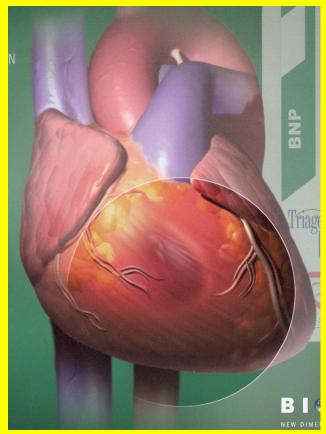
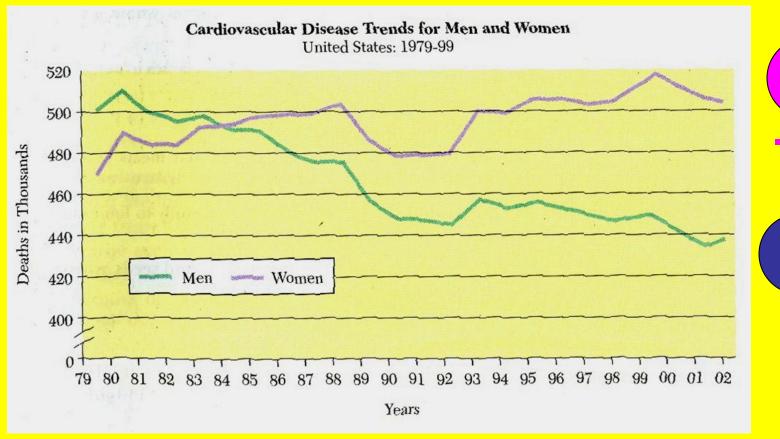
Cardiovascular Disease



Cardiovascular disease: heart & blood vessels (vascular)

- 1. > 70 million people in US
- 2. Economic cost: \$300 billion (2001)
- 3. #1 killer
- **4. 451,326** coronary heart disease deaths- 2004 (**1236/day**)
- Stroke- related vascular disease:#3 killer

- Heart disease: a man's disease?
- #1 killer American women: more than men





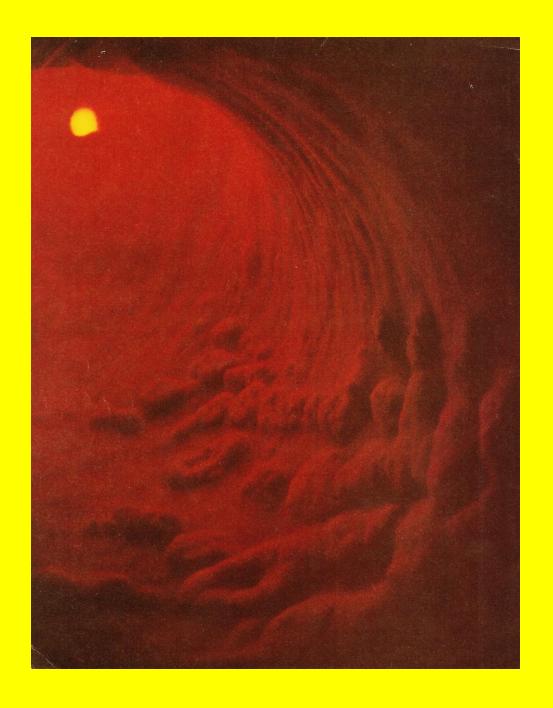
Underlying process:

Athere= porridge (Greek)

Sklerosis= hardness (Greek)

Arteriosclerosis: general- hardening of arteries

Atherosclerosis: arteries narrowed by <u>fatty deposits</u> (plaques)



Do you have atherosclerosis? **YES**

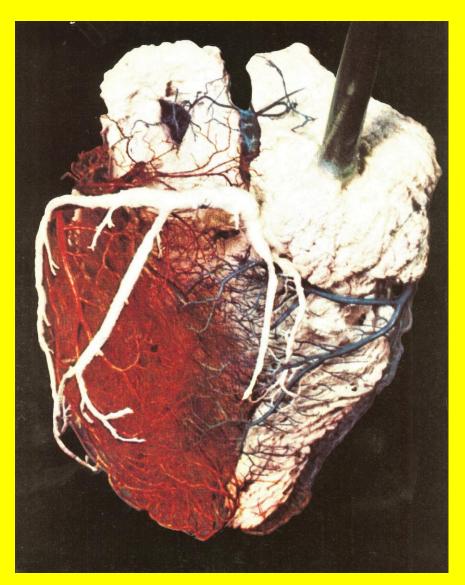
- All humans have this disease (susceptible)
- Dogs/rats: resistant
- Going on slowly, quietly in you now
- Deposits throughout your arteries:
 Heart, brain, neck, arms/legs
- Arms: feel- small hard "pipes" (peripheral artery disease)

Coronary= coronarius (Latin): a

crown or circle

Coronarycirculation:encircles heart

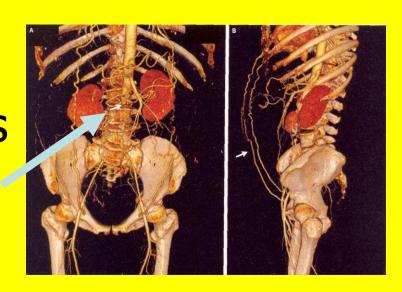
CoronaryArtery Disease



Peripheral Artery Disease

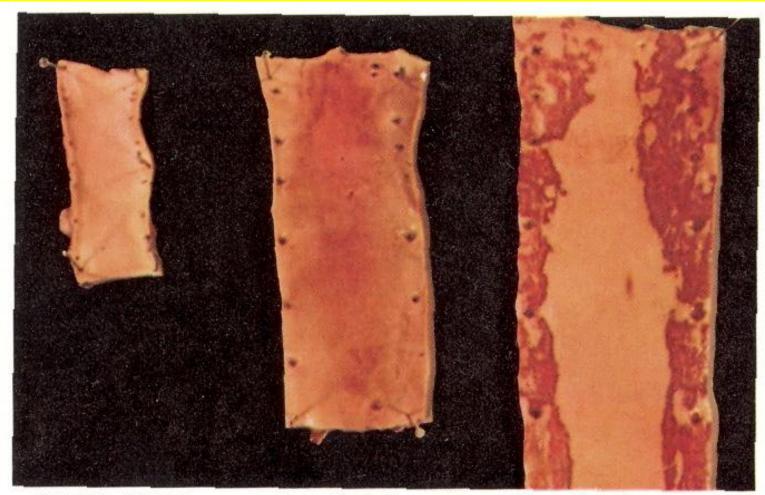


- 55 year old woman
 Awoke: numbness & weakness: both legs
- Smoker, † blood lipids
 Angiogram: blocked
 lower aorta
- Treatment: antiplatelet, statin therapy, stop smoking, exercise
- OK at next hospital visit



When does atherosclerosis start?

- Children: see artery thickenings
 & "fatty streaks" (5-12 years)
- Early lesions (injury): coronary arteries & aorta: seen sometimesnewborn babies & fetuses
- Suggests: prenatal environmentrole in atherosclerosis



Juvenile intimal thickening

Juvenile fatty streaks and diffuse sudanophilia

Transitional fatty streaks in a young adult

A Pediatric Disease



 Many doctors: atherosclerosis is a "pediatric disease": begin early

prevention

 2008 AHA study: **Thickening in** arteries: obese 10 year olds= 45 year old adult "You are as old as you arteries are"



6th International Pediatric Cardiovascular Symposium Novel Medical Interventions and Their Role in Children with Heart Disease **Evolution of atherosclerosis:**

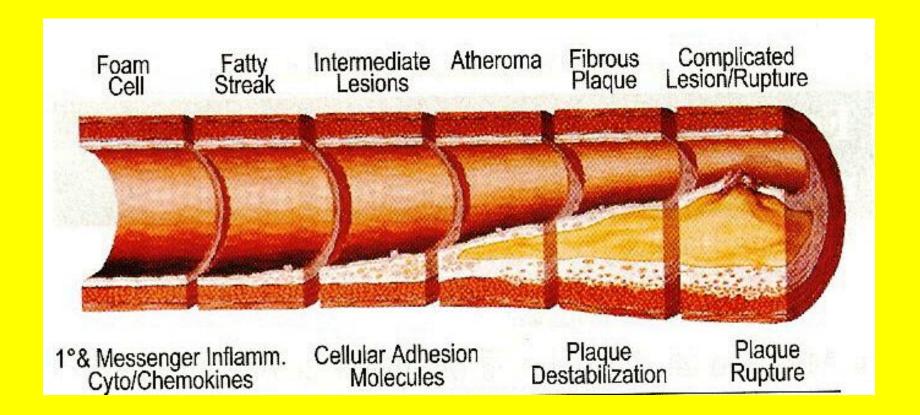
Early thickenings <

fatty streak

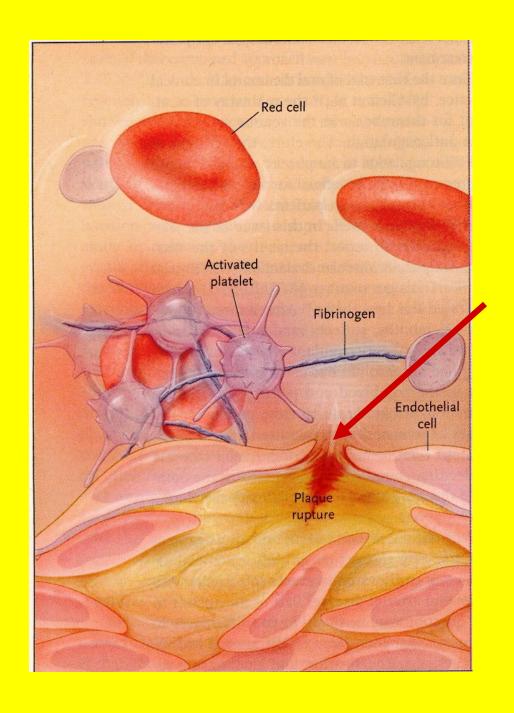
fibrous plaque

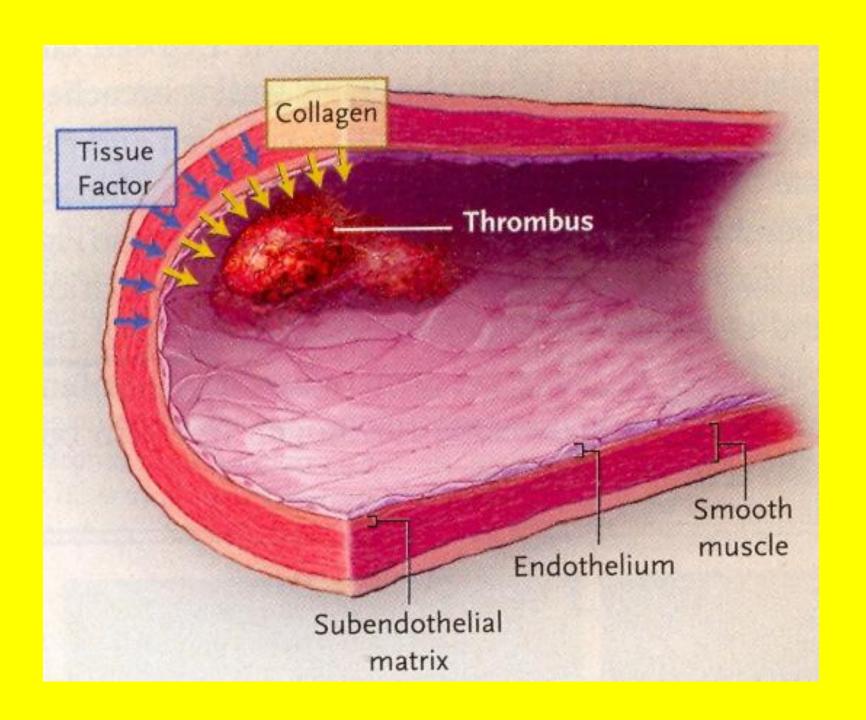
advanced, complicated lesion

(vulnerable to burst)

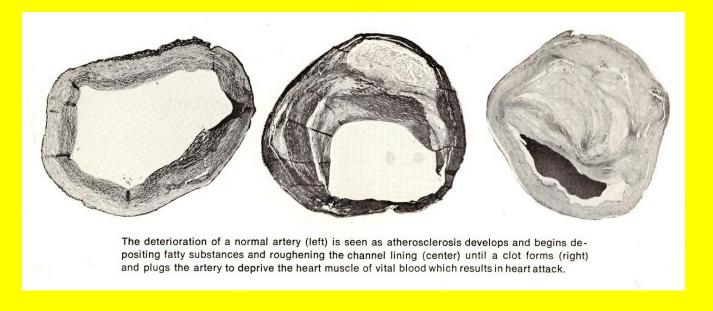








- American soldiers (19-20) killed:
 Korean War
 Viet Nam War
- Autopsies: extensive atherosclerosis



- Thomas Herrion: 23 year old,
 6' 3", 315 pound lineman: San Francisco 49ers
- 2005: died suddenly after exhibition game



- Significant blockage: right coronary artery
- Enlarged heart; no drug abuse

1984 Stormie Jones: 6 year old girl

Texas

Wartlike bumps:
 elbows, knuckles,
 knees, toes:
 started:
 age 3 months



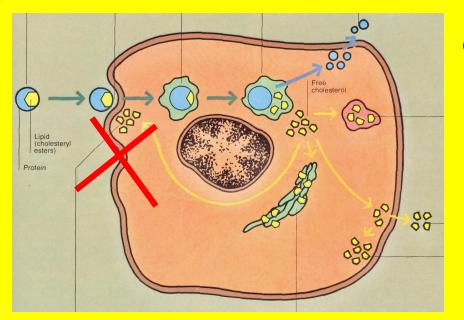
Bumps: cholesterol deposits under skin





- Sign of: Familial
 Hypercholesterolemia
- LDL cholesterol: 9X normal
- Genetic defect: 2 bad copies of gene → LDL receptor
- 1 in million people

- LDL receptors: membranes of liver/other cells
- Like "magnets" pull LDL out of blood
- No receptors: LDL stays in blood



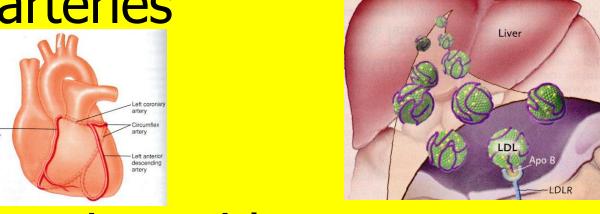
atherosclerosis

- October 12, 1984: heart attack
- Days later: chest pains, 2 bypass operations- no help
- Last ditch effort: 15 hour operation- transplant heart & liver



Why double transplant?

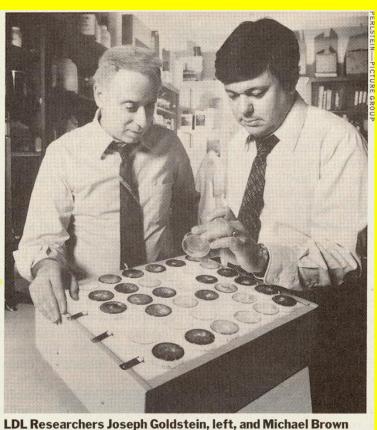
She received heart without clogged arteries



She received good liver
 with active LDL receptors:
 help lower blood cholesterol

- Stormie Jones helped Drs. Michael Brown & Joseph Goldstein (UT) discover LDL receptor defect
- Nobel prize 1985

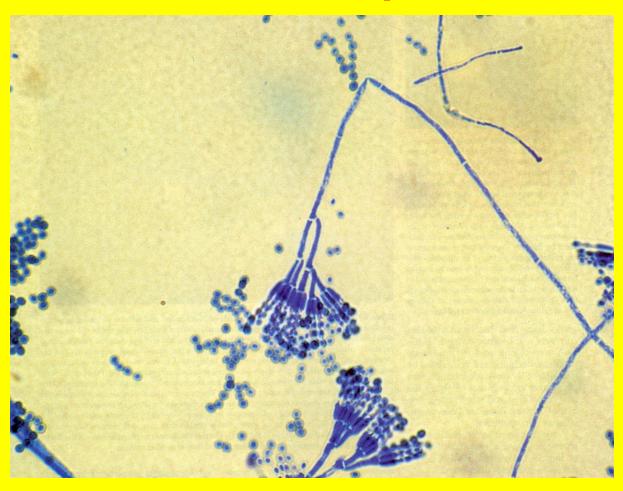




Basis of **statin** therapy (Lipitor)

In patients with multiple risk factors for heart disease, Lipitor reduces risk of heart attack ^{by} 36% DR. ROBERT JARVIK ~Inventor of the Jarvik Artificial Heart and Lipitor User If you have risk factors such as family history, high blood pressure, age, low HDL ('good' cholesterol) or smoking.

First statin isolated from fungus (*Penicillium citrinum*)

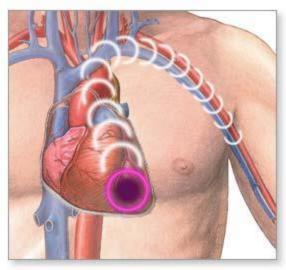


Atherosclerosis: What are its symptoms?

None: early on

Later: artery clogged in heart:

heart attack



Pain radiating down arm might signal heart attack



- Myocardium- heart muscle
- Infarct: tissue death/no blood supply

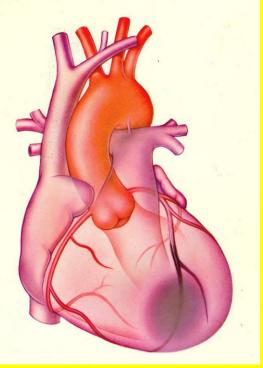
MI

Uncontrolled high blood pressure increases the risk of ...

Heart attack

- One of the arteries supplying the heart with blood can become completely blocked.
- The part of the heart muscle that doesn't get blood dies from lack of oxygen. This can be life-threatening.

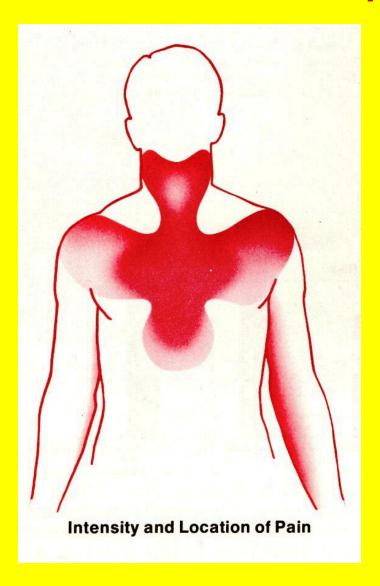
Medical term: Myocardial infarction (MI)



Heart attack: Warning signs

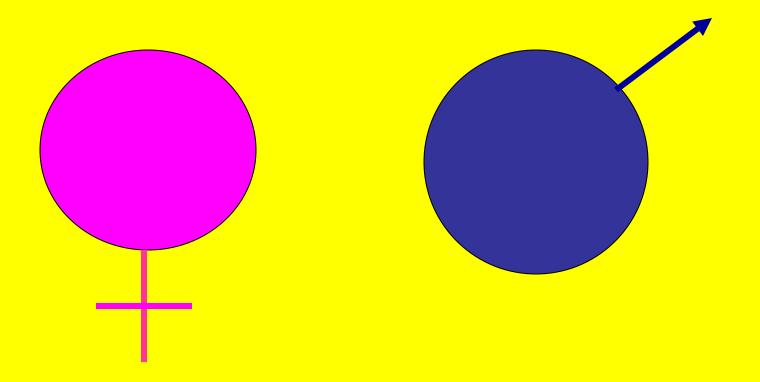
- Heavy pressure, fullness, squeezing pain in center of chest
- Pain may spread: arms, back, neck, jaw, or stomach
- Cold sweat
- Nausea and vomiting
- Lightheadedness

Heart Attack Pain: may spread



Heart Disease: Women vs. Men

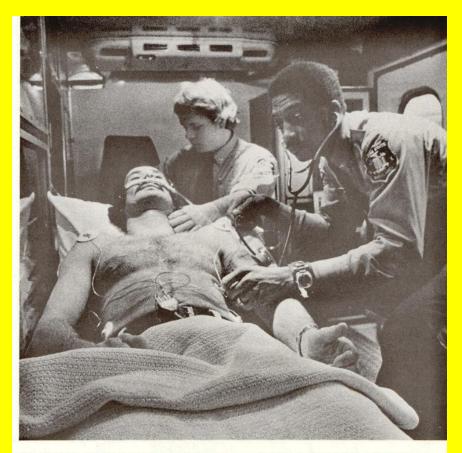
Men affected by heart disease 10 years earlier than women



- Until puberty: boys & girls same
 HDL levels
- At puberty: boys \ \ HDL \ girls \ \ HDL \ \ LDL \ (estrogen)
- With menopause (35-58):
 - ↓ estrogen † weight † heart risk

 Men more likely: blockages: big coronary arteries: crushing

chest pains

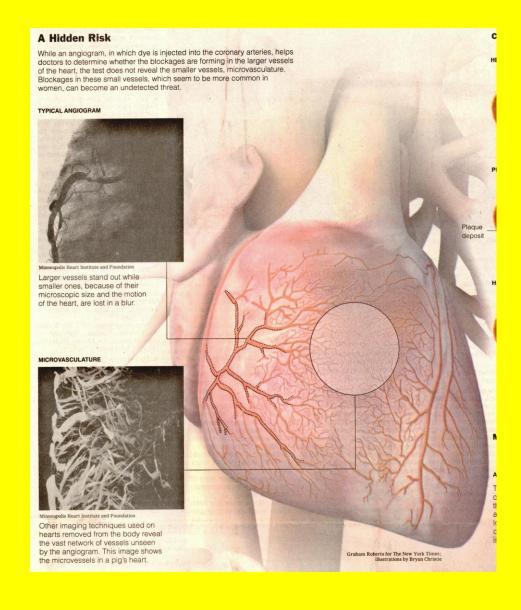


A heart attack victim treated by an emergency rescue service (ERS) has an increased chance of reaching the hospital alive and surviving the ordeal.

Women: more common:

- "microvascular disease"thickening, stiffening of smaller arterioles- supply heart
- Don't dilate very well
- Heart muscle-starved O2
- Chest pains, abnormal stress test

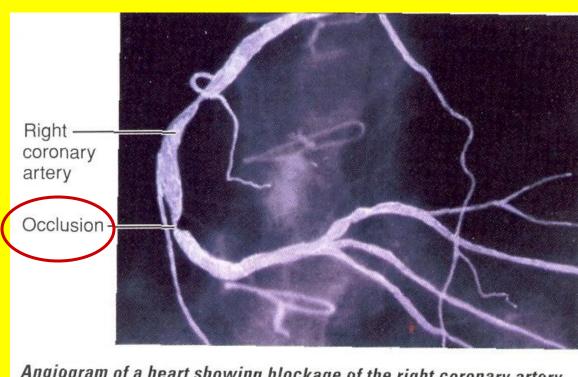
Microvascular Disease



 Standard <u>angiogram</u>: inject dye, X-Ray coronary arteries (big)

Only 1/3 women show big

blockages



Angiogram of a heart showing blockage of the right coronary artery.

 Rest of heart disease: missed in angiograms of women

 3 million American women- this type of heart disease: "coronary microvascular syndrome"

 Further tests: women: arterioles don't dilate, \ \ blood flow

Women's Warning Signs

- Chest discomfort
- Mild/severe pressure, fullness, or pain: center of chest
- Discomfort: arms, back, neck, jaw, stomach
- Shortness breath
- Nausea, light headedness or sudden cold sweat
- Extreme fatigue

Angina: may be warning sign: heart attack on the way

Angina from "angere" (Latin):

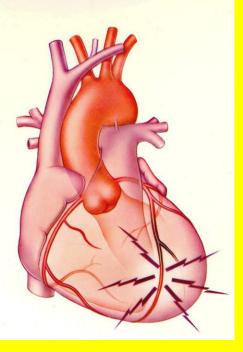
choke

Uncontrolled high blood pressure increases the risk of ...

Chest pain

- High blood pressure can increase the risk of clogged narrowed blood vessels. This results from a buildup of fatty deposits.
- Blood flow into the heart is reduced, and an increase in exertion can cause a sudden vise-like chest pain or discomfort.

Medical term: Angina pectoris



Angina:

- 1. Pain: tight, crushing, suffocating, beneath breastbone
- 2. Heaviness/tightness- chest
- 3. Occurs: exercise (exertion), emotional stress
- 4. Lasts: 2-15 minutes- goes away

Angina cause:

1. Spasm- coronary arteriesinsufficient blood to heart muscle= myocardial ischemia

2. Result of: atherosclerosiscoronary arteries

Heart disease: Who's at risk?

- Framingham Heart Study (1948): followed participants → today
- Identify "risk factors"
- Risk factors:

```
Having 1 = BAD
```

2 = Worse

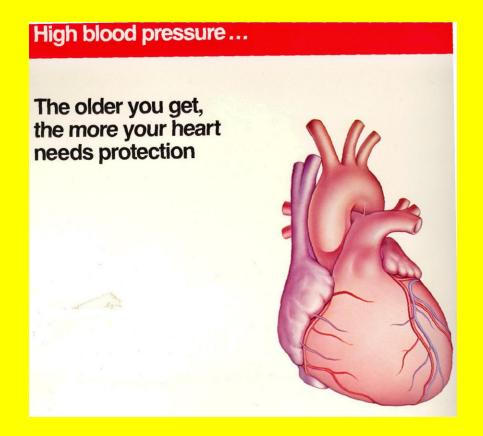
3 = Terrible

Risk Factors: Uncontrollable

- 1. Sex: Increased risk: men \geq 45 women \geq 55
- Family history: increased risk if:
 Male relative- heart disease
 before age 55
 Female relative- heart disease
 before age 65

Risk Factors: Uncontrollable

3. † Age † Risk 4/5 people die of heart disease > 65

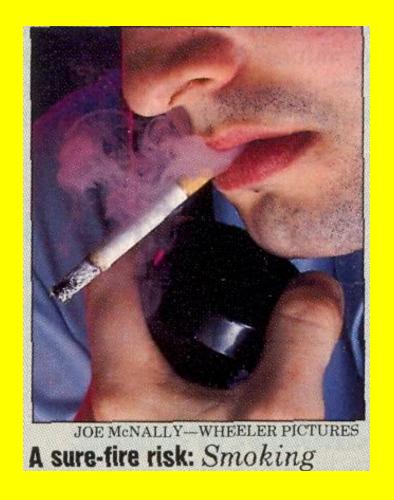


Risk Factors: Uncontrollable

- 4. Genetics | Risk
 - A) African Americans (high blood pressure)
 - B) Mexican Americans, Native Americans, Hawaiians (diabetes & obesity)

Risk Factors: Controllable

5. Cigarette smoking



Tobacco Smoke

- 1. **↓ HDL**
- 2. Platelets sticky- blood clot
- 3. CO: reduce blood oxygen to heart
- 4. Nicotine: arterial cell toxin
- 5. † adrenaline, heart rate, blood pressure, arrhythmias

Tobacco Smoke

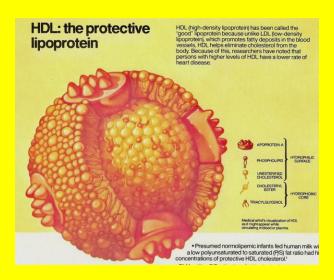
- 6. Heart works harder but can't get enough oxygen (CO)
- 7. Mutagens, carcinogens, allergens, radioactivity
- 8. Nicotine: addictive signs- 2 days start smoking: young people

2008 Dutch Study

- Pregnant women who **smoked**
- Their children years later
 (age 28)
- † Thicknesscarotid arteries



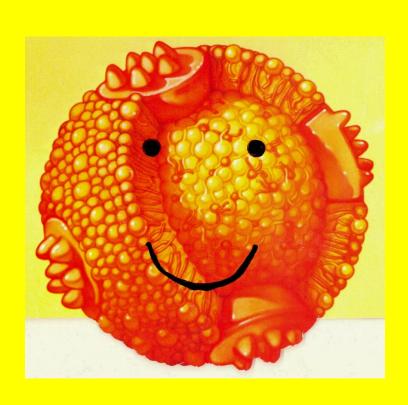
6. Blood fats (increased risk) LDL cholesterol > 100 mg HDL cholesterol < 40 mg Total cholesterol > 200 mg Triglycerides: > 150 mg

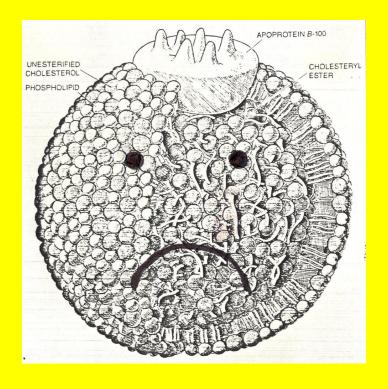


Cholesterol

The Good and The Bad HDL

LDL



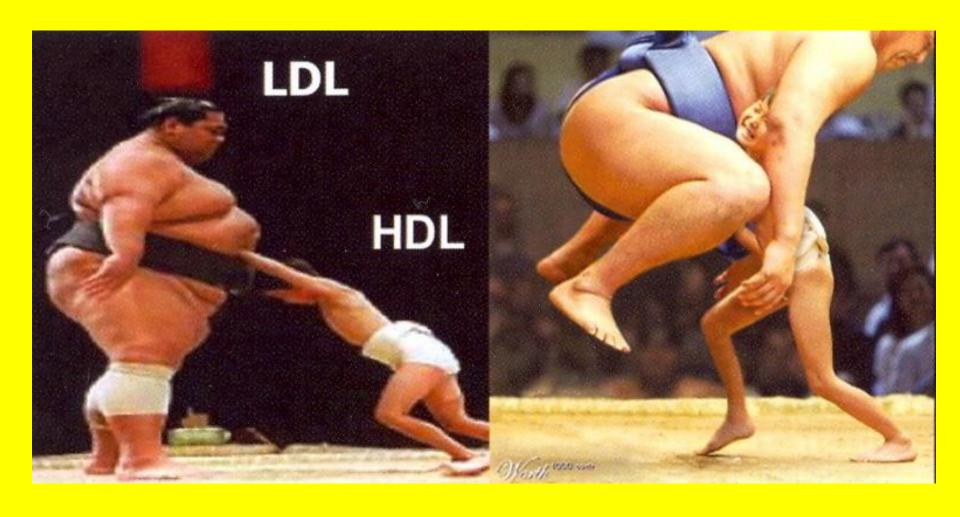


- Newborn babies: LDL 40-50 mg
- Populations: low risk, low fat diets:
 - LDL < 100 mg throughout life
- Brown/Goldstein:

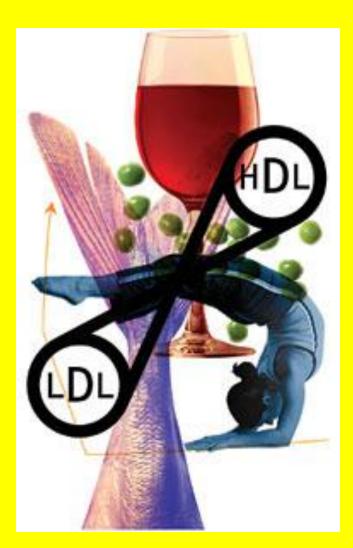




LDL vs. HDL: Balance is important



Bottom line: Keep LDL low and HDL high



7. High Blood Pressure: > 140/90

NUTRITION ACTIONS HEALTH LETTER

CENTER FOR SCIENCE IN THE PUBLIC INTEREST

Volume 22/Number 6

One Nation, Under Pressure

igh blood pressure.
The words don't exactly strike fear into most Americans' hearts. After all, it's not painful, like cancer. It doesn't sound deadly, like a heart attack. And besides, *you* probably don't have it.

But you probably will.

By about age 60, six out of ten
Americans have blood pressure
that's high enough to treat with
drugs. Millions more have pressure that's
high enough to raise their risk of a heart
attack or stroke.

"We're talking about a problem where, if you live long enough, only a minority of Americans escape," says
Jeffrey Cutler, an epidemiologist at the National
Heart, Lung and Blood
Institute in Bethesda,
Maryland. "All families will
be touched by it. If it's not
me, it's my spouse."

But it's not inevitable.

"Among the risk factors for stroke and heart disease, one of the most preventable is high blood pressure," says Paul Whelton, director of the Welch

Center for Prevention, Epidemiology, and Clinical Research at The Johns Hopkins Medical Institutions in Baltimore.

How to prevent it? Researchers know...but the public doesn't.

CONTINUED

ON PAGE 6

8. Diabetes: fasting blood sugar:≥ 126 milligrams



Figure 4.16 Monitoring blood glucose requires pricking the fingers each day and measuring the blood using a glucometer.

9. ObesityOverweight

BMI > 25

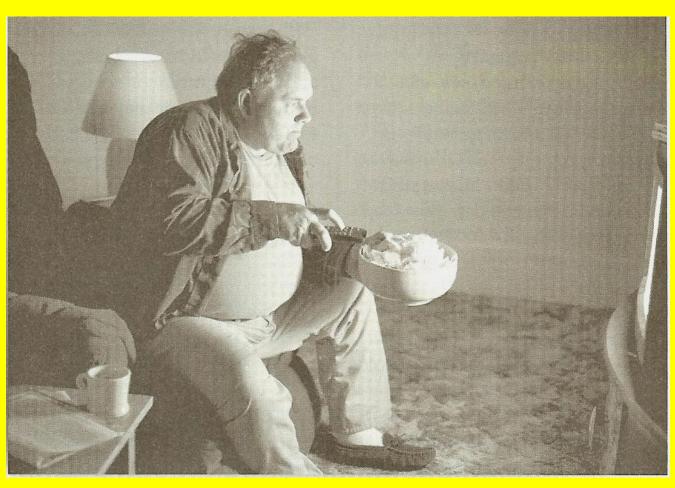
and



waist circumference:

- > 35 inches- women
- > 40 inches- men

10. Sedentary Lifestyle (inactivity)



Boston Irish Brothers Study

- Large study: 1 brother immigrated to Boston, other stayed Ireland
- Ireland brother ate ¼ more food/day but weighed 10 pounds less
- Ireland brothers: less heart disease
- Ireland brothers: more exercise/physical activitycompensated for excess food

11. Diet & Coronary Risk

Saturated fat, trans fat, cholesterol

Fiber, fruits, vegetables

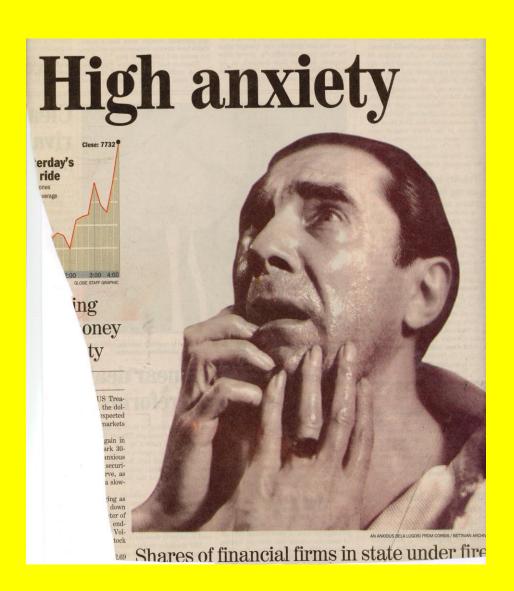


Other risk factors

- † C Reactive Protein † Risk
 Indication of inflammation in body (arteries)
- Blood homocysteine † Risk
 (amino acid)
 Vitamins B6, B12, folic acid
 lower homocysteine
 Foods: fortified grains (cereals, breads), fruits, veggies

Other risk factors

Stress

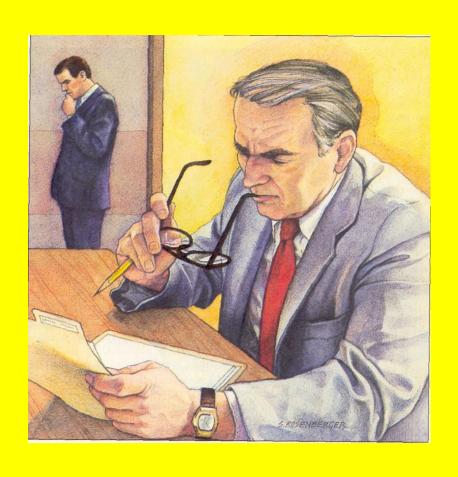


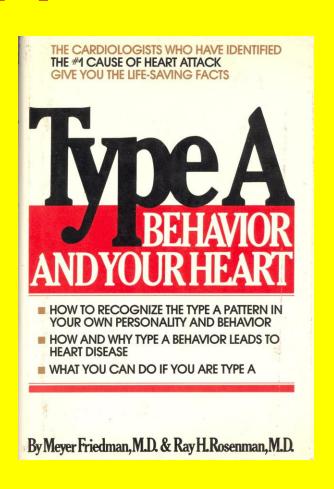
Stress: Job, society, school, peers

- † Stress † Angina & MI
 - 1. Some people: prone to emotional stress- worsen blood pressure, angina
 - 2. Long-term † adrenaline: heart rate, blood pressure, blood glucose
 - 3. Stress & overeating, smoking

Personality Type

Type A: Coronary prone





Type A:

Time urgency, impatient, competitive, aggressive

Subtype: hostile, cynical, increased adrenaline stress response: †risk

Type B: more relaxed, less time conscious: ‡ risk

2006 Dutch "Outlook on life" study: men 64-84 followed for 15 years "I still expect much from life" "I am still full of plans" 50% lower risk dying heart disease

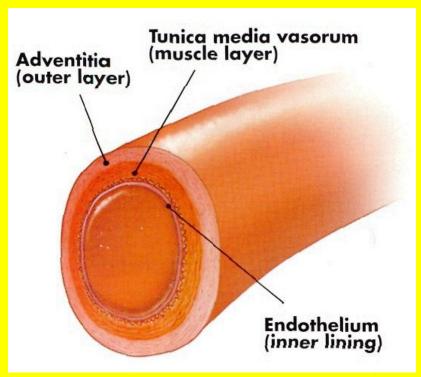
How does atherosclerosis begin?

Atherosclerosis: accumulation: lipids, protein, calcium, **scar tissue** in arteries: atherosclerotic plaque

Artery: | elastic (hardened), blood flow eventually blocked

Atherosclerosis Sequence

1. Injury (insult) to inner lining of artery wall



Injury: Different factors 1

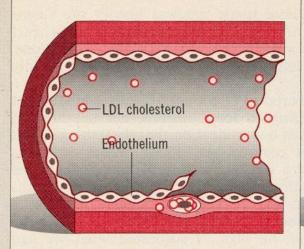
- LDL (oxidized)
- Glucose
- Homocysteine
- Blood pressure
- Free radicals- cigarette smoke
- Diabetes
- Infection- virus: Herpes virus detected in atherosclerotic plaque

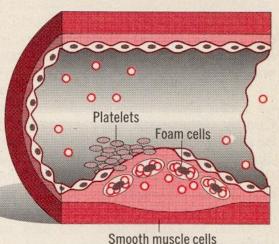
- 2. Inner lining: develops openings
- LDL moves in from blood

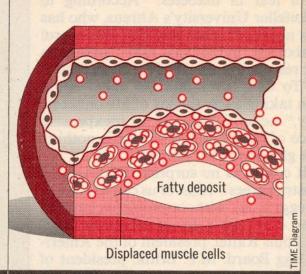
 Platelets attach to injured lining: release growth factors

 Smooth muscle cells → divide: thickening (like cancer)

HOW CHOLESTEROL CAN CLOG YOUR ARTERIES







Atherosclerosis is believed to begin when the lining of an artery, the endothelium, is damaged by factors including high blood pressure, elevated cholesterol levels or infection. 2 Two forms of blood cells accumulate in the damaged vessel wall: platelets and macrophages. The latter become foam cells as they gorge on cholesterol. When they burst, a fatty deposit forms.

3 Smooth muscle cells migrate from the layer below the endothelium and multiply wildly. Over a period of years, this proliferating jumble blocks the flow of blood, leading to a heart attack or stroke.

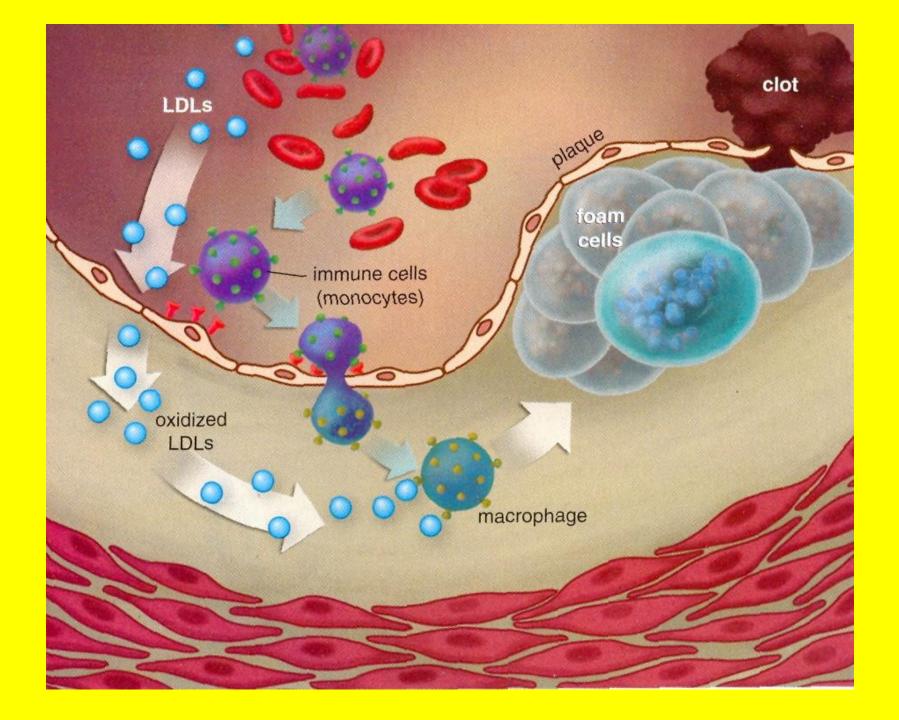
3. LDL inside artery- **oxidized:** dangerous

- Triggers inflammation
- White cells in blood → artery wall

macrophages

- Gobble up oxidized LDL bag of fat: foam cells
- Foam cells burst: release fat

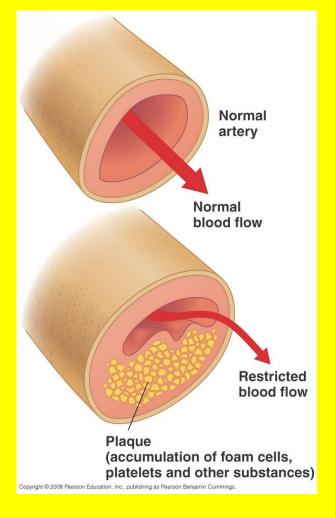
fatty streak



- 4. Injury (lesion) grows → plaque
- Cap (cover) of protein forms:

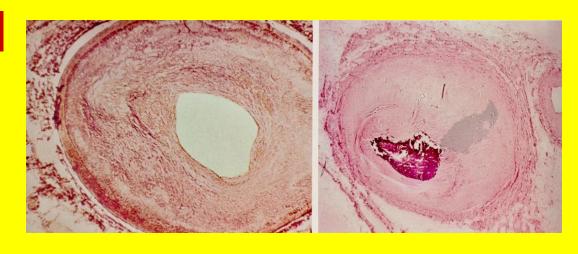
fibrous plaque

- Attempt to "wall off" damaged artery
- Immune cells in plaque break down
 cap: ruptures

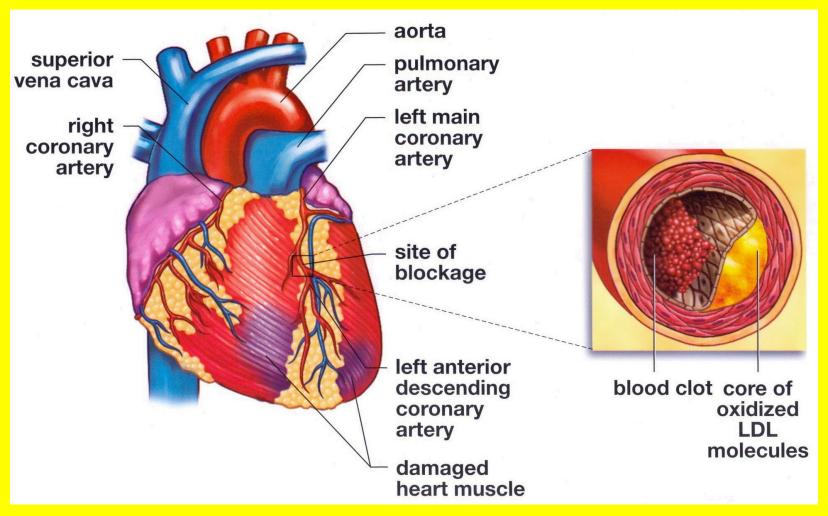


- 5. Clot forms on roughened surface
- Thrombosis (thrombus)
- Heart attack:

myocardial infarction



Heart attacks: more common morning, on birthdays



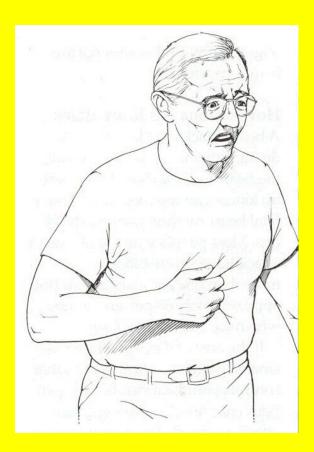
- 6. Damage to heart muscle triggers: abnormal heart rhythms (cardiac arrhythmias)
- Most dangerous: ventricular fibrillation
- Heart quivers, stops pumping
- "Bag of worms"

Ventricular fibrillation loss of consciousness, death quickly

- A. Do CPR
- B. Shock heart back into normal rhythm: **defibrillator** (paddles)-airplanes, airports

Heart Attack

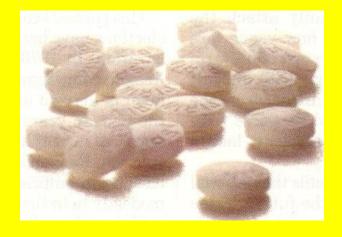
Classic "Hollywood heart attack"person clutching chest



Heart Attack

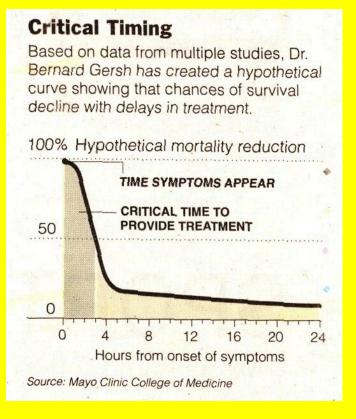
- Not always true
- Sometimes-less distinct symptoms (women & elderly)
- Discomfort/pressure- chest
- Exhaustion: just walking across room
- Break out: cold sweat
- Diabetics: sudden extreme fatigue:
 "silent heart attacks" (scar tissue)

- Heart attack may last 4-6 hours
- With each passing minute: heart tissue → no O2 → dies
- If conscious: suggestion- "chew" on aspirin- prevent further clotting/help blood flow

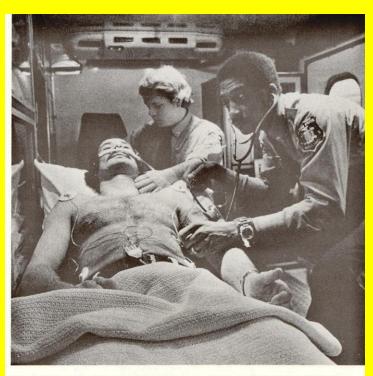


Regardless of type:

- Every minute counts
- "Golden hour": "Time is muscle"
- ~ 1 hour:
 get arteries open prevent permanent
 heart damage



Problem: 1/2 people with heart attacks don't call ambulance



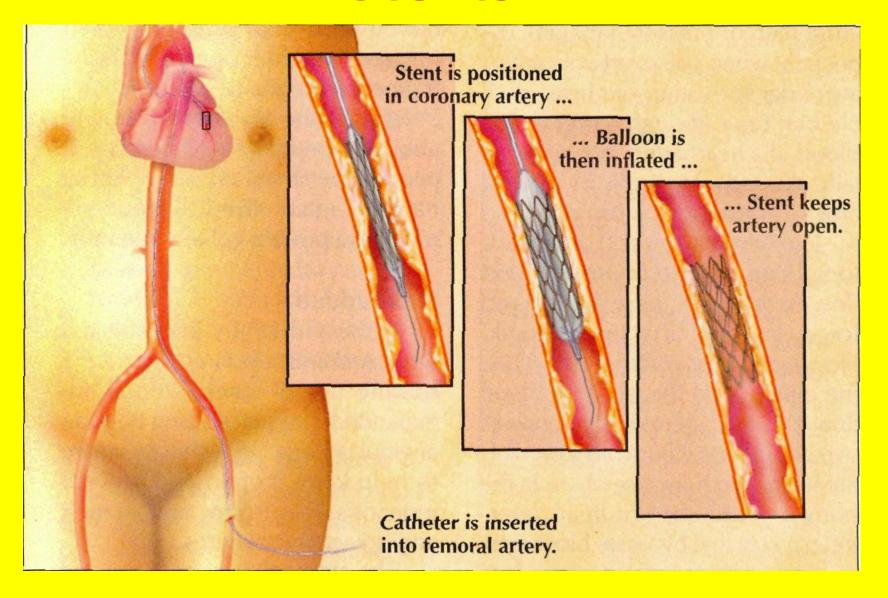
A heart attack victim treated by an emergency rescue service (ERS) has an increased chance of reaching the hospital alive and surviving the ordeal.

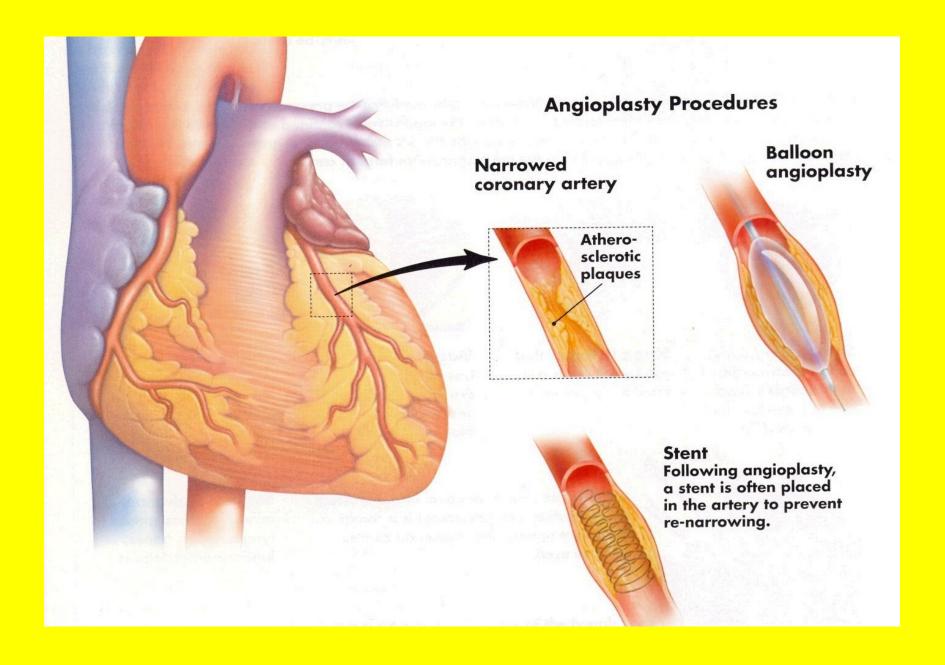


MI: 2 treatments at hospital

- Clot buster: tissue
 plasminogen activator
 (tpa): not perfect- only opens
 60-70% blockages
- 2. Balloon angioplasty + stent (stainless steel mesh)- keeps artery open

Stents

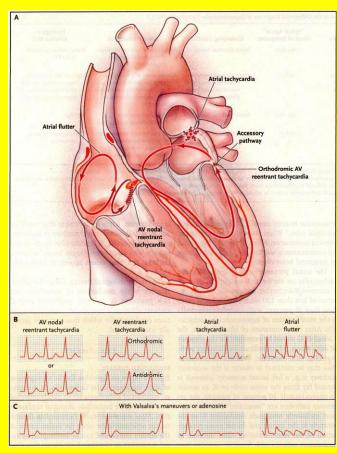




Heart Disease: How do you detect it?

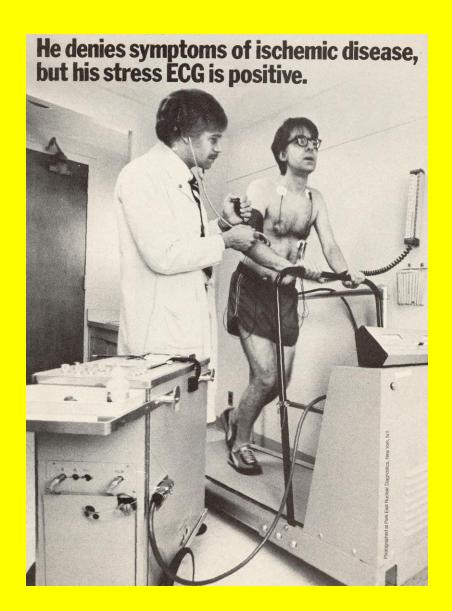
Electrocardiogram (ECG): look for

abnormal rhythms



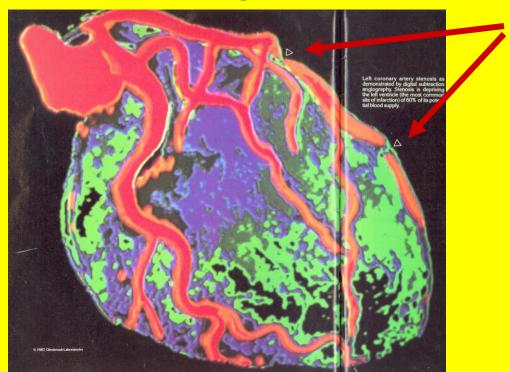
Cardiac stress test: treadmill +

ECG



 Coronary angiography: gold standard

Catheter → coronary arteries blockages ← X-Ray movies ← dye



Coronary
Angiogram
53 year old
man

Severe blockage



How do you treat heart disease?

- 1. Healthy diet
- 2. Exercise
- 3. Stop smoking







Whole fruits and vegetables can reduce your risk for cardiovascular disease.

- 4. Medications:
 - A) Statins
 - B) Bile acid-binding resins (sequestrants)

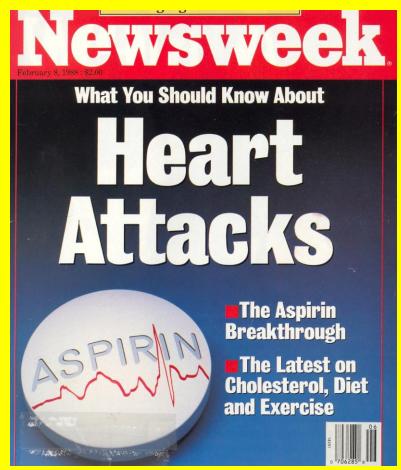
Both deplete liver- cholesterol

† Liver LDL receptors ↓ blood LDL

C) Aspirin- baby aspirin (81 mg): may prevent clots, protect against

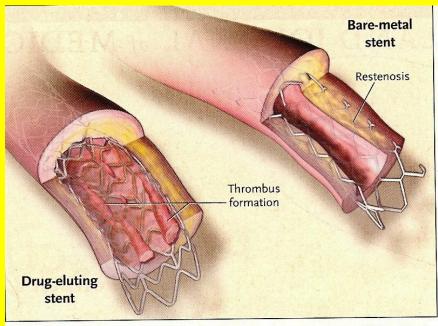
heart attack/stroke

Higher dosemay be harmful: GI bleeding



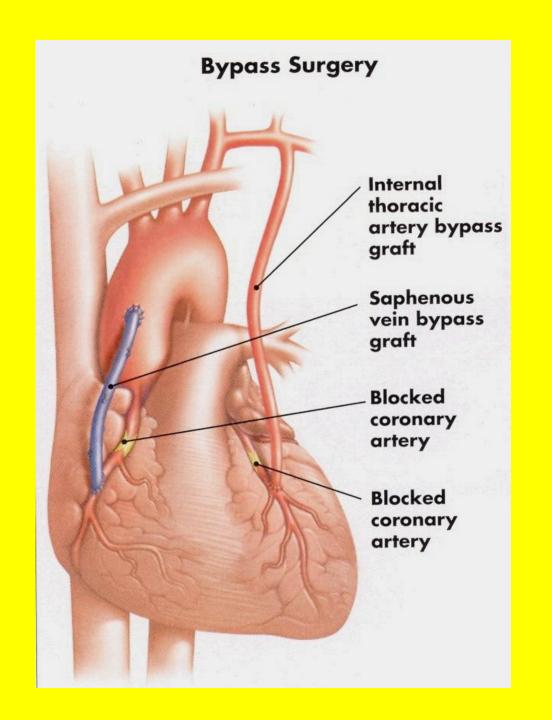
D) Niacin- B vitamin: ↓ LDL ↑ HDL

5. Coronary angioplasty + stent



Contrasting Mechanisms of Obstruction of Bare-Metal Stents and Drug-Eluting Stents. Bare-metal stents may be narrowed or obstructed by ingrowth of tissue. With drug-eluting stents, this process is inhibited, but since the struts remain uncovered, they may be prone to thrombosis after antiplatelet therapy is discontinued.

- 6. Coronary Artery Bypass Graft (CABG): improve blood flow
 - A) Use vein from leg/arm or
 - B) Mammary artery grafted around blocked artery
- President Clinton: multiple bypasses



Dietary Factors: to reduce <u>progression</u> of atherosclerosis

1. † Whole grains | Heart risk

Contain: fiber, vitamins, minerals, antioxidants (LDL), phytochemicals

Also control blood glucose, blood pressure, prevent obesity

2. † Simple sugars† Blood triglycerides† Heart risk

Limit: cookies, high sugar drinks, snacks, candy

3. Soluble fiber Heart Risk
| Cholesterol & bile acid
| absorption- intestine: | LDL

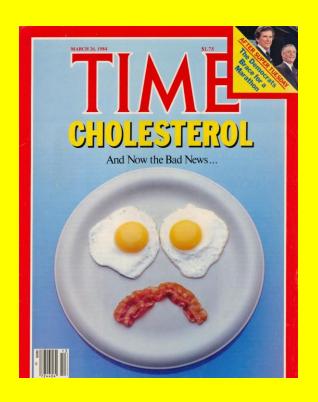
Soluble fiber sources:

Oat bran, oats, oatmeal, peas, beans, apples, flaxseed, psyllium (Metamucil), pears, peaches, plums, oranges, broccoli, Brussels sprouts

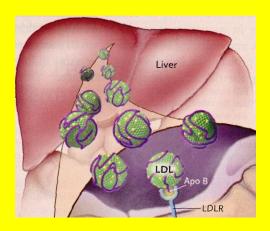
4. † Cholesterol † Heart Risk

20% cholesterol= food

80% cholesterol = made in



your body (liver)



5. † Total Fat † Heart Risk **Exceptions:**

- A) Greenland Inuits:
 - tomega 3 fats (fish)
 - **↓** heart disease
- B) Mediterranean diet: high monounsaturated fats, whole grains, fruits/veggies, wine, low animal foods \ heart disease

6. | Saturated fat | Heart risk | Meats, dairy products (whole milk, cheese, ice cream), prepared (frozen) foods

↓ LDL receptors- liver ↑ LDL

Limit: 20 grams/day (< 10% calories)

Where the saturated fat is at

Animal fat:

Beef: 50%

Chicken: 30%

Pork: 39%

Tropical oils

Coconut: 87%

Palm oil: 49%

Palm kernel oil:

82%

Low saturated fat:

Vegetable oils

Canola: 6%

Corn: 13%

Cottonseed: 26%

Olive: 13%

Peanut: 17%

Safflower: 9%

Sesame: 14%

Soybean: 15%

Sunflower: 10%

7. ↑ Trans fat ↑ Heart risk("partially hydrogenated")↑ LDL ↓ HDL

Keep as low as possible in diet

Veggies, nuts, corn, soybean, safflower, sunflower oils, soft/liquid margarines

↓ LDL but also slight **↓ HDL**

Fish, fish oil, flaxseed, soybean oil, canola oil, walnuts

Eat fish: 2-3 times/week

↓ Triglycerides ↓ LDL ↑ HDL Good heart rhythms

Olive oil, canola oil, high "oleic" safflower & sunflower oils, nuts

↓ Blood pressure, ↓LDL ↓ LDL oxidation

Polys + monos = **45** grams/day

Keep homocysteine low homocysteine tatherosclerosis

Sources: enriched grains, fruits, veggies

† HDL ↓ Blood clotting

Ethanole wine beer mixed de

Ethanol: wine, beer, mixed drinks

Red wine: polyphenols

(phytochemicals): ↓ LDL oxidation

Moderate limit: 2 drinks/day men

1 drink/day women

13. Soy products

Soy protein, phytoestrogens

↓ LDL may be **↑ HDL**

Cholesterol-lowering effect- not as dramatic as once thought

Reduce cholesterol absorption-intestine **LDL**

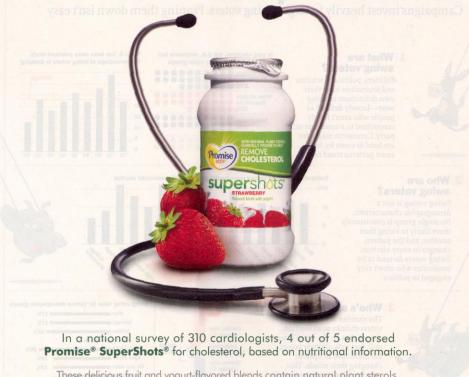
Small amounts: fruits, veggies, nuts, seeds, cereals, peas, beans, vegetable oils

Now added to: salad dressings, OJ, margarines (Benecol, Take Control)



's only natural that Maria Angeles got such spectacular results.





These delicious fruit and yogurt-flavored blends contain natural plant sterols, ingredients clinically proven to help remove cholesterol from your body.

Enjoy daily with meals as part of a diet low in saturated fat and cholesterol, and you could see reduced cholesterol levels.

For more information on plant sterols, go to WebMD.

Plant Sterols

WebMD'

supershots



TRY ALL FOUR FRUIT FLAVORS!

Strawberry, Peach, Raspberry, Bluebern

Foods containing at least 0.4 grams per serving of plant sterols, eaten twice a day with meals for a daily total intake of at least 0.8 grams, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. A serving of this product provides 2 grams of plant sterols. ©2008 Unitever

15. Caffeinated beverages

Elderly † caffeinated drinks heart disease death risk But people with MI in hospitals High coffee intake: risk ventricular arrhythmias

16. DASH Diet Blood pressure

↓ Heart risk

Eat more: Fruits, veggies, whole grains, low-fat dairy products, poultry, fish, nuts

Eat less: Total fat, red meat, sweets, sugary drinks

17. Meal frequency

NIH High Blood Pressure in Adults Expert Panel

- Eat throughout day
- Smaller meals & snacks (healthy, low calorie)
- Instead of: 1 large meal in evening, before bed

18. Activity/exercise

- Be active most days of week:
 30-60 minutes
- Maintain healthy body weight
- 2007 study: people use pedometers: more motivated
- ↓ BMI ↓ Blood Pressure
- +2000 steps/day = 1 mile

19. Antioxidants

- Inconsistent results
- Some studies: † fruits/veggies
 - ↓ heart disease
- † Vitamin E- smokers | coronary deaths
- Other studies: Vitamin E: people at risk heart attack/stroke: No effect; ditto: Vitamin C, Beta carotene

Do Hershey's Kisses lower blood pressure?



- German study 2007:
- People- blood pressure: 147/86
- Ate: 6 grams white or dark chocolate (equal in amount to 1.5 Hershey's Kisses per day)
- Dark chocolate from cocoa- rich in flavonoids
- After 18 weeks: systolic ↓ 3 points
 (dark) diastolic ↓ 2 points

Flavonoids:

- 1. Decrease LDL oxidation
- 2. Lower LDL, raise HDL
- 3. Vasodilation
- 4. Decrease inflammation
- 5. Decrease blood pressure
- 6. Decrease platelet clumping
- 7. Increase insulin sensitivity

Flavonoids in black tea

- Netherlands study
- > 3 cups black tea/day
- I heart attack rate
 Green Tea (catechins)
- LCRP (inflammation)
- Antioxidant abilities



Flavonoids -other sources:

Green/black tea, cherries, purple grapes, blackberries, raspberries, blueberries, cranberries, plums, bran, red apples, pears, red wine, strawberries, grapefruit, prunes

*Organic tomatoes higher in flavonoids

 Problems: Current way manufacturers make cocoa & chocolate: destroys most flavonoids

Chocolate: high in calories & fat

