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Lecture: “The Inflammatory Cascade” by Dr. Geert Schmid-Schonbein, part I.
Given August 7, 2006 during the GEM4 session at MIT in Cambridge, MA.

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The Inflammatory Cascade:

Shock and Multi-organ Failure

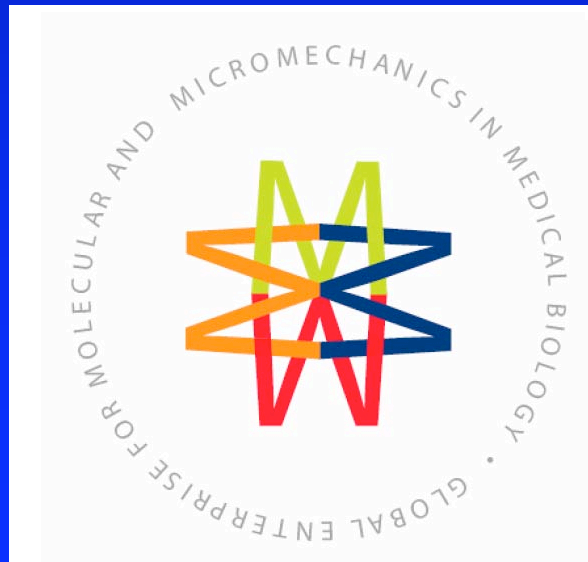
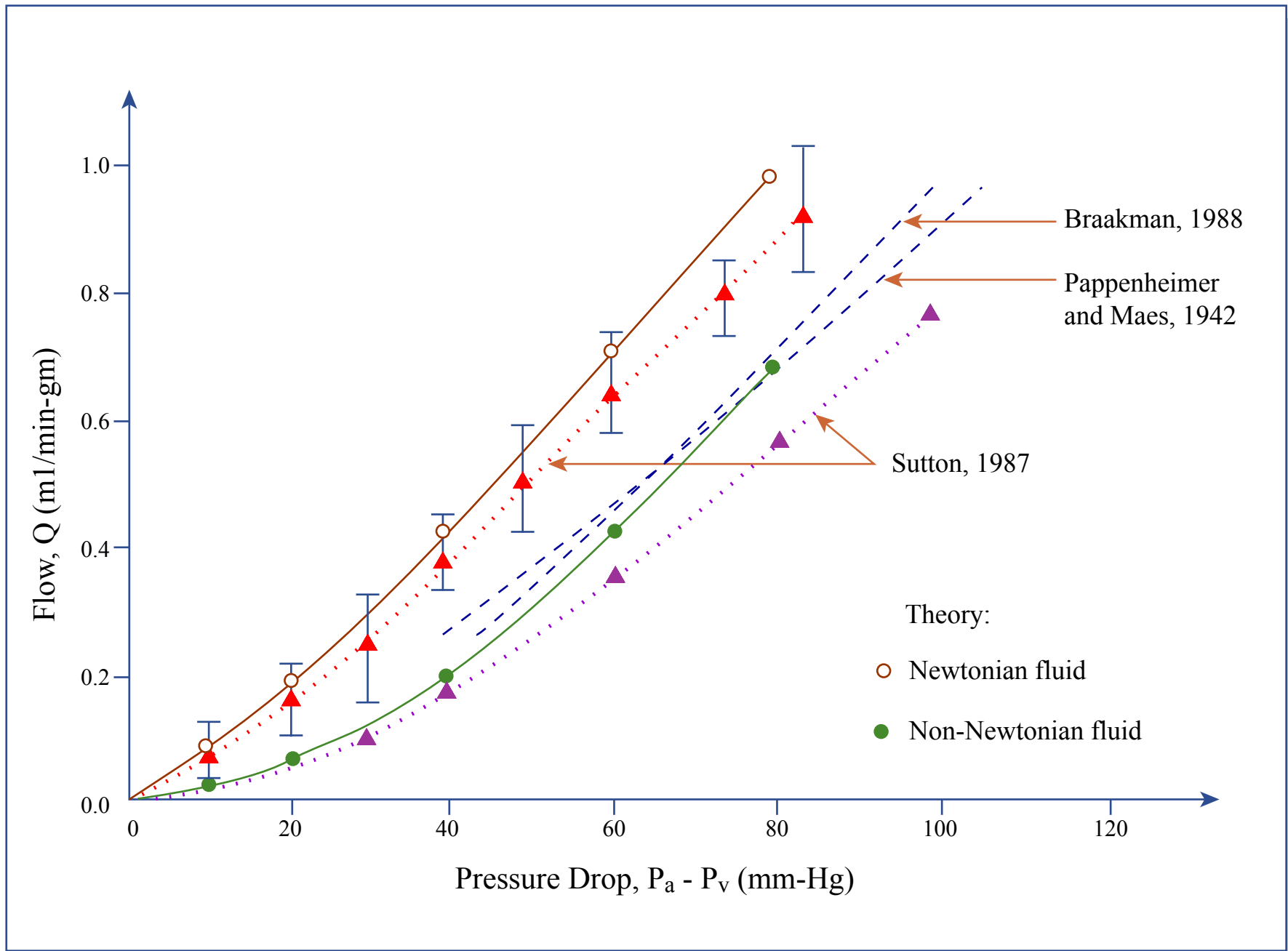


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Please see Fig. 4 in Schmid-Schonbein, et al. *Microvascular Networks: Theoretical and Experimental Studies*. Farmington, CT: S. Karger, 1986, p. 44.

Pressure-Flow Relationship in Skeletal Muscle Microcirculation



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

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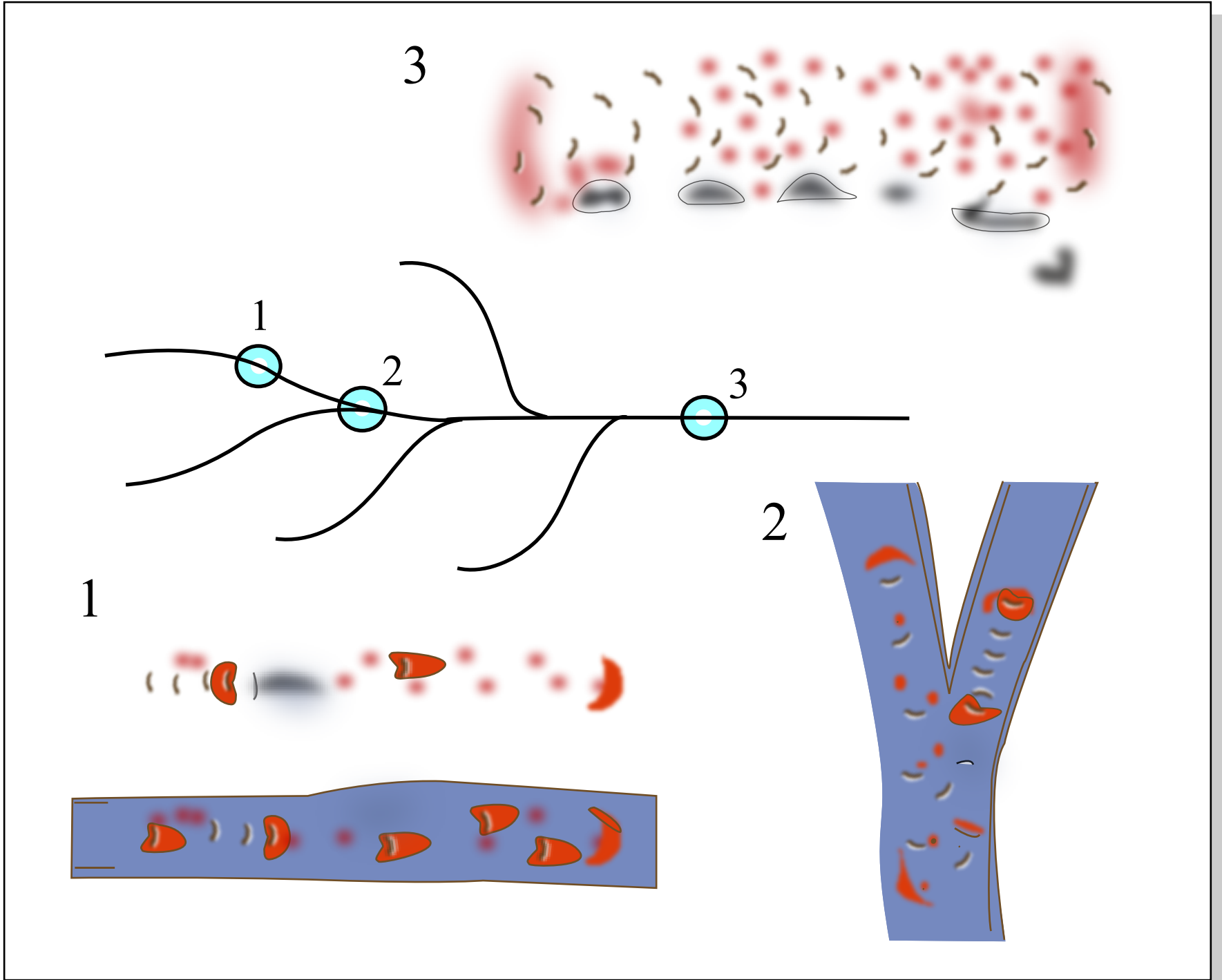


Figure by MIT OpenCourseWare.

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

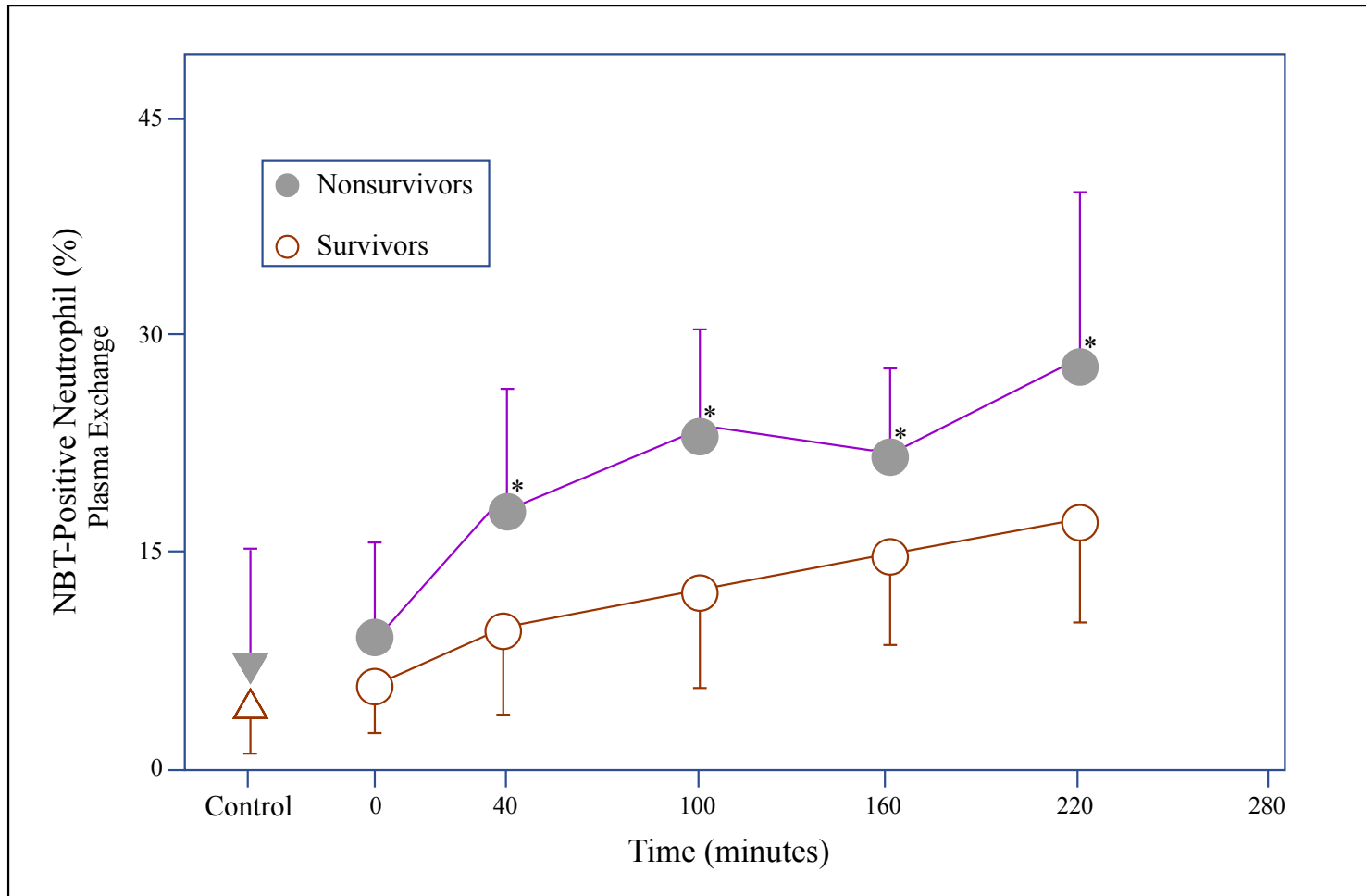


Figure by MIT OpenCourseWare.