

ARTERIAL BLOOD SUPPLY AND TISSUE NEEDS

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Contents

1. Introduction
 2. Elementary Hemodynamics and Wall Mechanics
 - 2.1. Laminar and Turbulent Flow
 - 2.2. Hydrodynamic Resistance
 - 2.3. Blood Viscosity
 - 2.4. Parameters of Artery Wall Elasticity
 3. Biological Design of Arteries
 - 3.1. Arterial Tree
 - 3.2. Geometric Design of Arterial Segments
 - 3.3. Arterial Viscoelasticity. Effects of Smooth Muscle Contraction-relaxation
 - 3.4. Histologic Design
 - 3.5. Angiogenesis, Remodeling of Arteries
 4. Cytophysiology of Artery Wall Components
 - 4.1. Arterial Smooth Muscle Cells
 - 4.2. Endothelial Cell
 - 4.3. Connective Tissue
 5. Pressure in Arteries
 - 5.1. Measurement of Arterial Pressure
 - 5.2. Arterial Pressure Curve
 - 5.3. Values of Arterial Blood Pressure
 - 5.4. Arterial Pressure Wave
 6. Blood Flow in Arteries
 - 6.1. Measurement of Arterial Blood Flow
 - 6.2. Pulsatile Flow
 7. Different Segments of The Arterial Tree
 - 7.1. Windkessel Arteries
 - 7.2. Distributing (large muscular) Arteries
 - 7.3. Resistance Arteries
 8. Control of Arterial Contractility
 - 8.1. Neural Control
 - 8.2. Endocrine Control
 - 8.3. Local Control of Arteries
 - 8.4. Myogenic Control of Arteries
 9. Organ Blood Flows and Needs
 10. Blood Pressure Control
 11. Pathophysiology of Arteries
- Glossary

Bibliography

Biographical Sketch

Summary

Success of vertebrates in the animal kingdom is well founded by their excellent double convection system for oxygen supply. The motoric force for oxygen transport in blood circulation is given by the *heart* (with rhythmically contracting skeletal muscles assisting the venous circulation). Pressure in vessels leaving the heart, called *arteries*, is higher than in *veins*, which collect blood and bring it back to the heart. This pressure difference, produced by the continuous function of the heart, keeps the blood in motion and helps deliver oxygen to tissues. Arteries are tubes. Their main function is to conduct blood. Some elementary laws of hydrodynamics have to be kept in mind to understand dynamics of blood flow in arteries. A cylindrical shape is optimal for even distribution of distending forces on the wall. In our arterial system, daughter artery diameters are consequently less, in forthcoming branchings more and more resistant arteries are formed. Our cardiac output at rest is about 5 liters/min; it is distributed to different organs and tissues through small arteries in which the mean arterial pressure drops from 90 mmHg to about 40 mmHg. In systole, the heart pushes about 70 ml of blood into the ascending aorta. This induces a wave of pressure rise here which moves at a speed of about 5 m/sec toward the periphery. The explanation of this pressure wave is that a small particle of blood when pushed a little bit further will push the neighboring particle, and so on. Thus the movement of the pressure wave is much faster than the movement of the blood particles themselves (average speed of flow in the aorta is only about 0.3 m/sec). Pressure wave propagation velocity is reduced by wall elasticity, as blood particles can accumulate in a distensible segment of the artery instead of pushing other particles further. Among our tissues, the brain, especially certain cortical and subcortical neurons, are most sensitive to a reduction of blood supply. Oxygen consumption of the brain (about 20% of resting whole body level) and its circulation (15-20% of cardiac output) are very high in comparison with brain mass (2% of body mass), especially, when taking into consideration that brain tissue is not involved in mechanical work. Most arteries have a *sympathetic* innervation. The alteration of sympathetic outflow to the artery is one important way of smooth muscle control in many vessels. The level of sympathetic tone under basal conditions is different in different vascular territories, also there are large differences as to the level of general contribution to setting total peripheral resistance (e.g. in frame of the baroreceptor reflex) and in accommodation to specific physiological functions. Major part of the tissue arteries e.g. in the muscles, gut and skin contract or dilate due to increased physical activity in muscles, during digestion in the gut and during the heat dissipation in skin. There is metabolic control of tissue blood flow in the brain and coronary (heart) circulations. Thus the arteries are active throughout our life. All this explains that arterial diseases, mostly due to the extreme mechanical tear and wear as well as due to our unhealthy lifestyle (especially diet) are common and major causes of death.

1. Introduction

In unicellular organisms, oxygen has to diffuse just a few micrometers from the surface to the interior of the cells. In larger multicellular animals most of the cells are located far from the skin. Relying on simple diffusion alone would limit their speed of

metabolism and functions. As a solution, in the diverse groups of multicellular animals, oxygen contained in either water or air is moved into the depth of the body or tissue fluids circulate between the surface and deeper layers: convection helps diffusion.

Success of vertebrates in the animal kingdom is well founded by their excellent double convection system. Oxygen rich water (*gills*) or air (*lungs*) is brought into contact with tissue fluids by convection in a process we call *respiration* (see *Respiration*). In addition, a separated compartment of tissue fluids (called *blood*) is moved in a closed system of vessels to and fro between the respiratory organs and tissues. This latter convection is called *circulation*. Blood might have been propelled by contractions of the vascular wall itself in early vertebrates (similarly to the function of the gut), but in species living today the ability to provide motor force for blood circulation is concentrated in the *heart*. Pressure in vessels leaving the heart, called *arteries*, is higher than in *veins* that collect blood toward the heart. This pressure difference produced by the continuous function of the heart keeps the blood in motion.

In mammals, the separation of the *pulmonary* and *systemic circulations* is complete: in *pulmonary arteries* exhausted blood is propelled from the right ventricle of the heart to the lung, while oxygen enriched blood is pumped by the left ventricle into the *systemic arteries*. Another (functional) characteristic of the mammalian circulation is the relative high systemic arterial pressure. It is not too difficult to understand that higher pumping pressures can provide higher blood flow through the tissues. But the situation is more complicated than that. The pressure drop in larger arteries leading toward the tissues (over about 500 micrometers of inner diameter) is negligible. Most of the pumping energy will be lost, to become virtually useless, in a relative short portion of the arterial tree located in the target tissues, called *resistance arteries*. These vessels have inner diameters from around 500 micrometers down to about 20 micrometers. Such "hydrodynamic resistors" separate larger arteries with systemic mean arterial pressure around 90 mmHg (12 kPa), from capillaries with pressures around 40 mmHg, 5.3 kPa, at their arterial end. The large pressure drop at these vessels means a higher potential for flow control located in the distal parts of the arterial tree. Indeed, by contraction or relaxation of these vessels, in certain cases, 30-50 times alterations in local blood flow can be achieved, without alteration in arterial pumping pressures. However, for this advantageous higher setting of pumping pressure, a double price should be paid. Pumping energy of the heart is "unnecessarily" lost especially at times when tissue perfusion is set to low values by resistance artery constriction. The other is that tissue of the arterial wall of mammals has to endure the large pulsating distending pressure throughout life, which is an unparalleled situation in animal biology. In the case of the heart, skeletal muscle, tendon and bone, a contraction is always interrupted with relaxation; times of heavy mechanical stress alternate with periods of ease, which can be used to recover (see *Heart*). But in arteries, the cyclic change of higher (systolic) and somewhat less high (diastolic) pressures never give a break. Few plastic materials could endure such wear and tear.

In addition, the endothelial surface of arteries is subjected to the shearing effect of the blood flow, which, like a speedy river erodes its bank, tries to remove the inner cell layers. We will see later that according to present knowledge, certain forces of morphogenesis (*angiogenesis* in this case) are at a slow but continuous work in the arterial wall, even under adult basal conditions, to ensure the integrity of the vessel wall

subjected to such a wide range of damaging mechanical forces. Higher distending forces can be matched with higher wall thicknesses to reduce stress on wall components. But high tissue pressures in the inner wall of arteries would compress capillary vessels if they were present here. Indeed, the *vasa vasorum*, the small vessels supplying the arterial wall itself are entirely missing from the inner third of the wall of larger arteries. These inner layers being entirely avascular, have to rely solely on diffusion for exchange of materials. Avascular tissues are not too frequent in the mammalian body. The cornea and lens of the eye, hyaline cartilage of joints, epidermis of skin, and enamel of teeth are other members of the list—visibly a group laden with geriatric problems.

Deviations of human creatures from "natural" ways of life put even more burden on these vascular tissues. The higher than optimal salt intake of Western people, stresses of overcrowded industrial cities, reduced level of stimulating physical exercise at mechanized working places, obesity (as a result of general availability of cheap food), use of psychostimulating substances, general aging of the population, move more than 10% of the population of developed countries into the range of *elevated arterial blood pressure*.

Smoking and exposition to several other toxic materials damages the sensitive *endothelium* of arteries. Historically, the people of modern industrialized society have been subjected to a roller-coaster ride of changing feeding habits. There has not been time for full genetic or cultural adaptation to develop. By turning to hunting early humans improved their diet with meat of other mammals. Use of fire for cooking caused strange new oxidized products to appear in the food. With the invention of the boat a very productive settled way of life was achieved, initially based on the rich fish resources of waters. Paradoxically, these same brave boaters were able to cover several hundreds of miles in a few weeks of expedition, following seashores and rivers. This was accompanied, needless to say, by exchange of foodstuffs, weapons, working instruments, microbial parasites, cultural and genetic information.

Early agricultural civilizations were restricted to a safer but more monotonous than natural diet, the main component of which was starch (they are the "wheat eating people" of civilized shores in the *Odysseia*). While meat was highly esteemed and rare in most antique and medieval societies, another group of people has been formed with just the opposite feeding problems. The nomads possessed abundant meat and milk, but no bread. Improving living standards in the European countries elevated meat consumption, but the meat at hand was mostly from animals genetically selected to produce cheap animal fat. In recent centuries, modern science has demonstrated to politicians that animal protein is required for optimal working, military and reproduction capacity of the population they governed. Different political interest groups paved the way for milk and egg producing farms, which surround the affluent new industrial cities. Animal protein intake was thus greatly improved, but at the expense of consuming more *cholesterol*. For the modern kitchen higher temperatures are more easily accessible for cooking, which induced again the appearance of new oxidized products. Strangely, all the above listed historical changes in feeding habits drastically altered the availability of different forms of lipids, such as unsaturated fatty acids, cholesterol and their oxidized products. We will see later in this chapter that the main event in human *arteriosclerosis*, which kills many tens of thousands each day, is

nothing else but accumulation of cholesterol in the inner layers of arteries (see also EOLSS chapters on Sterols and Fatty acids).

Another common form of arterial damage is also attributable to achievements of civilization. Honey was the only sweetener for millennia; cane sugar was hardly more than a decoration in golden containers on the table of the most affluent. Consumption of soluble sugars was restricted merely by the volume of fruits which contained them. Strangely, in modern industrialized countries, sugar proved to be one of the cheapest, most readily available sources of foodstuff energy. The insulin producing beta cells of our pancreas do not seem to be genetically prepared for such an invasion of water soluble sugars. The result is that in industrial countries about 2% and now increasingly more of the population is to some degree *diabetic*. Insufficiently treated diabetes, in 10-15 years, induces serious damage to several tissues, including, not surprisingly, the arterial wall with its vulnerable metabolism.

2. Elementary Hemodynamics and Wall Mechanics

2.1. Laminar and Turbulent Flow

Arteries are tubes. Their main function is to conduct blood. Some elementary laws of hydrodynamics have to be kept in mind to understand the dynamics of blood in arteries.

The amount of fluid which passes the cross section of the tube in unit time is called *volume flow* ($Q = dV/dt$). The velocity of a particle of blood is called *linear velocity* ($v = ds/dt$). In arteries, linear velocities are different in different points of the cross section. Linear velocities and volume flow also change with time; blood flow in arteries is *not constant*.

If a viscous fluid is flowing in a tube, energy requirements to keep the fluid moving will vary, depending on whether the flow is *laminar* or *turbulent*. In the case of laminar flow, the different layers of fluid slide over each other. The outermost layer sticks practically motionless to the wall, linear velocities will be higher the closer the given layer is to the axis of the tube. A parabolic linear velocity profile can be observed. If speed of flow is elevated into a "dangerous" range or blood particles are forced to an irregular course by artery wall irregularities, the laminar flow pattern will be destroyed. Vortices will appear in it, which is accompanied by a sudden rise of mechanical energy dissipation, such flow is called turbulent. The normal biological design of the shape of arteries ensures that despite disturbing pulsatility, flow is essentially laminar in the whole arterial system. Exceptions are places just above the aortic valve and at the carinas of bifurcations. Turbulency, however, frequently disturbs blood flow at pathological wall deformations and strictures.

2.2. Hydrodynamic Resistance

Poiseuille's Law describes what a volume flow can be expected in case of a rigid, cylindrical tube, at constant, linear flow with a fluid of constant viscosity:

$$Q = (\pi/8) * (r^4/\eta) * ((p_1-p_2)/l),$$

where Q is the volume flow, r is the inner radius, p_1 and p_2 are the pressures at the inlet and outlet of the tube, η is the viscosity of the fluid and l is the length of the tube. It can be written in analogy with Ohm's law, $I = U/R$, where the current (I) corresponds to volume flow (Q), voltage difference (U) corresponds to pressure difference ($p_1 - p_2$), and the resistance is represented by $(8/\pi) * ((\eta l) / r^4)$. This latter term, expresses what a pressure difference should be established to keep a unit volume flow and will be defined as hydrodynamic (hemodynamic) resistance.

We have to keep in mind now that if the above restrictions are valid, hydrodynamic resistance is linearly changing with tube length and fluid viscosity, but it is inversely proportional to the fourth power of the inner radius. We can compose complex systems by adding together individual hydrodynamic resistances serially and in parallel. In analogy with electric resistances, at serial connections the resulting resistance will be the sum of individual units, i.e. higher pressure will be needed to keep the same volume flow through the series of resistances. With parallel connection, the sum of the reciprocals of individual resistances will give the reciprocal of resulting resistance. The result will be more flow when the same pressure difference is kept.

Applying all this to artery networks, hydrodynamic resistance will increase when the length of an artery is longer, and even slight decreases in lumen diameter will induce large elevations. Opening of new collaterals (connected parallelly) decreases hemodynamic resistance.

2.3. Blood Viscosity

With the application of the symbol η above we erroneously suggested that its value is constant. Blood is a typical non-Newtonian fluid, the value of viscosity is massively dependent on the velocity difference between neighbouring fluid layers (shear rate). In non-Newtonian fluids, viscosity decreases with increasing shear rate as elongated particles arrange along the lines of flow, setting less resistance to sliding of neighboring sheets of fluid along each other (see *Blood Rheology and Hemodynamics*). In the case of blood the situation is further complicated, as the size of red blood cells is not negligible, when compared to the diameter of smaller vessels: viscosity will also be dependent on vessel lumen. In arteries below about 600 micrometers of inner diameter, red blood cells will crowd in the axial flow, where friction between neighbouring moving fluid layers is less. The result is that measured (apparent) viscosity is about 5 times that of water in arteries over this range, but it decreases to a value only about 3 times water viscosity toward the range of smallest resistance arteries (about. 20 micrometers). This unusual viscotic behaviour of blood massively reduces the energy requirements of the whole circulation.

2.4. Parameters of Artery Wall Elasticity

Contrary to the restrictions of Poiseuille's Law, the arteries are not rigid tubes. Elasticity of arteries is essential to transform the periodic pumping function of the heart into a fairly continuous pressure and flow at the level of the microcirculation. The elastic arterial system behaves as a pressure reservoir from which the microcirculation is

supplied.

In a closed elastic container filled with some incompressible fluid, pressure can be established only, if more fluid is pumped into it, than needed to fill it at zero pressure level. The extra volume of fluid will induce elastic distension of the wall, the elastic forces of the wall "try" to shrink the fluid volume and thus they elevate fluid pressure. The conclusion is that pressure in a vessel will be determined by the amount of blood in it and by wall elasticity. Vessels which are able to enclose large extra volumes with small rises in fluid pressure are called compliant. Compliance (C) is defined as $C = \Delta V / \Delta p$, where ΔV is the added volume, Δp is the observed pressure rise. More elastic vessels will be more compliant, increasing their volume more at the expense of smaller pressure rises. Still, compliance will not be characteristic only for vessel wall elasticity. If original volume is high, large volume changes can occur even in rigid vessels in response to unit pressure rise in the lumen. This problem is eliminated when distensibility (D) is computed. It expresses relative change in lumen volume in response to unit pressure rise ($D = \Delta V / (V * \Delta p)$, where V is the original volume of the vessel). Computing distensibility now will answer the question what an elastic behaviour from a vessel as a whole can be expected. A low distensibility, however, can be explained not only by the rigidity of the wall material alone. A thicker wall will produce the same result. Wall material elasticity is expressed in the form of an elastic modulus, in general $E = \Delta \sigma / \Delta \epsilon$, where $\Delta \sigma$ is the elevation of distending force per unit surface, $\Delta \epsilon$ is the relative change of length. E is called the (Young's) elastic modulus. Rigid materials have higher moduli.

3. Biological Design of Arteries

3.1. Arterial Tree

The systemic arterial tree begins at the aortic valve of the heart. The main artery of the body, the *aorta* initiates its route almost vertically upward, than it turns vertically downward while forming the aortic arch. Two coronary arteries supplying the heart originate just above the aortic valve, and the four large arteries emerging from the aortic arch supply the neck and head (left and right common carotid arteries) and upper extremities (left and right subclavian arteries).

The thoracic aorta descends at the hind wall of the chest and after piercing the diaphragm it routes downward at the hind wall of the abdominal cavity as abdominal aorta. The renal arteries are paired branches of the abdominal aorta. Three unpaired large arteries supply the stomach, liver, spleen and guts: the celiac trunk, and the upper and the lower mesenteric arteries. In the pelvic cavity, the abdominal aorta finally branches into two large arteries, the left and right common iliac arteries, supplying the pelvic organs and the lower extremities.

Approaching their target tissue, the arteries branch several times forming more and more in their number but less and less in diameter branches. Such a system of an artery with all of its branching is called the *arterial tree*.

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Biographical Sketch

György L Nádasy was born in 1951. He studied at the Semmelweis University, Budapest, Hungary, finished his MD in 1975, and defended his PhD dissertation in 1994 (Hungarian Academy of Sciences). He has been working in the Experimental Research and Human Physiological Institute, Semmelweis University Budapest, Hungary, in the field of vascular physiology and pathology from 1967 as a high school student, a member of medical students' scientific group, scientific trainee, assistant professor and associate professor. Senior associate professor of physiology from 1998. Member of several clinical and pathological cooperation studies in the field of vascular sciences. He was a visiting scientist in 1979-1981 at the Cerebrovascular Research Center, University of Pennsylvania, Philadelphia, Pa, US, and in 1997 at the Physiology Dept of the New York Medical College, Valhalla, NY, US. Shorter visits in other circulatory laboratories in Germany, Poland, Russia and US. At present he is senior associate professor of physiology at the Institute of Human Physiology and Clinical Experimental Research, Semmelweis University Budapest, Hungary. His main research area has been circulation. He has published 101 papers in refereed journals, among them 5 reviews. He has contributed to 5 books. He is assistant editor of the *Acta Physiologica Hungarica*.