VENOUS SYSTEM

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Summary

The venous system is the major collecting blood conduit canalicular system of an organism. It performs several important physiological functions, contributing substantially to maintaining homeostatic conditions in the fluids of the extracellular space for optimal survival and functions of the cells (see *Homeodynamics*).

Approximately one tenth of the whole human population on Earth suffers from venous disorders or diseases. Results of scientific studies suggest that the probability of development of venous pathology can be significantly reduced by an adequate healthy attitude and practice.

Despite several significant new scientific achievements in venous physiology, the importance of research in this field still remains underestimated relative to arteries.

Many efforts should be made in the future to improve our understanding of normal and pathological functions of the venous system.

1. Introduction

Interest in the veins has a very long history. Two and a half thousand years ago, a Greek named Lysimachides from Acharnes had made a beautiful thanksgiving votive marble panel for the sanctuary of Doctor Amynos, which depicts a human leg with varicosities. This marble leg is the first known illustration of varicous veins (Figure 1).

Figure 1. The oldest known illustration of a venous disease (fourth century B.C.). The original marble panel is exposed in the Greek National Archeological Museum in Athens.

Interest in venous diseases has sometimes been motivated by erroneous beliefs and misunderstandings. Nowadays, however, this interest is intensified due to special problems related to high morbidity and mortality caused by venous disorders, throughout the whole word.

The incidence of venous diseases (varicosities, hemorrhoids, deep vein thrombosis, etc.) is much higher than that of the peripheral arterial disorders. At least one tenth of the whole human population suffers from various venous disorders or diseases. Experimental and clinical data indicate that disturbances of venous function can contribute even to the development and maintenance of arterial hypertension disease. An increasing clinical interest in physiological properties of the veins is due to the fact that healthy autologous vein grafts are frequently used for replacement of arteries affected by pathological processes or other injuries.

The impact of physiological significance of veins has been revised in recent decades, as new scientific discoveries and their practical applications have verified the multiple role of the venous system in various organismic mechanisms. For example: its overall function in supporting orthostatic tolerance of the organism both at rest and during physical exercise; special immune functions of the venular endothelium, etc. Other data, as specified later, emphasize specific regional functions of the venous system in different species (e.g. the role of the facial vein in the cranial thermoregulation and even in emotional blushing).

Despite the new achievements and valuable discoveries, the importance (and hence level of scientific research) of the field of venous physiology and pathophysiology, compared to that of arteries, still remains under-estimated. There are at least two reasons that might explain this. Until recently, venous diseases were thought not to be directly associated with human mortality, so clinicians and physiologists showed less interest in the studying physiology and pathophysiology of the venous system, than for the arteries. Another reason is the extreme difficulty associated with experimental research into vein function, even in animal models. The special fine structure of the vein tissue, the high variability in vein geometry, wide ranges of intravenous pressure and flow values, susceptibility to different external stimuli, as well as vulnerability, make research and data interpretation in this field very difficult.

It was only in the 1990s that scientists recognized that veins are not merely passive blood conduits. In fact they comprise a specific organ system with multiple distributed functions in the body. Based on the results of recent research, we summarize the physiological functions of the venous system at different organization levels (organism, organ, tissue, vessel wall, endothelium, and the smooth muscle cells). Some of these findings are specific to the veins, whereas other features apply also to the arterial system.

2. Survey of Physiological Functions of the Venous System

2.1. Collecting Blood Conduit Network System with Unidirectional Valves

Despite the fact that in 1628 William Harvey had correctly described the complete blood circulation of the body and the hemodynamic role of the vein valves in his world-famous publication entitled ”Excitatio Anatomica de Motu Cordis et Sanguinis in Animalibus”, and soon after that "venous tone" and the role of venoconstriction in limb circulation was recognized, the medical profession until recently, has still considered the veins only as passive blood collectors. It is now accepted that this "blood collecting" system, of 450-500 km length in humans, involves complex morphological, geometric, biochemical, biophysical, and functional properties with multilevel physiological regulation, like that of the arteries (see *Arterial Blood Supply and Tissue Needs*). Apart from the systemic control mechanisms (vis a tergo and vis a fronte exerted by the heart activity, venous "pumps" in extremity muscles, thoraco-abdominal “pump”, blood volume and venous tone set by neurohormonal reflexes), a variety of local biomechanical, hormonal, ionic, metabolic, and neural factors contribute to the adaptability of the venous circulation.

Recognition of the crucial role of the venous valve insufficiency in the pathomechanism of varicosity disease, with subsequent extravasal correction, as well as the development of the technical basis of clinical diagnostics, have increased interest in the venous valves. These bicuspidal valves with their packeted leaflets maintain a unidirectional flow of blood from the extremities towards the heart. The free edges of leaflets in the superficial veins are parallel to the skin surface. The sinus shaped valve section of the vein is always larger than the diameter of the vessel before and behind it—hence the cusps of an open valve never adhere to the vein wall, but are kept floating by the axial blood flow. It is an ideal situation that results in immediate closure of the valve when filled with blood, if a retrograde flow occurs. Probably, even the open cusps contain a certain amount of blood, which might explain why vein thrombosis usually starts in the sinuses of the vein valves. Adequate valve function depends not only on the cusp movement, but is also related to the distensibility of the vein wall. In less distensible veins the cusps fail to close appropriately, allowing a retrograde blood flow, because the edges of the cusps remain loose and they can prolapse, thus resulting in an insufficiency. Normally, the valves, consisting only of thin collagen layer covered with endothelium, are very strong. Biomechanical data indicate an extremely high maximum tensile stress of the cusps (in circumferential direction this stress in the valves of human femoral veins amounts to 8-10 N/m^2). Their mechanical load-bearing capacity is 2-3 times higher than that of the vein wall itself. In contrast to the valve-free areas of the vein, the wall of the venous sinuses at the site of the valves is more elastic in circumferential, than in longitudinal direction. This direction-dependent elasticity contributes to an easier vaulting of the sinus wall, so when filled with blood it forms a tightly closing spheric structure.

The inferior caval vein and the common iliac vein contain no valves at all, while the external iliac and femoral veins contain 75% and 25% of the valves respectively. It is assumed that the lack of valves in the caval veins might contribute to a progressive descending valvular insufficiency that leads to varicosity disease. The veins under the inguinal ligament have an increasing number of valves, up to one per 5 cm in the calf. Valves occur in small veins of 1 mm in diameter, but smaller veins and venules have no valves.

2.2. Selective Barrier Function

The vein wall is a distinct barrier between the intra- and extravasal spaces, being at the level of the venules especially selective, regionally differentiated, and regulated. It is known that apart from the capillaries, venules also participate in the microcirculatory transport processes, e.g. in the resorption of interstitial fluid, diapedesis of neutrophil leukocytes, and extravasation of the plasma macromolecules, especially during inflammation. Inflammatory mediators bind to the endothelial receptors eliciting contraction of the endothelial cells with a reversible formation of junctional gaps between the neighboring cells. It is noteworthy that the white blood cells can also mediate permeability changes. It is assumed that, like the arteries, transmural transport occurs also in the larger veins both in the luminal and abluminal directions. A pathologically high macromolecular plasma influx occurring in vein segments grafted in the arteries and exposed to the relatively high physiological hemodynamic load might contribute to fibrotic cell proliferation and thickening of the intima. This influx can also contribute to other processes that induce phlebosclerosis.

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Biographical Sketch

Dr. Emil Monos studied at the Semmelweis Medical University, Budapest, and he received his MD in 1959. Since then he has consistently worked at this institution, presently called Clinical Research Department and Institute of Human Physiology, Faculty of Medicine, Semmelweis University, Budapest. He obtained his PhD and DMSci in physiology at the Hungarian Academy of Sciences in 1974 and1982, respectively. He was appointed full professor in 1983. Dr. Monos was director of the Institute (1990-2000) and deputy-rector of the University (1995-1999), since 2005 he has been an emeritus professor of physiology at the same institution. Since 1990 he has been an adjunct professor of physiology at the Department of Physiology, Medical College of Wisconsin, Milwaukee, USA, where he worked as a visiting professor for more than two years. He teaches medical physiology in Hungarian and in English for graduate and post-graduate students in medicine, pharmacy, and biomedical engineering. Dr. Monos is author and co-author of five books and about 400 articles in the fields of cardiovascular physiology and pathophysiology, endocrinology, neurophysiology, and biomedical engineering. He is editor-in-chief of the Acta Physiologica Hungarica, and serves on the editorial board of a number of scientific journals. He was president of the Hungarian Physiological Society (1990-98), and the International Society for Pathophysiology (2002-2006). He is a full member of the American Physiological Society, the Academia Europaea, the Academia Scientiarum et Artium Europae, and the European Academy of Sciences. A number of university and governmental honours have been conferred upon him. Dr. Monos and his co-workers have discovered a number of important mechanisms participating in physiological control of blood vessel functions, including those of capacity autoregulation of veins. His present research interests are in the regulation of orthostatic tolerance and the adaptation of extremity vessels to long-term gravitational stress.