FLUID MECHANICS OF ARTIFICIAL BLOOD VESSELS

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OVERVIEW
• Anatomy and Physiology of Blood Vessels
• Properties of Blood Flow
• Artificial Blood Vessels
• History
• Pathologies
• Failure of Artificial Blood Vessels
• Future and Current Research
• References
INTRODUCTION

TYPES OF BLOOD VESSELS

Major blood vessels
- Arteries: carry blood away from the heart
- Capillaries: enable the actual exchange of water and chemicals between the blood and the tissues
- Veins: carry blood from the capillaries back toward the heart

Secondary blood vessels
- Pulmonary Arteries and Veins: connect the heart and lungs
- Arterioles: small diameter blood vessels which extend for the Artery and lead to the capillaries
- Venules: small diameter blood vessels that allow deoxygenated blood to return from the capillaries to the veins
TYPES OF BLOOD VESSELS
DID YOU KNOW?

If you took all of the blood vessels out of an average child, and laid them out in one line, the line would be over 60,000 miles long. An adult's blood vessels would extend to 100,000 miles!
STRUCTURE OF ARTERIES & VEINS

Tunica Intima
Consists of two parts:
1. Simple squamous epithelium, called endothelium
   - Physically influences blood flow, secreting locally acting chemical mediators, and assists with capillary permeability
2. Basement membrane deep to the endothelium
   - provides a physical support base for the epithelial layer
STRUCTURE CONT’

* Tunica Media
  * Thickest of all three layers
  * Comprised mainly of smooth muscle cells and substantial amounts of elastic fibers
  * Functions as a blood flow and pressure regulator
**Tunica Externa**

- The outer covering of a blood vessel
- consists of elastin and collagen fibers
- Supplies the vessel wall with nerves and self vessels (tiny blood vessels that supply the tissue of the vessel wall)
PROPERTIES OF BLOOD

• Blood consists of 3 types of cells.
  • Red blood cells (erythrocytes)
    • constitute between 38 and 48% of the whole blood composition
  • White blood cells (leucocytes)
    • < 1% total volume
  • Platelets (thrombocytes)
  • Plasma
    • 52 and 62% of whole blood composition
    • 91% water
    • protein
    • Hormones
    • Vitamins
    • Wastes
• Densities of blood
• Which of the following densities belong to blood?
  A. 1060 kg/M³.
  B. 992.2 kg/M³.

Note: blood density above is the average blood density.
PROPERTIES OF BLOOD

VISCOELASTICITY

- Viscous behaviour
- Elastic behaviour

Which section of the circulatory system would region 3 represent?
Aorta
FLOW TYPES

Laminar flow
- Laminar Streamlined
- Movements occur in the center of the vessel, results in less friction with the walls of the vessel (Less shear Stress)
- Re<2000

Pulsatile Flow
- Rhythmic, intermittent propagation of a fluid through a blood vessel or piping system
- in contrast to constant, smooth propagation, which produces laminar flow.

Turbulent Flow
- Random direction of flow of blood
- Produces friction (Increased Sheer Stress)
- Re>4000
Table 3.1. Some properties of the circulation and blood

<p>| | | | | | | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Number of red blood cells ($\text{mm}^{-3}$)</td>
<td>$5 \times 10^6$</td>
<td>Specific gravity</td>
<td>1.06</td>
<td></td>
<td></td>
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<tr>
<td>Number of white blood cells ($\text{mm}^{-3}$)</td>
<td>$10^4$</td>
<td>Heart rate ($\text{min}^{-1}$)</td>
<td>60–70</td>
<td></td>
<td></td>
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<tr>
<td>Blood volume (L)</td>
<td>5–6</td>
<td>Cardiac output ($\text{L min}^{-1}$)</td>
<td>5–6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viscosity of whole blood (mPa s; cP)</td>
<td>3–4*</td>
<td>Stroke volume (mL)</td>
<td>70</td>
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</table>

<table>
<thead>
<tr>
<th>Vessels</th>
<th>Diameter (mm)</th>
<th>Length (cm)</th>
<th>Wall thickness (mm)</th>
<th>Contained volume (cm$^3$ or mL)</th>
<th>Mean pressure (mmHg)</th>
<th>Average velocity (cm s$^{-1}$)</th>
<th>Reynolds number</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Aorta</td>
<td>25.0</td>
<td>40.0</td>
<td>2.0</td>
<td>100</td>
<td>100(avg.)</td>
<td>40(avg.)</td>
<td>3000</td>
<td>8500</td>
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<tr>
<td>Arteries</td>
<td>15–0.15</td>
<td>15.0</td>
<td>0.8</td>
<td>350</td>
<td>90(avg.)</td>
<td>40–10</td>
<td>500</td>
<td>1000</td>
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<tr>
<td>Arterioles</td>
<td>0.14–0.01</td>
<td>0.2</td>
<td>0.02</td>
<td>50</td>
<td>60</td>
<td>10–0.1</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Capillaries</td>
<td>0.008</td>
<td>0.05</td>
<td>0.001</td>
<td>300</td>
<td>30–20</td>
<td>&lt;0.1</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Venules</td>
<td>0.01–0.14</td>
<td>0.2</td>
<td>0.002</td>
<td>300</td>
<td>20</td>
<td>&lt;0.3</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Veins</td>
<td>0.15–15</td>
<td>18.0</td>
<td>0.6</td>
<td>2500</td>
<td>15–10</td>
<td>0.3–5</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Vena cava</td>
<td>30.0</td>
<td>40.0</td>
<td>1.5</td>
<td>300</td>
<td>10–5</td>
<td>5–30</td>
<td>3000</td>
<td></td>
</tr>
</tbody>
</table>

* In the larger vessels.

Fig. 3.4 Pressure variation in the systemic circulation.
BIFURCATION

Steady flow
• Explained in terms of the conservation rules of fluid flow.

Pulsatile flow
• the effects of pulse reflections and propagation at branches must be considered.

Fig. 3.10 Simple bifurcation of a parent vessel into two smaller vessels.

Fig. 3.11 Change in arterial pressure pulse with increasing distance from the heart.
ARTIFICIAL BLOOD VESSELS

- Tubes that are made from synthetic materials used to restore blood circulation

- There are three basic elements required for the construction of an artificial blood vessel (tissue engineering)

1. Structural scaffold made of either Collagen or a Biodegradable polymer
2. Vascural tissue (Xylem & phloem)
3. Nutrituning environment
ARTIFICIAL BLOOD VESSELS CONT’

- Mechanical properties of the artificial vessels are enhanced by bioreactors that mimic the environment of the vascular cells by producing pulsatile flow.

- Alternative approaches include the production of fibrocollagenous tubes within the recipient’s own body (subcutaneous tissue or peritoneal cavity) and the construction of an artificial vessel from an acellular native tissue.
Did you know?

The most successful artificial blood vessels in use today come from surgical techniques developed in the 1940s and 1950s.
A BRIEF HISTORY

- Goyannes first used an autogenous popliteal vein graft for popliteal aneurysm repair in 1906.

- During World War I (1914-1918) Alexis Carrel perfected a procedure for sewing the ends of blood vessels together. Carrel also made artificial blood vessels with tubes of glass and aluminum.

- A femoropopliteal bypass with a reversed saphenous vein graft was first performed by Kunlin in 1948.

- At the same time, the first fresh arterial allografts (foreign tissue of the same species) began to be used in human vascular reconstructive surgery.

- A porous synthetic material called vinyon was first used on humans in 1953.
In the early 1980s Donald Lyman synthesized a polymer which reduced clot formation due to a high attraction for albumin (the protein in blood serum).

Research Industries of Salt Lake City began testing Lyman's vessels on humans in 1988.

In 1990 Organogenesis began animal testing of its living blood vessel equivalent. This artificial vessel features a smooth inner layer grown in the laboratory from human cadaver artery cells and tubules strengthened with Dacron mesh.
PATHOLOGIES THAT REQUIRE ARTIFICIAL BLOOD VESSELS

Atherosclerosis
- cholesterol accumulates in the walls of the arteries, making them narrower, and thus impairing blood flow

- Blockage from the neck to the brain can cause a stroke

- Blockage to the coronary artery can lead to angina pectoris and myocardial infarction or a heart attack

- Blockage to the leg arteries causes pain due to ischemia and
Aneurysm

-Fatty deposits of cholesterol accumulate on the walls of the blood vessels but also may result from infection or from trauma or be congenital.

-The wall of a blood vessel begins to inflate, once the blood vessel gives away it is a medical emergency which may result in death.
Intestinal Ischemic Syndromes
-occur when blood flow to the bowel or gastrointestinal system is decreased because of a blood vessel blockage

-The three major abdominal blood vessels that may become blocked include the celiac artery, superior mesenteric artery or inferior mesenteric artery

-The tissues below the blocked vessel will be starved for oxygen-rich blood and die
**Thrombosis**

- formation of a blood clot inside a blood vessel, obstructing the flow of blood through the circulatory system

- blood flow to the tissue supplied is reduced enough to cause symptoms because of decreased oxygen and accumulation of metabolic products like lactic acid and may result in cell death
Did you know?

- Cardiovascular diseases are the number one cause of death in the western world today. Cardiovascular diseases alone account for approximately 30% of all global deaths, and in 2005 an estimated 17.5 million people died from CVDs which will reach 20 million a year by 2015.
ARTIFICIAL VESSELS BASED ON BIODEGRADABLE SCAFFOLDS

- Scaffold degrades as the artery is formed and remodelled.

- Polyglycolic acid is the most commonly used polymer in this application (combined with several copolymers to improve the physical properties).

- Collagen and DNA content, as well as the mechanical strain-stress curve, approached those of the native aorta over time.

- Tissue-engineered grafts were used to replace infrarenal aortic segments in seven lambs and all remained patent for up to 5 months.
ARTIFICIAL VESSELS BASED ON BIODEGRADABLE SCAFFOLDS

- Clinical application of an artificial vessel based on a biodegradable scaffold was reported in. The graft was used for the reconstruction of an occluded pulmonary artery in a 4-year-old girl. Seven months after implantation, the patient was doing well, with no evidence of graft occlusion or aneurysm formation.
ARTIFICIAL VESSELS BASED ON HUMAN TISSUE

- The grafts is derived entirely from the patient's own tissues, which lowers the odds of a harmful immune reaction.
- Starts by harvesting skin cells known as fibroblasts and growing these in a sheet. The sheet is then rolled up to allow the cells to produce an interpenetrating mixture of structural support proteins.
- Fibroblasts can transform into smooth muscle cells that can eventually clog the vessel so it has to be removed after the protein has formed.
Last step to add a layer of the patient's own endothelial cells, which promote smooth blood flow, on the inside of the vessel.

Implantation into ten kidney dialysis patients yielded:
- Three patients failed in the first three months.
- Two other patients didn't finish the study for reasons unrelated to the grafts.
- In the remaining five patients, the engineered grafts functioned normally to the study's conclusion, which was between 6 months and 20 months.
BIOSYNTHETIC/BIOHYBRID VASCULAR GRAFTS

- Introducing viable biological components into an artificial material-based vascular graft
- A viable endothelial layer is the best anti-thrombogenic surface.
- The concept of seeding endothelial cells onto the graft lumen before implantation was experimentally implemented and managed to improve the patency of human Dacron prostheses
- Endothelialized bypass grafts have been reported to close the gap between prosthetic and vein grafts
To regulate cell attachment, biomaterials are coated with ECM proteins such as collagen, laminin, and fibronectin.

Alternative approach aimed at improving seeding efficiency is to use bone marrow cells.

directly load the materials with anticoagulant, anti-inflammatory and cell growth-regulating substances, such as heparin and heparin-like molecules.
<table>
<thead>
<tr>
<th>Composite grafts</th>
<th>Biosynthetic grafts</th>
<th>Totally engineered blood vessels</th>
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<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td><strong>Experimental</strong></td>
<td><strong>Clinical</strong></td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td>Antithrombogenic, better patency</td>
<td>Responsiveness, non-thrombogenicity, self-repair, growth, metabolically active, potentially cost-effective</td>
</tr>
</tbody>
</table>

| Disadvantages | Technically demanding, prolonged surgery time | No emergency use, cell amplification problems, cell culture contamination risk | Demanding fabrication, time- and cost-consuming, bioreactor cell laboratory, specialized centers only |

<table>
<thead>
<tr>
<th>Vascular substitute choice</th>
<th>Vascular regions</th>
<th>Hemodialysis arterio-venous access</th>
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<tbody>
<tr>
<td><strong>Large-caliber arteries</strong> (≥ 8 mm)</td>
<td>Aorta, arch vessels, iliac and common femoral arteries</td>
<td>Superior and inferior vena cava, ilio-femoral veins, portal vein, visceral veins</td>
</tr>
<tr>
<td><strong>Medium-caliber arteries</strong> (6-8 mm)</td>
<td>Carotid, subclavian, common femoral, visceral and above-the-knee arteries</td>
<td>Upper &gt; lower extremity</td>
</tr>
<tr>
<td><strong>Small-caliber arteries</strong> (≤ 6 mm)</td>
<td>Coronary, below-the-knee, tibial and peroneal arteries</td>
<td></td>
</tr>
<tr>
<td><strong>Venous reconstructions</strong></td>
<td>Saphenous spiral vein graft, deep venous autograft</td>
<td></td>
</tr>
<tr>
<td><strong>Hemodialysis arterio-venous access</strong></td>
<td>Native material</td>
<td></td>
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**1st choice**
- Prosthesis (Dacron, ePTFE)
- Prosthesis or autograft (equal)
- Arterial or venous autograft
- Saphenous spiral vein graft, deep venous autograft

**2nd choice**
- Allograft, deep venous autograft
- Prosthesis or autograft
- Composite graft, vein interposition, prosthesis (ePTFE, Dacron), allograft, biosynthetic
- Allografts, ePTFE, biografts, TEBV (clinical trial)
TERMINOLOGY

- **Anastomosis** - The connection of normally separate parts or spaces so they intercommunicate. (Eg. Connection between two blood vessels.)
- **Hyperplasia** - Increased cell production in a normal tissue or organ
- **Vascular occlusion** - a sudden blockage of a blood vessel. It can be used to describe any form of blockage, not just one formed by a clot
Question

- Which of the following vascular structures are more prone to failure (surgical reconstruction)?
- A. Major blood vessels (Eg: aorta, iliac & femoral arteries)
- B. Coronary arteries and lower extremity peripheral arteries
FAILURE OF ARTIFICIAL BLOOD VESSEL CONT’

LOCAL BLOOD FLOW IN END-TO-END ANASTOMOSES

Intimal hyperplasia
• narrowing of the pathway

REASON:
• Lumen stricture (stenosis)
• Intimal flaps
• Suture mismatch in size and compliance between the graft and the host artery

FLOW DISTURBANCES
• Flow separation (flow stagnation point)
• Low shear stress around the walls (more prone to fracture)
FAILURE OF ARTIFICIAL BLOOD VESSEL CONT’

- http://www.youtube.com/watch?v=94QocnjgW_U
FAILURE OF ARTIFICIAL BLOOD VESSEL CONT’

LOCAL BLOOD FLOW IN DISTAL END TO SIDE ANASTOMOSES

FLOW DISTURBANCES

- Flow separation- (Flow stagnation point)
- Angle of anastomoses (<15°) = No flow disturbances or separation
- Secondary flow pattern – superimposed primary flow pattern

COMPLICATIONS

- Intimal thickening
  - At suture line *
  - Along the floor of the host artery *

Figure 1. Sketch of end-to-side anastomosis construction from Grevious et al. (2003).
FAILURE OF ARTIFICIAL BLOOD VESSEL CONT’

- Flow Direction
- front aorta
- joint
- graft
- rear aorta

(a) Forward facing graft
(b) Backward facing graft

- B: Bed
- H: Heel
- T: Toe
- Inner Wall
- Outer Wall
The formation of a stagnation point at the toe.

Velocity magnitude was generally small, as the inlet flow began to accelerate.
STAGNATION POINT CONT’

- At $t_3=1.8\ s$, when flow was decelerating -A VORTEX

- The centre of the joint, which induced some fluid in the grafts to reverse its flow direction near the inner wall.

- The existence of vortex combined with reversed flow near the heel reduced the effective flow flux of the graft.
STAGNATION POINT CONT’

(d) $t_4=1.85 \text{ s}$

(e) $t_5=2.1 \text{ s}$

(f) $t_6=2.4 \text{ s}$

(g) Time intervals in the cycle
STAGNATION POINT CONT’

- At \( t_5 = 2.1 \) s, the net inlet flow was in the reverse direction, dominated by backflow from the graft.
- For \( t_6 = 2.4 \) s backflow in the graft had disappeared;
  - fluid had moved downstream of the aorta.
  - Note: At peak flow rate, the flow separation could be found along the graft inner wall immediately downstream of the heel.
ANGLE OF ANASTOMOSIS

- From $45^\circ$ to $135^\circ$ (namely, $45^\circ$ backward-facing graft)
  - Flow separation region reduces in size
  - More restricted to the region close to the inner wall

- The vortex reduced in length when plane A moved to B
  - Increase in the cross-sectional area.

- The presence of vortex
  - Increase contact between blood and the thrombogenic surface (platelet activation)

- Increasing the cross-sectional area may be beneficial to graft patency.
ANGLE OF ANASYOMOSIS

FAILURE OF ARTIFICIAL BLOOD VESSEL CONT’

- **THROMBOSIS**
  - Formation or presence of a blood clot in a blood vessel. (vein or artery)

- **THROMBOSIS THRESHOLD VELOCITY**
  - Time average velocity at which more that 50% of the graft surface is covered with thrombus deposits.

Below threshold- thrombus will accumulate on graft surface leading to occlusion.

Above threshold- thrombus is prevented from forming on the wall (due to shear forces)
WHICH OF THESE CAN AID ARTIFICIAL BLOOD VESSELS RESEARCH?

1. Printing
2. Lightning
3. Salamon
FUTURE AND CURRENT RESEARCH

The search for the ideal artificial blood vessel which will include the following properties:

- composed of viable tissue
- able to contract in response to hemodynamic forces and chemical stimuli
- able to secrete normal blood vessel products
- allow complete healing without any immunologic reaction and remodelling according to the needs of the environment
- high and long-term patency rates, high burst strength, low compliance mismatch
- lack of thrombogenicity, resistance to infections and off-the-shelf availability
FUTURE AND CURRENT RESEARCH
CONT’

3D printing
-The vessels are being created using 3D printing and multiphoton polymerization, a process in which monomers are used as the building blocks in order to create more complex structures.
-The materials used includes synthetic polymers to avoid degradation and an anti rejection biomolecules to provide biocompatibility.
-Introduction of endothelial cells that attach themselves to the inside of the vessel tubes to avoid the blood from sticking to the synthetic component.
Lighting

- "frozen lightning", created by striking an electrically charged block of plastic with a nail

- Adding human blood vessel cells to the tunnels could create a template upon which an artificial organ could grow

- The artificial organs begin as clear blocks of biodegradable plastic. An electron beam fills the block with electricity, then a nail is driven into either end of the plastic block
Researchers have created artificial blood vessels using collagen derived from the skin of salmon.

- There are no known viruses transmitted from salmon to humans, so the use of salmon collagen is regarded as relatively safe.

- Salmon collagen had to be reformed to raise its heat resistance.

- The heat-resistant collagen was used to create blood vessels with an internal diameter of 1.6 mm and a wall thickness of 0.6 mm.
THANKS FOR LISTENING!

Questions?
Ask A Scientist!
And F.A.Q...
REFERENCES


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REFERENCES CONT’

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