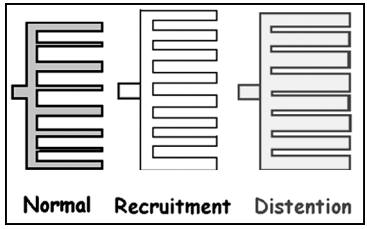
The pulmonary circulation serves as a blood reservoir and the volume in the lung capillaries is approximately equal to the stroke volume of the right heart. Pulmonary vessels also contribute to the metabolism of vasoactive hormones. For example angiotensin I is activated and converted to angiotensin II by angiotensin-converting enzyme which is located on the surface of the endothelial cells of the pulmonary capillaries.

The differences between the pulmonary and the systemic circulation:

1. The pressures in the pulmonary circulation are remarkably low: The pressure in the main pulmonary artery is 25 mm Hg (systolic) and 8 mm Hg (diastolic), in average 15 mm Hg. This is a very

lowpressure compare to the pressure in aorta, 100 mm Hg.

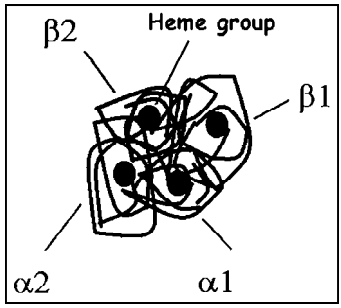
2. Another striking property of the pulmonary arteries is their exceedingly thin walls. This anatomical adaptation of the lung is critically important for its function: The lung is required to receive the whole of the cardiac output at all times. Keeping the pulmonary pressure as low as possible allows the right heart answer this demand with a minimum work.
3. Unlike the systemic capillaries, which are organised as tubular network with some interconnections, the pulmonary capillaries mesh together in the alveolar wall so the blood flows as a thin sheet (capillary bed).
4. Another unique property of the pulmonary circulation is its ability to decrease resistance as cardiac output increases. Two mechanisms are responsible for this function.
   - Capillary recruitment: opening of initially closed capillaries when cardiac output increases.
   - Capillary distension: The decrease in pulmonary pressure with increased cardiac output has several beneficial effects: It
     i. Minimise the load on the right heart,
     ii. Prevents pulmonary oedema,
     iii. Maintains the adequate flow rate of the blood in the capillary, and
     iv. Increases the capillary surface area.



GAS TRANSPORT TO THE PERIPHERY

Oxygen

Oxygen is carried in the blood in two forms, dissolved and combined with haemoglobin (Hb). Dissolved Oxygen: The amount of oxygen dissolved in the blood is proportional to its partial pressure (Henry's Law). 100 ml of arterial blood with normal oxygen partial pressure (100 mm Hg) contains 0.3 ml oxygen. By this way amount of oxygen delivered to the tissues is only about 90 ml/min. Taking in to account that the tissue requirements are about 3000 ml Oxygen/min, it is obvious that this way of transporting oxygen is not adequate for human.



Haemoglobin

Haemoglobin (Hb) = Heme (iron-porphyrin) + globin (protein) Globin has 4 protein polypeptide chains: 2 alpha (each has 141 aa) and 2 beta (each has 146 aa). Differences in the amino acid sequence of these chains give rise to various types of Hb.

- Hb-A: Normal adult Hb.
- Hb-F: Foetal Hb, which makes part of the total Hb at birth and is gradually, replaced by Hb-A.
- Hb-S: S stands for sickle. This Hb has valine in the beta chain instead of glutamic acid. Deoxygenated form of this Hb is poorly soluble and crystallises in the erythrocytes which results in changes in red cell

shape. The fragility of the red cells is increased and there is a tendency to thrombus formation. Each polypeptide chain is combined with one heme group. In the centre of each heme group there is one atom of iron, which can combine with one oxygen molecule. Thus one Hb molecule can bind 4 oxygen molecules. Heme contains iron in the reduced form (Fe^{++}, ferrous iron). In this form the iron can share electrons and bond with oxygen. Oxygen forms a reversible combination with Hb.

$$O_2 + Hb \leftrightarrow HbO_2 (\text{oxyhemoglobin})$$

When oxyhemoglobin dissociates to release oxygen to the tissues (the heme iron is still in ferrous form) and the Hb is called deoxyhemoglobin (reduced Hb). Oxyhemoglobin is not same with oxidised Hb (or methemoglobin) in which iron is in the oxidised (Fe^{+++}, ferric) form. Because methemoglobin lacks the electron necessary to bind oxygen, it does not participate in oxygen transport.

The oxygen carrying capacity of the blood is determined by the Hb concentration. If it is below normal, anaemia, the oxygen concentration of the blood is reduced. When the Hb concentration is high, polycythemia, the oxygen carrying capacity of the blood is increased.

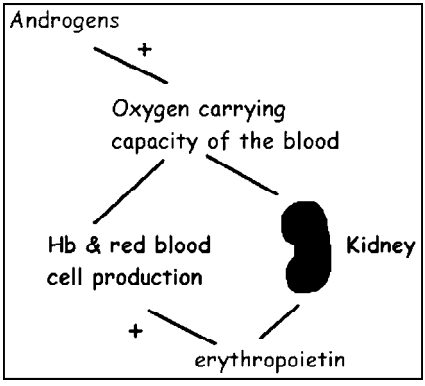
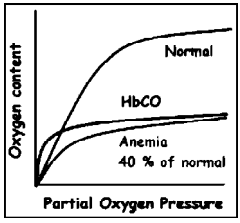


Fig. The Oxygen Saturation of Hb O_2 Combined with Hb/O_2 Capacity

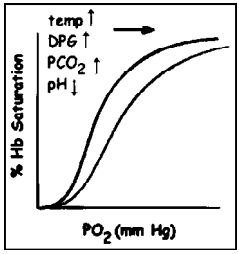
The Hb and red blood cell production in the body is under control of erythropoietin, which is produced by the kidneys. Its production is stimulated when the amount of oxygen delivered to the kidneys is lower than normal. Normally Hb concentration in men is higher then women, because the red cell production is also stimulated by androgen.

- One gram of Hb can combine with 1.39 ml oxygen and because normal blood has 15 mg of Hb/100 ml and the oxygen capacity of the 100 ml blood is 20.8 ml.
- Oxygen saturation of the arterial blood (PO2=100 mm Hg) is 97.5 per cent while oxygen saturation of the venous blood (PO2= 40 mm Hg) is 75 per cent.



Why is the Relationship between PO_2, O_2 Saturation and O_2 Concentration Important

In anaemic patients Hb concentration can be as low as 10 mg/100ml blood. In such patient with normal respiratory functions (PO_2 = 100 mm Hg), O_2 capacity will be lower (20.8 × 10/15 = 13.9 ml/100 ml blood) and though the O_2 saturation still be 97.5 per cent, the amount of oxygen combined with Hb will be lower. Because the reduced Hb is purple a low arterial oxygen saturation causes cyanosis.



The oxygen dissociation curve is shifted to the right by:

- An increase in H^+ concentration,
- An increase in PCO_2 (Bohr effect),
- An increase in temperature,
- An increase in 2,3-diphosphoglycerate (DPG). A rightward shift means more unloading of oxygen at a given PO_2 in a tissue capillary. DPG is an end product of red cell metabolism and an increase in its concentration occurs in chronic hypoxia (*e.g.* at high attitude or in patients with chronic lung disease).

Because CO has a much higher affinity to Hb (forms carboxyhemoglobin, COHb), even small amounts of CO bind the large proportion of Hb making it unavailable for oxygen: The Hb concentration and PO_2 of blood may be normal but its oxygen content is grossly reduced.

Carbon-dioxide

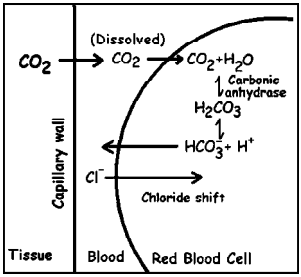
CO_2 is carried in the blood in three forms: Dissolved CO_2, as bicarbonate and as carbamino compounds (combined with proteins). Dissolved CO_2: Because CO_2 is more soluble than oxygen this fraction of CO_2 in the blood plays an important role in its transport (about 10 per cent). Bicarbonate:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

The first reaction is very fast and involves carbonic anhydrase enzyme, which is present in red cells, while the second reaction does not involve an enzyme. When the concentrations of the products of the carbonic acid dissociation reaction bicarbonate diffuses into the blood but not hydrogen ion because the red cell membrane is relatively impermeable to the positively charged ions. In order to maintain electrical neutrality Cl^- ions diffuse into the red cells according to the Gibbs-Donnan equilibrium (chloride shift). Some of the H^+ are bound to Hb:

$$H^+ + HbO_2 \leftrightarrow H^+Hb + O_2$$

The reduced Hb is a better proton acceptor than oxygenated Hb meaning deoxygenation of the blood increases its ability to carry CO_2 = Haldane effect.



Carbamino compounds: CO_2 is also bond by terminal amine groups of several blood proteins. Such as (the most important one) globin of Hb (carbamino-haemoglobin). In arterial blood CO_2 is carried 90 per cent as bicarbonate, 5 per cent combined with carbamino proteins and 5 per cent as dissolved CO_2. In venous blood these values are 60, 30 and 10, respectively.

ACID-BASE REGULATION

By altering the CO_2 elimination the lungs can control the acid-base balance of the body.

$$H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

$$K_A\left(H_2CO_3\right) = \left(H^+ + HCO_3\right) / H_2CO_3$$

$$K_A = \left(H^+ + HCO_3\right) / CO_2$$

$$\log K_A = \log H^+ + \log\left(HCO_3^- / CO_2\right)$$

$$-\log H^+ = -\log K_A + \log\left(HCO_3^- / CO_2\right)$$

$$pH = pKA + \log\left(HCO_3^- / CO_2\right)$$

$$pH = pKA + \log\left(HCO_3^- / 0.03\, PCO_2\right)$$

$$pH = 6.1 + \log 24 / 0.03 \times 40$$

$$pH = 6.1 + \log 20$$

$$pH = 6.1 + 1.3 = 7.4$$

In the human body bicarbonate concentration is regulated by mainly the kidneys and the PCO_2 by the lungs.

Respiratory Acidosis

It is due to an increase in PCO_2 (*e.g.* hypoventilation, ventilationperfusion inequality). Whenever PCO_2 is increased the bicarbonate concentration is also rises due to dissociation of carbonic acid but nevertheless HCO_3^-/PCO_2 falls. In response to these changes the kidneys start conserving HCO_3^-.

$$pH = 6.1 + \log 24 / 0.03 \times 40 = 6.1 + \log 20 = 7.4 \text{ (Normal)}$$

$$pH = 6.1 + \log 28 / 0.03 \times 60 = 6.1 + \log 15.6 = 7.29 \text{ (Respiratory acidosis)}$$

$$pH = 6.1 + \log 33 / 0.03 \times 60 = 6.1 + \log 18.3 = 7.36 \text{ (compensated res. acidosis)}$$

Respiratory Alkalosis

It is caused by a decrease in PCO_2 (which in turn increases the HCO_3^-/PCO_2) due to hyperventilation (*e.g.* at high attitude, voluntary). The kidneys compensate it by increasing the HCO_3^- excretion.

Metabolic Acidosis

Metabolic refers changes in HCO_3^-. In this case HCO_3^-/PCO_2 decreases by lowering HCO_3^- in the blood. It occurs in conditions accompanied by an accumulation of acids in the blood (*e.g.* diabetes mellitus, lactic acid accumulation after tissue hypoxia) Respiratory compensation occurs by an increase in ventilation that lowers PCO_2. This stimulation is mainly due to stimulation of peripheral chemoreceptors by H^+.

Metabolic Alkalosis

An in crease in HCO_3^- raises the HCO_3^-/PCO_2. Common reasons are excessive ingestion of alkalis and loss of gastric acid due to vomiting. In response the metabolic acidosis a reduction in alveolar ventilation occurs and PCO_2 is increased.

RESPIRATORY SYSTEM UNDER STRESS

Exercise

During exercise the rate and the depth of breathing are increased. This increase in ventilation (hyperpnea) matches the simultaneous increase in oxygen consumption and carbon dioxide production that the arterial blood carbon dioxide and oxygen partial pressures and pH do not change dramatically.

The mechanism underlying the exercise-induced changes in ventilation is not clear:

- Neurogenic mechanisms:
  - Stimulation of respiratory system muscles by sensory nerve activity from exercising limbs, probably via activating brain stem respiratory centres and/or via spinal reflexes.
  - Stimulatory inputs from cerebral cortex.
- Chemical mechanisms: Because partial pressures of carbon dioxide and oxygen do not change during exercise it is difficult to explain possible chemical factors. However, the focal changes in these parameters near chemoreceptor area may contribute to the exercise-induced changes in ventilation.

Anaerobic Threshold

The maximum rate of oxygen consumption than can be attained before blood lactic acid levels rise as a result of anaerobic respiration. Lactic acid concentration is increased due to anaerobic limitations in the muscle cells during heavy exercise. [The cardiovascular system maintains an adequate amount of oxygen to the tissue that mitochondria can carry out oxidative phosphorylation. Oxidative phosphorylation is an oxygen consuming process by which energy derived from substrate oxidation is stored in ATP as a chemical energy. When the oxygen consumption is increased (*e.g.* heavy exercise) or at low PO_2 (*e.g.* cellular hypoxia) anaerobic glycolysis becomes

a major mechanism for cellular ATP formation and glucose is reduced to lactate.]

Acclimatization to High Altitude

In the high altitude the human body compensates the low partial oxygen pressure by changing ventilation or affinity of Hb to oxygen or total Hb concentration.

Hypoxic Ventilatory Response

Hyperventilation induced by the decreased partial oxygen pressure. This lowers the arterial partial carbon dioxide pressure and causes respiratory alkalosis. The rise in blood pH in turn set the ventilation to a more stable but still slightly higher levels. Hyperventilation increases the tidal volume and reduces the proportion of the anatomical death space in the inspired air. This also improves the oxygenation of the blood. However, in spite of all these adaptation mechanisms, the partial oxygen pressure in the arterial blood can not be increased more than the partial oxygen pressure in the inspired air.

As a result partial pressure of oxygen in the arterial blood decreases with increasing altitude. At sea levels arterial blood loses 22 per cent of its oxygen load in tissues: The oxygen saturation of the arterial and venous blood is 97 per cent and 75 per cent, respectively. At high altitude the low oxygen content of red blood cells stimulates 2-DPG production and decreases the affinity of Hb to oxygen, which in turn facilitates the oxygen transport to the tissues. However, at very high altitudes increase in blood pH causes a shift to the left in the oxygen saturation curve and increases the affinity of Hb to oxygen.

This second step is indeed beneficial at very high altitude by increasing the oxygenation of the blood in the lungs. Due to low oxygen partial pressure in the arterial blood at high altitude the tissue hypoxia occurs and in response the kidneys secrete erythropoietin hormone. Erythropoietin stimulates the production of red blood cells resulting in polycythemia, which can cause oedema, ventricular hypertrophy and heart failure.

DIGESTIVE SYSTEM

The digestive system is made up of the digestive tract—a series of hollow organs joined in a long, twisting tube from the mouth to the anus—and other organs that help the body break down and absorb food. Organs that make up the digestive tract are the mouth, esophagus, stomach, small intestine, large intestine—also called the colon—rectum, and anus. Inside these hollow organs is a lining called the mucosa. In the mouth, stomach, and small intestine, the mucosa contains tiny glands that produce juices to help digest food. The digestive tract also contains a layer of smooth muscle that helps break down food and move it along the tract. Two "solid" digestive organs, the liver and the pancreas, produce digestive juices that reach the intestine through small tubes called ducts. The gallbladder stores the liver's digestive juices until they are needed in the intestine.

When you eat foods—such as bread, meat, and vegetables—they are not in a form that the body can use as nourishment. Food and drink must be changed into smaller molecules of nutrients before they can be absorbed into the blood and carried to cells throughout the body. Digestion is the process by which food and drink are broken down into their smallest parts so the body can use them to build and nourish cells and to provide energy.

HOW IS FOOD DIGESTED

Digestion involves mixing food with digestive juices, moving it through the digestive tract, and breaking down large molecules of food into smaller molecules. Digestion begins in the mouth, when you chew and swallow, and is completed in the small intestine.

Movement of Food through the System

The large, hollow organs of the digestive tract contain a layer of muscle that enables their walls to move. The movement

of organ walls can propel food and liquid through the system and also can mix the contents within each organ. Food moves from one organ to the next through muscle action called peristalsis. Peristalsis looks like an ocean wave travelling through the muscle. The muscle of the organ contracts to create a narrowing and then propels the narrowed portion slowly down the length of the organ.

These waves of narrowing push the food and fluid in front of them through each hollow organ. The first major muscle movement occurs when food or liquid is swallowed. Although you are able to start swallowing by choice, once the swallow begins, it becomes involuntary and proceeds under the control of the nerves. Swallowed food is pushed into the esophagus, which connects the throat above with the stomach below.

At the junction of the esophagus and stomach, there is a ringlike muscle, called the lower esophageal sphincter, closing the passage between the two organs. As food approaches the closed sphincter, the sphincter relaxes and allows the food to pass through to the stomach. The stomach has three mechanical tasks. First, it stores the swallowed food and liquid. To do this, the muscle of the upper part of the stomach relaxes to accept large volumes of swallowed material.

The second job is to mix up the food, liquid, and digestive juice produced by the stomach. The lower part of the stomach mixes these materials by its muscle action. The third task of the stomach is to empty its contents slowly into the small intestine. Several factors affect emptying of the stomach, including the kind of food and the degree of muscle action of the emptying stomach and the small intestine. Carbohydrates, for example, spend the least amount of time in the stomach, while protein stays in the stomach longer, and fats the longest.

As the food dissolves into the juices from the pancreas, liver, and intestine, the contents of the intestine are mixed and pushed forward to allow further digestion. Finally, the digested nutrients are absorbed through the intestinal walls and transported throughout the body. The waste products of this process include undigested parts of the food, known as fibre,

and older cells that have been shed from the mucosa. These materials are pushed into the colon, where they remain until the feces are expelled by a bowel movement.

Production of Digestive Juices

The digestive glands that act first are in the mouth—the salivary glands. Saliva produced by these glands contains an enzyme that begins to digest the starch from food into smaller molecules. An enzyme is a substance that speeds up chemical reactions in the body. The next set of digestive glands is in the stomach lining. They produce stomach acid and an enzyme that digests protein. A thick mucus layer coats the mucosa and helps keep the acidic digestive juice from dissolving the tissue of the stomach itself.

In most people, the stomach mucosa is able to resist the juice, although food and other tissues of the body cannot. After the stomach empties the food and juice mixture into the small intestine, the juices of two other digestive organs mix with the food. One of these organs, the pancreas, produces a juice that contains a wide array of enzymes to break down the carbohydrate, fat, and protein in food. Other enzymes that are active in the process come from glands in the wall of the intestine.

The second organ, the liver, produces yet another digestive juice—bile. Bile is stored between meals in the gallbladder. At mealtime, it is squeezed out of the gallbladder, through the bile ducts, and into the intestine to mix with the fat in food. The bile acids dissolve fat into the watery contents of the intestine, much like detergents that dissolve grease from a frying pan. After fat is dissolved, it is digested by enzymes from the pancreas and the lining of the intestine.

Absorption and Transport of Nutrients

Most digested molecules of food, as well as water and minerals, are absorbed through the small intestine. The mucosa of the small intestine contains many folds that are covered with

tiny fingerlike projections called villi. In turn, the villi are covered with microscopic projections called microvilli. These structures create a vast surface area through which nutrients can be absorbed. Specialized cells allow absorbed materials to cross the mucosa into the blood, where they are carried off in the bloodstream to other parts of the body for storage or further chemical change. This part of the process varies with different types of nutrients.

Carbohydrates

The *Dietary Guidelines for Americans 2005* recommend that 45 to 65 per cent of total daily calories be from carbohydrates. Foods rich in carbohydrates include bread, potatoes, dried peas and beans, rice, pasta, fruits, and vegetables. Many of these foods contain both starch and fibre. The digestible carbohydrates—starch and sugar—are broken into simpler molecules by enzymes in the saliva, in juice produced by the pancreas, and in the lining of the small intestine. Starch is digested in two steps.

First, an enzyme in the saliva and pancreatic juice breaks the starch into molecules called maltose. Then an enzyme in the lining of the small intestine splits the maltose into glucose molecules that can be absorbed into the blood. Glucose is carried through the bloodstream to the liver, where it is stored or used to provide energy for the work of the body. Sugars are digested in one step. An enzyme in the lining of the small intestine digests sucrose, also known as table sugar, into glucose and fructose, which are absorbed through the intestine into the blood.

Milk contains another type of sugar, lactose, which is changed into absorbable molecules by another enzyme in the intestinal lining. Fibre is undigestible and moves through the digestive tract without being broken down by enzymes. Many foods contain both soluble and insoluble fibre. Soluble fibre dissolves easily in water and takes on a soft, gel-like texture in the intestines. Insoluble fibre, on the other hand, passes essentially unchanged through the intestines.

Protein

Foods such as meat, eggs, and beans consist of giant molecules of protein that must be digested by enzymes before they can be used to build and repair body tissues. An enzyme in the juice of the stomach starts the digestion of swallowed protein. Then in the small intestine, several enzymes from the pancreatic juice and the lining of the intestine complete the breakdown of huge protein molecules into small molecules called amino acids. These small molecules can be absorbed through the small intestine into the blood and then be carried to all parts of the body to build the walls and other parts of cells.

Fats

Fat molecules are a rich source of energy for the body. The first step in digestion of a fat such as butter is to dissolve it into the watery content of the intestine. The bile acids produced by the liver dissolve fat into tiny droplets and allow pancreatic and intestinal enzymes to break the large fat molecules into smaller ones. Some of these small molecules are fatty acids and cholesterol.

The bile acids combine with the fatty acids and cholesterol and help these molecules move into the cells of the mucosa. In these cells the small molecules are formed back into large ones, most of which pass into vessels called lymphatics near the intestine. These small vessels carry the reformed fat to the veins of the chest, and the blood carries the fat to storage depots in different parts of the body.

Vitamins

Another vital part of food that is absorbed through the small intestine are vitamins. The two types of vitamins are classified by the fluid in which they can be dissolved: water-soluble vitamins (all the B vitamins and vitamin C) and fat-soluble vitamins (vitamins A, D, E, and K). Fat-soluble vitamins are stored in the liver and fatty tissue of the body, whereas

water-soluble vitamins are not easily stored and excess amounts are flushed out in the urine.

Water and Salt

Most of the material absorbed through the small intestine is water in which salt is dissolved. The salt and water come from the food and liquid you swallow and the juices secreted by the many digestive glands.

THE DIGESTIVE PROCESS CONTROLLED

Hormone Regulators

The major hormones that control the functions of the digestive system are produced and released by cells in the mucosa of the stomach and small intestine. These hormones are released into the blood of the digestive tract, travel back to the heart and through the arteries, and return to the digestive system where they stimulate digestive juices and cause organ movement.

The main hormones that control digestion are gastrin, secretin, and cholecystokinin (CCK):

- Gastrin causes the stomach to produce an acid for dissolving and digesting some foods. Gastrin is also necessary for normal cell growth in the lining of the stomach, small intestine, and colon.
- Secretin causes the pancreas to send out a digestive juice that is rich in bicarbonate. The bicarbonate helps neutralize the acidic stomach contents as they enter the small intestine. Secretin also stimulates the stomach to produce pepsin, an enzyme that digests protein, and stimulates the liver to produce bile.
- CCK causes the pancreas to produce the enzymes of pancreatic juice, and causes the gallbladder to empty. It also promotes normal cell growth of the pancreas.

Additional hormones in the digestive system regulate appetite:

- Ghrelin is produced in the stomach and upper intestine in the absence of food in the digestive system and stimulates appetite.
- Peptide YY is produced in the digestive tract in response to a meal in the system and inhibits appetite.

Both of these hormones work on the brain to help regulate the intake of food for energy. Researchers are studying other hormones that may play a part in inhibiting appetite, including glucagon-like peptide-1 (GPL-1), oxyntomodulin (+), and pancreatic polypeptide.

Nerve Regulators

Two types of nerves help control the action of the digestive system. Extrinsic, or outside, nerves come to the digestive organs from the brain or the spinal cord. They release two chemicals, acetylcholine and adrenaline. Acetylcholine causes the muscle layer of the digestive organs to squeeze with more force and increase the "push" of food and juice through the digestive tract. It also causes the stomach and pancreas to produce more digestive juice.

Adrenaline has the opposite effect. It relaxes the muscle of the stomach and intestine and decreases the flow of blood to these organs, slowing or stopping digestion. The intrinsic, or inside, nerves make up a very dense network embedded in the walls of the esophagus, stomach, small intestine, and colon. The intrinsic nerves are triggered to act when the walls of the hollow organs are stretched by food. They release many different substances that speed up or delay the movement of food and the production of juices by the digestive organs. Together, nerves, hormones, the blood, and the organs of the digestive system conduct the complex tasks of digesting and absorbing nutrients from the foods and liquids you consume each day.

EFFECTS OF EXERCISE ON THE DIGESTIVE SYSTEM

Mild exercise speeds digestion because it increases the

circulation of the blood but there comes a point where the exercise if it becomes too heavy then the body must choose between digesting food or the exercise. If the person is very determined to exercise heavily the body will reject the food and throw it out as the digestion requires a lot of blood to accomplish and so does heavy exercise.

2

Physiologic Responses and Long-Term Adaptations to Exercise

INTRODUCTION

When challenged with any physical task, the human body responds through a series of integrated changes in function that involve most, if not all, of its physiologic systems. Movement requires activation and control of the musculoskeletal system; the cardiovascular and respiratory systems provide the ability to sustain this movement over extended periods.

When the body engages in exercise training several times a week or more frequently, each of these physiologic systems undergoes specific adaptations that increase the body's efficiency and capacity.

The magnitude of these changes depends largely on the intensity and duration of the training sessions, the force or load used in training, and the body's initial level of fitness. Removal of the training stimulus, however, will result in loss of the efficiency and capacity that was gained through these training-induced adaptations; this loss is a process called detraining. This stage provides an overview of how the body responds to an episode of exercise and adapts to exercise training and detraining.

The discussion focuses on aerobic or cardiorespiratory endurance exercise and resistance exercise (*e.g.*, strength-developing exercises). It does not address training for speed, agility, and flexibility. In discussing the multiple effects of exercise, this overview will orient the reader to the physiologic basis for the relationship of physical activity and health.

PHYSIOLOGIC RESPONSES TO EPISODES OF EXERCISE

The body's physiologic responses to episodes of aerobic and resistance exercise occur in the musculoskeletal, cardiovascular, respiratory, endocrine, and immune systems. These responses have been studied in controlled laboratory settings, where exercise stress can be precisely regulated and physiologic responses carefully observed.

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

The primary functions of the cardiovascular and respiratory systems are to provide the body with oxygen (O_2) and nutrients, to rid the body of carbon dioxide (CO_2) and metabolic waste products, to maintain body temperature and acid-base balance, and to transport hormones from the endocrine glands to their target organs. To be effective and efficient, the cardiovascular system should be able to respond to increased skeletal muscle activity. Low rates of work, such as walking at 4 kilometers per hour (2.5 miles per hour), place relatively small demands on the cardiovascular and respiratory systems. However, as the rate of muscular work increases, these two systems will eventually reach their maximum capacities and will no longer be able to meet the body's demands.

Cardiovascular Responses to Exercise

The cardiovascular system, composed of the heart, blood vessels, and blood, responds predictably to the increased demands of exercise. With few exceptions, the cardiovascular

response to exercise is directly proportional to the skeletal muscle oxygen demands for any given rate of work, and oxygen uptake increases linearly with increasing rates of work.

Coronary Circulation

The coronary arteries supply the myocardium with blood and nutrients. The right and left coronary arteries curve around the external surface of the heart, then branch and penetrate the myocardial muscle bed, dividing and subdividing like branches of a tree to form a dense vascular and capillary network to supply each myocardial muscle fibre. Generally one capillary supplies each myocardial fibre in adult humans and animals; however, evidence suggests that the capillary density of the ventricular myocardium can be increased by endurance exercise training.

At rest and during exercise, myocardial oxygen demand and coronary blood flow are closely linked. This coupling is necessary because the myocardium depends almost completely on aerobic metabolism and therefore requires a constant oxygen supply. Even at rest, the myocardium's oxygen use is high relative to the blood flow. About 70 to 80 per cent of the oxygen is extracted from each unit of blood crossing the myocardial capillaries; by comparison, only about 25 per cent is extracted from each unit crossing skeletal muscle at rest.

In the healthy heart, a linear relationship exists between myocardial oxygen demands, consumption, and coronary blood flow, and adjustments are made on a beat-to-beat basis. The three major determinants of myocardial oxygen consumption are heart rate, myocardial contractility, and wall stress. Acute increases in arterial pressure increase left ventricular pressure and wall stress. As a result, the rate of myocardial metabolism increases, necessitating an increased coronary blood flow.

A very high correlation exists between both myocardial oxygen consumption and coronary blood flow and the product of heart rate and systolic blood pressure (SBP). This socalled double product is generally used to estimate myocardial

oxygen and coronary blood flow requirements. During vigourous exercise, all three major determinants of myocardial oxygen requirements increase above their resting levels.

The increase in coronary blood flow during exercise results from an increase in perfusion pressure of the coronary artery and from coronary vasodilation. Most important, an increase in sympathetic nervous system stimulation leads to an increase in circulating catecholamines. This response triggers metabolic processes that increase both perfusion pressure of the coronary artery and coronary vasodilation to meet the increased need for blood flow required by the increase in myocardial oxygen use.

Respiratory Responses to Exercise

The respiratory system also responds when challenged with the stress of exercise. Pulmonary ventilation increases almost immediately, largely through stimulation of the respiratory centers in the brain stem from the motor cortex and through feedback from the proprioceptors in the muscles and joints of the active limbs. During prolonged exercise, or at higher rates of work, increases in CO_2 production, hydrogen ions (H^+), and body and blood temperatures stimulate further increases in pulmonary ventilation.

At low work intensities, the increase in ventilation is mostly the result of increases in tidal volume. At higher intensities, the respiratory rate also increases. In normal-sized, untrained adults, pulmonary ventilation rates can vary from about 10 litres per minute at rest to more than 100 litres per minute at maximal rates of work; in large, highly trained male athletes, pulmonary ventilation rates can reach more than 200 litres per minute at maximal rates of work.

Resistance Exercise

The cardiovascular and respiratory responses to episodes of resistance exercise are mostly similar to those associated with endurance exercise. One notable exception is the

exaggerated blood pressure response that occurs during resistance exercise. Part of this response can be explained by the fact that resistance exercise usually involves muscle mass that develops considerable force. Such high, isolated force leads to compression of the smaller arteries and results in substantial increases in total peripheral resistance. Although high-intensity resistance training poses a potential risk to hypertensive patients and to those with cardiovascular disease, research data suggest that the risk is relatively low and that hypertensive persons may benefit from resistance training.

SKELETAL MUSCLE

The primary purpose of the musculoskeletal system is to define and move the body. To provide efficient and effective force, muscle adapts to demands. In response to demand, it changes its ability to extract oxygen, choose energy sources, and rid itself of waste products. The body contains three types of muscle tissue: skeletal (voluntary) muscle, cardiac muscle or myocardium, and smooth (autonomic) muscle. This section focuses solely on skeletal muscle. Skeletal muscle is composed of two basic types of muscle fibres distinguished by their speed of contraction— slow-twitch and fast-twitch—a characteristic that is largely dictated by different forms of the enzyme myosin adenosinetriphosphatase (ATPase).

Slow-twitch fibres, which have relatively slow contractile speed, have high oxidative capacity and fatigue resistance, low glycolytic capacity, relatively high blood flow capacity, high capillary density, and high mitochondrial content. Fasttwitch muscle fibres have fast contractile speed and are classified into two subtypes, fast-twitch type "a" (FT_a) and fast-twitch type "b" (FT_b). FT_a fibres have moderately high oxidative capacity, are relatively fatigue resistant, and have high glycolytic capacity, relatively high blood flow capacity, high capillary density, and high mitochondrial content.

FT_b fibres have low oxidative capacity, low fatigue resistance, high glycolytic capacity, and fast contractile speed. Further, they have relatively low blood flow capacity, capillary

density, and mitochondrial content. There is a direct relationship between predominant fibre type and performance in certain sports.

For example, in most marathon runners, slow-twitch fibres account for up to or more than 90 per cent of the total fibres in the leg muscles. On the other hand, the leg muscles in sprinters are often more than 80 per cent composed of fast-twitch fibres. Although the issue is not totally resolved, muscle fibre type appears to be genetically determined; researchers have shown that several years of either high-intensity sprint training or high-intensity endurance training do not significantly alter the percentage of the two major types of fibres.

SKELETAL MUSCLE ENERGY METABOLISM

Metabolic processes are responsible for generating adenosine triphosphate (ATP), the body's energy source for all muscle action. ATP is generated by three basic energy systems: the ATP-phosphocreatine (ATP-PCr) system, the glycolytic system, and the oxidative system. Each system contributes to energy production in nearly every type of exercise. The relative contribution of each will depend on factors such as the intensity of work rate at the onset of exercise and the availability of oxygen in the muscle.

Energy Systems

The ATP-PCr system provides energy from the ATP stored in all of the body's cells. PCr, also found in all cells, is a high-energy phosphate molecule that stores energy. As ATP concentrations in the cell are reduced by the breakdown of ATP to adenosine diphosphate (ADP) to release energy for muscle contraction, PCr is broken down to release both energy and a phosphate to allow reconstitution of ATP from ADP. This process describes the primary energy system for short, highintensity exercise, such as a 40- to 200-meter sprint; during such exercise, the system can produce energy at very high rates, and ATP and PCr stores, which are depleted in 10–20 seconds,

will last just long enough to complete the exercise. At high rates of work, the active muscle cell's oxygen demand exceeds its supply.

The cell must then rely on the glycolytic energy system to produce ATP in the absence of oxygen (*i.e.*, anaerobically). This system can only use glucose, available in the blood plasma and stored in both muscle and the liver as glycogen. The glycolytic energy system is the primary energy system for all-out bouts of exercise lasting from 30 seconds to 2 minutes, such as an 800-meter run. The major limitation of this energy system is that it produces lactate, which lowers the pH of both the muscle and blood. Once the pH drops below a value of 6.4 to 6.6, enzymes critical for producing energy are no longer able to function, and ATP production stops.

The oxidative energy system uses oxygen to produce ATP within the mitochondria, which are special cell organelles within muscle. This process cannot generate ATP at a high enough rate to sustain an all-out sprint, but it is highly effective at lower rates of work (*e.g.*, long distance running). ATP can also be produced from fat and protein metabolism through the oxidative energy system. Typically, carbohydrate and fat provide most of the ATP; under most conditions, protein contributes only 5 to 10 per cent at rest and during exercise.

Metabolic Rate

The rate at which the body uses energy is known as the metabolic rate. When measured while a person is at rest, the resulting value represents the lowest (*i.e.*, basal) rate of energy expenditure necessary to maintain basic body functions. Resting metabolic rate is measured under highly controlled resting conditions following a 12-hour fast and a good night's sleep. To quantify the rate of energy expenditure during exercise, the metabolic rate at rest is defined as 1 metabolic equivalent (MET); a 4 MET activity thus represents an activity that requires four times the resting metabolic rate. The use of METs to quantify physical activity intensity is the basis of the absolute intensity scale.

Lactate Threshold

Lactate is the primary by-product of the anaerobic glycolytic energy system. At lower exercise intensities, when the cardiorespiratory system can meet the oxygen demands of active muscles, blood lactate levels remain close to those observed at rest, because some lactate is used aerobically by muscle and is removed as fast as it enters the blood from the muscle. As the intensity of exercise is increased, however, the rate of lactate entry into the blood from muscle eventually exceeds its rate of removal from the blood, and blood lactate concentrations increase above resting levels.

From this point on, lactate levels continue to increase as the rate of work increases, until the point of exhaustion. The point at which the concentration of lactate in the blood begins to increase above resting levels is referred to as the lactate threshold.

Lactate threshold is an important marker for endurance performance, because distance runners set their race pace at or slightly above the lactate threshold. Further, the lactate thresholds of highly trained endurance athletes occur at a much higher percentage of their VO_2 max, and thus at higher relative workloads, than do the thresholds of untrained persons. This key difference is what allows endurance athletes to perform at a faster pace.

HORMONAL RESPONSES TO EXERCISE

The endocrine system, like the nervous system, integrates physiologic responses and plays an important role in maintaining homeostatic conditions at rest and during exercise. This system controls the release of hormones from specialized glands throughout the body, and these hormones exert their actions on targeted organs and cells. In response to an episode of exercise, many hormones, such as catecholamines, are secreted at an increased rate, though insulin is secreted at a decreased rate. The actions of some of these hormones, as well as their specific responses to exercise.

IMMUNE RESPONSES TO EXERCISE

The immune system is a complex adaptive system that provides surveillance against foreign proteins, viruses, and bacteria by using the unique functions of cells produced by the bone marrow and the thymus gland. By interacting with neural and endocrine factors, the immune system influences the body's overall response to exercise. A growing body of literature indicates that the incidence of some infections may be influenced by the exercise history of the individual. Moderate exercise has been shown to bolster the function of certain components of the human immune system—such as natural killer cells, circulating T- and B-lymphocytes, and cells of the monocyte-macrophage system—thereby possibly decreasing the incidence of some infections and perhaps of certain types of cancer.

Exercise of high intensity and long duration or exercise that involves excessive training may have adverse effects on immune function. In general, a high-intensity, single episode of exercise results in a marked decline in the functioning of all major cells of the immune system. In addition, overtraining may reduce the response of T-lymphocytes to mutagenic stimulation, decrease antibody synthesis and plasma level of immunoglobins and complement, and impair macrophage phagocytosis. The reduced plasma glutamine levels that occur with high-intensity exercise or excessive training are postulated to contribute to these adverse effects on the immune system.

LONG-TERM ADAPTATIONS TO EXERCISE TRAINING

ADAPTATIONS OF SKELETAL MUSCLE AND BONE

Skeletal muscle adapts to endurance training chiefly through a small increase in the cross-sectional area of slow-twitch fibres, because low- to moderate- intensity aerobic activity primarily recruits these fibres. Prolonged endurance training (*i.e.*, months to years) can lead to a transition of FTb

fibres to FTa fibres, which have a higher oxidative capacity. No substantive evidence indicates that fasttwitch fibres will convert to slow-twitch fibres under normal training conditions.

Endurance training also increases the number of capillaries in trained skeletal muscle, thereby allowing a greater capacity for blood flow in the active muscle. Resistance-trained skeletal muscle exerts considerably more force because of both increased muscle size and increased muscle fibre recruitment. Fibre hypertrophy is the result of increases in both the size and number of myofibrils in both fast-twitch and slow-twitch muscle fibres. Hyperplasia, or increased fibre number, has been reported in animal studies, where the number of individual muscle fibres can be counted, and has been indirectly demonstrated during autopsies on humans by using direct fibre counts to compare dominant and non-dominant paired muscles.

During both aerobic and resistance exercise, active muscles can undergo changes that lead to muscle soreness. Some soreness is felt immediately after exercise, and some can even occur during exercise. This muscle soreness is generally not physically limiting and dissipates rapidly. A more limiting soreness, however, may occur 24 to 48 hours following exercise. This delayed-onset muscle soreness is primarily associated with eccentric-type muscle action, during which the muscle exerts force while lengthening, as can happen when a person runs down a steep hill or lowers a weight from a fully flexed to a fully extended position (*e.g.*, the two-arm curl).

Delayedonset muscle soreness is the result of structural damage to the muscle; in its most severe form, this damage may include rupture of the cell membrane and disruption of the contractile elements of individual muscle fibres. Such damage appears to result in an inflammatory response. Total inactivity results in muscle atrophy and loss of bone mineral and mass. Persons who are sedentary generally have less bone mass than those who exercise, but the increases in bone mineral and mass that result from either endurance or resistance training are relatively small.

The role of resistance training in increasing or maintaining bone mass is not well characterized. Endurance training has little demonstrated positive effect on bone mineral and mass. Nonetheless, even small increases in bone mass gained from endurance or resistance training can help prevent or delay the process of osteoporosis. The musculoskeletal system cannot function without connective tissue linking bones to bones (ligaments) and muscles to bones (tendons).

Extensive animal studies indicate that ligaments and tendons become stronger with prolonged and high-intensity exercise. This effect is the result of an increase in the strength of insertion sites between ligaments, tendons, and bones, as well as an increase in the crosssectional areas of ligaments and tendons. These structures also become weaker and smaller with several weeks of immobilization, which can have important implications for musculoskeletal performance and risk of injury.

METABOLIC ADAPTATIONS

Significant metabolic adaptations occur in skeletal muscle in response to endurance training. First, both the size and number of mitochondria increase substantially, as does the activity of oxidative enzymes. Myoglobin content in the muscle can also be augmented, increasing the amount of oxygen stored in individual muscle fibres, but this effect is variable. Such adaptations, combined with the increase in capillaries and muscle blood flow in the trained muscles, greatly enhance the oxidative capacity of the endurance-trained muscle.

Endurance training also increases the capacity of skeletal muscle to store glycogen. The ability of trained muscles to use fat as an energy source is also improved, and this greater reliance on fat spares glycogen stores.

The increased capacity to use fat following endurance training results from an enhanced ability to mobilize free-fatty acids from fat depots and an improved capacity to oxidize fat consequent to the increase in the muscle enzymes responsible for fat oxidation.

These changes in muscle and in cardiorespiratory function are responsible for increases in both VO_2 max and lactate threshold. The endurancetrained person can thus perform at considerably higher rates of work than the untrained person. Increases in VO_2 max generally range from 15 to 20 per cent following a 6-month training period. However, individual variations in this response are considerable. In one study of 60- to 71-year-old men and women who endurance trained for 9 to 12 months, the improvement in VO_2 max varied from 0 to 43 per cent; the mean increase was 24 per cent.

This variation in response may be due in part to genetic factors and to initial levels of fitness. To illustrate the changes that can be expected with endurance training, a hypothetical sedentary man's pretraining values have been compared with his values after a 6-month period of endurance training and with the values of a typical elite endurance runner. Responses to endurance training are similar for men and women. At all ages, women and men show similar gains in strength from resistance training and similar gains in VO_2 max from aerobic endurance training.

CARDIOVASCULAR AND RESPIRATORY ADAPTATIONS

Endurance training leads to significant cardiovascular and respiratory changes at rest and during steadystate exercise at both submaximal and maximal rates of work. The magnitude of these adaptations largely depends on the person's initial fitness level; on mode, intensity, duration, and frequency of exercise; and on the length of training.

Long-Term Cardiovascular Adaptations

Cardiac output at rest and during submaximal exercise is essentially unchanged following an endurance training programme. At or near maximal rates of work, however, cardiac output is increased substantially, up to 30 per cent or more. There are important differences in the responses of stroke volume and heart rate to training. After training, stroke volume

is increased at rest, during submaximal exercise, and during maximal exercise; conversely, posttraining heart rate is decreased at rest and during submaximal exercise and is usually unchanged at maximal rates of work.

The increase in stroke volume appears to be the dominant change and explains most of the changes observed in cardiac output. Several factors contribute to the increase in stroke volume from endurance training. Endurance training increases plasma volume by approximately the same percentage that it increases stroke volume. An increased plasma volume increases the volume of blood available to return to the right heart and, subsequently, to the left ventricle. There is also an increase in the end-diastolic volume because of increased amount of blood and increased return of blood to the ventricle during exercise.

This acute increase in the left ventricle's end-diastolic volume stretches its walls, resulting in a more elastic recoil. Endurance training also results in long-term changes in the structure of the heart that augment stroke volume. Short-term adaptive responses include ventricular dilatation; this increase in the volume of the ventricles allows end-diastolic volume to increase without excessive stress on the ventricular walls. Long-term adaptive responses include hypertrophy of the cardiac muscle fibres.

This hypertrophy increases the muscle mass of the ventricles, permitting greater force to be exerted with each beat of the heart. Increases in the thickness of the posterior and septal walls of the left ventricle can lead to a more forceful contraction of the left ventricle, thus emptying more of the blood from the left ventricle. Endurance training increases the number of capillaries in trained skeletal muscle, thereby allowing a greater capacity for blood flow in the active muscle.

This enhanced capacity for blood flow is associated with a reduction in total peripheral resistance; thus, the left ventricle can exert a more forceful contraction against a lower resistance to flow out of the ventricle. Arterial blood pressure at rest, blood pressure during submaximal exercise, and peak blood

pressure all show a slight decline as a result of endurance training in normotensive individuals.

However, decreases are greater in persons with high blood pressure. After endurance training, resting blood pressure will decrease on average -3/-3 mmHg in persons with normal blood pressure; in borderline hypertensive persons, the decrease will be -6/-7 mmHg; and in hypertensive persons, the decrease will be -10/-8 mmHg.

Respiratory Adaptations

The major changes in the respiratory system from endurance training are an increase in the maximal rate of pulmonary ventilation, which is the result of increases in both tidal volume and respiration rate, and an increase in pulmonary diffusion at maximal rates of work, primarily due to increases in pulmonary blood flow, particularly to the upper regions of the lung.

MAINTENANCE, DETRAINING, AND PROLONGED INACTIVITY

Most adaptations that result from both endurance and resistance training will be reversed if a person stops or reduces training. The greatest deterioration in physiologic function occurs during prolonged bed rest and immobilization by casts. A basic maintenance training programme is necessary to prevent these losses in function.

MAINTAINING FITNESS AND MUSCULAR STRENGTH

Muscle strength and cardiorespiratory capacity are dependent on separate aspects of exercise. After a person has obtained gains in VO_2 max by performing cardiorespiratory exercise six times per week, two to four times per week is the optimal frequency of training to maintain those gains.

Further, a substantial part of the gain can be retained when the duration of each session is reduced by as much as two-

thirds, but only if the intensity during these abbreviated sessions is maintained at ≥ 70 per cent of VO_2 max. If training intensity is reduced by as little as one-third, however, a substantial reduction in VO_2 max can be expected over the next 15 weeks. In previously untrained persons, gains in muscular strength can be sustained by as little as a single session per week of resistance training, but only if the intensity is not reduced.

DETRAINING

With complete cessation of exercise training, a significant reduction in VO_2 max and a decrease in plasma volume occur within 2 weeks; all prior functional gains are dissipated within 2 to 8 months, even if routine low- to moderate-intensity physical activity has taken the place of training. Muscular strength and power are reduced at a much slower rate than VO_2 max, particularly during the first few months after an athlete discontinues resistance training. In fact, no decrement in either strength or power may occur for the first 4 to 6 weeks after training ends. After 12 months, almost half of the strength gained might still be retained if the athlete remains moderately active.

PROLONGED INACTIVITY

The effects of prolonged inactivity have been studied by placing healthy young male athletes and sedentary volunteers in bed for up to 3 weeks after a control period during which baseline measurements were made. The resulting detrimental changes in physiologic function and performance are similar to those resulting from reduced gravitational forces during space flight and are more dramatic than those resulting from detraining studies in which routine daily activities in the upright position (*e.g.*, walking, stair climbing, lifting, and carrying) are not restricted.

Results of bed rest studies show numerous physiologic changes, such as profound decrements in cardiorespiratory

function proportional to the duration of bed rest. Metabolic disturbances evident within a few days of bed rest include reversible glucose intolerance and hyperinsulinemia in response to a standard glucose load, reflecting cell insulin resistance; reduced total energy expenditure; negative nitrogen balance, reflecting loss of muscle protein; and negative calcium balance, reflecting loss of bone mass. There is also a substantial decrease in plasma volume, which affects aerobic power. From one study, a decline in VO_2 max of 15 per cent was evident within 10 days of bed rest and progressed to 27 per cent in 3 weeks; the rate of loss was approximately 0.8 per cent per day of bed rest.

The decrement in VO_2 max from bed rest and reduced activity results from a decrease in maximal cardiac output, consequent to a reduced stroke volume. This, in turn, reflects the decrease in end-diastolic volume resulting from a reduction in total blood and plasma volume, and probably also from a decrease in myocardial contractility. Maximal heart rate and $A-\bar{v}O_2$ difference remain unchanged. Resting heart rate remains essentially unchanged or is slightly increased, whereas resting stroke volume and cardiac output remain unchanged or are slightly decreased.

However, the heart rate for submaximal exertion is generally increased to compensate for the sizable reduction in stroke volume. Physical inactivity associated with bed rest or prolonged weightlessness also results in a progressive decrement in skeletal muscle mass and strength, as well as an associated reduction in bone mineral density that is approximately proportional to the duration of immobilization or weightlessness.

The loss of muscle mass is not as great as that which occurs with immobilization of a limb by a plaster cast, but it exceeds that associated with cessation of resistance exercise training. The muscle groups most affected by prolonged immobilization are the antigravity postural muscles of the lower extremities. The loss of normal mechanical strain patterns from contraction of these muscles results in a corresponding loss of density in

the bones of the lower extremity, particularly the heel and the spine. Muscles atrophy faster than bones lose their density.

For example, 1 month of bed rest by healthy young men resulted in a 10 to 20 per cent decrease in muscle fibre cross-sectional area and a 21 per cent reduction in peak isokinetic torque of knee extensors, whereas a similar period of bed rest resulted in a reduction in bone mineral density of only 0.3 to 3 per cent for the lumbar spine and 1.5 per cent for the heel. Quantitative histologic examination of muscle biopsies of the vastus lateralis of the leg following immobilization shows reduced cross-sectional area for both slow-twitch and fast-twitch fibres, actual necrotic changes in affected fibres, loss of capillary density, and a decline in aerobic enzyme activity, creatinine phosphate, and glycogen stores.

On resuming normal activity, reversibility of these decrements in cardiorespiratory, metabolic, and muscle function is fairly rapid. By contrast, the reversal of the decrement of bone mineral density requires weeks to months.

SPECIAL CONSIDERATIONS

The physiologic responses to exercise and physiologic adaptations to training and detraining, reviewed in the preceding sections, can be influenced by a number of factors, including physical disability, environmental conditions, age, and sex.

DISABILITY

Although there is a paucity of information about physiologic responses to exercise among persons with disabilities, existing information supports the notion that the capacity of these persons to adapt to increased levels of physical activity is similar to that of persons without disabilities. Many of the acute effects of physical activity on the cardiovascular, respiratory, endocrine, and musculoskeletal systems have been demonstrated to be similar among persons with disabilities, depending on the specific nature of the disability. For example,

physiologic responses to exercise have been studied among persons with paraplegia, quadriplegia, mental retardation, multiple sclerosis, and postpolio syndrome.

ENVIRONMENTAL CONDITIONS

The basic physiologic responses to an episode of exercise vary considerably with changes in environmental conditions. As environmental temperature and humidity increase, the body is challenged to maintain its core temperature. Generally, as the body's core temperature increases during exercise, blood vessels in the skin begin to dilate, diverting more blood to the body's surface, where body heat can be passed on to the environment (unless environmental temperature exceeds body temperature).

Evaporation of water from the skin's surface significantly aids in heat loss; however, as humidity increases, evaporation becomes limited. These methods for cooling can compromise cardiovascular function during exercise. Increasing blood flow to the skin creates competition with the active muscles for a large percentage of the cardiac output. When a person is exercising for prolonged periods in the heat, stroke volume will generally decline over time consequent to dehydration and increased blood flow in the skin.

Heart rate increases substantially to try to maintain cardiac output to compensate for the reduced stroke volume. High air temperature is not the only factor that stresses the body's ability to cool itself in the heat. High humidity, low air velocity, and the radiant heat from the sun and reflective surfaces also contribute to the total effect. For example, exercising under conditions of 32°C (90°F) air temperature, 20 per cent relative humidity, 3.0 kilometers per hour (4.8 miles per hour) air velocity, and cloud cover is much more comfortable and less stressful to the body than the same exercise under conditions of 24°C (75°F) air temperature, 90 per cent relative humidity, no air movement, and direct exposure to the sun.

Children respond differently to heat than adults do. Children have a higher body surface area to body mass ratio

(surface area/mass), which facilitates heat loss when environmental temperatures are below skin temperature. When environmental temperature exceeds skin temperature, children are at an even greater disadvantage because these mechanisms then become avenues of heat gain.

Children also have a lower rate of sweat production; even though they have more heat-activated sweat glands, each gland produces considerably less sweat than that of an adult. The inability to maintain core temperature can lead to heat-related injuries.

Heat cramps, characterized by severe cramping of the active skeletal muscles, is the least severe of three primary heat disorders. Heat exhaustion results when the demand for blood exceeds what is available, leading to competition for the body's limited blood supply.

Heat exhaustion is accompanied by symptoms including extreme fatigue, breathlessness, dizziness, vomiting, fainting, cold and clammy or hot and dry skin, hypotension, and a weak, rapid pulse. Heatstroke, the most extreme of the three heat disorders, is characterized by a core temperature of 40°C (104°F) or higher, cessation of sweating, hot and dry skin, rapid pulse and respiration, hypertension, and confusion or unconsciousness.

If left untreated, heatstroke can lead to coma, then death. People experiencing symptoms of heat-related injury should be taken to a shady area, cooled with by whatever means available, and if conscious given non-alcoholic beverages to drink.

Medical assistance should be sought. To reduce the risk of developing heat disorders, a person should drink enough fluid to try to match that which is lost through sweating, avoid extreme heat, and reduce the intensity of activity in hot weather.

Because children are less resistant to the adverse effects of heat during exercise, special attention should be given to protect them when they exercise in the heat and to provide them with extra fluids to drink. Stresses associated with exercising in the extreme cold are generally less severe.

For most situations, the problems associated with cold stress can be eliminated by adequate clothing. Still, cold stress can induce a number of changes in the physiologic response to exercise. These include the increased generation of body heat by vigourous activity and shivering, increased production of catecholamines, vasoconstriction in both the cutaneous and non-active skeletal muscle beds to provide insulation for the body's core, increased lactate production, and a higher oxygen uptake for the same work.

For the same absolute temperature, exposure to cold water is substantially more stressful than exposure to cold air because the heat transfer in water is about 25 times greater than in air. Because the ratio of surface area to mass is higher in children than in adults, children lose heat at a faster rate when exposed to the same cold stress. The elderly tend to have a reduced response of generating body heat and are thus more susceptible to cold stress. Altitude also affects the body's physiologic responses to exercise.

As altitude increases, barometric pressure decreases, and the partial pressure of inhaled oxygen is decreased proportionally.

A decreased partial pressure of oxygen reduces the driving force to unload oxygen from the air to the blood and from the blood to the muscle, thereby compromising oxygen delivery. $A-\bar{v}O_2$ max is significantly reduced at altitudes greater than 1,500 meters. This effect impairs the performance of endurance activities.

The body makes both short-term and long-term adaptations to altitude exposure that enable it to at least partially adapt to this imposed stress. Because oxygen delivery is the primary concern, the initial adaptation that occurs within the first 24 hours of exposure to altitude is an increased cardiac output both at rest and during submaximal exercise. Ventilatory volumes are also increased.

An ensuing reduction in plasma volume increases the concentration of red blood cells, thus providing more oxygen molecules per unit of blood.

Over several weeks, the red blood cell mass is increased through stimulation of the bone marrow by the hormone erythropoietin. Exercising vigourously outdoors when air quality is poor can also produce adverse physiologic responses. In addition to decreased tolerance for exercise, direct respiratory effects include increased airway reactivity and potential exposure to harmful vapors and airborne dusts, toxins, and pollens.

3

The Effects of Physical Activity on Health and Disease

OVERALL MORTALITY

Persons with moderate to high levels of physical activity or cardiorespiratory fitness have a lower mortality rate than those with sedentary habits or low cardiorespiratory fitness. For example, compared with people who are most active, sedentary people experience between a 1.2-fold to a 2-fold increased risk of dying during the follow-up interval. Associations are generally stronger for measured cardiorespiratory fitness than for reported physical activity. Blair, Kohl, and Barlow showed that low levels of cardiorespiratory fitness were strongly associated with overall mortality for both women and men.

The association with physical inactivity was weaker for men, and there was no association for women. Though cardiorespiratory fitness may be the better indicator of regular physical activity, the level of reported physical activity has been associated with reduced all-cause mortality. Paffenbarger, Lee, and Leung evaluated several types of recalled activity (walking, stair climbing, all sports, moderatelevel sports, and total energy expended in activity per week) as predictors of

all-cause mortality among male Harvard alumni. Among these men, the relative risk of death within the follow-up period was reduced to 0.67 with walking 15 or more kilometers per week, to 0.75 with climbing 55 or more flights of stairs per week, to 0.63 with involvement in moderate sports, and to 0.47 with 3 or more hours of moderate sports activities per week.

Most importantly, there was a significant trend of decreasing risk of death across increasing categories of distance walked, flights of stairs climbed, and degree of intensity of sports play. Researchers have also examined age-specific effects of different levels of physical activity on allcause mortality. Kaplan and colleagues have shown that physical activity level has an effect on death rates among both older and younger persons. Data from a study of 9,484 Seventh-Day Adventist men aged 30 years or older in 1958 who were followed through 1985 indicated that both moderate and intense levels of activity reduced overall risk of death even late in life. Both moderate and vigourous levels of activity were equally protective at age 50 years.

The protective effect of high levels of activity lasted only until age 70, but the protective effect for moderate activity lasted beyond age 80. The studies cited thus far in this section assessed physical activity or cardiorespiratory fitness at baseline only and then followed up for mortality. A stronger test for a causal relationship is to examine the effect that changing from lower to higher levels of physical activity or cardiorespiratory fitness has on subsequent mortality. Two large studies provide such evidence.

Among middle-aged Harvard male alumni who were sedentary in 1962 or 1966, those who took up moderately intense sports activity during the study's 11 years of follow-up had a 23 per cent lower death rate than those who remained sedentary. Men 45–84 years of age who took up moderately intense sports extended their longevity on average by 0.72 years; added years of life were observed in all age groups, including men 75–84 years of age. Similar reductions in death rates with increases in cardiorespiratory fitness were reported

for men in the Aerobics Center Longitudinal Study. Blair and colleagues reported a reduction in death rates among healthy men who improved their initially low levels of cardiorespiratory fitness.

The men performed two maximal exercise tests an average of 4.8 years apart; follow-up for mortality after the second test occurred an average of 4.7 years later. Among men in the bottom fifth of the cardiorespiratory fitness distribution, those who improved to at least a moderate fitness level had a 44 per cent lower death rate than their peers who remained in the bottom fifth. After multivariate adjustment, those who became fit had a significant 64 per cent reduction in their relative mortality rate. In comparison, men who stopped smoking reduced their adjusted RR by about 50 per cent.

CARDIOVASCULAR DISEASES

Despite a progressive decline since the late 1960s, cardiovascular diseases and stroke, remain major causes of death, disability, and health care expenditures in the United States. In 1992, more than 860,000 deaths in the United States were attributed to heart disease and stroke. High blood pressure, a major risk factor for CVD, affects about 50 million Americans, including an estimated 2.8 million children and adolescents 6–17 years of age. The prevalence of CVD increases with age and is higher among African Americans than whites. The majority of population-based research in the area of physical activity and health has focused on some aspect of CVD.

CARDIOVASCULAR DISEASES COMBINED

Most of the reported studies relating physical activity to CVD have reported CVD mortality as an endpoint; two also reported on non-fatal disease, and one reported on CVD hospitalization. Seven cohort studies evaluated the association between level of physical activity and the risk of total CVD. All relied on a single point-in-time estimate of physical activity,

in some cases assessed as long as 26 years before the end of the observational period, and four had follow-up periods of > 14 years.

Four of the seven studies found both an inverse association and a dose-response gradient between level of physical activity and risk of CVD outcome. One study among men found an inverse association among the moderately active group but less of an effect in the vigourously active group. One study of women 50–74 years of age found no relationship of physical activity with CVD mortality. Five large cohort studies have related cardiorespiratory fitness to the risk of CVD mortality, but only one provided a separate analysis for women. Each of these studies demonstrated an inverse dose-response relationship between level of cardiorespiratory fitness and CVD mortality.

Three of the five studies relied on a maximal or near-maximal exercise test to estimate cardiorespiratory fitness. One study demonstrated that men with low cardiorespiratory fitness who became fit had a lower risk of CVD mortality than men who remained unfit. Taken together, these major cohort studies indicate that low levels of physical activity or cardiorespiratory fitness increase risk of CVD mortality.

Findings seem to be more consistent for studies of cardiorespiratory fitness, perhaps because of its greater precision of measurement, than for those of reported physical activity. The demonstrated doseresponse relationship indicates that the benefit derived from physical activity occurs at moderate levels of physical activity or cardiorespiratory fitness and increases with increasing levels of physical activity or higher levels of fitness.

CORONARY HEART DISEASE

Numerous studies have examined the relationship between physical activity and CHD as a specific CVD outcome. Reviews of the epidemiologic literature have concluded that physical activity is strongly and inversely related to CHD risk. Although physical exertion may transiently increase the risk

of an acute coronary event among persons with advanced coronary atherosclerosis, particularly among those who do not exercise regularly, physically active people have a substantially lower overall risk for major coronary events.

Thirty-six studies examining the relationship of physical activity level to risk of CHD have been published since 1953. Studies published before 1978 predominantly classified physical activity level by job title or occupational activities. Studies thereafter usually defined activity level by recall of leisure-time activity or by such activity combined with occupational activity. These later studies were also able to control statistically for many potentially confounding variables in addition to age. Most of these studies focused on men in the age ranges associated with increasing risk of CHD; only four included women.

Although in several studies, CHD mortality was the sole outcome variable, most included both fatal and non-fatal disease. All but one were cohort studies; lengths of follow-up from baseline assessment ranged from 4 to 25 years. All studies related a single baseline estimate of physical activity level to risk of CHD during the follow-up period. Some study populations have had more than one follow-up assessment for CHD. For example, three follow-up assessments have been reported for men in the Honolulu Heart Programme. Each represented follow-up further removed from the original determination of physical activity.

Thus, the diminishing effect seen over time might indicate changing patterns of physical activity—and thereby a lessening of validity of the original physical activity classification. Oddly, in the 12-year follow-up, the reduction in CHD risk observed among both active middle-aged men and active older men when compared with their least active counterparts was not diminished by bivariate adjustment for serum cholesterol, body mass index (BMI), or blood pressure. In the 23-year follow-up, however, the reduction in CHD risk among active men was greatly diminished by simultaneous adjustment for serum cholesterol, BMI, blood pressure, and diabetes, leading the

authors to conclude that the beneficial effect of physical activity on CHD risk is likely mediated by the beneficial effect of physical activity on these other factors.

These reports thus illustrate not only the problem of lengthy follow-up without repeated assessments of physical activity but also the problem of lack of uniformity in adjustment for potential confounding factors, as well as the underlying, thorny problem of adjustment for multiple factors that may be in the causal pathway between physical activity and disease. Studies have in fact varied greatly in the extent to which they have controlled for potential confounding and in the factors selected for adjustment. Although early studies were not designed to demonstrate a dose-response gradient between physical activity level and CHD, most found an inverse association: more active persons were found to be at lower risk of CHD than their more sedentary counterparts.

Of the 17 recent studies that found an inverse relationship and were able to examine doseresponse relationships, 13 demonstrated an inverse dose-response gradient between level of physical activity and risk of CHD, whereas 2 showed a dose-response gradient only for some subgroups. The relationship between cardiorespiratory fitness and risk of CHD was examined in seven cohort studies. All but two used estimates of aerobic power based on submaximal exercise testing.

None of these studies included women. Similar to the studies of physical activity and CHD, these all related a single baseline assessment of cardiorespiratory fitness to risk of CHD during the follow-up period. Most controlled statistically for possible confounding variables. All seven studies showed an inverse association between cardiorespiratory fitness and CHD. Of the six studies that had more than two categories of cardiorespiratory fitness, all demonstrated an inverse dose-response gradient.

Two recent meta-analyses of studies of physical activity and CHD have included independent scoring for the quality of the methods used in each study. Both concluded that studies with higher-quality scores tended to show higher relative risk

estimates than those with lower-quality scores. In the Berlin and Colditz quantitative meta-analysis, the pooled relative risk for CHD—comparing risk for the lowest level of physical activity with risk for the highest level— was 1.8 among the studies judged to be of higher quality. In contrast, the pooled relative risk for the studies with low-quality scores was in the null range.

CVD RISK FACTORS IN CHILDREN

Because CHD is rare in children, the cardiovascular effects of physical activity in children are assessed through the relationship of physical activity with CHD risk factors such as elevated low-density lipoprotein cholesterol, lowered high-density lipoprotein cholesterol, and elevated blood pressure. The presence of CHD risk factors in children is of concern because of evidence that atherosclerosis begins in childhood, that presence of CHD in adults is related to elevated blood lipids in children, and that CHD risk factor patterns persist from childhood to adulthood.

Recently, Armstrong and Simons-Morton reviewed the research literature on physical activity and blood lipids in children and adolescents, including over 20 observational and 8 intervention studies. They concluded that the cross-sectional observational studies did not demonstrate a relationship between physical activity level or cardiorespiratory fitness and total cholesterol, LDL-C, or HDL-C, especially when differences in body weight or fat were taken into account, suggesting that activity and body fat are not independently related to serum lipids.

However, highly physically active or fit children and adolescents tended to have higher HDL-C than their inactive or unfit peers. The intervention studies generally showed favourable effects of exercise on LDL-C or HDL-C only in children and adolescents who were at high risk for CHD because of obesity, insulin-dependent diabetes mellitus, or having a parent with three or more CHD risk factors. Alpert and Wilmore recently reviewed the research literature on

physical activity and blood pressure in children and adolescents, including 18 observational and 11 intervention studies.

These authors found evidence in studies of normotensive children and adolescents that higher levels of physical activity tended to be related to lower blood pressure. The associations were generally reduced in magnitude in those studies that adjusted for BMI, suggesting that lower body fat mass may at least partly explain why physical activity is related to lower blood pressure. Intervention studies tended to show that training programmes lowered blood pressure by 1–6 mm Hg in normotensive children and adolescents, although the effects were inconsistent for boys and girls and for systolic and diastolic blood pressure.

In hypertensive children and adolescents, physical activity interventions lowered blood pressure to a greater degree than in their normotensive peers, although statistical significance was not always achieved because of small sample sizes. Interpreting these studies on lipids and blood pressure in children and adolescents is hindered by several factors. Studies used a variety of physical activity categorizations, and the interventions covered a wide range of frequency, type, duration, and intensity, which were not all specified.

The difficulties of assessing physical activity by self-report in children and adolescents, together with the highly self-selected population in the observational studies, may account for the less consistent findings on lipids and physical activity that were reported for children and adolescents than for adults. The relationship between dose of physical activity and amount of effect on blood pressure or serum lipids in children has not been adequately addressed.

Nonetheless, there appears to be some evidence, although not strong, of a direct relationship between physical activity and HDL-C level in children and adolescents. There is also evidence that increased physical activity can favourably influence the lipid profile in children and adolescents who are at high risk of CHD. Similarly, the evidence suggests that

physical activity can lower blood pressure in children and adolescents, particularly in those who have elevated blood pressure.

STROKE

A major cardiovascular problem in developed countries, stroke is the third leading cause of death in the United States. Atherosclerosis of the extracranial and intracranial arteries, which triggers thrombosis, is thought to be the underlying pathologic basis of ischemic stroke. Cigarette smoking and high blood pressure are major risk factors for ischemic stroke, whereas high blood pressure is the major determinant of hemorrhagic stroke. The studies cited in this section examined the association between reported level of physical activity and stroke.

No published studies have examined the association between cardiorespiratory fitness and stroke. Fourteen population-based studies relate physical activity to risk of all types of stroke; these closely parallel the study designs and populations previously cited for CVD and CHD. Thirteen of the studies were cohort studies. Only eight found an inverse association. As with the earlier studies on CHD, the earlier studies of stroke did not permit a dose-response evaluation. Among later studies that could do so by virtue of design, half did not find a gradient.

This outcome, coupled with some suggestion of a "U-shaped" association in two studies, casts doubt on the nature of the association between physical activity and risk of both types of strokes combined. Because of their different pathophysiologies, physical activity may not affect ischemic and hemorrhagic stroke in the same way; this issue requires more research. Only one study distinguished between ischemic and hemorrhagic stroke.

In this study, inactive men were more likely than active men to have a hemorrhagic stroke; physical activity was also associated with a lower risk of ischemic stroke in smokers but not in non-smokers. Thus the existing data do not

unequivocally support an association between physical activity and risk of stroke.

HIGH BLOOD PRESSURE

High blood pressure is a major underlying cause of cardiovascular complications and mortality. Organ damage and complications related to elevated blood pressure include left ventricular hypertrophy (which can eventually lead to left ventricular dysfunction and congestive heart failure), hemorrhagic stroke, aortic aneurysms and dissections, renal failure, and retinopathy. Atherosclerotic complications of high blood pressure include CHD, ischemic stroke, and peripheral vascular disease.

Although rates of hypertension have been declining in the United States since 1960, nearly one in four Americans can be classified as being hypertensive. Several cohort studies have followed male college alumni after graduation. One found later development of hypertension to be inversely related to the reported number of hours per week of participation in sports or exercise while in college.

In a later follow-up of the same cohort, using information on physical activity during mid-life, vigourous sports were associated with a 19–30 per cent reduction in risk of developing hypertension over the 14-year period. Follow-up of a different cohort of male college alumni similarly showed the least active men to have a 30 per cent increased risk of developing hypertension.

In a study of 55- through 69-year-old women followed for 2 years, the most active women were found to have a 30 per cent reduced risk of developing hypertension. One randomized trial for the primary prevention of hypertension has been conducted. A 5-year trial of a nutrition and physical activity intervention showed that the incidence of hypertension for the intervention group was less than half that of the control group.

Participants in the intervention group lost more weight than those in the control group, reduced more of their sodium

and alcohol intake, and were more likely to become more physically active. Although the effects of the nutritional and physical activity components of this intervention cannot be separated, the study does show that the risk for developing hypertension among persons who are at high risk for the disease can be lowered by weight loss and improvements in dietary and physical activity practices.

Like physical inactivity, low cardiorespiratory fitness in middle age is associated with increased risk for high blood pressure. After adjustment for sex, age, baseline blood pressure, and body mass index, persons with low cardiorespiratory fitness had a 52 per cent higher risk of later developing high blood pressure than their fit peers. Taken together, the cohort studies show that physical inactivity is associated with an increased risk of later developing hypertension among both men and women.

Three of the studies had more than two categories of physical activity for comparison, and each demonstrated a dose-response gradient between amount of activity and degree of protection from hypertension. Point estimates for quantification of risk suggest that those least physically active have a 30 per cent greater risk of developing hypertension than their most active counterparts. Unfortunately, none of these studies was conducted in minority populations, which have a disproportionate burden of hypertensive disease.

Several randomized controlled trials have been conducted to determine the effects of exercise on blood pressure in people with elevated blood pressure levels. The reduction of elevated blood pressure is important for preventing stroke and CHD, for which high blood pressure is a risk factor with a dose-response relationship. Thirteen controlled trials of habitual activity and blood pressure were analysed in a meta-analysis by Arroll and Beaglehole and nine randomized controlled trials of aerobic exercise using the lower extremities and blood pressure were analysed in a meta-analysis by Kelley and McClellan. The two meta-analyses independently concluded that aerobic exercise decreases both systolic and diastolic blood

pressure by approximately 6–7 mm Hg. Some of the studies were conducted with persons with defined hypertension, and others were conducted with persons with high normal blood pressure. Most of the studies tested aerobic training of 60–70 per cent maximum oxygen uptake, 3–4 times/week, 30–60 minutes per session. Three trials have specifically examined the effect of different intensities of exercise on blood pressure.

Hagberg et al. randomly assigned 33 hypertensive participants to a non-exercising control group and to two groups participating in different intensities of exercise for 9 months. Both exercise groups had comparable decreases in diastolic blood pressure, and the lower-intensity group had a greater decrease in systolic blood pressure than the higherintensity group. All the decreases were statistically significant when compared with the control group's blood pressure level, except the 8 mm Hg decrease in systolic blood pressure in the higher-intensity group.

Matsusaki and colleagues randomly assigned 26 mildly hypertensive participants to two exercise intensities for 10 weeks. The pretest-to-posttest decreases in systolic and diastolic blood pressure in the lower-workload group were significant, but those in the higher-intensity group were not. Marceau and colleagues used a randomized crossover design to compare intensities of 50 per cent and 70 per cent V O_2 max training on 24-hour ambulatory blood pressure in persons with hypertension.

A similar reduction in 24-hour blood pressure was observed for both training intensities, but diurnal patterns of reduction were different. These trials provide some evidence that moderateintensity activity may achieve a similar, or an even greater, blood-pressure-lowering effect than vigourous-intensity activity. Because few studies have directly addressed the intensity question, however, the research base is not strong enough to draw a firm conclusion about the role of activity intensity in lowering blood pressure. It is not clear, for example, how the findings could have been affected by several issues, such as use of antihypertensive medications, changes in body

weight, lack of direct interventioncontrol comparisons, dropout rates, and total caloric expenditure.

BIOLOGICAL PLAUSIBILITY

Multiple physiological mechanisms may contribute to the protective effects of physical activity against CVDs. Postulated mechanisms involve advantageous effects on atherosclerosis, plasma lipid/lipoprotein profile, blood pressure, availability of oxygenated blood for heart muscle needs, blood clotting, and heart rhythm disturbances. Other effects of activity that may be associated with modifications of CVD risk include reduced incidence of obesity, healthier distribution of body fat, and reduced incidence of non–insulindependent diabetes.

Atherosclerosis

Atherosclerosis begins when cholesterol is transported from the blood into the artery wall by lipoproteins, particularly LDL. The formation of atherosclerotic plaques is increased at sites where the blood vessel lining is injured, which may occur in areas where blood flow is uneven (*e.g.*, near the origin or branching of major vessels). An inflammatory reaction leads to the formation of atherosclerotic plaques in the wall of the artery. In animal studies, exercise has been seen to protect against the effects of excess cholesterol and other contributors to the development of atherosclerosis.

In addition, longitudinal studies of men with coronary artery disease have shown that endurance training, together with a cholesterol-lowering diet and interventions for other CVD risk factors, can help prevent the progression or reduce the severity of atherosclerosis in the coronary arteries. There is also an inverse relationship between cardiorespiratory fitness and ultrasound-measured severity of atherosclerosis in neck arteries to the head.

Plasma Lipid/Lipoprotein Profile

The relationships of physical activity to blood lipid and

lipoprotein levels in men and women have been reviewed extensively. Of more than 60 studies of men and women, about half found that exercise training is associated with an increase in HDL. HDL, a lipid scavenger, helps protect against atherosclerosis by transporting cholesterol to the liver for elimination in the bile. Cross-sectional studies show a dose-response relationship between the amount of regular physical activity and plasma levels of HDL.

In these studies, the HDL levels of endurance-trained male and female athletes were generally 20 to 30 per cent higher than those of healthy, age-matched, sedentary persons. Moderate-intensity exercise training appears to be less likely to increase HDL levels in young to middle-aged women than men in the same age range. Moderate-intensity exercise was seen to increase HDL as much as more vigourous exercise in one randomized controlled trial of women.

Studies have found that even a single episode of physical activity can result in an improved blood lipid profile that persists for several days. Evidence also shows that exercise training increases lipoprotein lipase activity, an enzyme that removes cholesterol and fatty acids from the blood. Exercise training also reduces elevated levels of triglycerides, another blood lipid associated with heart disease.

Blood Pressure

The mechanisms by which physical activity lowers blood pressure are complicated and are mentioned only briefly here. Blood pressure is directly proportional to cardiac output and total resistance in the peripheral blood vessels. An episode of physical activity has the immediate and temporary effect of lowering blood pressure through dilating the peripheral blood vessels, and exercise training has the ongoing effect of lowering blood pressure by attenuating sympathetic nervous system activity.

The reduced sympathetic activity may reduce renin-angiotensin system activity, reset baroreceptors, and promote arterial vasodilatation—all of which help control blood

pressure. Improved insulin sensitivity and the associated reduction in circulating insulin levels may also contribute to blood pressure reduction by decreasing insulin-mediated sodium reabsorption by the kidney.

Ischemia

Clinical symptoms of atherosclerotic CHD occur when the heart muscle needs more oxygen than can be supplied from blood flowing through narrowed coronary arteries. This oxygen shortage leads to ischemia in the heart muscle—that is, to inadequate oxygenated blood for myocardial demand. Adaptations to a gradual reduction in blood flow may reduce the likelihood of myocardial ischemia. For example, new blood vessels may develop from other coronary arteries to provide an auxiliary blood supply.

A person with advanced atherosclerotic CHD may remain free of symptoms at rest but may develop ischemic chest pain or electrocardiographic changes during physical exertion, which generally result from too high a myocardial oxygen demand for the blood supply available through partially occluded coronary arteries and collateral vessels. Less commonly, angina pectoris may result from transient constriction of a large coronary artery, generally at the site of an atherosclerotic plaque, or from spasm of small arterial vessels that have no evidence of plaque formation. A recent review has summarized adaptations in the coronary circulation that are induced by endurance exercise training and that can decrease the likelihood of ischemia.

Data obtained primarily from research on animals have demonstrated that exercise leads to a greater capacity to increase coronary blood flow and an improved efficiency of oxygen exchange between blood in the capillaries and the heart muscle cells. These functional changes are the result of a remodelled vascular structure, improved control of blood flow dynamics, and promotion of biochemical pathways for oxygen transfer. The first and most consistent structural adaptation to exercise is an increase in the interior diameter of the major

coronary arteries and an associated increase in maximal coronary blood flow.

The second vascular adaptation is the formation of new myocardial blood vessels. Animal studies also have shown that exercise training alters coronary vascular reactivity and thereby improves control of blood flow and distribution. This adaptation may reduce the incidence of spasms in the proximal coronary arteries and arterioles. In addition, exercise training results in a reduced workload on the heart due to both an increase in compliance of the heart and a relative reduction in peripheral resistance; together, these reduce myocardial oxygen demand.

Thrombosis

An acute coronary event is usually initiated by disruption of an atherosclerotic plaque within an artery. Platelet accumulation at the injury site initiates a cascade of processes leading to clot formation, which further reduces or completely obstructs coronary flow. A major obstruction of flow in a coronary artery may lead to the death of heart muscle in the area served by that artery. These obstructions can, in addition, trigger potentially lethal disturbances in the rhythm of the heart.

Thrombosis, usually occurring at the site of rupture or fissuring of an atherosclerotic plaque, is the precipitating event in the transition of silent or stable coronary artery disease to acute ischemic events, such as unstable angina, acute myocardial infarction, or sudden cardiac death, and in the occurrence of ischemic stroke. Endurance training reduces thrombosis by enhancing the enzymatic breakdown of blood clots and by decreasing platelet adhesiveness and aggregation.

Arrhythmia

Although persons with coronary artery disease have an increased risk of ventricular fibrillation during acute physical activity, persons with a healthy cardiovascular system do not

incur this elevated risk. Exercise training may reduce the risk of ventricular fibrillation in healthy persons and in cardiac patients by improving myocardial oxygen supply and demand and by reducing sympathetic nervous system activity. Evidence from epidemiologic studies shows that a physically active lifestyle reduces the risk of sudden cardiac death. A meta-analysis of studies that examined use of physical activity for cardiac rehabilitation showed that endurance exercise training reduced the overall risk of sudden cardiac death even among persons with advanced coronary atherosclerosis.

CANCER

Cancer, the second leading cause of death in the United States, accounts for about 25 per cent of all deaths, and this percentage is increasing. The ACS has estimated that 1,359,150 new cases of cancer and 554,740 cancer-related deaths will occur among Americans during 1996. Physical inactivity has been examined as an etiologic factor for some cancers.

COLORECTAL CANCER

Colorectal cancer has been the most thoroughly investigated cancer in epidemiologic studies of physical activity. To date, nearly 30 published studies have examined the association between physical activity and risk of developing colon cancer alone. Studies that combined colon and rectal cancers as a single endpoint—colourectal cancer—are only briefly reviewed here because current research, summarized in this section, suggests that the relationship between physical activity and risk of colon cancer may be different from that for rectal cancer.

Among nine studies that have examined the relationship between physical activity and colourectal cancer, one reported an inverse relationship, and three reported positive associations that were not statistically significant. One reported no significant associations, and in the four other studies, the associations lacked consistency in subpopulations within the

study, anatomic subsites of the large bowel, or measures of physical activity. Colourectal adenomas are generally thought to be precursors to colourectal cancers. A single study of colourectal adenomatous polyps has reported an inverse relationship between risk of adenomas and level of total physical activity. Another study of colourectal adenomas also found an inverse association, but only for running or bicycling, and only with one of two different comparison groups.

Colon Cancer

Of the 29 studies of colon cancer, 18 used job title as the only measure of physical activity and thus addressed only occupational physical activity. These studies are a mix of mortality and incidence studies, and few have evaluated possible confounding by socioeconomic status, diet, and other possible risk factors for colon cancer. Nonetheless, findings from these 18 studies have been remarkably consistent: 14 studies reported a statistically significant inverse relationship between estimated occupational physical activity and risk of colon cancer.

Four studies found no significant relationship between occupational physical activity and risk of colon cancer. The 18 studies were conducted in a variety of study populations in China, Denmark, Japan, New Zealand, Sweden, Switzerland, Turkey, and the United States. Eleven studies assessed the association between leisure-time or total physical activity and colon cancer risk in 13 different study populations. These studies either measured physical activity and tracked participants over time to ascertain colon cancer outcomes or compared recalled histories of physical activity among colon cancer patients with those among controls.

In eight study populations, an inverse association was reported between physical activity and risk of colon cancer, and results were generally consistent for men and women. The three studies that examined the effect of physical activity during early adulthood found no effect, which could indicate that the earlier activity did not affect risk of colon cancer later

in life. In studies that used more than two categories of physical activity, 10 potential dose-response relationships between level of physical activity or cardiorespiratory fitness and colon cancer risk were evaluated. Five of these showed a statistically significant inverse dose-response gradient, one showed an inverse dose-response gradient that was not statistically significant, three showed no gradient, and one showed a positive relationship that was not statistically significant.

Two studies of colon adenomas reported an inverse relationship between leisure-time physical activity and risk of colon adenomas. Dietary factors may confound or modify the association between physical activity and colon cancer risk. Together, the research on occupational and leisure-time or total physical activity strongly suggests that physical activity has a protective effect against the risk of developing colon cancer.

Rectal Cancer

Many of the studies on physical activity and colon cancer risk also studied rectal cancer as a separate outcome. Of 13 studies that investigated occupational physical activity alone, 10 reported no statistically significant association with rectal cancer risk, two reported significant inverse associations and one reported a significant direct association. Six of the studies that investigated the association between leisure-time or total physical activity and the risk of developing rectal cancer failed to find a significant association. In another study, Whittemore and colleagues observed a statistically significant inverse association in one study population and no effect in the other. Paffenbarger, Hyde, and Wing found an inverse relationship in one cohort and a direct relationship in the other. Taken together, study results on both occupational and leisure-time or total physical activity suggest that risk of rectal cancer is unrelated to physical activity.

HORMONE-DEPENDENT CANCERS IN WOMEN

Of the epidemiologic studies examining the relationship

between physical activity and hormonedependent cancers in women, 13 have investigated the risk associated with breast cancer, two with ovarian cancer, four with uterine corpus cancer, and one with a combination of cancers. It should be noted that studies of physical activity in women have been especially prone to misclassification problems because they did not include household work and child care in their assessment.

Breast Cancer

Four of the 13 breast cancer studies considered only occupational physical activity. Two of those studies described significant inverse associations, and two others reported no significant association. Only two adjusted for socioeconomic status, and none gathered information about reproductive factors and thus could not control for those potential confounding variables. The epidemiologic studies of leisure-time or total physical activity and breast cancer risk have yielded inconsistent results. Of these 10 studies, two reported a significant inverse association, three reported an inverse association that was not statistically significant, three reported no relationship.

The other two reported a direct association, although in one this did not reach statistical significance, and in the other it remained statistically significant only for physical activity at age 30– 39 years. Even among the studies that controlled for potential confounding by reproductive factors, findings were inconsistent. Results were inconsistent as well among studies that included primarily postmenopausal women. Nonetheless, it is possible that physical activity during adolescence and young adulthood may protect against later development of breast cancer. Five of the studies cited here have examined this possibility. Among these five studies, two found a strong and statistically significant reduction in risk, one found a non-significant reduction in risk, and two found a null association. These studies thus lend limited support to the hypothesis that physical activity during adolescence and young adulthood may be protective against later development of breast cancer.

Other Hormone-Dependent Cancers in Women

Too little information is available to evaluate the possible effect of physical activity on risk of ovarian cancer. Zheng and colleagues found no significant associations between occupational physical activity and risk of ovarian cancer. On the other hand, data from the Iowa Women's Health Study showed that risk of ovarian cancer among women who were most active was twice the risk among sedentary women. Findings are limited for uterine corpus cancers as well. Zheng et al. found no relationship between physical activity and risk of cancer of the uterine corpus.

Among the endometrial cancer studies, one found a decreased risk associated with non-occupational activity, and one found combined recreational and non-recreational activity to be protective. Another study found no protective effect of non-occupational activity in any age group and a possible protective effect of occupational activity among younger women but not among older women. In Frisch and colleagues' study of the combined prevalence of cancers of the ovary, uterus, cervix, and vagina, nonathletes were 2.5 times more likely than former college athletes to have these forms of cancer at follow-up.

Because these cancers have different etiologies, however, the import of this finding is difficult to determine. Thus the data are either too limited or too inconsistent to firmly establish relationships between physical activity and hormone-dependent cancers in women. The suggestive finding that physical activity in adolescence and early adulthood may protect against later development of breast cancer deserves further study.

CANCER IN MEN

Prostate Cancer

Among epidemiologic studies of physical activity and cancer, prostate cancer is the second most commonly studied,

after colourectal cancer. Results of these studies are inconsistent. Seven studies have investigated the association between occupational physical activity and prostate cancer risk or mortality. Two described significant inverse dose-response relationships. Two showed a non-significant decreased risk with heavy occupational activity. In one publication that presented data from two cohorts, there was no effect in either.

The remaining study reported inconsistent findings by age: increasing risk with increasing activity among men aged 70 years or older and no relationship among men younger than age 70. The 10 studies of leisure-time physical activity, or total physical activity, or cardiorespiratory fitness and risk of prostate cancer have also produced inconsistent results. Two of the studies described significant inverse relationships, although one of these observed this relationship only among men aged 70 years or older.

Four studies found inverse relationships but these were not statistically significant, and one of the four showed this relationship only for those aged 60 years or older. Two studies found that men who had been athletically active in college had significantly increased risks of later developing prostate cancer. One study found no overall association between physical activity and prostate cancer risk but found a higher risk of more aggressive prostate cancer.

The two studies of the association of cardiorespiratory fitness with prostate cancer incidence were also inconsistent. Severson and colleagues found no association between resting pulse rate and subsequent risk of prostate cancer. Oliveria and colleagues found a strong inverse dose-response relationship between fitness assessed by time on a treadmill and subsequent risk of prostate cancer. Thus the body of research conducted to date shows no consistent relationship between prostate cancer and physical activity.

Testicular Cancer

Two studies investigated physical activity and risk of developing testicular cancer; again, results are inconsistent. A

case-control study in England found that men who spent at least 15 hours per week in recreational physical activity had approximately half the risk of sedentary men, and a significant trend was reported over six categories of total time spent exercising.

A cohort study in Norway was limited by few cases. It showed no association between leisure-time physical activity and risk of testicular cancer, but heavy manual occupational activity was associated with an approximately twofold increase in risk, although this result was not statistically significant. Thus no meaningful conclusions about a relationship between physical activity and testicular cancer can be drawn.

OTHER SITE-SPECIFIC CANCERS

Few epidemiologic studies have examined the association of physical activity with other site-specific cancers. The totality of evidence provides little basis for a suggestion of a relationship.

BIOLOGICAL PLAUSIBILITY

Because the data presented in this section demonstrate a clear association only between physical activity and colon cancer, the biologic plausibility of this relationship is the focus of this section. The alteration of local prostaglandin synthesis may serve as a mechanism through which physical activity may confer protection against colon cancer.

Strenuous physical activity increases prostaglandin F2 alpha, which strongly increases intestinal motility, and may suppress prostaglandin E2, which reduces intestinal motility and, released in greater quantities by colon tumour cells than normal cells, accelerates the rate of colon cell proliferation. It has been hypothesized that physical activity decreases gastrointestinal transit time, which in turn decreases the length of contact between the colon mucosa and potential carcinogens, cocarcinogens, or promoters contained in the fecal stream. This hypothesis could partly explain why physical activity has been

associated with reduced cancer risk in the colon but not in the rectum. Physical activity may shorten transit time within segments of the colon without affecting transit time in the rectum. Further, the rectum is only intermittently filled with fecal material before evacuation. Despite these hypothetical mechanisms, studies on the effects of physical activity on gastrointestinal transit time in humans have yielded inconsistent results.

NON–INSULIN-DEPENDENT DIABETES MELLITUS

An estimated 8 million Americans have been diagnosed with diabetes mellitus, and it is estimated that twice that many have diabetes but do not know it. More than 169,000 deaths per year are attributed to diabetes as the underlying cause, making it the seventh leading cause of mortality in the United States. However, underestimates the actual death toll: in 1993, more than twice this number of deaths occurred among persons for whom diabetes was listed as a secondary diagnosis on the death certificate.

Many of these deaths were the result of complications of diabetes, particularly CVDs, including CHD, stroke, peripheral vascular disease, and congestive heart failure. Diabetes accounts for at least 10 per cent of all acute hospital days and in 1992 accounted for an estimated $92 billion in direct and indirect medical costs.

In addition, by age 65 years, about 40 per cent of the general population has impaired glucose tolerance, which increases the risk of CVD. Diabetes is a heterogeneous group of metabolic disorders that have in common elevated blood glucose and associated metabolic derangements. Insulindependent diabetes mellitus is characterized by an absolute deficiency of circulating insulin caused by destruction of pancreatic beta islet cells, thought to have occurred by an autoimmune process.

Non–insulin-dependent diabetes mellitus is characterized either by elevated insulin levels that are ineffective in

normalizing blood glucose levels because of insulin resistance, largely in skeletal muscle, or by impaired insulin secretion. More than 90 per cent of persons with diabetes have NIDDM. Non-modifiable biologic factors implicated in the etiology of NIDDM include a strong genetic influence and advanced age, but the development of insulin resistance, hyperinsulinemia, and glucose intolerance are related to a modifiable factor: weight gain in adults, particularly in those persons in whom fat accumulates around the waist, abdomen, and upper body and within the abdominal cavity.

PHYSICAL ACTIVITY AND NIDDM

Considerable evidence supports a relationship between physical inactivity and NIDDM. Early suggestions of a relationship emerged from the observation that societies that had discontinued their traditional lifestyles experienced major increases in the prevalence of NIDDM. Additional evidence for the importance of lifestyle was provided by comparison studies demonstrating that groups of people who migrated to a more technologically advanced environment had higher prevalences of NIDDM than their ethnic counterparts who remained in their native land and that rural dwellers had a lower prevalence of diabetes than their urban counterparts.

Many cross-sectional studies have found physical inactivity to be significantly associated with NIDDM. Cross-sectional studies that have examined the relationship between physical activity and glucose intolerance in persons without diabetes have generally found that after a meal, glucose levels and insulin values were significantly higher in less active than in more active persons.

However, some crosssectional studies did not find that physical inactivity was consistently associated with NIDDM in either the entire population or in all subgroups. For example, the Second National Health and Nutrition Examination Survey and the Hispanic Health and Nutrition Examination Survey found that higher levels of occupational physical activity among Mexican Americans were associated with less NIDDM.

However, in contrast to findings from the First National Health and Nutrition Examination Survey, this association was not found for either occupational or leisuretime physical activity among blacks or whites.

Two case-control studies have found physical inactivity to be significantly associated with NIDDM. One was a population-based nested case-control study, in which women aged 55–69 years who had high levels of physical activity were found to be half as likely to develop NIDDM as were same-aged women with low levels of physical activity. Moderately active women had an intermediate risk. Prospective cohort studies of college alumni, female registered nurses, and male physicians have demonstrated that physical activity protects against the development of NIDDM.

A study of male university alumni demonstrated that physical activity was inversely related to the incidence of NIDDM, a relationship that was particularly evident in men at high risk for developing diabetes. Each 500 kilocalories of additional leisure-time physical activity per week was associated with a 6 per cent decrease in risk of developing NIDDM. This study showed a more pronounced benefit from vigourous sports than from stair climbing or walking.

In a study of female registered nurses aged 34–59 years, women who reported engaging in vigourous physical activity at least once a week had a 16 per cent lower adjusted relative risk of self-reported NIDDM during the 8 years of follow-up than women who reported no vigourous physical activity. Similar findings were observed between physical activity and incidence of NIDDM in a 5-year prospective study of male physicians 40–84 years of age. Although the incidence of diabetes was self-reported in these cohorts, concerns about accuracy are somewhat mitigated by the fact that these were studies of health professionals and college-educated persons.

In these three cohort studies, two found an inverse dose-response gradient of physical activity and the development of NIDDM. In a feasibility study in Malmo, Sweden, physical activity was included as part of an intervention strategy to

prevent diabetes among persons with impaired glucose tolerance. At the end of 5 years of follow-up, twice as many in the control group as in the intervention group had developed diabetes. The lack of random assignment of participants, however, limits the generalizability of this finding.

A study conducted in Daqing, China, also included physical activity as an intervention to prevent diabetes among persons with impaired glucose tolerance. After 6 years of follow-up, 8.3 cases per 100 person-years occurred in the exercise intervention group and 15.7 cases per 100 person-years in the control group. It has been recommended that an appropriate exercise programme may be added to diet or drug therapy to improve blood glucose control and reduce certain cardiovascular risk factors among persons with diabetes. Diet and exercise have been found to be most effective for controlling NIDDM in persons who have mild disease and are not taking medications.

However, excessive physical activity can sometimes cause persons with diabetes (particularly those who take insulin for blood glucose control) to experience detrimental effects, such as worsening of hyperglycemia and ketosis from poorly controlled diabetes, hypoglycemia either during vigourous physical activity or—more commonly—several hours after prolonged physical activity, complications from proliferative retinopathy, complications from superficial foot injuries, and a risk of myocardial infarction and sudden death, particularly among older people with NIDDM and advanced, but silent, coronary atherosclerosis. These risks can be minimized by a pre-exercise medical evaluation and by taking proper precautions. To reduce risk of hypoglycemic episodes, persons with diabetes who take insulin or oral hypoglycemic drugs must closely monitor their blood glucose levels and make appropriate adjustments in insulin or oral hypoglycemic drug dosage, food intake, and timing of physical activity sessions.

BIOLOGICAL PLAUSIBILITY

Numerous reviews of the short- and long-term effects of

physical activity on carbohydrate metabolism and glucose tolerance describe the physiological basis for a relationship. During a single prolonged session of physical activity, contracting skeletal muscle appears to have a synergistic effect with insulin in enhancing glucose uptake into the cells. This effect appears to be related to both increased blood flow in the muscle and enhanced glucose transport into the muscle cell.

This enhancement persists for 24 hours or more as glycogen levels in the muscle are being replenished. Such observations suggest that many of the effects of regular physical activity are due to the overlapping effects of individual physical activity sessions and are thus independent of long-term adaptations to exercise training or changes in body composition. In general, studies of exercise training have suggested that physical activity helps prevent NIDDM by increasing sensitivity to insulin.

These studies suggest that physical activity is more likely to improve abnormal glucose tolerance when the abnormality is primarily caused by insulin resistance than when it is caused by deficient amounts of circulating insulin. Thus, physical activity is likely to be most beneficial in preventing the progression of NIDDM during the earlier stages of the disease process, before insulin therapy is required.

Evidence supporting this theory includes intervention programmes that promote physical activity together with a low-fat diet high in complex carbohydrates or programmes that promote diet alone. These studies have shown that diet and physical activity interventions are much less beneficial for persons with NIDDM who require insulin therapy than for those who do not yet take any medication or those who take only oral medications for blood glucose control. Cross-sectional studies also show that, compared with their sedentary counterparts, endurance athletes and exercise-trained animals have greater insulin sensitivity, as evidenced by a lower plasma insulin concentration at a similar plasma glucose concentration, and increased I21I-insulin binding to white blood cells and adipocytes.

Insulin sensitivity and rate of glucose disposal are related to cardiorespiratory fitness even in older persons. Resistance or strength-training exercise has also been reported to have beneficial effects on glucose-insulin dynamics in some, but not all, studies involving persons who do not have diabetes. Much of the effect of physical activity appears to be due to the metabolic adaptation of skeletal muscle.

However, exercise training may contribute to improved glucose disposal and glucoseinsulin dynamics in both adipose tissue and the working skeletal muscles. In addition, exercise training may reduce other risk factors for atherosclerosis (*e.g.*, blood lipid abnormalities and elevated blood pressure levels), and thereby decrease the risk of macrovascular or atherosclerotic complications of diabetes.

Lastly, physical activity may prevent or delay the onset of NIDDM by reducing total body fat or specifically intra-abdominal fat, a known risk factor for insulin resistance. Physical activity is inversely associated with obesity and intra-abdominal fat distribution, and recent studies have demonstrated that physical training can reduce these body fat stores.

OSTEOARTHRITIS

Osteoarthritis, the most common form of arthritis, is characterized by both degeneration of cartilage and new growth of bone around the joint. Because its prevalence increases with age, osteoarthritis is the leading cause of activity limitation among older persons.

The etiology of osteoarthritis is unknown, and the risk factors and pathogenesis of osteoarthritis differ for each joint group. Whether an active lifestyle offers protection against the development of osteoarthritis is not known, but studies have examined the risk of developing it in relation to specific athletic pursuits. Cross-sectional studies have associated competitive—as opposed to recreational—running at high levels and for long periods with the development of osteoarthritis seen on x-rays.

On the other hand, both cross-sectional and cohort studies have suggested that persons who engage in recreational running over long periods of time have no more risk of developing osteoarthritis of the knee or hip than sedentary persons. There is also currently no evidence that persons with normal joints increase their risk of osteoarthritis by walking. Studies of competitive athletes suggest that some sports—specifically soccer, football, and weight lifting—are associated with developing osteoarthritis of the joints of the lower extremity.

Other competitive sports activities in which specific joints are used excessively have also been associated with the development of osteoarthritis. For example, baseball pitchers are reported to have an increased prevalence of osteoarthritis in the elbow and shoulder joint. These studies are limited because they involve small sample sizes. Further confounding these studies is the high incidence of fractures, ligamentous and cartilage injuries, and other injuries to joints that occur with greater-than-average frequency among competitive participants in these sports.

Because joint injury is a strong risk factor for the development of osteoarthritis, it may not be the physical activity but rather the associated injuries that cause osteoarthritis in these competitive athletes. In a study by Roos and colleagues, soccer players who had not suffered knee injuries had no greater prevalence of osteoarthritis than did sedentary controls. Regular non-competitive physical activity of the amount and intensity recommended for improving health thus does not appear harmful to joints that have no existing injury.

PHYSICAL ACTIVITY IN PERSONS WITH ARTHRITIS

Given the high prevalence of osteoarthritis among older people, it is important to determine whether persons with arthritis can safely exercise and be physically active. Experimental work with animals shows that use of injured joints inhibits tissue repair. More specifically, several studies

have indicated that running accelerates joint damage in animal models where osteoarthritis has been experimentally induced. In contrast, several short-term studies of human subjects have indicated that regular moderateexercise programmes, whether including aerobic or resistance training, relieve symptoms and improve function among people with both osteoarthritis and rheumatoid arthritis.

For example, it has been shown that after regular physical activity, persons with arthritis have a significant reduction in joint swelling. In other studies of persons with osteoarthritis, increased levels of physical activity were associated with improved psychosocial status, functional status, and physical fitness. Furthermore, regular physical activity of moderate intensity has been found to raise the pain threshold, improve energy level, and improve self-efficacy among persons with osteoarthritis.

BIOLOGICAL PLAUSIBILITY

The biologic effects of physical activity on the health and function of joints have not been extensively investigated, but some level of physical activity is necessary to preserve joint function. Because hyaline cartilage has no blood vessels or nerves, mature cartilage cells receive nourishment only from the diffusion of substances through the cartilage matrix from joint fluid. Physical activity enhances this process. In the laboratory, putting pressure on cartilage deforms the tissue, creating pressure gradients that cause fluid to flow and alter osmotic pressures within the cartilage matrix. The effect of such loading on the metabolism of chondrocytes is not well described, but when loading is performed within the physiologic range, chondrocytes increase proteoglycan synthesis.

In contrast, high-intensity loading and repetitive highimpact loads disrupt the cartilage matrix and inhibit proteoglycan synthesis. The role of normal loading is confirmed by the effect of inactivity on articular cartilage. Immobility leads to decreased cartilage proteoglycan synthesis, increased

water content, and decreased cartilage stiffness and thickness. Disuse may make the cartilage more vulnerable to injury, and prolonged disuse causes loss of normal joint function as the joint cavity is obliterated by fibrous tissue. Studies of running on joint function in dogs with normal joints have confirmed that running does affect the proteoglycan and water content of cartilage and does not lead to degeneration of articular surfaces or to degenerative joint disease. In contrast, in dogs with injured joints, running has been shown to cause arthritis.