좋은 아침입니다
(Cho Eun Achim Yip Ni Da)

저를 초대해 주셔서 감사합니다
(Jeo Reul Cho Dae Hae Joo
Seuh Seo, Kam Sa Hap Ni Da)

PLEASE JOIN US

13TH INTERNATIONAL CONGRESS OF BIORHEOLOGY

and

6TH INTERNATIONAL CONFERENCE ON CLINICAL HEMORHEOLOGY

PENN STATE UNIVERSITY
STATE COLLEGE, PA, USA
JULY 9-13, 2008

(ABSTRACT DEADLINE: MAY 1, 2008)

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FUNDAMENTALS OF HEMORHEOLOGY: BASIC SCIENCE AND CLINICAL ASPECTS

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PRESENTATION TODAY

- Historical Perspectives
- Principles of Rheology
- Rheology of Blood
- Determinants of Blood Rheology
- Relevance to Atherosclerosis

EARLY WORKERS IN HEMORHEOLOGY

- **POISEUILLE** (1797-1869)

  "Poiseuille's Law"

  $Q = K (\Delta P)(D^4) / (L)(\eta)$; η = viscosity

  Resistance to flow = $\Delta P / Q = K (L)(\boldsymbol{\eta}) / D^4$

- **FÅHRAEUS – LINDQVIST** (1929, 1931)

  Blood viscosity and hematocrit in narrow tubes

  "Fåhraeus – Lindqvist Effect"

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RHEOLOGICAL APPROACH

- **DEFORMING FORCE = STRESS**

  Pressure gradient in tube, torque on viscometer surfaces

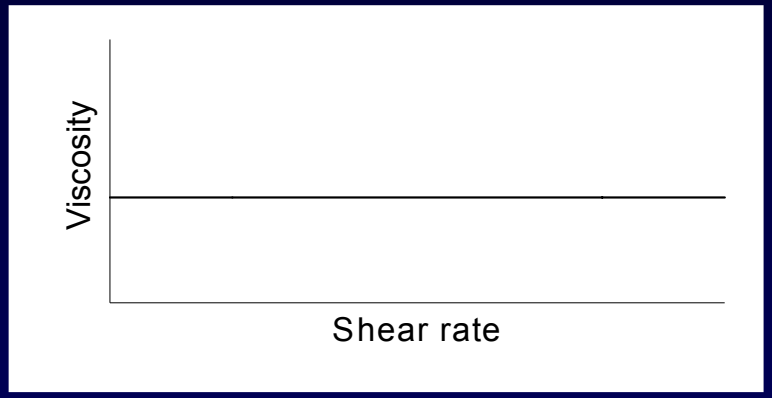
- **DEFORMATION = STRAIN ≈ SHEAR RATE**

  Flow rate in tube, viscometer rotational speed

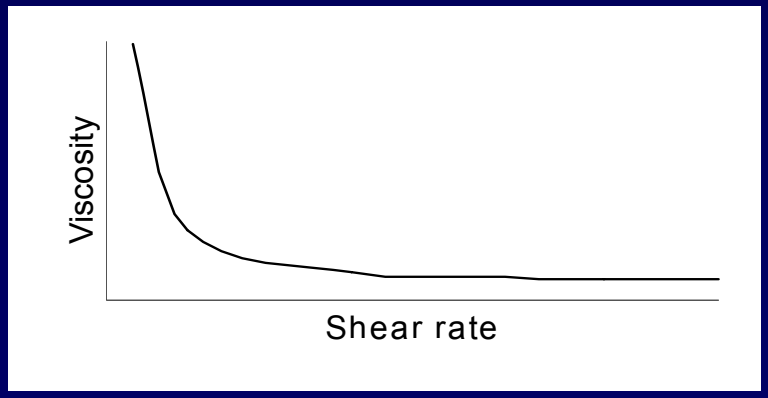
- **STRESS / STRAIN** = Mechanical Property ≈ Viscosity

RHEOLOGY OF FLUIDS

Newtonian



Non-Newtonian



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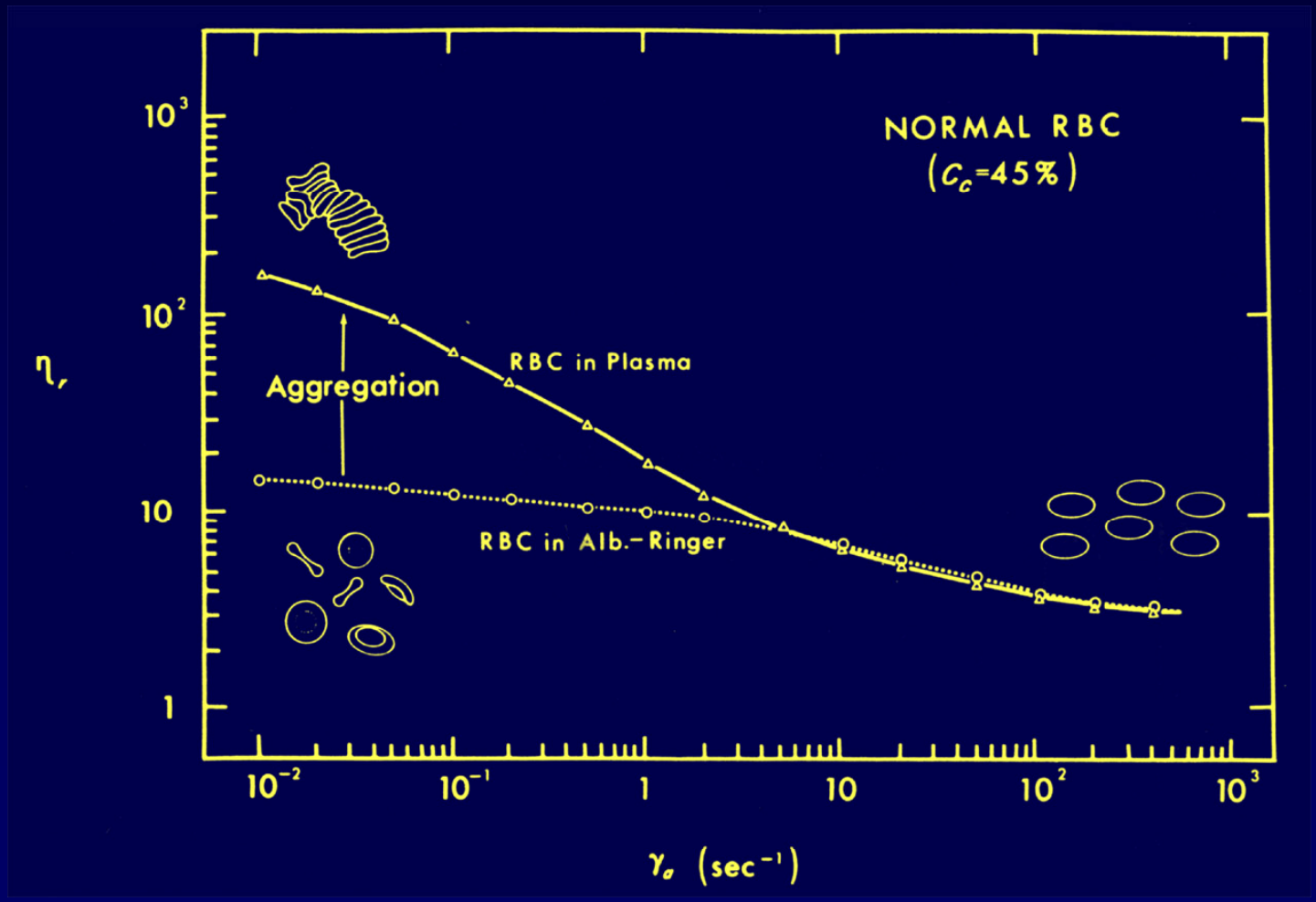
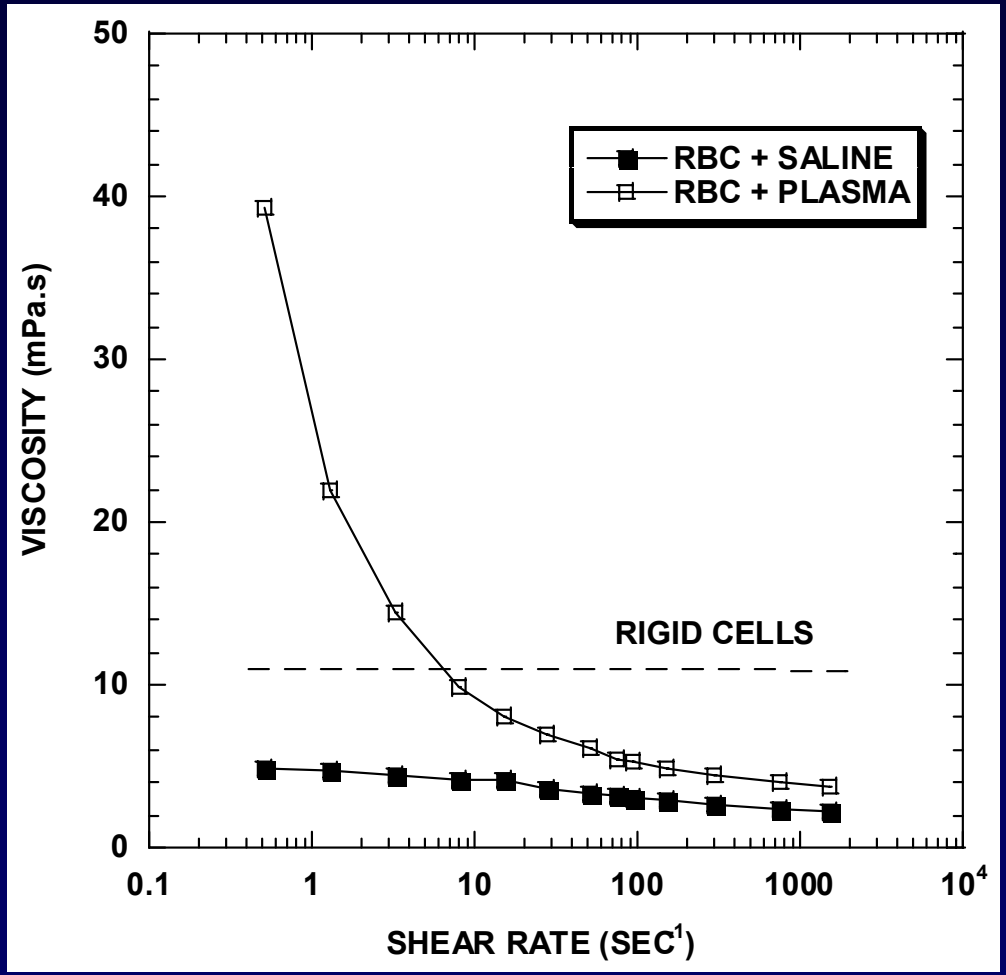
SHEAR RATE – VISCOSITY RESULTS



Viscosity – Shear Rate Relations



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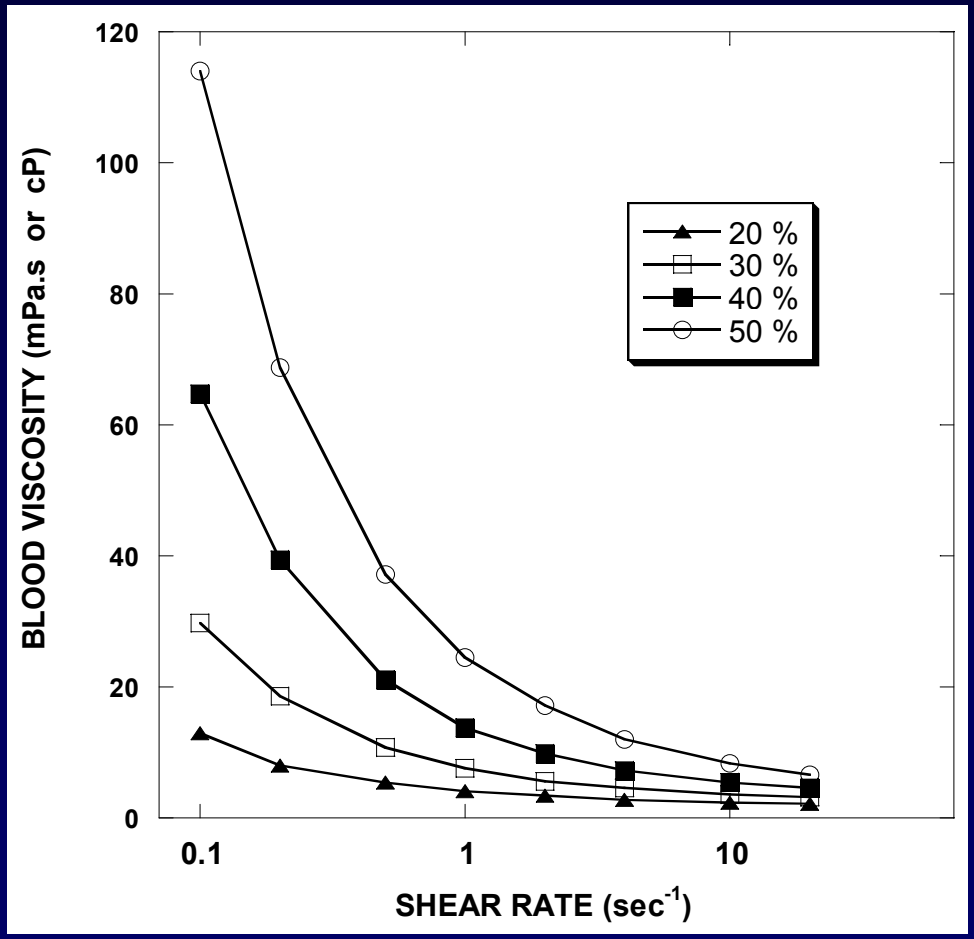
RBC MOTION IN TUBE FLOW: IMPORTANCE OF RBC DEFORMABILITY

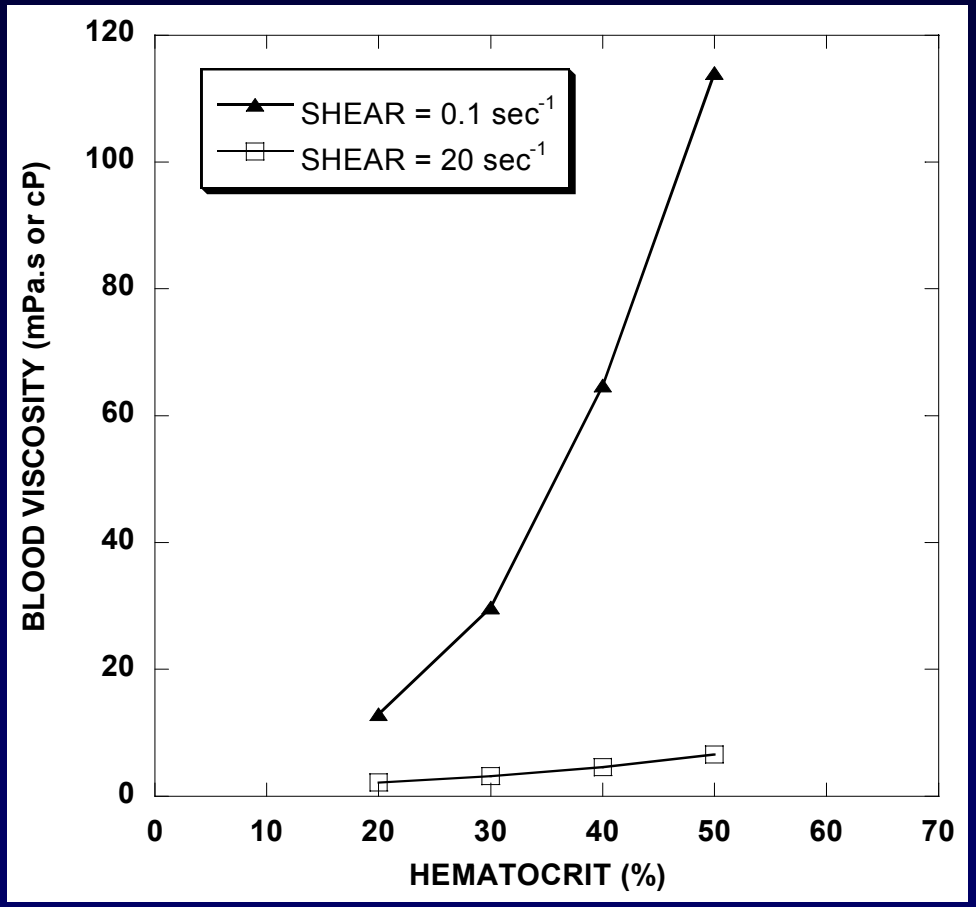
DILUTE RBC SUSPENSION

INTACT RBC IN CROWDED GHOST SUSPENSION

EFFECT OF HEMATOCRIT ON BLOOD VISCOSITY



SENSITIVITY OF VISCOSITY TO HEMATOCRIT: EFFECT OF SHEAR RATE



RED BLOOD CELL AGGREGATION AT STASIS OR LOW FLOW

RBC AGGREGATION MECHANISMS

BRIDGING MODEL:

- larger proteins or polymers bind to adjacent cells
- tends to “link” or “bridge” cells together

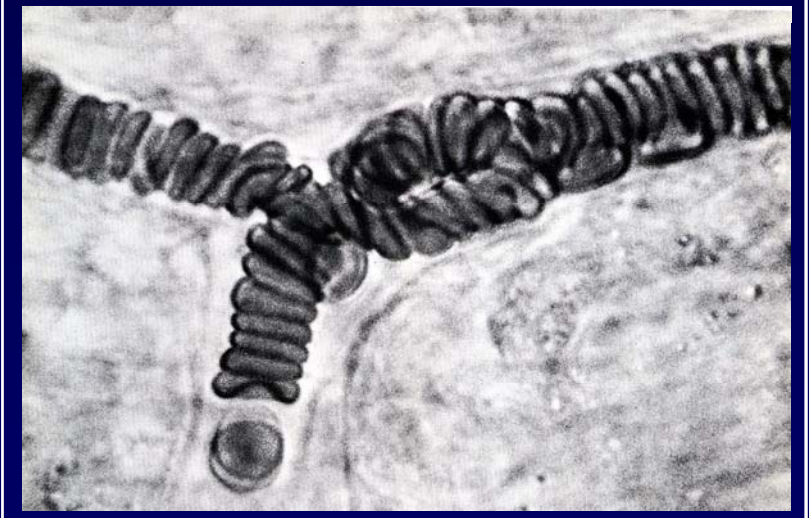
DEPLETION MODEL:

- depletion of protein or polymer concentration (versus bulk phase) near the cell surface
- exclusion of macromolecules leads to an osmotic gradient and thus attractive forces between cells

RBC BEHAVIOR *IN VIVO*

HIGH FLOW RATES: **DEFORMATION**

LOW FLOW RATES: **AGGREGATION**



STASIS: **AGGREGATION**

INCREASED RBC AGGREGATION IN PATHOLOGICAL STATES

- Diabetes
- HIV Infection
- Lipid Disorders
- Macroglobulinemia
- Myocardial Infarction
- Sepsis
- Stroke

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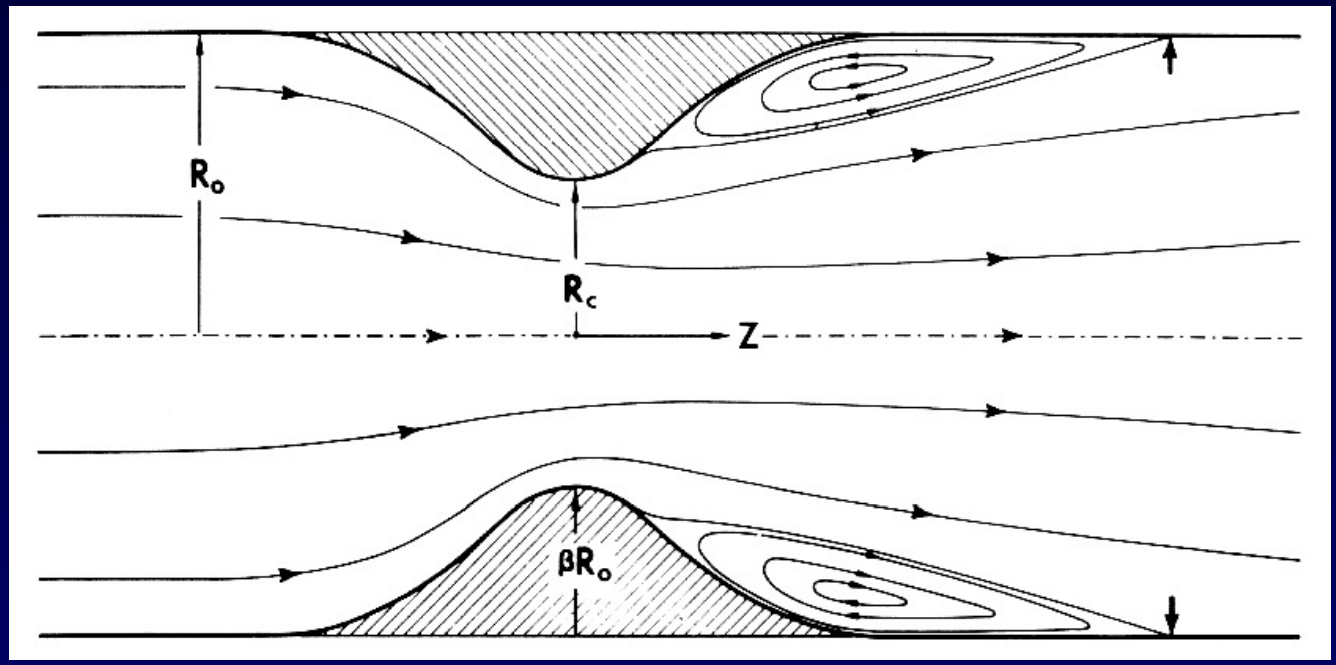
ATHEROGENESIS AND ATHEROSCLEROSIS LINKS WITH HEMORHEOLOGY (A)

- High levels of fibrinogen strongly correlate with frequency of atherosclerosis and stroke
- High levels of fibrinogen cause increased extent and strength of RBC aggregation
- RBC aggregation enhanced in regions of low flow or stasis
- Enhanced RBC aggregation promotes margination of leucocytes to vessel wall

ATHEROGENESIS AND ATHEROSCLEROSIS LINKS WITH HEMORHEOLOGY (B)

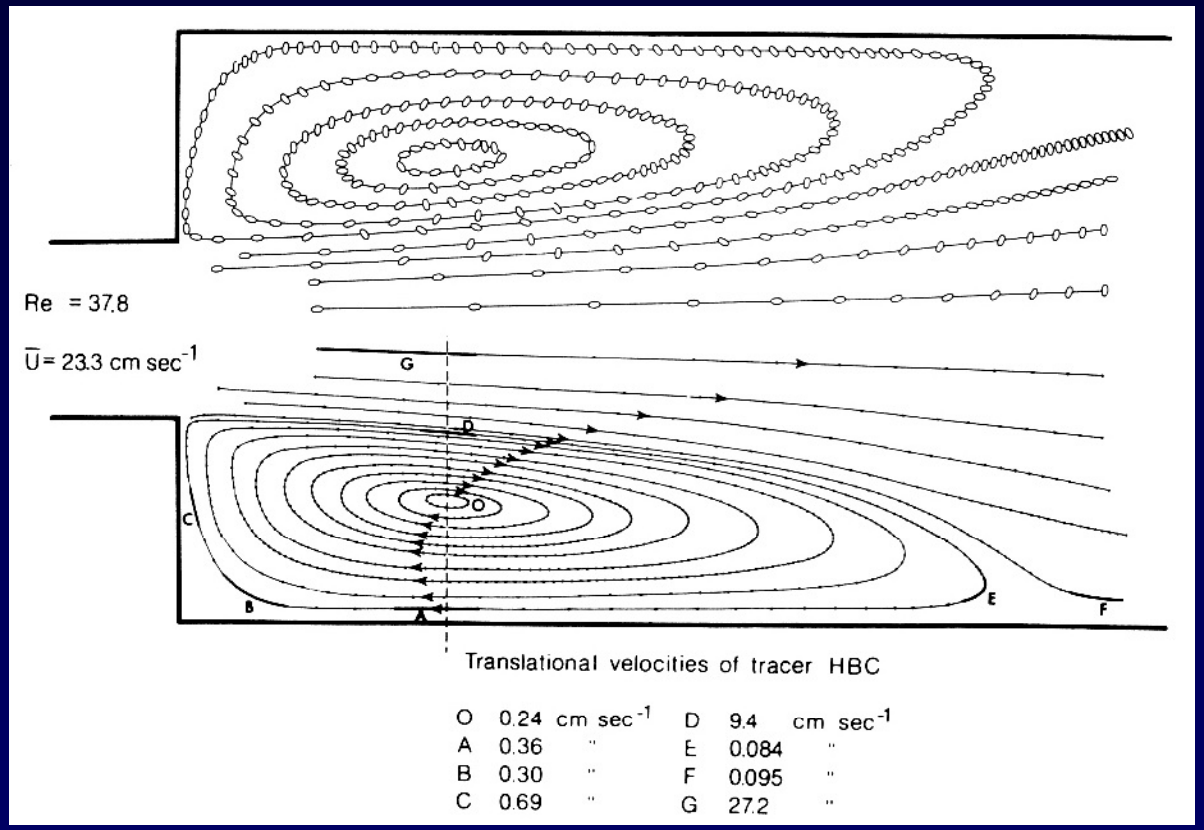
- Uniform laminar flow is “atheroprotective”
- Regions of disturbed flow (branches, curves) preferred sites for atherosclerotic disease
- Low or zero shear rate in regions of disturbed flow are regions of higher blood viscosity
- Long residence times for cells (RBC, WBC) and solutes (ADP) in regions of disturbed flow

FLOW THROUGH SYMMETRIC CONSTRICTION



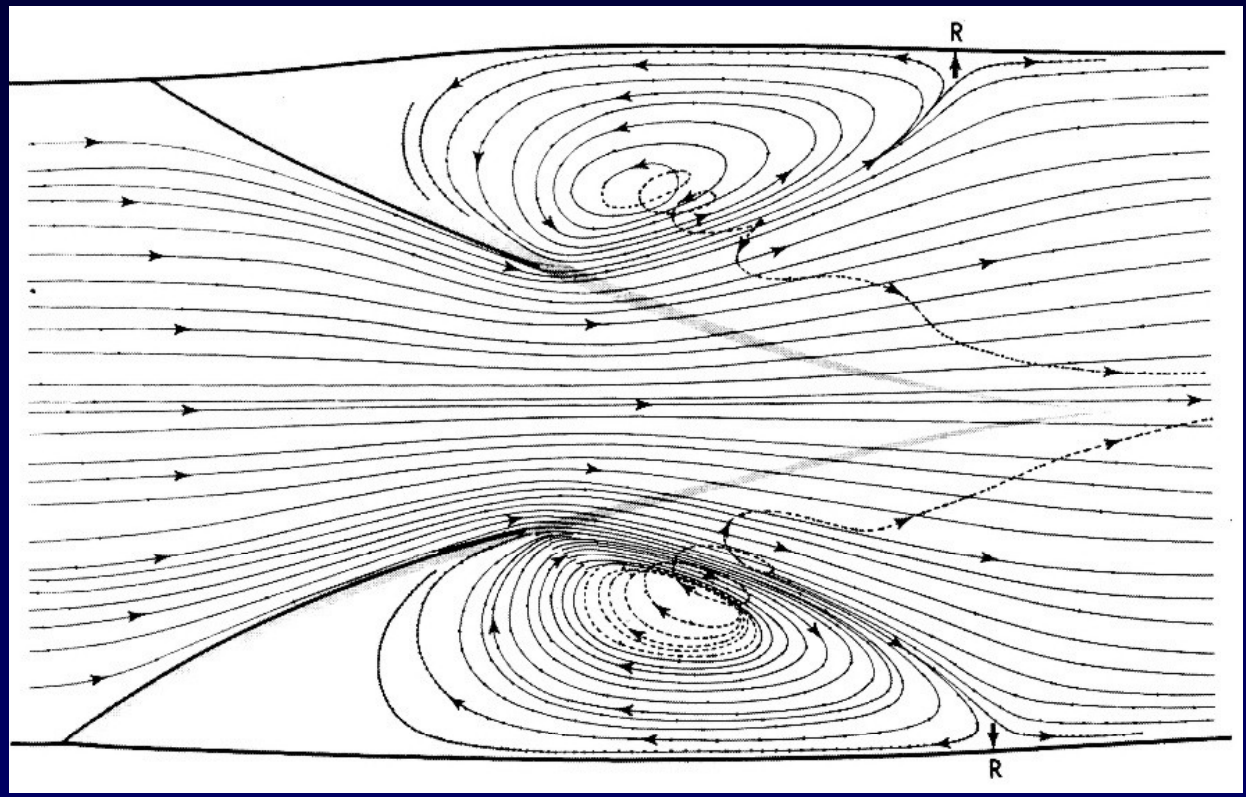
Karino, Goldsmith, et.al, 1987

FLOW THROUGH SUDDEN EXPANSION



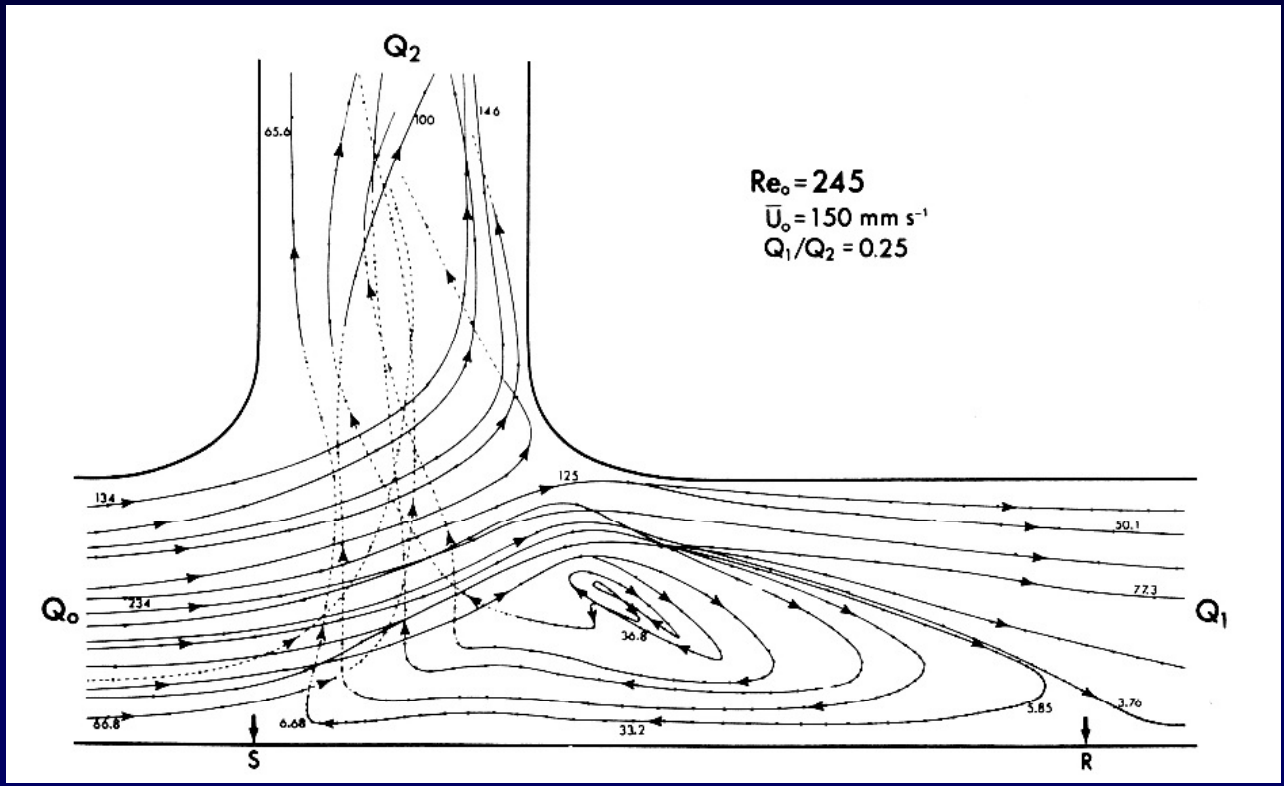
Karino, Goldsmith, et. al, 1987

FLOW THROUGH VALVE LEAFLETS (DOG SAPHENOUS VEIN)



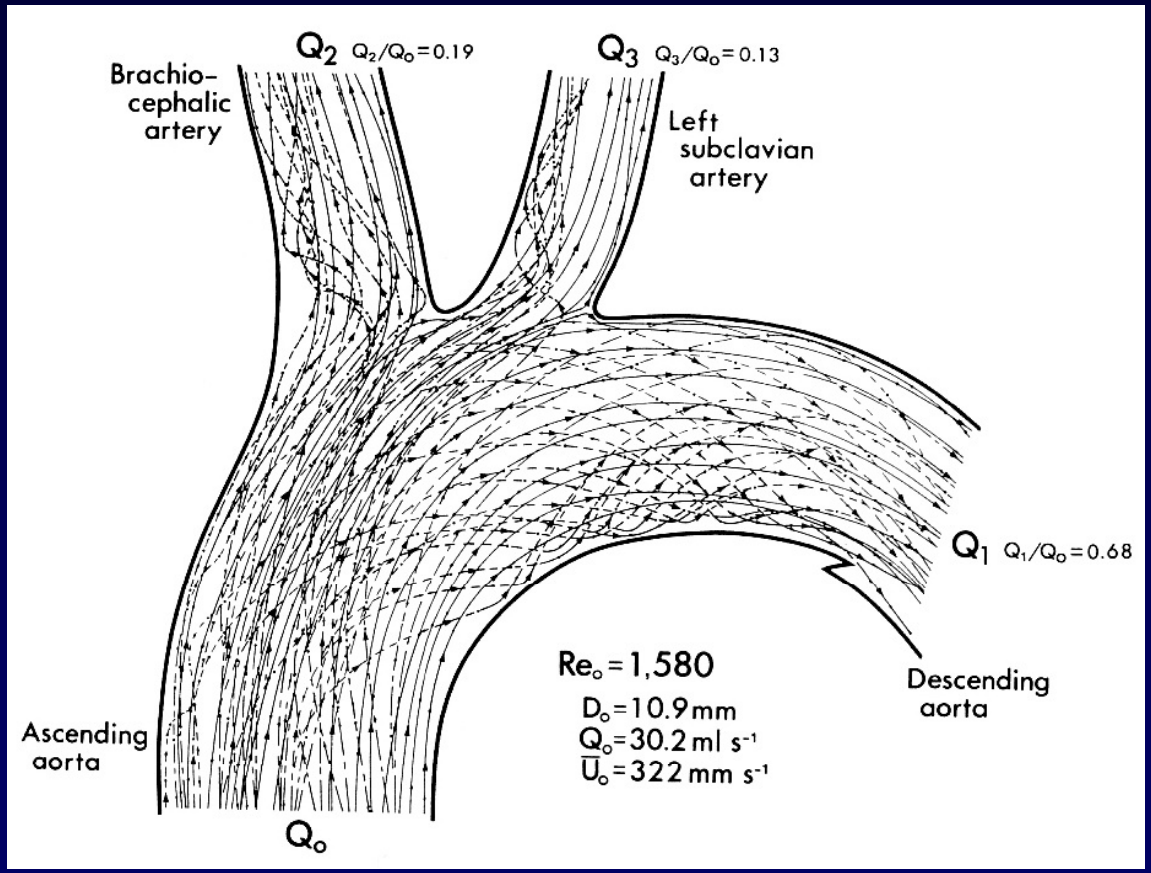
Karino, Goldsmith, et. al, 1987

FLOW THROUGH 90 DEGREE BRANCH



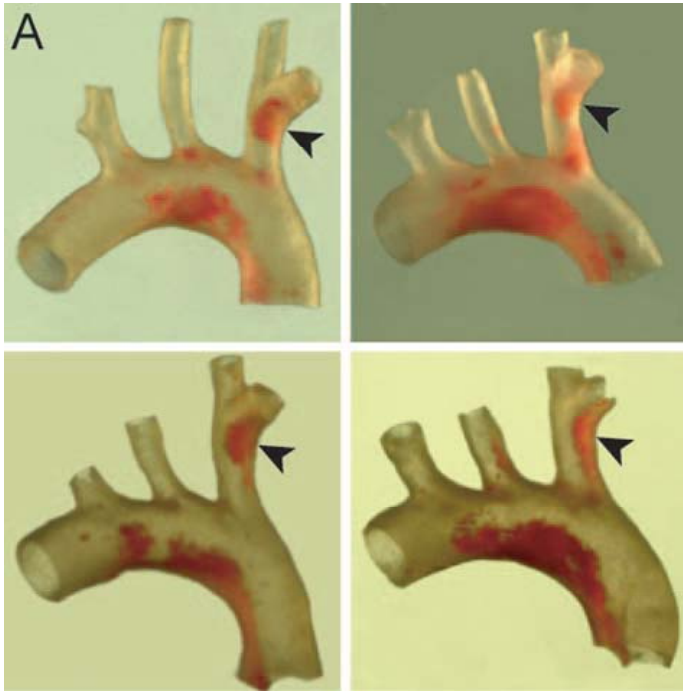
Karino, Goldsmith, et. al, 1987

FLOW PATTERNS IN DOG AORTIC ARCH



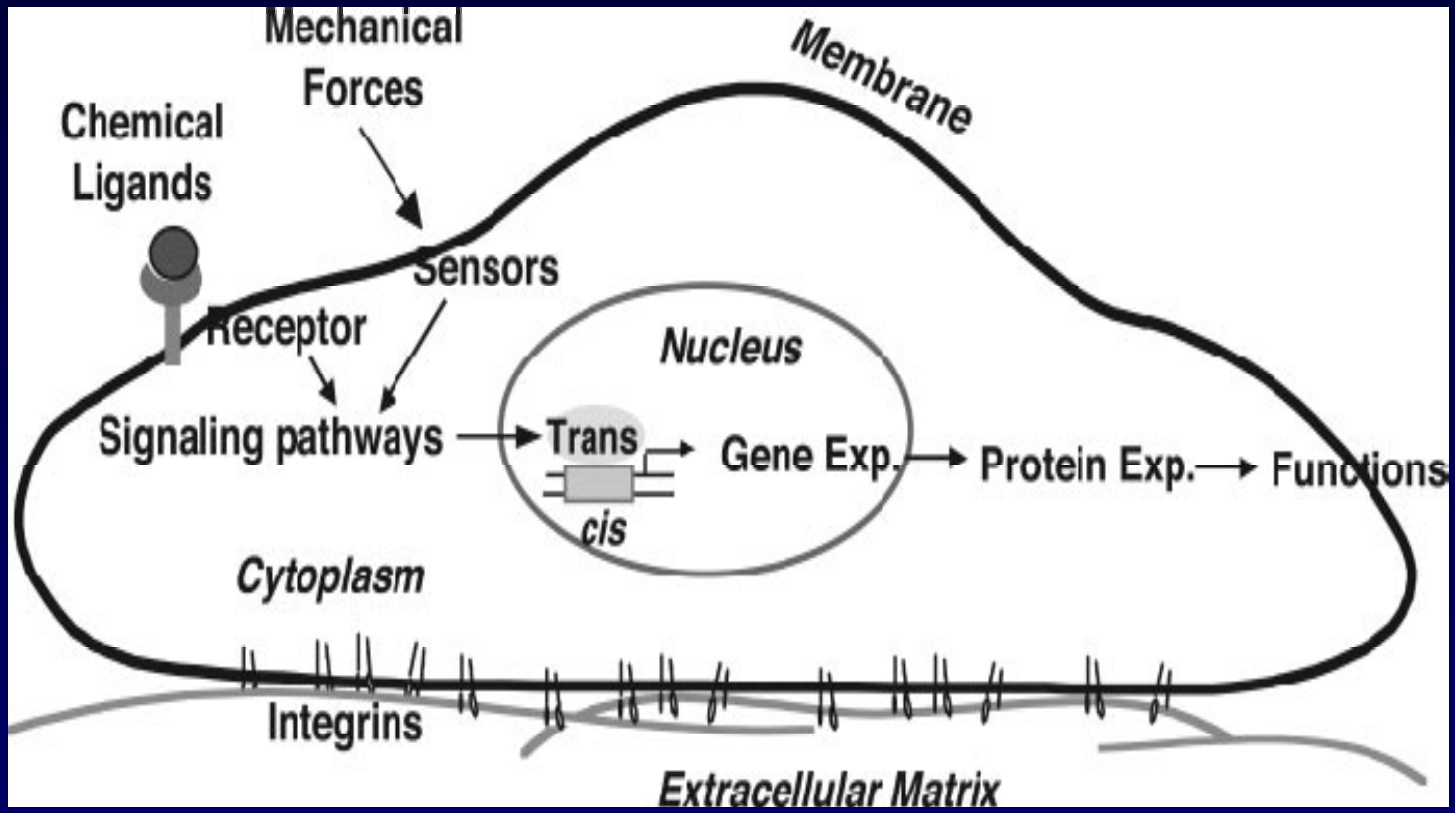
Karino, Goldsmith, et. al, 1987

ATHEROSCLEROSIS PRONE OR RESISTANT REGIONS (MOUSE BRACHIOCEPHALIC TRUNK)



Won, et al., Am. J. Path., 2007

CHEMICAL LIGANDS AND MECHANICAL FORCES STIMULATE ENDOTHELIAL CELLS



Chien, Am. J. Physiol., 2007

CONCLUSIONS

- Blood is a non-Newtonian fluid: viscosity increases as flow slows and shear decreases
- Viscosity function of hematocrit, RBC rigidity, RBC aggregation, plasma proteins
- Disturbed flow regions have low or zero shear rate and are preferred sites for atherosclerotic disease ; laminar flow “athero-protective”
- Disturbed flow regions: higher blood viscosity, margination of cells, long residence times for cells (RBC, WBC) and solutes (ADP)

경청해 주셔서 감사합니다
(Kyung Chung Hae Joo Seuh Seo,
Kam Sa Hap Ni Da)