

GEM4 Summer School OpenCourseWare

<http://gem4.educommons.net/>

<http://www.gem4.org/>

Lecture: “The Inflammatory Cascade” by Dr. Geert Schmid-Schonbein, part I.

Given August 7, 2006 during the GEM4 session at MIT in Cambridge, MA.

Please use the following citation format:

Schmid-Schonbein, Geert. “The Inflammatory Cascade, Part I.” Lecture, GEM4 session at MIT, Cambridge, MA, August 7, 2006. <http://gem4.educommons.net/> (accessed MM DD, YYYY). License: Creative Commons Attribution-Noncommercial-Share Alike.

Note: Please use the actual date you accessed this material in your citation.

The Inflammatory Cascade:

Shock and Multi-organ Failure

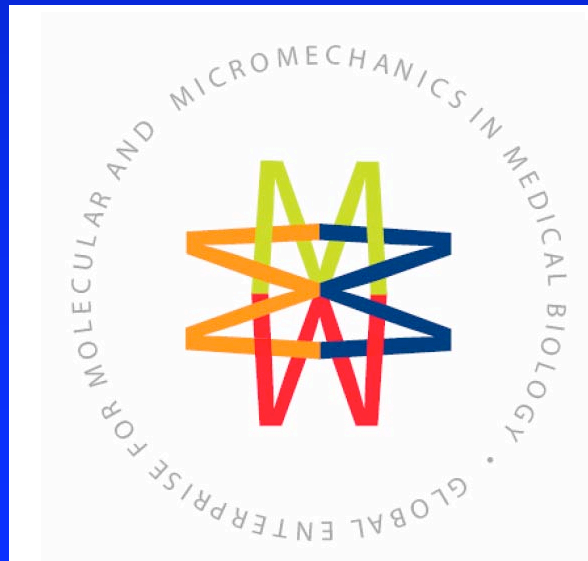


Image removed due to copyright restrictions.

Please see Fig. 4 in Schmid-Schonbein, et al. *Microvascular Networks: Theoretical and Experimental Studies*. Farmington, CT: S. Karger, 1986, p. 44.

Pressure-Flow Relationship in Skeletal Muscle Microcirculation

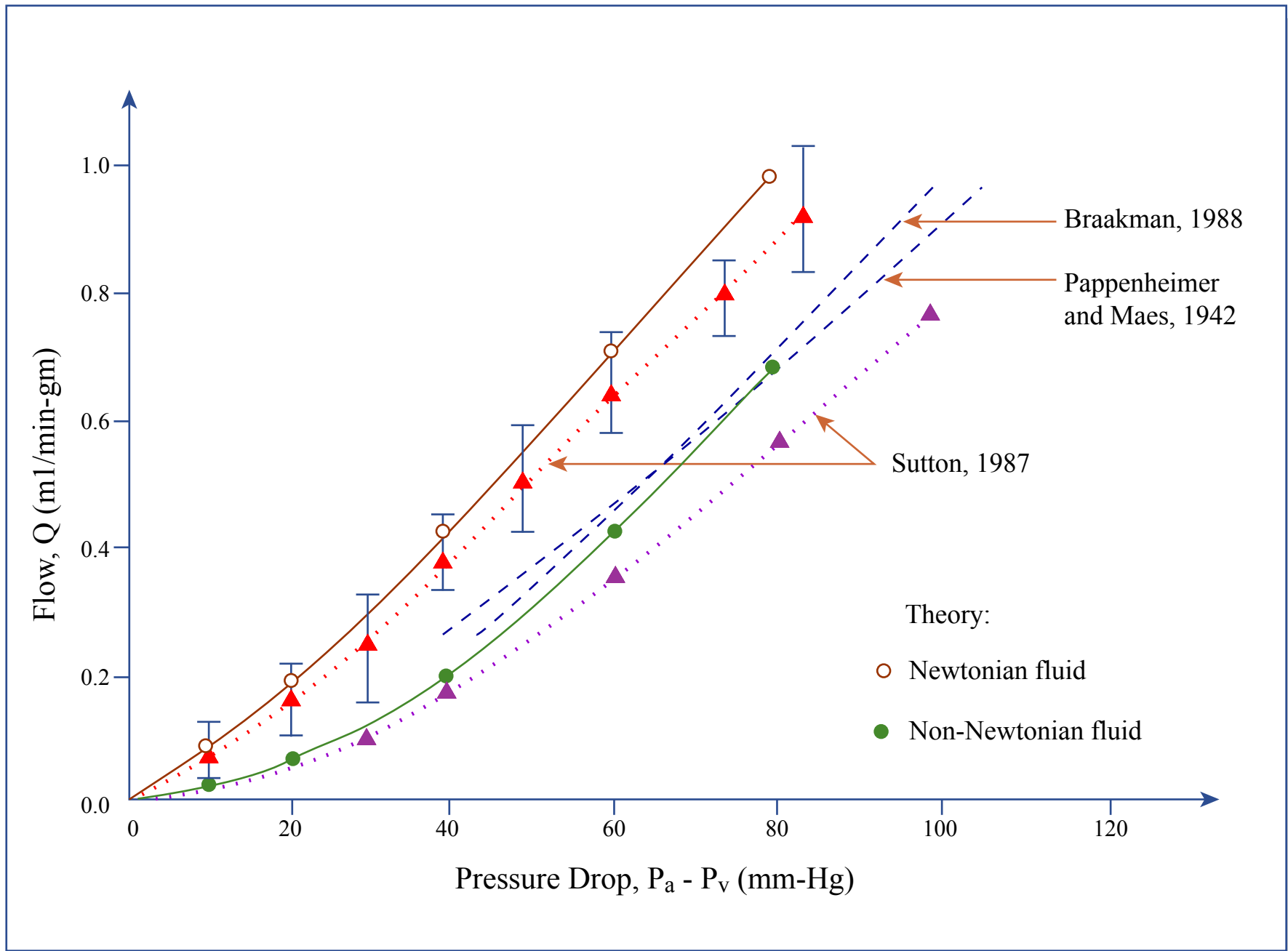


Figure by MIT OpenCourseWare.

Cardiovascular Disease is Accompanied By Cell Activation and Inflammation

- ✓ Infectious Diseases
- ✓ Chronic Degenerative Diseases
(arthritis, retinopathy, dementia,
venous disease, coeliac disease, ...)
- ✓ Diabetes
- ✓ Cardiovascular Risks (smoking, obesity)
- ✓ Myocardial ischemia
- ✓ Stroke
- ✓ Atherosclerosis
- ✓ Arterial Hypertension
- ✓ Cancer
- ✓ Physiological Shock

The Inflammatory Cascade

Trigger mechanism

Early Cell Responses:

- Ion exchange
- Pseudopod formation by actin polymerization/depolymerization
- Degranulation
- Production and release of inflammatory mediators
- Enhancement of endothelial permeability
- Upregulation of membrane adhesion molecules

Tissue Degradation:

- Neutrophil entrapment in microvessels, transvascular migration
- Platelet attachment, aggregation, thrombosis, red cell aggregation
- Protease release and activation
- Oxygen free radical formation
- Apoptosis
- Organ dysfunction

Initial Repair:

- Downregulation of anti-inflammatory genes
- Upregulation of pro-inflammatory genes (cytokines, etc.)
- Monocyte and T-Lymphocyte infiltration

Repair:

- Release of growth factors
- Connective tissue growth
- Revascularization
- “Resolution of Inflammation”

Inflammation in the Microcirculation

Images removed due to copyright restrictions.

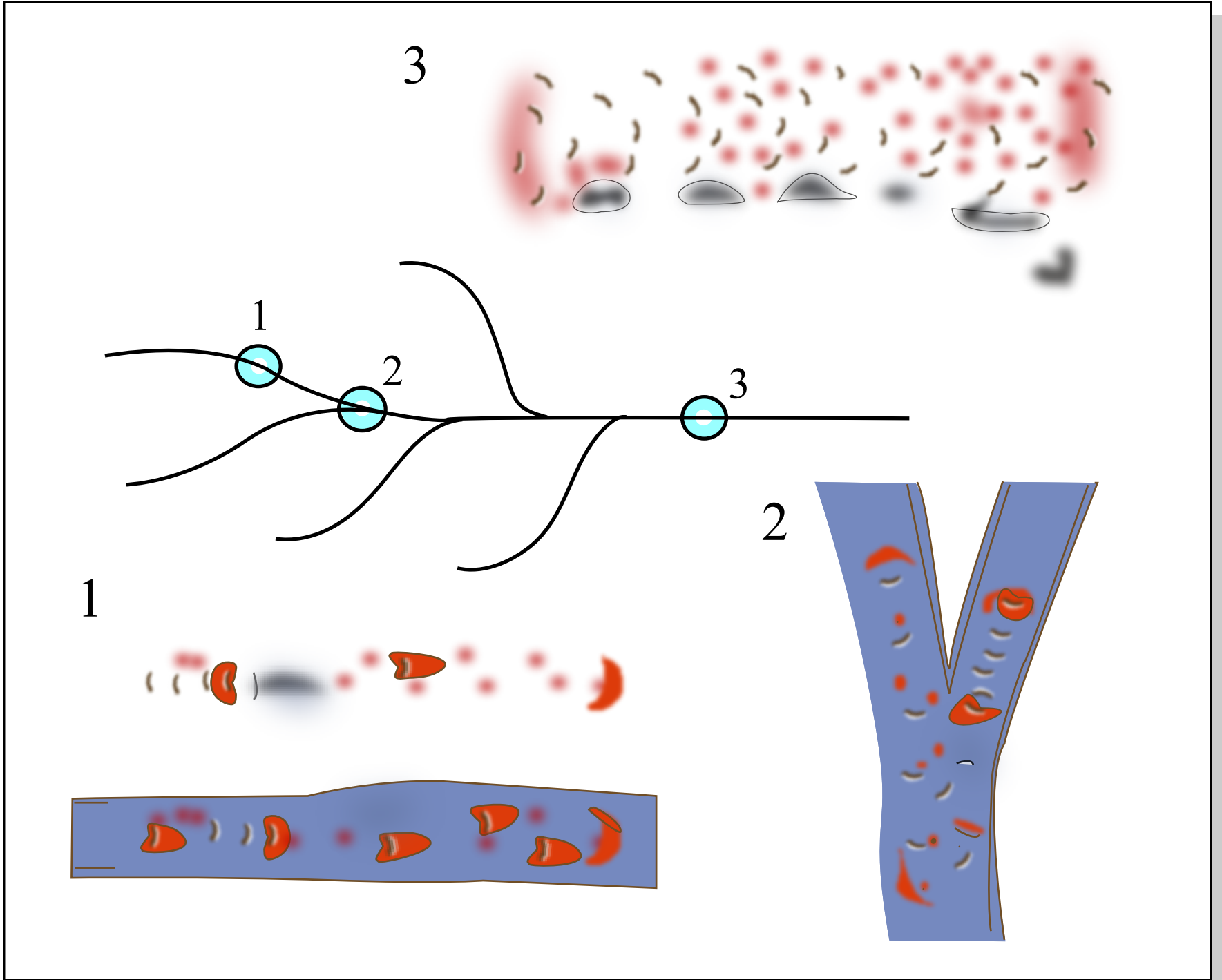


Figure by MIT OpenCourseWare.

Trigger Mechanisms for Cardiovascular Cell Activation

- Inflammatory mediators (bacterial/viral/fungal sources, endotoxins, cytokines, histamine, oxidized products, complement fragments, LTB₄, PAF, etc.)
- Depletion of anti-inflammatory mediators (nitric oxide, IL-10, glucocorticoids, albumin, etc.)
- Fluid stress
- Transients of Gas Pressure or Temperature
- Juxtacrine Activation
- Bio-Implant Interfaces

Plasma Derived Inflammatory Mediators in Hemorrhagic Shock

Leukotaxin Peptide

Myocardial Depressing Factor

Clastogenic factor

T-Lymphocyte proliferation depression factor

Neutrophil activating factor

Leukocyte Chemotactic Factor

Neurin

Inflammatory Mediators in Hemorrhagic Shock

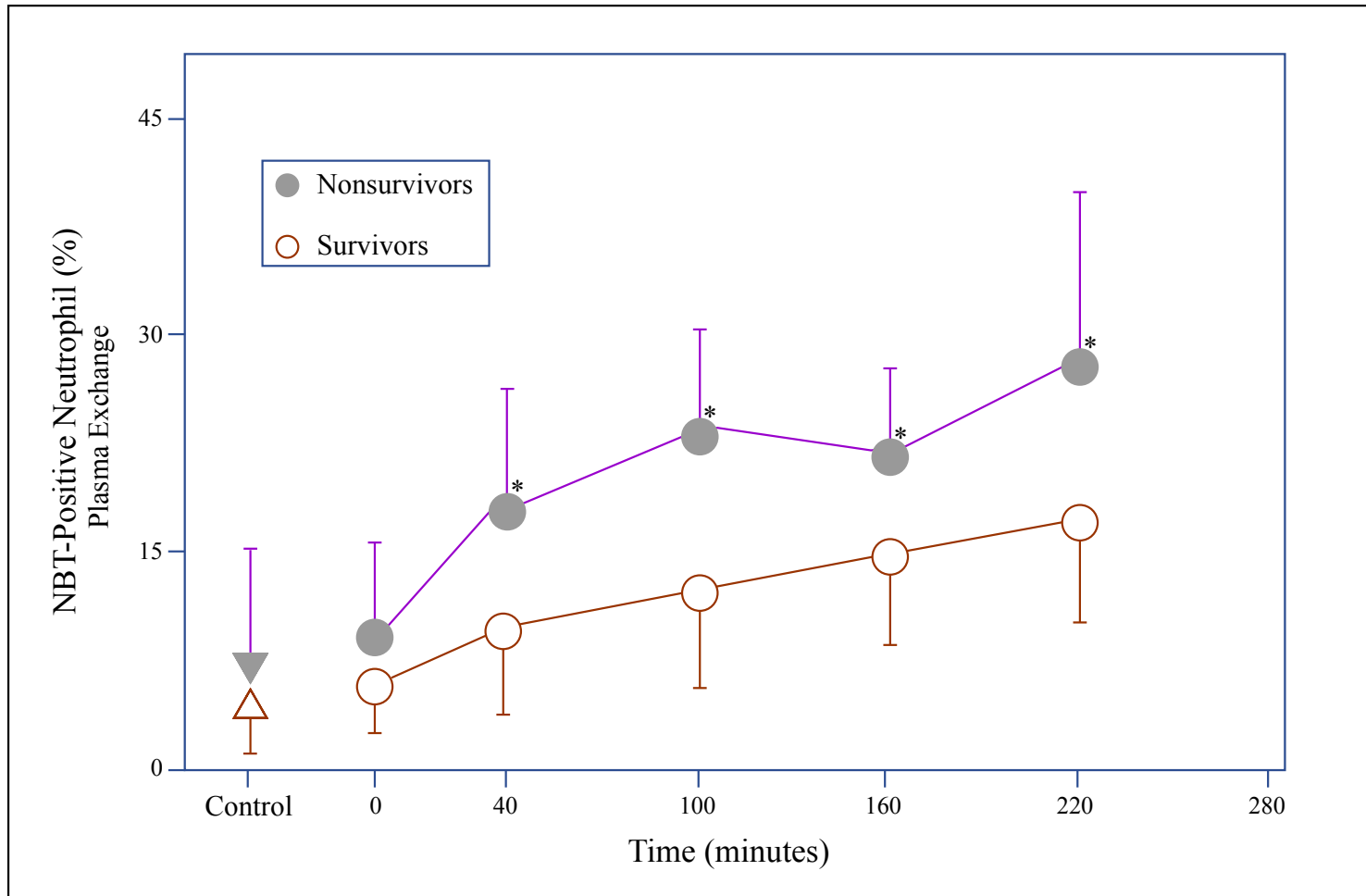


Figure by MIT OpenCourseWare.