

# BIOL 342

## Cardiovascular Disease and Pathology



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# About Me



BSc from McGill University  
Major: Biochemistry



PhD from University of British Columbia  
Major: Biochemistry and Molecular Biology  
Mentor: Dr. Christian Kastrop



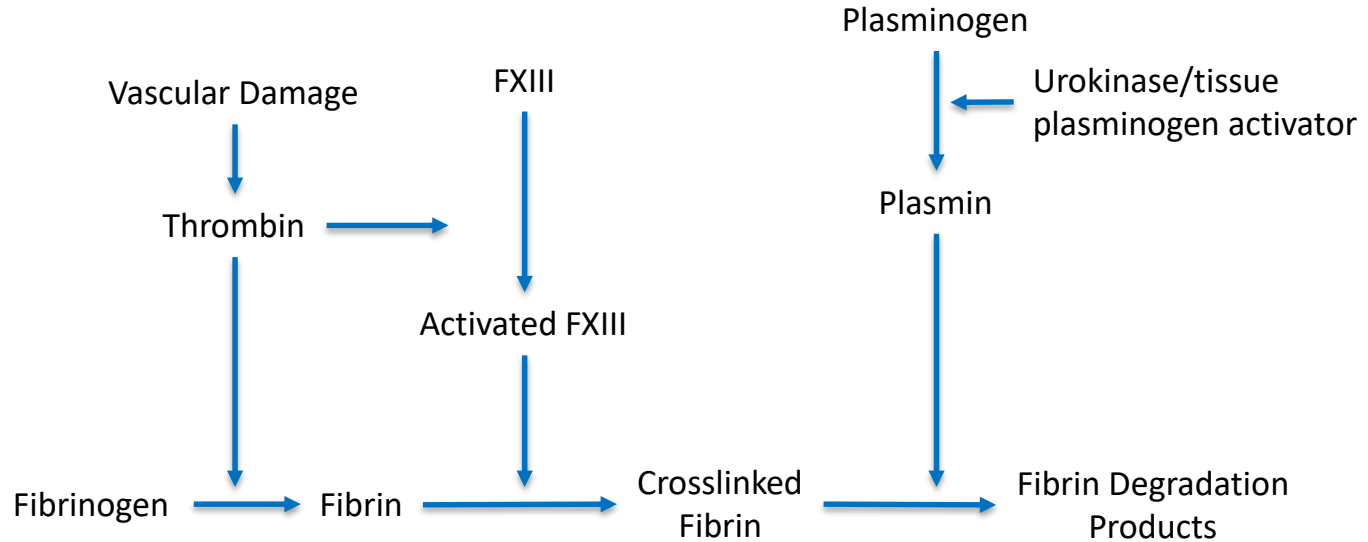


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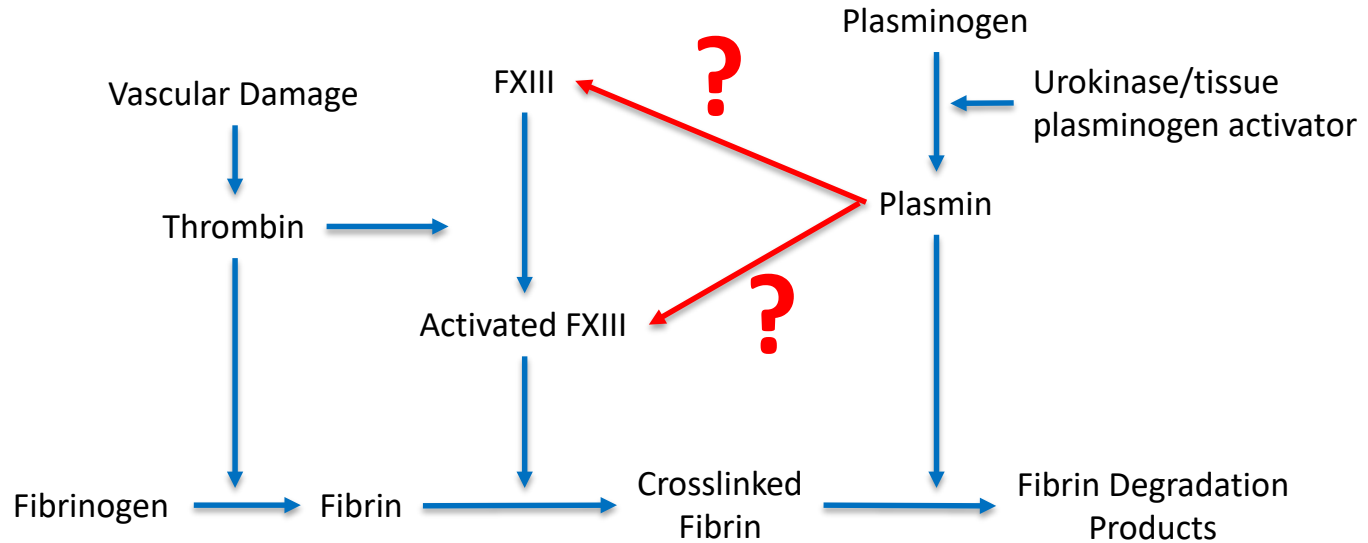


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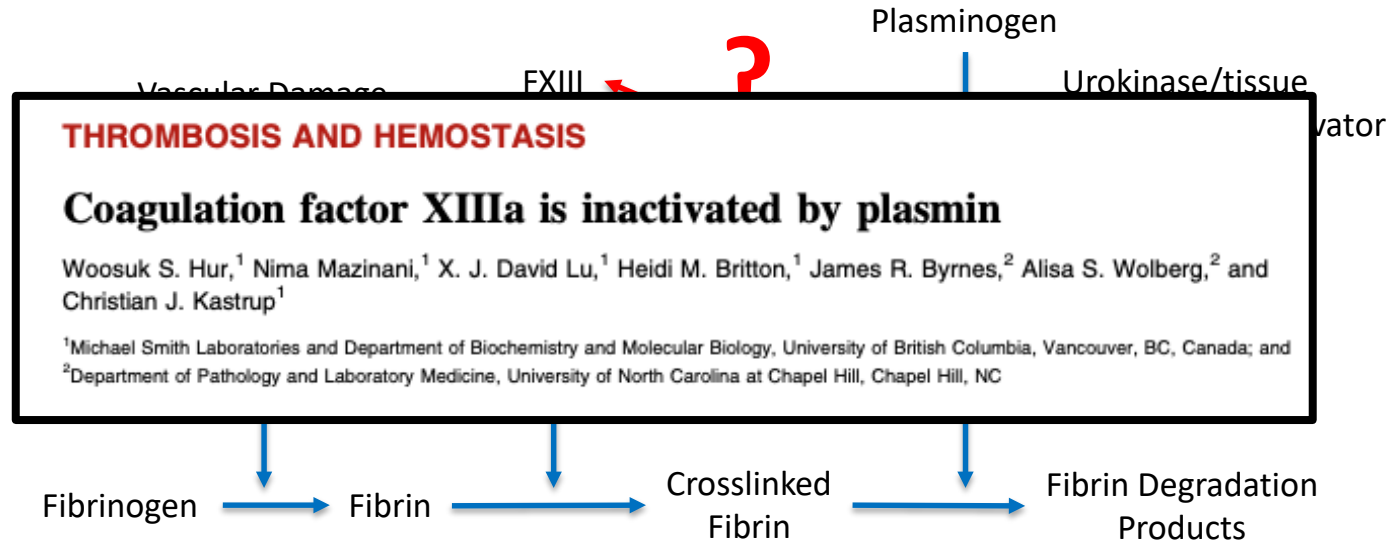


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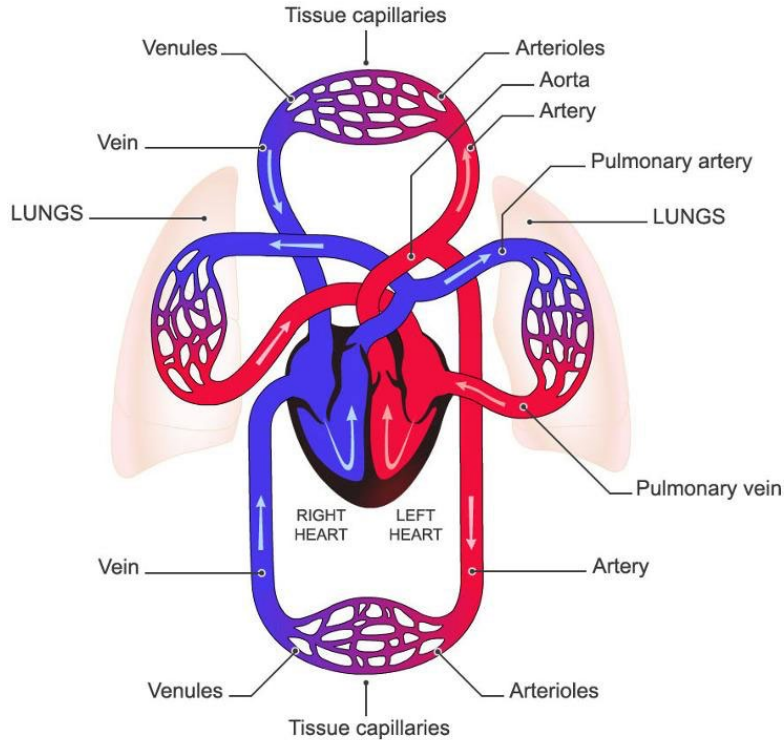
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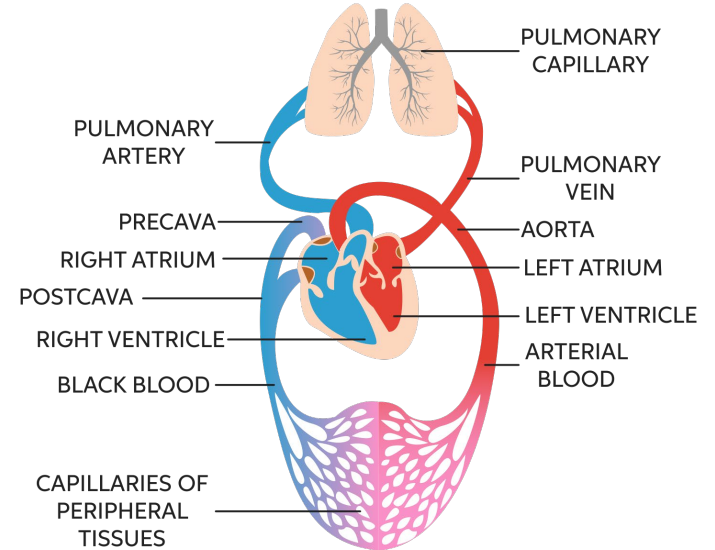


# Circulatory System



— Arterial circulation  
— Venous circulation

## Circulation



Source: <http://humananatomybody.info/neck-arteries-model-labeled/>

<https://www.chegg.com/learn/biology/anatomy-physiology-in-biology/components-of-circulatory-system>



# Cardiovascular Diseases

Name some cardiovascular diseases

Please type your answers in the zoom chat!



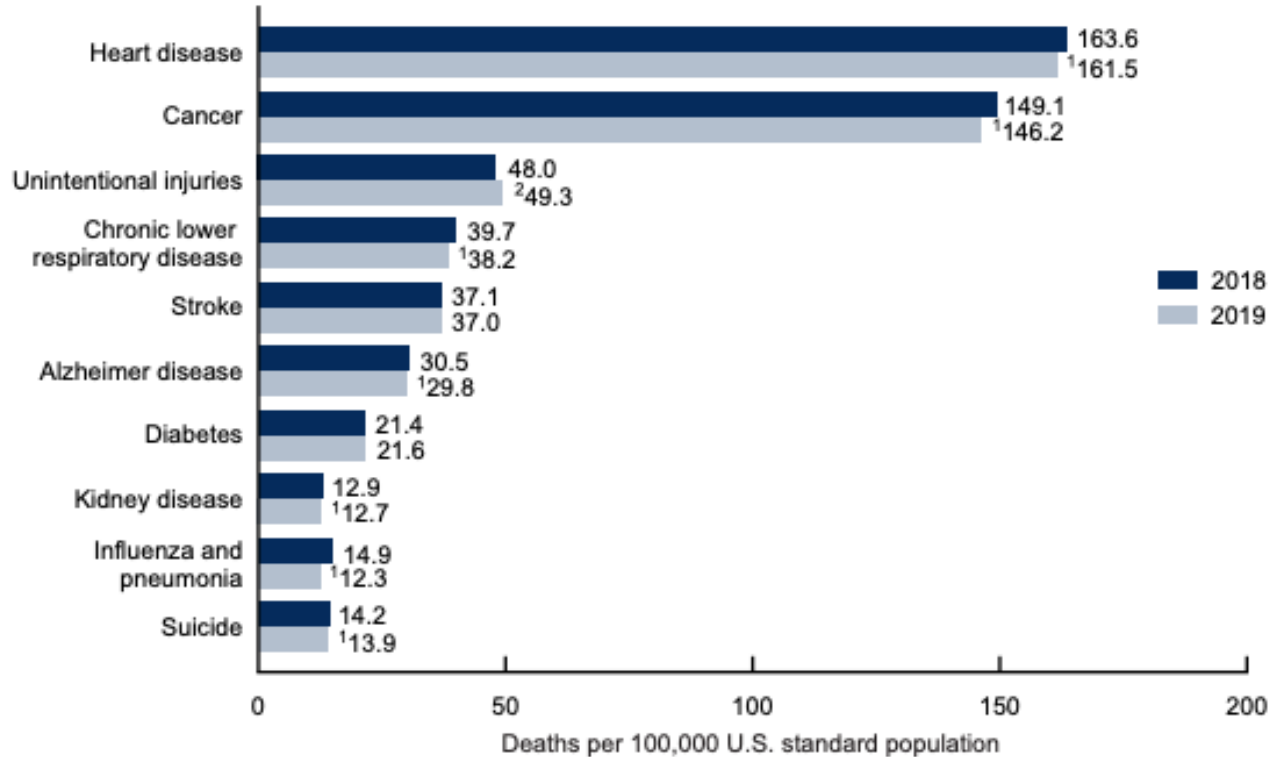
# Cardiovascular Diseases

- 🔴 Atherosclerosis
- 🔴 Heart Attack
- 🔴 Heart Failure
- 🔴 Heart Valve Problems
- 🔴 Arrhythmia
- 🔴 Stroke
  - 🔴 Ischemic
  - 🔴 Hemorrhagic





# Cardiovascular Diseases



🔥 Leading cause of death in US

🔥 National Heart, Lung and Blood Institute Funding: **\$3 Billion.**



# Risk Factors for Cardiovascular Diseases

Name some risk factors for cardiovascular diseases

Please type your answers in the zoom chat!



# Risk Factors for Cardiovascular Diseases

## 🔥 Diabetes

🔥 High cholesterol (hypercholesterolemia)

🔥 High blood pressure (hypertension)

## 🔥 Obesity

🔥 Unhealthy diet

🔥 Physical inactivity

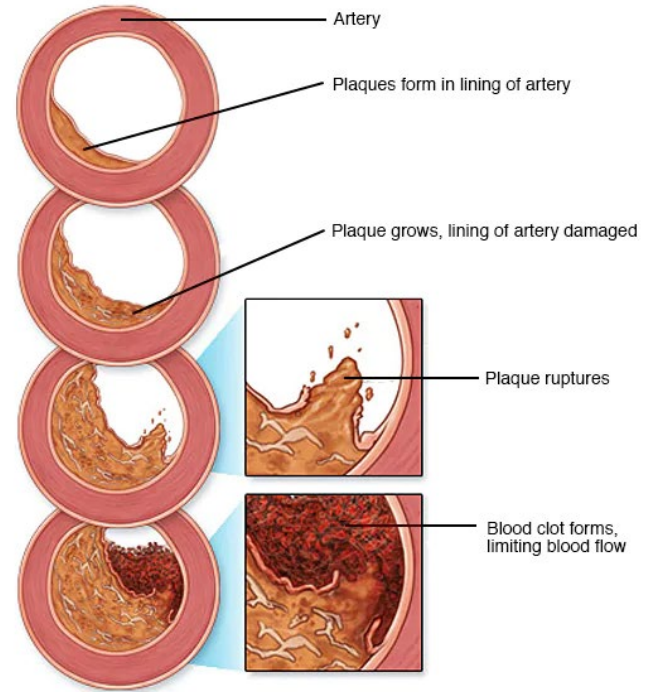
🔥 Smoking

🔥 Heavy alcohol consumption



# Atherosclerosis

- 🔥 Buildup of fatty deposits in the blood vessel.
- 🔥 Arteries become thick and stiff.
- 🔥 Reduces blood flow through vessels.
- 🔥 Can rupture, leading to thrombosis.

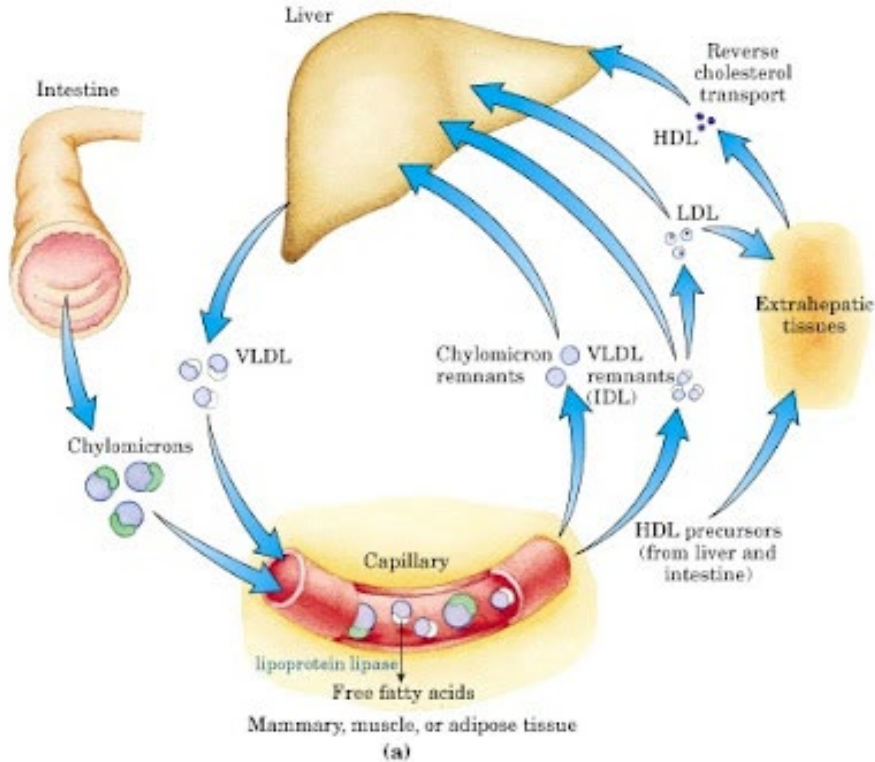


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<https://www.mayoclinic.org/diseases-conditions/arteriosclerosis-atherosclerosis/symptoms-causes/syc-20350569#dialogId40591634>



# Cholesterol Metabolism



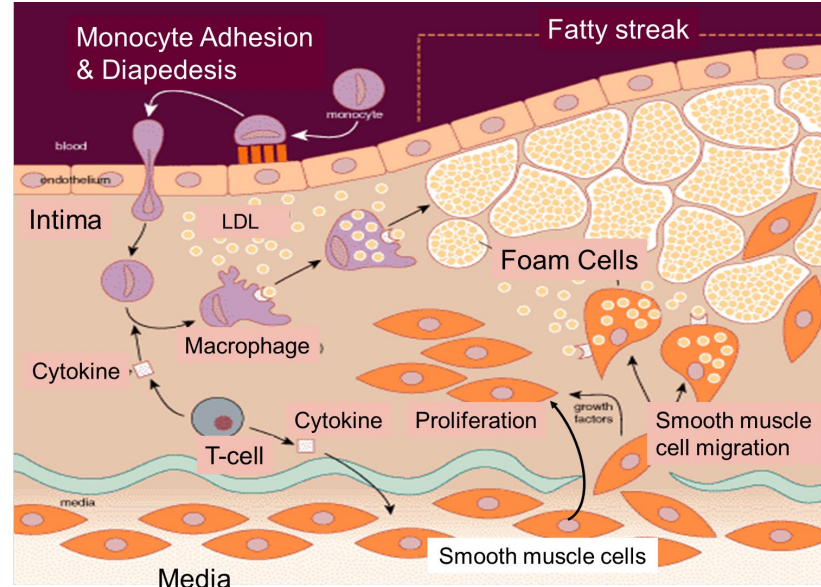
- 🔥 Cholesterol and fatty acids hydrophobic and circulates bound to lipoproteins.
- 🔥 Liver releases VLDL, which circulate to deliver cholesterol and fatty acids to periphery.
- 🔥 HDL returns to liver for reverse cholesterol transport.

<http://thescienceofhealthyscepticism.blogspot.com/2011/03/healthy-harmonious-lipoprotein-cycle.html>



# Pathogenesis of Atherosclerosis

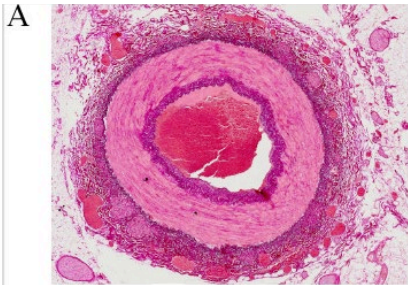
- LDL-cholesterol complex is endocytosed, leading to accumulation of fat deposits.
- Macrophages are activated and phagocytose cholesterol and other lipids.
  - Become foam cells.
  - Release cytokines that recruit smooth muscle cells and their proliferation.
- This early stage: fatty streak



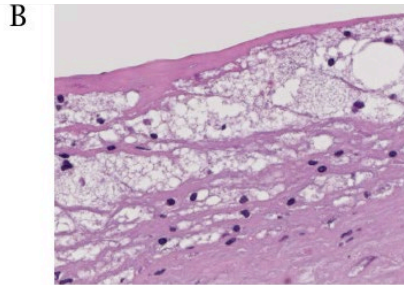
[https://sphweb.bumc.bu.edu/otlt/mph-modules/ph/ph709\\_heart/ph709\\_heart\\_print.html](https://sphweb.bumc.bu.edu/otlt/mph-modules/ph/ph709_heart/ph709_heart_print.html)



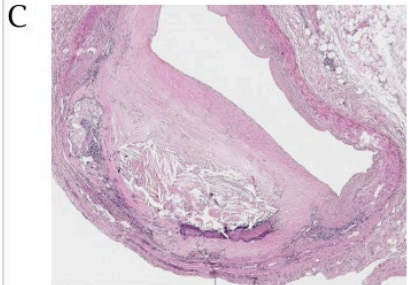
# Pathogenesis of Atherosclerosis



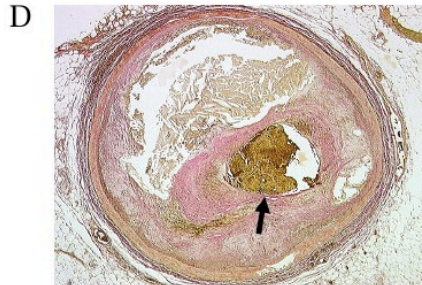
Normal artery



Foam cells in early lesion



Detritus, fibrosis in advanced lesion



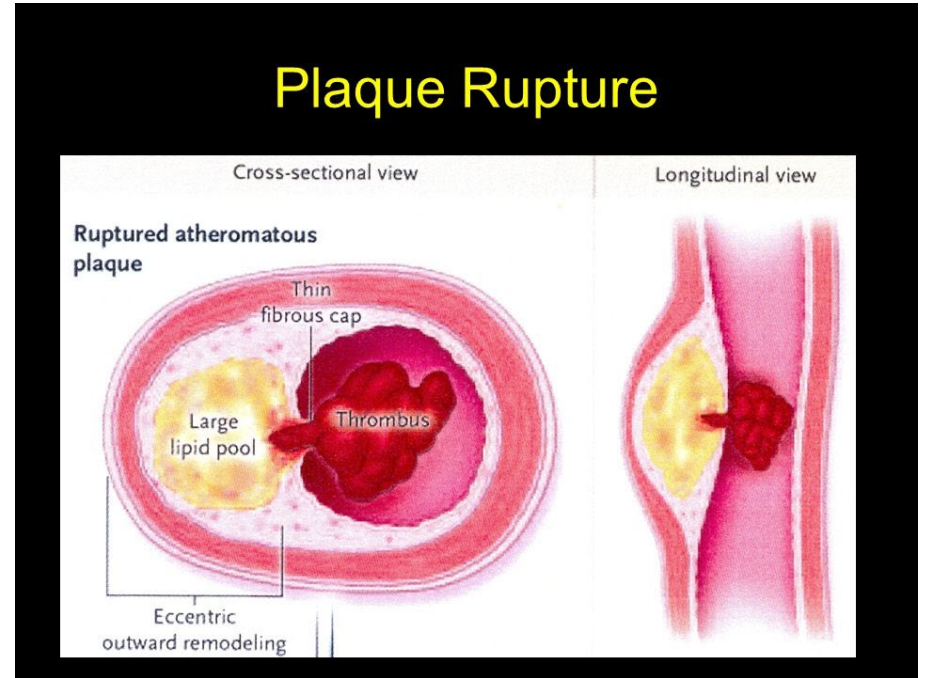
High-grade stenosis, thrombus

<http://watcut.uwaterloo.ca/webnotes/Metabolism/Cholesterol.html>

- 🔥 Lipid core grows
  - 🔥 Foam cells die from too much lipids and release their content
- 🔥 Smooth muscle cells reproduce and proliferate
  - 🔥 Leads to bulging arteries
- 🔥 Calcification occurs
- 🔥 Fibrous collagen caps form

# Pathogenesis of Atherosclerosis

- 🔥 The fibrotic cap becomes eroded
  - 🔥 By shear
  - 🔥 By macrophage-derived enzymes
- 🔥 Thrombus formation
  - 🔥 Release from sight → embolism

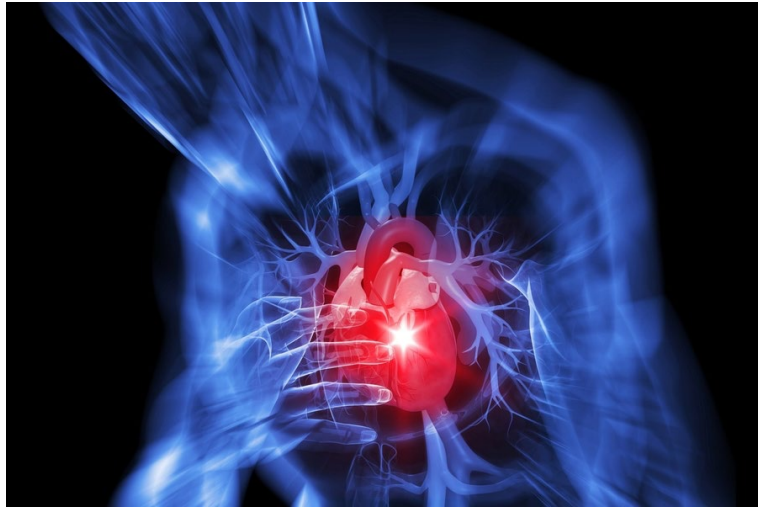


<https://slideplayer.com/slide/4289862/>





# Prevalence of Atherosclerosis



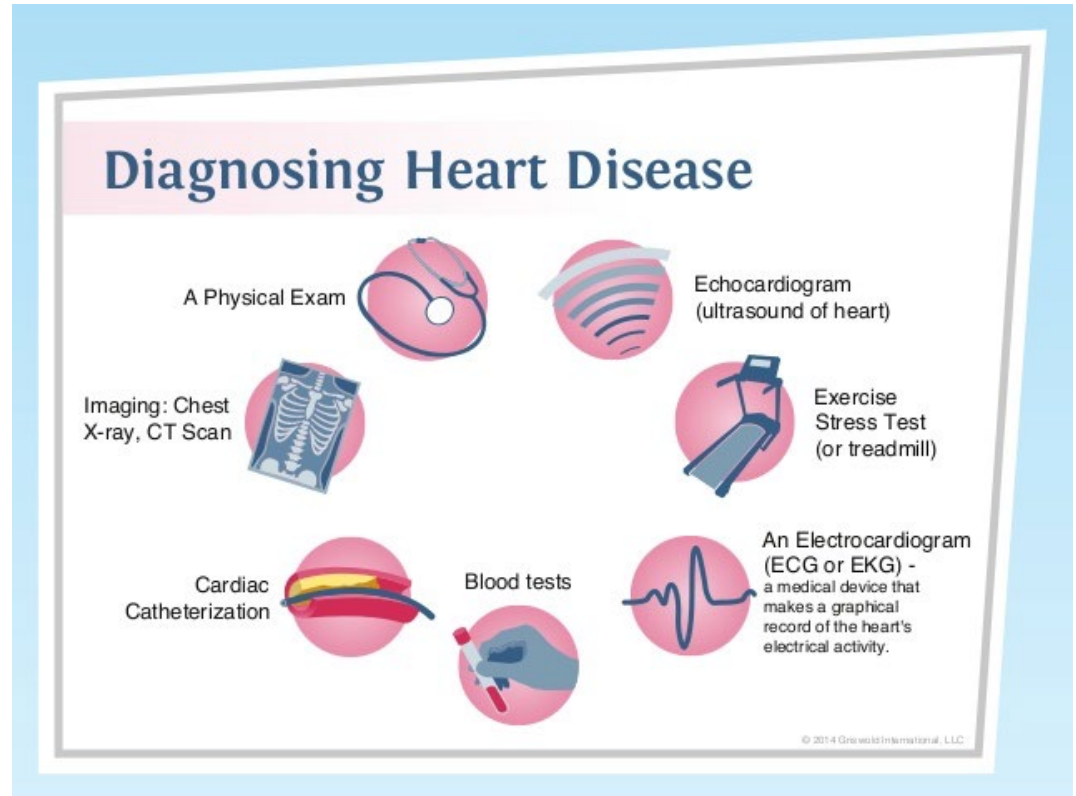
- 🔴 No one knows
  - 🔴 Asymptomatic unless problematic
- 🔴 Identified due to angina, heart attack and/or stroke
- 🔴 Can form as early as –teens.

<https://news.mit.edu/2019/machine-learning-shows-no-difference-angina-symptoms-between-men-and-women-1106>



# Diagnosis of Atherosclerosis

- 🔥 Blood test
- 🔥 EKG
- 🔥 X ray
- 🔥 Echocardiography
- 🔥 Angiography
- 🔥 No clear BIOMARKER

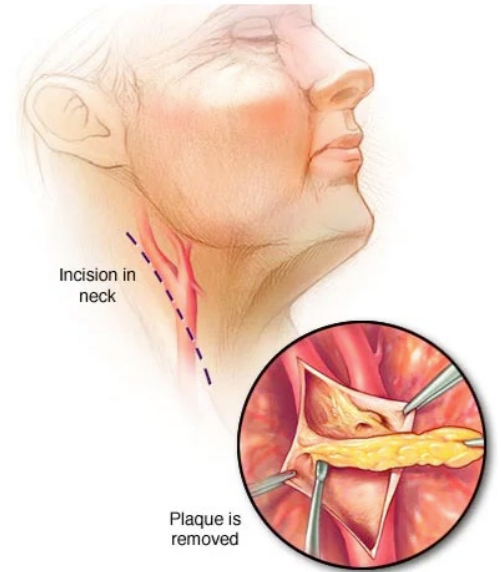
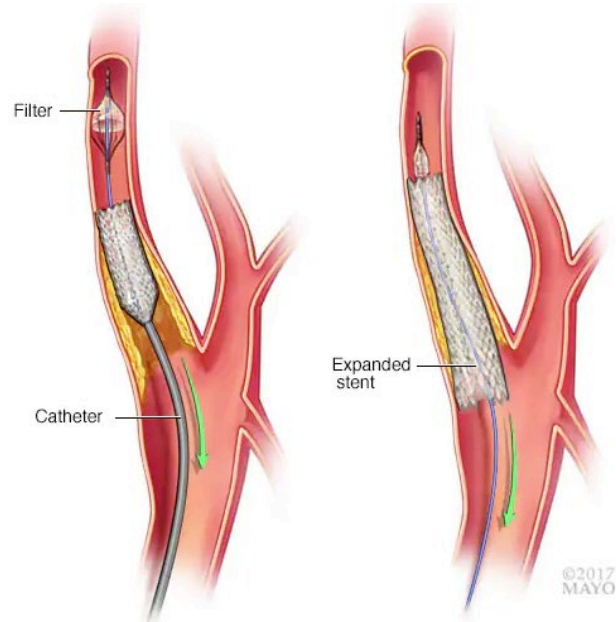


<http://heartdiseasendsublog.blogspot.com/2018/03/diagnosis-and-treatment.html>



# Treatment for Atherosclerosis

- 🔥 Lifestyle changes
- 🔥 Lowering cholesterol levels in blood – statins
- 🔥 Lowering high blood pressure
- 🔥 Anticoagulants
- 🔥 Coronary angioplasty
- 🔥 Bypass surgery
- 🔥 Atherectomy



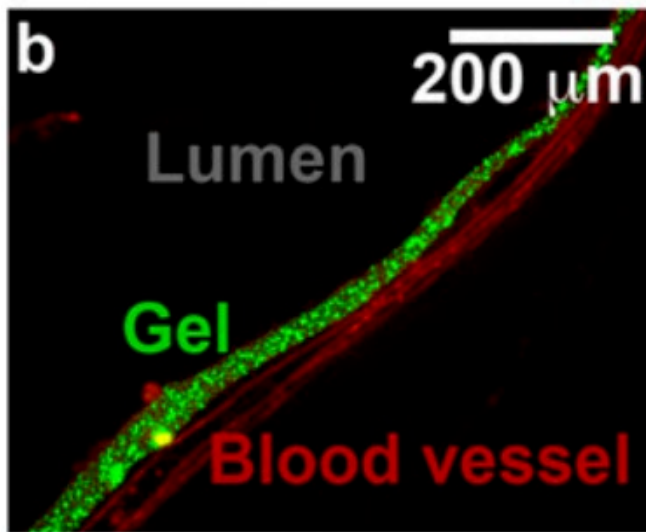
# Ongoing Research of Atherosclerosis

- 🔥 Imaging technologies
- 🔥 Biomarkers
- 🔥 Differences in women and ethnic minorities
  - 🔥 Multi-ethnic study of atherosclerosis (MESA)
  - 🔥 Atherosclerosis risk in communities (ARIC)
- 🔥 Genetic risk factor identification and personalized medicine
- 🔥 Novel therapies to reduce atherosclerotic plaques
  - 🔥 Anti-inflammatory treatment
  - 🔥 Bempedoic acid (ATP citrate lyase inhibitor)



# Painting blood vessels and atherosclerotic plaques with an adhesive drug depot

Christian J. Kastrup<sup>a,b</sup>, Matthias Nahrendorf<sup>c</sup>, Jose Luiz Figueiredo<sup>c</sup>, Haeshin Lee<sup>d</sup>, Timothy Lee<sup>a</sup>, Seung-Woo Cho<sup>e</sup>, Rostic Gorbатов<sup>c</sup>, Yoshiko Iwamoto<sup>c</sup>, Tram T. Dao<sup>b</sup>, Hao Cheng<sup>a,f</sup>, Christopher D. Pritchard<sup>a</sup>, Arturo J. Vegas<sup>a</sup>, Cory D. Siegel<sup>c</sup>, Samantha Anh Thai<sup>a</sup>, James R. Stone<sup>g</sup>, Arthur J. Coury<sup>h</sup>, Ralph Weissleder<sup>c</sup>, Robert Langer<sup>a,i</sup>

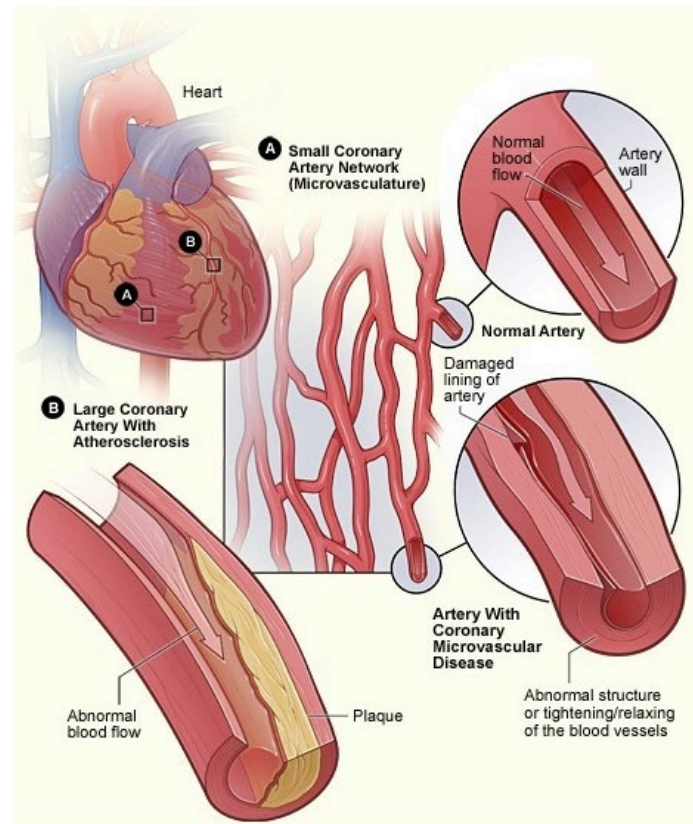


- 🔥 Developed a method to coat atherosclerotic plaques to prevent rupture
- 🔥 Can also incorporate drugs to be released at the atherosclerotic plaques
- 🔥 Stable for over 4 months in mice



# Coronary Heart Disease

- 🔥 When arteries of the heart cannot deliver oxygen-rich, nutrient-rich blood to the heart.
  - 🔥 Heart attacks,
  - 🔥 Heart failures,
- 🔥 Leading cause of death in US
  - 🔥 1 in 36 seconds, someone dies of CVD
- 🔥 Classified as obstructive or non-obstructive
  - 🔥 Obstructive = >50% blocked
  - 🔥 Non-obstructive
    - 🔥 Unresponsive to vasoconstriction/vasodilation
    - 🔥 Vasospasm



<https://www.nhlbi.nih.gov/health-topics/coronary-heart-disease>





# Risk Factors of Coronary Heart Disease

## 🔥 Age

- 🔥 >45 for men,
- 🔥 ~>55 for women (menopause)

## 🔥 Genetics / family history

## 🔥 Lifestyle habits

### 🔥 **Obesity**

### 🔥 Abnormal sleep quality

- 🔥 Daylight saving time

### 🔥 Stress

### 🔥 Smoking

## 🔥 Underlying disease

### 🔥 **Diabetes**

## 🔥 Race or ethnicity

- 🔥 Asian Americans have lower incidence

## 🔥 Sex

- 🔥 Obstructive: Men>Women

- 🔥 Non-obstructive: Men<Women

<https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/>





# Risk Factors of Coronary Heart Disease

Race of Ethnic Group	% of Deaths	Men, %	Women, %
American Indian or Alaska Native	18.3	19.4	17.0
Asian American or Pacific Islander	21.4	22.9	19.9
Black (Non-Hispanic)	23.5	23.9	23.1
White (Non-Hispanic)	23.7	24.9	22.5
Hispanic	20.3	20.6	19.9
All	23.4	24.4	22.3



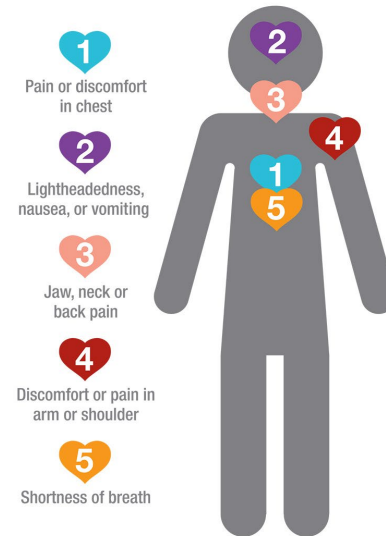


# Symptoms of Coronary Heart Disease

- 🔥 Angina
  - 🔥 Behind breastbone, arm, shoulder, jaw, throat, back
- 🔥 Cold sweats
- 🔥 Dizziness
- 🔥 Light-headedness
- 🔥 Neck pain
- 🔥 Shortness of breath
- 🔥 Sleep disturbances
- 🔥 Fatigue
- 🔥 Nausea



## Common Heart Attack Warning Signs



Learn more at [Heart.org/HeartAttack](https://www.heart.org/HeartAttack).

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# Complications of Coronary Heart Disease

CARDIAC  
ARREST

VS

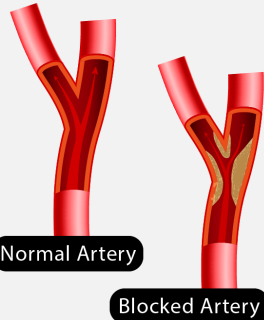
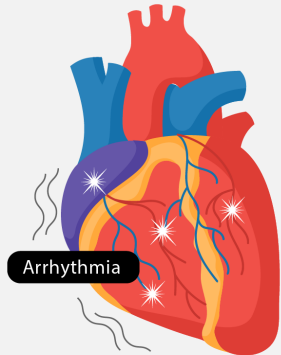
HEART  
ATTACK



Cardiac arrest is an **ELECTRICAL** problem.



A heart attack is a **CIRCULATION** problem.

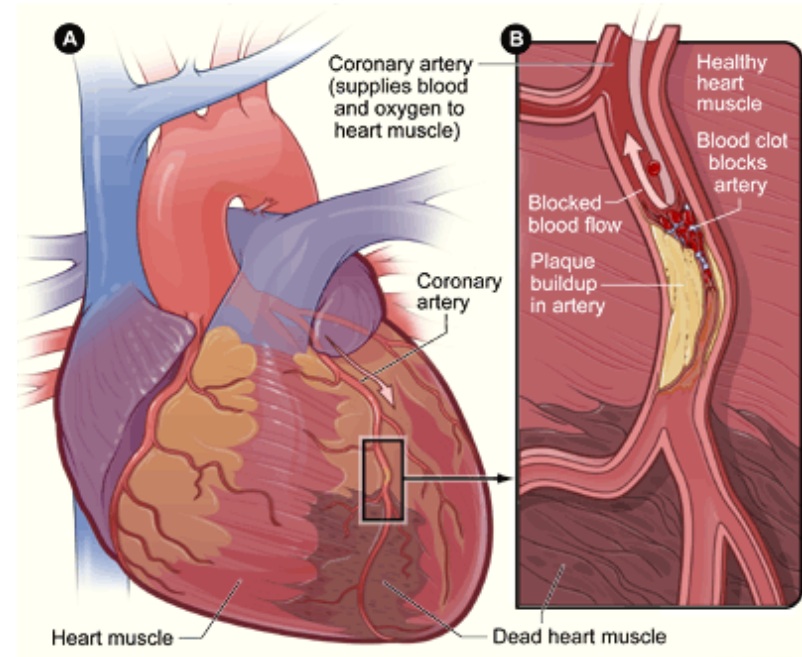


- 🔥 Can lead to
  - 🔥 Heart attack
  - 🔥 Arrhythmia
    - 🔥 Sudden cardiac arrest
  - 🔥 Heart failure
    - 🔥 Cardiogenic shock



# Heart Attacks

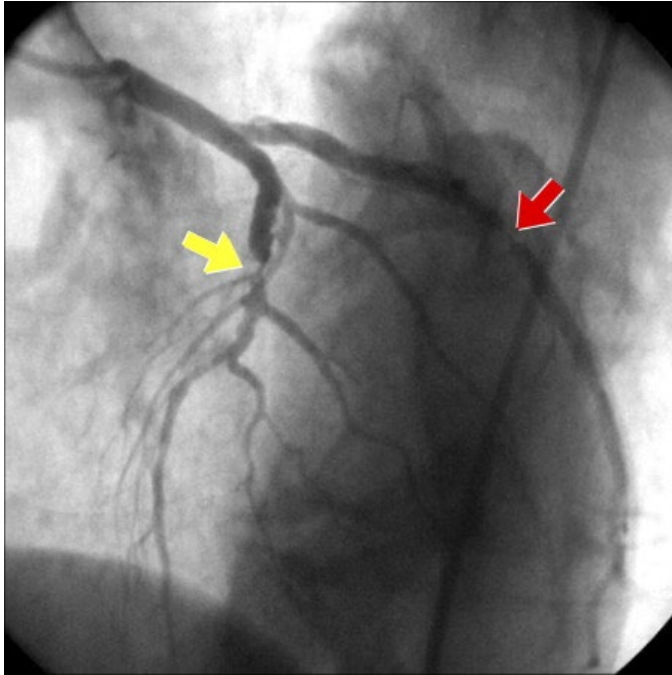
- 🔥 Myocardial Infarction
- 🔥 Flow of oxygen-rich, nutrient-rich blood is suddenly blocked.
  - 🔥 Heart muscles (cardiomyocytes) start to die
- 🔥 If not treated quickly, can lead to death of heart muscles and be replaced by scar tissue
  - 🔥 Can cause future problems
- 🔥 Mostly from atherosclerosis and associated thrombosis



<https://www.nhlbi.nih.gov/health-topics/heart-attack>



# Diagnosis of Heart Attacks



[https://www.amjmed.com/article/S0002-9343\(08\)01018-8/fulltext](https://www.amjmed.com/article/S0002-9343(08)01018-8/fulltext)

🔥 Electrocardiogram

🔥 Blood test

🔥 Troponin tests

🔥 CK test

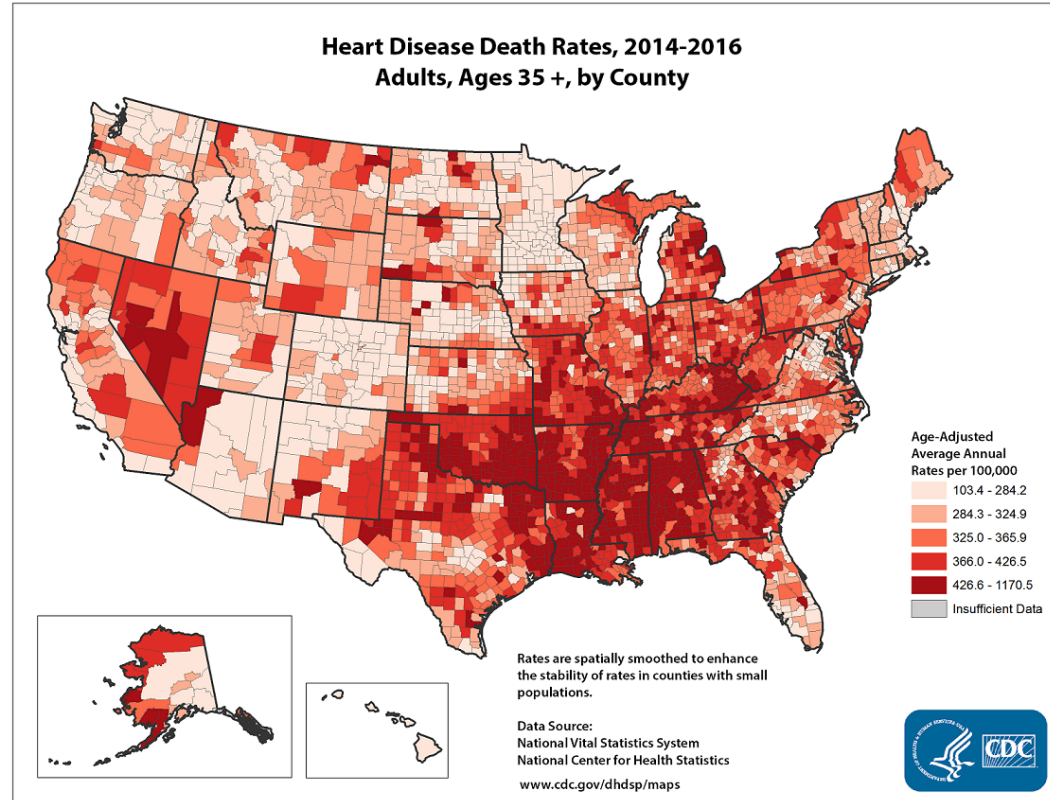
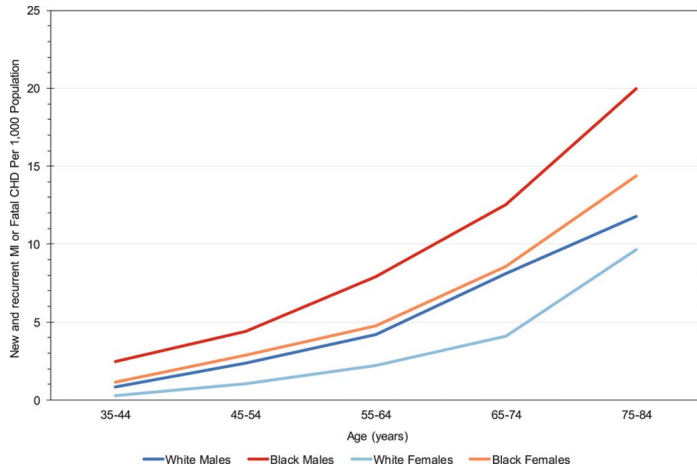
🔥 Serum myoglobin tests

🔥 Coronary angiography



# Prevalence of Heart Attacks

- Someone has a heart attack every 40 seconds in US.
- 805 000 Americans have a heart attack each year.
  - 605 000 are first time.
- 1 in 5 are silent.
- Mortality: 108 610 (2018)











# Treatment for Heart Attacks

MEDICAL-SURGICAL NURSING: CARDIOVASCULAR CARE NURSING

## NURSING MNEMONICS & TIPS

### IMMEDIATE TREATMENT OF MYOCARDIAL INFARCTION

#### "MONA TASS"

<b>M</b>	<b>MORPHINE</b> Analgesic drugs such as morphine are to reduce pain and anxiety, also has other beneficial effects as a vasodilator and decreases the workload of the heart by reducing preload and afterload.	
<b>O</b>	<b>OXYGEN</b> To provide and improve oxygenation of ischemic myocardial tissue; enforced together with bedrest to help reduce myocardial oxygen consumption. Given via nasal cannula at 2 to 4 L/min.	
<b>N</b>	<b>NITROGLYCERIN</b> First-line of treatment for angina pectoris and acute MI; causes vasodilation and increases blood flow to the myocardium.	
<b>A</b>	<b>ASPIRIN</b> Aspirin prevents the formation of thromboxane A2 which causes platelets to aggregate and arteries to constrict. The earlier the patient receives ASA after symptom onset, the greater the potential benefit.	
<b>T</b>	<b>THROMBOLYTICS</b> To dissolve the thrombus in a coronary artery, allowing blood to flow through again, minimizing the size of the infarction and preserving ventricular function; given in some patients with MI.	
<b>A</b>	<b>ANTICOAGULANTS</b> Given to prevent clots from becoming larger and block coronary arteries. They are usually given with other anticoagulating medicines to help prevent or reduce heart muscle damage.	
<b>S</b>	<b>STOOL SOFTENERS</b> Given to avoid intense straining that may trigger arrhythmias or another cardiac arrest.	
<b>S</b>	<b>SEDATIVES</b> In order to limit the size of infarction and give rest to the patient. Valium or an equivalent is usually given.	

© 2016 Nurseslabs.com

**LEARN MORE: MONA AND MYOCARDIAL INFARCTION**

MONA is a mnemonic for the four primary interventions that are performed when treating a patient with Myocardial Infarction (MI). However, MONA does not represent the order and prioritization of administering them. Aside from MONA, TASS is also given which includes thrombolytic drugs are also given within 6 hours of onset to interrupt MI evolution. Anticoagulant therapy reduces the risk of recurrent infarction and death in patients with ST-segment elevation. Stool softeners are used to avoid straining of stool, and sedatives and tranquilizers to increase rest.

DO NOT REPRESENT THE ORDER AND PRIORITIZATION OF ADMINISTERING DRUGS

SEE ALL MNEMONICS AND TIPS AT:  
<http://nurseslabs.com/mnemonics>

nurseslabs.com  
FOR ALL YOUR NURSING NEEDS

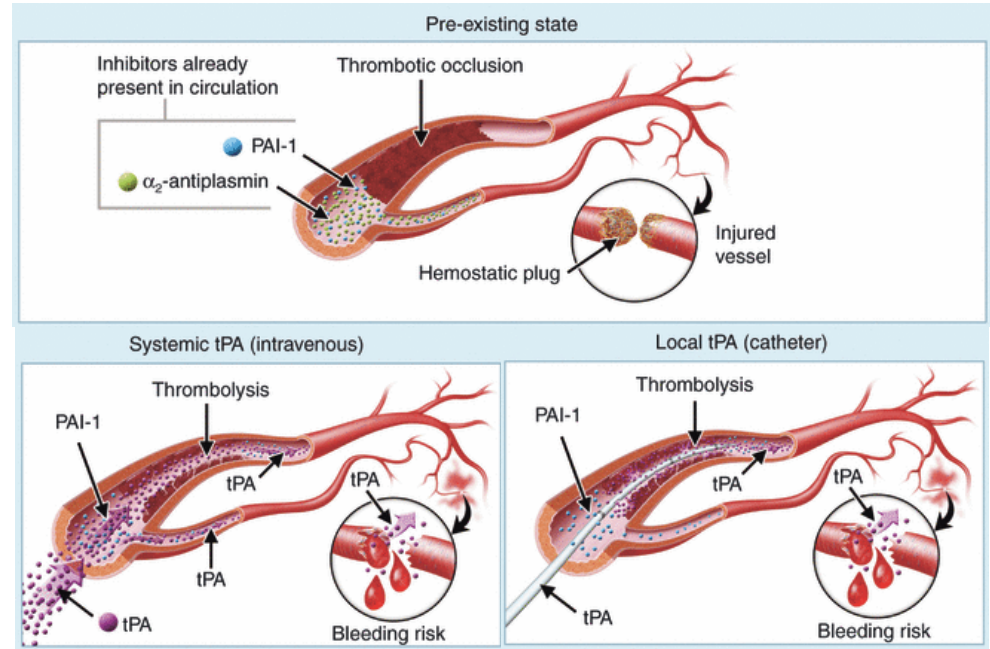
fb.com/nurseslabs  
@nurseslabs  
+nurseslabs

- 🔥 Aspirin
- 🔥 Nitroglycerin
- 🔥 Beta blockers
- 🔥 Oxygen therapy
- 🔥 Thrombolysis
- 🔥 Anticoagulants
- 🔥 Coronary angioplasty



# Thrombolytic Therapy

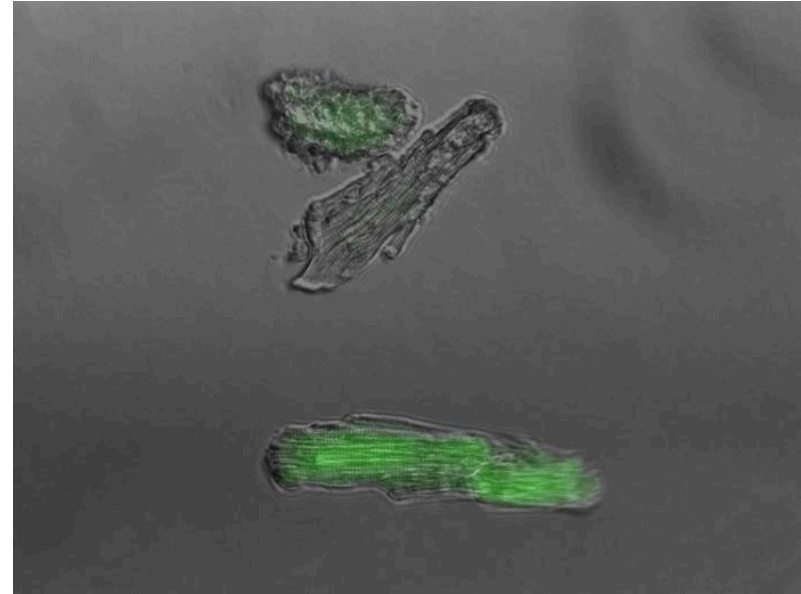
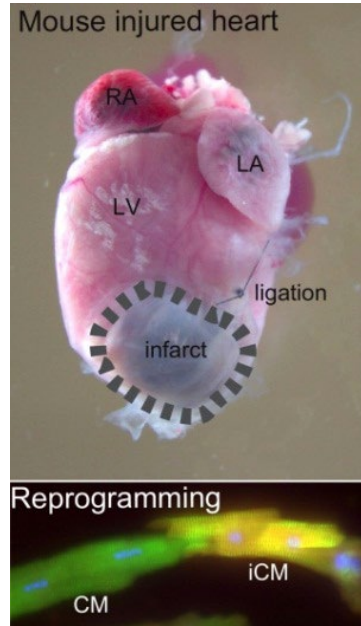
- 🔥 Administration of enzymes that degrade the blood clot.
- 🔥 Associated with increased risk of bleeding
  - 🔥 Major bleeding (drop in hemoglobin, or transfusion)
  - 🔥 Intracranial hemorrhages



<https://onlinelibrary.wiley.com/doi/full/10.1111/j.1538-7836.2011.04370.x>

# Ongoing Research for Heart Attacks

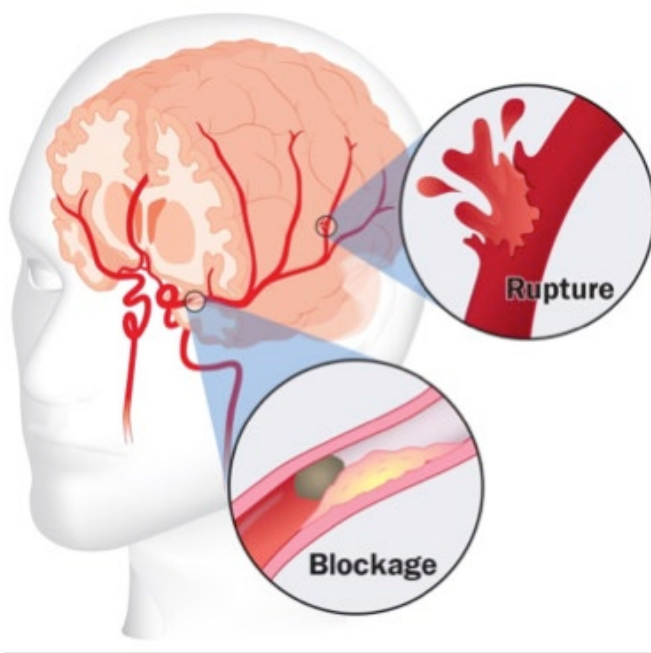
- 🔥 Identifying genetic and environmental risk factors
- 🔥 Improving treatments
- 🔥 Reversing scarred tissues



Qian et al., Nature, 2012



# Stroke

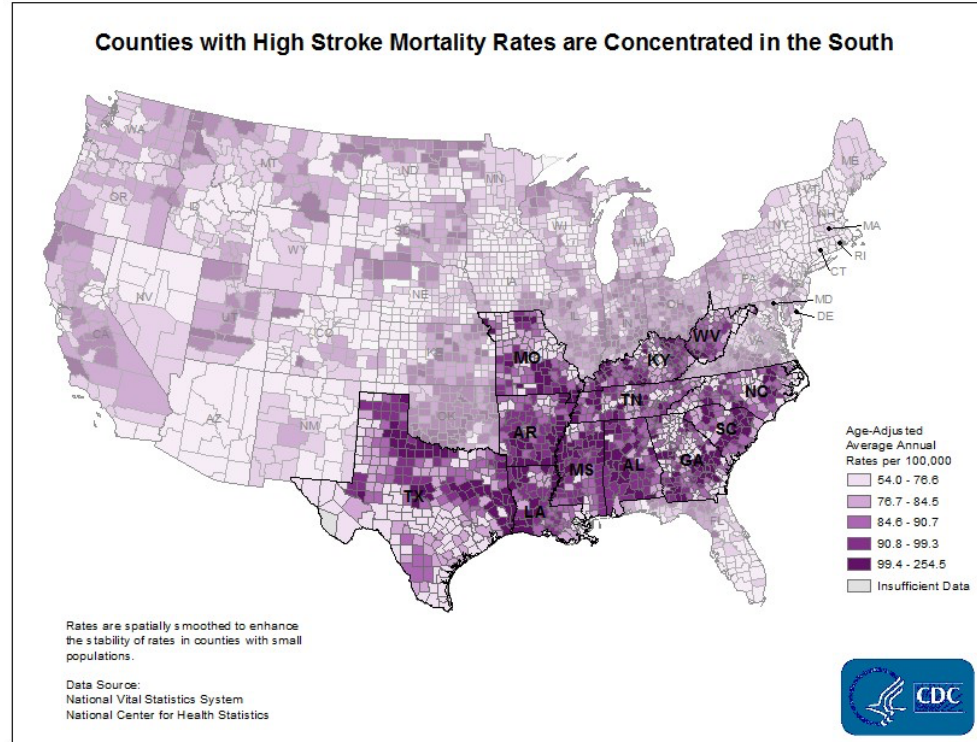


<https://med.uth.edu/neurology/specialty-programs/ut-stroke/stroke-symptoms-prevention-and-background/>

- 🔥 When the brain does not receive sufficient oxygen and nutrients
- 🔥 2% of body weight, yet 20% of oxygen usage
- 🔥 2 types
  - 🔥 Ischemic (80%)
  - 🔥 Hemorrhagic (20%)

# Prevalence of Stroke

- 🔥 1/6 CVD disease is due to stroke.
- 🔥 Someone suffers from stroke every 40 seconds and someone dies every 4 min.
- 🔥 185 000 stroke/year
- 🔥 Leading cause of long-term disability.
- 🔥 Risk of having the first stroke is twice as high for the Black population compared to the White population.



# Symptoms and Diagnosis of Stroke

# F

## Face Drooping

DOES ONE SIDE OF THE FACE DROOP OR IS IT NUMB?

Ask the person to smile. Is the person's smile uneven?

# A

## Arm Weakness

IS ONE ARM WEAK OR NUMB?

Ask the person to raise both arms. Does one arm drift downward?

# S

## Speech

IS SPEECH SLURRED?

Is the person unable to speak or hard to understand? Ask the person to repeat a simple sentence, like "The sky is blue."

# T

## Time to Call 9-1-1

If someone shows any of these symptoms, even if the symptoms go away, call 9-1-1 and get to a hospital immediately.

Check the time so you'll know when the first symptoms appeared.

🔥 Blood tests

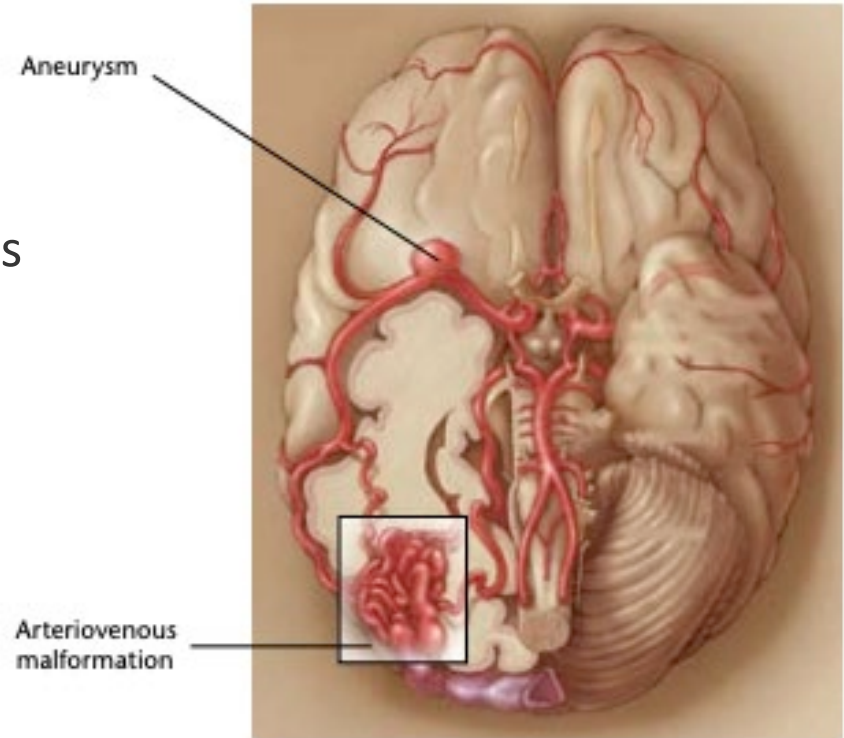
🔥 EKG

🔥 MRI/CT



# Treatment for Stroke

- 🔥 Ischemic stroke
  - 🔥 Thrombolytic therapy
  - 🔥 Anticoagulant/antiplatelet drugs
  - 🔥 Thrombectomy
- 🔥 Hemorrhagic stroke
  - 🔥 Surgery
  - 🔥 Blood clotting reagents



# Risk Factors for Stroke

🔥 **Obesity**

🔥 **Diabetes**

🔥 High blood pressure

🔥 High cholesterol

🔥 Smoking

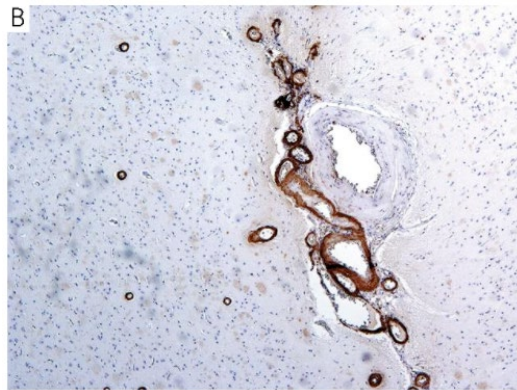
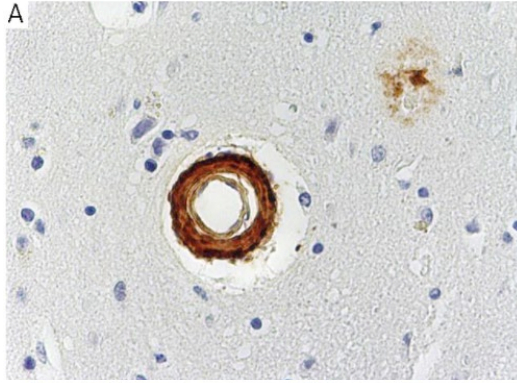
🔥 Cerebral amyloid angiopathy

🔥 Build up of amyloid beta proteins along brain blood vessels

🔥 Risk factor for bleeding in thrombolytic therapy



# Cerebral Amyloid Angiopathy (CAA)



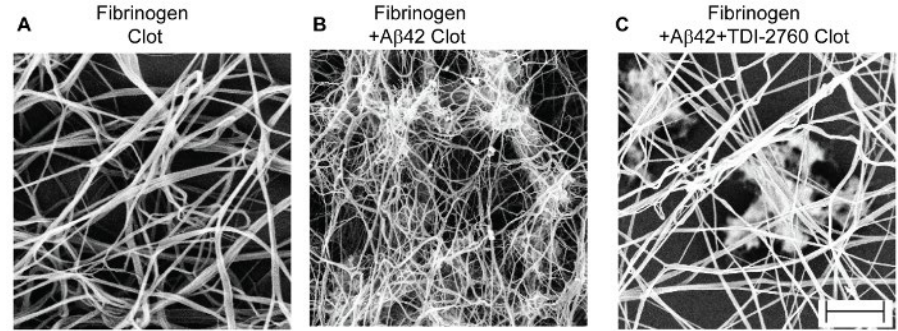
- 🔥 Build-up of amyloid beta proteins along the blood vessels of the brain
- 🔥 Highly associated with the development of Alzheimer's disease (AD)
- 🔥 Genetic risk factors and environmental risk factors of CAA and AD
- 🔥 Risk factor for thrombolysis

<https://www.semanticscholar.org/paper/The-development-of-cerebral-amyloid-angiopathy-in-A-Mendel-Wierzba-Bobrowicz/b2b17e4572384cd7bc779193e912636a12aa5df9>



# Cerebral Amyloid Angiopathy and Coagulation

- 🔥 Fibrin deposits are found in CAA
- 🔥 Co-localizes with sites of vascular damage
- 🔥 Fibrinogen worsens inflammation and subsequently AD and CAA development.
- 🔥 FXIIIa crosslinks amyloid beta proteins to itself and to fibrin.



<https://www.jove.com/t/58475/analysis-amyloid-induced-abnormalities-on-fibrin-clot-structure>

## JBC ARTICLE



### Coagulation factor XIIIa cross-links amyloid $\beta$ into dimers and oligomers and to blood proteins

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# Ongoing Research for Stroke

- 🔥 Identify new genetic risk factors
- 🔥 Find new biomarkers of atherosclerosis
- 🔥 Improve thrombolytic therapy
- 🔥 Develop new drugs to prevent/reduce neurological damage





# Cardiovascular Health in African Americans

## 🔥 Coronary Heart Disease:

- 🔥 -3.2%/y vs -6.5%/y (men) -4.0%/y vs -5.2%/y (women)

- 🔥 2.18 (men) and 1.63 (women) more likely of fatal CHD

## 🔥 Stroke

- 🔥 Mortality is higher in non-White population

  - 🔥 Reduced from 4.5-fold in 1950s to ~2-fold in 1999.

  - 🔥 Risk disparity decreases with increasing age

## 🔥 Obesity

- 🔥 58% in Black women, 38% in Black men, 34% in white men and 33% in white women

## 🔥 Diabetes

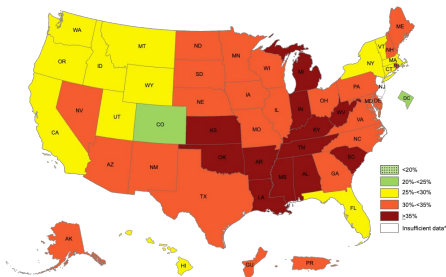
- 🔥 Prevalence: 21.8% in Blacks vs 11.3% in Whites

  - 🔥 Black men are 1.5 times and women are 2.1 times more likely to develop diabetes.

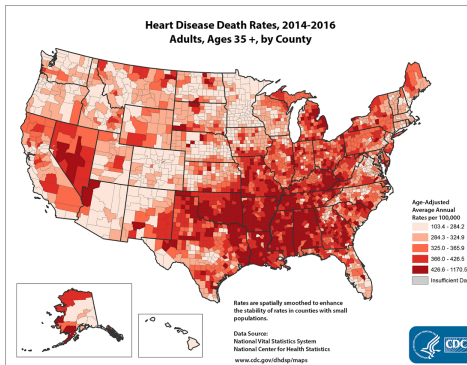


# Obesity is a Major Risk Factor for CVD

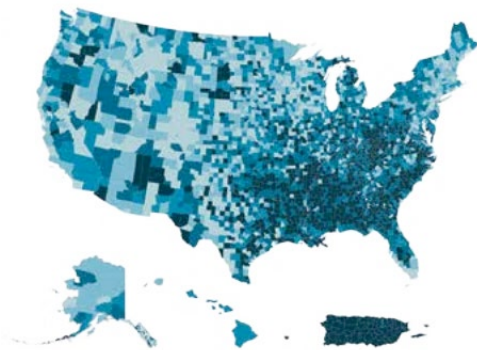
## Obesity



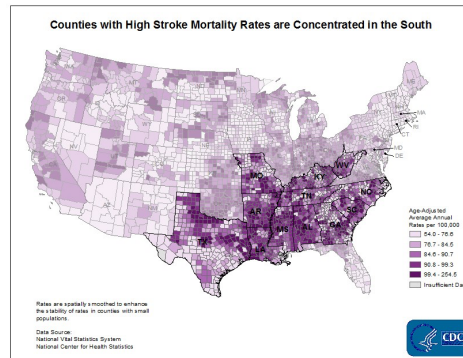
## Heart Attack



## Diabetes

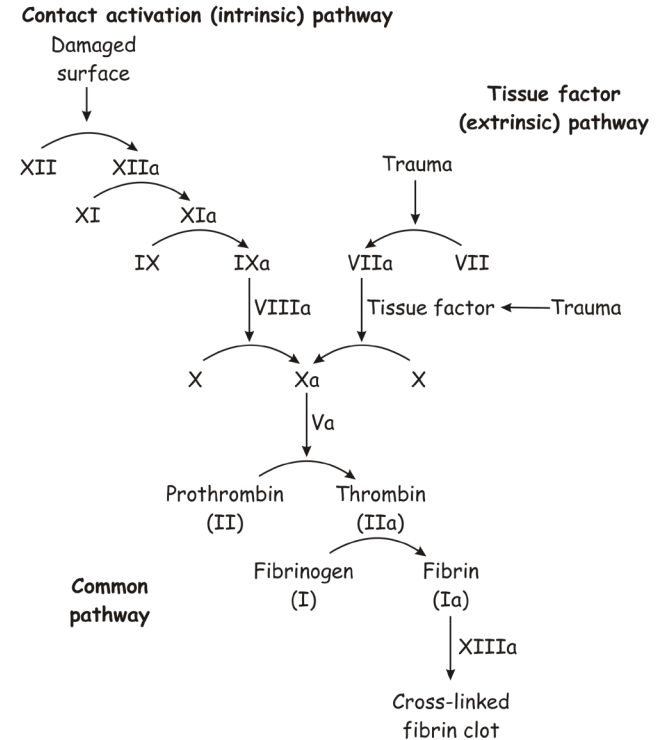


## Stroke

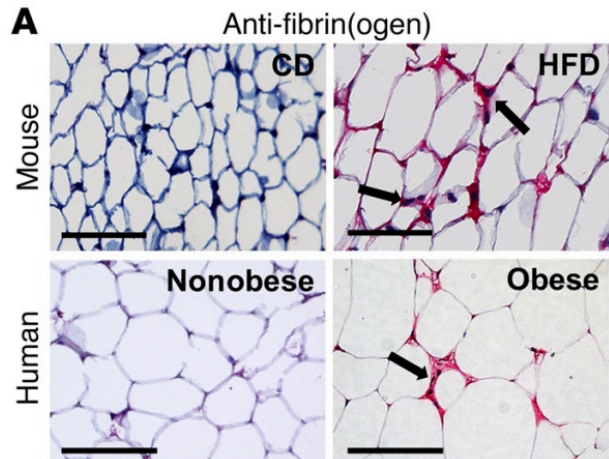


# Obesity Leads to Dysregulation of Hemostasis

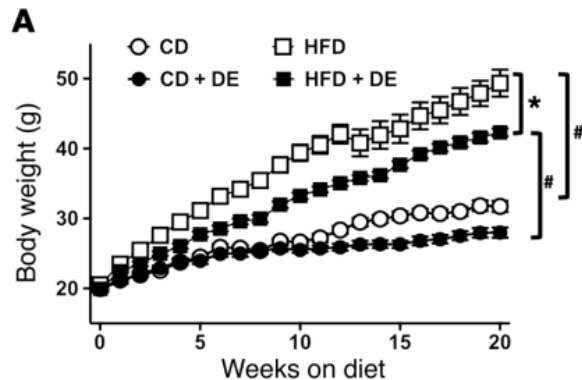
- 🔥 Enhanced platelet activation
- 🔥 Increased levels and activities of VWF, FVIII, FIX, FXI, FXII
- 🔥 Impaired fibrinolysis
  - 🔥 Reduced plasmin generation
  - 🔥 Reduced plasmin activity



# Inhibition of Coagulation Prevents Obesity



- 🔥 Fibrin deposits are found within livers and white adipose tissues of obese mice and men.
- 🔥 Fibrin increases the accumulation of pro-inflammatory macrophages in these tissues.
- 🔥 Inhibition of thrombin activity prevented weight gain.





# Questions?

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