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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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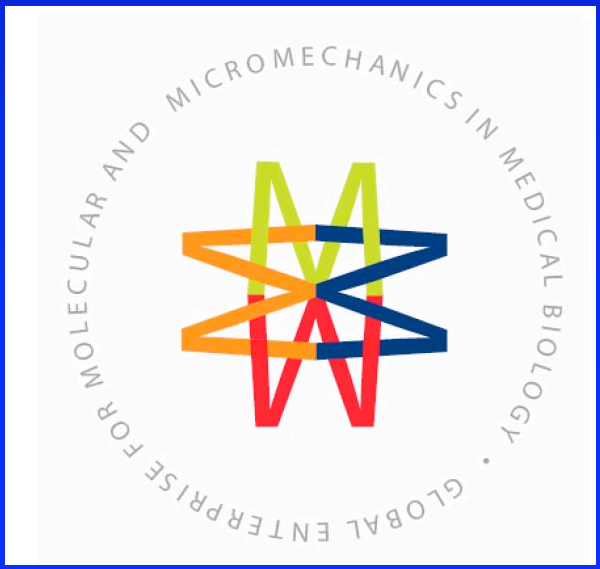
The Inflammatory Cascade:

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

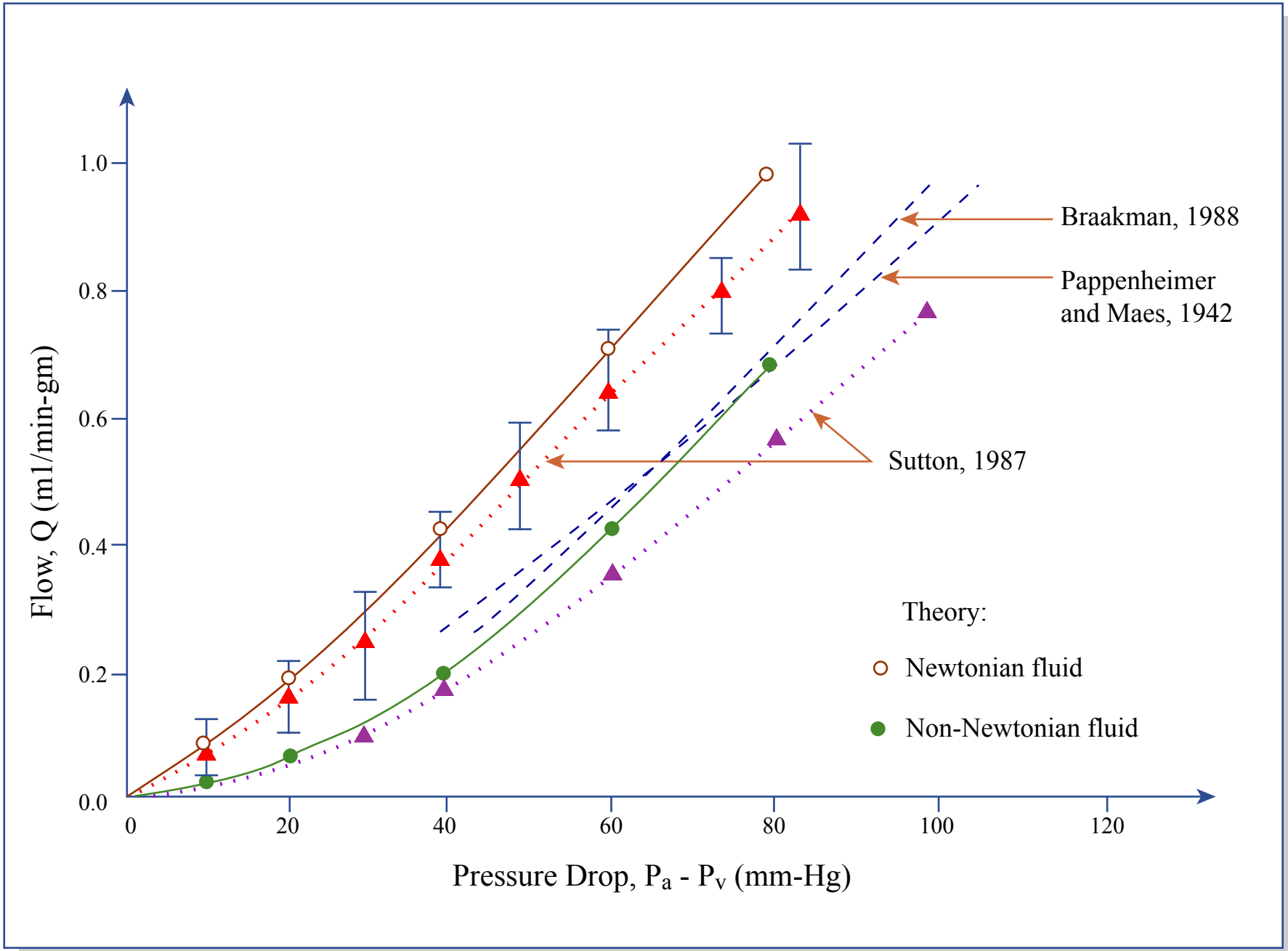

Figure by MIT OpenCourseWare.

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

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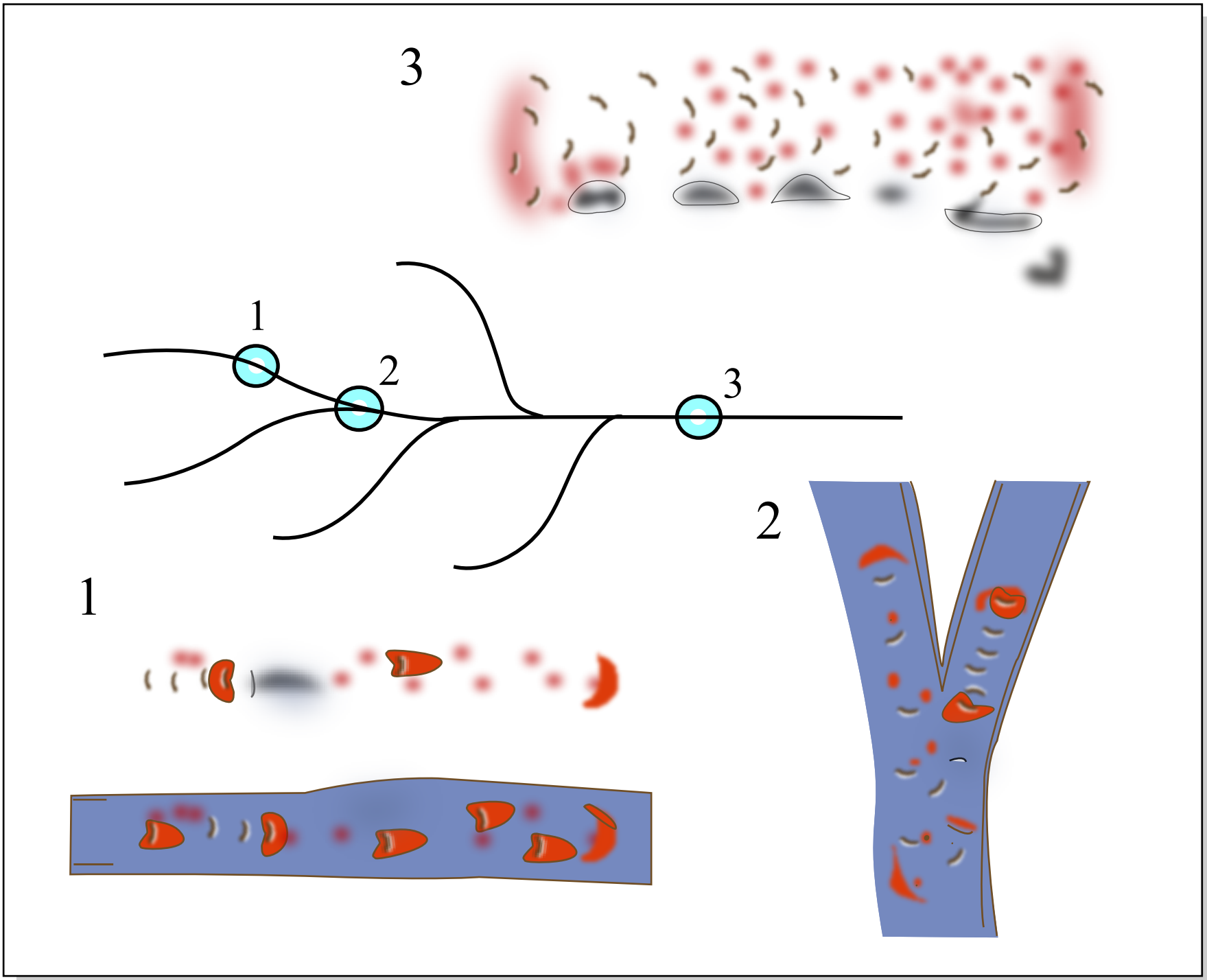

Figure by MIT OpenCourseWare.

Trigger Mechanisms for Cardiovascular Cell Activation

- Inflammatory mediators (bacterial/viral/fungal sources, endotoxins, cytokines, histamine, oxidized products, complement fragments, LTB_4, 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

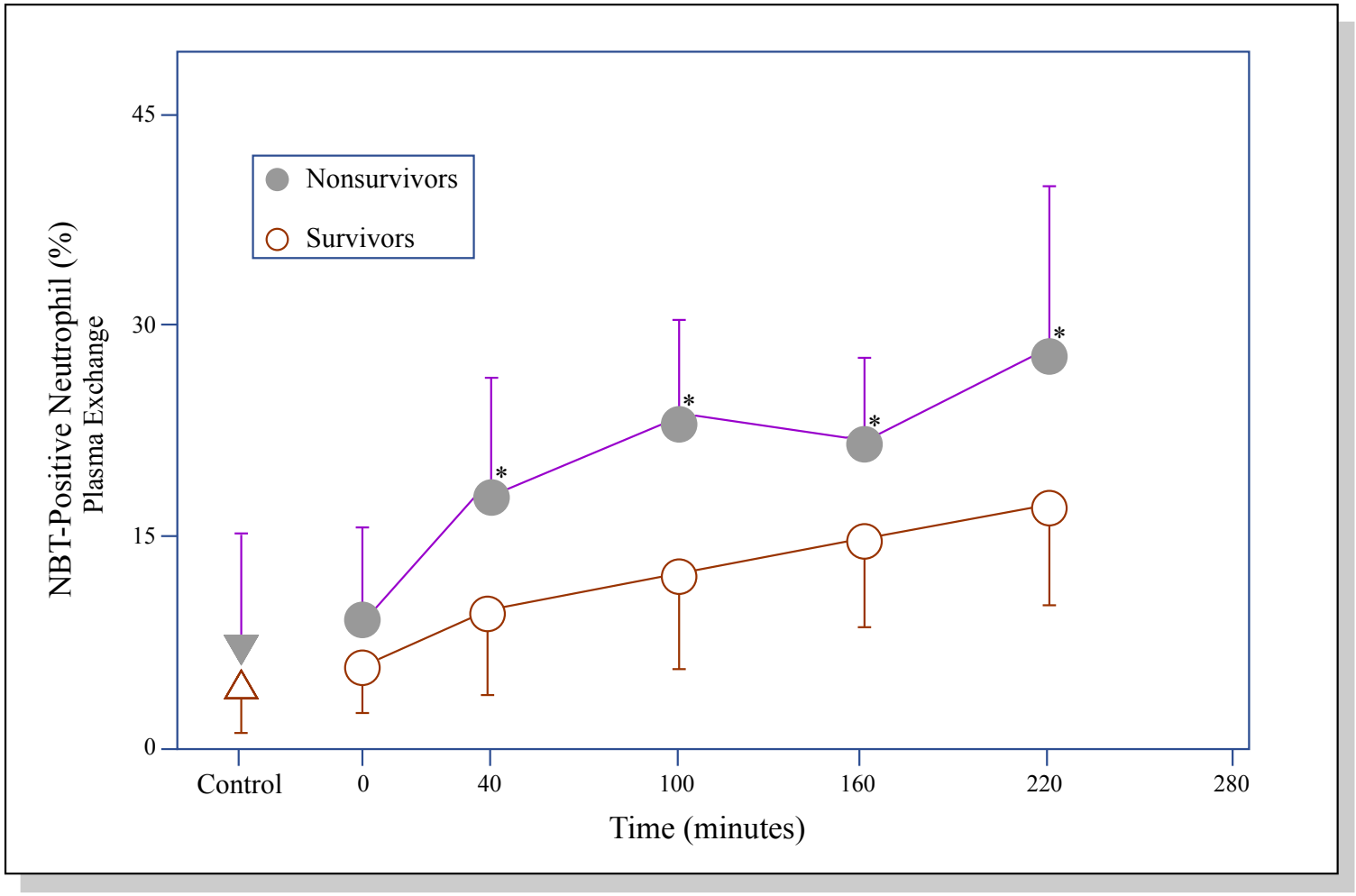

Figure by MIT OpenCourseWare.