An Introduction to Cardiovascular Health and Disease

February 9, 2023

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Presentation to the Northern Virginia Baptist Association

Heart Disease comprises a wide variety of different diseases including:

- <u>Coronary artery disease</u> (<u>Atherosclerosis</u> of the coronary arteries) which is responsible for the vast majority of heart attacks leading either to death or chronic heart failure ("Congestive Heart Failure")
- Heart valve diseases which can cause chronic heart failure
- <u>Inflammations and infections of the heart</u> (myocarditis, infectious endocarditis) causing heart failure.
- Abnormal heart rhythms (e.g. atrial fibrillation which can lead to strokes, ventricular fibrillation which is a cause of sudden death)
- <u>Infiltrative diseases</u> such as amyloidosis which stiffens the heart causing heart failure.
- <u>Scarring of the pericardium</u> which impairs heart muscle motion causing heart failure.
- <u>Cardiomyopathies</u> (=muscular dystrophy-like conditions which cause a weakening of the heart muscle). Some are caused by abnormal genes or alcoholism but the causes of most are unknown.

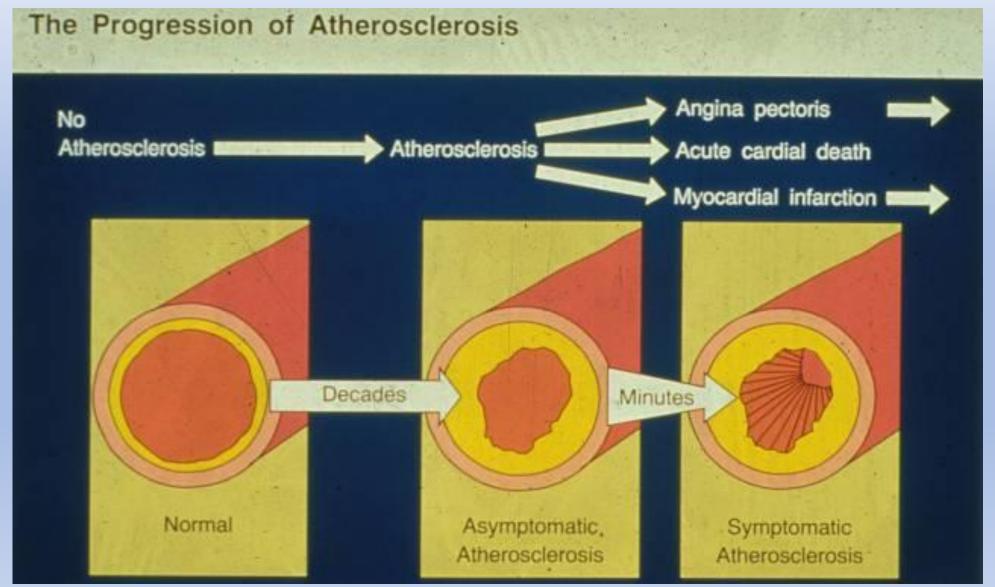
Main topics to be covered today:

- Atherosclerosis ("hardening of the arteries")
 - Pathology
 - Risk factors
- "Heart attacks"
 - Myocardial infarction
 - Arrhythmias and sudden death
- Strokes
- <u>High blood pressure</u>:
 - Definition and causes
 - Symptoms
 - Kidney failure
 - Hypertensive congestive heart failure
 - Aortic Dissection
- Anything else folks want to talk about!

Atherosclerosis ("hardening of the arteries") is by far the most common disease process underlying all sorts of cardiovascular disease.

The build up of chronically inflamed scar tissue within our major arteries (mainly aorta, coronary arteries, arteries of the legs, arteries feeding the brain)

Atherosclerosis is not just cholesterol deposits on the inside of arteries.

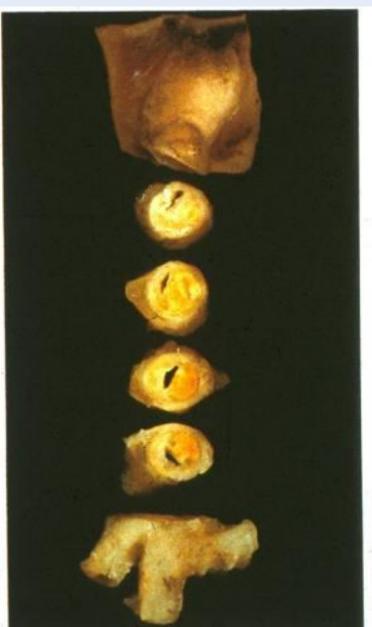


"Solvents" such as alcohol consumption will not help you here!

Focal Coronary Arterial Involvement

Human coronary artery and branches

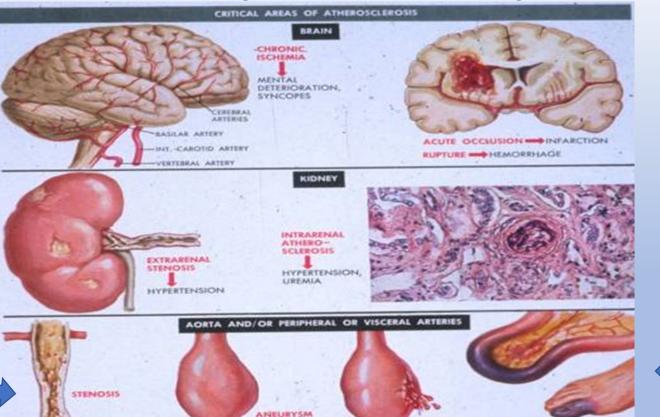




Atherosclerosis related problems depend on the

arteries invo

Aortic occlusion or aneurysm; peripheral vascular disease



HEART

MYOCARDIAL

... Hobosiste the heart; and nephrologists, the

Stroke

Kidney damage

Gangrene of tissues

Myocardial infarction ("heart attack")

VISCERAL OR

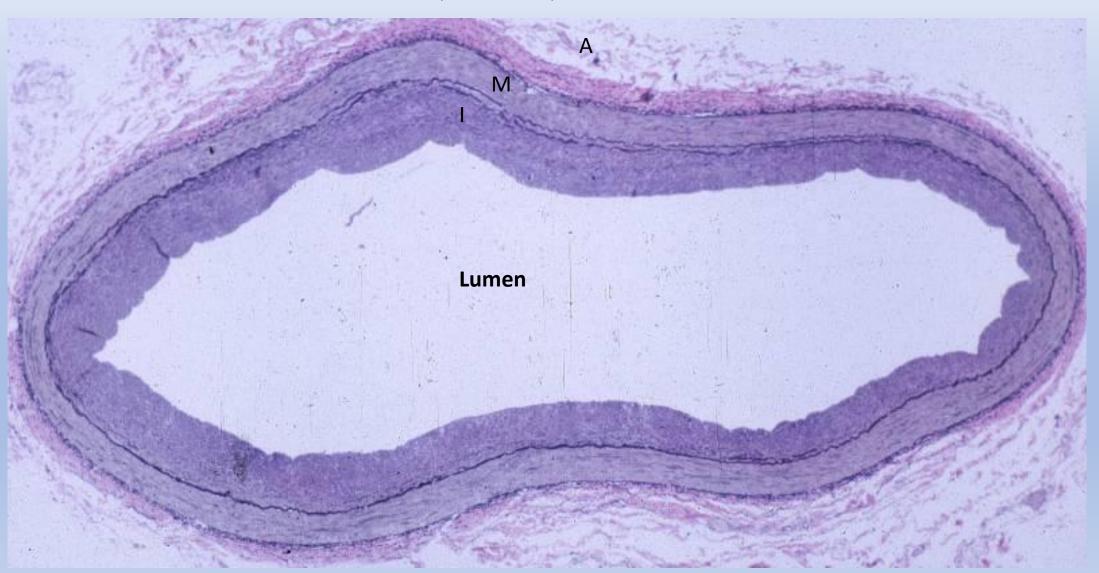
concurrent treatment of both the hypertension as

PERIPHERAL GANGRENE

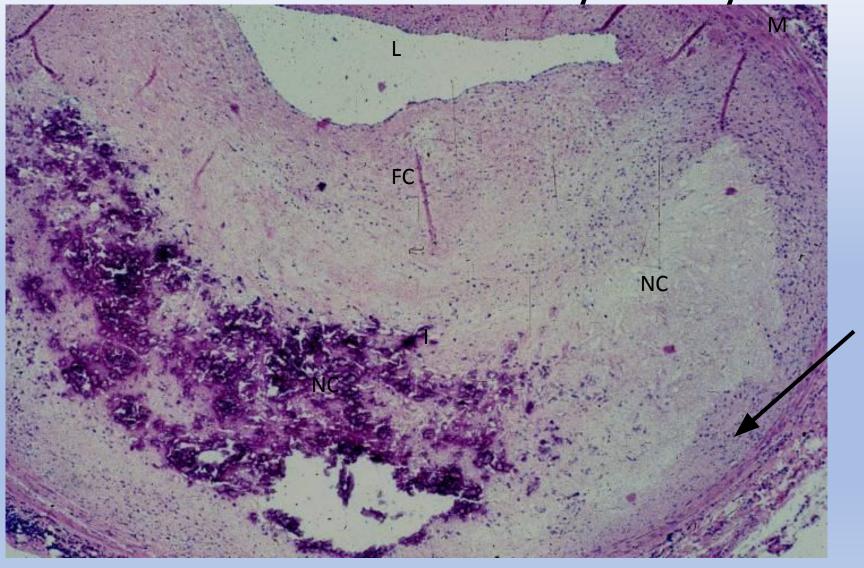
MYOCARDIAL INFARCTION

Normal adult coronary artery

I= intima; M= media; A= adventitia



Atherosclerotic Coronary Artery



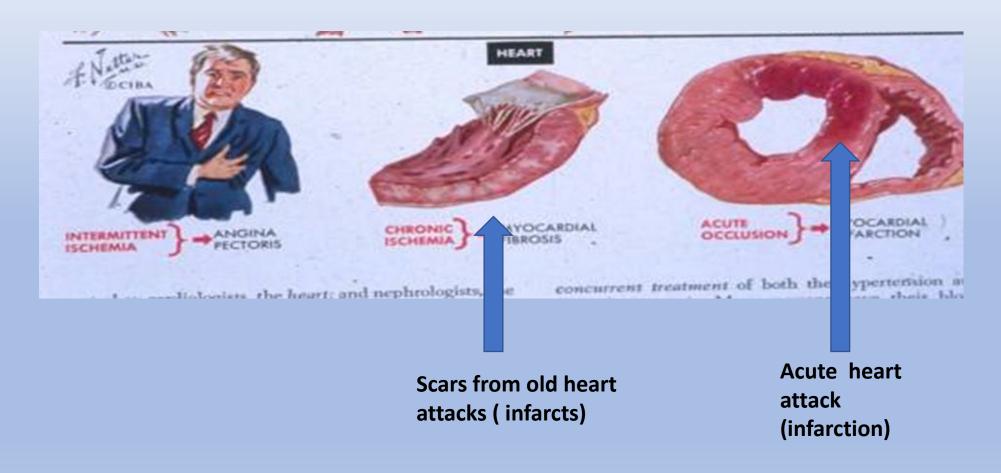
Angina:

- Clinical syndrome of chest "pain/pressure, discomfort" and pump dysfunction brought on by exertion, excitement and things which increase heart work and oxygen consumption.
- Caused by a narrowed coronary artery which can deliver enough blood flow for <u>resting</u> periods, but which can <u>not</u> deliver the increased blood flow demands associated with exertion and increased heart work.

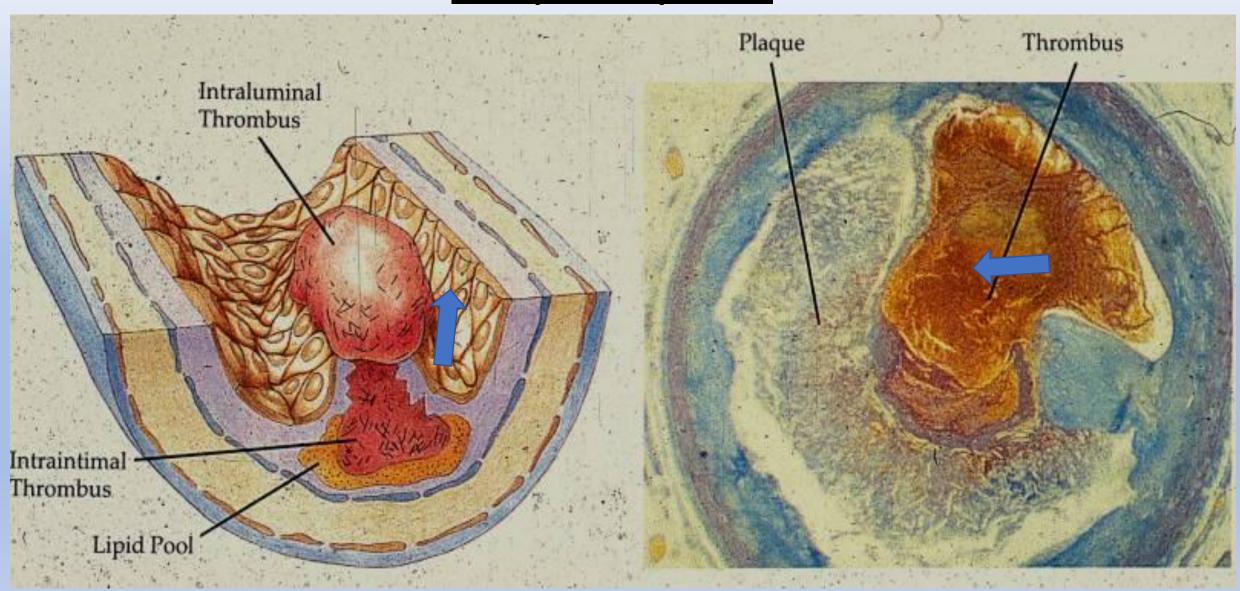
Major clinical risk factors for atherosclerosis:

- Hypercholesterolemia* (= high blood cholesterol, particularly LDL elevation >190 mg/dl) Irritates the inner lining of arteries causing inflammation and the build up of plaques which narrow the arteries and can close them off with clot formation.
- Hypertension (= high blood pressure)*
 - Pushes cholesterol and other plasma proteins into the arteries causing inflammation and the build up of plaques as above.
 - Thickens the blood vessels in the kidney and eventually closes off the ability of the kidney to do its normal filtration function and rid the body of impurities, plus maintain proper water and electrolyte balance.
- Diabetes*
 - Damages the proteins of the arteries in ways that promote inflammation and the buildup of plaques as above.
 - Secondarily thickens small vessels in the kidney causing kidney function impairment.
- Cigarette smoking*
- Age
- Male sex
- Increased general inflammatory state? (C-reactive protein elevations)
- Genetics

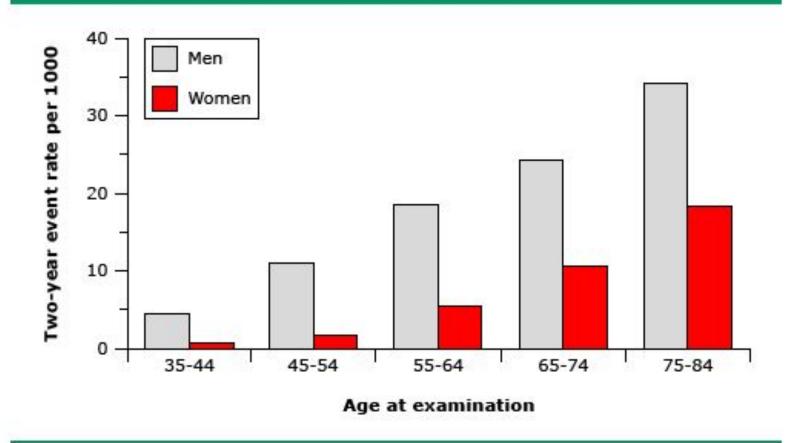
Atherosclerotic coronary artery disease causing a heart attack (myocardial infarction)



Plaque rupture



Incidence of myocardial infarction in men and women

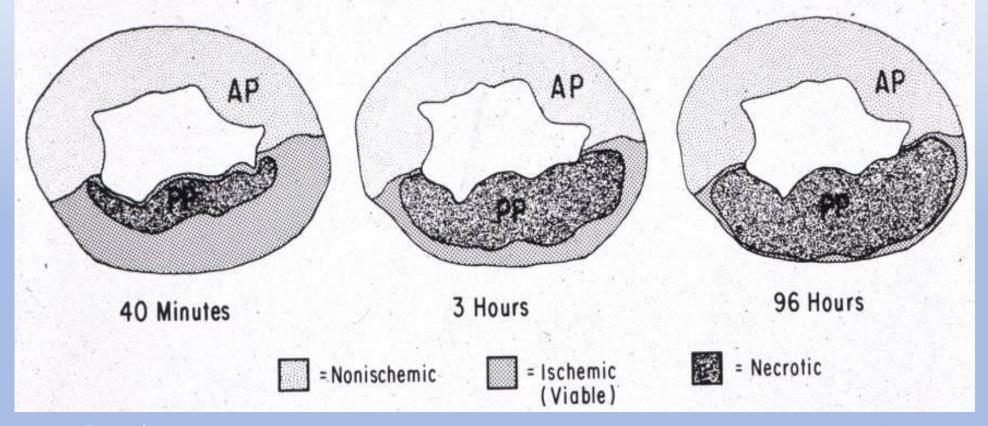


Incidence of myocardial infarction by age and sex in a 26-year follow-up in the Framingham study. The incidence increases with age in both sexes, but occurs later (primarily after menopause) in women.

Data from: Lerner DJ, Kannel WB. Am Heart J 1986; 111:383.



Wave front phenomenon justifies early reperfusion.



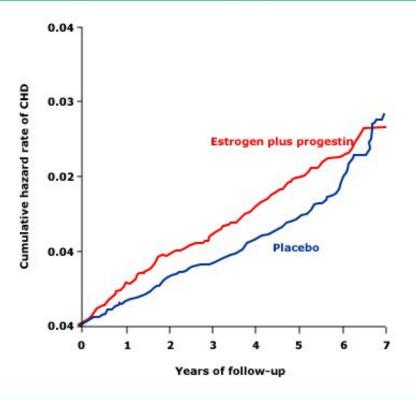
Clinical: Early reperfusion preserves more muscle. Reperfused infarcts also heal somewhat faster.

This is why getting to a hospital ASAP if your have chest pain which lasts several minutes even at rest is so important!

Major Risk Factors for Cardiovascular Disease <u>Unique to Women</u>:

- Post-menopausal status
- Pregnancy-related complications (e.g., eclampsia, preeclampsia, gestational hypertension, gestational diabetes)
- Prior hysterectomy
- Oral contraceptive use

Women's Health Initiative: Risk of heart disease

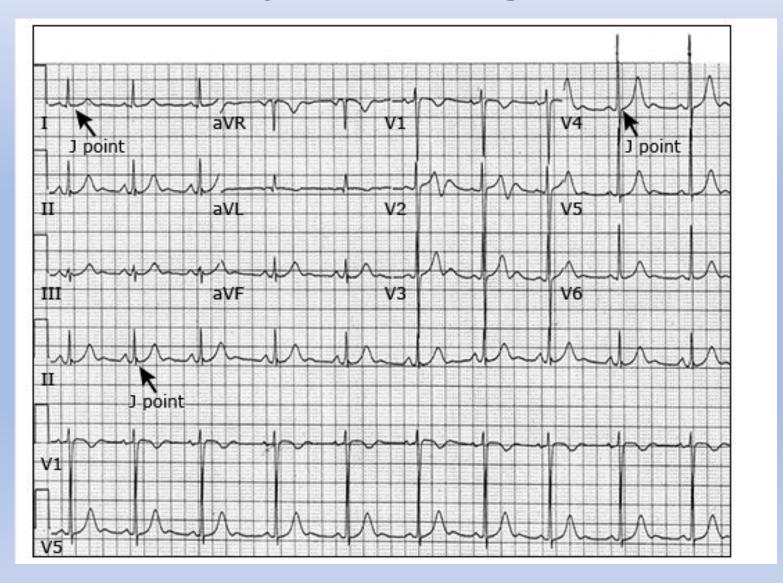


Kaplan-Meier estimates of cumulative hazard rates of CHD. In the Women's Health Initiative, combined estrogen-progestin therapy was associated with a significant increase in coronary events. CHD included nonfatal myocardial infarction and death due to CHD. The overall hazard ratio for CHD was 1.24 (nominal 95% CI, 1.00-1.54).

CHD: coronary heart disease.

Data from: Manson JE, Hsia J, Johnson KC, et al. Estrogen plus progestin and the risk of coronary heart disease. N Engl J Med 2003; 349:523

Normal heart rhythm is regular

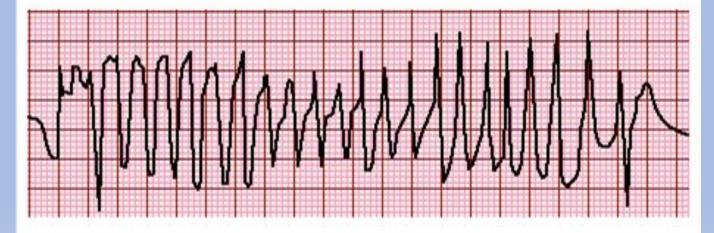


Damaged heart muscle can also cause arrhythmias: Ventricular Tachycardia

The damaged heart cannot tolerate this for very long and will eventually fail.

Medicines and electro-shocks are used to treat this.

Single lead electrocardiogram (ECG) showing polymorphic ventricular tachycardia (VT)



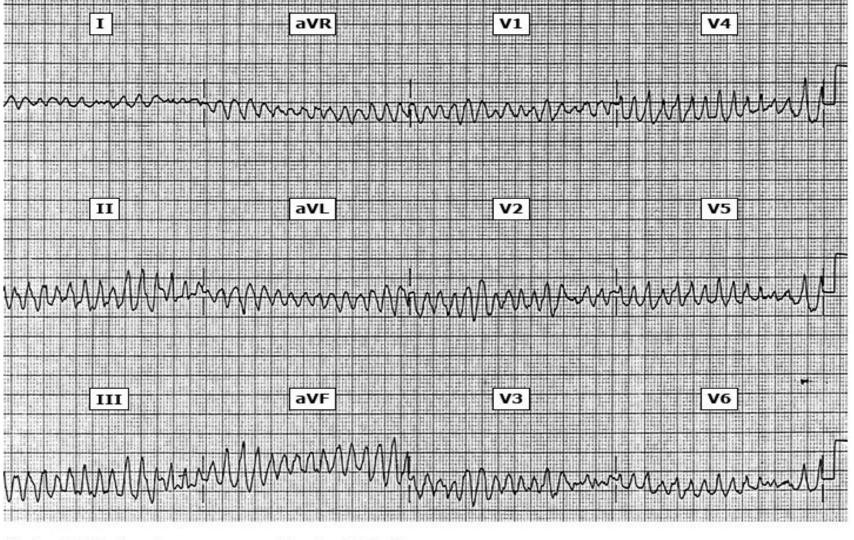
This is an atypical, rapid, and bizarre form of ventricular tachycardia that is characterized by a continuously changing axis of polymorphic QRS morphologies.

Ventricular Fibrillation: heart beating so chaotically and not uniformly, that it does not push out blood.

This requires electro-shocks to stop, otherwise the patient will die.

Very frequent cause of sudden death in the setting of a heart attack, and sometimes with just severely narrowed coronary arteries (making the heart muscle irritable).

ECG 12-lead ventricular fibrillation



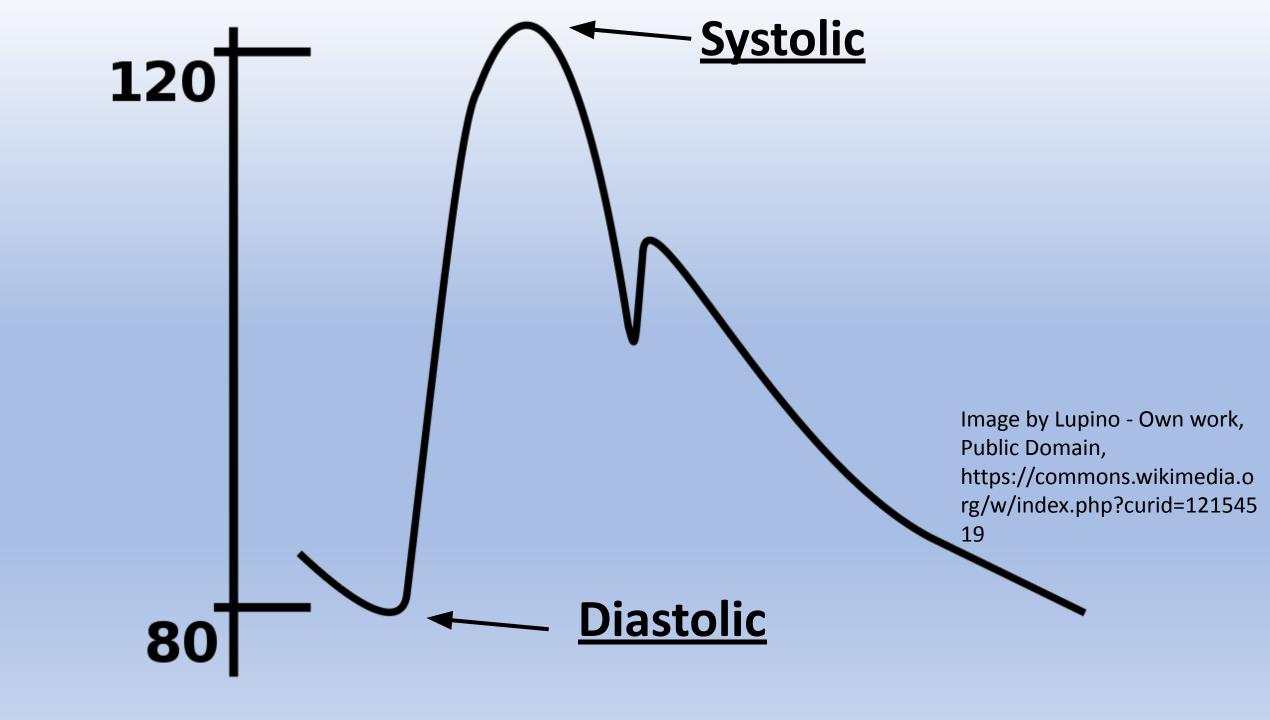
12-lead ECG showing course ventricular fibrillation.

ECG: electrocardiogram.

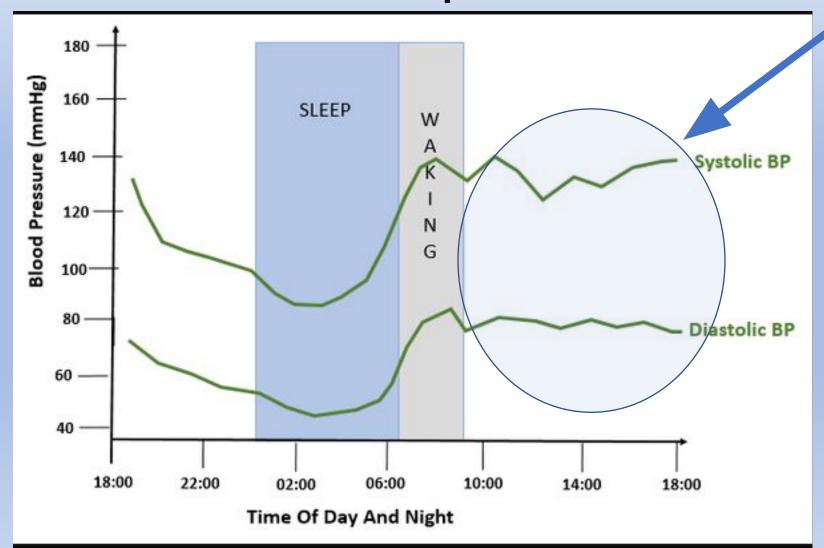


Hypertension (high blood pressure), diabetes, and heart diseases are multiple, overlapping disease entities which strongly affect men, particularly African American men.

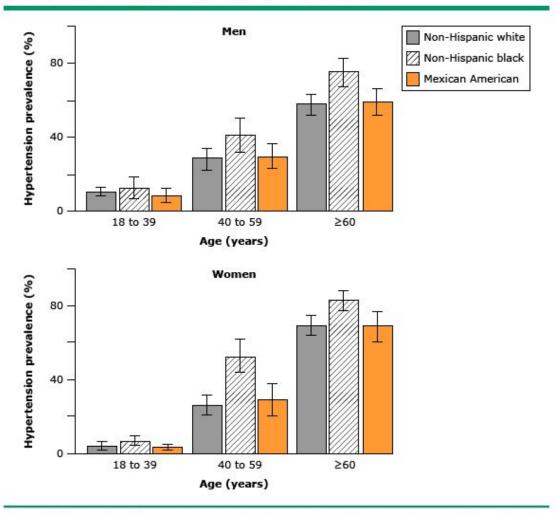
- High blood pressure definition:
 - Systolic (peak) blood pressure >120-130 mmHg and/or
 - Diastolic (trough) blood pressure > 80 mmHg
 - Promotes: Atherosclerosis ("hardening of the arteries") which causes the most deaths of any disease category in the U.S.
 - Also promotes:
 - Kidney damage and failure
 - Heart attacks and sudden death
 - Heart failure
 - Strokes
 - Aneurysm and aortic splitting/rupture



Blood pressure varies throughout the day and with different activities. Best to measure your blood pressure during the day, either at the same time or multiple times.



Prevalence of hypertension in the United States



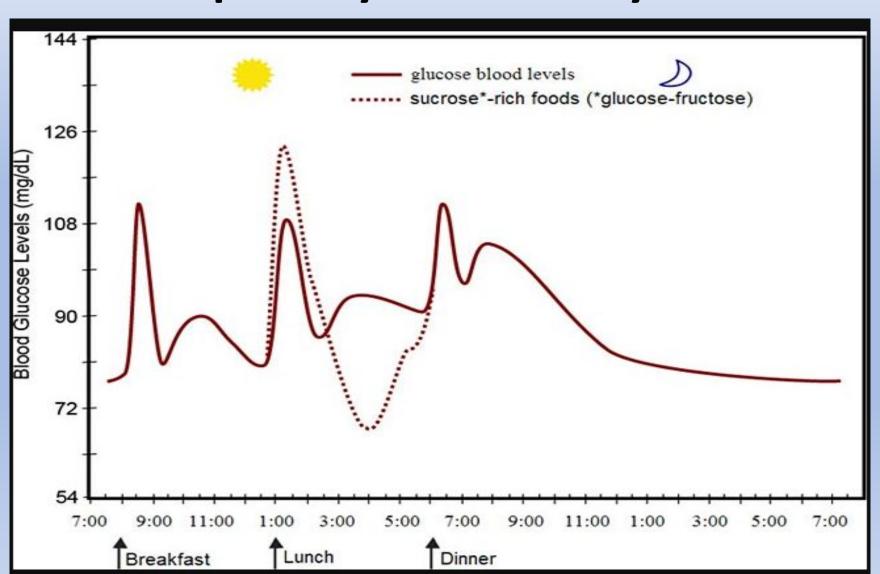
Prevalence of hypertension in men (upper graph) and women (lower graph) according to age and race/ethnicity in the United States from the National Health and Nutrition Examination Survey (NHANES). Hypertension occurs earlier and more frequently in non-Hispanic blacks.

Data from: Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. JAMA 2010; 303:2043.

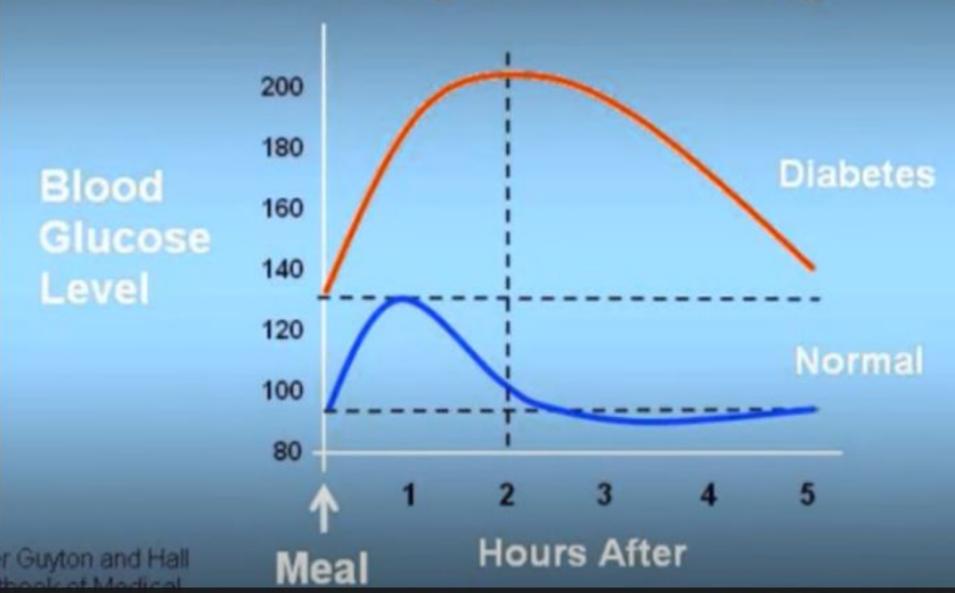
Diabetes:

- Defined as poor control of blood sugar levels such that rather the normal variations being about 70-120 mg/dl to marked elevations above 120 mg/dl, and with some treatments, even low levels below 70 mg/dl. Also Hemoglobin A1C <6%.
- Causes numerous diseases linked to how poorly the blood sugar is controlled, including:
 - Atherosclerosis: ("hardening of the arteries") which causes the most deaths of any disease category in the U.S.
 - Nerve damage causing pains and numbness in feet or hands
 - Kidney damage and failure (Note: hypertension and/or diabetes account for the vast majority of kidney failure cases in the U.S. requiring dialysis)
 - Sometimes brain damage with cognitive impairment
 - Suppressed immune system making one more susceptible to infections, and poor healing of infections and injuries.
 - Bowel problems including diarrhea

Blood glucose also varies throughout the day, especially with what you eat.



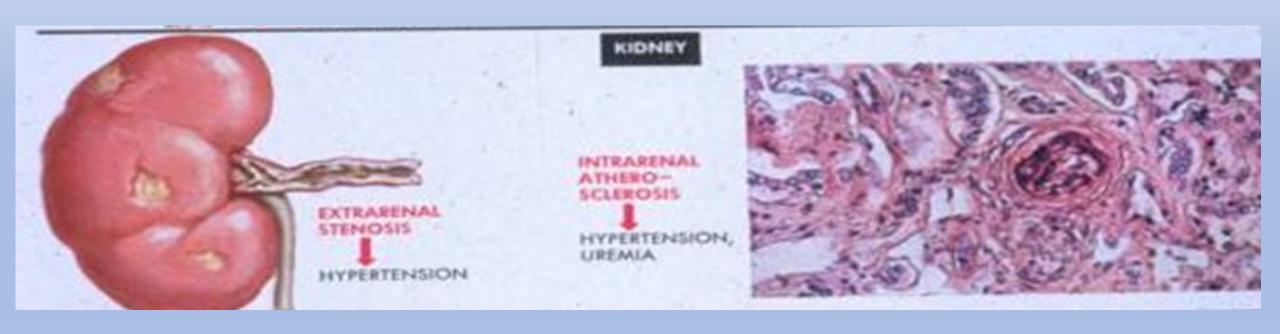
Blood Sugar After Eating



Diabetic Medications:

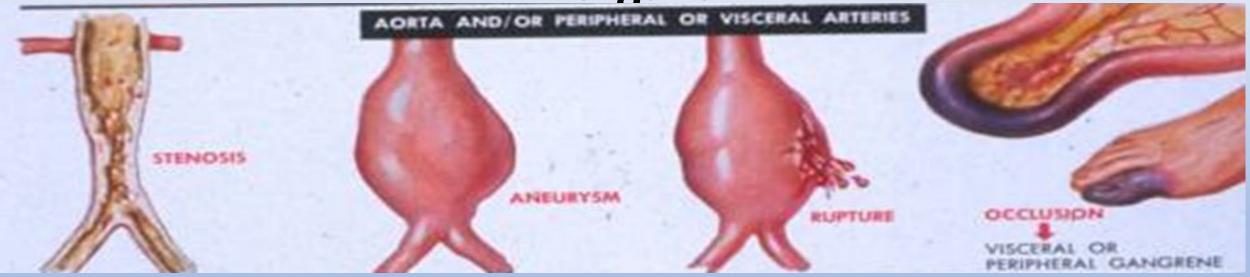
- 1) Metformin:
 - a) Action: works by lowering the amount of sugar produced in the liver, and also increasing the sensitivity of muscle cells to insulin.
 - b) Other names: Glucophage, Glumetza, Riomet, Fortamet, and Glucophage XR
- 2) Glucagon-like peptide-1 (GLP-1) receptor agonist (liraglutide, semaglutide, dulaglutide)
- 3) <u>Sodium-glucose co-transporter 2 (SGLT2) inhibitor</u> (<u>empagliflozin</u>, <u>canagliflozin</u>, <u>dapagliflozin=Farxiga</u>). reduce blood glucose by increasing urinary glucose excretion. Adverse effects include an increased incidence of genital and urinary tract infections. There are a growing number of reports of necrotizing fasciitis of the perineum (Fournier's gangrene)
- 4) <u>Sulfonylureas (Glipizide)</u>: directly stimulate release of insulin from pancreatic beta cells
- 5) <u>Dipeptidyl peptidase-4 inhibitor</u>: (e.g. <u>Januvia</u>=sitagliptin, Janumet, biguanide) Sitagliptin prolongs the action of GLP-1 (*glucagon-like peptide-1*) and GIP (*glucose-dependent insulinotropic polypeptide*). By enhancing active incretin levels, sitagliptin increases insulin production and lowers glucagon secretion from alpha cells, which decreases hepatic glucose overproduction. This results in enhancement of glucose-dependent insulin secretion, slowed gastric emptying, and reduction of postprandial glucagon and of food intake
- 6) Meglitinides: directly stimulate release of insulin from pancreatic beta cells
- 7) <u>Insulins (Long acting and short acting)</u>:
- a) <u>Lantus</u>: (Insulin glargine, Basaglar) is a long-acting insulin that starts to work 2- several hours after _{Copyrights apply}injection and keeps working evenly for 24 hours.

Renal artery involvement can lead to infarcts in the kidney



Aortic disease and embolism to affected

organs



Aortic occlusion

Aortic aneurysm

Aortic aneurysm rupture

Intestine and toe gangrene

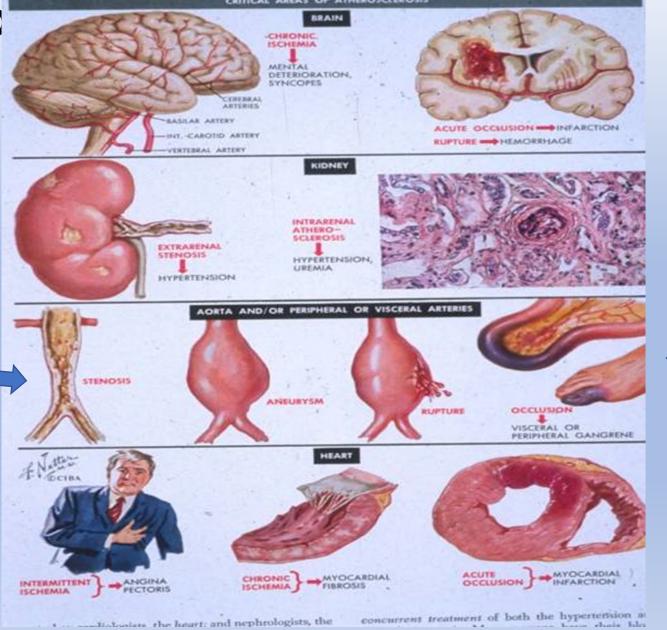
Atherosclerosis related problems depend on the

arteries invo

Aortic

occlusion or

aneurysm



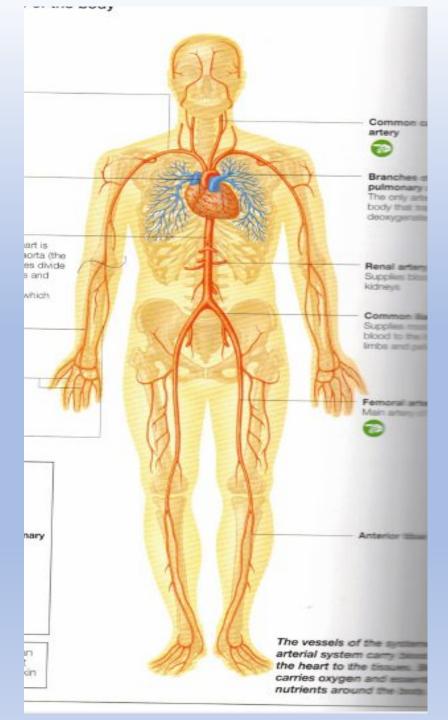
Stroke

Kidney damage

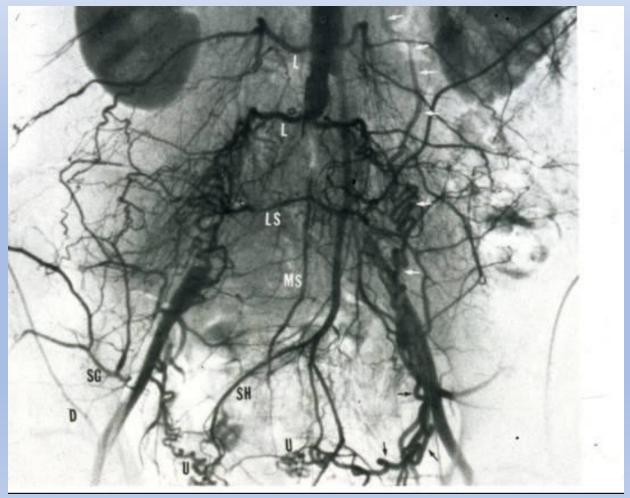
Gangrene of tissues

Myocardial infarction ("heart attack")

Normal arterial tree



Peripheral arterial disease:



Spontaneous revascularization of aortic occlusive disease.

Intermittent claudication:

- Clinical syndrome similar to angina but related to the extremities (especially legs) upon exertion. Patients experience cramping leg pain in the affected muscles upon exertion (e.g. walking up a flight of stairs).
- Caused by narrowed peripheral artery (e.g. femoral artery) which can deliver enough blood flow for resting periods, but which can not deliver the increased blood flow demands associated with exertion.

Prevention of atherosclerosis is better than treatment once you get atherosclerosis: High Blood Pressure

- Get your <u>blood pressure</u> measured either with a clinic check up, or by using a blood pressure measuring device at home (most pharmacies have these)
 - If normal, then check every 6 months.
 - If elevated then check every week and if consistently elevated, see your healthcare provider.
- Control your high blood pressure, if not with weight control, diet (including salt restriction) and exercise, then add medications to lower your blood pressure. High blood pressure usually causes no symptoms and just because you don't feel anxious doesn't mean you don't have it.

• Medications:

- Diuretics
- Direct vasodilators (including calcium channel blockers)
- Angiotensin system inhibitors (ACE inhibitors and ARBs)
- Stop medications which raise blood pressure (e.g. epinephrine-like decongestants).

<u>Prevention of atherosclerosis is better than</u> <u>treatment: High Cholesterol</u>

- High cholesterol levels are also asymptomatic. Get your blood tested, especially if there is a family history of heart disease, stroke, or sudden death.
 - If normal, then can wait to check again at your usual clinic visit.
 - If abnormal, then try diet, exercise, and if this does not work (as is often the case), then ask your clinician for medical treatment:
 - <u>Statin drugs</u> are the usual ones prescribed. Some may give you side effects such as muscle fatigue, but the doses and/or medicine types can be changed around to find what is best for you.
 - Cholesterol absorption inhibitors
 - Diet

Prevention of atherosclerosis is better than treatment:

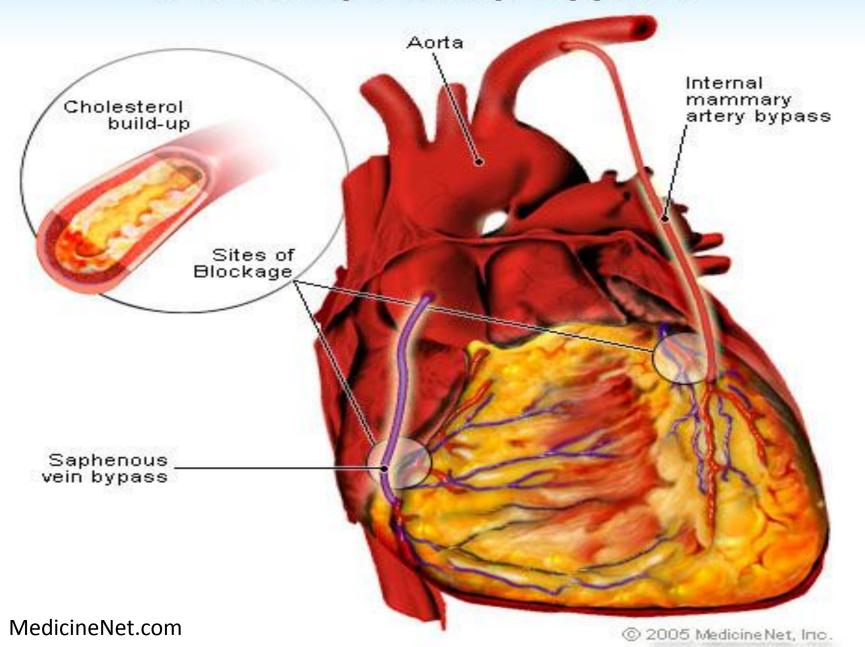
- <u>Diabetes</u> (usually Type II diabetes) is often asymptomatic or minimally symptomatic in its early stages.
 - May have frequent urination, thirst, may have light headedness, blurry vision, all of which are reversible.
 - Don't wait until you get actual arterial narrowing, kidney damage, nerve damage, etc. since these are generally NOT reversible.
- Get your blood sugar tested in the clinic, either as a fasting blood sugar, or better get a hemoglobin A1C test (a measure of blood sugar control over the past few months).
- If your blood sugar is elevated, may be able to control with weight control, diet and exercise.
- If not controlled by the above then there are a series of drugs which can be added:
 - a) Metformin
 - b) sulfonylureas and other drugs
 - c) Insulin forms (short acting and long acting)
 - d) Combinations of the above drugs

Treatments once you have significant atherosclerosis:

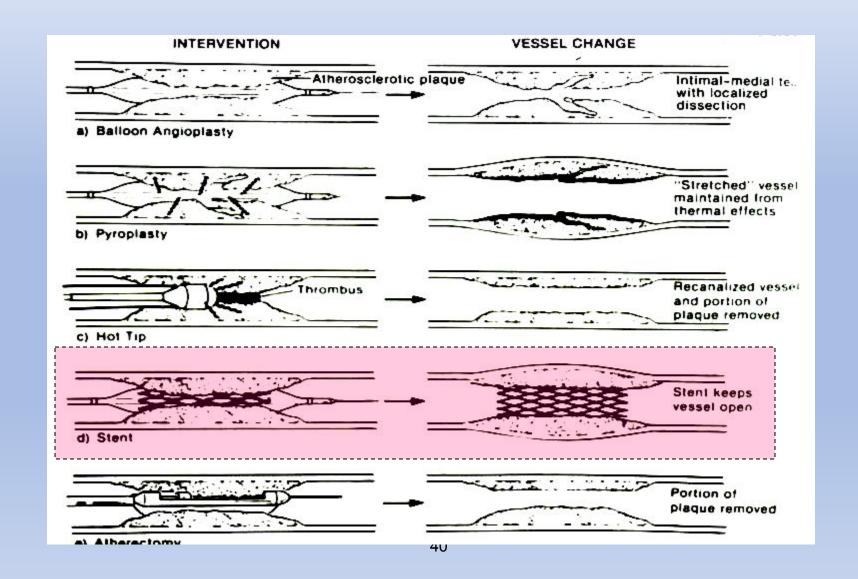
•Surgical interventions:

- Endarterectomy if very focal arterial disease
- Coronary and other arterial system angioplasty and stenting
- Bypass surgery
- Organ transplant (heart, kidney)
 - Organs are often in short supply
 - Entails a whole new set of medications and periodic studies to prevent the body from rejecting the transplanted organ
 - May eventually fail due to inflammatory rejection or to the development of "transplant arterial narrowing."

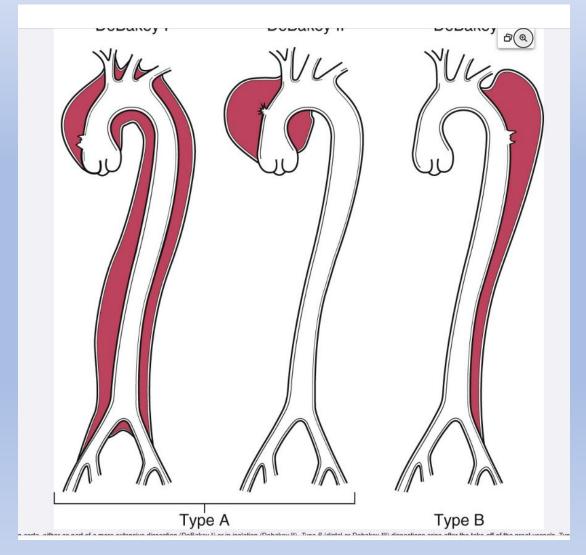
Coronary Artery Bypass



Mechanical plaque disruption / resection:



Aortic dissection: Caused mostly by uncontrolled hypertension, but also some genetic causes



Other aneurysms of the aorta:

Thoracic aortic aneurysm (TAA)

- 60% involve aortic root and/or ascending aorta, 40% involve the descending aorta
- Etiology

 Syndromic: Marfan syndrome, vascular Ehlers-Danlos syndrome, Loeys-Dietz syndrome, Turner syndrome.

 Non syndromic: bicuspid aortic valve, Sporadic TAA, familial TAA.

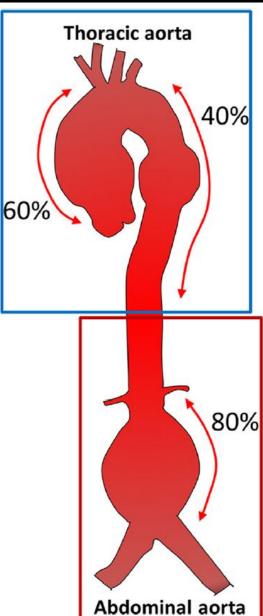
Descending .

Root and

ascending

aorta

- Atherosclerosis
- Aortitis (non-infectious): Takayasu, Giant-cell,
- Aortitis (infectious): Syphilis, mycotic
- Trauma



Abdominal aortic aneurysm (AAA)

- 80% of cases located infra renal arteries
- Etiology (The majority are atherosclerotic)
 - Atherosclerosis Risk factors
 - Smoking
 - Age
 - Hypertension
 - Hyperlipidemia
 - Male sex
 - Family history of AAA
 - Other cardiovascular disease
 - Inflammatory aneurysm, IgG4-RD,
 - Infectious aneurysm

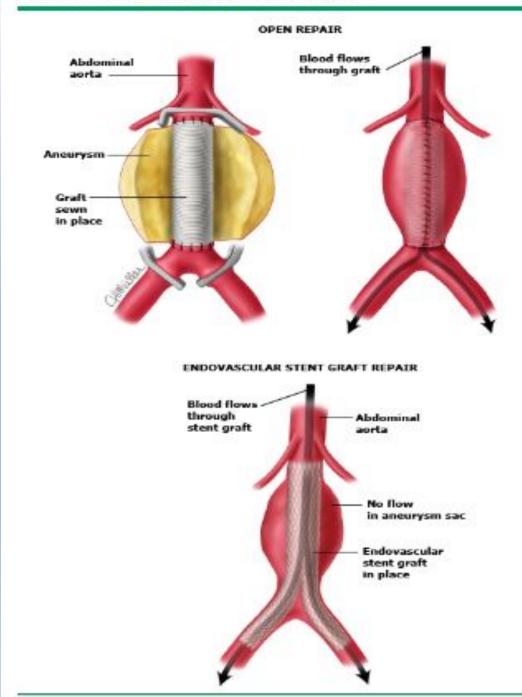
Aneurysms usually cause <u>no symptoms</u> until they burst or otherwise bleed!

- Tell my personal story with aneurysms
- These are best screened for, especially if there is any family history of aneurysms.
 - Usually, CT x-ray studies of the chest and abdomen
 - Some ultrasound methods can be used, for those near the heart.
- Usual symptoms are sudden in onset and may include:
 - Chest or back pain.
 - Fainting and collapse

• <u>Treatment</u>:

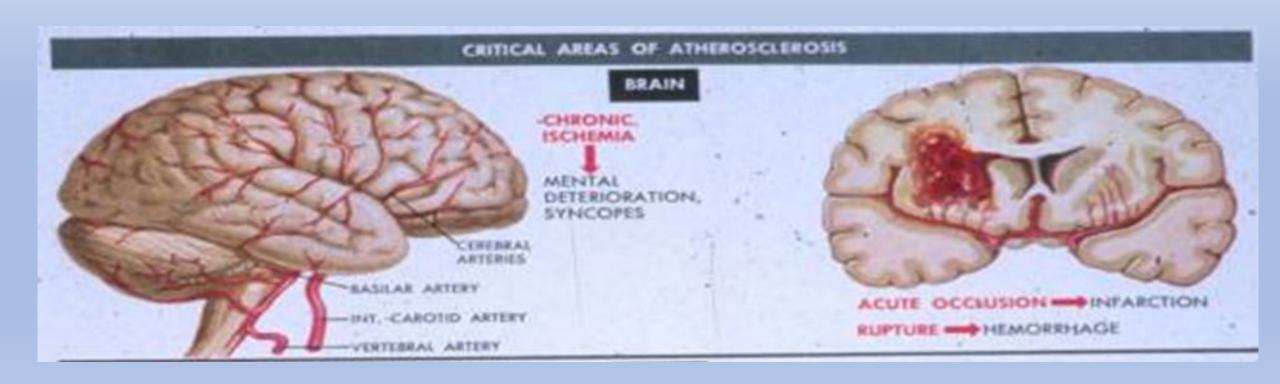
- Small aneurysms can be followed over time and if they enlarge (to ~5 cm diameter for the aorta) should be pre-emptively surgically corrected. Some amenable to stents, others need open graft replacement.
- No heavy lifting (e.g., less that 10-15 pounds) and keep your blood pressure low.

Abdominal aortic aneurysm repair



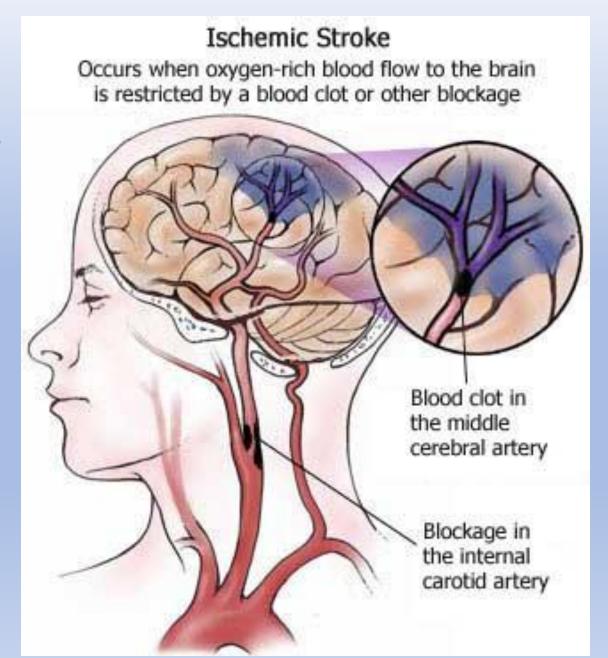
UpToDate 2018

Cerebral artery involvement can lead to brain strokes and hemorrhages.



Cerebral infarction = Stroke:

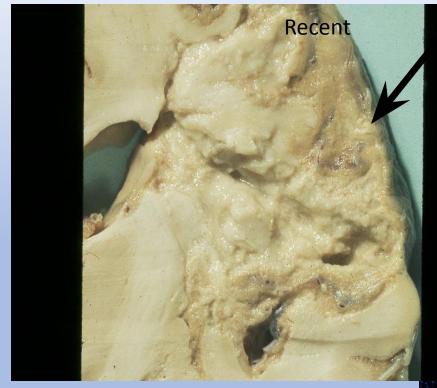
Cerebrovascular disease: the third leading cause of death in the U.S. Such infarcts of brain tissue are caused by carotid or cerebral artery occlusion due to atherosclerosis and thrombosis.







Cerebral infarction=Stroke:



Here are some examples of old and recent cerebral infarcts.

http://www.path.sunysb.edu/faculty/woz/NPERESS/webclass.htm



<u>Danger signs that you may be having a stroke</u>:

- Sudden arm or leg or other numbness
- Sudden slurring of speech
- Facial droop and drooling
- Sudden fall from leg weakness
- New onset seizure.

• If you have any of these, get to a hospital ASAP since they may be able to open the blocked artery to your brain and salvage much brain tissue (leading to much lesser disability).

Biological mechanisms for benefit of exercise

Ant	tiatherogenic effects
	Reduction of adiposity, particularly in those with excess upper body and abdominal fat
8	Reduction of elevated blood pressure
	Reduction of elevated plasma triglycerides (and associated small dense LDL particles)
3	Increase in HDL cholesterol levels
	Improvement in insulin sensitivity and glucose use and reduction in risk of type 2 diabetes
Ant	tithrombotic effects
En	dothelial function alteration
Aut	tonomic functional changes
Ant	ti-ischemic effects
Ant	tiarrhythmic effects

Also reduction in general inflammation.

LDL: low-density lipoprotein; HDL: high-density lipoprotein.

Reproduced with permission from: Fletcher GF, Balady GJ, Amsterdam EA, et al. Circulation 2001; 104:1694.



The importance of having a primary care doctor:

- This is the doctor who puts your whole medical situation together and knows your overall health status.
- Arranges for you to see specialists as needed.
- Will follow established guidelines for specific screening tests (e.g., blood tests, imaging studies, screens for depression/anxiety)
- Integrates all your medications and along with the pharmacy (best to have only one pharmacy) looks our for medication interactions that may be harmful.

Don't wait for symptoms to occur, get a primary care doctor today (if you don't already have one).

Questions: