

# Aspects Of Immunopathology in Emergence and Development of Atherosclerosis: Review

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**Annotation.** The authors offer a review of the literature on various aspects of immunopathology in the occurrence and development of atherosclerosis, and provide information on a number of theories of the pathogenesis of atherosclerosis. Data is shown on both fundamental theories and current research of today.

**Key words:** atherosclerosis, aspects, immunopathology, theories.

## Introduction.

Among the diverse problems of modern medicine, the issues of etiology and pathogenesis of atherosclerosis are very current trends and continue to attract the attention of numerous researchers around the world [1, 2]. Scientific research on this track is really active, as well as discussions about various mechanisms of the pathogenesis of atherosclerotic vascular damage.

## Materials and methods.

The material for this report was numerous scientific papers posted in the public domain on the Internet resources of scientific platforms, journals, collections, monographs. An analytical review of publications and literature sources in the PubMed, Medline, Web of Science and Cochrane Library databases is presented in this article.

## Results and discussion.

One of the early theories is the cholesterol or infiltration theory of atherosclerosis. It was proposed by the prominent pathologist N.N. Anichkov. in 1913. Together with Khalatov S.S., they caused atherosclerotic changes in blood vessels by adding pure cholesterol to rabbit food [3, 4, 5].

There have been numerous studies, in particular, interesting experimental work on the involvement of endocrine system organs in the mechanisms of occurrence and development of atherosclerosis: the thyroid gland [6, 7, 8], adrenal glands [9, 10], pituitary gland [11, 12].

It seems obvious that this theory was not the last in a series of other hypotheses, since it did not answer questions, including those concerning the occurrence of atherosclerosis in the absence of the cholesterol factor. Since the main postulate of this theory: “No cholesterol, no atherosclerosis” does not always work, other theories began to appear regarding the causes and development of this disease.

Today, various theories of atherogenesis are simultaneously on the platform of this problem. In addition to the above cholesterol, infiltration-hyperplastic theory, the following stage theories of the development of atherosclerosis are presented. The lipid theory was proposed in 1865 by R. Virchow, who considered the primary damage to the vascular endothelium with subsequent deposition of lipids. K. Rokitansky in 1884 proposed a theory in which the main role was assigned to thrombus formation [13, 14].

The idea of I.V. Davydovsky seems interesting, he believed that atherosclerosis is not a disease, but a manifestation of age and, thus, a problem of gerontology [15]. In contrast, another theory may be proposed for consideration, according to which atherosclerosis is a childhood disease that manifests itself at a late age. Studies have shown that the first signs of atherosclerosis in the vessels of children appeared before the age of 10, and by the age of 13–15, atherosclerotic plaques formed [14].

There is also a generally accepted theory in which dyslipidemia is considered the main cause of the development of atherosclerosis and associated cardiovascular diseases [13, 14, 15]. Bacterial translocation and endotoxemia, developing as a result of dysbiotic changes in the intestine, lead to impaired liver function, which, in turn, leads to the occurrence of atherogenic dyslipidemia. On the other hand, non-alcoholic fatty disease appears in the liver, which is the target organ. The latter is recognized by a number of authors as one of the main risk factors for cardiovascular diseases, as well as a factor significantly inhibiting the possibility of adequate lipid-lowering therapy [16, 17].

The above allows us to consider the existence of the hepatocellular or enterohepatic theory of atherosclerosis, which represents atherosclerosis as a disease of the hepatocyte, as justified.

Summarizing this part of the message, we can say that discussions about the etiopathogenic aspects of the development of atherosclerosis have been going on for more than 100 years. Today, in addition to those mentioned above, theories such as lipid theory exist and coexist, in the new version it is presented as a pathology of essential polyene fatty acids [14], endothelial damage [18], inflammatory [19], oxidative stress [16], infectious [20], monoclonal, metabolic [21], hormonal, viral, chlamydia [13], genetic [17, 22], cytokine [20, 23, 24].

Such a wide variety of theories is due to the fact that none of them fully responds to the emerging contradictions: the standard morphology of the atherosclerotic process, regardless of the type of dyslipidemia, the focality of the event, the appearance of atherosclerosis with normal indicators of lipid metabolism, the subendothelial location of atherosclerotic plaques and others.

Moving on to the essence of this message, I would like to say that at the present stage of ongoing research in this area, the participation of the immune system in the pathogenesis of atherosclerosis is undeniable [16, 18, 19, 22, 25]. The fundamental autoimmune theory proposed in 1987-1990 is well known. A.N. Klimov. According to this theory, the atherosclerotic process is triggered not so much by lipoproteins as by autoimmune complexes containing lipoproteins as antigens. These autoimmune complexes damage the endothelium of arteries and accelerate the penetration of lipoproteins into their walls; they have also been found to prolong the circulation of lipoproteins in the blood and delay the oxidation and excretion of cholesterol with bile, and have a cytotoxic effect, being fixed and deposited in the walls of blood vessels [26]. Research in this area was carried out by V.A. Nagorneva and colleagues at the Laboratory of Atherosclerosis named after N.N. Anichkov Research Institute of Experimental Medicine of the North-Western Branch of the Russian Academy of Medical Sciences in St. Petersburg. Through their efforts, an in-depth study of cell kinetics in the dynamics of atherosclerosis in humans was carried out. It has been established that blood cells migrating in the intima come into contact with the cells of the vascular wall and do not ignore the surrounding low-density lipoproteins and other tissue components of antigenic value. It has also been determined that the selective accumulation of macrophages and T lymphocytes in the intima of arteries can play a significant role in the immunoinflammatory reaction during atherogenesis in humans [18, 27].

Interesting work on the study of autoimmune reactions of humoral and cellular types in patients with stable angina and their relationship with the degree of coronary damage and multifocal atherosclerosis. The results obtained indicate the importance of the status of cellular and humoral immunity in the progression of atherosclerosis; the use of determining the level of circulating immune complexes as a marker of the progression of atherosclerosis is proposed. The latter is justified by the fact that the severity of stenotic lesions of various vascular beds linearly correlates with its concentration in the blood [13].

Research by M.I. Kazakova [28] expand the existing information about the mechanisms of immunoregulation of the vascular wall from the point of view of the cellular composition of atherosclerotic plaques. Data are presented on subtypes of T lymphocytes considered anti-inflammatory due to their association with macrophages and secretion of interferon- $\gamma$ . Another subclass of T cells can dampen inflammation by releasing anti-inflammatory cytokines. Lymphocytes that synthesize cytokines, which enhance the immune response and contribute to the progression of atherosclerosis, were also found in the atherosclerotic plaque.

### **Conclusion.**

The content of the article does not pretend to be a complete statement of everything that has been published about atherosclerosis. The authors sought to highlight the work of many researchers to resolve the most pressing problem, which is the leading cause of death and disability in people - diseases of the cardiovascular system. There is no doubt that research on this track of medical science will continue for a long time. In this changing world, there will always be a demand for effective preventive and therapeutic methods for atherosclerosis, since the solution to the issue of improving the situation with cardiovascular diseases is very far from being resolved.

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