on T extrasystole). See fig. 3.53 on page 248 and fig. 3.54 on page 248.

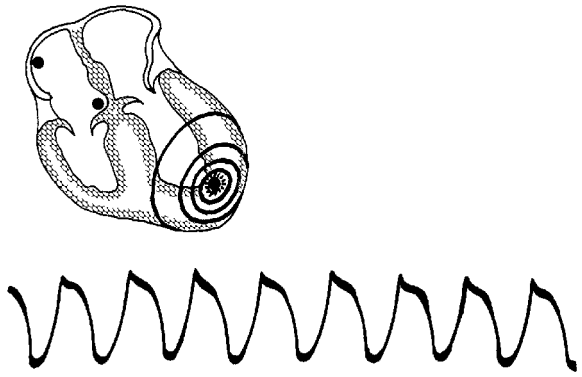

Figure 3.53: Ventricular flutter

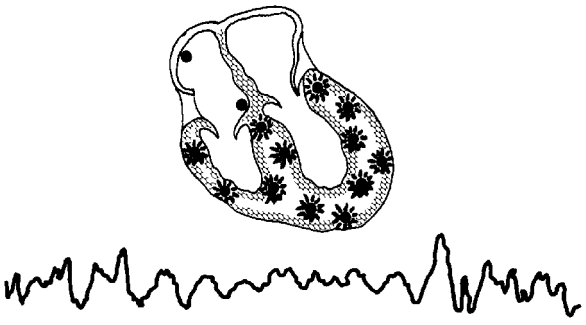

Figure 3.54: Ventricular fibrillation

3.27.5 Pathophysiological outcomes of antiarrhythmic treatment

In antiarrhythmic treatment it is necessary to consider all the pathological changes, which can cause arrhythmia, maintain it, or initiate it. The removal of these nonsuitable conditions is first aim. Then we have to consider the fact that antiarrhythmic drugs have proarrhytmogenic effect. The aim of treatment can be to terminate arrhythmia or to prevent its occurrence.

The choice of the proper antiarhythmics is quite difficult. Antiarrhythmics have some exactly defined characteristics, considering their effect on the electric process on the cellular membranes. Yet the doctor does not know how these processes take place on the patients cellular membranes. He only knows the result which is arrhythmia. That is why we recently appreciate testing the effects of antiarhytmics in programmed stimulation. For example: in induced ventricular tachycardia we found out that antiarrhythmics really lead to the prevention of ventricular tachycardia after stimulation. Yet programmed stimulation and intravascular catheterization are procedures which have some limits due to many risks.

Antiarrhythmics are agents that affect the depolarizing Na^{2+} and Ca^{2+} ion currents, the process of action potential, and cellular automacity. For example, if we depress the depolarizing currents, slowing in the impulse conduction will be resulted and so we can terminate arrhythmia by blocking the impulse conduction in these areas where they are already slow. Another type of antiarrhytmics lead to the prolongation of action potential and hence the prolongation of the refractory period. These effects are defined precisely on isolated myocytes. The effect of antiarrhytmic drug in vivo may differ. Besides the fact that the heart architecture is very complicated and we can not calculate with it in using of antiarrhythmics. Arrhythmia usually have a morphological substrate for a reentry mechanism, in which some cells or cardiac areas are incorporated. But antiarrhythmic drugs effect all cardiac cells equally. Therefore, it is necessary to reevaluate the proarrhythmogenic effects of antiarrhythmics in each individual patient.

3.28 Diseases of the venous system

Veins are capacity vessels which secure the venous return of blood to the heart. Changes in the venous return affect the minute heart volume. The entire

venous circulation is affected to a decisive extent by **central venous pressure**, i.e. blood pressure in large veins, in clinical practice being measured in the right atrium (0,8 kPa, event. 6 torr). It is determined by the equilibrium between the heart pumping function and venous return.

The low-pressure easily distensible venous system contains 60--80 % of the total blood volume. Changes in the capacity of this system are conditioned by passive dilatation (e.g. hydrostatic pressure effect), as well as active venoconstriction. General venoconstriction increases the venous return. It is applied in situations requiring an increased minute heart volume, e.g. due to muscle excercise and stress, or due to a pathologically decreased minute heart volume, e.g. due to failure of the left ventricle.

Veins of the lower extremities are formed by superficial and profound venous systems which are transconnected by a system of joining veins. Under physiological conditions, the venous return leads blood from the superficial veins to those profound. The superficial veins lead 10 % and those profound (the so-called collecting veins) 90 % of blood.

In addition to mechanisms which support the blood flow in veins (changes in intrathoracic pressure, pulsation pressure of arteries upon the venous wall), the venous return is secured by two compensatory mechanisms which maintain pressure in the venous system on a relatively low level. They are **venous bicuspidal valves**, the number of which decreases in the proximal direction, and the muscle-veins pump which functions on the principle of rhythmic compression and decompression of veins owing to the work of the lower extremities muscles.

Contraction of limb muscles augments pressure upon the due segment of the profound vein seven fold. The valves under the site of compression close, those above the compression site open and thus blood flows toward the heart. During the relaxation phase the pressure situation reverses. The pressure in the due segment of the profound vein decreases rapidly; that in the cranial and distal segments, as well as in the superficial venous system, increases. The valves in cranial segments of the profound vein close and inhibit the backflow of blood towards the periphery. The valves localized more distally, as well as the valves of joining veins and valves of the superficial venous system open and the due segment refills with blood.

Dysfunction of these compensatory mechanisms (insufficiency of venous valves, long lasting immobilization of patients) augments the hydrostatical pressure in veins and causes the development of venous insufficiency.

The most important diseases of the venous system are represented by varices. thrombophlebitis and phlebothrombosis. The most serious consequences of these states are chronic venous insufficiency and pulmonary embolism.

3.28.1 Varices

Varices are sack-shaped bulges of superficial veins due to which they acquire a tortuous course. They are most frequently localized on the lower limbs (**varics cruris**) and inflict women twice as often as men. Their origin is stimulated by a long-term elevation of venous pressure in the lower limbs (professions performed in upright position and associated with lifting of heavy burdens, obesity, wearing compressing suspenders, the pressure of a pregnant womb upon large venous trunks, etc.) **Primary varices** originate due to an inborn weakness of the connective tissue (collagen) in vein walls, which results in loss of resistance against overstrain. **Secondary varices** originate due to impairment of compensatory mechanisms and venous hypertension, Most frequently, they originate due to inflammation of the profound venous system after trauma, or due to arteriovenous fistula. Secondary varices represent channels which compensate the impairment of the venous return via profound veins.

Pathologically, varices are based on venous valvular insufficiency leading to severe haemodynamical changes. Blood flows in an opposite direction as under physiological conditions, thus the venous return directs from the profound (collecting) veins towards the superficial veins. The muscle-vein pump is in consequence of valvular insufficiency dysfunctional and in such cases gait does not improve circulation. Superficial veins are overfilled, the blood flow deteriorates, venous pressure is not improved by gait, on the contrary, it elevates. Venous hypertension supervenes (mean venous pressure in the dorsum of the foot increases above 4,0 kPa, event. 30 torr) and the superficial veins distend.

The first stage of the disease involves simple dilatation of veins without valvular impairment. An unimpaired valvular apparatus secures reduction of

pressure in veins during orthostasis or gait, therefore swellings do not occur. **The second stage of the disease** merely involves valvular insufficiency of superficial veins. The venous pressure does not decrease during gait or orthostasis. It is reduced only due to obviation of filling of superficial veins with blood due to compression of the limb, namely cranially from the inflicted site. **The third stage** supervenes when valves of the profound venous system become also inflicted and thereby the venous pressure does not decrease due to muscular contraction during gait or orthostasis. **In the fourth stage**, valves of the joining veins, and/or in the ostia of v.saphena magna or v.saphena parva are insufficient. Decompensation of the venous system supervenes and **chronical venous insufficiency** develops, manifesting itself by a picture of varicose complex: swelling of the limb, hyperpigmentation of the skin, subcutaneous inflammation with a subsequent induration, eczema, and the most severe complication -- ulcus cruris.

Varices occur also in the rectum (nodi haemorrhoidales externi et interni). They originate in consequence of the development of a collateral circuit. Their origin is stimulated by sedentary mode of life, constipation, or on the contrary, by diarrhoea. Portal hypertension often brings about, due to the development of collateral circuits, the oesophageal varices. Their rupture usually results in fatal bleeding.

3.28.2 Thrombophlebitis

Thrombophlebitis **is inflammation of the venous wall secondarily accompanied by formation of thrombus**. The thrombus firmly adheres to the vessel wall and causes its partial or total occlusion. Thrombophlebitis inflicts prevailingly the veins of the superficial venous system. It is three times more frequent in women than in men and its incidence increases with age. Embolization is rare.

Pathogenetically, phlebitis is caused by irritation of the venous wall and subsequent inflammation, the irritation being of chemical, microbic, mechanical, or other character, eventually by pervasion of the inflammatory process from the surrounding tissues (periphlebitis). In the consequence of inflammatory impairment of the vascular endothelium, the blood corpuscles get into contact with subendothelially layed collagen fibrils which in turn stimulate blood coagulation. Haemocoagulation is enhanced by the slowing of the blood flow and changes in blood clotting. The predisposition factors of thrombophlebitis include the following: surgical interventions, injuries, infectious diseases, intravenous injections, lasting immobilization, obesity, and hereditary dispositions.

According to its ethiology, thrombophlebitis can be of primary or secondary character. **The primary** thrombophlebitis includes idiopathic thrombophlebitis which occurs in healthy people without an obvious reason, and thrombophlebitis migrans which represents the initial symptom of thrombangiitis obliterans. **The secondary** thrombophlebitis occurs more often. It can be of local, superficial or profound character.

Superficial thrombophlebitis occurs most frequently. It manifests itself by the reddening and warming of the skin, swelling, tension and pain along the inflicted vein. It represents the least serious process. When there are no complications, there is no threat of embolization.

Profound thrombophlebitis is more serious, as it disables drainage from a larger area and endangers the patient by the possibility of occurence of thromboembolic complications. Most frequently it inflicts veins of the lower limbs, it may though occur in other sites. The visceral thrombophlebitis is also known to occur (in kidneys, spleen, liver, intestines, uterus, prostate, cerebral hemispheres, eyes, etc.)

3.28.3 Phlebothrombosis

Phlebothrombosis is an intravital blood coagulation within veins. It inflicts the veins of the profound system. In contrast with thrombophlebitis, the thrombi in phlebothrombosis are formed primarily, and not in consequence of inflammation. The thrombi are loose, later they may, often only partially, adhere to the venous wall. They can evoke a reactive inflammation, and the profound phlebothrombosis can turn during several hours or days into thrombophlebitis. These facts represent the reason why it is often impossible to distinguish phlebothrombosis from thrombophlebitis and vice versa in clinical practice. The most feared complication of phlebothrombosis is migration of the torn off thrombi into the lungs, thus causing pulmonary embolism. Phlebothrombosis occurs more frequently in women than in men and its incidence increases with age.

Since 1856, the **main** ethiological factors of the phlebothrombosis origin are being considered to be

three compounds of the Virchow's triade: slowing down of blood flow, vessel wall lesion, and changes in blood coagulation. Aggregation of thrombocytes and their adhesion to the vessel wall takes place at the beginning of thrombosis, though minute thrombi adhering to the vessel are dissolved by the fibrinolytic system. Later, the balance between the coagulation and fibrinolytic systems becomes disturbed and phlebothrombosis is at its onset. The origin of phlebothrombosis is usually evoked by participance of the following factors: surgical intervention, bone fracture, tissue contussion, bleeding, lasting immobilization, parturition, abortion, infectious diseases, malign neoplasms, etc.. The **predisposition** factors of the phlebothrombosis origin include: obesity, ageing, lack of excercise, disturbances of lipid metabolism, and cardiac decompensation.

The veins obstructed with thrombi disable drainage from the due area, subsequently transsudation of fluids into the surrounding tissue supervenes and edema originates. The status can be deteriorated by reflex spasms in the surrounding veins. The healing is secured by spontaneous fibrinolysis which leads to a partial or entire recanalization of the vein. The healing though, is not absolute, the valves remain permanently impaired and the disease leads to a chronic venous insufficiency (postthrombotic syndrome).

Many cases of profound phlebothrombosis are clinically latent, and they often become clinically manifested later by pulmonary embolism.

3.28.4 Pulmonary embolism

Pulmonary embolism is a pathophysiological and clinical status which is inaugurated by occlusion of a.pulmonalis vascular network. It originates most frequently along with the thromboembolic disease, the cause of occlusion being the embolus originating in the venous system by thrombus liberation. Less frequent etiologic factors of pulmonary embolism include drops of fat, air bubbles, aggregations of leucocytes, or loosened pieces of neoplasms, eventually amnionic fluid, etc.. Pulmonary embolism represents the third most frequent cardiovascular disease.

Etiopathogenesis of the thromboembolic disease is partially described in the article dealing with phlebothrombosis. Emboli have their source prevailingly in the profound venous system of the lower limbs (90 %), less frequently in plexuses of the small pelvis and abdomen. Emboli from the right chambers of the heart originating due to arrhythmias, especially due to fibrillations of atrii also occur. The supporting factors of pulmonary embolism include inactivity and immobilization, especially in older patients, those with tumours or hemiplegias, after surgery, protracted parturitions, severe injuries, massive bleeding, etc.. Embolization often takes place after an abrupt change of a recumbent to an erect position (after prolonged confinement in bed), or at defecation. Pulmonary embolism often represents the first symptom of venous thrombosis. In some patients neither repeatedly performed examinations make it possible to discover the particular source of embolization.

Embolization of a.pulmonalis may be clinically manifested in an acute or chronic form. The **acute form** includes massive pulmonary embolism and multiple embolism. The course of **the chronic form of embolism** of a. pulmonalis bears the character of pulmonary microembolization.

The primary event in **massive pulmonary embolism** is the occlusion of one or both main branches of a.pulmonalis, thus excluding more than 50 % of the pulmonary vascular network. Such a state imminently endangers life. 50 % of such cases result in sudden death, in the rest of them the clinical picture is severely dramatic (severe dyspnoe, retrosternal pain, cough, hemoptysis, tachycardia, anxiety, restlessness, cyanosis and cardiogenic shock). Massive pulmonary embolism often immitates the picture of acute cardiac infarction.

Multiple pulmonary embolism inflicts some lobal and segmental branches of a.pulmonalis. It represents the most frequent form of pulmonary embolism. It manifests itself as **pulmonary infarction**. It originates due to insufficiency of nutritive bronchial circulation in consequence of pulmonary venostasis or a major decrease of the systemic pressure.

Microembolization of the lungs manifestats itself as a chronic form of a.pulmonalis embolism. It involves the occlusion of arterioles and capillaries of the pulmonary vascular network. It occurs in cases of succesive multiple embolization of the lungs, which leads to gradual obturations of the peripheral branches of a. pulmonalis.

Respiratory, hemodynamic and metabolic acute manifestations are very variable and depend on the severity of the disease. Though the part of the lungs

behind the site of obstruction in pulmonary embolism is ventilated, it is not perfused. Ventilation of the nonperfused pulmonary region does not fulfill its function. There occurs an intrapulmonary, so-called *dead space*. Within this space, bronchioloconstriction takes place due to alveolar hypocapnia. The origin of alveolar collapse and subsequent atelectasis occur later as a consequent of a partaking decrease of lipoproteins (surfactant) which maintain the alveolar surface tension. A 50 % reduction of the pulmonary vascular capacity increases the pulmonary resistance and subsequently leads to pulmonary hypertension which possibly results in an acute heart failure (cor pulmonale acutum). The acute hypertension overstrains the right heart, the pressure in the right ventricle elevates at the end of diastola. In consequence of an insufficient blood inflow towards the left heart, the minute heart expenditure decreases and the systemic pressure in spite of tachycardia rapidly drops. Severe embolization causes a shock or sudden death due to circulation failure or ventricular fibrillation.

Besides the mechanical obstruction, microembolization of the lungs involves also vasoconstriction and bronchiololconstriction of the uninflicted area. It is not clear if the process involves a reflex mechanism, or whether it originates due to humoral stimulation of local mediators arisen from the ischaemic area. Microembolization of the lungs takes place without any specific clinical symptoms, sometimes symptomless and cor pulmonale chronicum develops only after repeated embolization.

The process of healing of pulmonary embolization involves two mechanisms, the fibrinolytic process and thrombus organization. The majority of emboli is relatively quickly dissolved and the occluded vessels recanalize. Minority is subdued to organization resulting in small mural scars and intravascular *bridges*.

Paradoxical embolism supervenes when thrombi arisen from the venous system cause embolization of the systemic circulation circuit. It may occur in patients with an inborn defect of the atrial septum during the change of the left-right shunt to the right-left shunt.

3.28.5 Chronic venous insufficiency

The chronic venous insufficiency may represent consequence, eventually the complication of any of vein diseases. Most frequently it develops after thromboses of the profound veins (the so-called post-thrombotic syndrome), less frequently after inflammation of the superficial veins (the so-called post-phlebitis syndrome), or after extensive varices, often without clear precedent signs of thrombosis or phlebitis (the so-called varicose complex).

Manifestation of chronic venous insufficiency is composed of three groups of symptoms: swelling of the limbs, hyperpigmentation of the skin, subcutaneous inflammation with subsequent induration, eczema, and the most serious complication – ulcus cruris.

Pathophysiologically, the chronic venous insufficiency is based on **permanent venous hypertension**. At the mean venous pressure being above 6,0 kPa, eventually 45 torr, the venostasis and venous hypertension increase to such an extent that it interferes also the capillary network. The balanced state becomes impaired, filtration prevails resorption, thus resulting in edema formation. The origin of such local hydrostatic edema is later also affected by participation of capillary permeability alteration which supervenes due to hypoxia. The growth of protein content in the edema fluid is caused also by compression of lymphatic capillaries, which leads to abrogated elimination of proteins from the interstice. Hence, in final consequence, the impairment of both venous and lymphatic drainage participate in the edema origin in venous diseases.

Diapedesis of erythrocytes and macromollecular proteins, and stagnation of metabolites lead to secondary skin alterations. Hyperpigmentation supervenes due to presence of hemosiderin caused by break-down of erythrocytes. Macromollecular proteins act as alien material and thus cause sterile imflammation, in turn leading to proliferation of the connective tissue, subcutaneous induration, skin atrophy, and finally to ulcus cruris. The chronic venostatic eczema represents a sign of impaired skin trophicity.

Advanced stages of chronic venous insufficiency may display subcutaneous bone metaplasis and restriction of anckle movement.