which is the result of another primary disease).

Pathophysiological aspects in the therapy of acute myocardial infarction

1. From the awareness of the pathogenesis of the acute myocardial infarction we conclude, that an important therapeutic step lies in the reperfusion of the coronary field by the help of thrombolysis (via a chemical way, e.g. streptokinase as an infusion or a mechanical way e.g. PTCA = percutaneous transluminal coronary angioplasty).

2. Application of betablockers (intravenously or orally) is very useful mainly because they lead to a decrement in the oxygen requirement by the myocardium.

3. The use of an antiaggregatory substances (salicylic acid alone or in combination with dipyridamol) as a prevention of reocclusion of the coronary artery.

In the region of a palliative therapy the greatest attention is given to:

1. The reconstruction of the diseased coronary arteries (meanwhile the main problem is to overcome the restenotization of the artery in the region of the attempt, for example through the use of cellular proliferation inhibitors).

2. Changing the myocardial tolerance to the ischemia. Only recently it was found that, the myocardial tolerance to ischemia can be changed not depending on the perfusion at rest that is obtained by the collateral arteries. This tolerance could be trained by short occlusions of the coronary circulation (for 5-15 min.). It actually delays the occurrence of necrosis yet it does not prevent it. It was found that by this way it is possible to raise the gene expression for a whole series of proteins HSP 70, that have a protective function during many insults (such as heat, radiation). A high tolerance for ischemia is possible to imagine by the help of substances that are activated by the ischemia that would completely exclude the contractile apparatus of the myocardium during the earliest signs of ischemia (e.g. when pH drops). The spared oxygen will be then disposed for keeping the integrity of the myocardium.

3. Attempts made in the region of infarction healing. The modern moleculo-biological methods in animal experiments proved by the use of a cardio-specific genes to stimulate the cardiomyocytes to devide. It is hence possible to hope for the regeneration of the vascular system of the myocardium.

4. The hit in protecting the myocardium is what is known by preconditioning. In life the prevention must be sleep and glycosides, that can keep a high ATP level in the myocardium.

3.24 Pathophysiology of the brain circulation

Vascular supply of the brain

Brain is supplied by blood through 4 large vessels – 2 carotids and 2 vertebral arteries. The left carotid artery (a. carotis communis sinistra) is branching right out of the aortic arch, the right (a. carotis communis dextra) is branching from the brachiocephalic trunk. The carotid sinus lies at the level of C_3–C_4 where the common carotid artery branches into the internal and external carotid arteries. This sinus has special receptors for pressure changes (baroreceptors) and the afferent impulses travel through the glossopharyngeal nerve into the vasoregulatory centers. A. carotis interna enters the intracerebral cavity at the base of the skull through the carotid canal, then forms the S shape and passes through the sinus cavernosus. A. opthalmica which is the first branch of the internal carotid artery anastomosis with the a. carotid externa. Another branch of the internal carotid artery is a. communicans posterior. The internal carotid artery ends as a bifurcation into anterior and median cerebral arteries.

85 % of the blood supply of the brain is passing through the carotids and the rest through the **2 vertebral arteries**. The vertebral arteries in their extravertebral course (after branching from a. subclavia) are in close relation to the neck vertebrae.

The vertebral arteries run in the foramena costotransversaria of the cervical vertebrae C_6 and above. The left and right vertebral arteries are united at the lower end of the pons and form a. basilaris. A. basilaris is then devided into 2 aa. cerebri posteriores at the upper end of the pons. They are connected to the carotid field by joining aa. communicantes posteriores. The communicans anterior artery connects both anterior cerebral arteries.

By this vascular anastomosis **circulus anteriosus Willisi** is formed and through this circle it is possible to compensate the obliteration of any mentioned artery. The deep structures of the brain are supplied by short perforating arteries. The superficial structures of the cortex are supplied by long arteries. Three main arteries emerged from the circle of Willis being: anterior cerebral artery, medial cerebral artery, and posterior cerebral artery which communicate by anastomosis. The amount of blood supply is more in the gray matter than the white matter, this is related to the intensity of the metabolic rate.

There is what is called **haematoencephalic barrier** (blood brain barrier – BBB). The importance of this lies in that the exchange of material in the brain vessels is markedly different from other parts of the body where the capillary supply is usually present. The speed of exchange is very slow and in the normal situation many substances cannot pass through the BBB from the blood to the brain. But this permeability changes during some diseases.

The veins of the brain are devided into the superficial (which carry the blood into the sinuses of dura mater) and into deep veins (which empty into the inferior or the great cerebral vein that in turn empties into the rectus sinus).

The intracranial venous sinuses (s. sagittalis superior and inferior, rectus, transversi, sigmoidei, cavernosus) are placed between the lists of dura mater and all flow into the v. jugularis interna.

There are no lymphatics in the brain, the perivascular spaces take the function of lymphatics.

The collateral blood supply is present in some areas of the brain, but in other areas, such as internal capsule, basal ganglia, the thalamus only few anastomosis are present.

The sensory inervation of the brain vessels comes from the V., IX., X. cranial nerves and the upper cervical roots.

Vasoconstriction is mediated through the cervical sympathetic fibers and the vasodilatatory parasympathetic fibers are in the cranial nerves III., VII., X.

Regulation of the brain blood flow

The human brain represents nearly 2–3 % the complete weight of the organism. Yet for the oxidation that takes place in the brain nearly 20 % of the whole oxygen is needed. The neurons cannot work with low oxygen supply. The damage of the neurons may result also from the depletion of glucose, phosphates rich with energy, some aminoacids, vitamins and other substances. **Nearly 15 % of the minute blood volume is passing through the brain. This is 750 ml/min.** (Compared to the myocardium where it is 250 ml/min). This amount represents a large circulatory reserve. During the childhood the blood flow through the brain is twice as much as the flow in elderly when it is usually the least.

The brain utilizes oxygen merely for glucose oxidation. The gained energy is largely transformed into macroenergetic phosphate bonds. The total oxygen store of the brain is 315 mmol/g and is mostly contained in the brain vessels and with a sudden interruption of the oxygen supply by blood this store enables the survival of the neurons for only 8 minutes. The dysfunction of the neurons takes place after nearly 10 sec. The brain of the newborns can tolerate anoxia more than in the adulthood.

The oxygen supply is 1/4–1/2 larger than the actual amount utilized. By this way the brain is protected against the oxygen depletion which takes place during blood pressure changes.

The basis of the adequate oxidation of the brain tissue is the perfusion pressure which is given in the following relation:

$$CRP = MAP - (CPP + CVP)$$

where: CPP – cerebral perfusion pressure
          MAP – median arterial pressure
          ICP – intracranial pressure
          CVP – central venous pressure

The intracranial space is strongly limited by the bony parts and filled with 3 noncompressible components - the brain tissue, blood, liquor (the cerebrospinal fluid or CSF). The change of volume in any of these components is accompanied by the change in ICP which ranges physiologically between 0,9–

1,9 kPa. When ICP reaches over 6,6 kPa the brain circulation will stop.

The venous pressure in the brain is only 0,7 kPa.

In normal conditions the CPP ranges between 6,6–20 kPa. The critical level of the MAP needed to keep the blood flowing through the brain is about 8 kPa. Any decrease below this level, specially if sudden, can lead to failure of the brain circulation.

Another condition for normal functional activity of the brain is an intact BBB. As well as other criteria, such as enough glucose supply.

The normal blood flow through the brain is about 50–60 ml/100 g tissue/min. When this is lowered to 20 ml/100 g tissue/min, the functional activity of the neurons decreases and this is presented very fast in the cerebral cortex. **The structural changes in the brain neurons take place after few minutes when the blood flow level is decreased to 10 ml/100 g tissue/min**. The most sensitive are the neurons, then the glial cells and finally the endothelial cells of the brain vessels.

During the passive changes in the systemic arterial pressure the brain circulation is not affected due to the **autoregulatory compensatory mechanisms.**

Yet those regulatory mechanisms do not start working immediately after the drop of blood pressure, but with a 1–2 min latency, during which the blood pressure may get below the critical level needed to keep the CPP. In hypertensive and atherosclerotic patients has been noticed that the critical level needed to keep the CPP is relatively higher than in normal individuals. Decrease in blood pressure to 70 % of its original level in hypertonic patients may have serious outcomes.

The brain vessels are very much adapted to deal with any decrease in the brain perfusion by an adequate vasodilatation. At the same time vasoconstriction takes place of the peripheral structures and by this mechanism a redistribution of blood supplies adequate amounts of blood to the brain. The mechanism which leads to vasodilatation in the brain vessels is yet unknown but many opinions point to the role of carbon dioxide and its effect on the brain vessels.

On the other hand when there is an increase in the blood pressure (for instance an increase in the MAP up to the level of 20 kPa) the arteriol field reacts by increasing the vasoconstriction. Any deviation of pressure changes above or below the previous mentioned levels leads to the failure of autoregulatory mechanisms. Carbon dioxide can affect the brain vessels in 3 manners:

- through the pCO_2 level in the arterial blood

- indirectly acting on the vasomotor center in the medulla oblongata

- through pH changes in the tissue which may have an influence on contractile elements in vascular wall

Hypercapnia leads to vasodilatation of the brain vessels, acidosis in the perivascular space and in the smooth muscle cells in the vascular wall leads to vasodilatation as well.

The metabolic results of **hypoxia** (decrease in the hydrogen ions concentration, increase K^+ and Ca^{2+} concentration, increase the level of catecholamins, and adenosin level increase in the tissues surrounding the arterioles) may lead to vasodilatation.

On the other hand hypocapnia, alkalosis, and hyperoxia have a blocking effect on the vasodilatation and have vasoconstrictory effect. Some other substances with vasoconstrictory effect are acetylcholine, norepinephrine, dopamin, serotonin, histamine, thromboxan A_2, haemoglobin, prostaglandin E_2 etc.

The neurogenic regulation is less prominent than the chemical regulation in the brain circulation and it has an adjusting action. The outcome of this regulation comes from the baroreceptors in the aortic arch and the carotid sinus. These are stimulated by any change in the diameter of the vessel where they are located. The role of the sympathetic nerves lies in protecting the brain against any sudden increase in the blood pressure. The stimulation of the sympathetic fibers leads usually to vasoconstricion similarly to the stimulation of the a-adrenergic receptors, on the contrary the stimulation of the b-adrenergic receptors leads to vasodilatation.

3.24.1 Stroke – acute cerebrovascular accident

Cerebrovascular accident – CVA (apoplexia, ictus) is a localized cerebral damage which results from a sudden drop of blood perfusion in a certain area of the brain tissue (**local brain ischaemia**) or a sudden distraction of the brain tissue by a haemorrhage which is localized in a certain area (**cerebral haemorrhage).**

3.24.1.1   Localized ischaemia of the brain

Is a condition **of decreased perfusion in a limited area of brain tissue resulting from cerebrovascular insufficiency**. Cerebrovascular insufficiency can occur, when cerebrovascular resistance increases with a normal haemodynamics (eg.atherosclerotis or obliterations) or the resistance is unchanged but the haemodynamics are decreased (eg. hypotension).

The decrease in the brain perfusion by 30–50 % can pass with no neurological signs and with no switching on of the regulatory mechanisms, yet any further reduction in the brain circulation leads to switching on of compensatory mechanisms.

Yet, when the cerebrovascular insufficiency leads to a perfusion decrease of about 20 ml/100 g/min, then the compensatory mechanisms are not capable any more to deal with the perfusion drop in the brain. So the cerebral blood flow is no more sufficient for the adequate oxygen and nutrition supply of the brain and the clearance of the metabolic products. Here an area of a permanent ischaemia is formed (with the changes of pH of the perivascular fluid, and the resulting pathological vasodilatation, hyperaemia and brain oedema).

Brain ischaemia can occur as well during an abnormal increase in brain function beyond the physiological ability where the compensatory mechanisms are no more capable of adapting the increasing requirements.

Brain ischaemia can occur due to acute **hypotension** specially in patients with cardiocirculatory insufficiency with hypertension, atherosclerosis or other pathological disorders. In these patients even a physiological drop of the blood pressure in such conditions as rising up, long standing, after meals, after hypotensive therapy, may lead to brain ischaemia.

Localized brain ischaemia can occur as well with a **pathological** drop of the blood pressure e.g. in shock, haemorrhage, MI, Adam's stroke syndrom, narcosis.

bn The cerebrovascular insufficiency may be a result of the circulatory failure in cardiocirculatory diseases:

- myocardial infarction (MI)
- cardiac arrhythmias
- heart failure
- cor pulmonale with decompensation
- mitral valve diseases
- others

Lowering the heart function in these cases leads to the decrease in the amount and the speed of cerebral blood flow.

Generally there are some hypoxic factors which correlate with other factors predisposing to the acute regional brain ischaemia.

These are: increased blood viscosity, anaemia, polycythaemia, change in blood temperature, coagulation disorders, disorders in glucose utilization, lipaemia, cytotoxic changes in the cells, haemoconcentration, respiratory disorders.

The most effective factor among them is **diabetes mellitus** (DM), with bad glucose tolerance and utilization. Diabetic microangiopathy of the brain arteries may cause their dysfunction and respectively the failure of their autoregulatory function. Polycythaemia may lead to high blood viscosity which increases the cerebrovascular resistance and decreases the cerebral blood flow.

Anaemia with a low haemoglobin concentration worsens the brain supply with oxygen. In **lipaemia** there is also an increase in blood viscosity. Another hypoxic factor is an increase in the thrombocyte aggregation, which leads to a microcirculatory failure.

A localized atherosclerosis in regions of branching, bifurcations, and bendings of carotid, vertebral and cerebral vessels **is the most common cause of the cerebrovascular failure**. It causes chronic stenosis and represents also one of the pathogenic factors in acute brain ischaemia.

Atheromatous changes lead to the narrowing of the vascular lumen and hence they become less translucent. The endothelium is destroyed and then sloughed during the process of atherosclerosis leading eventually to a marked loss of vasoconstricting endothelines, which more over induces the loss of thromboxanes being another effective vasoconstricting agents present in the platelets. Atheromatous lesions may also lead to microembolization.

The atherosclerotic changes are usually found on the extracerebral part of the carotid arteries.

The vascular anomalies such as (absence of a vessel, their tortuosity, etc.) occur mainly in the regions of the vertebrobasilar and carotid vessels. The cerebrovascular insufficiency arises from the slow blood flow through the abnormal vessels mainly in the elderly. There are also some other mechanical factors

that affect the circulation (for example the vertebral artery is closely related to the bodies of the vertebrae, to the intervertebral discs and to the spinal nerves). Thus change in the position of the head together with additional factors may play a role in cerebrovascular insufuciency.

The cerebral arteries (with the exception of the circle of Willis) have a very weakly developed tunica muscularis media and hence a weak ability to contract. Apart from this penetrating cerebral arteries loose the periarterial inervation when penetrating the brain tissue and as a result they loose the neurogenic regulation of their contraction.

The **ischaemic tissue** from the pathological point of view contains devitalized central areas (where the blood flow is below $10 \, \text{ml}/100 \, \text{g}$ of tissue/min) as well as vital peripheral parts in which the perfusion reaches about 10-20ml/100 g /tis/min but these parts due to their dysfunction are also considered "lost" parts.

The initial **functional** change is the loss of neuronal membrane polarity. The initial **structural** change after few minutes of ischaemia is the enlargement of the mitochondria (and hence the damage of their membrane) which is essential for the oxidative phosphorylation). In the nucleus there is loss of proteosynthesis, free oxygen radicals are released as well. These radicals react with some phospholipids in the cell membrane leading to it dysfunction. After few hours of ischaemia due to the rupture of the cell membrane the hydrolytic enzymes are spread into the interstitium.

The first morphologically detected change in the ischaemic area is the **intracellular oedema**. Hypoxia leads to the depletion of ATP due to low aerobic glycolysis. This eventually leads to the dysfunction of Na^+–K^+ pump in the cell membrane. There is an influx of Na^+ intracellularly leading to intracellular oedema. Ca^{2+} plays a key role in cell damage hence it flows intracellulary and activates the phospholipase enzymes. Free oxygen radicals represent other factors in the cellular damage.

Later the tissue **necrosis** develops. The pathologicanatomical picture of the necrotizing area is **malatia alba**, less frequent is **malatia rubra** being a haemorhagic infarct which occur when there is venous stasis in the cerebral circulation. The final picture which is the result of the macrophage action after weeks and months is what is known as **post-**malatia pseudocyst** being a cavity filled with serous fuild.

Between day 7 and day 30 of the CVA a **defect in the blood brain barrier** is noticed. The hypoxia not only affects the neurons and the glia but as well destroys the vascular endothelium. The damage of the blood brain barrier during the ischaemia is an important factor in other 3 processes being :

1. The passage of the serum proteins extravascularly lead to the formation of extracellular oedema.

2. The abnormal permeability of pharmacologically active substances leads to a change in the vascular smooth muscle cells reactivity.

3. There is a disturbed permeability for some tissue metabolites and some local toxic products to vascular lumen (this leads to the accumulation of lactic acid in the interestitium and hence an increase in the water binding capacity).

Brain oedema is an increase in the water content in the brain tissue. Since the brain is contained in limited and closed intracranial space, this phenomena is very dangerous. The increasing brain volume leads to deformation of the brain ventricles and other liquor filled spaces, a deviation of the midline and even herniation of the brain tissue to intracranial spaces like to foramen occipitale magnum.

Ischemic oedema marks the hyperhydratation of the infarcted area which results from the tissue hypoxia. It starts as intracellular hyperhydration and later the vasogenic oedema takes place. The effect of oedema on the nervous tissue lies in the formation of bad condition for neuronal transmission. Global hypoxic damage of the brain can be the end result and this is manifested as a state of deep coma after the cardiopulmonary resuscitation. The picture of this state is a multicentric necrosis.

3.24.1.2 Brain haemorrhage

The basis of **brain haemorrhage is a gush of blood through a vascular rupture into the brain tissue**, or into **the cerebrospinal fluid** (CSF) of a ventricle or the leptomeningeal cisternae.

The degenerative vascular changes render the vessels liable for rupture. The usual site is the internal capsule and the most common artery affected is the Charcots artery.

The etiopathogenesis lies in a lower local resistance of a given artery in combination with a sudden or a continuous increase in a cerebral arterial blood pressure. An arterial spasm can precede the haemorrhage causing a functional distraction to the vessel wall and then its easy rupture in case of any increase in the blood pressure. A decrement in the mechanical strength of the cerebral arteries is mostly caused by the atherosclerotic changes.

At the moment of the arterial wall rupture the blood gushes out, and the pressure is markedly decreased intravascularly leading to the vascular smooth muscle contraction. The narrow lumen leads to thrombus formation. The flow of blood continues till the decreasing intravascular pressure is in equilibrium with the increasing intracranial pressure.

Haemorrhage causes a disruption in the brain tissue along the axons can completely destroy the tissue despite its anatomical structure. The increase in the intracranial pressure leads to the failure of the venous return and hence venous congestion leads to malacia rubra.

3.24.2   Subarachniod haemorrhage

Is a spontaneous intracranial haemorrhage which spreads in the leptomeningeal space between the arachnoid and pia mater. Frequently it is associated with a cerebrovascular haemorrhage which is the primary event and the passage of blood to the leptomeningeal space is the secondary event. **The vascular aneurysms are the usual source of the subarachnoid haemorrhage**. This condition usually occurs suddenly and hence the term ictus.

The clinical picture of the subarachnoid haemorrhage is usually pain as a dominating symptom which is frequently accompanied by alteration of consciousness. The location of the pain usually corresponds to the site of rupture. Meningeal syndrom develops 6–12 hours later when the meningies respond to the presence of blood by a sterile inflammation. In cases where the aneurysmal blood affected the surrounding brain tissue, here a loss of individual functions may occur.

3.24.3   Aneurysms

Intracranial aneurysm is **an abnormally located dilatation of a cerebral artery** which usually develops in a weakened area of the vessel wall. It can be **congenital**, **traumatic**, **arteriosclerotic** or **inflammatory**.

Congenital and traumatic aneurysms are the commonest causes of the subarachnoid haemorrhage.

Besides the congenital aneurysms there are also the required ones usually due to mycotic embolisation. Some aneurysms have elastic wall and their rupture occur very rarely. So they are manifested by their pressure on the brain tissue or the cranial nerves.

3.24.4   Generalized arteriosclerosis of the small cerebral arteries

The pathologicanatomical finding of the cerebral arteriosclerosis is the picture **status verminosus** of the cerebral cortex (being the extinction of the ganglion cells due to ischaemia), **status cribrosus** of the basal ganglia being a widening of the perivascular spaces, and status lacunaris (being small cavities or post malatia pseudocysts).

In the elderly the brain tissue is subjected to a **diffuse slowly progressing arteriosclerosis**. The arteriosclerotic changes seems to develop gradually reaching the small vessels. During life a gradual hyalinization of the vessels takes place, particularly in hypertensive individuals, which is followed by fibrosis and necrosis. Thus the vessels loose their elasticity and the ability of dilatation.

The illness **usually starts as pseudoneurosthenia being** (tiredness, irritability, apathic behavior). We can notice some memory problems, emotional liability, and some sleep disturbance.

3.24.5   Thrombosis and thrombophlebitis of the cerebral veins and sinuses

Venous obliteration can result from **inflammation** of the venous wall and **disturbances of the haemodynamics** with venous stasis.

Thrombophlebitis results from a generalized or a localized inflammation such as sinusitis, otitis media etc.

On the other hand, **phlebothrombosis is mainly caused by** a **disturbance in the haemodynamics**. It can manifest itself in patients with an increased haemocoagulation and in cases of venous stasis.

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-