

Cardiovascular disease, studies at the cellular and molecular level

Linda Lowe-Krentz

Bioscience in the 21st Century

November 14

Risk Factors

- High blood pressure (above 120/80 mm Hg)
- Serum cholesterol [aim for below 100 mg/dL LDL cholesterol and above 50 mg/dL HDL, or aim for total cholesterol below 180 mg/dL]
- Body Mass index (BMI) [between 18.5 and 24.9]
- Smoking
- Drinking
- Diabetes

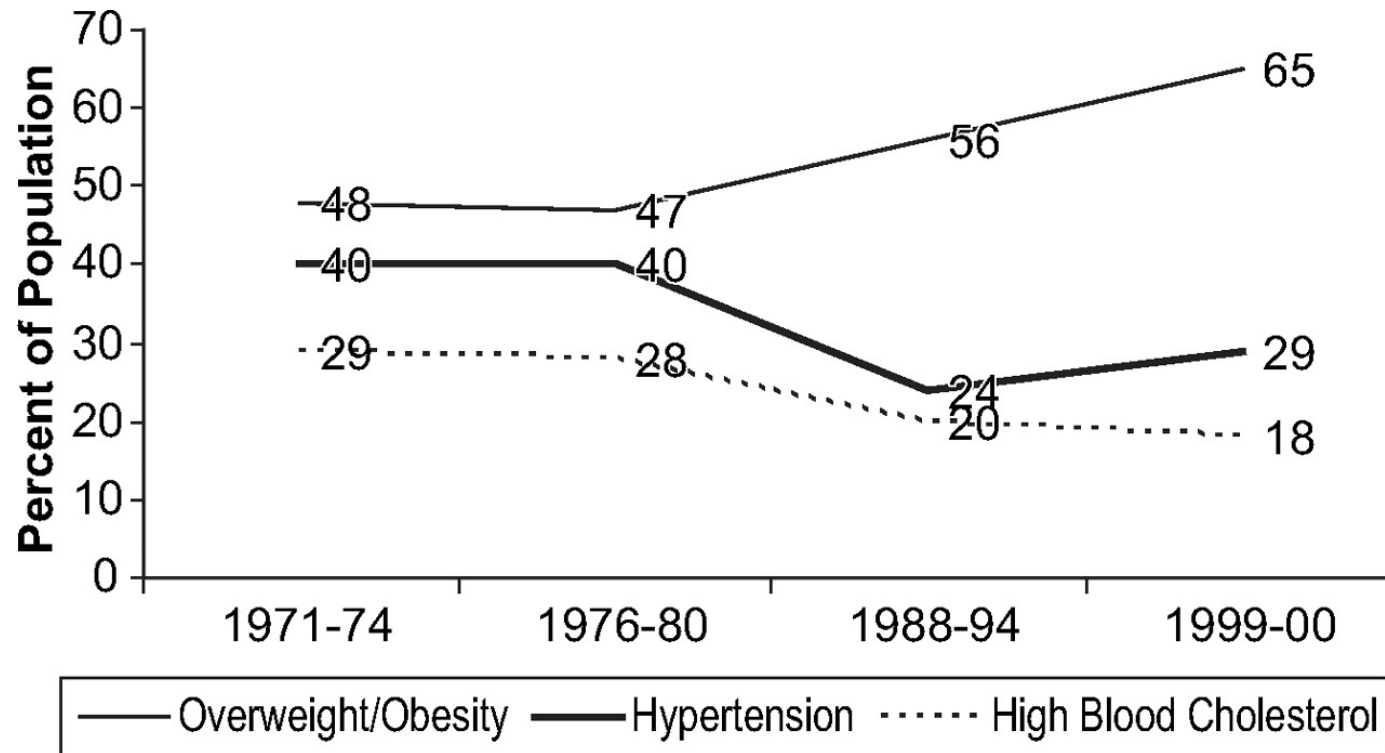
Compare to Metabolic Syndrome

- Abdominal obesity
- High blood pressure
- High fasting blood glucose
- High triglycerides
- Low HDL

Statistics

- Compiled and presented in the Journal Circulation – published by the American Heart Association

**Chart 2-1 Trends in the age-adjusted prevalence of health conditions
US adults ages 20 to 74**

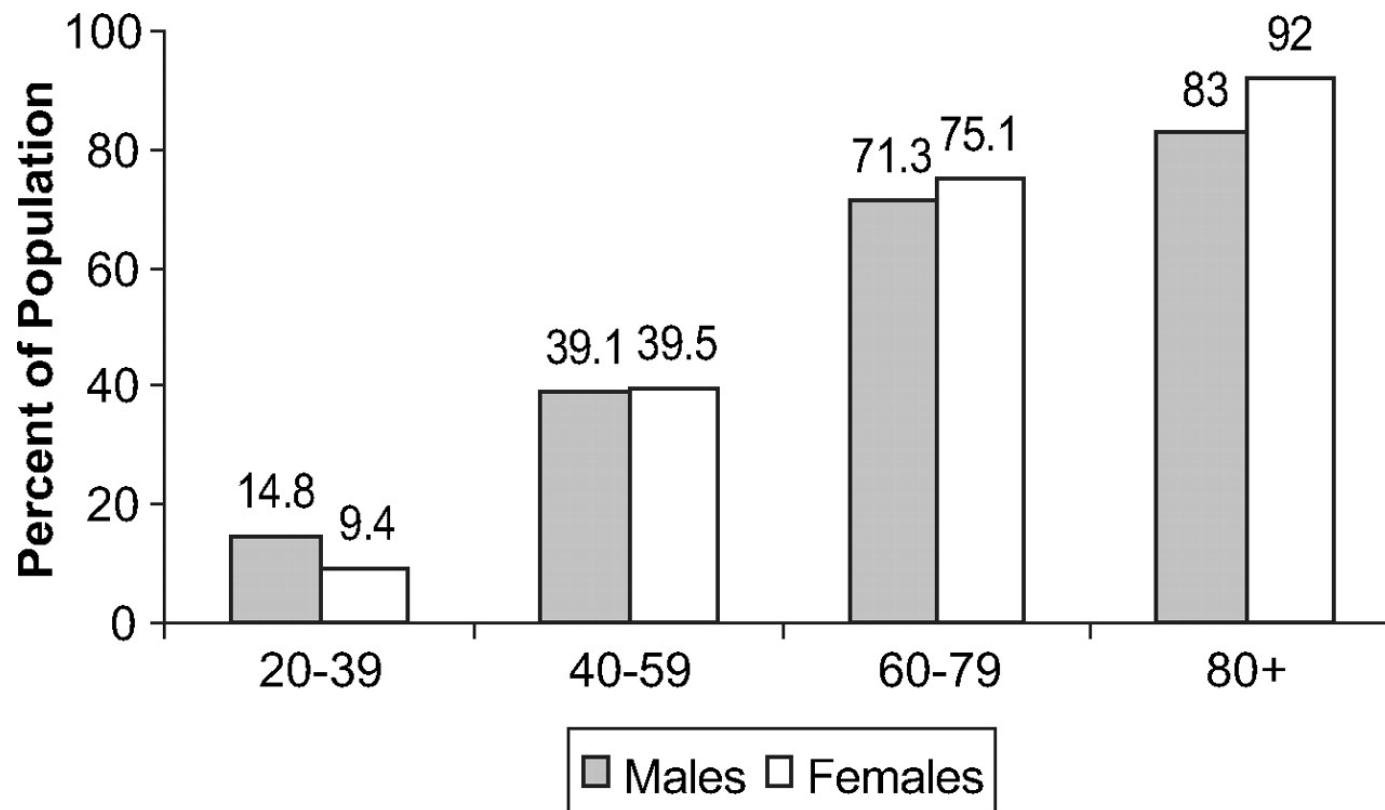


Rosamond, W. et al. *Circulation* 2007;115:e69-e171

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Chart 2-2. Prevalence of CVDs in adults age 20 and older by age and sex. (1999-2004)

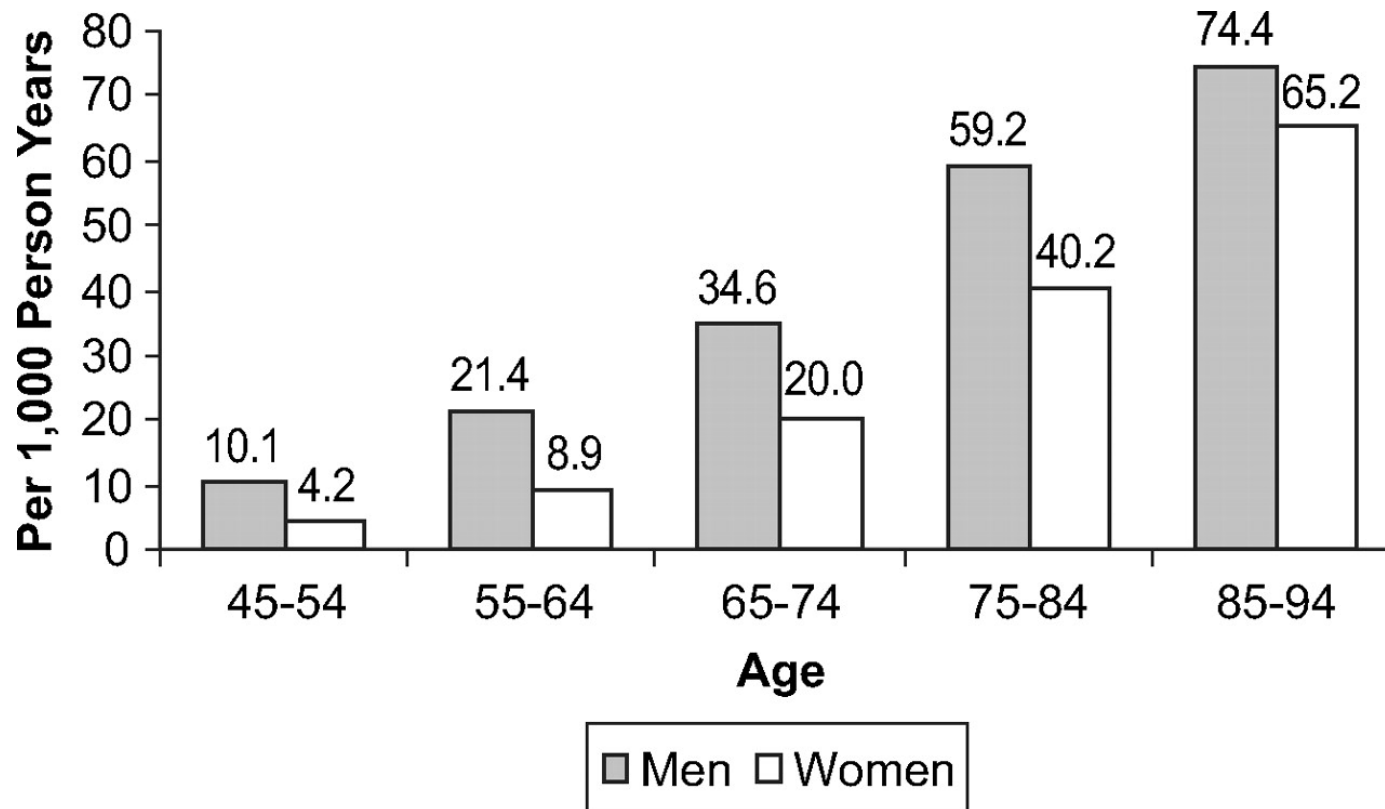


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Chart 2-3. CVD without including hypertension

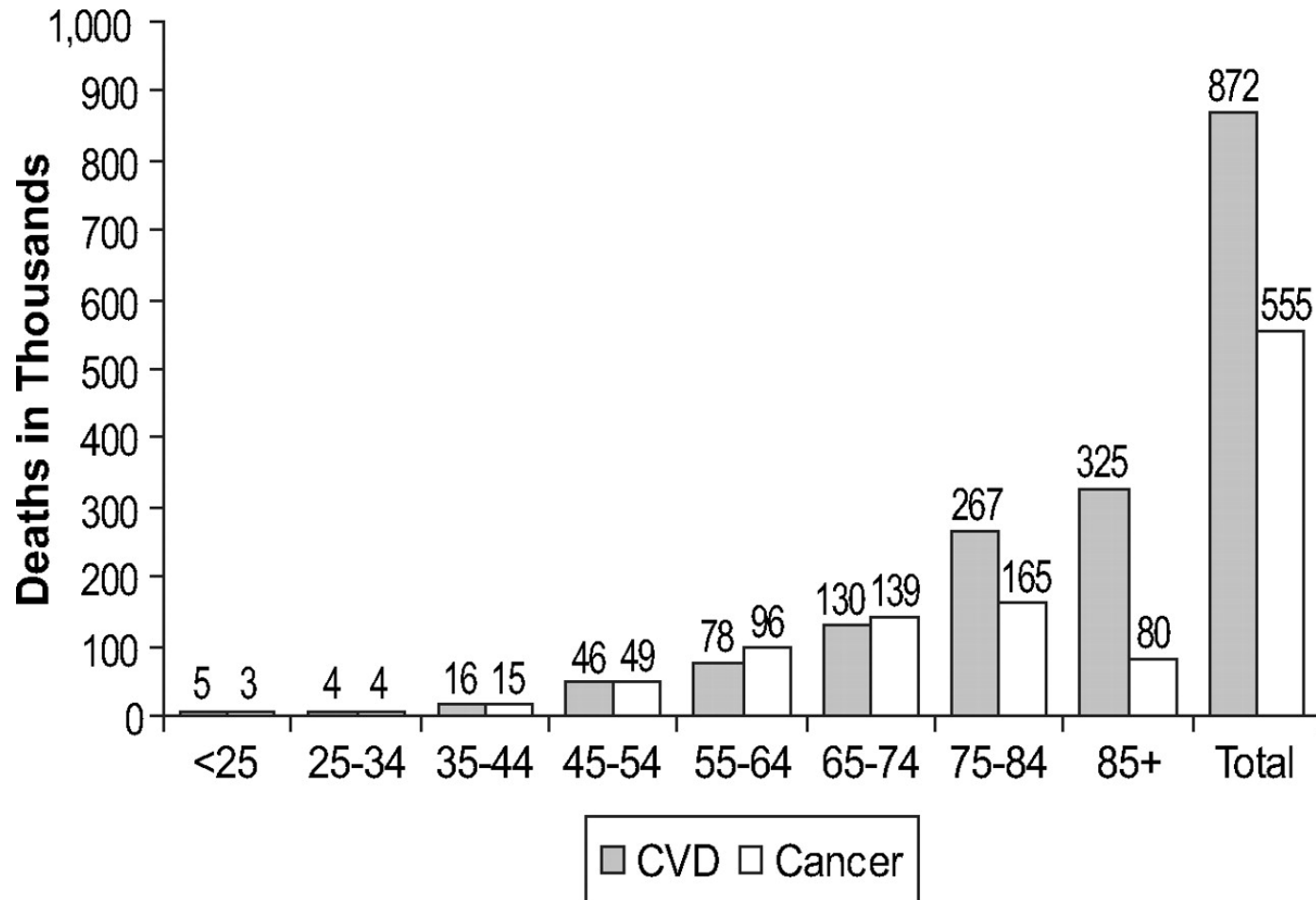


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**Chart 2-6. CVD deaths vs cancer deaths by age.
(2004)**



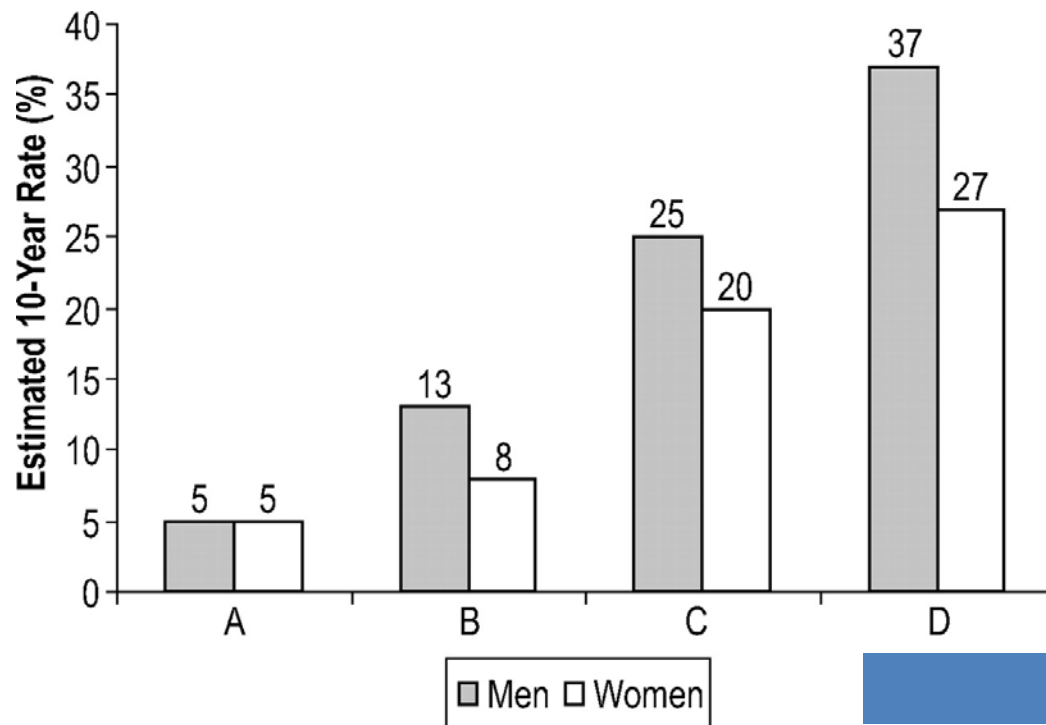
Rosamond, W. et al. *Circulation* 2007;115:e69-e171

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Chart 3-6. Ten year risk for CHD by risk factors



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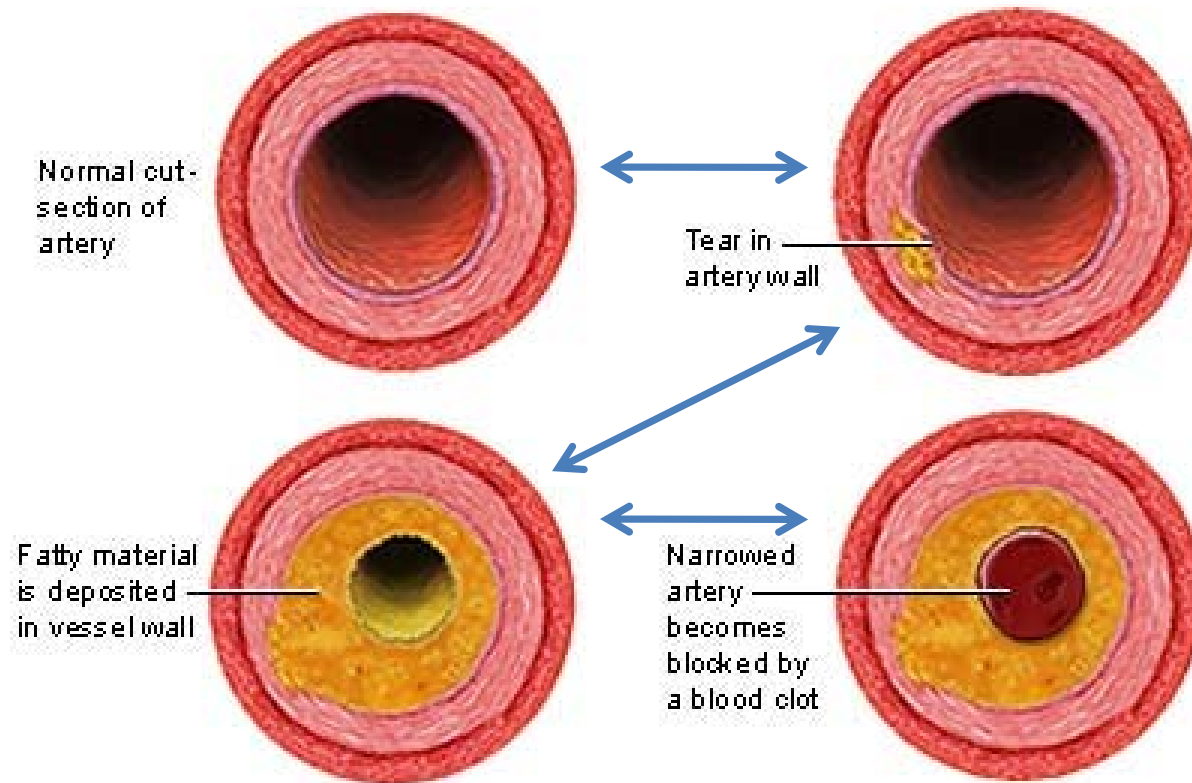
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	A	B	C	D
BP, mm HG	120/ 80	140/ 90	140/ 90	140/ 90
mg/dL, Total Cholesterol	200	240	240	240
Mg/dL HDL cholesterol	50	50	40	40
Diabetes	No	No	Yes	Yes
Cigarettes	No	No	No	Yes

Recommendations

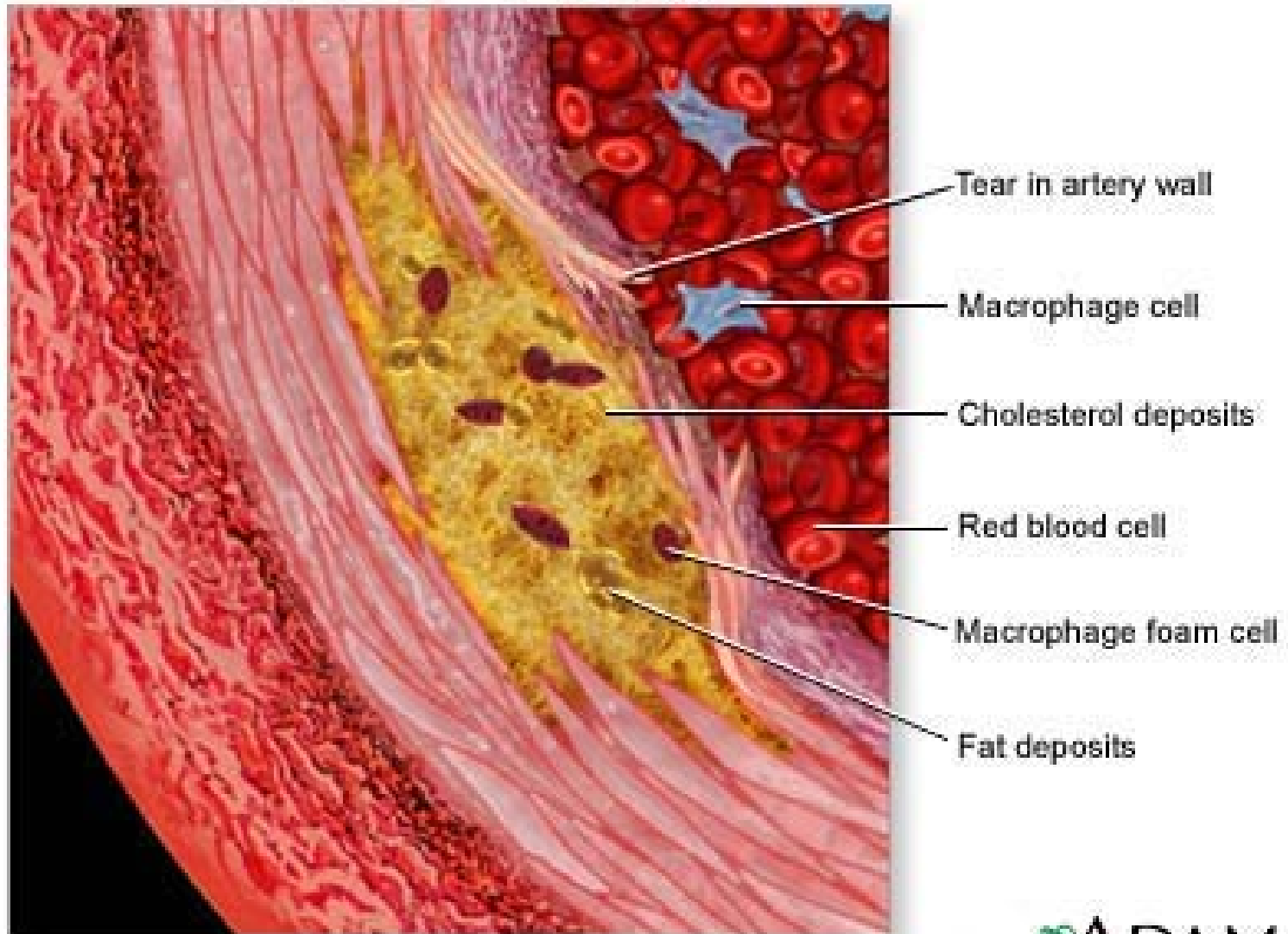
- Eat less than 7% of your calories from sat. fat
- Consume less than 200 mg/day cholesterol
- Eat 25-35% of your daily calories in fat
- Diet options for lowering cholesterol
 - Plant sterols and/or soluble fiber
- Eat only enough calories to maintain weight (or reach a healthy weight)
- At least 30 min of moderate physical activity/day

Progression of Vascular Disease

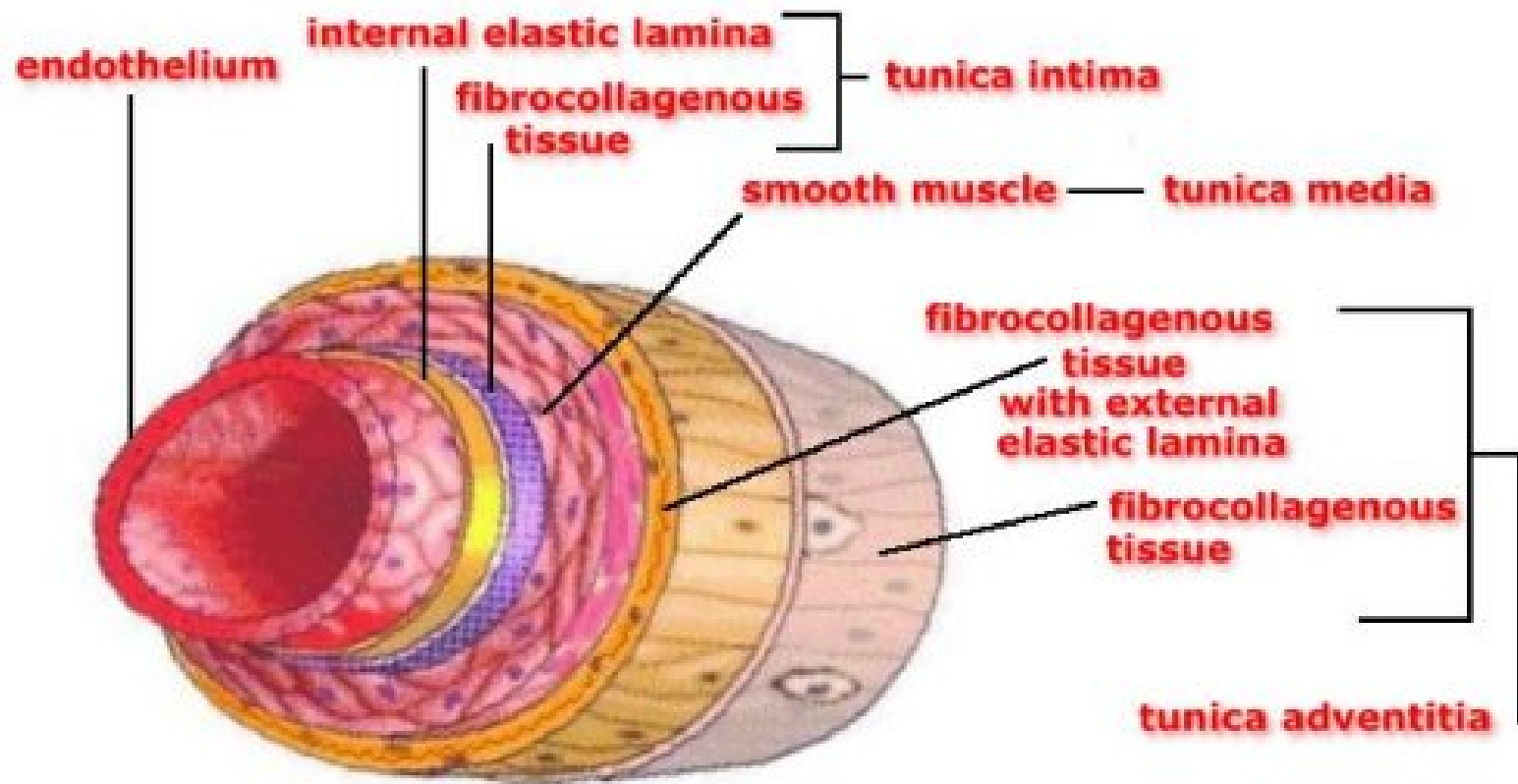


ADAM.

Cut-section of artery

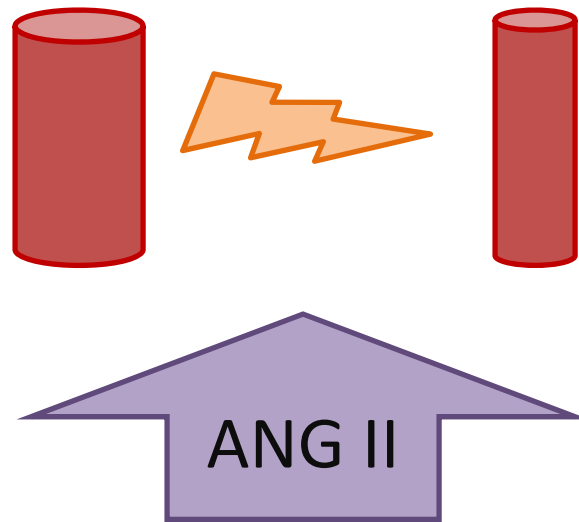


 ADAM.



Contraction of blood vessels

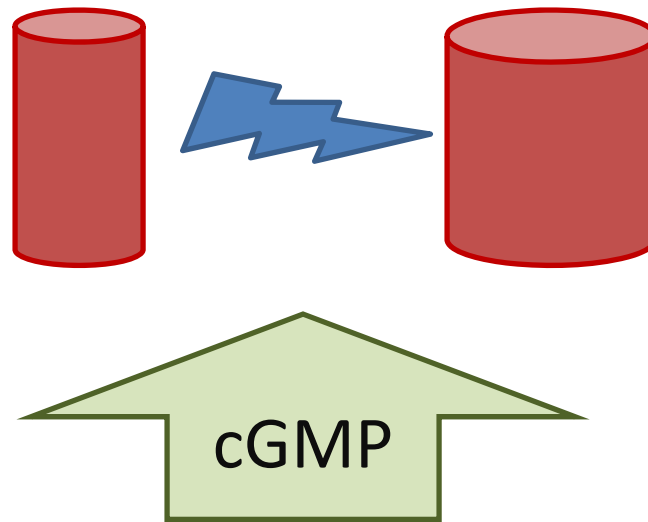
- Angiotensin is a major contraction signal that increases blood pressure transiently



Ace inhibitors,
 β -blockers

Relaxation of blood vessels

- NO (nitric oxide) and atrial natriuretic factor both cause increases in cGMP



Nitroglycerin

- But cGMP is typically rapidly degraded by proteins called PDEs



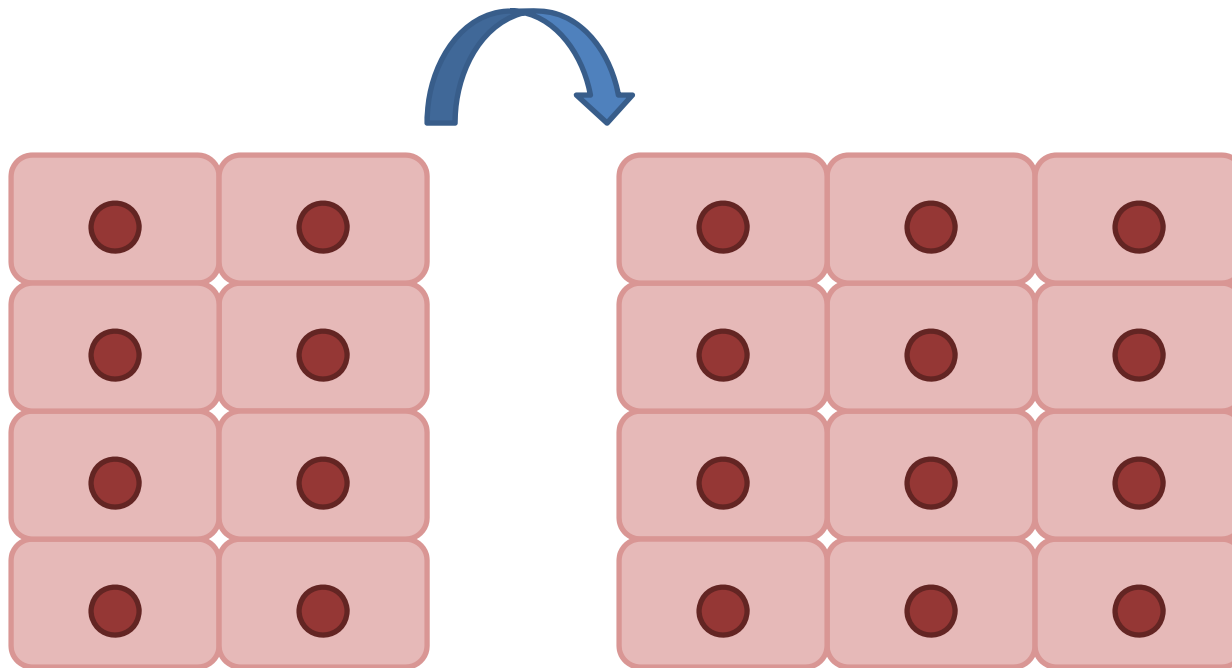
- PDE3 is primarily in cardiac muscle
- PDE6 is primarily in the retinas
- PDE5 is primarily in vascular smooth muscle

Sildenafil citrate

- Blocks PDE5 80 to 4000 times more effectively than it blocks other PDE isoforms (except PDE6)
- Therefore in vascular smooth muscle cells cGMP remains elevated longer.
- Viagra is the trade name for sildenafil citrate

Cell proliferation and wound repair

- Lack of contact, damaging chemicals, etc.
- Growth factors, Angiotensin
- Immune system

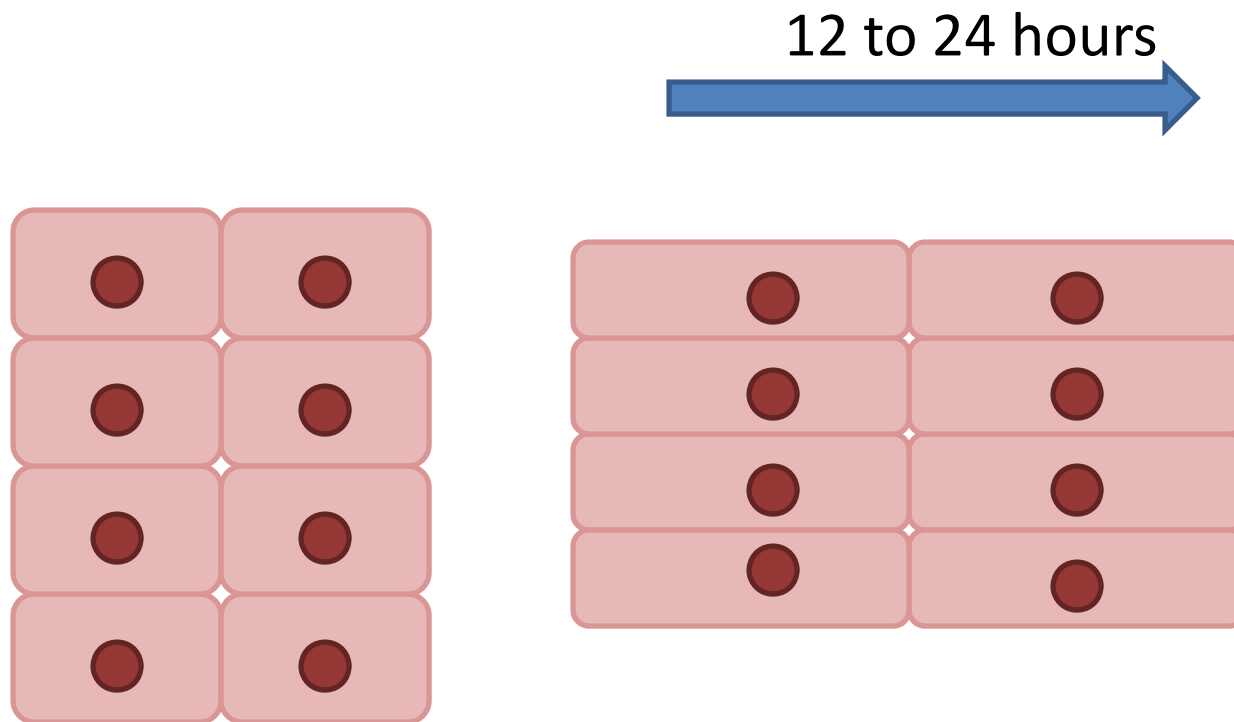


Excessive damage

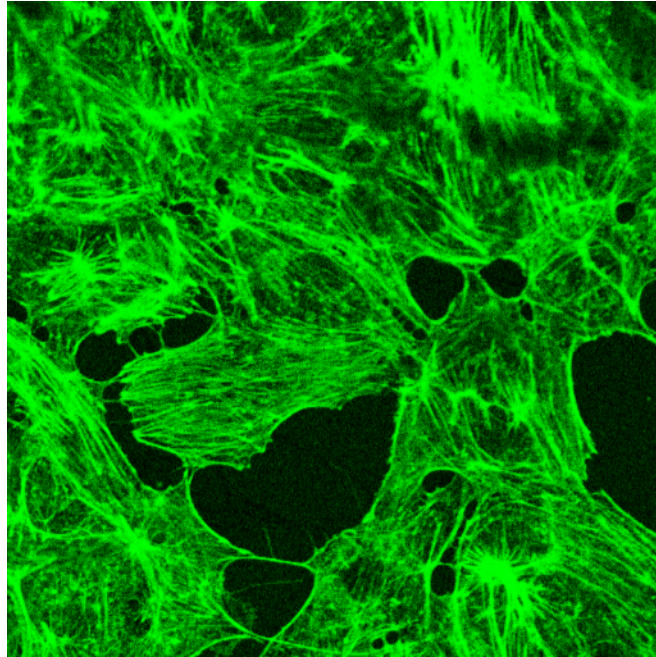
- Occurs where physical stress from blood flow also is present
- Occurs when excessive chemical agents damage cells (e.g. high cholesterol)
- Occurs if there is constant infiltration by cells from the immune system
- How can the cells stop the injury cycle?

Effects of flow on cell morphology

- Models helpful in the study of molecular events in cell culture

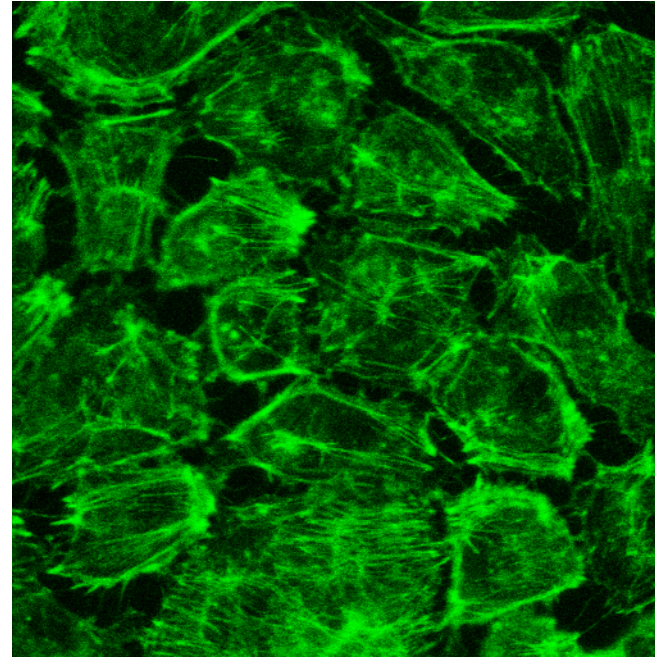
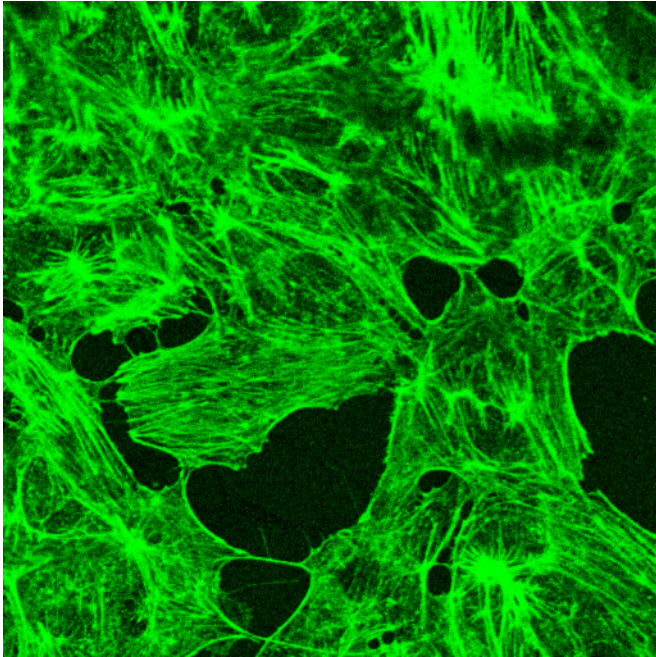


Cultured Endothelial cells



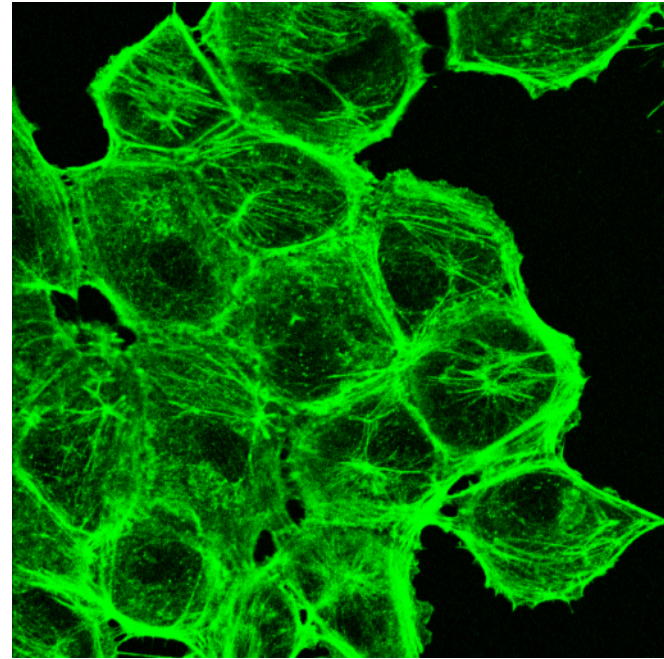
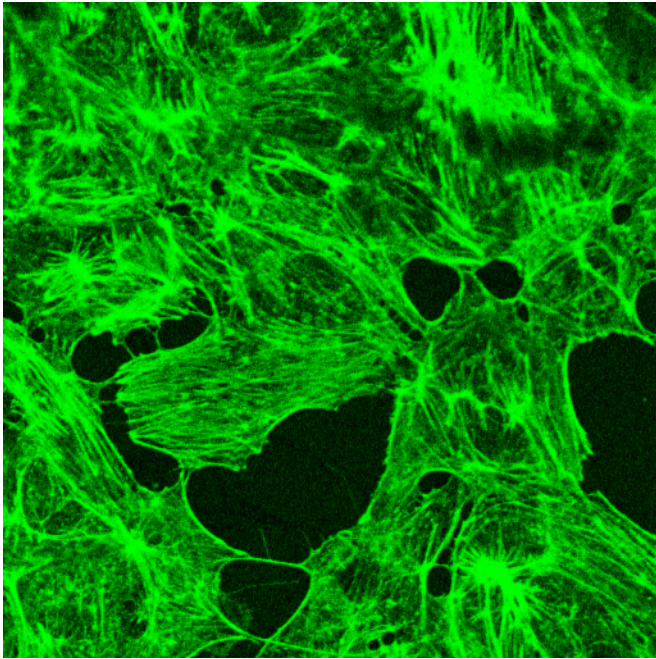
Actin Staining

Chemical treatments



TNF α for 15 min

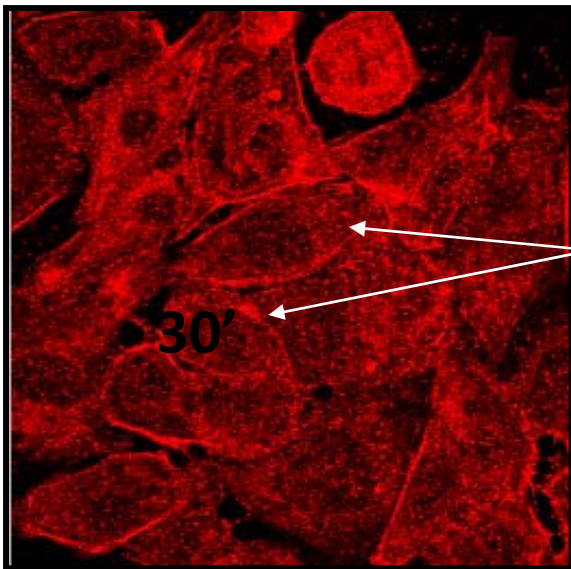
Flow induced changes



Flow for 15 min

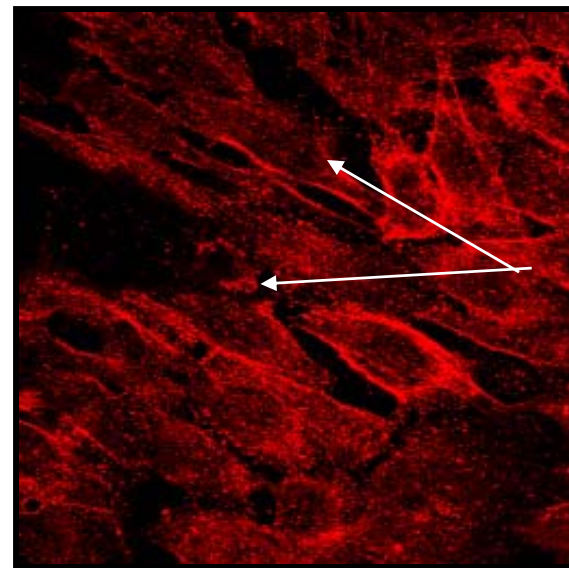
Actin Remodeling Under Shear Stress

Low shear flow for 60'



Flow ←
Cortical actin No alignment

High shear flow for 60'



Flow ←
F-Actin starts to align in the direction of flow

Cells and their actin filaments begin to align in the direction of flow after 60' of high shear flow exposure. No change under low shear stress

Flow with an inhibitor

