

CARDIO CARE

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Circulation

Coronary Artery Bypass Graft Surgery (CABGS) is one of the options available to the patient of heart disease. Over 500,000 Americans have bypass surgery annually, involving replacement of one or more arteries.

CABGS attaches a blood vessel from another part of the body to the injured artery of the heart downstream from the blockage to restore normal blood flow. Normally, the donor tissue (a vein) is from the leg of the patient. However, this is not always possible and tissue from other donors is not always available.

Tissue replacement therapy, using grafts constructed in vitro from living human cells and man-made or natural biopolymers is becoming a viable and desirable alternative. During

the past several years, the Division of Cell & Tissue Engineering, under the direction of S. Dan Dimitrijevič, Ph.D., has been successful in constructing models of the human skin and

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Division of Cell & Tissue Engineering Meet the Division Director..



S. Dan Dimitrijevič Ph.D. directs the Division of Cell & Tissue Engineering. He is Associate Research Professor in the Department of Integrative Physiology at the University of North Texas Health Science Center. His research interest is in the role of cell-matrix interactions in maintenance (homeostasis) and repair of human tissue. He has developed in vitro models of living human tissues (*skin, cornea and conjunctiva*), and using gene transfer techniques, is pioneering the concept of “cell engineering” to convert potentially passive grafts into implants that will actively participate in their integration with the host.

His NASA sponsored studies of tissue assembly in simulated zero gravity have resulted in the development of the Double Chamber Rotating Wall Vessels.

Dr. Dimitrijevič is a Fellow of the Royal Chemical Society (UK), Member of Association for Research in Vision and Ophthalmology, Member of the Society for Tissue Repair and Regeneration, and is a consultant to a number of pharmaceutical companies, including Johnson & Johnson.

The Cardiovascular Research Institute was established in 1995 as an Institute of Discovery of the UNT Health Science Center. It is a multidisciplinary program designed to promote basic and clinical research, education, clinical practice and community outreach programs in the prevention, diagnosis, treatment and rehabilitation of cardiovascular disease of human beings of all ages.

The Heart... the beginning of circulation

Circulation of blood through the body begins when the left ventricle of the heart contracts, pumping blood into the aorta through the aortic valve. The aorta, the main artery of the body, leaves the heart as one artery and quickly branches into smaller arteries which continue to branch into even smaller arteries as the blood travels. The smallest of the arteries are called arterioles.

Arterioles connect to capillaries. It is within the capillaries where oxygen is exchanged for waste (normally in the form of carbon dioxide). Once the oxygen has been

delivered and the waste collected, the blood continues through the capillaries, which come together to form venules, which increase in size to form veins, which carry the deoxygenated blood back to the heart. Arriving back at the heart, blood cells pass through the lungs in much the same way as they travel through the body, except that in the lungs, carbon dioxide is exchanged for oxygen and the cycle begins again.

As adults, we have about 100,000 miles of blood vessels in our bodies! This 100,000 miles of vessels are generally made up of arteries, arterioles, capillaries, venules and veins.

Arteries, Capillaries, and Veins

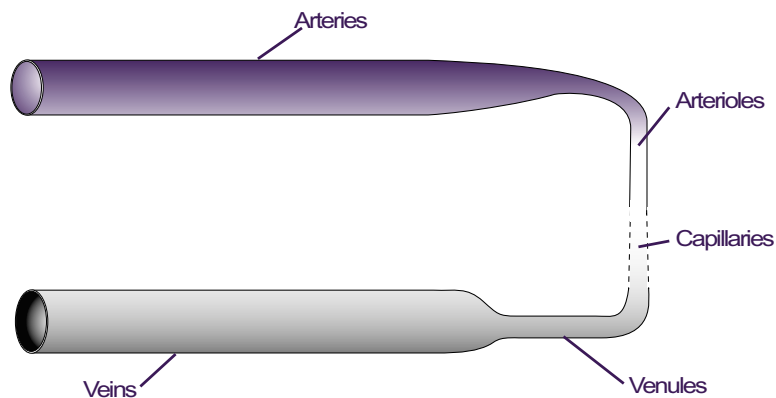
Arteries, pressure vessels, are strong enough to withstand the force of the contraction and expansion of the left ventricle. To accomplish this, arteries have a middle layer that is muscular, expanding and contracting to accommodate the flow of blood circulation.

Capillaries are very thin. So thin that red blood cells flow through single file. Blood needs the thin walls to allow the exchange of oxygen and carbon dioxide. Once this exchange is made, the blood continues through the capillaries into the veins.

Veins are quite similar to arteries, except that they

- transport blood at a lower pressure, and
- rather than transporting oxygen rich blood, veins transport blood filled with waste (carbon dioxide)

Structure of the Circulatory System



How Blood Moves

Just as there are two sides of the heart, there are two “parts” to the circulatory system: arterial, which carries blood rich with oxygen away from the heart and venous, which carries blood with carbon dioxide (waste) back to the heart. To deliver the oxygenated (arterial) blood to our tissues, pressure from the left ventricle keeps it moving through the arteries. However, on the venous side æthe “return” side, circulation depends on the contraction of skeletal muscles to squeeze the veins, thereby pushing the deoxygenated blood forward to complete the cycle. Just as there are one-way valves in the heart to control the flow of blood, there are venous valves in veins that keep blood constantly moving toward the heart.

How does blockage occur?

Arteries and veins become restricted due to cholesterol deposits. Low-density lipoprotein (LDL), referred to as “bad” cholesterol, binds with oxygen molecules and deposits as soft layers of oxidized cholesterol on the walls of arteries and veins. As the cholesterol collects, it eventually hardens into plaque. The immune system sees plaque as an injury and releases macrophages, a form of white blood cells. Macrophages try to remove the plaque, but in the process also become attached causing a further inflammation. In response to this increased threat, the immune system sends out additional white blood cells and causes the liver to produce blood clotting factors. Eventually, the vein or artery becomes calcified and loses elasticity (known as atherosclerosis) and the flow of blood becomes restricted.

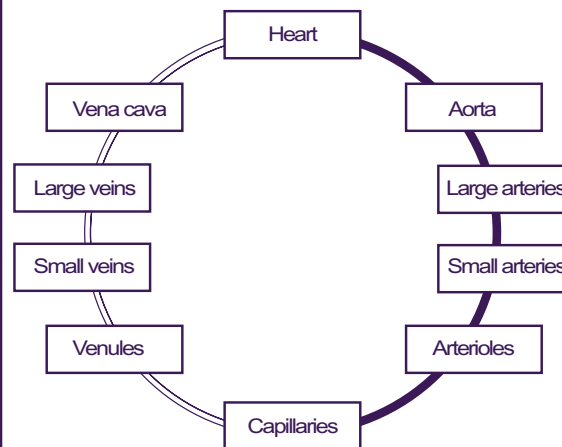
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cornea. Currently, Dr. Dimitrijeviç is working on construction of a human vascular tissue equivalent – an artery.

A human vascular tissue equivalent is composed of a matrix containing collagen that is densely populated with vascular smooth muscle cells. This tissue will be lined with human artery cells on one side and a collagen gel containing a sparse population of human dermal fibroblasts on the other side. In some cases, it would be possible for the human artery to be constructed using the patient’s own cells.

The application for this technology would include every one of the bypass surgeries performed every year, plus many other uses in vessel replacement therapy.

How Blood Moves



Glossary of Terms used in this issue:

in vitro: in an artificial environment, such as a laboratory setting.

matrix: a scaffolding substance used to support a growing biological structure.

collagen: the major structural protein of connective tissues in mammals.

vascular smooth muscle cells: cells capable of contraction and expansion that make up blood vessel walls.

dermal fibroblasts: those cells which can develop into skin.

cholesterol: the most abundant steroid in human tissue and also found in fat rich foods.

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