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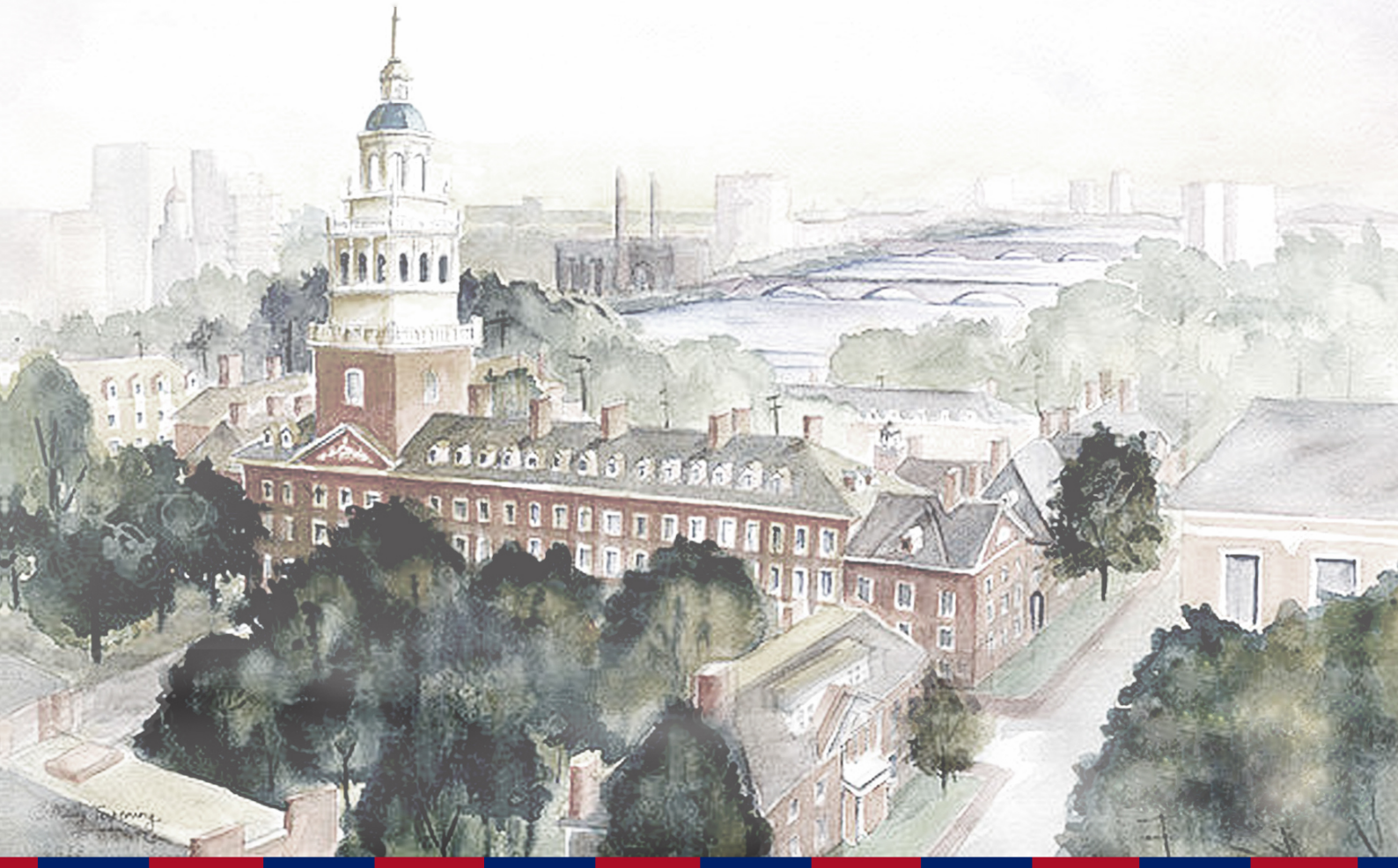

SECTION XXIV. MEDICAL SCIENCES AND PUBLIC HEALTH

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ENDOTHELIAL DYSFUNCTION IN NON-ALCOHOLIC FATTY LIVER DISEASE

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In the modern concept of the pathogenesis of nonalcoholic fatty liver disease (NAFLD), endothelial dysfunction occupies one of the leading places. The mechanism of endothelial involvement in the occurrence and development of various pathological conditions is multifaceted and is associated not only with the regulation of vascular tone and protection of vascular wall integrity, but also with participation in atherogenesis and thrombosis [1]. Normally, endothelial cells enhance the synthesis of substances: nitric oxide (primarily), endothelium-dependent hyperpolarization factor, which causes relaxation of smooth muscle cells of the vascular wall [2]. The structure and functions of the endothelium in different organs are not equivalent. The liver uses enhanced synthesis of nitric oxide to protect the body's internal environment from microorganisms, toxic substances entering the body through mucous membranes and skin. The synthesis of nitric oxide by the liver increases in the presence of virulent bacteria, proinflammatory cytokines in the internal environment of the body. Of all the factors synthesized by the endothelium, the role of regulator of the basic functions of the endothelium belongs to the endothelial relaxation factor, or NO. Disruption of lipid metabolism promotes the expression of adhesion molecules on the surface of endothelial cells, resulting in the formation of atheroma [3].

Damage to the vascular endothelium and exposure of the subendothelial layers triggers aggregation reactions, coagulation, preventing blood loss, causes vascular spasm, stops the formation of antiplatelet agents. At short-term action of damaging agents the endothelium interferes with blood loss that is its protective function. But, according to many researchers, with prolonged damage, the endothelium begins to play a key role in the pathogenesis of a number of systemic pathologies [4]. Platelets can, under certain circumstances, bind to endothelial cells, where they can cause

leukocytes to adhere to the vessel wall [5]. In case of functional insufficiency of intracellular mechanisms of homocysteine utilization and excessive intake of methionine, homocysteine is excreted from the cell into the extracellular space and further into the blood, thus preventing the toxic effect of homocysteine on the cell. At the same time, given the low filtration of even healthy kidneys, the concentration of homocysteine in the blood increases, which contributes to hyperhomocysteinemia and the effect of homocysteine on endothelial cells [6]. It was proved that in patients with NAFLD in the blood plasma the level of homocysteine was higher than in healthy subjects [7]. A strong inverse correlation was found between the level of homocysteine and vitamin B12 [8], and the pathophysiological mechanisms of hepatocyte damage in vitamin deficiency states were described [9, 10].

The presence of anticoagulants and vasodilators on endothelial cells in physiological conditions ensures adequate blood flow, especially in the vessels of microcirculation. Although on the other hand, an excess of nitric oxide impairs endothelial function, suppresses the production of endothelial nitric oxide and suppresses myocardial contractile function. Exposure of subendothelial layers in case of damage to vascular endothelium and triggers aggregation reactions, coagulation, which prevent blood loss [11]. Nitric oxide is a key compound in the microcirculation regulation system.

In creating a model of steatohepatitis and its correction, we identified correlations between systemic inflammation, endothelial dysfunction and insulin resistance as the causes of cardiovascular complications in NAFLD. Adiponectin has also been shown to prevent endothelial apoptosis. We found that in patients with NAFLD with overweight and obesity, increased leptin levels, decreased serum adiponectin levels were associated with increased body mass index, insulin resistance, increased concentration of highly sensitive CRP [12].

Conclusion. There is accumulated evidence that by modulating endothelial dysfunction, fatty degeneration of the liver can stimulate inflammatory processes, which, in turn, mediate the atherosclerotic process. The search for methods of early diagnosis and a new direction of treatment of NAFLD, taking into account the development of endothelial dysfunction, is promising.

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