LYMPHATIC SYSTEM PUMPING CHARACTERISTICS

HOW DOES THE BODY'S SEWER SYSTEM PUMP UPHILL?

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Lymphatic System Overview

Fluid and protein balance

Collect fluid, protein, cells and foreign bodies from tissues

Important for immune response

Cell trafficking

Lipid uptake

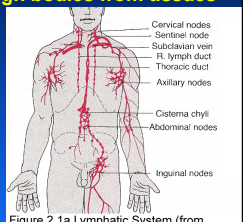


Figure 2.1a Lymphatic System (from Guyton and Hall, 1996)

Fluid and Protein Balance

Approximate daily totals:

- Cardiac output: 8000 liters
- Outflow from capillaries: 20 liters
- Inflow to capillaries: 16 liters
- Lymph flow: 4 liters

50% of blood proteins lost through capillaries

Return to venous system is one of main jobs

Also serves immune system transport role

Moves foreign invaders from tissues to lymph nodes

Immune cell trafficking

- Monocytes to lymph nodes
  One way trip; macrophages for ~1 month
- Lymphocytes continuously circulate
  Distribute memory of antigens

Processing in lymph nodes

Pumping challenges

Tissue pressures are low or negative

Much of lymph has to go "uphill"

Can only account for <3% of total lymph flow

Table 2.3a Tissue pressures

Tissue	Pressure (mmHg)
Corneal Stroma	-55
Umbilical cord	-10
Lung	-7
Subcutis	-5
Skeletal muscle	-3
Stomach	+0.5
Small intestine	+1.5
Brain	+5
Kidney	+6
Liver	+6
Left ventricle	+15

From Granger et al., 1984

Pumping function

Check valves all along system, including terminal level (Schmid-Schoenbein)

"Lymphangion" = vessel segment between valves

Muscle pump (like veins) + some tissue pressure (Extrinsic pumping mechanisms)

Lymphatic smooth muscle (Intrinsic pumping mechanism)

- Most mitochondria of any SMC
- Extensive blood vessel supply

Importance in Disease Conditions

Lymphedema
- Incurable
- Affects cancer patients who have nodes removed
- Congenital (relatively rare)
- Contracted through filaria parasite (elephantiasis)

Cancer
- Lymphangiogenesis in tumor development
- Route for metastases of most dangerous forms

Wound healing
- Arteries shut down
- Lymphatics keep pumping to drain

Cellular Signaling for Pumping

Stretch induces contraction, increases frequency

Flow inhibits contraction

Sensitivity to both depends on anatomical location
- Implication: Asynchronous network

Lymphatic endothelial cells

- Endothelin-1 (ET-1) - Vasoconstrictor
- Nitric Oxide (NO) - Vasodilator
- Expression of both is τ dependent for blood EC

Overall Research Goals:

Construct network model of lymphatic circulation

Include regional variability in pumping function

Model disease states

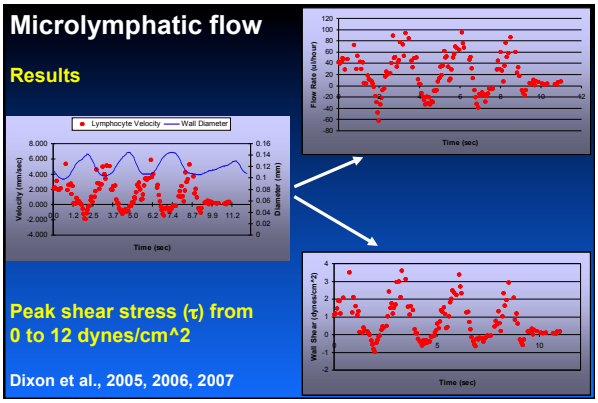
Work thus far:

High-speed video "DPIV" in microlymphatics

Network model underway

Microlymphatic flow

Results



Peak shear stress (τ) from 0 to 12 dynes/cm^2

Dixon et al., 2005, 2006, 2007

Lymph flow and vessel contraction

- **Fluid fluctuates roughly 90 degrees out of phase with contraction cycle**
- **Particle Velocity: -4 to 9 mm/sec, mean: 0.9 mm /sec**
- **Diameters: 24 µm to 165 µm, mean: 90 µm**
- **Contraction velocity: -0.4 mm/sec to 0.4 mm/sec, rms 40 µm/sec**

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