Thrombophlebitis and thrombosis of the cerebral venous system lead to a picture of **pseudotumorous encephalopathy** (being an elevated intracranial pressure with no proved expanding process). Thrombosis and thrombophlebitis have a relatively higher incidence during gravidity and puerperium. The reason of this is the higher heamocoagulability, arterial infections of the genitalia which is common in these situations as well as the possible migration of the thrombophlebitis from the pelvic area intracranially through the vertebral plexuses.

The clinical manifestation of this condition is usually headache, symptoms of a space occupying lesion (SOL) in the brain, signs of an elevated intracranial pressure, and possibly signs of infection.

3.25 The basis of the electrical action of the heart

The cell is a structural unit in all living organisms. The cellular membrane has an important role in all the electric events that precede the contraction. **Cellular membranes** are complicated structures that protect the intracellular environment. They have special systems which have the ability to recognize structures being that is known as massangers. These can carry information to internal organelles. Membranes are lipid structures or layers which are interrupted by protein molecules. Soluble substances in the extra cellular space can pass intracellulary by simple diffusion or active transport where the protein receptors in the cell membrane take part. Phospholipids are the building units apart from them are the neutral fat and glycolipids. The lipids form polar hydrophilic heads and non polar hydrophobic ends.

The membrane proteins are arranged asymmetrically. Sometimes they surround lipid rings and hence form some non specific hydrophilic configurations which act as channels through which electrolytes can pass. Some membrane protein are mobile, they can rotate or change their position in the membrane.

The transmembrane transport (flux) can be active or passive. Influx means the in–flow of solutes and the out–flow is know as efflux. The passive transport takes place along the electrochemical gradient and depends on the concentration gradient of the solutes. The active transport occur against the electrochemical gradient, still not all the power sources taking place in the active transport are known. The active transport needs energy supply which is mainly from the ATP. Most probably the active transport is the result of no equilibrium of ions and electric charges on both sides of the membrane. Na^+ and Cl^- are predominantly extracellular ions whereas K^+ is main intracellular ion. Nernst equation shows the state of equilibrium:

$$V_x = -61,5 \cdot \frac{1}{z} \cdot \log \frac{ion_i}{ion_e}$$

ion_e = extracellular concentration of the ion;
ion_i = intracellular concentration of the ion;
z = the ion charge, e.g.: +1 for K^+, +2 for Ca^{2+}, -1 for Cl^-)
V_x = the equilibrium state (tension) for choice ion.

The ATP-ase enzyme is unequally distributed in the cell membrane and it can change its position. When the ATP-ase is directed intracellularly (to the inside) it has a high affinity to Na^+. When it is directed to the outside it has a higher affinity to K^+. The Na^+–ATP-ase binding leads to ATP-ase hydrolysis which first step is the enzyme phosphorilation. The following conformation change rotates the enzyme along with the bound Na+ to face the extracellular fluid, in this condition the affinity to Na^+ decreases with a simultaneous increase in the affinity to K^+. The phosphorilated enzyme then makes an exchange by giving Na^+ and taking K^+ instead.

Then another conformation change will rotate the K^+–ATP-ase to face intracellularly where the K+ ion is exchanged by Na^+. This process continues and the in-flowing Na^+ is expelled extracellularly when on the other hand the lost K^+ions are returned back into the cell. Yet this process is not equivalent because for pumping 3 Na^+ moles extracellularly only 2 K^+ moles are returned back and one mole of ATP is used. This mechanism is known as the Na^+–K^+ pump.

Many living cells make use of the differences in the electric charge across the membranes in regulating physiological functions. Muscle fibers and neurons make use of the electric charge of their membranes in the regulation of their permeability, releasing neu-

rotransmitters, Ca^{2+} release for contraction, and in the secretion of some substances.

With the appropriate stimulation the neurons and muscle fibers have the ability to change their electrical characteristics – A wave of excitation can take place in the membranes or the near by cells which will eventually lead to a change in the electrical character of these membranes. As a result there is an influx of the positive charged particles (Na^+ and K^+) into the cells. The influx of these ions is mediated by special sensors for voltage changes. The polar molecules in the membranes represent those sensors and they have high charge resp. high dipole moment. These polar highly charged molecules change their conformation as a response to the electric changes.

Channels present in the cell membrane by which the Na^+ influx takes place are known as the fast channels. These channels are regulated by 2 gates being the m and h gate which are localized one behind the other. At rest the gate h is opened end gate m is closed. When the cell is stimulated and the potential reaches -60 mV (-40 mV) (this is known as the threshold potential) the gate m opens fast mean while the gate h starts to close. The closure of gate h is 3-4 times slower than the gate m opening and due to this there will be a small portion of time when both gate m and gate h are opened so that the Na^+ ions enter the cell due to the electrochemical gradient. It is very likely hat the gate system is in a continuous transitional state, all the time moving from active to inactive and back to the active state and so on, and hence the resulting state of the membrane depends on the total number of the opened channels in a given time. The gate m is an activatory gate and the gate h is an inactivatory one. The channel is activated when gate m is opened and it is inactivated when gate h is closed. In conclusion the channel can exhibit 4 different states according to the position of the gates and the channel is considered to be open only when both gate h and m are opened (see fig. 3.23 page 213).

In some excitable cells there are **similar channels for Ca^{2+} ions** and other ions which have a similar diameter to the Ca^{2+} ions (e.g. Ba^{2+}, Mn^{2+}, Mg^{2+}). These channels are controlled by 2 gates known as d and f. They are known as the slow channels and a continuous supply of energy is needed to keep them active. In addition another ions can pass through the slow channels such as Ba^{2+}, Mn^{2+}, Mg^{2+} and others. Ca^{2+} is very important for the regulation of myocardial contractility. In the resting state of the cell the Ca^{2+} ions are expelled out of the cell by Na^+–Ca^{2+} transport mechanism. This mechanism is voltage depended. During the plateau of the action potential the transporting mechanism is changed into a pump which enables a faster Ca^{2+} ions influx to the cell.

3.25.1 The resting (membrane) potential

In the living cells the ions are unequally distributed on both sides of the cell membrane. As a result of this fact a potential difference is formed between both sides of the membrane, this is known as the **resting potential**. It is negative on the internal side of the membrane. Many factors share the task of keeping this potential. The active Na^+–K^+ transport (Na^+ is transported to the outside and K^+ to the inside) is one of the most important factors and as a result of the action of Na^+–K^+ pump the K^+ concentration intracellulary is 40 times higher than extracellularly and the Na+ concentration is intracellularly 15 times lower than extracellularly. In the resting state the membrane permeability for Na^+ ions is very small. This means that even the Na+ conduction (g Na) is very small and hence the concentration gradient for Na^+ can not be turned by the passive diffusion of Na+ back to the cell. The proteins on the other hand are carriers of the negative charge intracellularly and they similarly to $H_2PO_4^-$ and HPO_4^{2-} can not leave the cell because of the low permeability of the cell membrane to these molecules. The cellular membrane permeability for K^+ ions is relatively high. The difference of the K^+ concentration is considered the generating power for this ion diffusion. K^+ ions have the tendency for increasing the positive charge on the outer side of the membrane but this positive charge will return the positive charged particles back to the cell. Both the opposing electric power and the concentration gradient (which act in opposite directions) are equal for the K^+ ion when it is in the state of equilibrium. Nernst equation applies in the equilibrium state and the K^+ voltage in the equilibrium state equals –100 mV. Using the Nernst equation we can calculate the voltage of other ions in the equilibrium state. So for Na^+ it is V_{Na} = +60 mV and for Ca^{2+} it is V_{Ca} = +100 mV. So

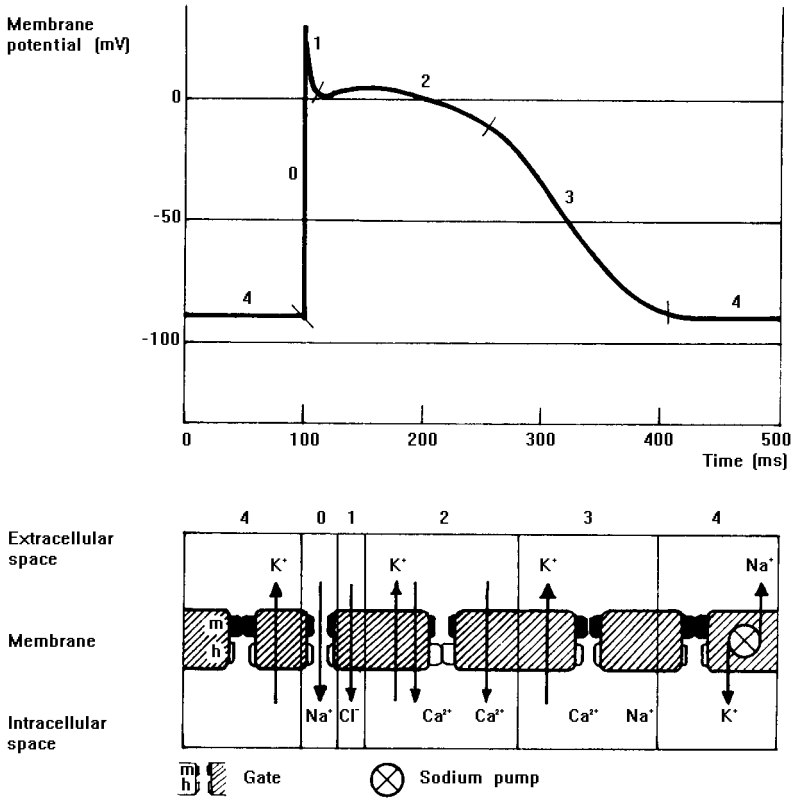

Figure 3.23: Influx of ions in cell via the slow and fast channels

the current size for any ion (I_x) is determined by the membrane conduction for this ion (g_x and the driving voltage can be obtained by calculating the difference between the actual voltage on the membrane (V) and the given ion voltage in state of equilibrium (V_x).

All the living membranes have their resting potential but only the muscle fibers and the neurons have the ability to change their permeability upon the stimulation. By this some large potential depend on the activity of the Na–K pump and the higher is the pump activity the higher is the resting potential.

3.25.2 The action potential

Upon stimulating the myocardial cell a characteristic change takes place, this change is known as the bn action potential. The resting potential in these cells ranges round –90 mV. Upon adequate stimulation the resting potential starts to change. This adequate stimulation may be an electrical stimulation from the outside or an activation which is transmitted from a neighbouring cell, on the other hand a mechanical or a chemical stimulation can be an adequate impulse or stimulus is followed by a change in the membrane permeability and a change in the state of the gates in the membrane channels. The membrane activation icreases the membrane permeability for Na by opening the m gates in the fast Na^+ channels and by this Na^+ ions can flow freely along their electrochemical gradient entering the cell (Na^+ influx) I_{Na}. The Na influx causes the extinction of the Na gradient between the intra and extracellular spaces. The Na influx cancels potential difference of the membrane. This process is very fast lasting only 2–4 ms and hence its name being the fast depolarizing influx I_f or I_{qi} (fast, quick). On the transmem-

brane action potential curve this change (the **fast depolarization**) is shown as **phase 0**. The Na^+ influx changes the membrane potential which further leads to opening of the Na^+ channel. So there is a positive connection in which an increasing Na^+ influx will fascilitate even more Na^+ influx. This relation is known as the regenerative depolarization. The potential changes its value to become near 0. Usually there is an overshooting of the potential value reaching +20 mV. This overshoot will cause the Na^+ influx inactivation. The sharp change in the potential in 0 phase is known as the steep edge of the action potential. So the steepness of the curve decides the quality of spread of the action potential to the neighbouring cells.

During the membrane fast depolarization by the Na^+ influx the Ca^{2+} channels will open when the membrane potential reaches -40 mV. This will facilitate the Ca^{2+} ions to flow or (influx) along their electrochemical gradient. This ion flow is known as the slow inward influx $I_{SI.}$.

So influx of the Ca^{2+} ions join the influx of Na+ ions in the process of membrane depolarization. The K^+ ion escape from the cell occurs simultaneously with the continuation of the membrane depolarization and by this the process of repolarization actually begins. The fast K^+ ion efflux starts with the overshoot to +20 mV, and a quick K^+ repolarization I_{qr}. This is known as **phase 1. In this phase the Na influx slows down whereas the** Ca^{2+} **influx continues**. Here the membrane potential doesnt change because the Ca^{2+} influx equalizes the K^+ efflux. This equilibrium represents a process of remedy, or rectification. Because the K^+ ion efflux is opposed by a high resistence, **the** Ca^{2+} **flow stops at the end of phase 2**.

In phase 3 only the K^+ **flow remains**. This is known as the late K^+ flow I_{x1} and later flow I_{x2}. This condition could be reffered to as the late (true) rectification. The membrane potential gradually returns to the original value at the end of phase 4. Yet the ion balance is markedly different from the original state. There is a surplus of Na^+ and Ca^{2+} ions with a depletion of K^+ ion. The correction of the ion levels start after reaching the original potential. Ca^{2+} ions are exchanged by Na^+ ions (the action of Na–Ca pump) and the Na+ ions surplus is then corrected by the Na–K pump. So during phase 4 there is an intensive exchange of ions with no change in the membrane potential. The myocardial cells mainly are concerned with this process. (See fig. 3.24 page 215). During the phase 0, 1, 2 it is not possible to stimulate the cell membrane by any impulse or stimulus because stimulating the membrane in other words means its depolarization. Because **we cannot depolarize a depolarized membrane**. That is why these phases are called the **absolute refractory phase**. At the end of phase 3 the membrane renewes its excitability (ability to be excited, sensitivity to stimuli) due to its partial repolarization. So we can stimulate the cell by an impulse which is over threshold and we can achieve a depolarization which is slower than the normal repolarization. This period is known as the relative refractory period or phase. The membrane potential should be -45 mV at least and the depolarization in this situation (with over treshold impuls) is achieved by the slow Ca^{2+} influx.

In pathological conditions repolarization is not necessary completed in phase 3 so the membrane potential doesn't reach the level -70 mV to -90 mV as it is suppose to be but it only reaches -30 mV to -40 mV. **In this condition a new depolarization (phase 0) can be obtained by stimulating the cell membrane by under threshold impulse**. This process takes plase when there are membrane abnormalities or when there is an abnormal potential which is usually localised in the vicinity of the ischemic regions. In this situation the difference in the potential levels of the two neighbouring zones leads to a partial depolarization of the attached cells. Due to the effect of some substances there is an increase in the speed of Na^+ and Ca^{2+} influx and a dicrease in the K^+ efflux. A situation similar to the mentioned can occur when the cells are overfiled with Ca^{2+} ion due to different causes.

3.25.3 Automatic cells

In automatic or rythmogennic cells phase 4 doesn't represent the preciously described isoelectric interval. In the sinoatrial cells similarly to other cells in the conducting system of the heart upon reaching the maximal diastolic potential its negativity starts to decrease it gradually i.e. if –70 was its maximal diastolic potential it gradually reaches –60). This change is marked as the **spontaneous diastolic depolarization** which is caused by Na^+ ion influx. This is due to Na^+ inadequate pumping out which is caused by a low Na-K pump performance. The SA node

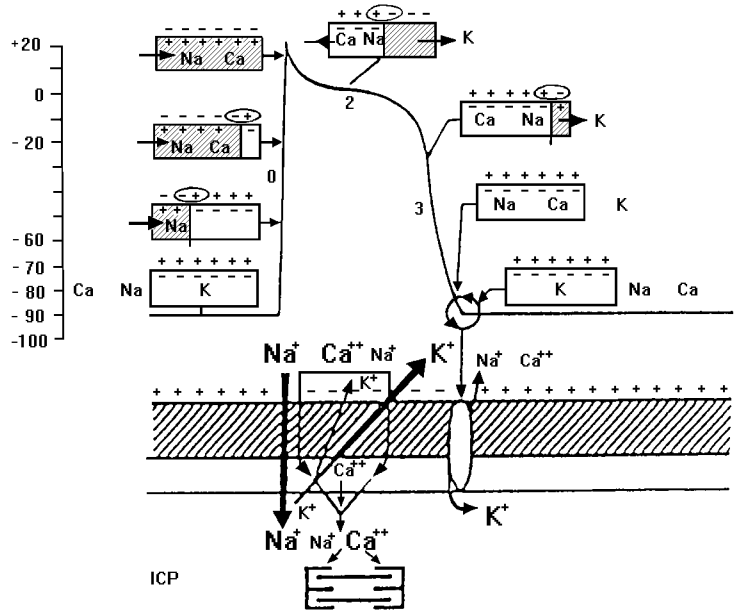

Figure 3.24: Transmembrane action potential of cardiomyocyte

cells have the steepest (fastest) diastolic depolarization. After reaching the threshold potential (–40 to –30 mV) phase 0 takes place (fast depolarization). The following phase (phase 1) is not as steep as in the myocardial cells. In the SA node cells the depolarization (phase 0) results from the Ca^{2+} ion influx and only partially due to the Na^{+} ion influx. The overshooting usually doesn't occur, plateau usually doesn't exist. The SA node cells don't need Ca^{2+} for contractions (an obvious plateau is present in the contractile cells). So in the action potential curve phase 1 is directly followed by phase 3.

The diastolic potential can only reach (–50 mV) – (–70 mV). The potassium potential is low. The spontanuous diastolic depolarization takes place in phase 4. The in-flowing Na+ ions cause the membrane potential to reach the threshold levels upon which phase 0 takes place (see fig. 3.25 page 215). The whole process is repeated approximately 70 times per minute. A similar process can occur in other rythmogenic cells in the conductive system of the heart,

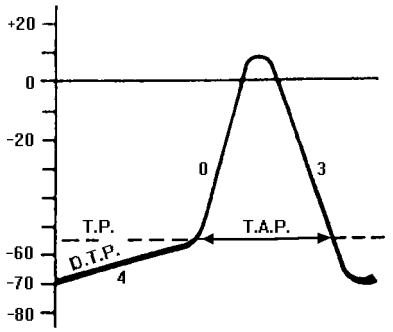

Figure 3.25: Transmembrane action potential of sinoatrial node

in this case phase 4 takes longer time. An impulse wave coming from the activated part of the conductive system of the heart reaches the myocardial cells

before they reach the threshold potential and here phase 0 starts. The refractory phase lasts for the whole action potential. This fact prevents the SA node from an immature activation as a consequence of activated atria. The spontanous depolarization of the SA node cells is not depended upon the Na^+ and K^+ concetration in the extracellular fluid. Yet the Ca^{2+} flow can affect the automacity. The **speed of the diastolic depolarization** determines the heart rate. Many substances achieve their action on the heart through changing the SA cells membrane permeability and hence change the length of phase 4.

From the electrophysiological point of view we can devide the heart cells into those having the ability to spontaneously depolarize, and those which need activation from the nearby cells to depolarize. The action potential of one cell shifts the resting potential of the neighbouring cell to the level of the threshold potential (by the ionic flow) and then the process of depolarization takes place as previously described. The action potential of an activated cell is the impulse which causes depolarization of the neighbouring cell, its effect is incresing with increasing its speed. That is why it is very easy for the steep 0 phase of the action potential to spread. It is very important to realize that after reaching the threshold potential through activating the cell by an action potencial of another cell, the coninuity of the event does not depend on the activating action potential but on electrophysiological properties of the activated cell.

3.25.4 The progress of activation

Stimulation passes from one cell membrane to the neighbouring cell membrane in the form of local electric currents which are generated between the polarised and the depolarized areas. These currents form circles on the still polarised cell membrane leading to the decrease of the membrane potential. And then decrease the resting potential to the threshold level. The local currents are generated during repolarization as well, yet they are weak and inadequate for activating cells which reached the relative refractory phase. The spread of the local current waves is affected by the characteristic of the conducting system as well as the characteristics of the myocardium which could be described as cable characters. We mainly deal with two constants being time and space. The space constant determines the extent of the local current waves, where as the time constant stands for the time needed to change the membrane potential. It is not easy to determine the time and space constants for the cardiac conductive system or for the myocardium. The Purkinje and myocardial fibers microstructure facilitate a longitudinal progress of activation. The intensity of the local current waves depends on the speed of the regenerative depolarization, which in turn depends on the membrane resting potential. So in conclusion the intentsity of the local current waves as well as their speed depend on the membrane resting potential.

The space constant of the myocardium and the conductive system is 1–2 mm. Local currents can then generate depolarization in the myocardial tissue. This depolarization can reach the distance of few millimeters. This will guarantee the progress of activation even in case of some inadequate cell function to conduct stimulation with the myocyte length about 100 mm. The local currents can even stand for a cable defect which is the representation of non functional myocytes.

The activation of the heart doesnt progress depending marely on the physical principles because if the conduction progresses by a cable mechanism only it would be gradually weaker and weaker. Yet the local current waves induce depolarization in the neighbouring cells which means that each cell generate another stimulus (when it depolarized). In other words the myocardial and the conductive system cells act as amplifieres of a continuously weakening stimulus and that is why activation is spread without any decreament. Moreover, the cellular activation (the process of action potential) presents the backward process of activation due to the refractivity phenomen.

The transfer of activation from cell to cell depend on the cellular membrane characteristics and on the time at which activation took place. When the impulse reaches the cell in phase 3 with no renewed diastolic potential, the Na^+ channel doesn't open. Yet another slow chanel opens and a regenerative depolarization takes place. In this case the membrane depolarization is slow and that is why phase 0 hasn't got a steep angle, the intensity of the local currents is lower, and the activation is progressing slowly. The spread in this case can dicrease gradually and the steepness of phase 0 is decreasing also till is finally dies out.

The absolute and fast transmission of activation

ensures a high and steep action potential and a polarised membrane with a low potential threshold. Na^+ channel disfunction can eventually lead to a conduction error. This effect could be achieved by using some antiarrhythmmic drugs. So the weak Na^+ current will cause the activation decreament and respectively its end.

A condution block occurs when the stimulus reaches a depolarized membrane, considering that a continuous depolarization can be caused by a high K^+ concetration intracellularly. In this case the normal impulse or stimulus is below the threshold level needed and by this there is a complete block of conduction. When the injury is less there wil be a conductive delay. The block can present only in one direction and hence the impulse conduction to other than the main side doesn't have to be blocked.

In some cases a functional block can occur and is usually caused by a continuous depolarization of the membranes. This continuous depolarization can be kept in some areas due to a repeated activation.

An abnormal conduction can occur during an increased membrane sensitivity of stimuli usually caused by catecholamines. In this case the slow Ca^{2+} channel is activated spontaneously and a slow wave of depolarization spreads to the membranes. This spread is due to the action potentials of the Ca^{2+} channels. This condition occurs in the ischemic zone of the myocardium and a conductive deffect can be furtherly complicated by the fact that the ischemia shortens the refractory phase. The short refractory phase when coupeled with a slow conduction is most dangerous. As a result of these facts, the slow conduction can reactivate the areas which have short refractory phase and a returning or (back going) activation occurs. This is known as (reentery) phenomena. In some cases the returning activation is progressing cross the Purkinje fibers and the myocardial fibers as well. The tract could be so long that it is possible to see the myocardial contraction in front of the stimulating wave and behind it, this is a case of macroreentery. Usually the returning activation (circulating wave) progresses in the same manner. In other situations the stimulus breaks up and the circulating wave moves in small circles, this is a case of microreentrery. A high susseptibility of the myocardium for micro and macro reentery renders the myocardium instable (an electric instable myocardium).

3.25.5 Anatomy and physiology of the conductive system of the heart

The awarness of the conductive system function and structure is crucial for understanding the basis of the electrophysiological processes in the heart and hence a right interpretation of the electrocardiogram.

In the heart there is a special conducting system which provides the automatic formation and propagation of the excitatory process in a way by which the heart can perfectly perform its pumping function. The conductive system of the heart differs functionally, histologically and evolutionally from a working myocardium. The automatic formation of a stimulus occurs in the sinoatrial node (SA node). The excitation spreads through the atria to the atrioventricular node (AV node). From this point the activation progress to the bundle of His, right and left bundle branches, to the Purkinje fibers and finally to the myocardium.

SA node The SA node develops during the embryonal period together with the compact AV node in the region where the right superior cardial vein is united with the sinus venosus. The AV node migrate internally to its definitive position whereas the SA node remains in its original position. It is situated in the vicinity of the enterance of superior vena cava to the right atrium, along the crista terminalis. Its internal end lies subendocardially. The SA node is 1–2 mm in width, 10–20 mm in length and it is pyramidal in shape, and cross section is triangular which base is directed towards the antrum of the right atrium. There is a small artery in the center of the triangle. This artery gives many small branches to provide the SA node with nutrition.

Besides the pacemaker function, the SA node monitors the central aortic pressure and the pulse. The SA node artery is the first branch of the right coronary artery. The substances that increase the SA node activity cause dilatation of the SA node artery and vise versa, the substances which depress the SA node activity cause constriction of the SA node artery. This feedback mechanism will provide stabilization of the SA rythm.

The fundamental **skeleton of the SA node** is thick callagenous connective tissue which surronds the central artery. It seems as the central artery adventitia. This connective tissue is composed of on irregularly distributed collagen fibers which forms a layer which encircles the central artery. On the edges of the node

the cells join to form the efferent pathways. The amount of collagen in SA node increases with age.

The centre of the SA node contains large number of nerve endings, and cholinergic ganglia are found on the peripheries. The afferent nerve fibers to the node join the nodal cells. The parasympathetic supply originate from the right vagus n. and the adrenergic supply comes from the post ganglionic sympathetic nerves.

There are at least 2 types of specialized cells in the SA node. The first type are small cells being round or oval in shape. The shape of the cells simulate the primitive myocardial cells having few organelles and pale cytoplasm. They are reffered to as P cells (pole cells) and contain large amount of glycogen. They are situated in the central area of the SA node and are organized into clusters. These cells are in direct contact with each other and they form the intercalated disks in areas of contact. Yet these are no nexuses which have the function of low resistence conection of the differentiated cells. The P cells preserved the ability to generate impulses endogenously from embryonal period.

Apart from P cells in the SA node there are also long thin myocytes with a longitudinally oriented myofibriles and multiple intercellular conections. These cells are refered to as transitional cells. They form a network of fibers and are mainly found on the SA node peripheries. They are attached to the P cells on one side and to the myocardial cells in the atria on the other side. By this way it is possible to provide the transmission of activation from the SA node to the atrial myocardium.

The main characteristic of the P cells is their automacity, being the ability to depolarize cellular membrane till reaching the threshold level without any external stimulation. This character is unique for the P cells being the fastest among the conductive system cells which have the ability to spontaneously depolarize the cellular membrane. And as a result of this they are known as the pacemaker cells. SA node is primary pacemaker.

It is possible that automacity can occur in other conductive system cells. But in the normal conditions the automacity of these cells doesnt express itself because of the dominance of the primary SA node activity.

The ways for the SA activation spread through the atria to the atrioventricular node (AV node) are not yet certain. There are three main conductive pathways, the anterior, the middle and the posterior, which provide internodal conduction between the SA node and the AV node. These pathways not only possess specialized cells but they are not continuous with each other (in other words they are interrupted). The cells in these pathways contain less myofillaments, yet they use multiple nexuses for connection (junction).

In normal conditions the task of the pathways being conducting stimuli to atrial muscles is not clear. It is possible that these tracts or pathways conduct activation during the pathological conditions and it was found that the posterior pathway has an important task during the shortening of P–Q interval. Those pathways don't have to exist as an exactly defined structures. They could be composed of groups of cells having different electrophysiological characteristics. These pathways are possible to be the basis for the reentery circles which occur during the cardiac arrythmias.

The activation of the atria reaches the atrioventricular junction which is a more complicated structure and could be anatomicallly divided into 4 parts.

1. The atrionadal region (junction) being a transitional zone
2. The compact AV node
3. The penetrating bundle (the proximal part of bundle of His)
4. The branching bundle (the distal part of bundle of His)

The mentioned parts in 1,2,3 are refered to as the junctional area. The branching bundle together with the bundle branches is referred to as the subjunctional area. (see fig. 3.26 on page 219).

The atrionodal region The atrionodal region or junction or what is known as the transitional zone is composed of groups of cells which are found between the atrial myocardium and the AV node. These cells (the transitional cells) are smaller than the active myocardial cells. They form tiny clusters which are separated by a conective tissue septi. These transitional cells enter the superficial and the deep part of the compact AV node.

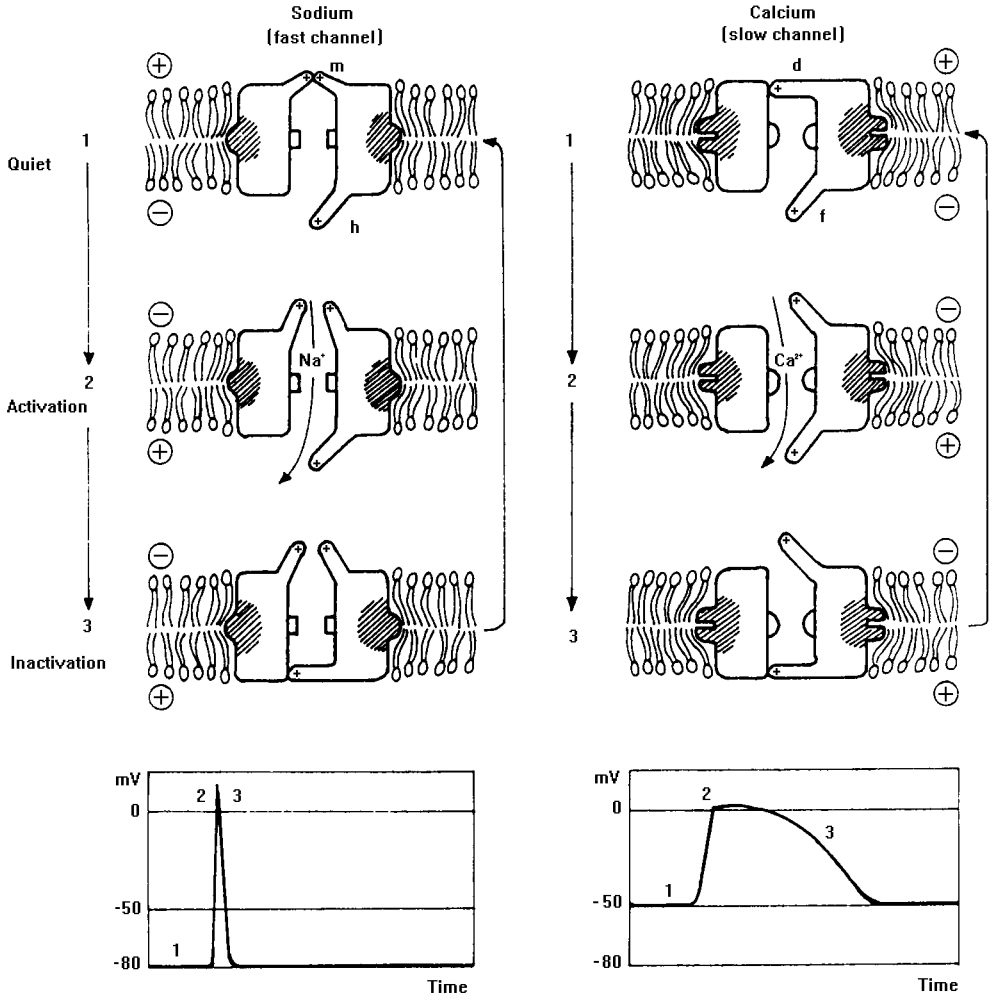

Figure 3.26: Sodium and calcium channels

The compact AV node The compact AV node is located in the posterobasal part of the interatrial septum. It is found between the isthmus of the coronary sinus and the medial cusp of the tricuspid valve. It's area is nearly 10 x 6 mm. From the electrophysiological point of view the AV area is divided into AN /atrionodal area), N (nodal area), and NH (nodal – His area). The AN area is composed of cells organized in a parallel way which gradually form a network when they reach the N area. The N area is considered to be the area of the slowest activation conducion. The atrionodal fibers can enter the SA node in this part. The NH part is composed of elongated cells which simulate the cells that form the bundle of His. The area where the AV junction crosses to the fibrous ring is considered to be the beginning of bundle of His.

Autonomic nerve fibers are found in the compact

AV node. They are in the vicinity of the arteries and veins. The parasympathetic n. fibers come from the left vagus n. and the sympathetic come from the postganglionic neurons. The blood supply is from the fibrous ring arteries.

The bundle of His The penetrating part and the remaining part of the branching bundle after giving its branches will pass through the annulus fibrosus as the continuity of the compact node then it passes through the membranous part of the interventricular septum. It starts to branch at the lower part of the membranous septum. The bundle of His is formed by parallel muscle fibers which are separated by connective tissue into a number of stripes. Its diameter can reach 3 mm and length 12 to 40 mm where its penetrating part forms about 8–10 mm.

Branching of bundle of His starts at the lower edge of the membranous part of the interventricular septum. The right bundle branch is the continuity of bundle of His, and its similar to it histologically. The proximal part of the right bundle branch is situated in the vicinity of the aortic and tricuspid valve. The distal part on the other hand is situated subendocardially near the septal papillary muscle, and it continues its pathway till reaching the apex of the right ventricle. The anatomical division of the bundle of His into right and left bundle branches is referred to as pseudobifurcation. The reason of this lies in that the bundle of His fibers are divided before the anatomical bifurcation, so they differ in function yet they still pass alongside together for a small distance. Analogical situation to this are present in the anterior (superior) and the posterior (inferior) branches of the left bundle. Their division already occurred in the bundle of His. So they run in the left bundle branch but they differ in their function. In some cases a third (branch) fasciculus is discribed to be present in the left bundle branch. The division of the bundle branches is very variable. There are some junctions between the branches. The bundle branches pass to Purkinje fibers at the apical part.

Purkinje fibers Purkinje fibers represent the peripheral branching of the bundle branches. They form an subendocardially situated network. Purkinje fibers contain myofibrils and are divided by collagen fibers so that to prevent the side way spread of activation. The Purkinje fibers spread among the fibers of the ventricular muscle fibers.

The compact AV node and the bundle of His is supplied by blood from the septal branch of the right coronary artery. The right bundle branch and the anterior fasciculus of the left bundle branch are supplied by blood through the descending branch of the left coronary artery. The terminal parts of the branches are supplied by blood through the right coronary artery.

3.25.5.1 Atrial activation

As mentioned above the **excitatory process begins in the SA node** and from the SA node the activation spreads radially and continuously across the atrial myocardium. In the beginning and after the rising of activation from the SA node, the right atrium is the first to be activated. Shortly afterwards the activation proceeds to the atrial septum and the left atrium respectively. For simplicity we can follow the atrial activation using three vectors, each one of them starts on the SA node. The **initial vector** of the atrial activation represents the activation of the right atrium and its direction is inferior, anterior and slightly to the right. The **second vector** represents the activation of the right and left atrium and it is directed inferiorly, to the right, and slight anteriorly or posteriorly. The **terminal vector** represents the activation of the left atrium and is oriented to the left, inferiorly, and posteriorly. The relation among these vectors on one plane is shown in fig. 3.27 on page 221.

The first half of the P wave is a picture of the right atrial activation whereas the **second half of the P wave** stands for the activation of the left atrium mainly. The average direction of maximal vector of the P wave is $+60^{o}$ in the frontal plane. The P wave being normally positive in leads I, II, AVL, but invered in the AVR lead. It is usually the highest in lead II. In the horizontal plane the maximal vector lies between 0^{o} and $+60^{o}$. The vector that represents the right atrial activation is partially anteriorly oriented whereas the vector that represents the activation of the left atrium is partially posteriorly directed and that is why the P wave is commonly biphasic in leads V_1 and V_2, being initially positive with a negative terminal part. The positive part represents the activation of the right atrium whereas the negative part represents the activation of the left ventricle. In the chest leads which are close to the heart the P wave is usually higher. In the left precordial leads the P wave is positive.

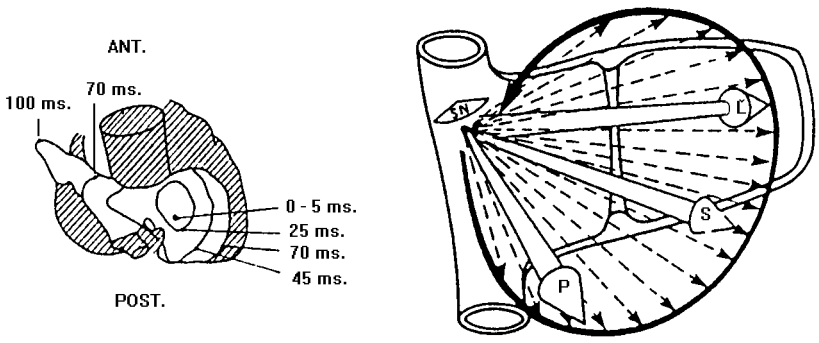

Figure 3.27: Activation of the atria and relationship between some vectors (left, right and maximal)

3.25.5.2 Atrial repolarization

The repolarization of atrial muscle fibers is related to its depolarization and it is represented as the T_p deviation (also referred to as T_a). It is usually not shown on the ECG and the reason is that the repolarization starts simultaneously with the ventricular depolarization and hence the two processes occur at the same time. On the ECG the atrial repolarization T_p is masked by the ventricular QRS complex. The direction of the T_p usually opposes the P wave. The atrial repolarization can cause pseudo depression of the ST segment in the J point (see fig. 3.28 page 222).

3.25.5.3 Ventricular activation

The activation of the ventricles can be divided into 4 phases for the purpose of which is an easy understanding of the ECG process yet actually the ventricular activation is one continuous event. Basically each deviation during the process of activation is shown immedialtedy as a projection on the corresponding axis of the lead.

The initial septal activation (0,01 s) The interventricular septum in the cavity of the left ventricle is the first to be activated during the activation of the ventricles. The interventricular septum is nearly parallel to the frontal plane of the human body. That is why the initial vector that represents the septal activation is directed anteriorly, slightly to the right and superiorly or inferiorly. The projection of this vector on chest lead axis will form the positive (r wave) on the right chest leads (V_1 and V_2) and a small negative wave (q wave) on the leads V_5 and V_6.

The progression of activation of the septal and apicoanterior parts of the right and left ventricles (0,02) During this phase the intervetricular septal activation continues from both sides. The electrical power are partially similar but a larger part of the septum is depolarized from the left side. So the net direction of the septal activation will be from the left ventricle to the right vetricle. The septal activation spreads from the apex to the heart base, and from the anterior to the posterior part simultaneously meanwhile the activation could spread fast to both ventricles. The apex of the heart, the lateral wall of the right ventricle, and the anterior apical part of the left ventricle are mainly activated during this phase. The sum of the dipoles in the left ventricle is higher than in the right ventricle and that is why the vector of activation is directed slightly anteriorly, to the left and partially inferiorly. There will be a positive wave in the chest leads as a result.

The complete activation of the interventricular septum, the right ventricle, and the larger part of the left ventricle (0,04–0,06 s) In this phase the activation of the septum and the right ventricle except its posterobasal part is completed. Most of the left ventricle is activated as well. Even in this phase the total sum of the potentials in the left ventricle is higher than in the right ventricle, and hence the resulting vector is large and left oriented, slightly backwards and inferiorly. This vector plays role in determining the final direction of the resulting QRS vector. The projection of this vector on the chest leads will even-

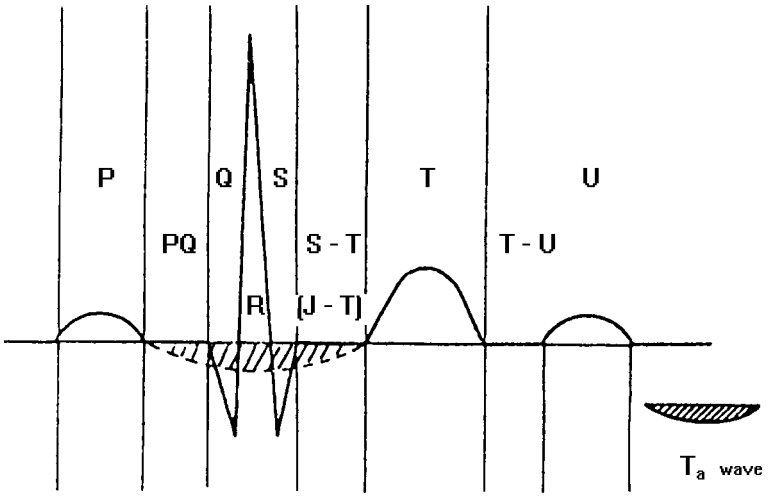

Figure 3.28: T_a wave

tually result in recording the shortest S wave in lead V1 and highest R in left chest leads.

Activation of the basal part of the interventricular septum and the posterobasal part of the left ventricle (0,06–0,08 s) This is the last event by which the activation of ventricles is completed (see fig. 3.29 on page 223 and fig. 3.30 on page 224).

At this time the activation of the pulmonary conus takes place yet its role in the activation is negligible. The terminal vector of the activation is backward directed and to the left or slightly to the right. This vector is the cause of the descending part of the R wave and the terminal part of the S wave in the left chest leads. Sometimes a small deviation is recorded being a normal variation in the lead V_1 it is usually found in young people and it refers to the activation of crista supraventricularis.

In Eithoven bipolar leads and in the unipolar limb leads the ECG deviation are recorded as the picture of the projection vectors on the frontal plane according to the corresponding phases. There is a certain variability in the ECG recording yet this variability is considered to be normal.

In conclusion during the ventricular activation the right precordial (chest) leads will record negative ventricular QRS complexes. On the other hand the complexes recorded by medial precordial (chest) leads will be equiphasic. During the ventricular activation we can register the loops representing the QRS complex from different planes. These loops are recorded in the frontal, horizontal and left sagittal planes.

3.25.5.4 Ventricular repolarization

Ventricular repolarization starts immediately after the completion of their activation. The direction of repolarization is generally opposite to the direction of activation, and that is why the resulting T vector in the adults is relatively parallel with the resulting QRS, or it is only slightly deviated. This means that in the ECG recording T wave is positive except in lead V_1. In the new-born and in children the resulting T vector is oriented to the left and posteriorly, and that is why T wave is negative in the leads V_1, V_2, and V_3. The direction of the T complex is usually similar to that of the QRS complex in each of the three used planes.

Arythmology is a new study concerned with the different mechanisms which take place in cardiac activation, whereas in the area of long monitoring of ECG there is the intensive development of the elec-

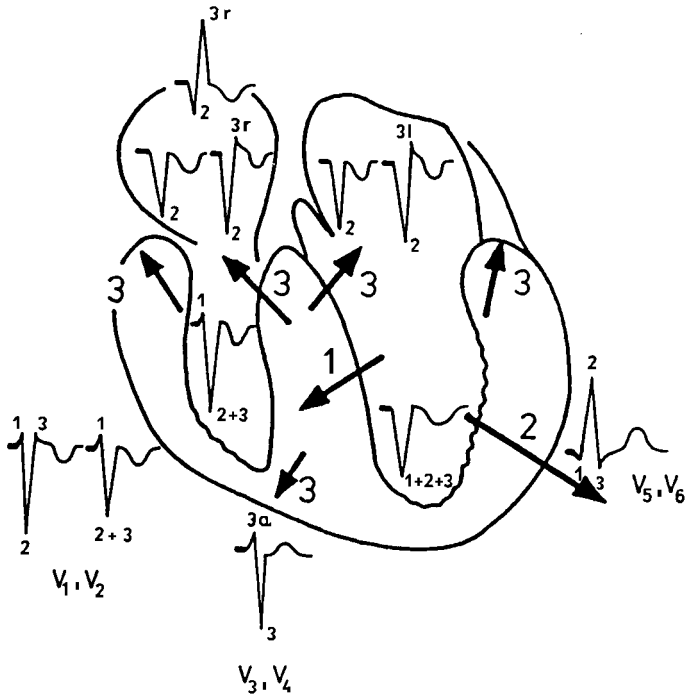

Figure 3.29: Vector representation of ventricular activation

trocardiograph, pacing, and some special methods which can detect the cardiac activation and markers of electrical instability. Recording the electrical activity of the heart can afford the most valuable information about the defect and the mechanisms that occur during the cardiac activity. That is why it is very important to be aware of the principles of the ECG because the ECG recording can provide us with information that can not be substituted regarding the cardiac activity and arrythmology, the pathophysiology of the heart, together with the electrocardiographic studies and explains some cardiac disorders and that is why were going to go through some of its most important principles.

Electrocardiogram The P wave represents the atrial activation (depolarization). The QRS complex represents the ventricular activation. The Q wave is a negative wave representing the initial stage of the QRS complex. R wave is the initial positive wave that immediately follows the Q wave. The S wave is a negative wave following the R wave. If instead of the QRS complex there is only negative wave which is followed by a positive wave it is then known as the S wave. Other waves of R or S are known as R' and S' waves. T wave represents the ventricular repolarization and sometimes is followed by U wave. The atrial repolarization is represented by T_a wave, this wave can occur in the PR interval. The section from the end of the QRS complex till the beginning of T wave is known as the ST segment. It is the segment between the ventricular depolarization and its fast repolarization. The PR or (PQ) interval is the interval between the beginning of the P wave and the beginning of the QRS complex, it usually lasts for 0,12–0,20 sec. The QRS complex takes about 0,04–0,10 sec. The QT represents the approximate refractory period of the ventricles.

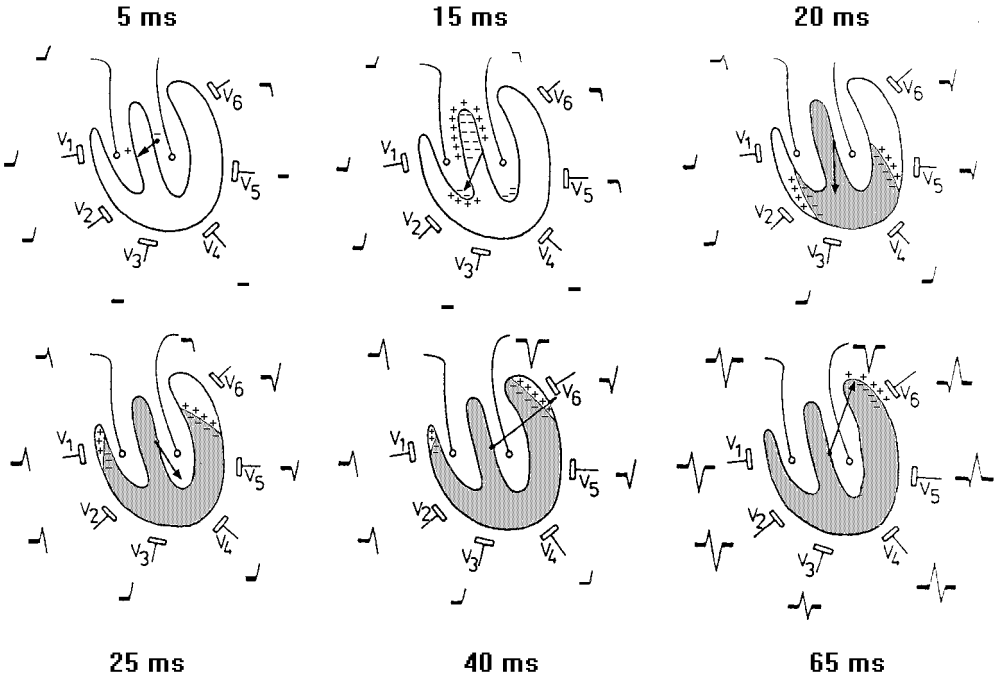

Figure 3.30: Time course of ventricular activation

3.25.6 The electrocardiographic changes in cardiac disorders

3.25.6.1 The electrocardiographic changes in ventricular hypertrophy

The left ventricular events are the dominating events shown in the ECG. During the ventricular hypertrophy the left ventricular activity and its share in the cardiographic changes is more obvious and clearly expressed.

The right ventricular hypertrophy will shift the cardiac axis (the main direction of activation) from being backwards and to the left to become forwards and to the right. On the ECG these changes are shown as a high R wave in the lead V_1 it may reach 0,5 mV or even exceed it. At the same time there is an abnormal S wave in leads V_5 or V_6 which may reach or exceed 0,7 mV. The QRS axis in the frontal plane is directed to the right, usually is more than 110 degrees. In a mild right ventricular hypertrophy there is a deep S wave in V_1 , and R wave, which voltage reaches the value of S wave, or there may be a normal R wave with a flat S wave in the lead V_2 with an obvious terminal S in the leads V_5 and V_6.

The left ventricular hypertrophy is usually presented as a high voltage in the leads that show the left ventricle. The R waves can exceed 2,0 mV in the standard leads meanwhile there is a tendency for a shift in the electrical axis of the QRS complex to the left in the frontal plane till -30 degrees. In leads V_1 or V_2 there is a deep S wave exceeding 2,5 mV. In the V_5 or V_6 leads there are R waves exceed 2,5 mV. It is very interesting that in young, thin and healthy people the voltage criteria of left ventricular hypertrophy can be found without actual hypertrophy. Usually there are no changes in the ST segment or T wave changes, and that is why their changes are the decisive criteria upon which we can say if there is left ventricular hypertrophy not in cases which are very suggestive of the left ventricular hypertrophy.

3.25.6.2 The electrocardiographic changes in acute myocardial infarction (MI)

From the pathological point of view an acute MI is a necrotic area which is surrounded by an ischemic zone which separate the necrotic zone from the surrounding healthy myocardium. The ischaemia is usually presented by certain changes in the T wave and the ST segment whereas necrosis is shown as changes in the QRS complex. **During the development of acute myocardial infarction** the signs of ischaemia are the first to be shown as a high peaked T waves, later these waves become inverted and symmetrical. The progressing ischaemia will lead to electrical integrity disorders of the cellular membranes. These are shown as the ST segment elevation in corresponding leads which face the ischaemia and as ST segment depression in the leads opposing the ischaemia. In case of transmural infarction the pathological Q wave will occur in leads where no Q wave was present before and it becomes very clear.

In myocardial infarction of the anterior wall most of the changes take place in leads AVL, V_2, V_3 whereas an inverted picture (ST depression) occur in leads II, III and AVF. The deepening of the Q wave is most obvious in leads AVL, V_1, V_3. The Q wave stays the same (see fig. 3.31 page 226).

In the posterior wall MI the ECG changes are exactly the opposite of those changes in the anterior wall infarction. Instead of the Q wave, ST segment elevation, and T wave inversion there is a tall R wave, ST segment depression and positive T waves. This type of infarction is usually combined with infarction of the inferior wall.

In the inferior wall myocardial infarction the most obvious changes are seen in those leads which picture the inferior wall of the left ventricle. These are the leads II, III, and AVF in which the Q wave appear combined with ST segment elevation, and T wave inverssion. The opposite changes being (ST depression and high T waves) are shown in the AVL.

If the infarct locus lies only in the subepicardial or subendocardial area there will be all signs of MI in the ECG except the Q wave which will be absent because Q wave is considered to be pathognomic to the transmural infarction. This ECG discovery is not totally corresponding with the post morten findings in dead patients due to MI, nevertheless we classify the MI according to the presence or absence of the Q wave.

The right ventricular MI is rare. It is usually combined with inferior wall infarction or MI of the posterior wall of the left ventricle. During the acute MI of the right ventricle the most typical changes are those occurring in leads V_6R, V_5R and V_6R.

3.25.6.3 The electrocardiographic changes in chronic ischemic heart disease

An important finding is the pathological Q wave of a previous MI. Other ECG changes are not specific. The patients usually use drugs which can markedly affect the ECG findings. Apart from this usually, those patients have a left ventricular hypertrophy which is shown on the ECG adding to this are some ST segment and T waves changes. A horizontal ST segment depression or S depression in the J point is an important landmark as well.

3.25.6.4 The ECG changes during the intraventricular conduction disorder

The conducting system of the heart and the myocardium could be the cause of intraventricular disorder of conduction. The basic disorder is slow ventricular activation which could accompany a diffuse or local disorder. The diffuse disorders of the activation progression is usualy caused by ventricular hypertrophy cardiomyopathy, or some metabolic disorders. On the other hand the local disorders of the activation progression is related to a partial or total block of the activation conduction in the left or right bundle branches of the bundle of His.

In right bundle branch block the activation is progressing normally in the beginning. Yet the block of activation transmission in the right bundle branch or the right ventricle is obvious in the terminal part of the QRS complex. There will be a wide S wave in lead I, AVL, and V_6. R wave occurs in V_1 and it is the picture of septal activation, it is then followed by S wave and R' wave. In cases of incomplete right bundle branch block there will be what is known as rSR' yet the QRS interval lasts for less than 0,12 sec. (see fig. 3.32 page 227).

During the left bundle branch block the QRS interval is prolonged as well. The progress of activation is disturbed immediately and simultaneously with the septal depolarization. And that is why there is no Q wave in leads I, AVL, and V_6. R wave could be absent or very small in lead V_1. There might be

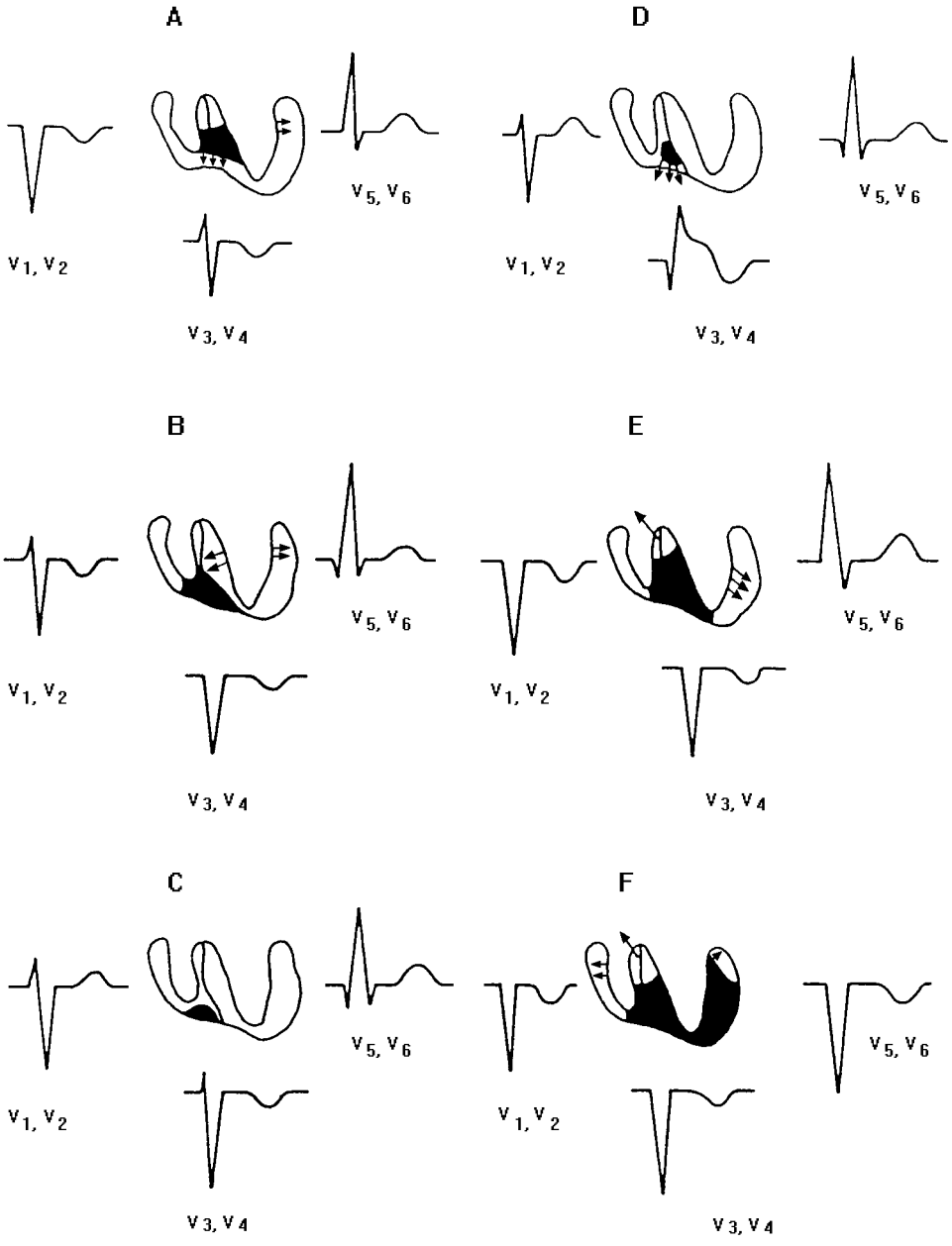

Figure 3.31: Myocardial infarction of vetricular septum and anterior left ventricular wall

some QRS changes (notches) in lead I and V_6. Secondary changes can occur in the T wave and the ST segment and this is the reason why it is very difficult to differentiate the ischemic heart disease changes from those of left bundle branch block. When the interval is prolonged due to intrinsic wave formation in leads V_5 or V_6 the QRS complex then is shorter than 0,12 sec and here we are talking about incomplete left bundle branch block (see fig. 3.33 on page 3.33).

As the left bundle branch block is accompanied

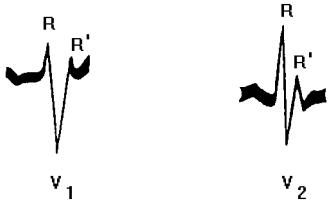

Figure 3.32: Right bundle branch block

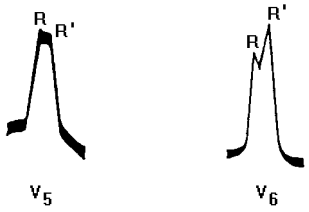

Figure 3.33: Left bundle branch block

with a marked left axis deviation, we can usually notice a clear left ventricular dysfunction. The left bundle branch gives many diffuse small branches, from these we can differentiate two parts. One is known as the anterior fasciculus and the other part is known as the posterior fasciculus. If a block occur in these fasciculi it is the known as a hemiblock.

In the left anterior fascicular block the activation conduction slows down in the upper part of the left ventricular wall and this is usually shown as QRS prolongation and a left axis deviation. It is not easy to differentiate between the fascicular block and a left ventricular hypertrophy. The hypertrophy of the left ventricle usually doesn't result in left axis deviation over –30 degrees in the frontal plane yet in the frontal hemicblock the deviation of electrical axis is -60 degrees or more. The ventricular QRS complex is usually typical. There is a mall Q wave in leads I, AVL and there is a small R and a deep S wave in lead II, III, and AVF.

In the left posterior fascicular block the progression of activation slows down in the posterior and inferior part of the free wall of the left ventricle. We can notice a prolongation of the QRS complex and a right axis deviation. there are no specific criteria for the posterior hemiblock and we usually reach the diagnosis by exclusion (excluding all other reasons of right axis deviation), and when no reason is found the finding is then considered a posterior fascicular block. The left fascicular blocks are frequently combined with a right bundle branch block. In this case we are talking about a bifascicular block. A trifascicular block on the other hand occur when the activation conduction is slow in each of the left branch fascicles and the right bundle branch.

3.25.6.5 The electrocardiographic changes in pericarditis

Acute pericarditis is presented by an isolated deviation of the ST segment in nearly all the leads. The ST segment deviation is not shown in the lead AVR and V_1. In a long lasting pericarditis the ST elevation could be normalized but an inversion of the T wave can appear. T wave inversion and other abnormalities can last for a very long time. Electrical alternations can occur when a large quantity of excudate is formed in the pericardial cavity. There might be a drop in the voltage in all complexes and waves in all the leads.

3.25.6.6 The electrocardiographic changes in myocarditis

The electrocardiographic changes occurring in the late stages of pericarditis. The ECG changes which point out to a myocardial injury are usually found in many infectious diseases as viral hepatitis, infectious mononucleosus (IMN), mumps, influenza, and others. Only some of these are presented with histological findings and the ECG changes are usually non specific. In a clinical case of myocarditis there are symmetrically inverted T waves in the standard leads and left chest leads. Different conduction disorders could appear, and arrhythmias are not unusual.

3.25.6.7 The electrocardiographic changes in cardiomyopathies

Signs of left ventricular hypertrophy are the most common signs of ventricular **hypertrophic cardiomyopathy**. There might be an abnormal Q wave in leads I, AVL, V_5 and V_6 and a tall initial R wave in V_1 in cases of the asymmetrical hypertrophy of the interventricular septum.

In congestive cardiomyopathy it is possible to notice an abnormal conduction in the ventricles which leads to some abnormalities in the QRS complex. We can notice the presence of some nonspecific ST segment and T wave changes as seen in other cardiomyopathies. In restrictive cardiomyopathies we can notice a low voltage QRS complex and disappearance of progression in the precordium.

3.25.6.8 Electrocardiographic changes in metabolic and electrolyte disorders

The cardiac tissue is electrically active, and that is why the electrolyte changes can affect its electrical activity.

In hyperkalaemia the appearance of tall T waves and a prolonged ventricular complex which becomes mated with the T wave to form one peak. P wave is small and PR interval is prolonged.

In hypokalaemia T waves become flattened or inverted. Whereas the U wave becomes very clear and the QT interval is markedly prolonged. Its prolongation is partly due to the U wave which is mated into the T wave. These signs signalize the possible occurrence of arrhythmias especially when digitalis or antiarrythmic drugs (group 1) are applied. The ECG changes in hypokalaemia are similar to those of hypocalcaemia. **Hypocalcaemia** prolongs the ST interval as well as the T wave, this will lead to QT interval prolongation. Hypocalcaemmia on the other side is not as dangerous as hypokalaemia in generating cardiac arrhythmias. Non specific ECG changes occur in hyperthyroidism, hypothyroidism, diabetic ketoacidosis, and of course after the use of antiarrythmic drugs. The prolongation of PR and QT interval as well as some non specific changes in ST segment and T wave are the most commonly seen.

3.26 The electrophysiological basis in the generation of cardiac arrhythmias

The term arrhythmia constitutes all changes of the cardiac rhythm that render the rhythm different from the normal sinus rhythm. The sinus rhythm is initiated in the SA node. The activation is progressing then from the atria to the ventricles having a normal PR interval that doesn't exceed 0,20 s and the heart rate in adults ranges between 60–100 /min.

The development of electrocardiology and especially the intracardial electrophysiological study and the Holter monitoring could influence many opinions about cardiac arrhythmias. Many findings were used to explain changes in the conventional electrocardiography.

From the histological and functional point of view we can differentiate two types of cardiac cells: contractile cells, which duty is to provide the pumping function of the heart and specialized cells for the formation and conduction of activation. The contractile cells have the ability to perform mechanical works and conduct electrical impulses from cell to cell.

The myocardial cells are connected to one another by intercalated disks by which they form interconnected muscle fibers. The intercalated disks serve the conduction of mechanical energy, yet they have electrical characteristics which render the activation conduction from cell to cell much easier.

The intercalated disks are formed by union of plasma membranes of the neighboring cells. It is actually a doubled plasma membrane. The junction is step, shaped with the alternation of areas oriented vertically and horizontally to the disk plane. This leads to an increment of the total surface area of the membranous contact. There are special junction structures in the intercalated disks being: The fascia adherens, macula adherens (desmosom), and a nexus (gap). Fascia adherens is the most common structure which form both plasmatic membranes which are wavy and inserted to each other. They run in a parallel manner and are separated by a 20–30 nm wide slot. Fascia adherens on the other side is the place where myofillaments are inserted. The