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THE ROLE OF ENDOTHELIUM, ENDOTHELIAL DYSFUNCTION, ATHEROSCLEROSIS AND NON-COMMUNICABLE DISEASES

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Non-communicable (civilization) diseases play a crucial role in nowadays hectic world, full of traps and surprises. They have become a world-wide problem. Civilization diseases are chronic and they make the quality of patients life to be worse. It can not be forgotten that this kind of diseases means also great social problem. Civilization diseases are the reason for many temporary and permanent disabilities. Coronary (atherosclerotic) disease is the most frequent fatality cause in industrially developed countries. Men are more often afflicted than women with the ratio of 4:1, however, at the age up to forty, it is as high as 8: 1, and at the age of seventy it is 1:1.

The clinical manifestation occurs most frequently at the age of 50–60 years by men, and at the age of 60–70 years by women. Cardiovascular diseases represent more than 10% of all diseases all around the world also at the end of the twentieth century (at the break of the millenniums). Atherosclerosis is a complex pathological process that includes lipoprotein accumulation, its further modification, increased peroxidase stress, as well as inflammatory, angiogenetic and fibroproliferatory responses mixed with extracellular matrix and accumulation of lipids.

Key words: cardiovascular diseases, risk factors, endothelium, atherosclerosis, prevention, nursing.

Civilization diseases became the most common health problem in last years not only for the patients with some of that sort of disease but for the whole community, too.

We should think about our lifestyle, about the importance of physical training, relaxation and about protecting our body, that have to serve us for the rest of the life. However, what about the hygiene – not only the physical part of it is important, for our health psychological hygiene is important, too. It is known that many of the civilization diseases are of psychological origin or can be influenced by it. Today we know that civilization diseases are responsible for increasing of morbidity and mortality especially among young adults.

Vascular system is complex, but individual blood vessels are among the simplest tissue structures in the body. A blood vessel consists of but two cell types: endothelial cells and smooth muscle cells. *The endothelium forms the lining of tunica intima, a single – celled layer at the interface between the blood and the extravascular fluid spaces.* Not many years ago the endothelium was considered a simple structural barrier that merely modulated permeation through the vessel wall by providing pores of appropriate size. The major cause of insufficient coronary flow leading to a heart attack is the presence of atherosclerosis in these vessels. Atherosclerosis (sometimes called «hardening of the arteries») is disease characterized by a thickening of the arte-

rial wall with (1) large numbers of abnormal smooth-muscle cells and (2) deposits of cholesterol and other substances in the portion of the vessel wall closest to the lumen. The mechanisms that initiate the thickening are not clear, but it is known that cigarette smoking, high plasme cholesterol concentration, hypertension, diabetes, and several other factors increase the incidence and the severity of the atherosclerotic process. To decrease cardiovascular mortality and morbidity, three additional strategies will be necessary: 1. Enlarging and widening of public health sector (detection, medical care training, preventive interventions...). 2. Identification of risk factors. 3. Allocation of sources aimed at acute and chronic disease therapy, focused mainly on secondary prevention. All these strategic techniques are to be enlarged equally as for both prevention and therapy for the whole population, regardless their race, ethnic and socio-economic group. Function of nursing in prevention, therapy and dispensarization of cardiovascular diseases ought to cooperate with experimental and clinical medicine. Nursing is a scientific branch which integrates knowledge of other branches dealing with study of man, society and environment. The characteristic feature of nursing is a complex approach towards an individual by preserving and supporting health, by prevention and care of the sick. The aim of nursing is to help a human being, family, group, community, and carry out those activities which in health or disease contribute to health, cure, or peaceful and dignified dying

and death, that could have been done by the patient himself if he had the necessary strength, will, or knowledge.

Results and Discussion

Cardiovascular diseases represent worldwide more than 10% of the total number of mortalities also at the end of 20th century (as well as at the break of the millenniums). They represent more than a half of all mortalities in industrially developed countries, and 25% in developing countries. In 2020, 25 million of people will die from cardiovascular diseases whereby heart diseases will be in the first place of mortality and morbidity rate, much ahead of contagious diseases. This increase of cardiovascular diseases results from the dramatic shift in the state of individual health worldwide also at the break of the millenniums. Lasting shift of dominant profile and distribution of diseases – cardiovascular and oncological diseases, is equally dominant. Contagious diseases and malnutrition were the main death causes in the year 1900. However, thanks to the changed life style, nutrition, and other risk factors, these were replaced by cardiovascular and oncological diseases as the main cause of morbidity and mortality. This is the reason why cardiovascular diseases will dominate as the main mortality cause in the year 2020, when every third death will be a result of cardiovascular disease. The morbidity and mortality shift is caused by the «lion's share», known as an epidemiological shift. The above mentioned epidemiological shift is never isolated and is tightly connected with personal and communal changes (personal and communal well-being) – economic shift, demographic and social structure changes. Since the economic shift is connected with evolution and social and economic force, it is performed at a different speed in different parts of the world. Although there are changes of health state of the inhabitants in each part of the world, at the beginning of the third millennium the national health and disease profile broadly varies according to the country and region. For example, the average life expectancy in Japan is 80 years, which is twice as high as in Sierra Leone, where it is only 37,5 years [1; 15;16; 25].

In 2020, a population increase is expected to reach the number of 7.8 billion; the highest one is expected mainly in the developing countries. Population increase in the developed countries will only be by 13%, from 798 million in 1990 to 905 million, though mainly as a result of immigration, and the similar situation is expected in so called «socialistic states», which is a reduced decrease in their own population, and population increase from 346 to 365 million.

On the other hand, in the developing countries (the third world countries), the population will considerably increase by more than 60%, from 4.1 billion in 1990 to 6.6 billion in 2020 and will represent 84% of the world's population. From the total number 54.8 million mortalities in 2020, 25 million will die of cardiovascular diseases, which

makes 36.3%. Whereas the number of community disease mortalities will show a sinking tendency from 32.2% to 15.1%, an increasing trend is expected in cardiovascular diseases. Cardiovascular diseases will always have a multifactorial character!!! (Table 1) [1;5;7;13;23;24].

Table 1

Main groups of myocardial ischemia risk factors

Genetic demographic, somatic and character factors (ICHs occurrence in the family, age, sex, race and similar factors).
Characteristics found by physical and auxiliary examination (hypertension, obesity, abnormal ECG etc.).
Factors connected with biochemical changes (increased cholesterol and triacylglyceride levels, some enzymatic changes (hyperhomocysteinemia).
Thrombocyte and haemocoagulation disorders.
Factors of lifestyle, habits and psychosocial influences (smoking, lack of exercise, mental stress, etc.).
Factors reflecting environmental influences (noise, drinkable water composition).
Signs reflecting an overall state of the organism (anginous pains, state of the bloodstream and others).
Factors marking an excessive diet, energy intake, cholesterol content in food, etc.
Factors showing the lack of some food components (insufficient intake of fibre, fruit, vegetables).
Ingestion of some medicaments (e.g. hormonal contraceptives, etc.).

Endothelial cells – function and dysfunction

Physiology, Pathophysiology,

Pharmacology, Cardiovascular Diseases

The functional and structural characteristics of the blood vessels change with successive branching. Yet the entire cardiovascular system, from the heart to the smallest capillary, has one structural component in common: a smooth, single-celled layer of endothelial cells, or *endothelium*, which lines the inner (blood containing) surface of the vessels [1;2;8;15;16;21–23;25]. Capillaries consist only of endothelium, whereas all other vessels have, in addition, layers of connective tissue and smooth muscle. Endothelial cells have a large number of active functions (Table 2).

Table 2

Functions of endothelial cells

Serve as a physical lining of heart and blood vessels.
Secrete endothelium-derived relaxing factor (EDRF), which mediate vascular smooth-muscle responses to many chemical agents and to mechanical force.
Secrete substances that stimulate angiogenesis (vessel growth).

Regulate transport of macromolecules and other substances between plasma and interstitial fluid.
Regulate platelet clumping, clotting and anticlotting.
Synthesize active hormones and other mediators.
Extract or degrade hormones and other mediators.
Undergo contractile activity, which regulates capillary permeability.
Influence vascular smooth-muscle proliferation in the disease atherosclerosis.

Endothelial cells and vessel wall

Vascular system is complex, but individual blood vessels are among the simplest tissue structures in the body. A blood vessel consists of but two cell types: endothelial cells and smooth muscle cells. *The endothelium forms the lining of tunica intima, a single cell layer at the interface between the blood and the extravascular fluid spaces.* Not many years ago the endothelium was considered a simple structural barrier that merely modulated permeation through the vessel wall by providing pores of appropriate size. Largely as a result of progress in tissue culture technology, we now know that endothelial cells accomplish a long list of metabolic functions (Table 3).

Table 3

Metabolic functions of endothelial cells of the blood vessels

Permeability barrier.
Antithrombic agent production: Prostacyclin (PGI ₂), adenine metabolites.
Prothrombic agent production: Factor VIIIa (von Willebrand factor).
Anticoagulant production: Thrombomodulin, other proteins.
Fibrinolytic agent production: Tissue plasminogen activator, urokinase-like factor.
Procoagulant production: Tissue factor, plasminogen activator/inhibitor, Factor V.
Inflammatory mediator production: Interleukin-1.
Provision of receptors for factor IX., Factor X., LDL, modified LDL, Thrombin.
Replication.
Growth factors: Blood cell colony stimulating factor, insulin-like growth factors, fibroblast growth factor, platelet-derived growth factor.
Growth inhibitors: Heparin.

Atherosclerosis

The major cause of insufficient coronary flow leading to a heart attack is the presence of atherosclerosis in these vessels. Atherosclerosis (sometimes called «hardening of the arteries») is disease characterized by a thickening of the arterial wall with (1) large numbers of abnormal smooth-muscle

cells and (2) deposits of cholesterol and other substances in the portion of the vessel wall closest to the lumen. The mechanisms that initiate the thickening are not clear, but it is known that cigarette smoking, high plasma cholesterol concentration, hypertension, diabetes, and several other factors increase the incidence and the severity of the atherosclerotic process [1;2;10;11;15;17;18;24].

The mechanism by which atherosclerosis reduces coronary blood flow is quite simple: The extra muscle cells and various deposits in the wall bulge into the lumen of the vessel and increase resistance to flow. This is usually progressive, often leading ultimately to complete occlusion. Acute coronary occlusion may occur because of (1) sudden formation of a blood clot on the roughened vessel surface, (2) the breaking off of a fragment of blood clot or fatty deposit that then lodges downstream, completely blocking a smaller vessel, or (3) a profound spasm of the vessel's smooth muscle. If the coronary occlusion is gradual, the heart may remain uninjured because, over time new accessory vessels supplying the same area of myocardium develop [3;6;11;19;20].

The question of whether regular exercise is protective against heart attacks is still controversial, although more and more circumstantial evidence favors this view. Certainly, modest exercise programs induce a variety of changes consistent with a protective effect: (1) increased diameter of coronary arteries, (2) decreased severity of hypertension and diabetes, which are risk factors for atherosclerosis, (3) decreased plasma cholesterol concentration (yet another risk factor) with simultaneous increase in the plasma concentration of a cholesterol-carrying lipoprotein thought to be protective against atherosclerosis and (4) improved ability to dissolve clots. Finally, the results of long-term studies that evaluated the effects of exercise on evidence of atherosclerosis are also suggestive of some degree of protection.

In a number of diseases, endothelial dysfunction (Table 4) is associated with the subendothelial accumulation of blood-borne materials. For example, the accretion of lipid beneath the endothelium in atherosclerotic lesion reflects the failure of the endothelium to serve as an effective barrier between tissue and plasma. Thus, a modern view of endothelium holds that the metabolic and endocrine functions of its cells play a critical role in disease [4;9;14].

Table 4

Factors, contributing to the endothelium dysfunction

- Dislipidemy and atherogenic modification of lipoproteins
- Elevation of LDL, VLDL, lipoprotein
- LDL modification (oxidation, glycation)
- Increased oxidation stress:
(Hypertension, Diabetes mellitus, Smoking)
- Estrogen insufficiency
- Hyperhomocysteinemy
- Higher age
- Genetic predisposition
- Infections

The endothelium acts as a charged semipermeable membrane, in which the exchange of plasma solutes with extracellular fluid is controlled by molecular size and charge. The endothelium also plays an active metabolic role by (1) synthesizing factors that influence the surrounding cells, (2) modifying molecules in transit across the endothelium, and (3) participating in the inflammatory response by synthesizing inflammatory mediators.

Permeability of capillaries depends on the ultrastructure of the capillary endothelial cells. Brain capillaries are highly impermeable because their endothelium has tightly sealed junctions between individual cells that prevent the exchange of proteins across the vessel wall. Transport in other capillary beds is mediated either by passage of molecules through incomplete cell junctions or by micropinocytosis, a process in which molecules transverse the cytoplasm «bucket brigade» fashion, via vesicular transport.

The complications of atherosclerosis, which include ischemic heart disease, myocardial infarction, stroke, and gangrene of extremities, account for more than half of the annual mortality. Ischemic heart disease is by itself the leading cause of death.

There are wide geographic and racial variations in the incidence of ischemic heart disease.

The atherosclerotic process indicates multiple etiologic factors in its pathogenesis. Epidemiologic studies have contributed greatly to the identification of the more influential factors. The risk factors outlined in Table 5 have been divided into two groups, (1) *nonmodifiable* and (2) *modifiable*. Of the numerous risk factors several have been shown to have greater importance, particularly a rich diet, hyperlipidemia, hypertension and cigarette smoking, whereas obesity and sedentary living appear to be of lesser importance.

Table 5

Risk factors for atherosclerosis

1. Nonmodifiable risk factors	- Age - Sex - Familial history of premature CAHD
2. Modifiable risk factors	<i>Major</i> - Elevated serum lipids (cholesterol and triglyceride) - Habitual diet high in total calories, total fats, saturated fats, cholesterol, refined carbohydrates, and salt - Hypertension - Cigarette smoking - Carbohydrate intolerance <i>Minor</i> - Obesity - Sedentary living - Personality type - Psychosocial tensions - Others

Conclusion

Function of medicine and nursing in prevention, therapy and dispensarization of cardiovascular diseases.

Prevention of cardiovascular diseases ought to concentrate on the development of cardiology:

- Elaboration of new, more sensitive diagnostic methods, improvement of diagnostics, mainly new non-invasive methods (ECHO CG, isotope methods, MRI...).
- Synthesis of new, more effective pharmacotherapeutical substances on molecular level (antihypertensives, antiarrhythmic drugs, diuretics, cardiotonics etc...).
- Broader application of preventive methods in the fight against cardiovascular diseases:
 - risk factors,
 - primary, secondary and tertiary prevention – lifelong prevention from the cradle to the grave,
 - healthcare education of all inhabitants, since health should be the matter of each individual, not only of the health care institutions (Table 6).

Table 6

Relations of the risk factors of cardiovascular diseases, the importance of their measurement, intervention response

1. Category (proved decrease of the risk of cardiovascular diseases, intervention, therapy)	Smoking LDL – cholesterol High level of fats and cholesterol in diet Hypertension Hypertrophy of the left heart ventricle
2. Category (presumably decreased risk of cardiovascular diseases, intervention – therapy)	Diabetes mellitus Physical inactivity HDL-cholesterol Triglycerides, VLDL-cholesterol Obesity Climacterium
3. Category (modification of the risk factors can decrease the risk of cardiovascular diseases)	Psychosocial factors Lipoprotein Homocystein Oxidation stress Alcohol abstinency
4. Category (Factors of a higher risk of cardiovascular disease that cannot be influenced)	Age Sex – male Low social end economic standards Family occurrence – in young age

To decrease cardiovascular mortality and morbidity, three additional strategies will be necessary: 1. Enlarging and widening of public health sector (detection, medical care training, preventive interventions...). 2. Identification of risk factors. 3. Allocation of sources aimed at acute and chronic disease therapy, focused mainly on secondary prevention.

All these strategic techniques are to be enlarged equally as for both prevention and therapy for the whole population, regardless their race, ethnic and socio-economic group [4;9;12;14;15].

Function of nursing in prevention, therapy and dispensarization of cardiovascular diseases ought to cooperate with experimental and clinical medicine. Nursing is a scientific branch which integrates knowledge of other branches dealing with study of man, society and environment. The characteristic feature of nursing is a complex approach towards an individual by preserving and supporting health, by prevention and care of the sick [15].

The aim of nursing is to help a human being, family, group, community, and carry out those activities which in health or disease contribute to health, cure, or peaceful and dignified dying and death, that could have been done by the patient himself if he had the necessary strength, will, or knowledge. Another aim of nursing is to help the patient to maintain independency as soon as possible. Among the main tasks of nursing are: a. To preserve and support an optimal state of an individual, family, group, and community in different situations. b. To gain an active interest of an individual and his family in the process of the health support, maintenance and treatment, as well as to support the family togetherness. c. To monitor nursing demands of an individual. d. To provide primary, secondary and aftercare. e. To harness scientifically justified working methods and techniques by qualified specialists in medicine and nursing.

Nursing plays a key and unique role in all levels of therapy, prevention and dispensarization of cardiovascular diseases. Nursing is a significant and irreplaceable phenomenon also in prevention, therapy, and dispensarization of cardiovascular diseases. Prevention plays a key, unique and irreplaceable role for both – medicine and nursing:

- *Primary prevention* of atherosclerosis consists of at least two parts: Global population strategy should lead to changes of lifestyles and changes of all social and economic determinants of the environment, called as angioepidemiology of 21st century. Individual risk strategy is a preventive care aimed at persons threatened by atherosclerosis which tends to the decrease or elimination of the risk factors. Its share in the control of atherosclerosis is of the foremost importance for an individual!
Prevention and therapy of the risk factors are to be complex and lifelong by the consequent monitoring.
- *Secondary prevention* of atherosclerosis should begin at the time of manifestation of the disease. The aim of early and adequate therapy is to manage the development of the pathologic process. Complex therapy (risk factors, pharmacotherapy, etc.) is also important.
- *Tertiary prevention* of atherosclerosis is therapeutical rehabilitation, comprising a complex of arrangements with an aim to maintain an optimal somatic, mental, and social state for an individual, enabling him to reach an adequate society status also in the tertiary stage of the disease with complications. Complex therapeutic rehabilitation has to be a part of secondary and primary prevention of atherosclerosis. Prevention and treatment should be complex, and not alternative. One constituent cannot be replaced by another one!!!

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Роль ендотелію, ендотеліальної дисфункції, атеросклерозу та неінфекційних захворювань

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Неінфекційні (цивілізаційні) захворювання стали глобальною проблемою. Захворювання цивілізації мають хронічний перебіг і погіршують якість життя пацієнтів. Вони становлять також велику соціальну проблему (є причиною значної тимчасової чи постійної інвалідності населення). Атеросклеротичні хвороби є найбільш частою причиною смерті в промислово розвинених країнах. Чоловіки частіше хворіють за жінок (співвідношення – 4:1), однак у віці 40 років різниця зростає (8:1), а у віці 70 років – становить 1:1. Клінічні прояви найчастіше зустрічаються у віці 50–60 років у чоловіків, і у віці 60–70 років у жінок. Серцево-судинні захворювання на рубежі тисячоліть складають понад 10% усіх захворювань у всьому світі.

Атеросклероз є складним патологічним процесом, який характеризується накопиченням ліпопротеїну та його подальшою модифікацією, збільшенням пероксидазного стресу, а також запальною, ангиогенетичною та фібропроліферативною відповіддю разом з позаклітинним матриксом і накопиченням ліпідів.

Ключові слова: серцево-судинні захворювання, фактори ризику, ендотелій, атеросклероз, профілактика, догляд.

Роль эндотелия, эндотелиальной дисфункции, атеросклероза и неинфекционных заболеваний

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Неинфекционные (цивилизационные) заболевания стали глобальной проблемой. Они имеют хронический характер течения, ухудшают качество жизни пациентов и составляют большую социальную проблему (являются причиной значительной части временной или постоянной инвалидности населения). Атеросклеротические болезни являются наиболее частой причиной смерти в промышленно развитых странах. Мужчины болеют чаще женщин (соотношение 4:1), однако в возрасте 40 лет разница возрастает (8:1), а в возрасте 70 лет – уже составляет 1:1. Клинические проявления чаще встречаются в возрасте 50–60 лет у мужчин, и в возрасте 60–70 лет у женщин. Сердечно-сосудистые заболевания на рубеже тысячелетий составляют более 10% всех заболеваний во всем мире.

Атеросклероз является сложным патологическим процессом, который характеризуется накоплением липопротеина с его последующей модификацией, увеличением пероксидазного стресса, а также воспалительным, ангиогенетическим и фибропролиферативным ответом вместе с внеклеточным матриксом и накоплением липидов.

Ключевые слова: сердечно-сосудистые заболевания, факторы риска, эндотелий, атеросклероз, профилактика, уход.

Рецензент: д.мед.н. В.Д. Парій.