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Cardiovascular diseases: review

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ABSTRACT

Cardiovascular disease (CVD) is a designation for multiple clinical phenotypes that result from the interaction of genetic variants, lifestyle choices, and environmental exposures. This article points to the utility of assessing a person's family history of CVD, which is the sum of genetic factors, environment and common lifestyle influences, which may be shared among family members and provides information useful for estimating risk for CVD. It also presents several approaches utilized in attempts to identify variants in genes that are involved in the etiology of CVD. Specifically, examples of the candidate gene approach to identify genetic risk factors for coronary heart disease from our own research are presented. The utilization of genetic profiling to predict an individual's long-term prognosis, to target preventive strategies, and to select the most efficacious drug for treatment are discussed, as well as, the need to consider newer approaches to understanding complex diseases.

Keywords: Shock, Disease of Blood Vessels, Disease of Blood Vessels, Disorder of Blood Pressure, Thrombosis.

INTRODUCTION

What is cardiovascular disease?

The cardiovascular system is made up of the heart and blood vessels. Cardiovascular disease (CVD) is defined as any serious, abnormal condition of the heart or blood vessels (arteries, veins). Cardiovascular disease includes coronary heart disease (CHD), stroke, peripheral vascular disease, congenital heart disease, endocarditis, and many other conditions. Many cardiovascular diseases are preventable.

What are the risk factors for CVD?

Risk factors are variables that predict who is most likely to develop CVD. Most of the risk factors for cardiovascular disease and stroke are modifiable or entirely preventable. By modifying risk factors, you decrease the chances of getting diseases. Modifiable risk factors include tobacco

use, high blood pressure, physical inactivity, high blood cholesterol, obesity, heavy alcohol consumption, and poor nutrition. Non-modifiable risk factors are age and family history. The more risk factors one has, the higher the risk of developing disease.

This document will enable communities to develop plans and strategies that will address CVD risk factors. *A Program Plan to Decrease Heart Disease in West Virginia* will assist local health advocates in implementing cardiovascular prevention efforts targeting the risk factors of tobacco use, physical inactivity, and poor nutrition.

This document may also be used by local and state policy makers in supporting the reduction of cardiovascular disease. There is much more that can be done to create environments conducive to promoting good health.

Goals of the plan

1. Raise awareness of the problem of cardiovascular disease.
2. Create an environment that supports and maintains health promotion behavior.
3. Encourage personal and public responsibility for good health (policy).
4. Stimulate community efforts to address risk factor prevalence and disease prevention.

The Number one killer in the United States and West Virginia today is cardiovascular disease.

Scope of the problem

The number one killer in the United States and West Virginia today is cardiovascular disease. In recent years, there has been a significant decline in the number of deaths from CVD due to changes in personal health behaviors as well as improvements in medical technology. However, the declines in West Virginia have been substantially lower than those experienced in the nation as a whole, especially in CVD mortality. In fact, while the rate of CVD mortality declined 44% nationwide between 1960 and 1990, the decline in West Virginia was only 32%.

Despite the declines, the toll from CVD mortality is high. The 1995 state age-adjusted rate of death due to heart disease was 328.2 deaths per 100,000 population, 17% higher than the national rate of 281.2 per 100,000. Tobacco use, high blood cholesterol, high blood pressure, and sedentary lifestyle, are modifiable risk behaviors that have been linked to cardiovascular disease.

Hypertension (high blood pressure) is another risk factor for heart disease and is the single most important risk factor for stroke. Diabetes substantially increases the risk of developing cardiovascular diseases. Persons with diabetes (depending on gender) are two to four times more likely to die of coronary heart disease, and twice as likely to die of stroke, as person without diabetes. The prevalence of all these risk factors have been found to be higher in West Virginia than in the nation as a whole.

Conditions associated with CVD (high blood cholesterol, diabetes, high blood pressure) are also affected by sedentary lifestyle, poor diet, and tobacco use. Decreasing the incidence of modifiable risk factors also decreases the risk of CVD-associated conditions (Refer to the risk factor chapters for interventions).

What is the connection between smoking and heart disease?

Coronary heart disease is the leading cause of death in the United States. Contrary to public perception, smoking-caused heart disease actually results in more deaths per year than smoking-caused lung cancer [1]. Thirty percent of all heart disease deaths are caused by cigarette smoking [2]. Smoking is the single largest preventable cause of heart disease in the United States.

Tobacco smoke contains high levels of carbon monoxide. Carbon monoxide affects the heart by reducing the amount of oxygen the blood is able to carry. This means that the heart, lungs, brain, and other vital organs do not always receive enough oxygen to perform everyday functions. At the same time, nicotine causes an increase in heart rate and blood pressure. Over time, this causes extraordinary "wear and tear" on the cardiovascular system. People who use tobacco are more likely to have heart attacks, high blood pressure, blood clots, strokes, hemorrhages, aneurysms, and other disorders of the cardiovascular system.

Smoking actually triples the risk of dying from heart disease. Cigarette smoking is a major cause of stroke by increasing clotting factors in the blood, decreasing HDL cholesterol levels, increasing triglyceride levels, and damaging the lining of

blood vessels. The risk for stroke increases as the number of cigarettes smoked increases.

What about secondhand smoke?

Secondhand smoke is a much greater problem than many people realize. Secondhand smoke is a combination of the smoke given off by the burning end of a cigarette, pipe, or cigar and the smoke exhaled from the lungs of smokers. This mixture contains more than 4,000 substances, more than 40 of which are known to cause cancer in humans or animals and many of which are strong irritants. Secondhand smoke has been classified by the United States Environmental Protection Agency (EPA) as a known cause of lung cancer in humans. Secondhand smoke causes 30 times as many lung cancer deaths as all regulated air pollutants combined [3]. Secondhand smoke is estimated by the EPA to cause approximately 3,000 lung cancer deaths in nonsmokers each year.

There is no evidence of a safe level of exposure to secondhand smoke. In fact, long-term exposure to secondhand smoke has been shown to cause a 30% increase in the risk of heart disease in nonsmokers. It is estimated that 37,000 coronary heart disease deaths per year are caused by exposure to secondhand smoke. Exposure to secondhand smoke also negatively affects cardiovascular health by decreasing exercise endurance, damaging blood vessel walls, and increasing the tendency of blood platelets to clot, contributing to heart attacks. Also, nonsmokers' bodies tend to react more dramatically to tobacco exposure than do smokers' bodies, so lower levels of smoke can cause adverse effects.

I've smoked for most of my life. Is it worth it to quit now?

YES. People who quit smoking dramatically reduce their risk of dying from heart disease. The body begins to repair itself almost immediately. Quitting can help people who already have heart disease. People who quit smoking can cut their risk of having another heart attack or dying of heart disease in half. When a smoker quits, the risk of heart disease death begins to fall almost immediately, but it takes ten years for the risk to approach that of a nonsmoker [4].

With five to 15 years, an ex-smoker's risk of having a stroke is the same as that of someone who never smoked Quitting also reduces the risk of other circulatory diseases. People who quit smoking cut their risk of abdominal aortic aneurysm in half. The risk of having a stroke or hemorrhage is also reduced. Within five to 15 years, an ex-smoker's risk of having a stroke is the same as that of someone who never smoked.

Won't I gain weight if I quit smoking?

Four out of five people who quit smoking gain a small amount of weight. The average is about five pounds. Some of this weight gain is due to a temporary increase in appetite caused by nicotine withdrawal. This usually goes away within a few weeks or months after quitting. The slight weight gain many ex-smokers experience is not a health risk.

Experts think that nicotine interferes with metabolism or some other digestive process. Smokers and nonsmokers tend to eat about the same amount, but smokers weigh slightly less and have less healthy distribution of body fat. Children who are exposed to secondhand smoke or who smoke or chew tobacco also exhibit high levels of overall cholesterol and low levels of high density lipoproteins or HDL ("good" cholesterol). This indicates that nicotine or some other component of tobacco interferes with normal digestion and metabolism.

It has been found that on average, smokers weigh only a few pounds less than nonsmokers of the same age and gender. Upon cessation, weight tends to increase only to a level the smoker would have attained/maintained if he/she had never smoked [5]. Smoking should not be used as a weight loss tool.

Most ex-smokers have higher levels of exercise endurance, improved cardiovascular functioning, and more energy than they did while they were smokers. Studies indicate that beginning an exercise program for a few weeks before attempting to quit, and maintaining exercise for several weeks after successfully quitting, can help to prevent both weight gain and relapse.

When can I expect to see the benefits of quitting?

As soon as a person quits smoking, his/her body begins to repair the damage caused by tobacco use. Within a few days or weeks, exercise endurance

and cardiovascular capacity improve, and HDL (protective, "good" cholesterol) increases. Within a year, the risk for most cardiovascular diseases will be cut in half. In 15 smoke free years, an ex-smoker's cardiovascular system will be as healthy as if he or she had never smoked.

Does smokeless tobacco cause heart disease?

Yes. Using smokeless tobacco increases the risk of high blood pressure, which can lead to cardiovascular disease [6]. It also increases the chances of cardiovascular stroke. Additionally, according to the Centers for Disease Control and Prevention, smokeless tobacco is highly addictive because of its high nicotine levels. It can be more difficult to quit this habit than smoking. Smokeless tobacco is not a safe alternative to cigarettes.(tobacco continued, select forward)

VARIOUS CARDIOVASCULAR DISEASES

Shock

Shock occurs when the metabolic needs of cells are not being met because of inadequate blood flow. In effect, there is a reduction in circulating blood volume, in blood pressure and in cardiac output. This causes tissue hypoxia, an inadequate supply of nutrients and the accumulation of waste products. A number of different types of shock are described:

1. Hypovolemic
2. Cardiogenic
3. Septic
4. Neurogenic
5. Anaphylactic.

Hypovolemic shock

This occurs when the blood volume is reduced by 15 to 25%. Reduced venous return and in turn cardiac output may occur following:

- Severe hemorrhage — whole blood is lost
- Extensive superficial burns — serum is lost and blood cells at the site of the burn are destroyed
- Severe vomiting and diarrhea — water and electrolytes are lost
- Perforation of an organ allowing its contents to enter the peritoneal cavity (peritonitis).

Cardiogenic shock

This occurs in acute heart disease when the damaged heart muscle cannot maintain an adequate cardiac output,
E.g. in myocardial infarction.

Septic shock (bacteraemic, endotoxic)

This is caused by severe infections in which endotoxins are released into the circulation from dead Gram-negative bacteria, e.g. *Enterobacteria, Pseudomonas*. The mode of action of the toxins is not clearly understood. It may be that they cause an apparent reduction in the blood volume because of vasodilatation and pooling of blood in the large veins. This reduces the venous return to the heart and the cardiac output.

Neurogenic shock (vasovagal attack, fainting)

The causes include sudden acute pain, severe emotional experience, spinal anaesthesia and spinal cord damage. Parasympathetic nerve impulses reduce the heart rate, and in turn, the cardiac output. The venous return may also be reduced by the pooling of blood in dilated veins. These changes effectively reduce the blood supply to the brain, causing fainting. The period of unconsciousness is usually of short duration.

Anaphylactic shock

In allergic reactions an antigen interacts with an antibody and a variety of responses can occur (p. 383). In severe Cases, the chemicals released, e.g. histamine, bradykinin, produce widespread vasodilatation and constriction of Bronchiolar smooth muscle (bronchospasm). The vasodilatation profoundly reduces the venous return and Cardiac output resulting in tissue hypoxia. Bronchospasm reduces the amount of air entering the lungs, increasing tissue hypoxia.

PHYSIOLOGICAL CHANGES DURING SHOCK

In the short term these are associated with physiological attempts to restore an adequate blood circulation. If the State of shock persists, the longer-term changes may be irreversible.

IMMEDIATE OR REACTIVE CHANGES

As the blood pressure falls, a number of reflexes are stimulated and hormone secretions increased in an attempt to restore homeostasis. These raise the blood pressure by increasing peripheral resistance, the blood volume and the cardiac output. The changes include:

1. Vasoconstriction, following:
   a) Stimulation of the baroreceptors in the aortic arch and carotid sinuses
   b) Sympathetic stimulation of the adrenal glands which causes increased secretion of adrenaline and noradrenaline
   c) Stimulation of the renin—angiotensin—aldosterone system by diminished blood flow to the kidneys
2. Increased heart rate, following sympathetic stimulation
3. Water retention by the kidney, following increased release of antidiuretic hormone by the posterior lobe of the pituitary gland, increasing salt and water retention. In shock of moderate severity the circulation to the heart and brain is maintained, in the short term.

Restlessness, confusion and coma occur as circulation to the brain is impaired. If shock is very severe there may not be time for the above changes to be effective. The severe hypoxia that occurs disrupts cell metabolism. In

The absence of adequate oxygen, cellular metabolism switches to less efficient anaerobic pathways, large amounts of lactic acid are formed and hydrogen ions accumulate, reaching dangerous levels in a few minutes. These are the changes that lead to the severe metabolic acidosis which occurs immediately prior to and following cardiac arrest.

LONG-TERM CHANGES ASSOCIATED WITH SHOCK

If the state of shock is not reversed, hypoxia and low blood pressure cause irreversible brain damage and capillary dilatation and a vicious circle of events is established.

Hypoxia

When this persists there is cell damage and a release of chemical substances that increase the permeability of the capillaries. More fluid enters the interstitial spaces, leading to further hypovolemia, further reduction in blood pressure and increased hypoxia.

Low blood pressure

As the blood pressure continues to fall, cerebral and myocardial hypoxia becomes progressively more marked and the reduced blood flow encourages the formation of thrombi and infarcts. There is acute renal failure and a marked reduction in the secretion of urine, leading to the retention of damaging metabolic waste products. If effective treatment is not possible these irreversible changes become progressively more severe and eventually may cause death.

DISEASES OF BLOOD VESSELS

Atheroma

Pathological changes

Patchy changes *(atheromatous plaques)* develop in the tunica intima of large and medium-sized arteries. These consist of accumulations of cholesterol and other lipid compounds, excess smooth muscle and fat-filled monocytes (foam cells). The plaque is covered with a fibrous cap. As plaques grow they spread along the artery wall forming swellings that protrude into the lumen. Eventually the whole thickness of the wall and long sections of the vessel may be affected. Plaques may rupture, exposing subintimal materials to the blood. This may cause thrombosis and vasospasm and will compromise blood flow. Arteries most commonly involved are those in the heart, brain, kidneys, and small intestine and lower limbs.

Causes of atheroma

The origin of atheromatous plaques is uncertain. *Fatty streaks* present in artery walls of infants are usually absorbed but their incomplete absorption may be the origin of atheromatous plaques in later life. Atherosclerosis is considered to be a disease of older people because it is usually in these age groups that clinical signs appear. Plaques, however, start to form in childhood in developed countries. The incidence of atheroma is widespread in developed countries. Why atheromatous plaques develop is not yet clearly understood but the

predisposing factors appear to exert their effects over a long period. This may mean that the development of atheroma can be delayed or even arrested by a change in lifestyle.

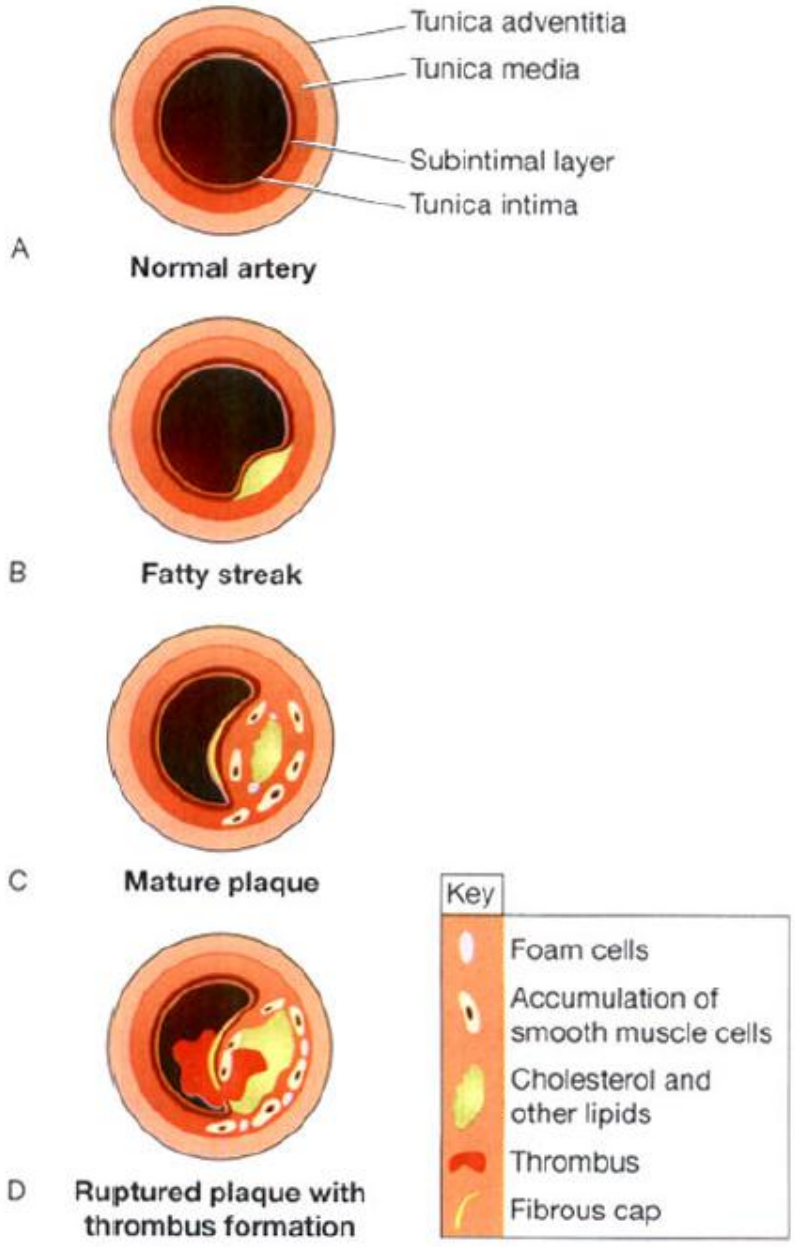

Figure No. 01: Stages in the development of an atheromatous plaque

Predisposing factors include:

- Heredity — family history
- Gender — males are more susceptible than females until after the menopause
- increasing age
- Hypertension
- Diabetes mellitus
- Smoking, especially cigarettes
- Excessive emotional stress in work or home environment
- Diet, e.g. high intake of refined carbohydrates and/or cholesterol and saturated fatty acids (from animal fats)
- Obesity
- Sedentary lifestyle
- Excessive alcohol consumption.

Effects of atheroma

Arteries may be partially or completely blocked by atheromatous plaques alone, or by plaques combined with a thrombus. This may reduce or completely block the blood supply. The effects depend on the site and size of the artery involved and the extent of collateral circulation. Commonly the arteries affected are those in the heart, abdomen and pelvis.

Narrowing of an artery

The tissues distal to the narrow point become ischaemic. The cells may receive enough blood to meet their minimum needs, but not enough to cope with an increase in metabolic rate, e.g. when muscle activity is increased. This causes acute cramp-like ischaemic pain. Cardiac muscle and skeletal muscles of the lower limb are most commonly affected. Ischaemic pain in the heart is called *angina pectoris* (p. 121), and in the lower limbs, *intermittent claudication.*

Occlusion of an artery

When an artery is completely blocked, the tissues it supplies rapidly undergo degeneration and die from *ischaemia* which leads to *infarction.* The extent of tissue damage depends on:

- The size of the artery occluded
- The amount and type of tissue involved
- The extent of collateral circulation, e.g. in the brain the circulus arteriosus (circle of Willis) provides extensive collateral blood vessels while in the heart there are very few. When a coronary artery is occluded *myocardial infarction* occurs. Occlusion of arteries in the brain causes cerebral ischaemia and this leads to *cerebral infarction* (stroke). Complications of atheroma.

Thrombosis and infarction

If the fibrous cap overlying a plaque breaks down, platelets are activated by the damaged cells and a blood clot (thrombus) forms, blocking the artery and causing ischaemia and infarction. Pieces of the clot (emboli) may break off, travel in the bloodstream and lodge in small arteries distal to the clot, causing small infarcts (areas of dead tissue).

Haemorrhage

When calcium salts are deposited in the plaques, the artery walls become brittle, rigid and unresponsive to rises in blood pressure and may rupture, causing haemorrhage.

Aneurysm formation

When the arterial wall is weakened by spread of the plaque between the layers of tissue, a local dilatation (aneurysm) may develop (see below). This may lead to thrombosis and embolism, or the aneurysm may rupture causing severe haemorrhage. The most common sites affected are the aorta and the abdominal and pelvic arteries.

ARTERIOSCLEROSIS

This is a progressive degeneration of arterial walls, associated with ageing and accompanied by hypertension.

Large and medium arteries

The tunica media is infiltrated with fibrous tissue and calcium. This causes the vessels to lose their elasticity. The lumen dilates and they become tortuous Loss of elasticity increases systolic blood pressure, and the *pulse pressure* (the difference between systolic and diastolic pressure).

Small arteries and arterioles

Hyaline thickening of the tunica media and tunica intima Causes narrowing of the lumen and they become tortuous. These arteries are the main determinants of peripheral resistance (p. 80) and narrowing of their lumens increases peripheral resistance and blood pressure. Ischaemia of tissues supplied by affected arteries may occur. In the limbs, the resultant ischaemia predisposes to gangrene which is particularly serious in people with diabetes mellitus.

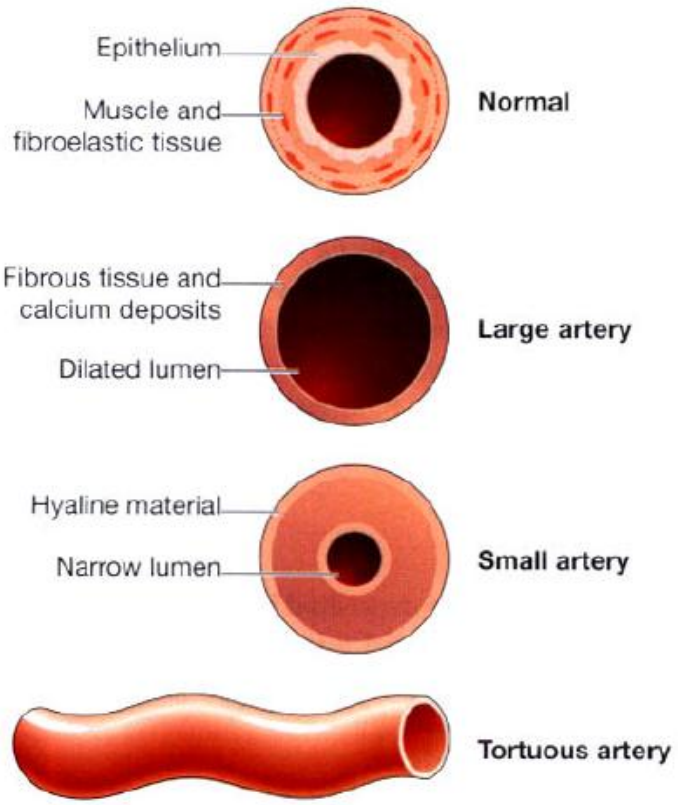

Figure No. 02: Arteriosclerotic arteries.

Senile arteriosclerosis

This is a condition affecting elderly people in which the progressive loss of elasticity and reduced arterial lumen leads to cerebral ischaemia and loss of mental function. There may or may not be evidence of hypertension.

THROMBOANGIITIS OBLITERANS (BUERGER'S DISEASE)

In this condition there is acute inflammation with thrombosis of the small arteries mainly in the lower limbs. It occurs most commonly in men between the ages of 20 and 40 years and is associated with heavy cigarette smoking. The condition may be caused by an immune response to an antigen, possibly a tobacco protein. The condition may become chronic and the vessel walls become f ibrosed, lose their elasticity and do not dilate during exercise. The individual suffers from acute ischaemic pain and, as the disease progresses, the distance walked with comfort is gradually reduced. In the long term the skin may ulcerate and, in extreme cases, gangrene may develop.

POLYARTERITIS NODOSA

This is a connective tissue disorder associated with inflammation of the tunica media of medium-sized arteries in any part of the body. The most common sites are the heart, kidneys, alimentary tract, liver, pancreas and nervous system. It is acute at first but frequently becomes chronic. Necrosis and rupture of blood vessels may occur in the acute phase followed by thrombosis, ischaemia, infarction and death. It is believed to be caused by an immune reaction. In most cases the antigen is not known but it may be a virus or drug such as a sulphonamide or antibiotic.

ANEURYSMS

Aneurysms are abnormal local dilatations of arteries which vary considerably in size (Fig. 3). The causes are not clear but predisposing factors

include atheroma, hypertension and defective formation of collagen in the arterial wall. *Fusiform* or spindle-shaped distensions occur mainly in the abdominal aorta and less commonly in the iliac arteries. They are usually associated with atheromatous changes.

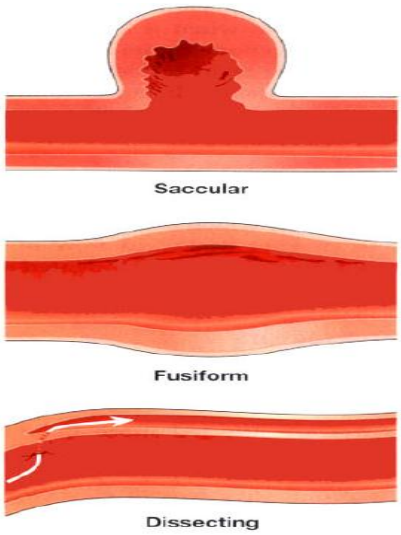

Figure No. 03: Types of aneurysm.

Saccular aneurysms bulge out on one side of the artery. When they occur in the relatively thin-walled arteries of the circulus arteriosus (circle of Willis) in the brain they are sometimes called 'berry' aneurysms. They may beassociated with defective collagen production, with atheromatous changes or be congenital.

Dissecting aneurysms occur mainly in the arch of the aorta due to infiltration of blood between the endothelium and tunica media, beginning at a site of endothelial damage.

Microaneurysms are fusiform or saccular aneurysms, occurring in small arteries and arterioles in the brain. They are associated with hypertension. Recurring small strokes (transient ischaemic attacks) are commonly due to thrombosis in the aneurysm or to haemorrhage when an aneurysm ruptures. Complications of aneurysms

Haemorrhage

A ruptured aneurysm may cause sudden death or disability of varying severity, depending on the size and site of the artery.

Pressure

Localized swelling may cause pressure affecting adjacent tissues including organs, blood vessels and nerves.

THROMBOSIS AND EMBOLISM

A blood clot (thrombus) may form in an artery where the endothelium has been damaged by an aneurysm. A piece of clot (embolus) may break off and travel in the bloodstream until it lodges in a small artery distal to the aneurysm and obstructs the blood flow, causing ischaemia and infarction.

Venous thrombosis

This may be superficial thrombophlebitis or deep vein thrombosis.

Superficial thrombophlebitis

In this acute inflammatory condition a thrombus forms in a superficial vein and the tissue around the affected vein becomes red and painful. The most common causes are:

- Intravenous infusion
- Varicosities in the saphenous vein.

Deep vein thrombosis (DVT) A thrombus forms in a deep vein commonly in the lower limb, pelvic or iliac veins, but occasionally in an upper limb. The thrombus may affect a long section of the vein and, after some days, fibrinolysis (p. 68) may enable recanalisation through the blockage. Deep vein thrombosis may be accompanied by pain and swelling, but is often asymptomatic. There are several predisposing factors.

Reduced rate of blood flow This may be caused by:

- Immobility associated with prolonged bed rest
- pressure on veins in the popliteal region by, e.g., a pillow under the knees in bed or sitting in a chair for long periods, as in long journeys
- Pressure on a vein by an adjacent tumor
- Prolonged low blood pressure, as in shock.

Changes in the blood These may trigger intravascular
Clotting, e.g.:

- Increased blood viscosity in, e.g., dehydration, polycythemia.
- Increased adhesiveness of platelets, e.g. associated with the use of some oral contraceptive drugs, and in some malignant diseases.

Damage to the blood vessel wall

This can result in intravascular clotting, e.g.:

- Accidental injury
- Surgery.

The most common complication of DVT is *pulmonary embolism*, which occurs when a large piece or several small fragments of a venous thrombus become detached and travel through the heart to lodge in the pulmonary artery or one of its branches. It causes infarction of lung tissue. A massive pulmonary embolism usually causes sudden collapse and death.

Varicose veins

A varicose vein is one which is so dilated that the valves do not close to prevent backward flow of blood. Such veins lose their elasticity, become elongated and tortuous and fibrous tissue replaces the tunica media. Predisposing factors

Heredity

There appears to be a familial tendency but no abnormal genetic factor has been identified.

Gender

Females are affected more than males, especially following pregnancy.

Age

There is progressive loss of elasticity in the vein walls with increasing age so that elastic recoil is less efficient.

Obesity

Superficial veins in the limbs are supported by subcutaneous areolar tissue. Excess adipose tissue may not provide sufficient support.

Gravity

Standing for long periods with little muscle contraction tends to cause pooling of blood in the lower limbs and pelvis.

Pressure

Because of their thin walls, veins are easily compressed by surrounding structures, leading to increased venous pressure distal to the site of compression.

Sites and effects of varicose veins

Varicose veins of the legs

When valves in the anastomosing veins between the deep and superficial veins in the legs become incompetent the venous pressure in the superficial veins rises. In the long term they stretch and become chronically dilated because the superficial veins are not supported by much tissue. Such areas are seen externally as *varicosities* (Fig. 5.56). The great and small saphenous veins and the anterior tibial veins are most commonly affected causing aching and fatigue of the legs especially during long periods of standing. These dilated, inelastic veins rupture easily if injured, and haemorrhage occurs. The skin over a varicose vein may become poorly nourished due to stasis of blood, leading to the formation of *varicose ulcers* usually on the medial aspects of the leg just above the ankle.

Haemorrhoids

Sustained pressure on the veins at the junction of the rectum and anus leads to increased venous pressure, valvular incompetence and the development of haemorrhoids (Fig. 4). The most common causes are chronic constipation, and the increased pressure in the pelvis towards the end of pregnancy. Slight bleeding may occur each time stools are passed and, in time, may cause anaemia. Severe haemorrhage is rare.

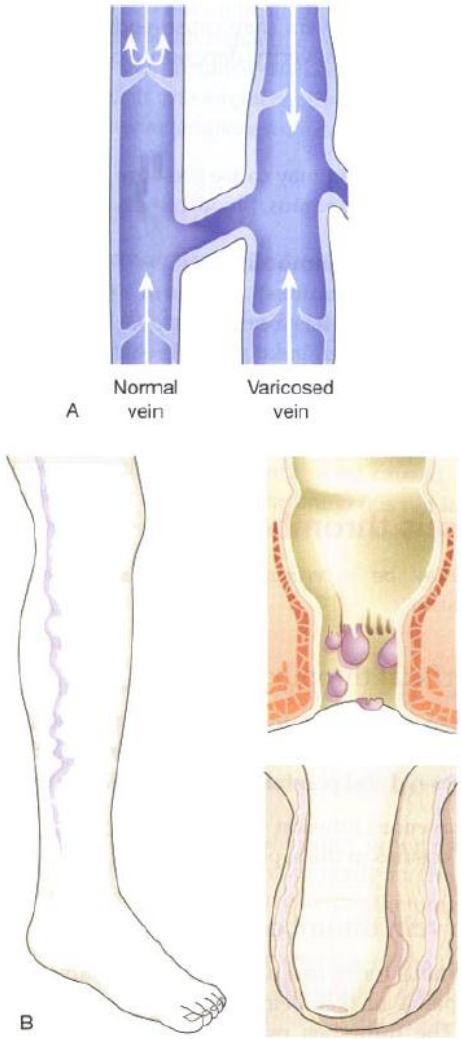

Figure No. 04: A. Normal and varicosed veins. B. Common sites for Varicosities - the leg, scrotum (varicocele) and anus (haemorrhoids).

Scrotal varicocele

Each spermatic cord is surrounded by a plexus of veins that may become varicosed (Fig. 4), especially in men whose work necessitates standing for long periods. If the varicocele is bilateral the increased temperature due to venous congestion may cause depressed spermatogenesis and result in infertility.

Oesophageal varices

The veins involved are at the lower end of the oesophagus. When the venous pressure in the liver rises, there is a rise in pressure in the anastomosing veins between the left gastric vein and the azygos vein. Sustained pressure causes varicosities to develop in the oesophagus (see Fig. 12.50, p. 321). The commonest causes of increased portal vein pressure are cirrhosis of the liver and right-sided cardiac failure. If the pressure continues to rise, inelastic varicosed veins may rupture causing severe haemorrhage, and possibly death.

TUMOURS OF BLOOD AND LYMPH VESSELS

Angiomas

Angiomas are benign tumours of either blood vessels (haemangiomas) or lymph vessels (lymphangiomas). The latter rarely occur, so angioma is usually taken to mean haemangioma.

Haemangiomas

These are not true tumours but are sufficiently similar to be classified as such. They consist of an excessive growth of blood vessels arranged in an uncharacteristic
Manner and interspersed with collagen fibres.

Capillary haemangiomas

Excess capillary growth interspersed with collagen in a localised area makes a dense, plexus-like network of tissue. Each haemangioma is supplied by only one blood vessel and if it thrombosis the haemangioma atrophies and disappears. Capillary haemangiomas are usually present at birth and are seen as a purple or red mole or birthmark. They may be quite small at birth but grow at an alarming rate in the first few months, keeping pace with the growth of the child. After 1 to 3 years, atrophy may begin and by the end of years in about 80% of cases the tumors have disappeared.

Cavernous haemangiomas

Blood vessels larger than capillaries grow in excess of normal needs in a localized area and are interspersed with collagen fibers. They are dark red in colour and may be present in the skin, though more commonly in the liver. They grow slowly, do not regress and may become large and unsightly.

THROMBOSIS, EMBOLISM AND INFARCTION

Factors which predispose to thrombus formation include

- An abnormality of the normally smooth endothelium,
  E.g. ruptured atheromatous plaque
- Abnormal blood flow in a vessel, especially venous stasis
- Increased coagulability of the blood.

If a fragment of thrombus, called an *embolus*, becomes detached, it travels in the bloodstream until it lodges in and blocks a smaller vessel. The tissue supplied by the vessel becomes ischaemic and dies; this is *infarction.* An *embolus* is a mass of any material carried in the bloodstream and large enough to block a blood vessel. Most emboli consist of fragments of thrombi but other materials include:

- Fragments of atheromatous plaques
- Fragments of vegetation from heart valves, e.g. infective endocarditis
- Tumour fragments that may cause metastases
- Amniotic fluid, during childbirth
- Fat, from extensive bone fractures
- Air, iatrogenic or following puncture of a blood vessel in the lung by a broken rib
- Nitrogen in decompression sickness — 'the bends'
- Pus from an abscess
- Clumps of platelets with adherent microbes.

Emboli in veins move towards the heart and lodge in the smaller vessels of the lungs or the liver (an important cause of metastases in tumours of the alimentary tract). Those in arteries travel away from the heart and lodge in smaller arteries or arterioles. The effects of an embolus are determined by the site and size of the blood vessel occluded, not its composition.
Common serious consequences include:

- Myocardial infarction
- Cerebral infarction
- Pulmonary embolism

OEDEMA

Diseases of the heart diseases of the heart

Cardiac failure

The heart is described as failing when the cardiac output is unable to maintain the circulation of sufficient blood to meet the needs of the body. In mild cases, cardiac output is adequate at rest and becomes inadequate only when increased cardiac output is required, e.g. in exercise.

Heart failure may affect either side of the heart, but since both sides of the heart are part of one circuit, when one half of the pump begins to fail it frequently leads to increased strain on, and eventual failure of, the other half. The main clinical manifestations depend on which side of the heart is most affected.

Compensatory mechanisms

In heart failure when heart failure happens acutely, the body has little time to make

compensatory changes, but if the heart fails over a period of time the following changes are likely to occur in an attempt to maintain cardiac output and tissue perfusion, especially of vital organs.

- The cardiac muscle fibres enlarge and increase in number, which makes the walls of the chambers thicker
- The heart chambers enlarge
- Decreased renal blood flow activates the renin-angiotensin-aldosterone system (p. 223), which leads to salt and water retention. This increases blood volume and cardiac workload. The direct vasoconstrictor action of angiotensin 2 increases peripheral resistance and puts further strain on the failing heart.

ACUTE CARDIAC FAILURE

A sudden decrease in output of blood from both ventricles causes acute reduction in the oxygen supply to all the tissues. Recovery from the acute phase may be followed by chronic failure, or death may occur due to anoxia of vital centers in the brain. The commonest Causes are:

- Severe damage to an area of cardiac muscle due to ischaemia caused by sudden occlusion of one of the larger coronary arteries by atheroma or atheroma with thrombosis pulmonary embolism acute toxic myocarditis severe cardiac arrhythmia rupture of a heart chamber or valve cusp severe malignant hypertension. Chronic cardiac failure this develops gradually and in the early stages there may be no symptoms because certain compensatory changes occur as described above. When further compensation is not possible there is a gradual decline in myocardial efficiency. Underlying causes include:
- Chronic hypertension, myocardial fibrosis, valvular disease, lung diseases, anaemia
- Previous acute cardiac failure
- Degenerative changes of old age.

RIGHT-SIDED (CONGESTIVE) CARDIAC FAILURE

The right ventricle fails when pressure developed within it by the contracting myocardium is less than the force needed to push blood through the lungs. When compensation has reached its limit, and the ventricle is not emptying completely, the right atrium and venae cavae become congested with blood and this is followed by congestion throughout the venous system. The organs affected first are the liver, spleen and kidneys. *Oedema* of the limbs and *ascites* (excess fluid in the peritoneal cavity) usually follow. This problem may be caused by increased vascular resistance in the lungs, weakness of the myocardium and/or stenosis and incompetence of valves in the heart or great vessels.

Resistance to blood flow through the lungs

When this is increased the right ventricle has more work to do. It may be caused by:

- The formation of fibrous tissue following inflammation or chronic disease of the lungs
- back pressure of blood from the left side of the heart,

E.g. in left ventricular failure, when the mitral valve is stenosis and/or incompetent.

Weakness of the myocardium

This may be caused by ischaemia following numerous small myocardial infarcts.

LEFT-SIDED OR LEFT VENTRICULAR FAILURE

This occurs when the pressure developed in the left ventricle by the contracting myocardium is less than the pressure in the aorta and the ventricle cannot then pump out all the blood it receives. Causes include:

- Excessively high systemic (aortic) blood pressure
- Incompetence of the mitral and/or the aortic valve
- Aortic valve stenosis
- Myocardial weakness.

Failure of the left ventricle leads to dilatation of the atrium and an increase in pulmonary blood pressure. This is followed by a rise in the blood pressure in the right side of the heart and eventually systemic venous congestion. Congestion in the lungs leads to pulmonary oedema and dyspnoea, often most severe at night. This *paroxysmal nocturnal Dyspnoea* may be due to raised blood volume as fluid from peripheral oedema is

reabsorbed when the patient slips down in bed during sleep.

DISORDERS OF HEART VALVES

The heart valves prevent backflow of blood in the heart during the cardiac cycle. The left atrioventricular and aortic valves are subject to greater pressures than those on the right side and are therefore more susceptible to damage. Distinctive heart sounds arise when the valves close during the cardiac cycle (p. 88). Damaged valves generate abnormal heart sounds called *murmurs.A* severe valve disorder results in heart failure. The most common causes of valve defects are rheumatic fever, fibrosis following inflammation and congenital abnormalities.

Stenosis

This is the narrowing of a valve opening, impeding blood flow through the valve. It occurs when inflammation and encrustations roughen the edges of the cusps so that they stick together, narrowing the valve opening. When healing occurs fibrous tissue is formed which shrinks as it ages, increasing the stenosis and leading to incompetence.

Incompetence

Sometimes called *regurgitation*, this is a functional defect caused by failure of a valve to close completely, allow in blood to flow back into the ventricle when it relaxes.

ISCHAEMIC HEART DISEASE

Ischaemic heart disease is due to the effects of atheroma, causing narrowing or occlusion of one or more branches of the coronary arteries. The narrowing is caused by atheromatous plaques. Occlusion may be by plaques alone, or plaques complicated by thrombosis. The overall effect depends on the size of the coronary artery involved and whether it is narrowed or occluded. Narrowing of an artery leads to *angina pectoris*, and occlusion to *myocardial infarction*, i.e. an area of dead tissue.

When atheroma develops slowly, a *collateral arterial blood supply* may have time to develop and effectively supplement or replace the original. This consists of the dilatation of normally occurring anastomotic arteries joining adjacent branch arteries. When sudden severe narrowing or occlusion of an artery occurs the anastomotic arteries dilate but may not be able to supply enough blood to meet the needs of the myocardium.

ANGINA PECTORIS

This is sometimes called *angina of effort* because increased cardiac output required during extra physical effort causes severe ischaemic pain in the chest. The pain may also radiate to the arms, neck and jaw. Other factors which may precipitate angina include:

- Cold weather
- Exercising after a heavy meal
- Strong emotions.

A narrowed coronary artery may supply sufficient blood to the myocardium to meet its needs during rest or moderate exercise but not when greatly increased cardiac output is needed, e.g. walking may be tolerated but not running. The thick, inflexible atheromatous artery wall is unable to dilate to allow for the increased blood flow needed by the more active myocardium which then becomes ischaemic. In the early stages of development of the disease the chest pain stops when the cardiac output returns to its resting level soon after the extra effort stops.

MYOCARDIAL INFARCTION

An *infarct* is an area of tissue that has died because of lack of oxygenated blood. The myocardium is affected when a branch of a coronary artery is occluded. The commonest cause is an atheromatous plaque complicated by thrombosis. The extent of myocardial damage depends on the size of the blood vessel and site of the infarct. The damage is permanent because cardiac muscle cannot regenerate and the dead tissue is replaced with non-functional fibrous tissue. Speedy restoration of blood flow through the blocked artery using clot-dissolving (thrombolytic) drugs can greatly reduce the extent of the permanent damage and improve prognosis, but treatment must be started within a few hours of the infarction occurring.

The effects and complications are greatest when the left ventricle is involved

Myocardial infarction is usually accompanied by very severe crushing chest pain behind the sternum which, unlike angina pectoris, continues even when the individual is at rest.

Complications

These may be fatal and include:

- Severe arrhythmias, especially *ventricular fibrillation*, due to disruption of the cardiac conducting system
- Cardiac failure, caused by impaired contraction of the damaged myocardium and, in severe cases, cardiogenic shock
- Rupture of a ventricle wall, usually within 2 weeks of the original episode
- Pulmonary or cerebral embolism originating from a mural clot within a ventricle, i.e. a clot that forms inside the heart over the area of dead tissue
- Pericarditis
- Angina pectoris
- Recurrence.

RHEUMATIC HEART DISEASE

Rheumatic fever

This autoimmune disease occurs 2 to 4 weeks after a throat infection, caused by *Streptococcus* pyogenes (betahaemolytic Group A). The antibodies developed to combat the infection damage the heart. The microbes are not present in the heart lesion and the same infection in other parts of the body is very rarely followed by rheumatic fever. How the antibodies damage the heart is not yet understood. Children and young adults are most commonly affected. Death rarely occurs in the acute phase but after recovery there may be permanent damage to the heart valves, eventually leading to disability and possibly cardiac Failure.

Effects on the endocardium

The endocardium becomes inflamed and oedematous and tiny pale areas called *Aschoff's bodies* appear which, when they heal, leave thick fibrous tissue. Thrombotic fibrous nodules consisting of platelets and fibrin form on the free borders of the cusps of the heart valves. When healing occurs the fibrous tissue formed shrinks as it ages, distorting the shape of the cusps and causing stenosis and incompetence of the valve. The mitral and aortic valves are commonly affected, the tricuspid valve sometimes and the pulmonary valve rarely.

Effects on the myocardium

Aschoff's bodies form on the connective tissue between the cardiac muscle fibres. As in the endocardium, healing is accompanied by fibrosis which may interfere with myocardial contraction.

Effects on the pericardium

Inflammation leads to the accumulation of exudate in the pericardial cavity. Healing is accompanied by fibrous thickening of the pericardium and adhesions form between the two layers. In severe cases the layers may fuse, obliterating the cavity. Within this inelastic pericardium the heart may not be able to expand fully during diastole, leading to reduced cardiac output, generalized venous congestion and oedema.

Sydenham's chorea

This usually occurs between the ages of 5 and 15 years. The causes are unknown but it is commonly associated with streptococcal throat infection, rheumatic fever or endocarditis. There are rapid, uncoordinated, involuntary muscle movements. In mild cases recovery takes place within about 4 weeks. In some cases the initial recovery may be followed by recurrences.

Choreiform movements may occasionally occur during pregnancy, in women taking contraceptive pills and following cerebrovascular lesions, especially in the elderly.

Subclinical rheumatic heart disease

Valvular incompetence developing in older people who have a history of rheumatic fever many years previously is believed to be due to repeated subclinical attacks. These attacks are not associated with repeated episodes of sore throat so it is assumed that the original disease has remained active in a subclinical form. In some cases there is no history of rheumatic fever.

INFECTIVE ENDOCARDITIS

Pathogenic organisms in the blood may colonise any part of the endocardium but the most common sites are on or near the heart valves and round the margins of congenital heart defects. These areas are susceptible to infection because they are exposed to fast-flowing blood that may cause mild trauma.

The main predisposing factors are bacteraemia

Depressed immune response and heart abnormalities.

Bacteraemia

Microbes may or may not multiply while in the bloodstream and, if not destroyed by phagocytes or antibodies, they tend to adhere to platelets and form tiny infected emboli. Inside the heart the emboli are most likely to settle on already damaged endocardium. Vegetations consisting of platelets and fibrin surround the microbes and seem to protect them from normal body defences and antibiotics. Because of this, infection may be caused by awide range of microbes, including some of low pathogenicity, e.g.:

- Non-hemolytic streptococci, e.g. following tooth extraction, tonsillectomy
- *Escherichia coli* and other normal bowel inhabitants,
- E.g. following intestinal surgery
- *Staphylococcus aureus,* e.g. from boils and carbuncles
- Microbes from infections of, e.g., the biliary, urinary, respiratory tracts
- Microbes accidentally introduced during medical and nursing procedures, e.g. cystoscopy, bladder catheterisation, arterial and venous cannulation, surgery, wound dressing
- Low-virulence microbes that cause infection in people with reduced immune response.

Depressed immune response

This enables low-virulence bacteria, viruses, yeasts and fungi to become established and cause infection. These are organisms always present in the body and the environment.

Depression of the immune systems may be caused by

- Cytotoxic drugs
- ionizing radiation, e.g. X-rays used in cancer treatment
- Anti-inflammatory drugs, e.g. corticosteroids
- Malignant diseases, e.g. leukemia, tumours of lymphoid tissue
- Sharing of syringes by drug addicts, spreading human immunodeficiency virus (HIV).

Heart abnormalities

The sites most commonly infected are already abnormal in some way, e.g. valve cusps damaged by earlier attacks of rheumatic fever, endothelium damaged by the fast flow of blood through a narrow opening, such as a stenosed valve or congenital septal defect.

ACUTE INFECTIVE ENDOCARDITIS

This is a severe febrile illness usually caused by high virulence microbes, commonly *Staphylococcus aurous.* Vegetations grow rapidly and pieces may break off, becoming infected emboli. These settle in other organs where the microbes grow, destroying tissue and forming pus. The effects depend on the organ involved, e.g. brain or kidney infection may cause death in a few days. The causative microbes rapidly destroy heart valves, impairing their function and resulting in acute heart failure.

SUBACUTE INFECTIVE ENDOCARDITIS

This endocarditis is usually caused by low-virulence microbes, e.g. non-haemolytic streptococci or some staphylococci. Infected emboli may settle in any organ but do not cause suppuration and rarely cause death. Microbes in the vegetations seem to be protected by surrounding platelets and fibrin from normal body defences and antibiotics. Healing by fibrosis further distorts the shape of the valve cusps, increasing the original stenosis and incompetence. Heart failure may develop later.

CARDIAC ARRHYTHMIAS

The heart rate is normally initiated by intrinsic impulses generated in the SA node. The rhythm is determined by the route of impulse transmission through the conducting system. The heart rate is usually measured as the pulse, but to determine the rhythm, an electrocardiogram (ECG) is required (Fig. 5.58A). A *cardiac arrhythmia* is any disorder of heart rate or rhythm, and is the result of abnormal generation or conduction of impulses. The normal cardiac cycle (p. 88) gives rise to *normal sinus rhythm* which has a rate between 60 and 100 beats per minute.

Sinus bradycardia

This is sinus rhythm below 60 beats per minute. This may occur during sleep and is common in athletes. It is an abnormality when it follows myocardial infarction or accompanies raised intracranial pressure.

Sinus tachycardia

This is sinus rhythm above 100 beats per minute when the individual is at rest. This accompanies exercise and anxiety; but is an indicator of some disorders, e.g. fever, hyperthyroidism, some cardiac conditions.

ASYSTOLE

This occurs when there is no electrical activity in the ventricles and therefore no cardiac output. The ECG shows a flat line (Fig. 5A). Ventricular fibrillation and asystole cause sudden and complete loss of cardiac output, i.e. *cardiac arrest* and death.

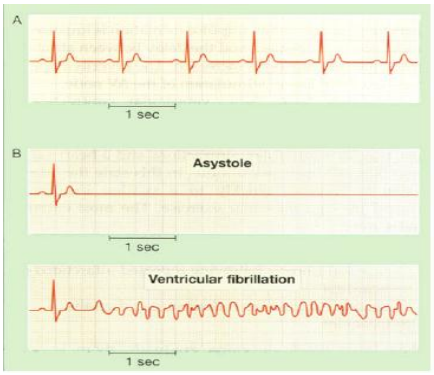

Figure No. 05: ECG traces: A. Normal sinus rhythm. B. Life-threatening Arrhythmias.

Fibrillation

This is the contraction of the cardiac muscle fibres in a disorderly sequence. The chambers do not contract as a whole and the pumping action is disrupted. In *atrial fibrillation* contraction of the atria is uncoordinated and rapid, pumping is ineffective and stimulation of the AV node is disorderly. Ventricular contraction becomes rapid and rhythm and force irregular; although an adequate cardiac output and blood pressure may be maintained, the pulse is irregular. The causes of increased excitability and disorganised activity are not always clear but predisposing conditions include:

- Ischaemic heart disease
- Degenerative changes in the heart due to old age
- Thyrotoxicosis
- Rheumatic heart disease.

In *ventricular fibrillation* there is disorganised and very rapid contraction causing disruption of ventricular function. Blood is not pumped from the heart into either the pulmonary or the systemic circulation. No pulses can be felt; consciousness is lost and breathing stops. The ECG shows an irregular chaotic trace with no recognizable wave pattern (Fig. 5B). If normal heart action cannot be restored quickly, death follows due to cerebral anoxia.

HEART BLOCK

Heart block occurs when impulse formation is impaired or conduction is prevented, and the delay between atrial and ventricular contraction is increased. The severity depends on the extent of loss of stimulation of the AV node. In *complete*

heart block, ventricular contraction is entirely independent of impulses initiated by the SA node. Impulses generated by the AV node result in slow, regular ventricular contractions and a heart rate of about 30 to 40 beats per minute. In this state the heart is unable to respond quickly to a sudden increase in demand by, e.g., muscular exercise. The most common causes are:

- Acute ischaemic heart disease
- Myocardial fibrosis following repeated infarctions or myocarditis
- Drugs used to treat heart disease, e.g. digitalis, propranolol.

When heart block develops gradually there is some degree of adjustment in the body to reduced cardiac output but, if progressive, it eventually leads to death from cardiac failure and cerebral anoxia. **Figure 6** The position of the ductus arteriosus in the fetus. The arrow indicates the direction of flow of blood from the pulmonary circulation into the aorta.

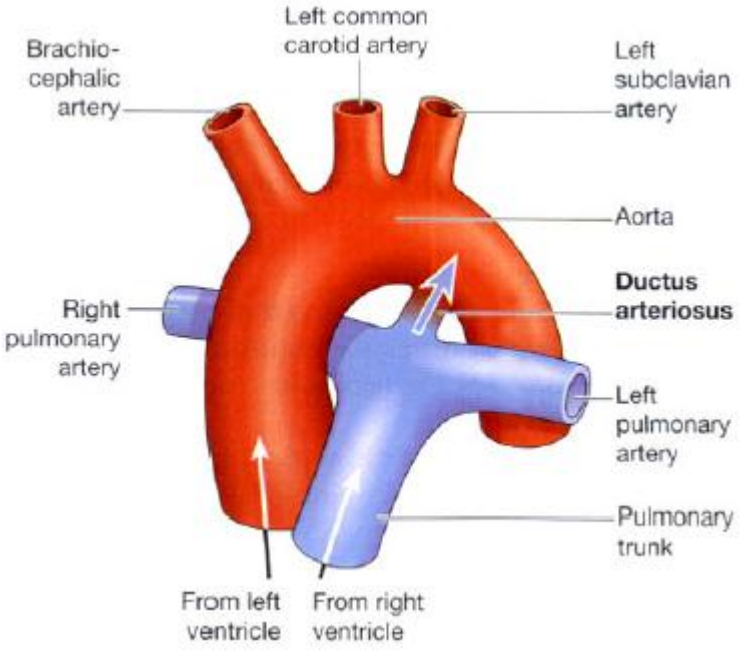

Figure No. 06: The position of the ductus arteriosus in the fetus. The arrow indicates the direction of flow of blood from the pulmonary circulation into the aorta.

CONGENITAL ABNORMALITIES

Abnormalities in the heart and great vessels at birth may be due to intrauterine developmental errors or to the failure of the heart and blood vessels to adapt to extrauterine life. Sometimes, there are no symptoms in early life and the abnormality is recognized only when complications appear.

Patent ductus arteriosus

Before birth the ductus arteriosus, joining the arch of the aorta and the pulmonary artery, allows blood to pass from the pulmonary artery to the aorta (Fig. 6). It carries blood pumped into the pulmonary trunk by the right ventricle into the aorta, bypassing the pulmonary circulation. At birth, when the pulmonary circulation is established, the ductus arteriosus should close completely. If it remains patent, blood regurgitates from the aorta to the pulmonary artery where the pressure is lower, reducing the volume entering the systemic circulation and increasing the volume of blood in the pulmonary circulation. This leads to pulmonary congestion and eventually cardiac failure.

Atrial septal defect

Before birth most oxygenated blood from the placenta enters the left atrium from the right atrium through the*foramen ovale* in the septum. There is a valve-like structure across the opening consisting

of two partly overlapping membranes. The Valve' is open when the pressure in the right atrium is higher than in the left. This diverts blood flow from the right to the left side of the heart, bypassing the pulmonary circulation. After birth, when the pulmonary circulation is established and the pressure in the left atrium is the higher, the two membranes come in contact, closing the 'valve'. Later the closure becomes permanent due to fibrosis (Fig. 5.60). When the membranes do not overlap an opening between the atria remains patent after birth. In many cases it is too small to cause symptoms in early life but they may appear later. In severe cases blood flows back to the right atrium from the left. This increases the right ventricular and pulmonary pressure, causing hypertrophy of the myocardium and eventually cardiac failure. As pressure in the right atrium rises, blood flow through the defect may be reversed, but this is not an improvement because deoxygenated blood gains access to the general circulation.

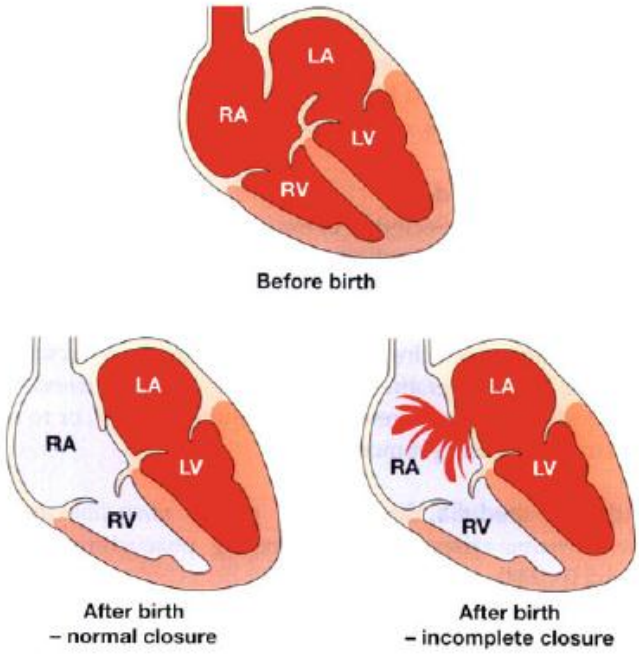

Figure No. 07: Atrioseptal valve: normal and defective closure after birth.

Coarctation of the aorta

The most common site of coarctation (narrowing) of the aorta is between the left subclavian artery and ductus arteriosus. This leads to hypertension in the upper body (which is supplied by arteries arising from the aorta proximal to the narrowing) because increased force of contraction of the heart is needed to push the blood through the coarctation. There is hypotension in the rest of the body.

Fallot's tetralogy

A characteristic combination of four congenital cardiac abnormalities, called the tetralogy of Fallot, causes cyanosis, growth retardation and exercise intolerance in babies and young children. The four abnormalities are:

- Stenosis of the pulmonary artery at its point of origin, which increases right ventricular workload
- Ventricular septal defect, i.e. an abnormal communicating hole between the two ventricles, just below the atrioventricular valves
- Aortic misplacement, i.e. the origin of the aorta is displaced to the right so that it is immediately above the septal defect
- Right ventricular hypertrophy to counteract the pulmonary stenosis. Cardiac function is inadequate to meet the needs of the growing child; surgical correction carries a good prognosis.

DISORDERS OF BLOOD PRESSURE

Hypertension

The term hypertension is used to describe blood pressure that is sustained at a higher than the generally accepted 'normal' maximum level for a particular age group,

e.g.:

- At 20years-140/90mmHg
- At 50years-160/95mmHg
- At 75 years -170/105 mmHg.

Arteriosclerosis contributes to increasing blood pressure with age but is not the only factor involved. Hypertension is described as *essential* (primary, idiopathic) or *secondary to other diseases*. Irrespective of the cause, hypertension commonly affects the kidneys

Essential hypertension

This means hypertension of unknown cause. It accounts for 85 to 90% of all cases and is subdivided according to the rate at which the disease progresses.

Benign (chronic) hypertension

The rise in blood pressure is usually slight to moderate and continues to rise slowly over many years. Sometimes complications are the first indication of hypertension.

E.g. heart failure, cerebrovascular accident, myocardial

Infarction. Occasionally the rate of progress increases and the hypertension becomes malignant.

Predisposing factors include

Inherited tendency obesity excessive alcohol intake cigarette smoking lack of exercise.

- Inherited tendency
- Obesity
- Excessive alcohol intake
- Cigarette smoking
- Lack of exercise.

Malignant (accelerated) hypertension

The blood pressure is already elevated and continues to rise rapidly over a few months. Diastolic pressure in excess of 120 mmHg is common. The effects are serious and quickly become apparent, e.g. haemorrhages into the retina, papilloedema (oedema around the optic disc), encephalopathy (cerebral oedema) and progressive renal disease, leading to cardiac failure.

Secondary hypertension

Hypertension resulting from other diseases accounts for 10 to 15% of all cases.

Kidney diseases

Raised blood pressure is a complication of many kidney diseases. The vasoconstrictor effect of excess *renin* released by damaged kidneys is one causative factor but there may be others, as yet unknown.

Endocrine disorders

Adrenal cortex

Secretion of excess *aldosterone* and *cortisol* stimulates the retention of excess sodium and water by the kidneys, raising the blood volume and pressure. Oversecretion of aldosterone (Conn's syndrome) is due to a hormone-secreting tumour. Oversecretion of cortisol may be due to overstimulation of the gland by *adrenocorticotrophic hormone* secreted by the pituitary gland, or to a hormone-secreting tumour.

Adrenal medulla

Secretion of excess *adrenaline* and *noradrenaline* raises blood pressure, e.g. phaeochromocytoma

Stricture of the aorta

Hypertension develops in branching arteries proximal to the site of a stricture. In *congenital coarctation* the stricture is between the ductus arteriosus and the left subclavian artery causing hypertension in the head, neck and right arm. Compression of the aorta by an adjacent tumour may cause hypertension proximal to the stricture.

Hypertension may be a complication of some drug Treatment

e.g.:

- Corticosteroids
- Non-steroidal anti-inflammatory drugs
- Oral contraceptives.

Effects and complications of hypertension

The effects of long-standing and progressively rising blood pressure are serious. Hypertension

predisposes to atherosclerosis and has specific effects on particular organs.

Heart

The rate and force of cardiac contraction are increased to maintain the cardiac output against a sustained rise in arterial pressure. The left ventricle hypertrophies and begins to fail when compensation has reached its limit. This is followed by back pressure and accumulation of blood in the lungs (pulmonary congestion), hypertrophy of the right ventricle and eventually to right ventricular failure. Hypertension also predisposes to ischaemic heart disease (p. 121) and aneurysm formation.

Brain

Stroke, caused by cerebral haemorrhage, is common, the effects depending on the position and size of the ruptured vessel. When a series of small blood vessels rupture, e.g. microaneurysms, at different times, there is progressive disability. Rupture of a large vessel causes extensive loss of function or possibly death.

Hypertensive encephalopathy

Hypertensive encephalopathy is a rare condition in which hypertension is accompanied by neurological disturbance, e.g. papilloedema, difficulty with speech, paraesthesia, convulsions and loss of consciousness. It is usually reversed when hypertension is controlled.

Kidneys

Essential hypertension causes kidney damage. If sustained for only a short time recovery may be complete. Otherwise the kidney damage causes further hypertension owing to activation of the renin-angiotensin-aldosterone system (p. 223), progressive loss of kidney function and kidney failure.

PULMONARY HYPERTENSION

Raised blood pressure in the pulmonary circulation is secondary to:

- Changes in blood vessels, described above chronic diseases of the respiratory system
- Diseases of the heart, e.g. congenital defects of the septum, stenosis and incompetence of the mitral or aortic valve, heart failure diseases of other organs that cause raised pressure in the left side of the heart, e.g. cirrhosis of the liver, thrombosis of the portal vein.

Hypotension

This usually occurs as a complication of other conditions, e.g.:

- Shock
- Addison's disease

Low blood pressure leads to inadequate blood supply to the brain. Depending on the cause, unconsciousness may be brief (fainting) or more prolonged, possibly causing death. *Postural hypotension syncope* (fainting) is due to sudden reduction in blood pressure on standing up quickly from a sitting or lying position. It occurs most commonly in the elderly. It may be caused by delay in response of the baroreceptors in the carotid sinuses to the gravitational effects of standing up. It may also occur when patients are being treated with antihypertensive drugs, especially when the most appropriate dose is being established.

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