

3.17.2.1 The vasodepressor syncope

The causative factor is a transient low activity of the sympathetic and a consequent dilatation of the peripheral vascular field. The typical representative is the vasovagal syncope. Occurs in some people upon fear, pain, and psycho emotional stress (venopunction, the sight of blood etc.). A predisposing factor is an upright posture and a residence in an oppressive environment. The cause is a reflex depression of the vasomotor center that causes dilatation of the peripheral vessels. The syncope is preceded by malaise, nausea, pallor, sweating, hyperventilation, confusion, blurred vision and tachycardia, that will change into bradycardia during the syncope. Putting the patient to the horizontal position the loss of consciousness will fade away and the patient returns to normal soon after.

Carotid sinus syndrome occurs in normal conditions upon massaging or exposing pressure on the carotid sinus that will lead to bradycardia and hypotension. In some cases and mainly in sick people with hypertension or atherosclerosis, loss of consciousness occurs upon a very slight stimulation of the carotid sinus (a narrow tight collar, pressure upon shaving, turning the head). Cardiac, vasomotor, and cerebral factors all share in the pathogenesis of its occurrence. That is why the sick carotid sinus syndrome might present in three variable types:

- the hypersensitive type, characterized by a prominent hypotension without changing the heart rate
- the cardioinhibitory type in which there is a prominent bradycardia without any change in the blood pressure
- a cerebral type where collapse occurs with no change in the heart rate or in the blood pressure, that indicate a disturbance in the higher regulatory centers

Syncope during miction occurs in men and it is mainly nocturnal after the intake of a large amount of fluids. It is most probably a case of some reflex mechanism (emptying the overfilled urinary bladder, Valsalva maneuver).

3.17.2.2 Syncope due to the primary failure of venous return

The primary failure of venous return can cause syncope upon venous stasis in the large dilated veins, during gravitational overload and during an increased intrathoracic pressure.

Orthostatic syncope is always characterized by an inadequate response of the sympathetic nervous system to the change of position from horizontal to vertical. The typical orthostatic syncope occur upon a sudden standing upright in those people with inadequate reactivity of the sympathetic nervous system, in patients treated with antihypertensive drugs, and also in cases of diseases of the central and peripheral nervous system (atherosclerosis of the CNS, diabetic neuropathy). Long standing may predispose to syncope in patients with tendency to cumulate blood in the lower limbs due to the insufficiency of the venous valves.

Gravitation syncope occurs with increasing the gravitation, and here it depends on the intensity of this increase, its direction (from head to feet), and upon previous experiences. In sensitive patients it might occur in elevators or upon a fast start. It occurs within 2–4 seconds after the beginning of gravitational overload and it gets soon to normal.

Syncope during cough: Syncope occurs in the case of heavy cough in patients with airway obstruction or pulmonary emphysema, where the increasing intrathoracic pressure will prevent the venous return. This case as well might occur in troublesome defecation – in old patients can a prolonged Valsalva maneuver be the cause of the transient lower venous return with the occurrence of syncope.

3.18 Shock states

The heart ensures blood flow via the vascular system. The speed of blood flow depends on the arterial pressure, that has to reach a certain value to obtain adequate perfusion via the large capillary network. The value of the blood pressure in the central area of the vessels is determined by two factors. **The**

first factor is the blood volume that is pumped per minute time. **The second factor is the resistance** to the blood flow imposed by the peripheral blood vessels. The resistance changes according to the muscle tension in the arterioles as well as according to the length of the vessels and the blood viscosity. The main determinant of the resistance is the total calibre of the vessels. From the below mentioned values in tab. 3.1 we might notice that venules and small veins together have a 5 folds larger calibre than the arteries and arterioles and that is why this part might be a reservoir of a large volume of blood.

aorta	2,5 cm ²
small arteries	20,0 cm ²
arterioles	40,0 cm ²
capillaries	2500,0 cm ²
venules	250,0 cm ²
small veins	80,0 cm ²
vena cava	8,0 cm ²

Table 3.1: Area of the calibres of different vessels of the circulation

The blood volume is not stationary, it might change accordingly with the actual needs. This change might occur via the neural or the humoral regulatory intervention only. Apart from those factors other constituents might be quite important for the blood flow but they are considered to be secondary.

The cardiac output is modulated and controlled by many factors, that are realized via the changes of the end diastolic volume of the ventricles, the quality of contraction and via changing the heart rate.

The arterial blood pressure is largely monitored by the vegetative nervous system. This has a prominent effect on the cardiac output and on the level of constriction of the resistance vessels (arterioles) and the capacitance vessels (veins and venules). The vegeta-

tive nervous system obtains the information about the actual state of pressure via the baroreceptors (receptors sensitive to the pressure and distention). They do present mainly in the carotid sinus, in the arch of aorta, heart ventricles, and in the lungs. Information from the baroreceptors are transferred to medulla oblongata. There are connections among the sympathetic and the parasympathetic nuclei. From medulla oblongata the information might be transferred to the cerebral cortex and the hypothalamic nuclei. By this way is the nervous regulation interconnected into the humoral regulation till the pituitary (hypophysis).

The permanent tension of the vascular wall continuously stimulates the baroreceptors. This information is processed centrally and according to the need it modulates the circulatory state.

A severe sudden lowering in the arterial pressure decreases the stimulation of baroreceptors, that causes changes in the sympathetic information and depresses the parasympathetic activity at the same time. The result is constriction of the smooth muscle of the arteriolar wall and venous wall and an increased myocardial contractility.

Consequently there will be an increased hormonal secretion from the adrenal cortex, the release of ADH, ACTH, renin and following aldosteron. Other substances share the regulation and those are some metabolites with vasodilatory effect such as adenosine, kinins, and prostaglandins. Changes in the volumes and in the electrolytes also take place in the process of maintaining the optimal blood pressure. The neural and humoral changes aim to renew the optimal level the blood pressure, to stay within an easily controllable and easily regulated range.

3.18.1 The adapting and compensatory mechanisms activated by the low tissue perfusion during shock

Shock is an emergency, that is characterized by its variable clinical presentation. It can be treated and managed successfully. Yet for this we need a clear appropriate medical care and a prompt and accurate monitoring of the haemodynamics.

The etiology of shock may be heterogenous. It is substantial, that in every case the circulation is deteriorated. Common sign of all shock types is the

disturbance of microcirculation. Impairment of the circulation system leads to decreased tissue perfusion and deterioration in cell function.

For understanding the pathophysiology and the treatment of the shock is necessary to know the principles of the circulation functions and of the control mechanisms involved in the shock development having the role of adaptation and compensation mechanisms.

3.18.1.1 Haemodynamic adaptation and compensation

The fundamental function of the circulation is the oxygen and nutrient supply for the tissues and the metabolic products removal from the tissues. This function of circulation is in all shock types insufficient. The degree of this disturbance determines the shock development and its clinical manifestation.

The perfusion of tissues is regulated by very complicated processes. There are some tens of determinants involved in the perfusion regulation: cardiac and vessel factors, and factors at the microcirculations level. The perfusion of organs depends on the systemic arterial blood pressure, on the resistance of vessels in the relevant organ, and on the state of capillaries inside of the organ.

The systemic arterial pressure depends of the cardiac output of all vessels resistance. The resistance of vessels is determined by their lumina, which are influenced by neural, humoral and muscular factors regulating the tension of vessels smooth muscle. The blood supply of every organ depends on the heart function, on blood vessel wall tension and on the calibre of resistant vessels and the vessel bed in the organ itself. The exchange of substrates between the tissue and the circulating blood depends of the microcirculation. Hence, the capillary network forms the interface between the circulation and the cells.

The left heart ventricle pumps five liters of blood each minute into the arterial circulation. The right ventricle pumps an equal volume of blood into the pulmonary circulation. If the cardiac output falls under 2 liters/min/m² of body surface the shock develops with all consequences. Particularly rapid is the development of shock if the fall of the cardiac output occurs rapidly.

The heart can pump the blood with great variability of the frequency. It is able to maintain the output volume per minute between 40 to 180/min.

Increase in the heart rate is the first compensatory change appearing during the fall of the systemic arterial pressure. The heart rate change is modulated by the autonomic nervous system. Increase in heart rate leads commonly to the cardiac output elevation. In heart rate elevation above 180/min., however, the diastole shortens so far that the phase of rapid ventricle filling becomes also shortened. During this heart rate the output volume is reduced owing to the heart filling decrease, and so does the output volume per minute. This situation results in the blood pressure fall. The condition may be very unfavourable, e.g. in acute myocardial infarction. The ventricular tachycardia or the atrial fibrillation result in reduced cardiac output, which is already decreased owing to the myocardial infarction itself. (the necrotic part of the ventricle does not contract).

This might result in the occurrence of cardiogenic shock, that is a very common dramatic situation with a lethal outcome. In this case the state of the haemodynamics is getting worse due to the higher heart rate. Sinus tachycardia alone is a useful compensatory mechanism. Yet it depends on the situation of its occurrence. It is a useful compensatory mechanism during febrile states, in anemia, or upon an acute blood loss. This is how we can explain tachycardia and the pathophysiology of its occurrence. It wouldn't be right to aim to treat a useful compensatory mechanisms in every situation. On the contrary **bradycardia** can also occur during a sudden drop of the cardiac output or during a sudden hypotension. This condition occurs mainly in situations where the low cardiac output and hypotension lead into hypoxia of the regulatory centers in the medulla oblongata. Bradycardia can occur upon treatment with many medicaments especially those leading to hypotension or upon blood loss. Bradycardia yet occurs even after myocardial infarction or in situations that lead to severe hypotension. This is not uncommon in cases of a sudden atrioventricular block.

Another factor that determines the state of haemodynamics is the **stroke volume**. It is the amount of blood expelled by the ventricle during each contraction. Low stroke volume can be the result of a low heart filling (preload), or a weak contractility (a negative inotropic state of the heart) and a high afterload. Preload is defined as the tension of the sarcomer at the very beginning of the ventricu-

lar contraction. Clinically the preload represents the ventricular filling at the end of the diastole. **Preload** shares in the determination of cardiac contraction by the means of Starling law. Preload is clinically measured as a pressure and not the filling of ventricle at the end of diastole. Yet we have to consider that the relationship between the pressure and volume is represented as compliance (dispensability) of the ventricle. Compliance represents the ratio between the volume changes and the pressure changes. (The inversion of the value of compliance is known as ventricular tension).

The most important factor, that determines the preload is the total volume of the circulating blood. **The volume of the circulating blood** can decrease relatively or actually. An actual decrement in the blood volume – hypovolemia – occurs upon the loss of blood or fluids. A worsening hypovolemia is the cause of hypovolemic shock. Such a state occurs during bleeding, exhausting vomiting, diarrhea, burns, abnormal loss of water by the kidneys, and upon an excessive sweating with no fluid intake. Hidden loss of fluids occur in peritonitis, pancreatitis, intestinal obstruction, splanchnic ischemia with necrosis, in haemoperitoneum, and in fractures with muscular bruising.

It is unbelievably important to realize that, the normal yet unchanged total **blood volume** is still not an indicator of an optimal haemodynamic. The volume of blood **has to be properly distributed** in the organism so that the preload would be good enough for the required stroke volume. The main factors that determine the distribution are the body position in relation to the gravity force, venous tension, intrathoracic and intrapericardial pressure and the pumping of blood in veins by the skeletal muscles. Cardiac compression for example in pericardial tamponade can limit its filling. Low venous return due to the absence of the negative intrathoracic pressure can occur in pneumothorax. A relative lowering of the blood volume can occur when losing the vascular tonus. This occur during anesthesia, injury to the medulla oblongata, and some disturbances of the vegetative nervous system.

Afterload be easily understood as the sum of forces, that has to be by the ventricle, to expel blood. Afterload is first of all determined by the diastolic arterial pressure at the beginning of aorta, the size of the ventricle, and vascular resistance. The dias-

tolic pressure at the beginning of the aorta depend on the total peripheral resistance, on the viscoelasticity of the arteries and on the volume of blood in the aorta at the beginning of systole. The resistance in this case is the sum of factors that try to prevent the blood to flow out of the ventricle. These are the continuation, the viscosity, the resistance, and the compliance. The resistance is shown by the dynamic relationship between the pressure changes and changes of the blood flow clinically it is only possible to count the resistance but not to measure all its constituents. The calculated resistance can be expressed as the systemic vascular resistance. We subtract the mean pressure in the right atrium from the mean systemic blood pressure and the difference is divided by the cardiac output.

In normal condition **the contraction of the atria** plays a negligible role in ventricular filling. Their share does not exceed 5–10%. In diseases of the heart the atrial contraction share about 40–50% of the ventricular filling and that is why in aortic stenosis or cardiomyopathy, the atrial fibrillation will worsen the heart failure.

The inotropic state of the heart determines the speed and the amount of the muscular contraction in the physiological conditions no matter how long was the sarcomer at the end of diastole. From the clinical point of view it is the power of contraction that is determined by multiple factors. Among those factors are the mass of the functioning myocardium, the myocardial perfusion, the controlling mechanism, and humoral factors. In some shock types we expect that the myocardial depressing factors has a certain role, that affects the contractility of the myocardium will result in a state where the heart can not maintain the cardiac output on the required level.

An important determinant of the myocardial contractility is **the state of the sympathetic nervous system**, that is realized via the activation of β – receptors in the heart. The result is a higher contractility of the heart and its frequency. This effect is obtained by the effect of the efferent sympathetic fibers of the myocardium, as well as the effect of the catecholamines produced by the adrenal medulla.

The cardiac activity depends on the relation between the myocardial requirements and the oxygen supply. **The supply of oxygen to the myocardium depends** on its perfusion, that is prominently determined by the arterial diastolic pressure and the state

of the coronary arteries. The state of the coronary arteries can be permanently changed by atherosclerosis of the coronary arteries or the change might be the result of a transient spasm. A prominent fast drop of the diastolic pressure can cause myocardial ischemia, the consequence of which is a lower cardiac output. If the coronary arteries are changed as well (narrowing in any segment by the atherosclerotic process), there will be vasodilatation after the constricted segment. It is caused by the accumulated metabolites, that have vasodilatory effects. In this situation the arterial blood pressure becomes a factor, that determines perfusion via the collateral arteries or via the narrowed coronary arteries.

3.18.1.2 Nervous regulation

An important part of the nervous regulation are the **receptors**, that are placed in strategic areas. The most important are the arterial baroreceptors in the carotid sinus area, in the aorta, the cardiopulmonary baroreceptor, chemoreceptor, and receptors of the skin and muscles. The vasomotor centers in the medulla oblongata are under the control of higher centers in the central nervous system. By this the sympathetic and parasympathetic regulation is modulated from the central nervous system.

The heart doesn't only work as a pump of blood even if this function is principally the most important one. The heart is a periphery sensory and endocrine organ. Baroreceptors are localized mainly in the posterior wall of the left ventricle. They are activated as **mechanoreceptors upon the relaxation and the contraction of the myocardium**. When the preload is increased the ventricular relaxation receptors are activated and work as an afferent inhibitors on the cardiovascular centers in the medulla oblongata. That is why the efferent sympathetic stimulation is decreased in these centers. On the contrary during hypovolemia or upon the standing position the afferent inhibition affect of the ventricular receptors on the centers in the medulla oblongata is suppressed. This is the reason why the afferent sympathetic activation is promoted, and this will result in vasoconstriction, tachycardia, and the release of renin. The ventricular relaxation receptors can signalize incorrectly during myocardial infarction that the tension in the ventricular wall is high.

The outcome of this there will be an inhibition of the cardiovascular centers, worsening the pump-

ing function of the heart and lowering the peripheral vascular resistance.

Arterial baroreceptors in the carotic sinus in the aortic arch are a high pressure mechanoreceptors, that are activated when increasing the arterial pressure. The activation of receptors is like an afferent inhibition of the vasomotor centers. Next the efferent sympathetic stimulation will be inhibited and hence the occurrence of vasodilatation and bradycardia. On the other hand when the blood pressure becomes low the afferent inhibition from the arterial baroreceptors on the vasomotor centers is. That is the reason why the sympathetic effect increases, resulting in vasoconstriction and tachycardia.

Both the mentioned systems are inhibitory. Apart from them there is a **peripheral excitatory system**, that makes use of the chemoreceptors that are localized in the carotic area. They are activated in shock when hypoxia takes place. Their activation has an excitatory effect on the medulla oblongata by means of the increased sympathetic activity and vasoconstriction. The other excitatory system is formed by the somatic receptors. These are actually **metabolic receptors** that are activated by the metabolic products in the working muscles.

The excitatory effect on the medulla oblongata resemble the sympathetic stimulation in the muscles, that yet effects merely the functioning muscles. The result is a useful redistribution of blood. In case of circulatory disturbances many reflex mechanisms might become interconnected. If eg. hypovolaemia is combined with hypoxia more mechanisms are activated. The result is not necessarily useful for the organism, because there might be the activation of opposing mechanisms. That is why in myocardial infarction due to the loss of a part of the contractile myocardium and a low cardiac output there will be hypotension. This hypotension will act on the arterial baroreceptor systems. At the same time there will be dyskinesia in the infarct area, that might cause a wrong information that signalizes a higher preload.

3.18.1.3 Humoral regulation

For optimizing the haemodynamics even **humoral factors** play an important role. **Renin**, primary synthesized in the juxtaglomerular apparatus and regulated by different stimuli, mainly the pressure in the afferent arteriole, the concentration of Na^+ in the region of macula densa, the stimulation of the renal

sympathetic fibers, the circulating **angiotensin II** and the concentration of electrolytes in plasma. Renin as a proteolytic enzyme converts angiotensinogen to angiotensin I. In the lungs angiotensin I is converted to angiotensin II and III by the effect of angiotensin converting enzyme. There are powerful vasoconstriction agents, that also facilitate a fast release of noradrenalin from the sympathetic nerve terminals. Vasoconstriction aims to increase the blood pressure. Angiotensin II increases the release of **aldosterone** with the resulting retention of Na^+ and water.

During hypovolemia and upon increasing the osmolarity vasopressin is released **from the posterior lobe of the pituitary**. Its vasoconstriction and antidiuretic effect is prominent during shock. **Vasopressin** stimulates the release of **ACTH and cortisol**. The release of vasopressin ceases upon stimulating the sensitive baroreceptors in the left ventricle, in hypervolemia, and arterial baroreceptors in hypertension. On the contrary the level of vasopressin is markedly increased in cases of hypotension. Lowering the blood volume by 10% its volume is a strong stimulus for the release of vasopressin. The vasopressin release is promoted by the central nervous system as well after the higher angiotensin level. It is very important to know that the release of vasopressin is stimulated by hypoxia and nausea as well and morfin. Catecholamines inhibit the release of vasopressin.

To maintain the haemodynamics many other **polypeptides with local vasodilatatoray effect** are of value. These polypeptides are formed by the effect of some proteolytic enzymes on plasma protein precursors. The classical prototype of this group of endogenous peptides is bradykinin. The role of these peptides is **the modulation of local perfusion** via some organs. Their effect is very prominent in case of inflammatory processes, that are accompanied with hyperemia. During shock they mainly influence the blood flow via the kidneys and pancreas. Renal kinins can increase diuresis and natriumuresis.

During shock **serotonin** is released **from the thrombocytes and histamine from mast cells**. They affect the local circulation. What is important is that they affect the capillary permeability. During hypoxia that results from shock some substances might be released and affect the formation of thrombi. Prostacyclin is synthesized from the endoperoxides

that are present in the vascular wall. **Prostacyclin** is vasodilatory agent that inhibits aggregation of thrombocytes and vasoconstriction. The formation of prostacyclines and **thromboxan** arises from the arachidonic acid, that is a part of the membranous phospholipids. The trigger for its release might be a very slight injury. In the first phase there is the formation of cyclic endoperoxid from which later prostacyclines and thromboxanes with their mentioned effects of thrombocytes aggregation are formed.

Haemodynamics during trauma and shock is affected even by **neuropeptides**. The most effective are endogenous opiates (β -endorphin), thyreotropin releasing hormone and ACTH. β -endorphin and ACTH are readily formed in the hypophysis and they are usually released during stress. They modulate the function of the vegetative nervous system. β -endorphins are usually of importance during hemorrhage and septic shock. They most probably have a direct or an indirect modulated depressor effect on the myocardium. Thyreotropin releasing hormone that is released during shock will improve the cardiorespiratory function.

Its function is probably an opposite to the β -endorphins function.

Catecholamines are important modulators of the cardiovascular function. Noradrenalin increases myocardial contractility and the heart rate via the activation of β -adrenoreceptors. That is why its function lies in the increase of the cardiac output. Noradrenalin however has mainly an α -adrenergic function and causes vasoconstriction in the skin vessels, muscles, splanchnic area but at the same time it has a β_2 -adrenergic mechanism and causes the vasodilatation in coronary arteries. Adrenaline has got both α , β_1 , β_2 effects, it causes a mild increase in the cardiac output. It causes redistribution of blood to the muscles.

3.18.1.4 Autoregulation of perfusion and changes in the microcirculation

Autoregulation of tissue perfusion is most important in the cerebral vasculature, in the coronary field, and in the renal vessels. Its function lies in maintaining the adequate perfusion even in cases where the arterial blood pressure is markedly low. In those vascular areas there are no specific mediators. The tension of the vascular wall is regulated by a combination

of changes of oxygen concentration, CO₂ concentration, pH, osmolarity, the level of adenosine and other metabolic substances.

The most difficult problem in the pathogenesis of shock is **microcirculation**. Every shock type is actually the outcome of microcirculatory failure. The redistribution or shift of an adequate volume of blood into a certain organ is not the guarantee that all parts of this organ and the capillaries will be perfused accordingly to their metabolic needs. **Blood in certain situations can leave a part of that organ without perfusion**. The total blood flow via the kidneys might be only slightly reduced. Blood can only flow via the medullary part and that is why some serious changes might occur in the cortex. Apart from this, blood flow is regulated via the capillary sphincters. Those sphincters are actually smooth muscles of the vascular wall, that is under the influence of many neurohumoral factors. In hypovolaemic shock the blood pressure drops and the activation of the sympathoadrenal system will result in vasoconstriction of the precapillary resistant vessels. As the result of all this the intracapillary pressure will reduce as well and hence fluid flows from the tissues intramuscularly. If this condition lasts for long time, vasoconstriction will gradually become weaker. It is caused by the fact that in the tissue becomes acidosis. At the same time the postcapillary resistance increases. In this stage fluid escapes from the intravascular spaces into the tissues (interstitium). This condition might be caused by catecholamines.

Changes of the precapillary and postcapillary resistance affect the shift of fluids between the intravascular space and the interstitium. Along with this it affects some colloid osmotic pressure changes that consequently change the capillary permeability. That is very important in some organs. Any change in the capillary permeability is sometimes so important that it causes escape of the plasma proteins into the extravascular spaces. These changes play an important role in the development of pulmonary shock.

During this shock there might be **erythrocyte, leukocyte or thrombocyte agglutinations**. These might obstruct capillaries and small arterioles. Thrombocytes activated by catecholamines can form individual clusters. Hypoxia causes injury to the endothelial cells, that will aggregate the accumulation of micro thrombi. Endothelium forms free oxygen radicals. These changes might worsen the state of

the micro circulation and the whole haemodynamics.

3.18.1.5 Hypoxia and acidosis

A very unfavorable factor that accompany shock is hypoxia and acidosis. **Tissue hypoxia** and its degree during shock is the factor that determines the clinical manifestation of the individual organ injury. It is yet natural that the degree of hypoxia also depends on the perfusion. Tissue hypoxia can not be separated from the value of oxygen saturation of the blood. The O₂ saturation in the arterial blood can be within the normal range and still the tissue hypoxia might occur (e.g. during a prominently low cardiac output).

Hypoxemia whether (**arterial or tissue**) causes vasodilatation in both the heart and the brain. Hypoxemia activates chemoreceptors sensitive to low O₂. The result will be sympathetic vasoconstriction in the vessels of the skeletal muscles, skin, and in the splanchnic area. Due to this vasoconstriction there will be redistribution of blood toward the vital organs, that have a high requirement for O₂ supply. Arterial hypoxemia with the secondary cellular hypoxia causes myocardial depression in many shock types. Acidosis is the result of anaerobic metabolism with the cummulation of lactate and organic acids due to the low renal perfusion.

Acidosis lowers myocardial contractility and the vasoconstriction caused by many endogenous and exogenous neurohumoral substances. We also have to think about the fact that the treatment of shock by using many substances can have other effects: their metabolism and excretion from the organism for example might be changed.

3.18.2 Shock

Shock is a state of the circulation, in which there is an acute and marked low tissue perfusion. Initially this state is reversible but later after its prolongation and worsening it becomes an irreversible cellular damage. The low tissue perfusion is the primary factor that results in other changes. During shock there are some changes that develop in the cardiovascular system, and metabolism, and these changes occur in a certain sequence and they are of different degrees. Almost in every case we can find a severe drop of the blood pressure and a low cardiac output. All this will consequently end up by an inadequate

blood flow through the tissues. **Tissue hypoxia** leads to acidosis and some complex hormonal and humoral changes.

The most important causes of shock are blood loss, trauma, dehydration, burns, toxemia, gastrointestinal perforation, myocardial infarction, anaphylaxis, septicemia, peritonitis, pancreatitis, pleural puncture and hydrocentesis (evacuation of large amounts of ascitic fluid).

The classical picture of shock is rather typical. There might be some consequence disturbances – irritability, apathy, confusion and coma. The skin is usually pale, covered with cold sweat. The peripheral pulses are weakly palpable or thready. There is usually tachycardia and a very weak unmeasurable blood pressure, oliguria or anuria.

The low cardiac output is the cause of low organ perfusion. Hypoperfusion might damage the heart alone or the cardiovascular apparatus as whole. A vicious circle would be closed by which the cardiac hypoperfusion worsens its own function and by the inadequate heart function hypoperfusion is getting more prominent and so on. From this point of view we might differentiate two different states of shock, the progressing state, and the non progressing shock state. See fig. 3.18 on page 179. (Blood transfusion performed in cases of irreversible shock state will only have a transitional haemodynamic effect but it cannot prevent the circulatory failure).

The development of shock can be prevented initially. Here we are talking about the **reversible stage** during which we can reverse the condition. But in cases where the tissue hypoperfusion already caused necrosis of cells in vital organs, shock is turning to become irreversible. In this stage there is cardiac injury as a result of the hypoperfusion with simultaneous hypoxia of the regulatory centers. Any approach, or even the removal of the shock cause cannot in this stage prevent death. See fig. 3.19 on page 179.

The low minute cardiac output is presented clinically as a **decrease in the arterial blood pressure**. There is a certain relation between the blood pressure measured in torr (i.e. in kPa) and the minute cardiac output. This relation is true and can only be applied for the diastolic values of the blood pressure before the occurrence of shock. See fig. 3.20 on page 180.

From the picture we can see, that the percentile decrement of the blood pressure is equal to the per-

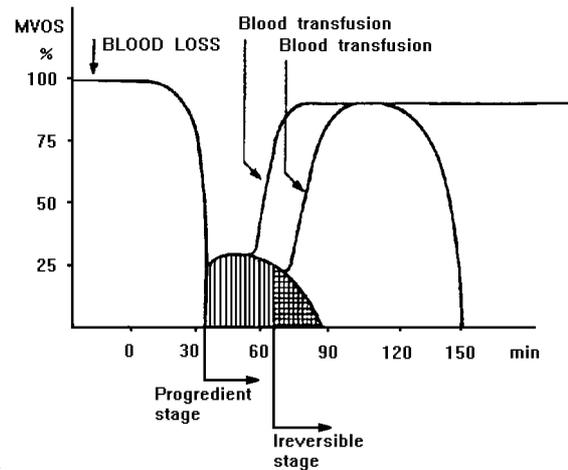


Figure 3.18: Development of the shock

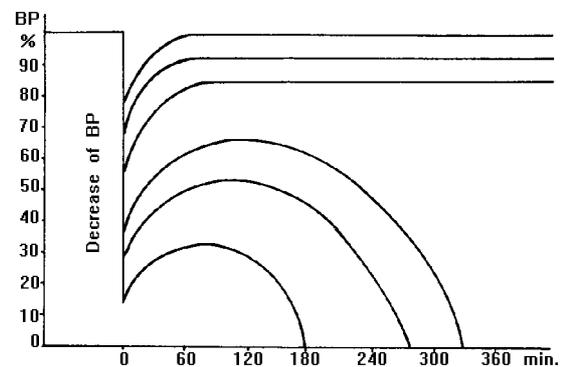


Figure 3.19: Acute decrease of blood pressure. The haemodynamic's fall down – see three bottom curves

centile drop of the minute cardiac output. In case we don't respect this fact, we could overlook or misjudge the hypoperfusion state as long as his arterial blood pressure is within the absolute physiological range of values. In hypertensive people shock may develop when there is lowering in the blood pressure by about 40 torr. That is why we consider measuring arterial pressure the fastest and the most easily approachable parameter in determining the develop-

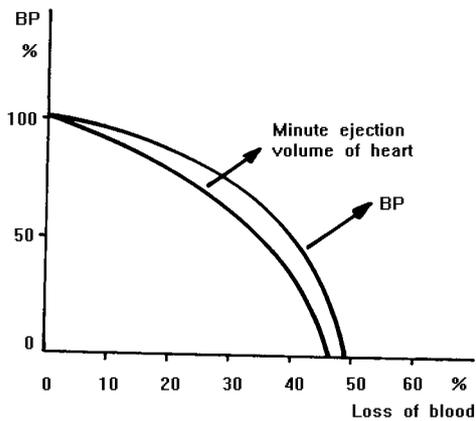


Figure 3.20: Relationship between % of blood pressure decrease and stroke volume of the heart

ment of shock state. To understand all the changes that occur in the organism during shock it is necessary to differentiate among individual types of shocks according to their etiology.

3.18.2.1 Hypovolemic, oligemic shock

Bleeding, or a heavy loss of fluids during vomiting, diarrhea, burns, and cases of dehydration cause decrement in the blood volume. That is why there will be low venous return and ventricular filling. This condition then shows itself, in form of low end-diastolic volume and pressure in both ventricles. The lowered preload results in lowered cardiac output. This is the most basic cause of many changes in the organism, which aim is to remove this unfavorable situation.

3.18.2.2 Normovolemic, distribution shock

Here the shock condition occur without any drop in the blood volume. An example for this is the traumatic shock, which triggering mechanism is pain. Another type of distribution shock is the anaphylactic and septic shock. In cases of distribution shock is the anaphylactic and septic shock. In cases of distribution shock the characteristic event is an enormously fast and markedly expressed lowering of the peripheral resistance in the resistant vessels. The

peripheral vascular spaces are actually filled with a large volume of blood. And in this condition blood does not return back to heart in adequate quantities. The circulation is failing due to incorrect distribution of blood. Sometimes there is a combination of septic and hypovolemic shock. It is a very complicated situation, from the etiologic as well as the therapeutical point of view.

3.18.2.3 Cardiogenic shock

It is basically a normovolemic shock which forms a separated condition because it differs from other types of normovolemic shocks. The basic difference lies in the fact that in cardiogenic shock the left ventricular filling pressure is increased. It occurs in myocardial infarction (MI) when due to necrosis more than 40% of the left ventricular muscle mass is not contractible. The left ventricle as a pump is failing. This condition may occur not only in cases of infarction, but even in acute myocarditis, depression of myocardial contractility, in cardiac arrest, and post a long lasting cardiosurgical insult. Cardiogenic shock occurs when, due to cardiac causes there is an acute drop down of the blood ejection to the aorta.

3.18.2.4 Extra cardiac obstructive shock

We are dealing with a type a shock, that develops during the pericardial tamponade. The low cardiac volume is in this case caused by the inability of the ventricle to expand and be filled during the presence a tamponade. Another type of the extra cardiac obstructive shock is a shock during a massive pulmonary embolism.

3.18.3 Some common signs of the individual types of shock

A common danger or risk of every shock is the cellular death. When a certain number of cells in vital organs (brain, heart, kidneys) are affected the shock is irreversible even when we remove its basic causes. The irreversible distraction of such a number of cells in this organ will lead to the failure of its function. This idea is very important mainly from the practical point of view as we want to prevent the irreversibility of the shock. Another common sign of the different types of shocks is lowering of the minute cardiac output. No matter what the causative agent

is, shock starts to develop, when the perfusion of life essential organs is low. At the very beginning thanks to the compensatory mechanisms the arterial blood pressure is kept within its normal levels. As the cause of shock is not removed, after a certain time the compensatory mechanisms become ineffective. Here there will be wide clinical manifestation of a shock. When the shock lasts for long there will be cellular death and patient is in the irreversible stage of shock.

The progression of hypovoleamic shock depends upon the volume of blood loss and the time period during which the loss occurred. Large volume loss during short time has unfavorable prognosis. The effect of compensatory mechanisms depends on whether we are dealing with a young healthy, or an older sick individual.

The clinical signs of shock appear after a blood loss that is 20–25% of the total blood volume. Despite an **intensive vasoconstriction** the minute cardiac output drops down and hypotension appears. In this situation the cardiac and brain perfusion is favoured and spared representing a marked compensatory mechanism. In some tissue the level of vasoconstriction is so intensive that it might result in tissue destruction and hence leads to ischemic necrosis. This might occur in the intestine, and the distal parts of limbs. During further progression of shock there will be a fast appearance of ARDS (adult respiratory distress syndrome), an acute renal failure, DIC (disseminated intravascular coagulation) and multiple organ injury. In this case we can not prevent death. The mechanism leading to the final event of heart failure is yet unknown. We may refer it to the effect to metabolites of ischemic tissues, that has some depressive effect on the myocardium. The cardiac arrest might as well be the result of inadequate coronary blood flow, acidosis, and the failure of regulatory center.

Lowering the minute cardiac output is always a potent **stimulus for baroreceptors**. The basic effect lies in lowering the arterial filling no matter what is the evoking factor. Noradrenalin is produced from the nerve endings. It stimulates a receptors in the arterial and venous blood field. a receptors are mainly situated in the splanchnic area, the kidneys, and the in skin. This is why vasoconstriction is most prominent in these areas. The simultaneous stimulation of b receptors in the heart has an effect of increasing

the contractility and tachycardia. Catecholamins are released from the adrenals, mainly adrenalin.

A powerful vasoconstriction mainly in the cortical area of the kidneys leads to low glomerular filtration eventually resulting in higher water and electrolyte reabsorption in the tubules. What favors this condition is the increasing level of **aldosteron and angiotensin** caused by the high rennin release. Due to the stimulation of osmoreceptors and volumereceptors there will be a release of ADH, that has itself a role in the water reabsorption in renal tubules. From the previous mentioned facts the final result might be oliguria and anuria. Vasoconstriction is generalized. Yet brain and heart are spared. Due to a marked vasoconstriction there is not enough clearance of acidic metabolites, that are formed in the tissues during hypoxia.

In the initial state of shock there will be an increment of the **precapillar resistance**, which effect lies in the resulting low filtration pressure and fluid reabsorption into the capillaries. Later and due to the effect of local products of anaerobic metabolism of **histamin and kinin** the precapillary resistance remains unchanged. This situation is shown as an increase in the filtration pressure with the consequences escape of fluids into the tissues. The capillary wall ischemia do further help the already present fluid loss across the capillary walls. As a result of this there will be very low oxygen transfer to the tissues. As a result of the previous facts the erythrocyte concentration is increasing. Small thrombotic loci are easily formed. Their formation amplifies a slow blood flow and thrombocyte aggregation.

In cases of a serious injury, that causes no blood loss shock might develop after few hours. This usually happens after skeletal muscle and bone injury. There might be loss of consciousness. The haemodynamic changes are similar to changes of distribution in the normovolemic shock. A heavy trauma causes pain and this pain has its inhibitory effect on the CNS and it inhibits the vasomotor center. As a result of vasomotor center inhibition, the vascular field capacity increases. And as a result there will be low venous return, and cardiac output. The progression of shock is accelerated by the production of toxic substances from the necrotic tissues.

A locus of infection is usually a predisposing factor for the occurrence of **septic shock**. Micro emboli of microbes are liberated from these loci. Other factors

released are histamin, kinins, prostaglandins, endorphins, TNF (tumor necrosing factor), interleukin 1 and interleukin 2 that cause vasodilatation. Vasodilatation overwhelms despite the fact that some prostaglandins and leucoteriens cause vasoconstriction. The heart reacts on this situation by an increased cardiac output. Later acidosis develops through the high cardiac output. This is most likely caused by the vasodilatation and elsewhere vasoconstriction that is caused by the circulating mediators.

At the beginning of the septic shock the cardiac output is high, which may appear on the first sight as a good functioning ventricles. Yet the ejection fraction is small and the ventricles are dilated. A high ventricular filling (preload) provide a normal cardiac output even in case of low ejection fraction. This is combined with tachycardia, and the result might be an increment of the cardiac output. The ejection fraction is still decreasing and the ventricles become even more dilated. Gradually there is a myocardial injury accompanied with the situation and this is most probably caused by some kind of myocardial depression that results from a circulating myocardial depressant factors the blood.

If the septic shock still continues, the peripheral vascular abnormalities becomes combined with the myocardial injury. In these cases the mortality rate might exceed 50%. Death is caused by hypotension and organ injury. Hypotension is usually severe and mostly irreversible. Myocardial depression and the drop of the cardiac output worsen the already present hypotension. Renal, cerebral, and hepatic insufficiency occur in this stage. Apart from the mentioned changes we sometimes notice neutrophilic aggregation, thrombus formation, and endothelial cell injury. The result will be a prominently disturbed micro circulation and perfusion.

A vast cellular death of important vital organs, shock becomes irreversible and despite all the care given the patient dies.

Anaphylactic shock occurs as a result of a generalized reaction of antigen with antibody. This leads to reaction of antigen with antibody. This leads to complement activation. The cascade system of complement activation leads to the release of many mediators of the anaphylactic reaction namely the anaphylatoxins C3 and C5. Even histamin is released. And the end result is a vast vasodilatation and high vascular permeability. From the haemodynamic point

of view we deal with an increased vascular capacity. Moreover plasma leaks out from the vessels so the hypovolemia becomes even more prominent. This condition develops within few seconds or minutes post allergen application. First of all there will be itching, generalized edema, later there might be headache, dyspnoe, stridor, nausea, vomiting and abdominal pain. The course of symptoms is very fast and dramatic which may many times end by excitus.

3.18.4 Clinical manifestation of shock

Some clinical manifestation of shock are similar for all types of shock. Clinically the most reachable parameter is the blood pressure as a value, that has a certain relationship to the cardiac output. Yet we have to keep in mind the fact that the mean arterial blood pressure has an informative value only when we already knew this value prior the occurrence of shock. Different mean arterial blood pressure during shock can be found in a normotonic individual, a hypertonic, or a chronic hypotonic. For normotonic and hypertonic individual can a drop of blood pressure for about 40 mmHg be considered to be a manifestation of hypotension.

Another common signs of shock are **tachycardia, oliguria, disturbances of consciousness**, as well as cold extremities with numbness due to the reduction of blood flow. There is also metabolic acidosis.

Other clinical symptoms are specific for individual types of shock. **Patients with cardiogenic shock** have the usual symptoms of a heart disease. They might have an increased filling pressure, gallop rhythm, and signs of acute heart failure when the cardiogenic shock results from mechanical causes, there will be the presence of some cardiac murmurs. This condition usually occurs in cases of acutely developing mitral regurgitation, or a ventricular septal defect. Patients with pericardial tamponade can have pulsus paradoxus. **Patients suffering of hypovoleamic (oligemic) shock** show an evident blood loss, commonly in cases of a gastrointestinal bleeding. There might be a clear loss of fluids in cases of diarrhea or vomiting. **Patients with a distribution shock** (in case of sepsis) have signs of infection, fever, vasoconstriction, and shivering.

Shock is a serious acute situation that requires treatment and hospitalization. **Everything should aim to prevent the irreversible injury of the vital organs.** That is why we first of all have to know the

causative factor and the degree of shock. Initially we have to prepare an X-ray of the chest, ECG, pO₂, pCO₂ of the arterial blood and the pH. Yet the only way to determine the state of haemodynamics is by performing the cardiac catheterization. Generally in every shock state we should provide an adequate flow of blood via the coronary field, the kidneys, the liver, the nervous system, and the lungs. To reverse the progression of shock it is necessary to keep the mean arterial blood pressure 60 mm Hg or more. The lactate value should be below 22 mmol/l.

In case of the cardiogenic shock the situation is always very serious. The mortality rate in patients with cardiogenic shock during myocardial infarction reaches 90%. Apart from the basic steps to handle shock we have to solve the problem of myocardial contractility and perfusion. The cardiac rhythm disturbances are other undesirable complication.

3.19 Septic shock and septicemia

When microorganisms and products of the inflammatory process reach the blood flow they might end up as a state known as **sepsis (septicemia)**. Septicemia is characterized by fever, rigor, tachycardia, tachypnoe, vasodilatation, and disturbances of consciousness at different levels. **When simultaneously with this there is a developing hypotension and hypo perfusion of organs** we name this condition as a state of **septic shock**. It has a very dramatic clinical symptomatology. Hypoperfusion is a result of a low vascular resistance, a low pumping function of the heart, and a disturbed micro circulation. Changes in the cardiac output in septic shock are known as the adapted compensatory mechanisms of shock. Hypoperfusion will lead to a diffuse cellular and tissue injury. Upon reaching a certain value the signs of multiple organ injury and failure become manifested. In this case and despite all the care given death can not be avoided.

Septicemia may result from all acute infections. Septic shock on the other hand usually occur in cases

of infections caused by the **gram-negative bacteria**. Staphylococci, pneumococci, streptococci, and other gram-positive microbes are a less common cause of septic shock. Some viruses, mycobacterium, fungi and protozoa play a particular role in developing of septicemia. It is not easy to prove the presence of microorganisms the blood by (haemoculture). Even in a fully manifested septicemia haemoculture might not reveal any microorganisms in the blood.

According to trustful statistics, during one year in USA there is around 500 000 cases of septic shock caused by gram-negative bacteria. Mortality rate reaches about 20%. We are usually dealing with patients suffering of diabetes mellitus, liver cirrhosis, alcoholic patients, patients with leukemia, lymphoma, and disseminated carcinoma. Further they are patients - who undergo cytostatic and immunosuppressive treatment and patients with neutropenia. It might as well occur in patients who are on the parenteral nutrition, in those having urinary tract infections and gastrointestinal infections including the gallbladder and the biliary tract. Another predisposed groups for septicemia are the new born and the elderly. Gram positive bacteria appear during the long lasting or repeated catheterization and with long lasting antibiotic or glucocorticoid therapy. Previously there was a high incidence of post abortive and post puerperal sepsis as a result of endometrial and its surrounding structures invasion by streptococci. This condition was usually complicated by septic thrombophlebitis of the pelvis, peritonitis, or the formation of abscess.

The clinical manifestation of septicemia and septic shock are based on the **simultaneous action of microorganisms with the immune and the mediator systems** of the concerned organism. At the level of micro circulation a vicious circle develops between the decreasing tissue perfusion and the worsening of the endothelial quality. This results in tissue injury. If we don't interrupt this vicious circle the condition usually ends by death.

Among the most important microbial factors, that initiate the changes of septic shock are the lipopolysaccharides of the gram-negative bacteria, specifically lipid A and peptidoglycans of the gram-positive bacteria. Even polysaccharides and extra cellular enzymes or toxins such as streptokinase and staphylococcal endotoxins can be manifested.

The mediators of the injured organ play a very