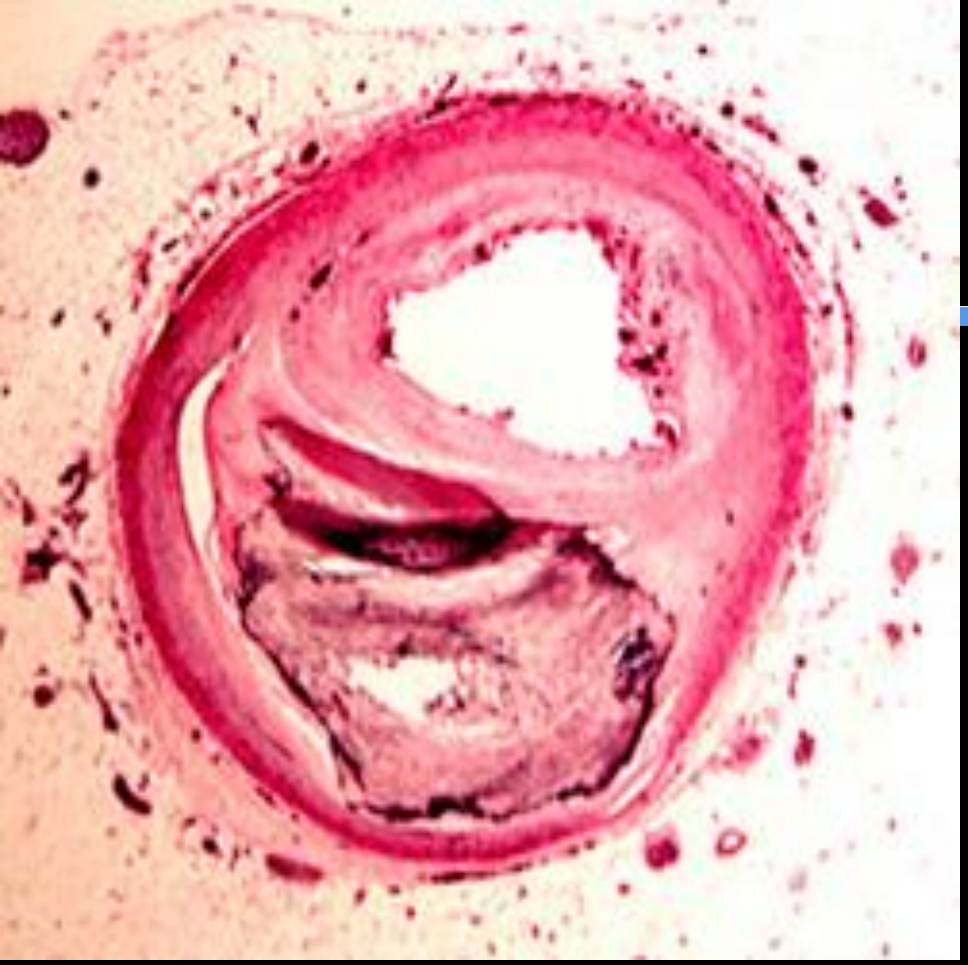


New Pathways in Lipid Care: Navigating the Latest Guidelines

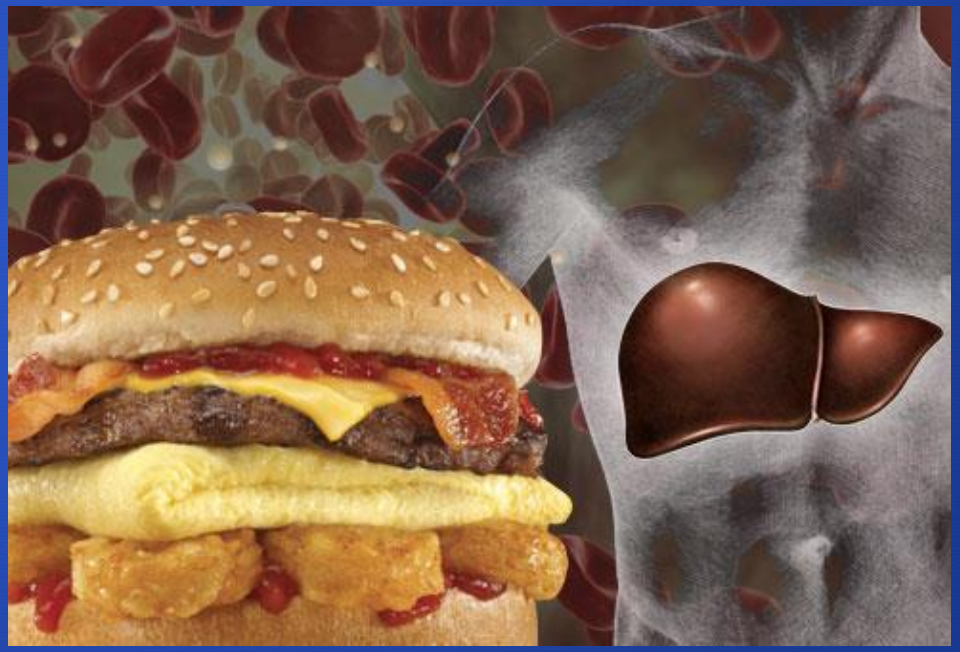
Harry Balian, MD, FACC, FSCAI
Armenian American Medical Society
September 2018

Disclosures

Nothing to disclose

Definition

- Cholesterol is a fatty substance manufactured in the liver and is carried throughout the body in the bloodstream.

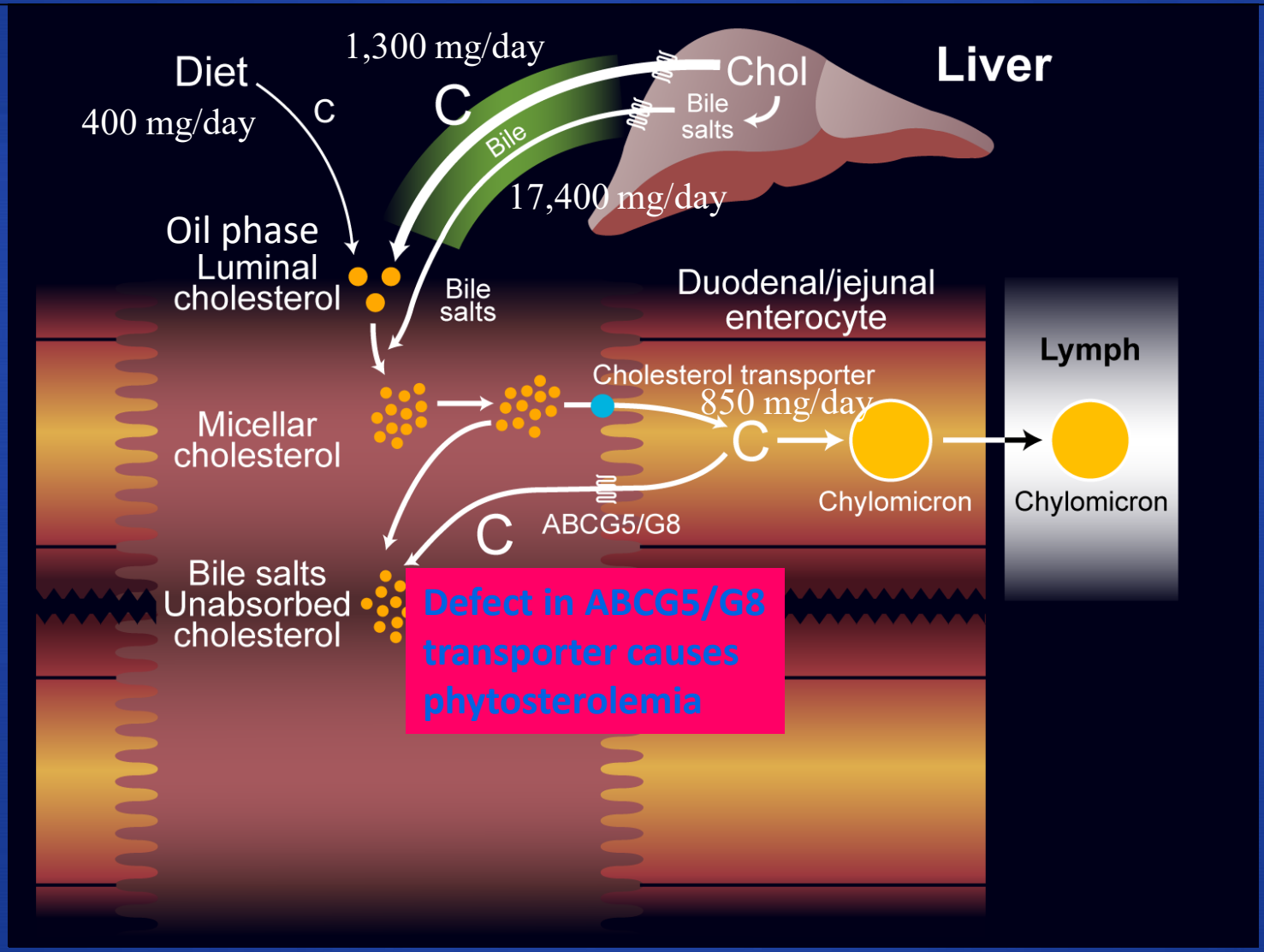


"I'M PUTTING YOU ON A 'WHATEVER TASTES GOOD, DON'T EAT IT' DIET."

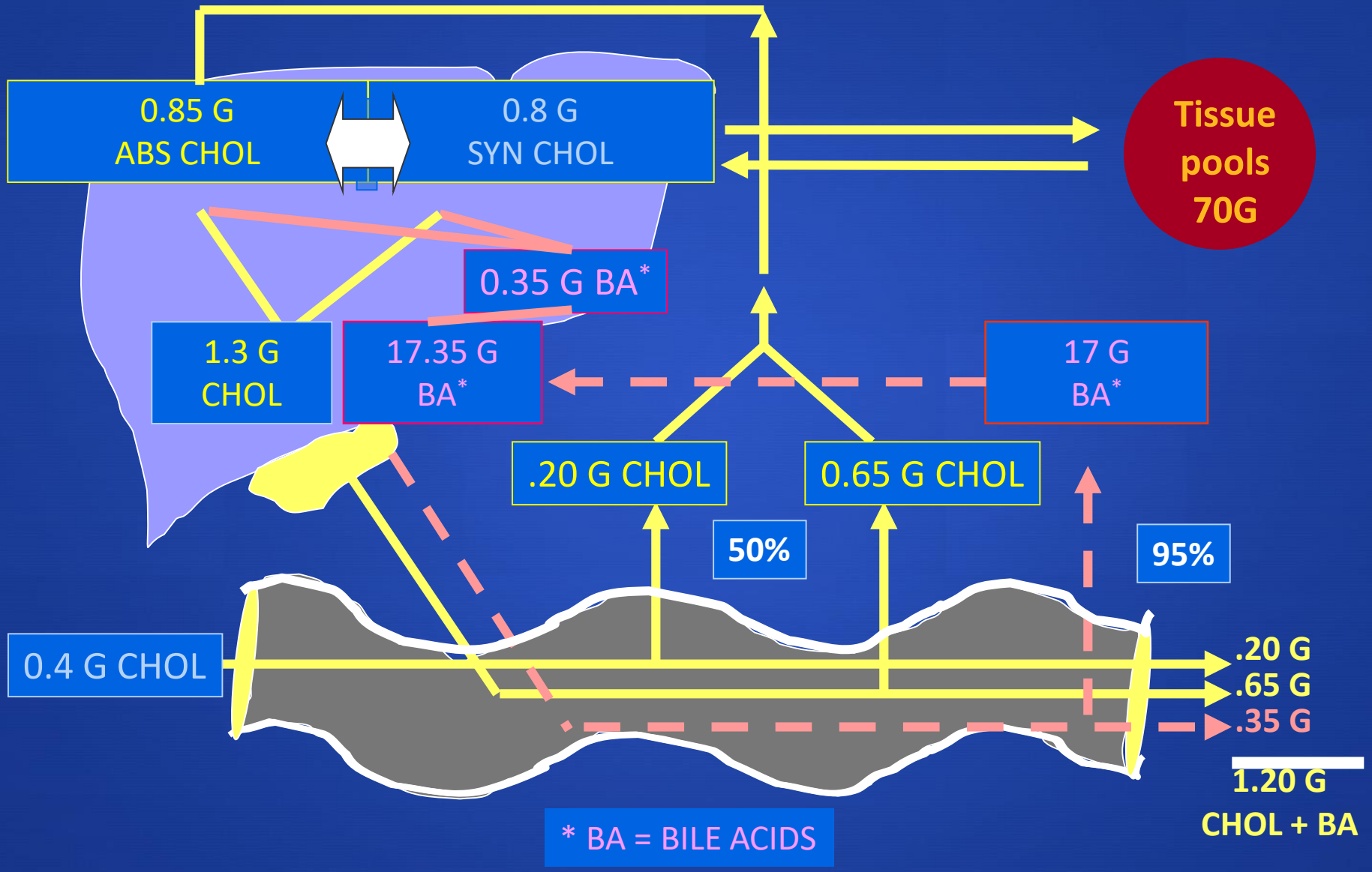
NORMAL CHOLESTEROL METABOLISM

- Synthesis
  - Primary synthetic sites are extrahepatic, but liver is key regulator of homeostasis
- Absorption
  - Largest source is biliary secretion, not diet.
  - Normal absorption: 50%
  - For cholesterol to be absorbed it must:
    - undergo hydrolysis (de-esterification by esterases)
    - be incorporated into micelles
    - be taken up by cholesterol transporter
    - be re-esterified and incorporated into chylomicrons

NORMAL CHOLESTEROL ABSORPTION



NORMAL CHOLESTEROL METABOLISM



Why High Cholesterol Matters

- High cholesterol is one of the major risk factors for coronary artery disease, heart attacks, and strokes. It also appears to boost the risk of Alzheimer's disease.
- High cholesterol leads to a buildup of plaque that narrows the arteries. The most dangerous or rupture-prone plaques are caused by lesions that were less than 70% stenotic and not by those with the most severe narrowing.

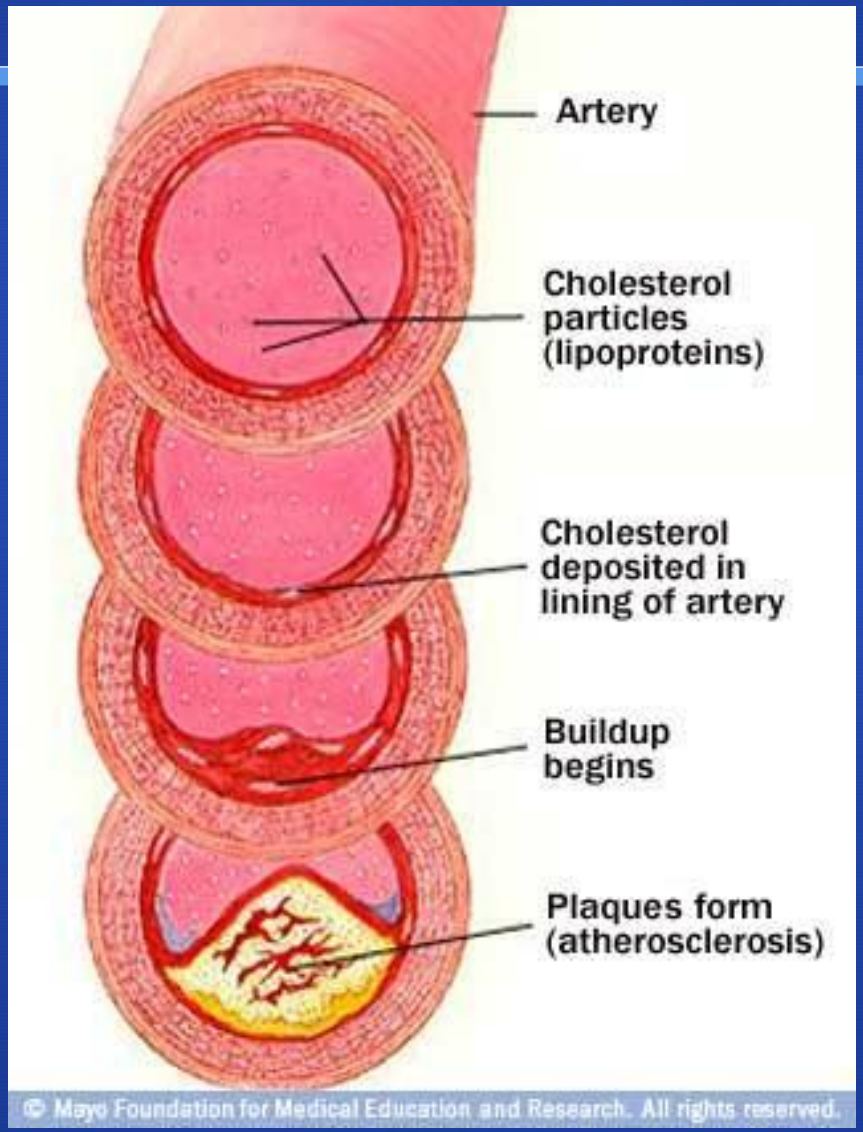
Prevalence

- About 50% of U.S. adults have an elevated total cholesterol level
- Majority of patients with atherosclerosis have some form of dyslipidemia
- 70-80% of individuals with dyslipidemia do not meet LDL cholesterol targets despite lipid therapy

Symptoms

- High cholesterol does not cause any symptoms.
- Too much cholesterol may lead to a buildup of plaque inside the arteries.
- This is known as atherosclerosis, a condition that causes narrowing of the space available for blood flow

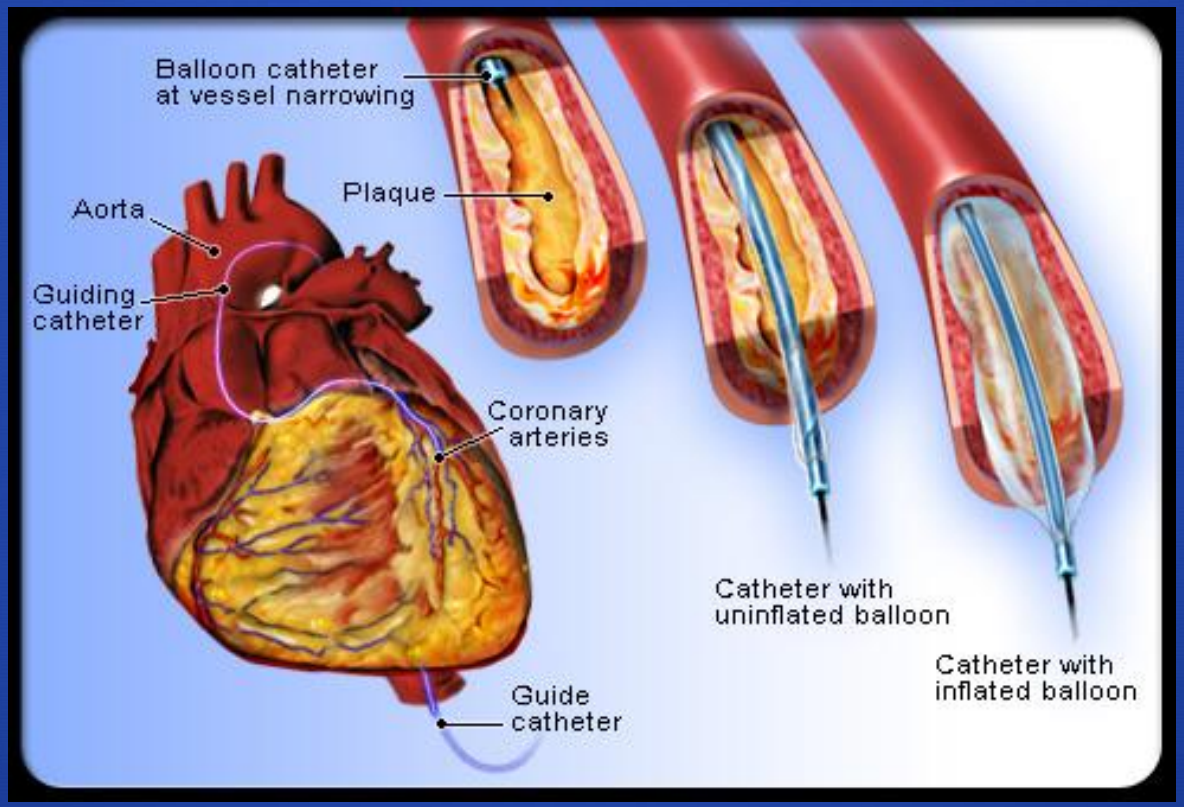
Development of Atherosclerosis



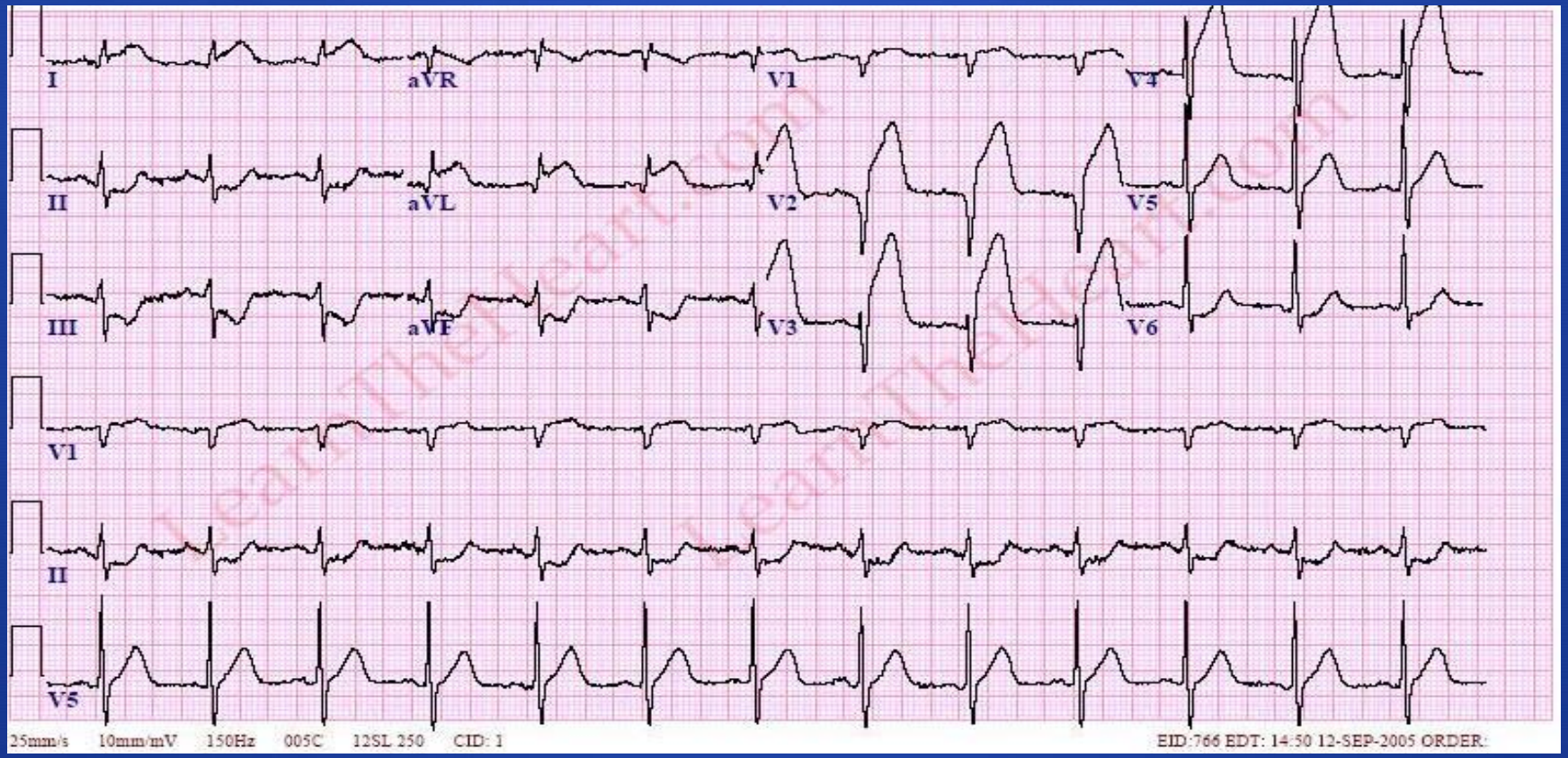
Atherosclerosis

- Leading cause of morbidity and mortality in the U.S.
- Accounts for more than 1/3 of all deaths each year
- About 13 million Americans have coronary heart disease (CHD)
- Dyslipidemia is the most prevalent and important modifiable risk factor for atherosclerosis

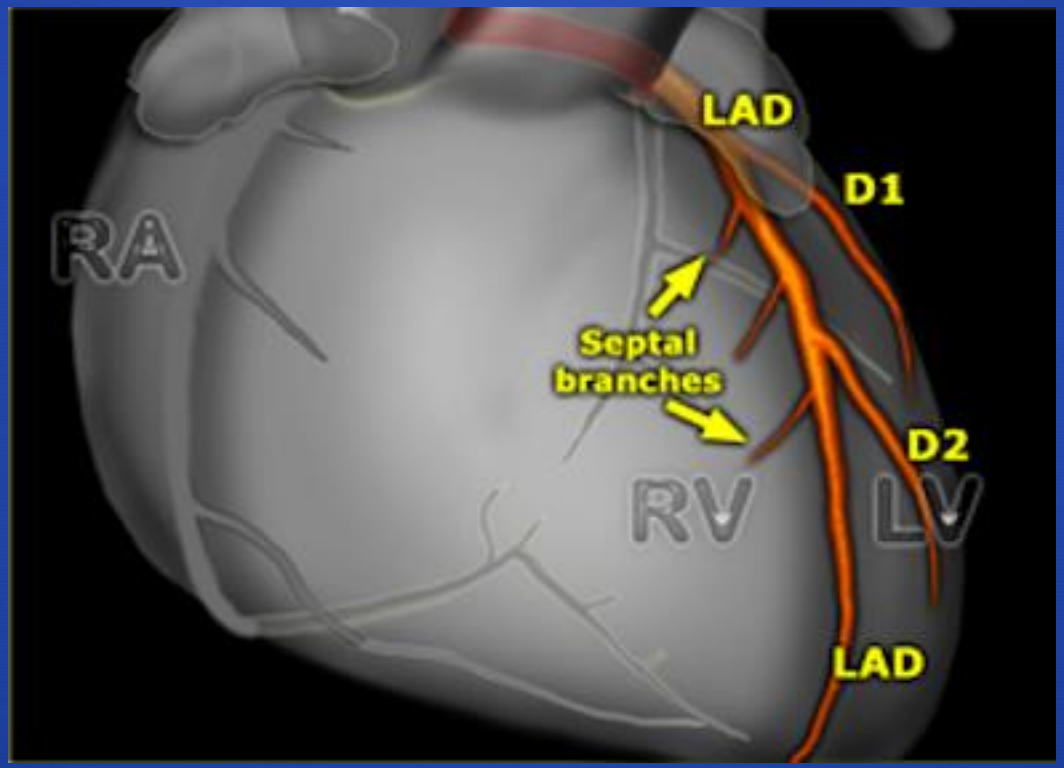
Coronary Artery Disease



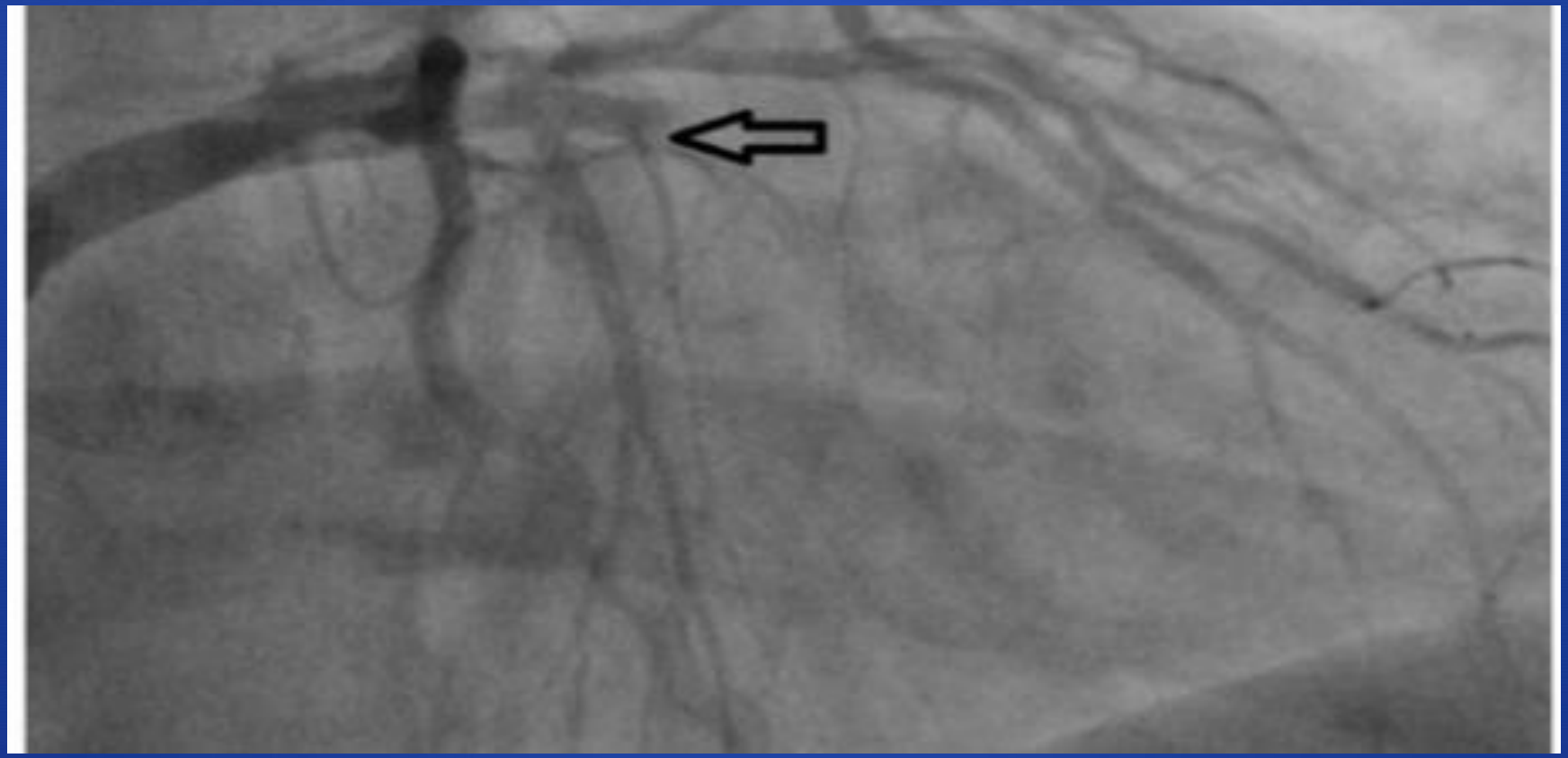
Acute Anterior MI

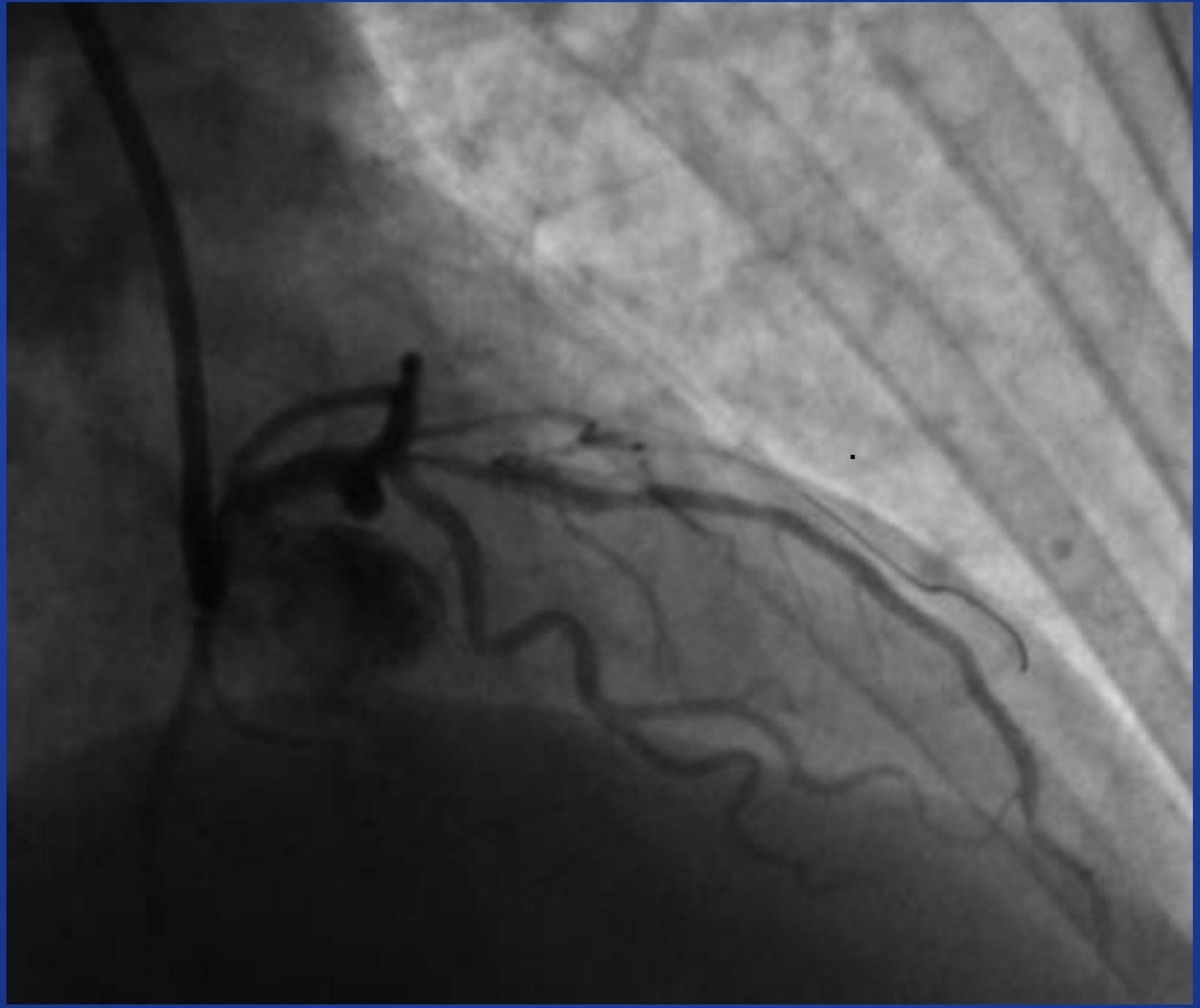


LAD anatomy

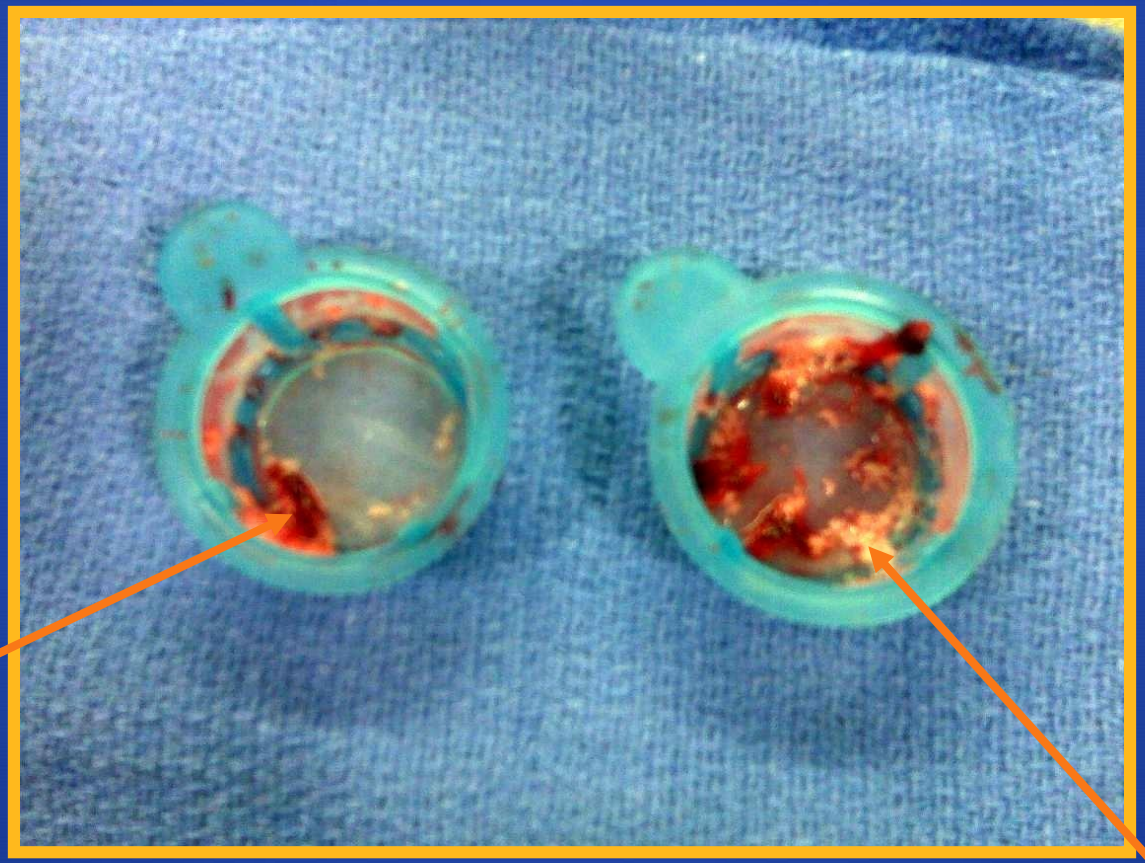


Emergent Cath



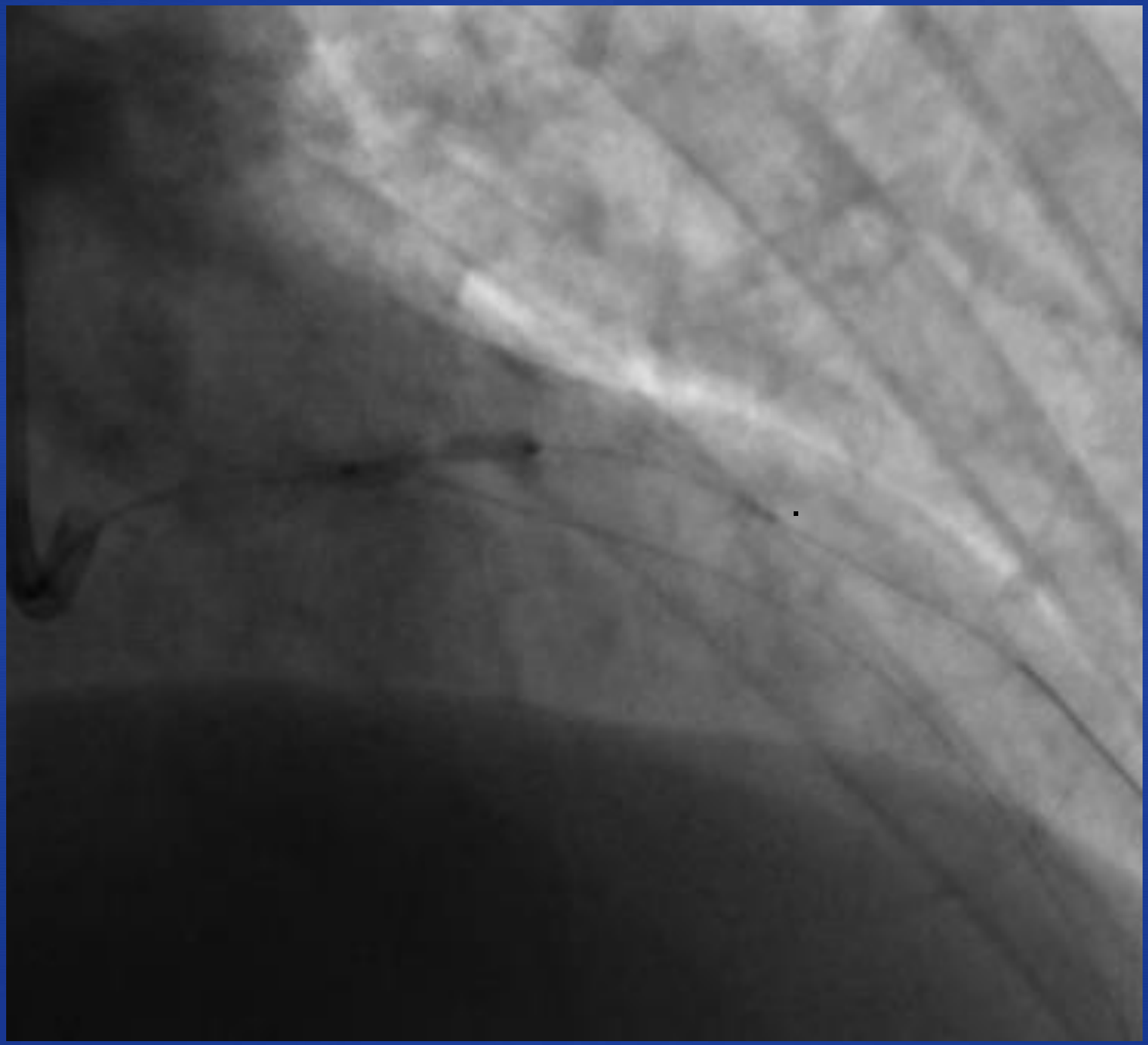


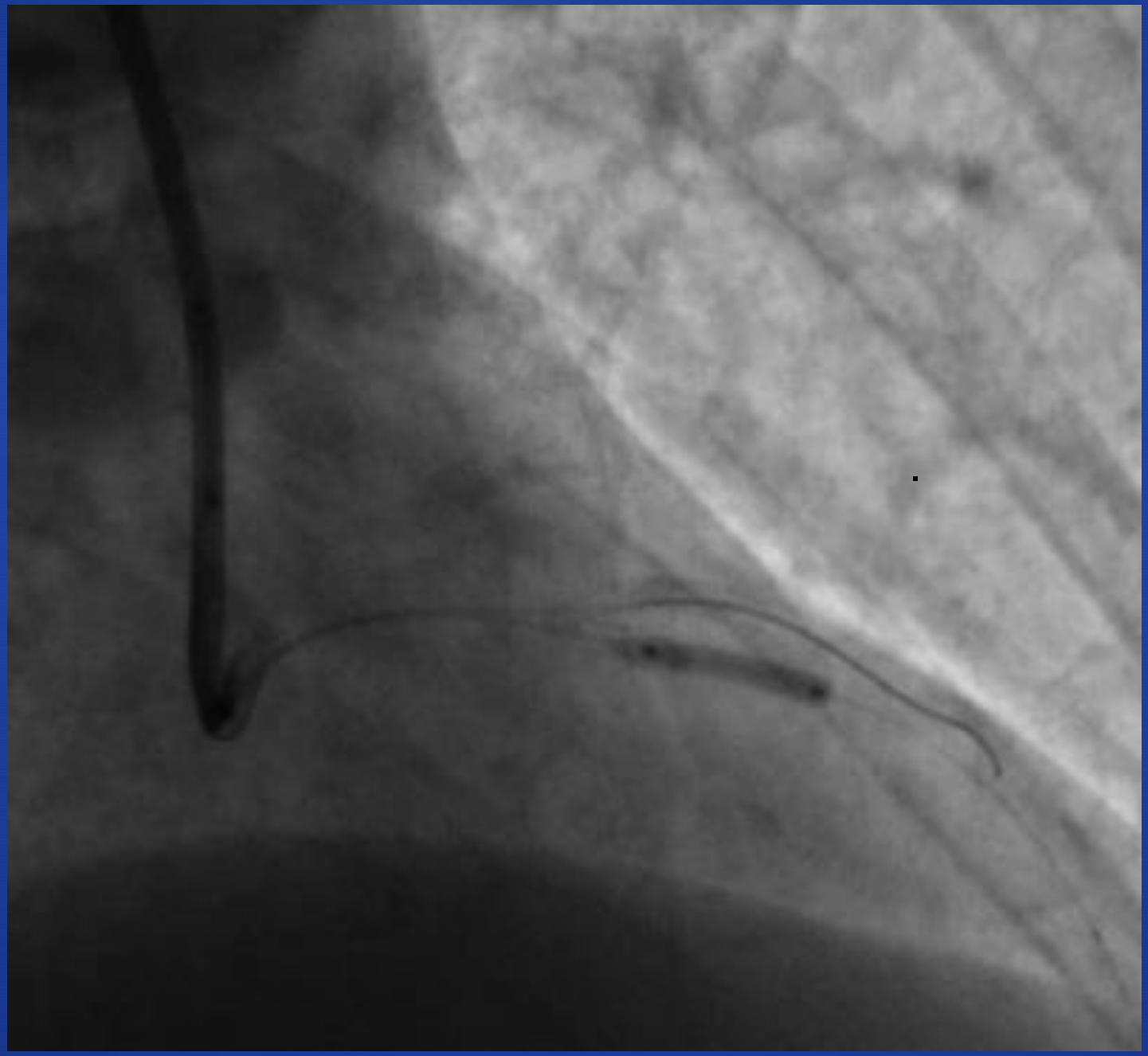
fatty deposits and clots removed from coronary arteries during the myocardial infarction



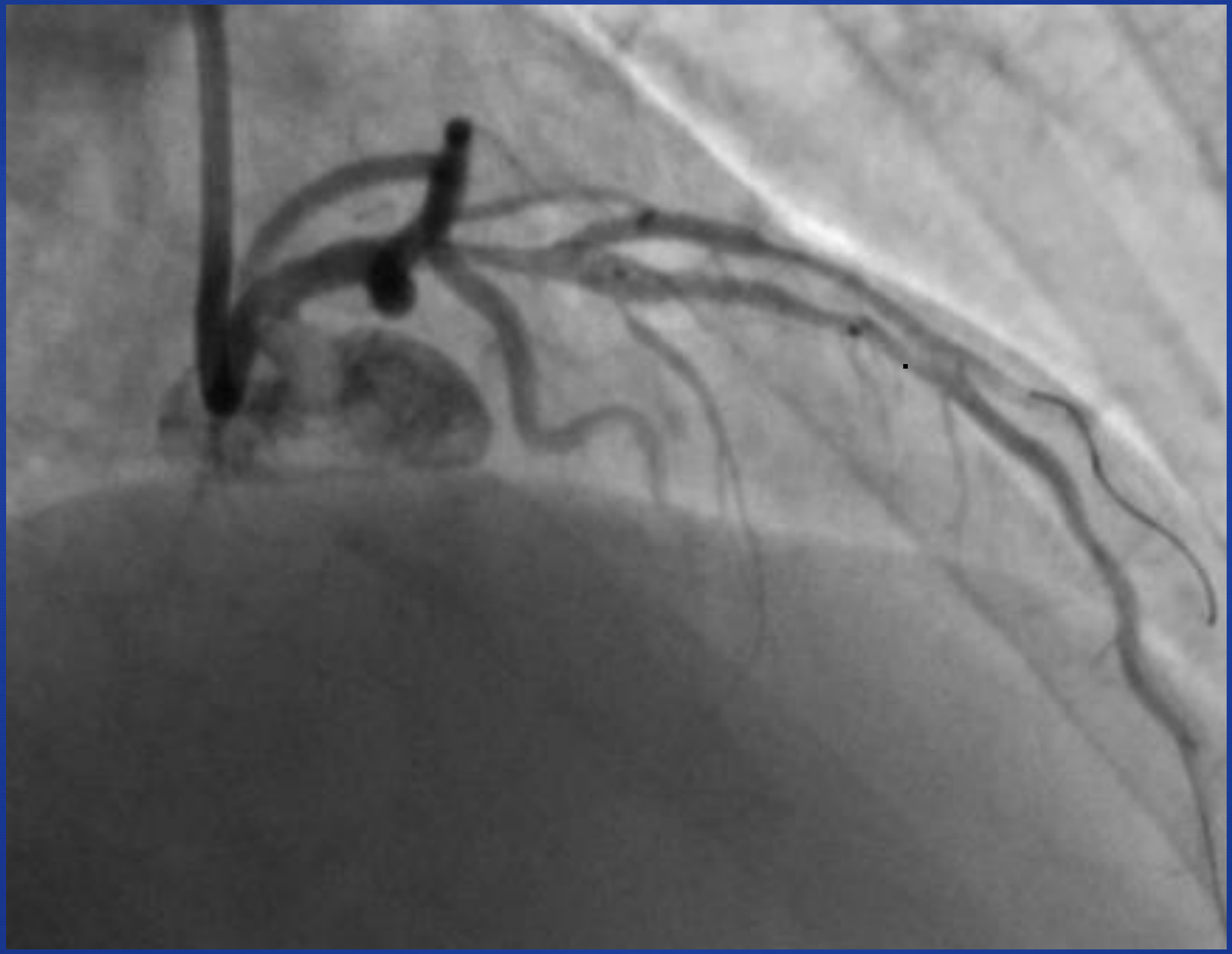
CLOTS

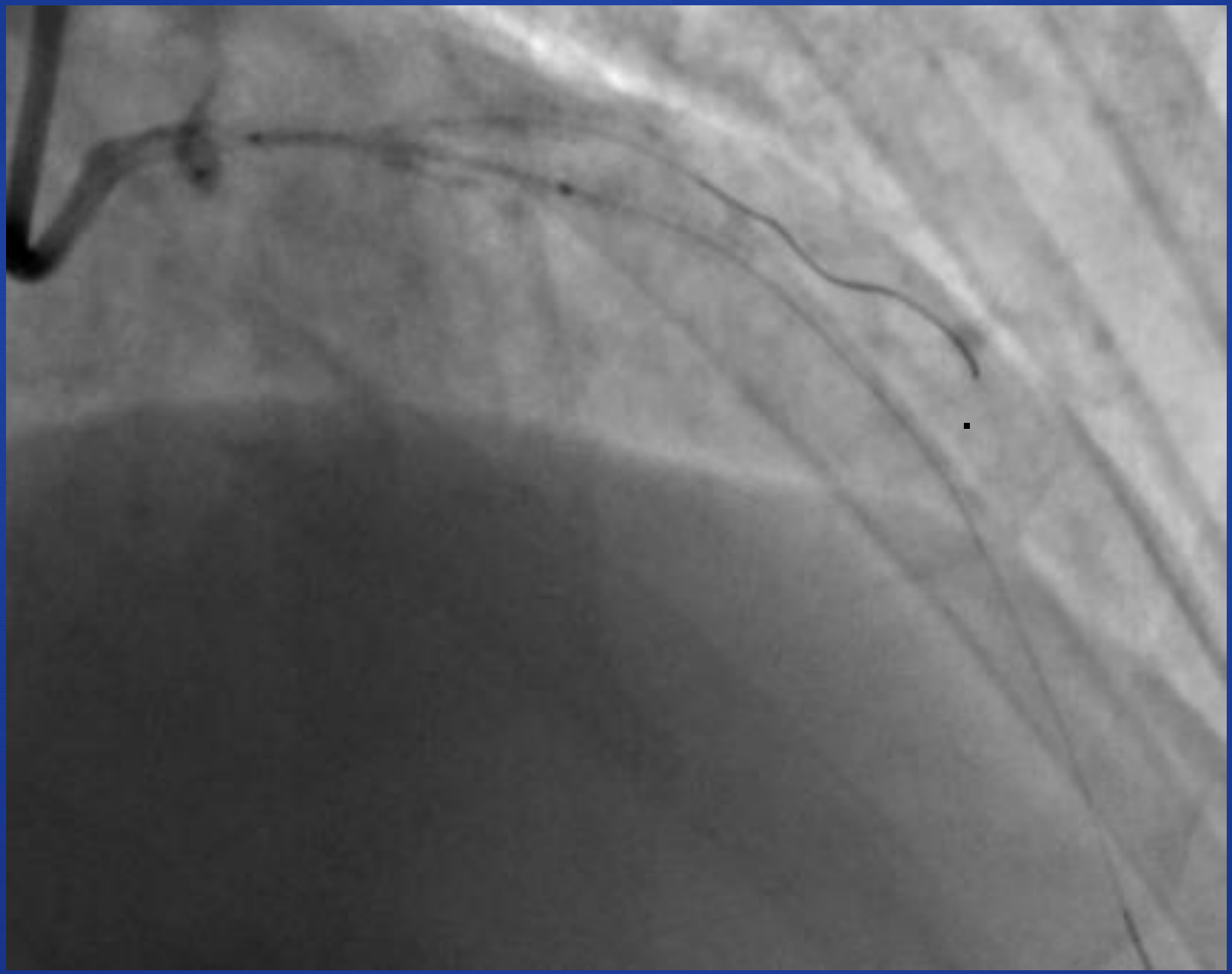
FATTY DEPOSITS

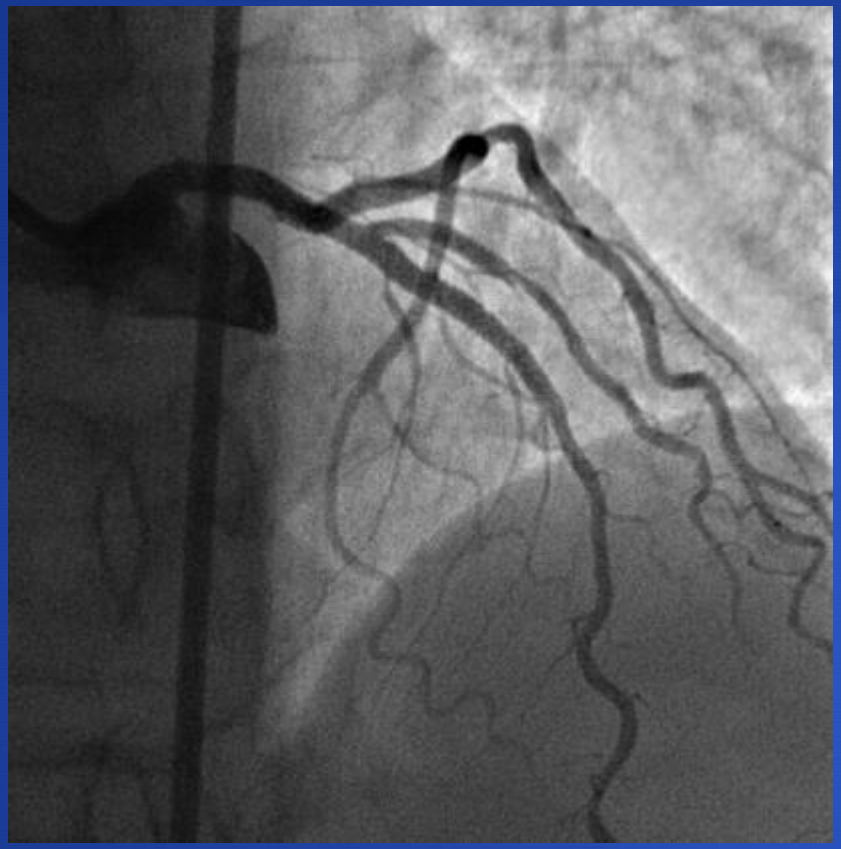


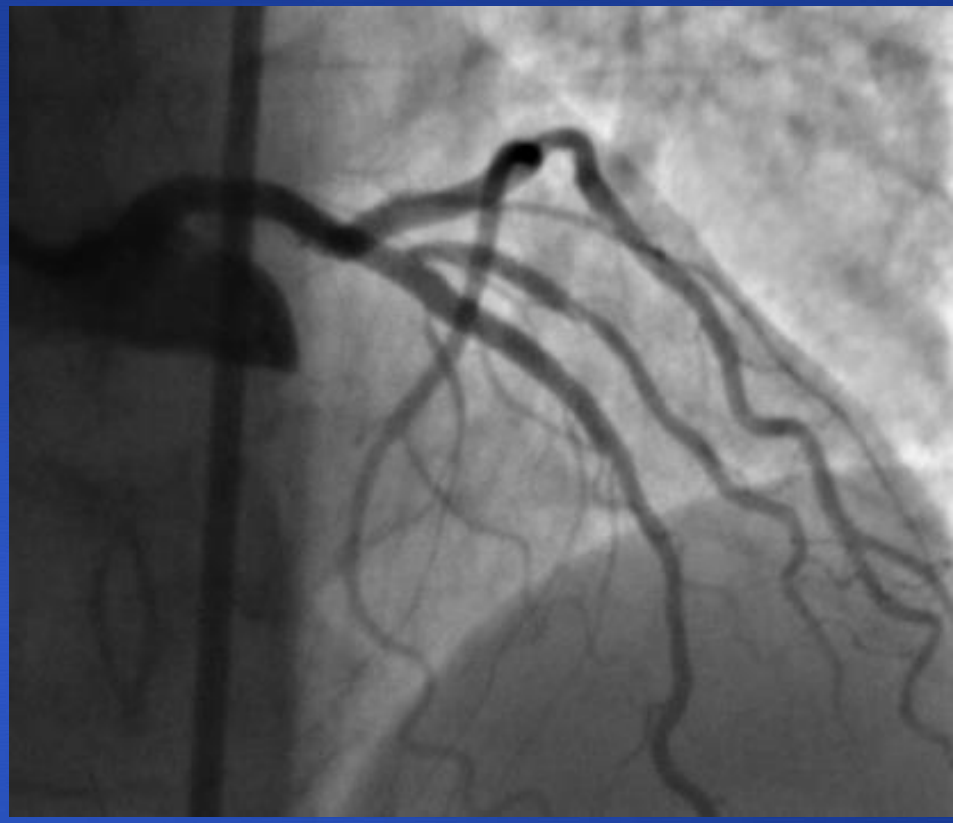


Treated with coronary stents





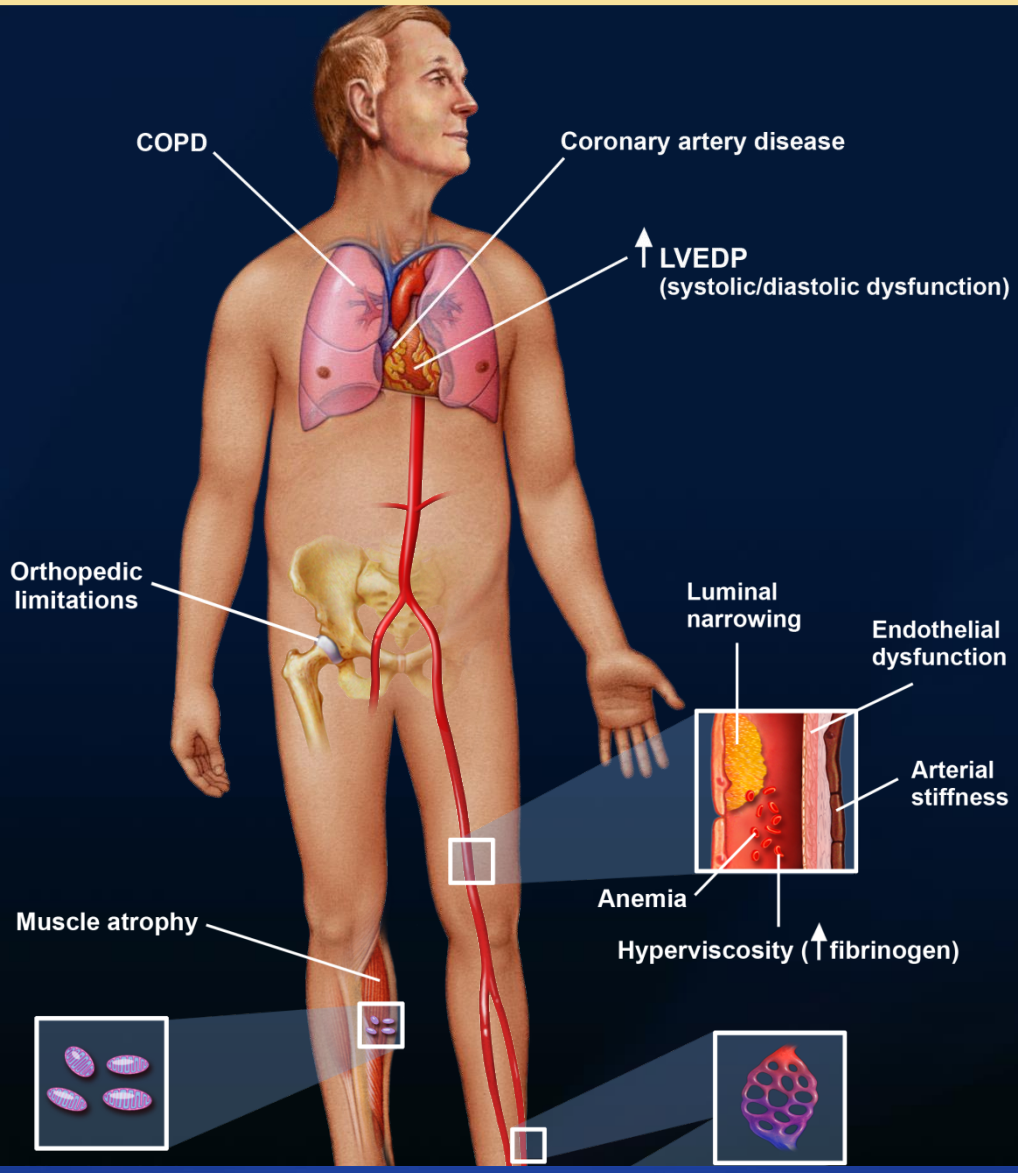




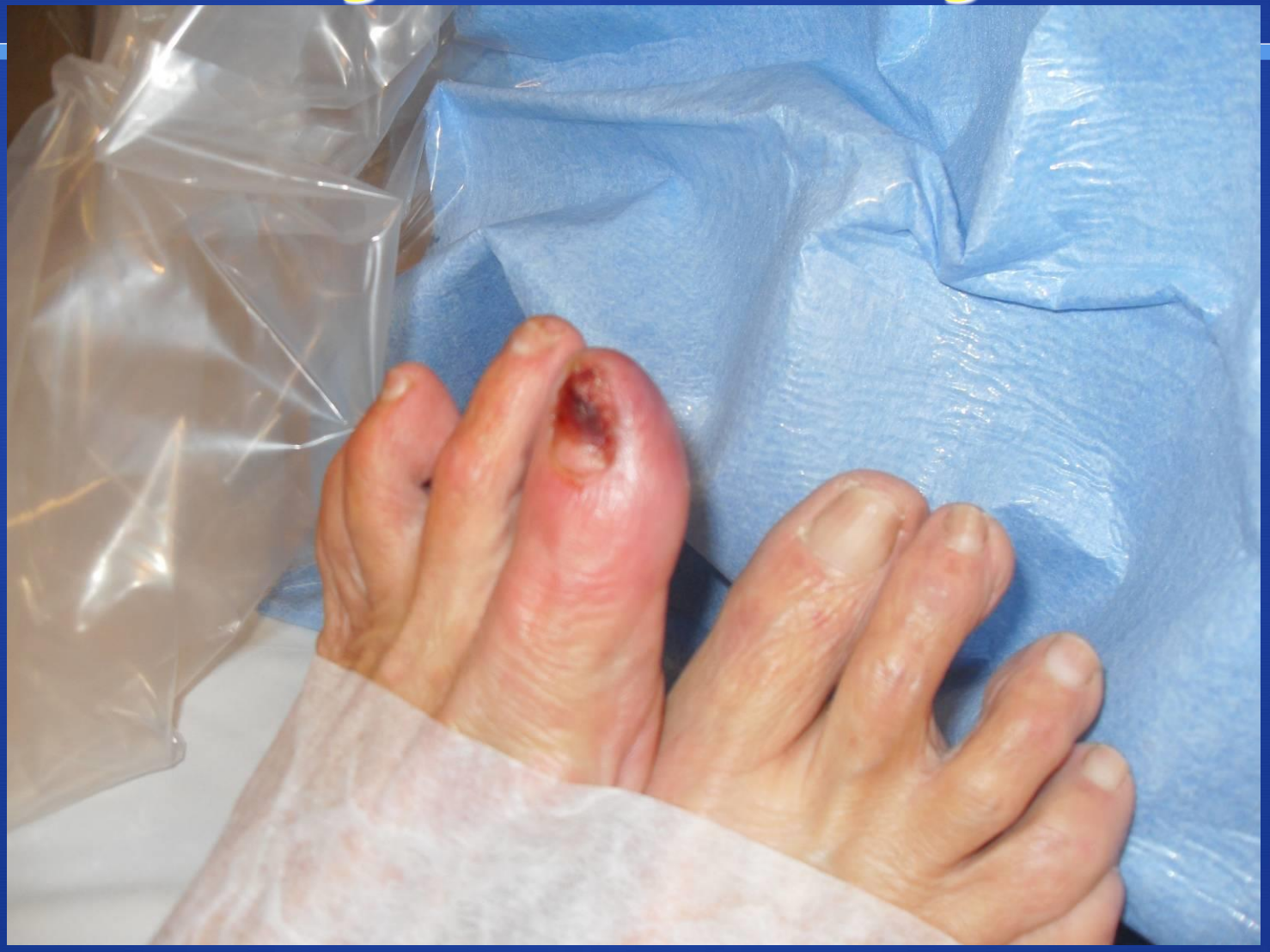
Risk Factors for PAD

- *Male gender*
- *Older age*
- *Hyperhomocysteinemia*
- *Lp(a)*
- *Tobacco*
- *High TG level*
- *DM*
- *HTN*

Functional impairment in PAD

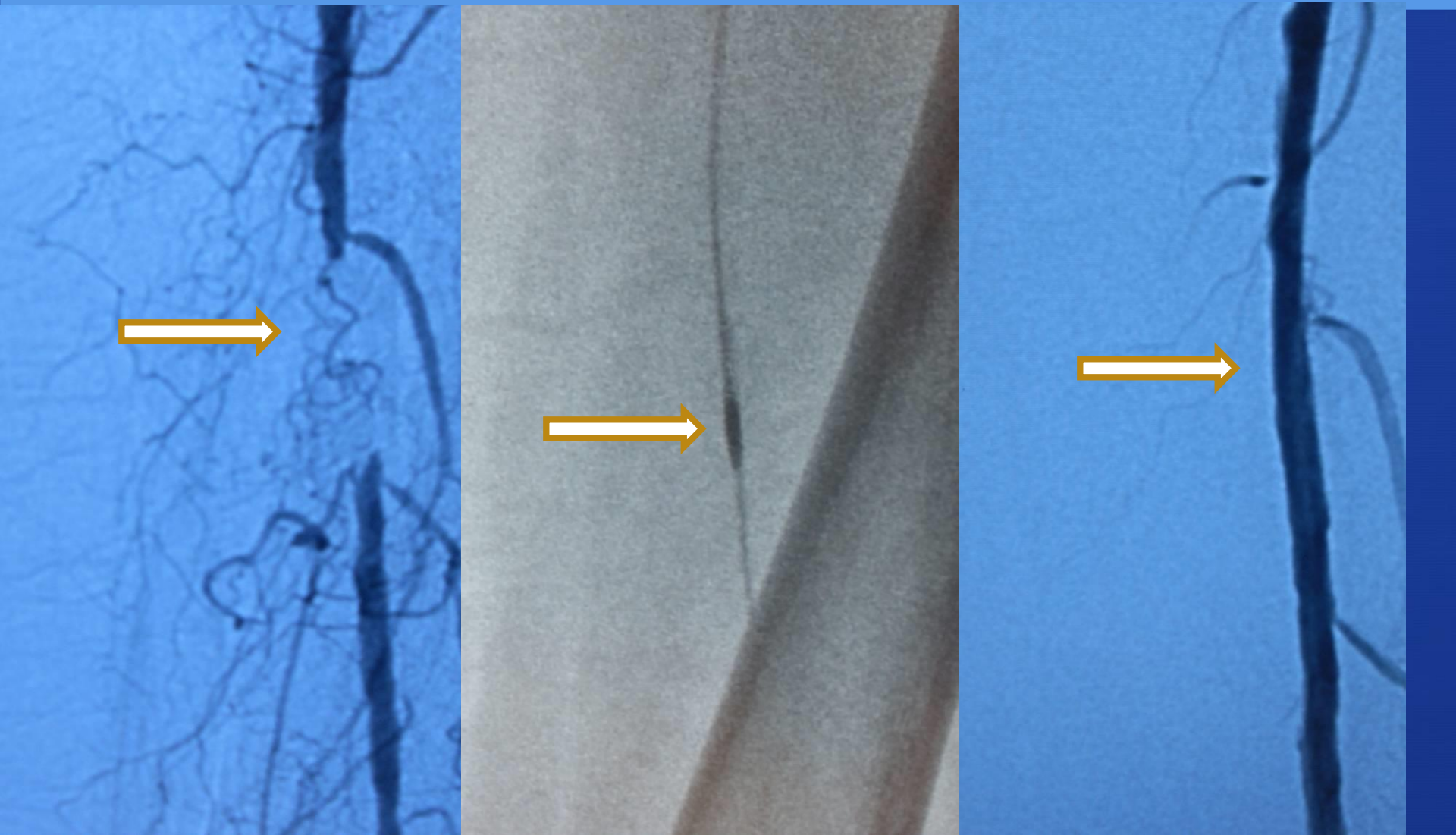


Left Big Toe Non Healing

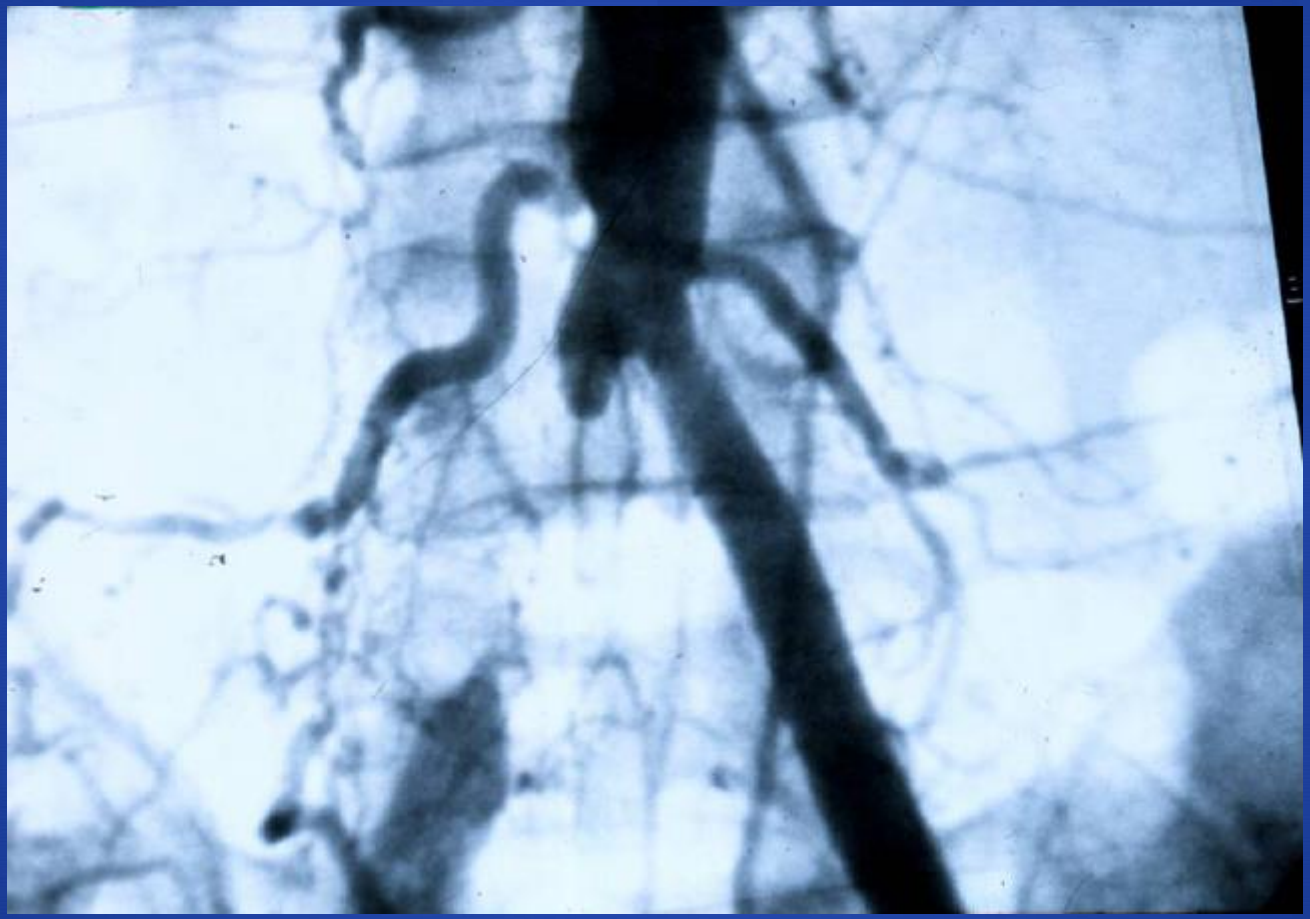


Calcified SFA debulked with a 2.25 Solid Crown.
50-75% of the Calcium/Plaque removed to change the Vessel compliance.
Followed by a low pressure balloon

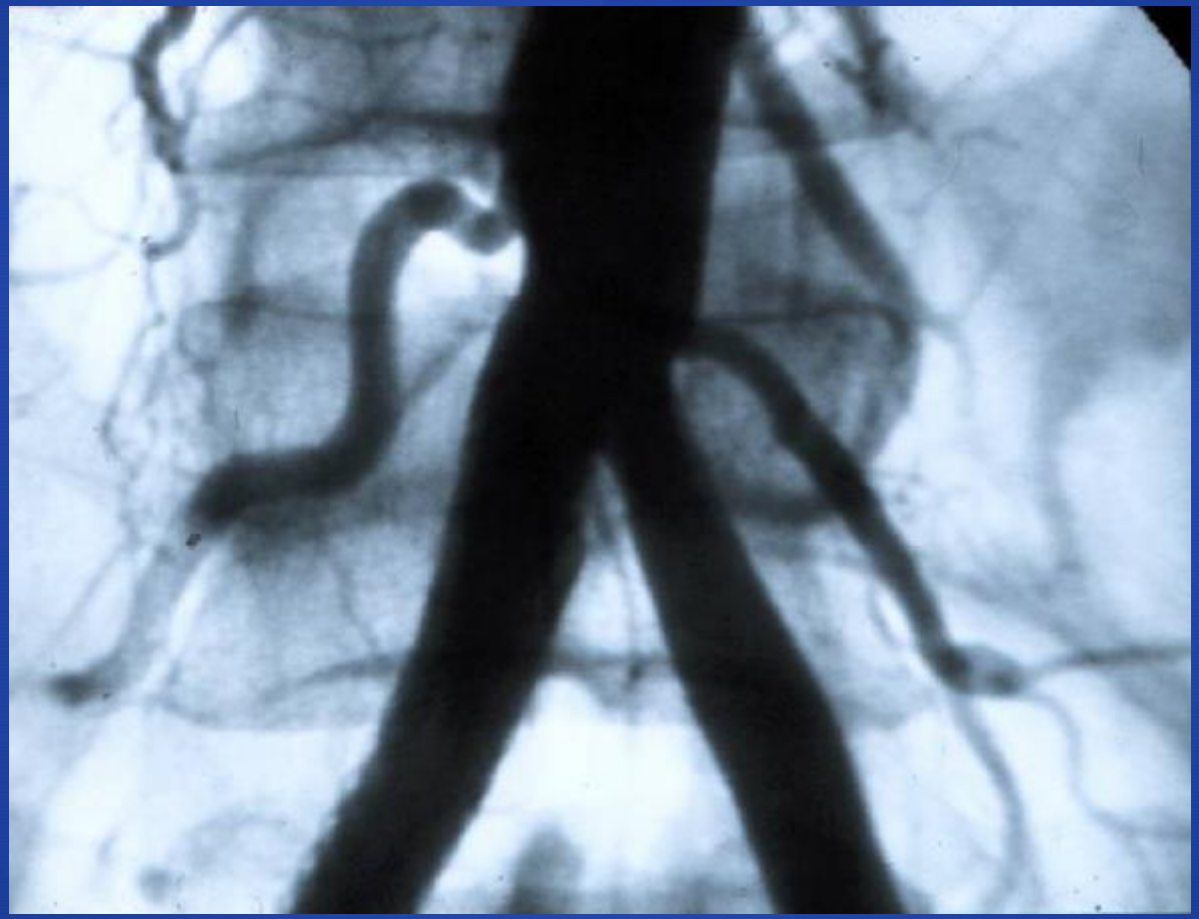
No Stent.



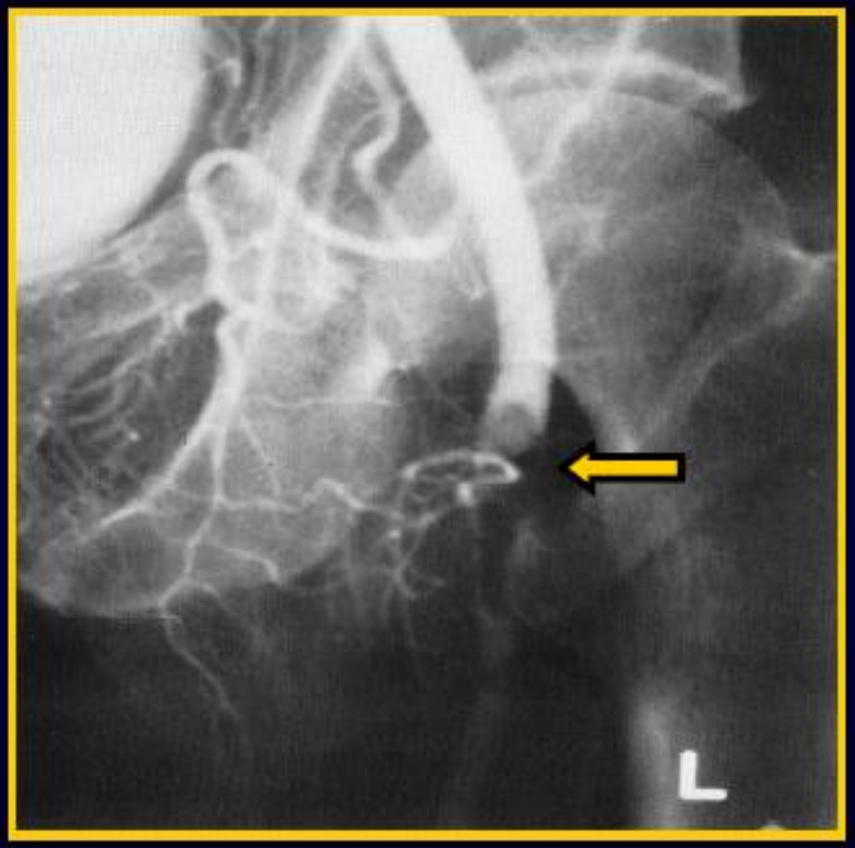
64 y/o diabetic male w/ acute R thigh/buttock pain with pulseless R leg

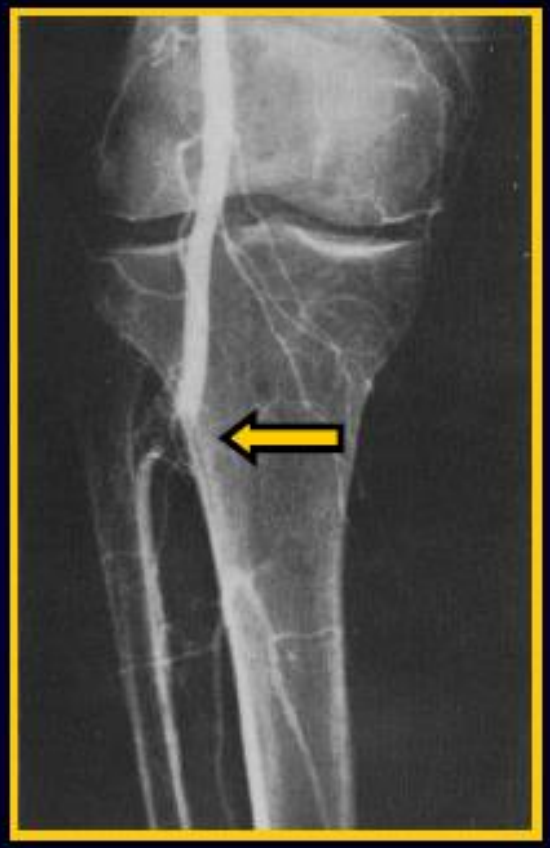


s/o PTA and Stenting of the common iliac artery-pt’s sxs resolved



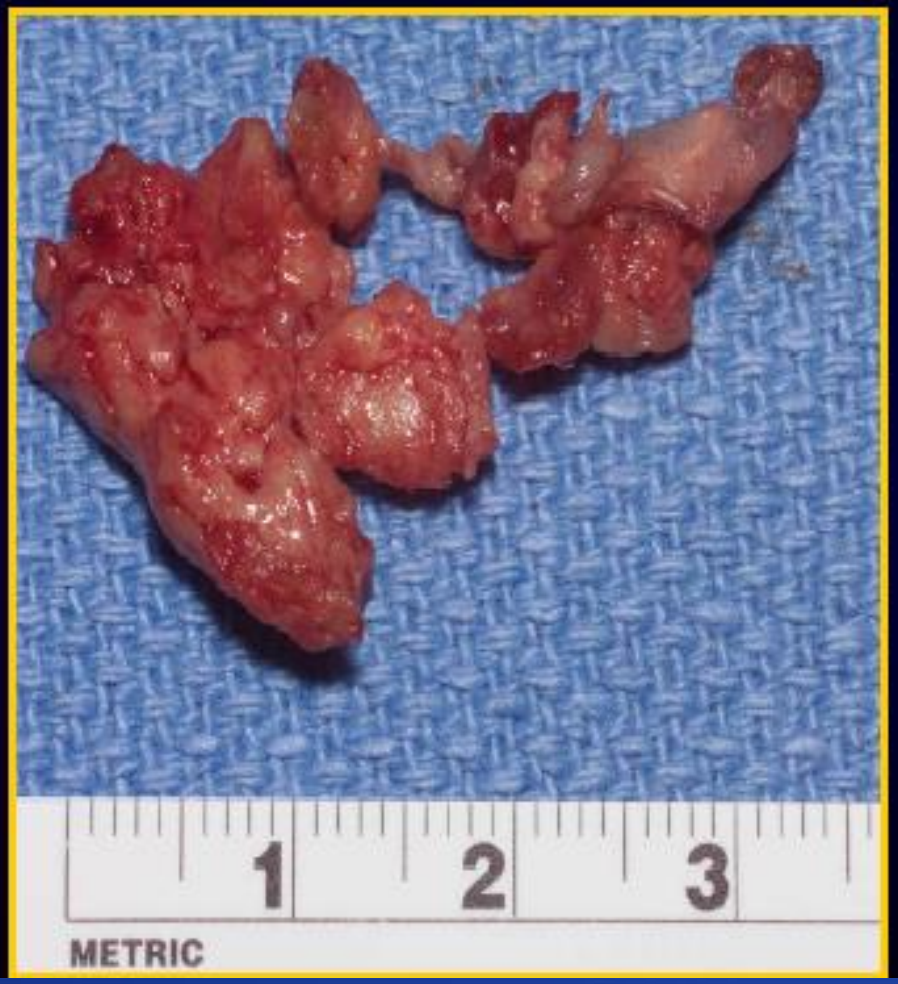
Angiogram





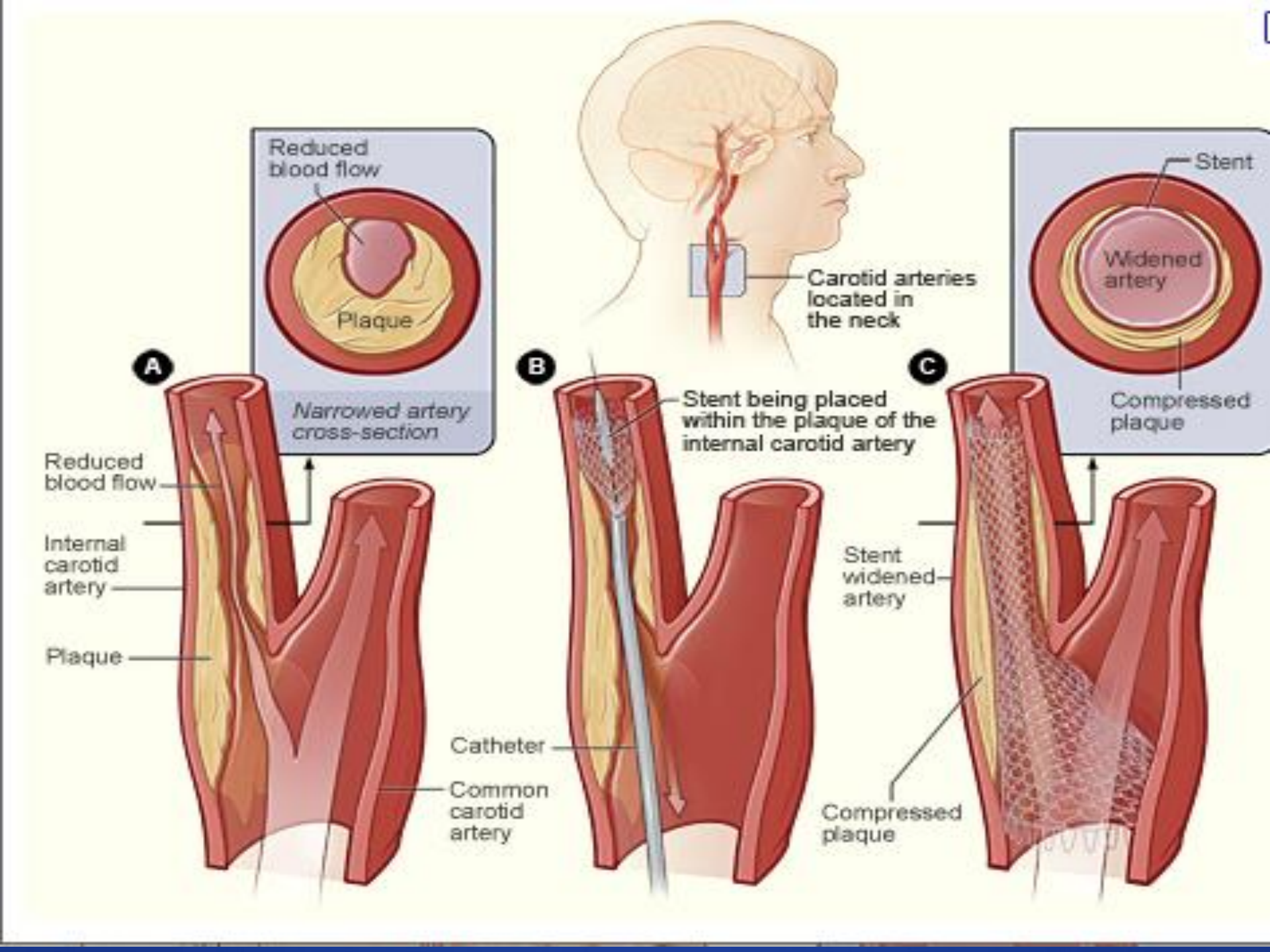
- Abrupt cut off (meniscus)
- No collaterals

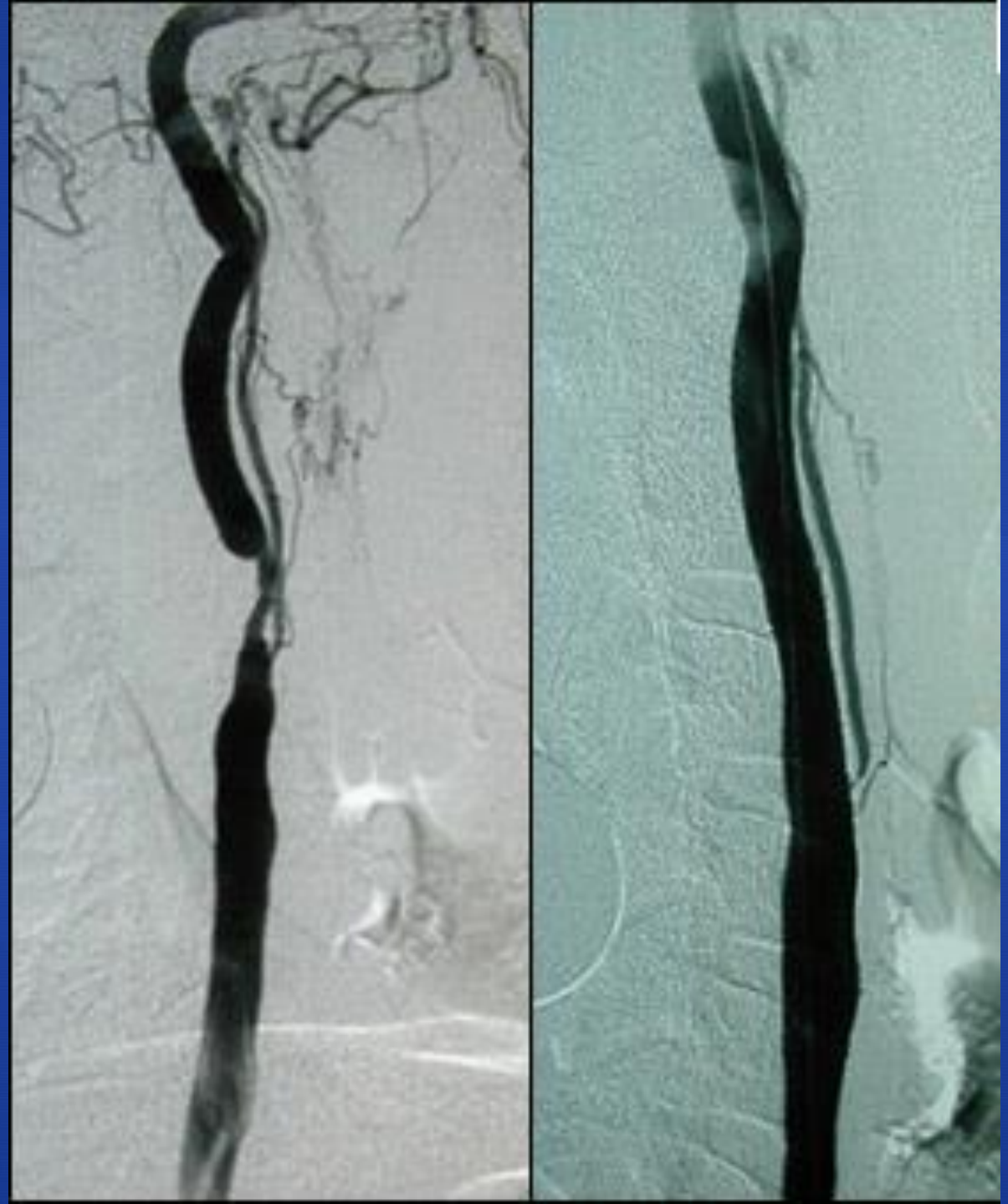
Thromboembolic Material

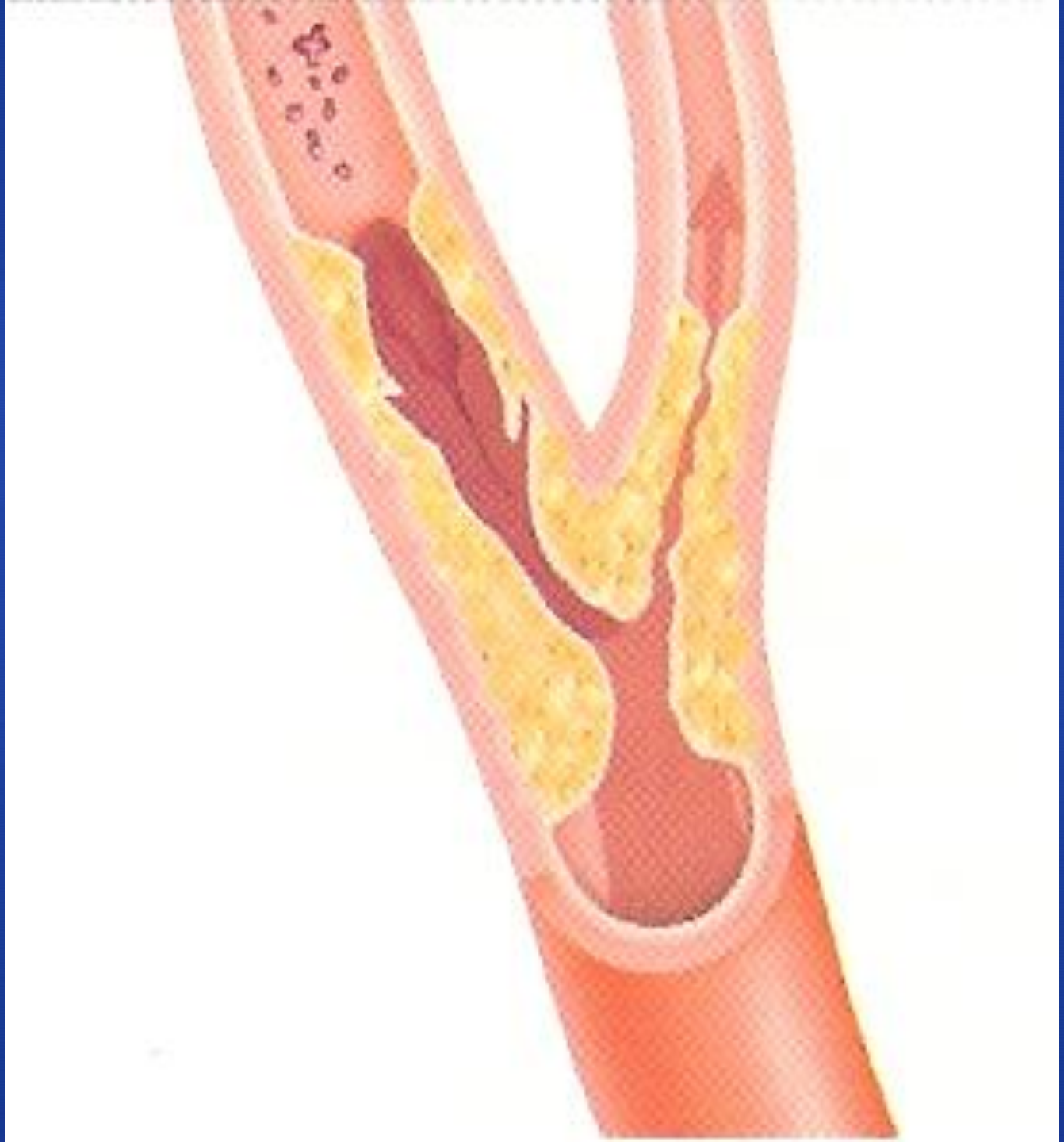


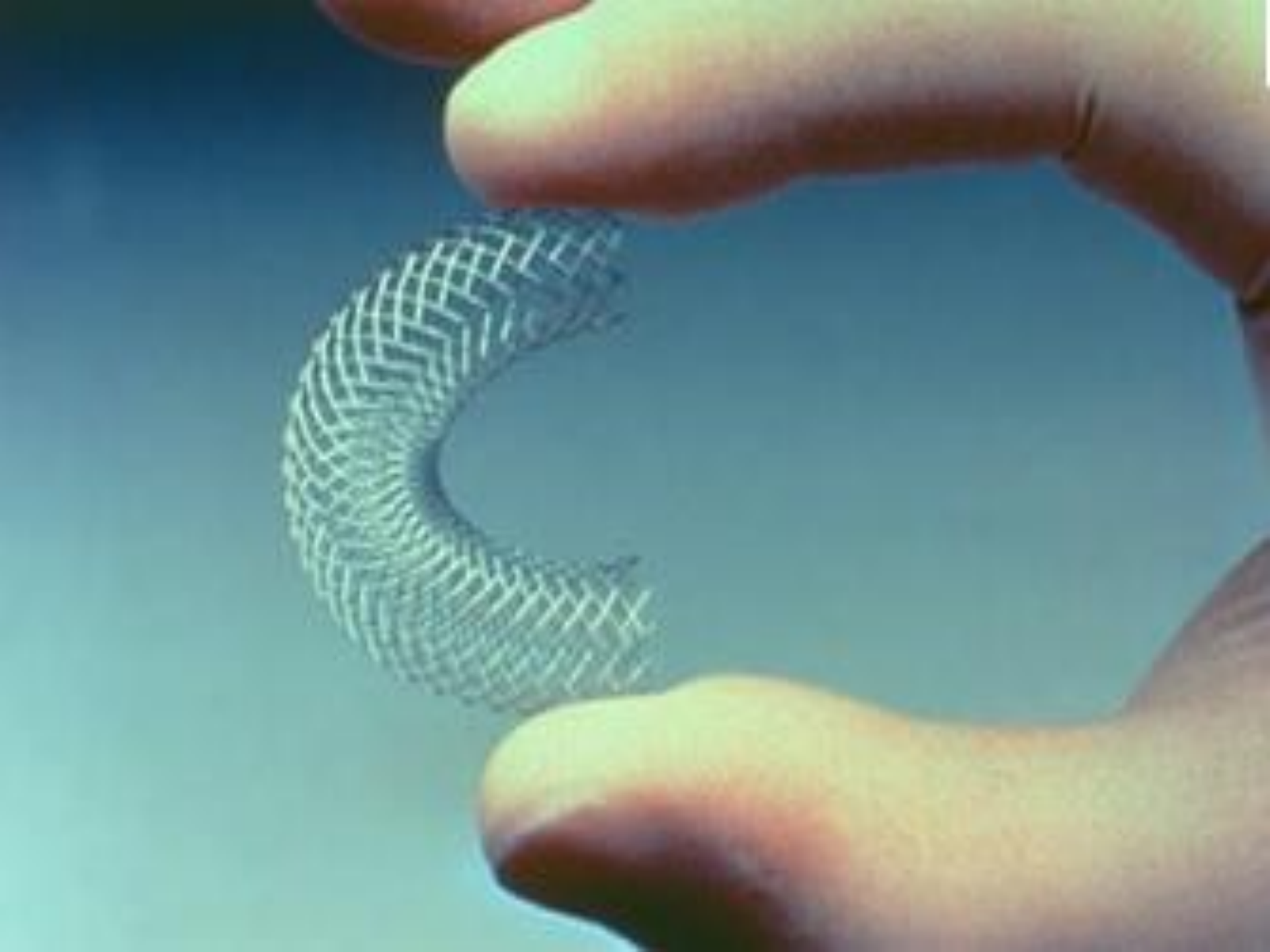
Always send for histology to confirm the absence of tumor

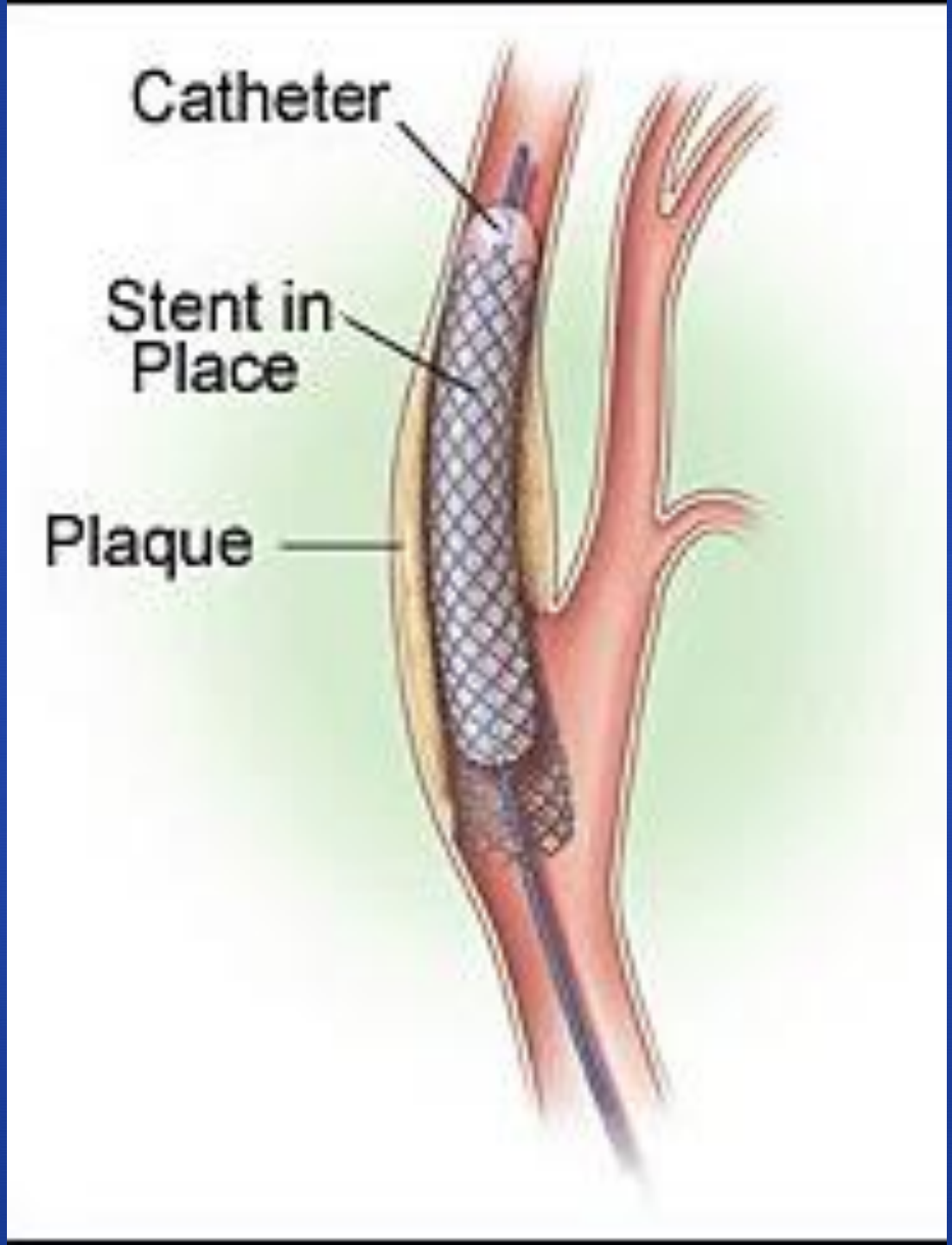
Carotid Artery Disease

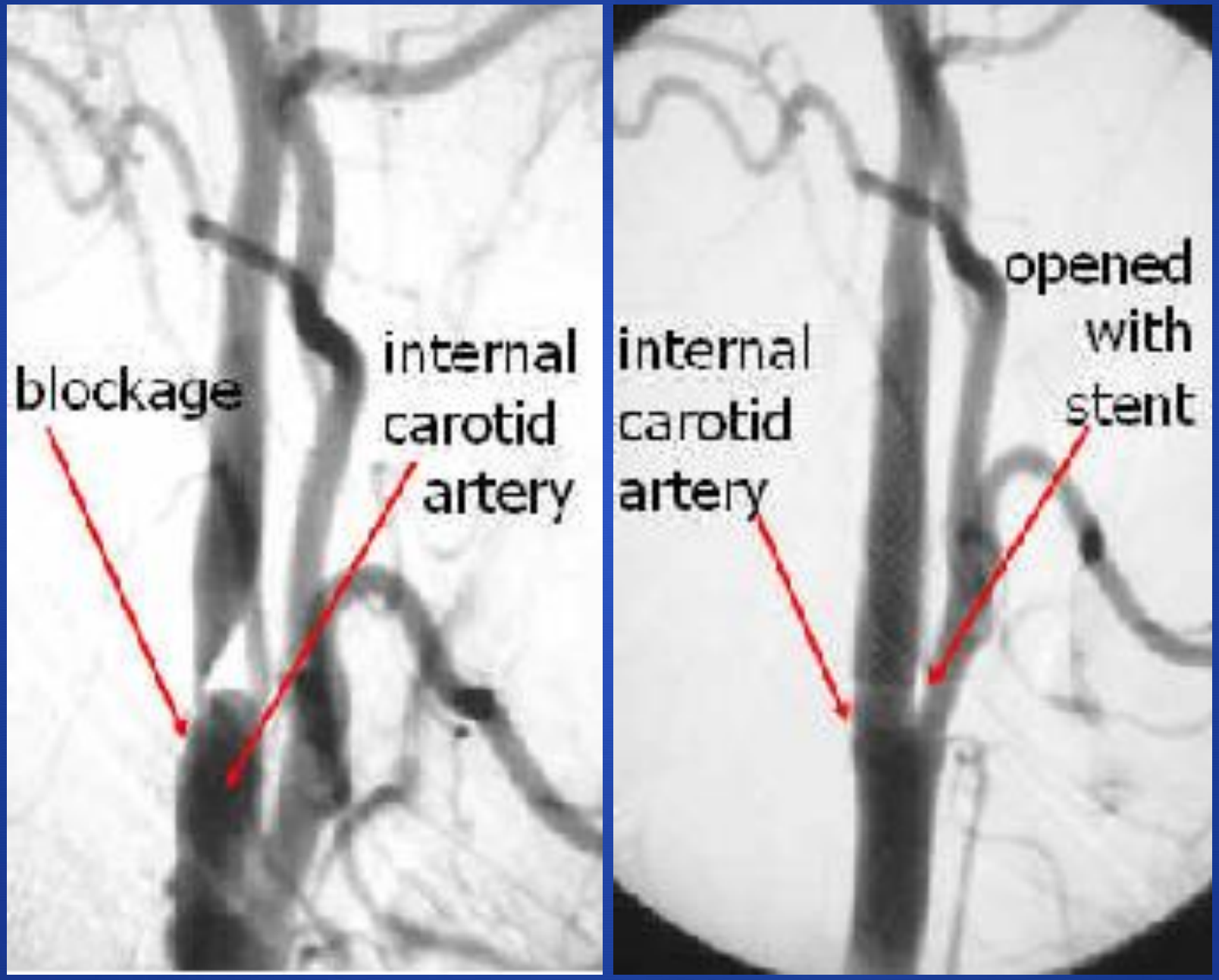

Reduced blood flow
Plaque
Narrowed artery cross-section
Carotid arteries located in the neck
Stent
Widened artery
Compressed plaque
A
B
C
Reduced blood flow
Internal carotid artery
Plaque
Stent being placed within the plaque of the internal carotid artery
Catheter
Common carotid artery
Stent widened artery
Compressed plaque



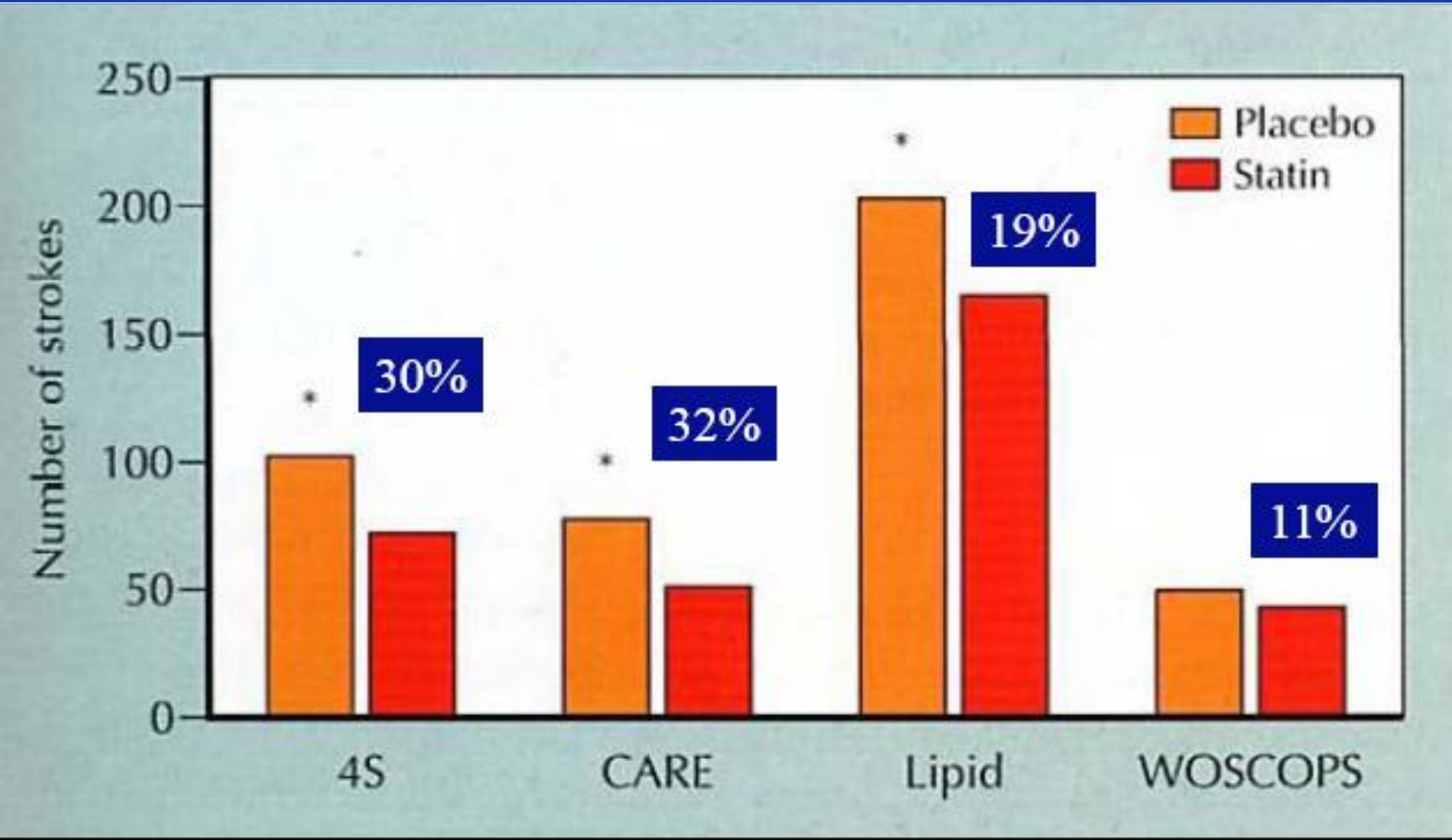





Catheter
Stent in Place
Plaque

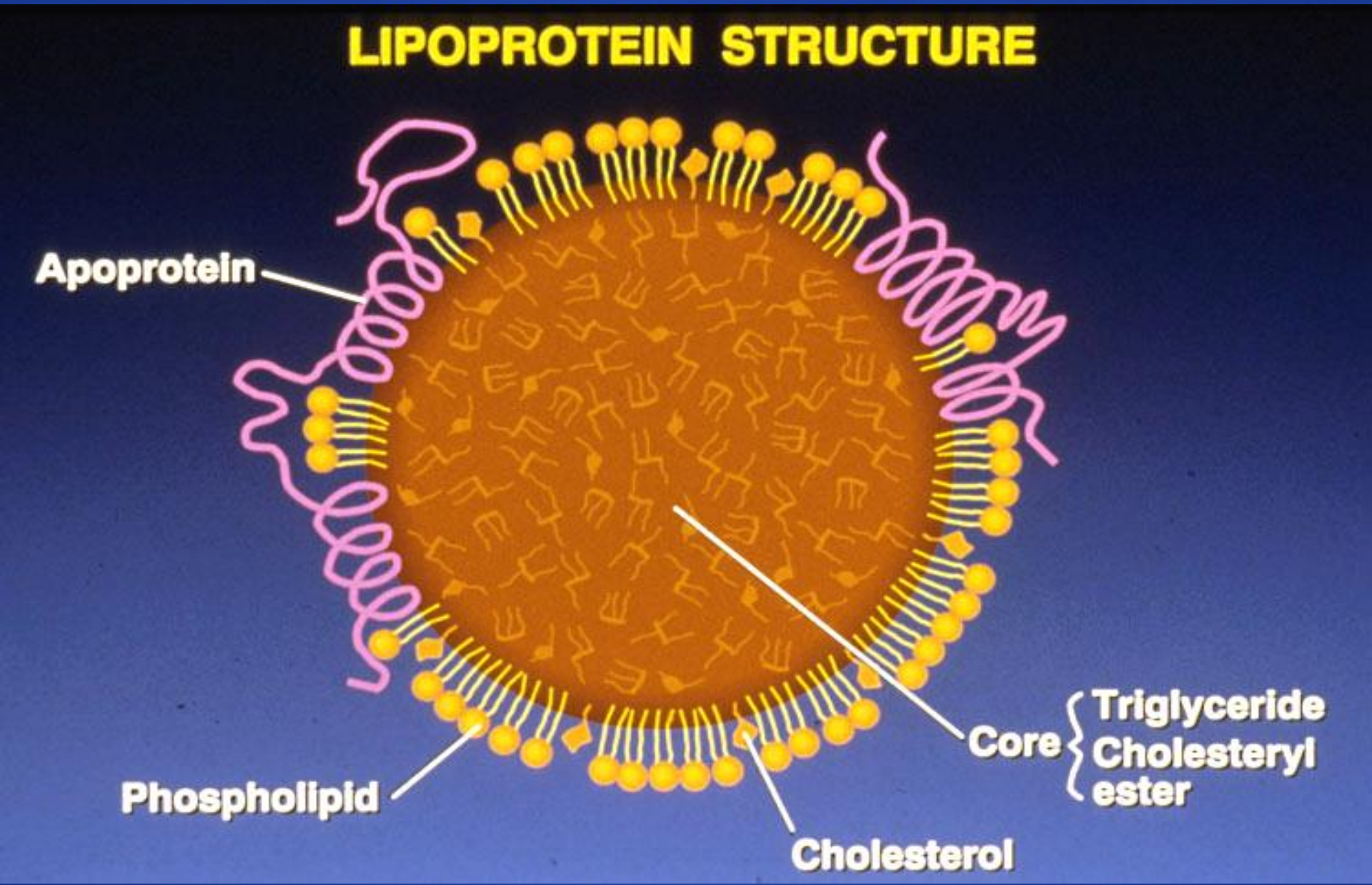

blockage
internal carotid artery
internal carotid artery
opened with stent

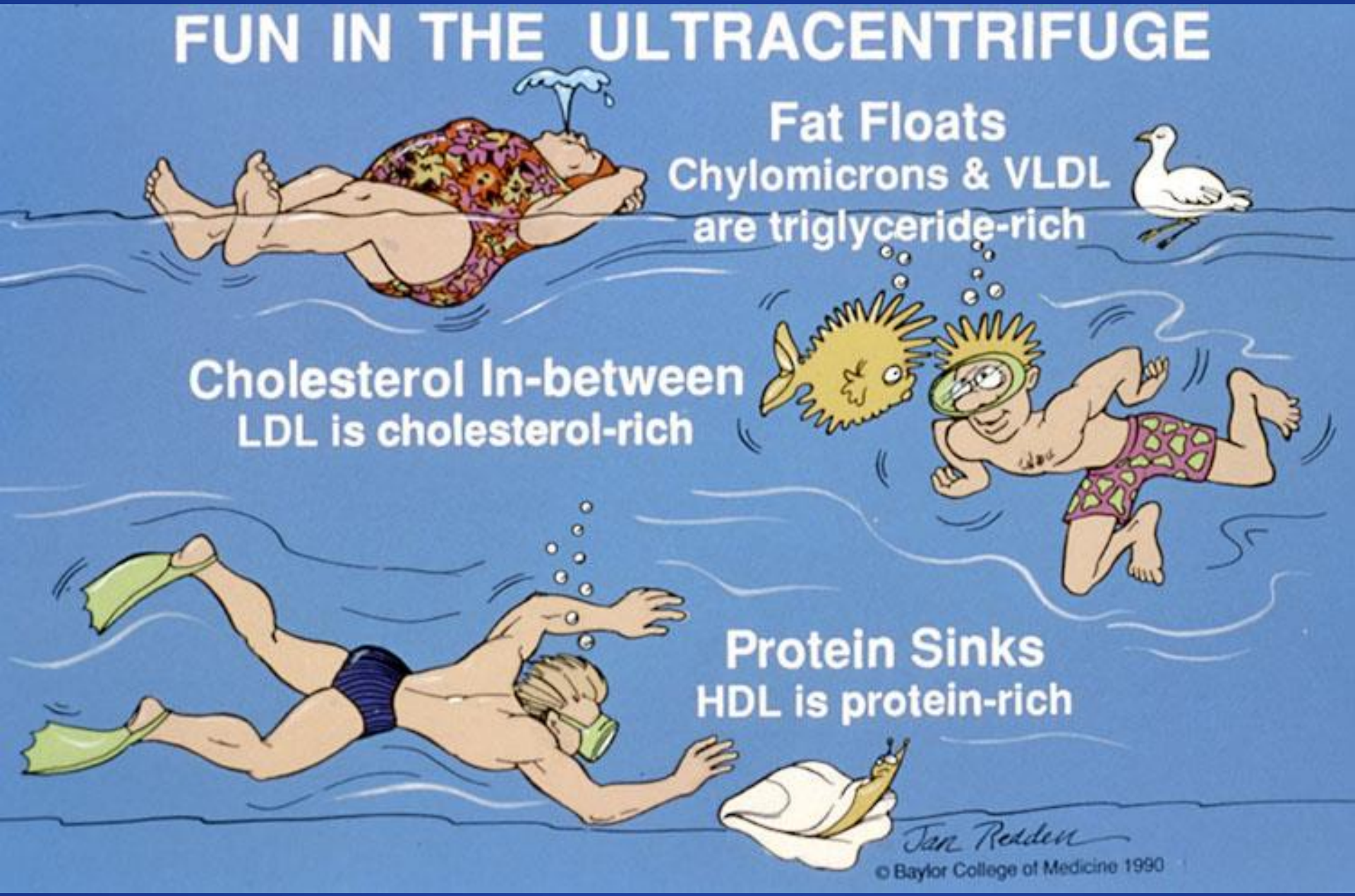
Lipid Lowering Trials



Total Cholesterol

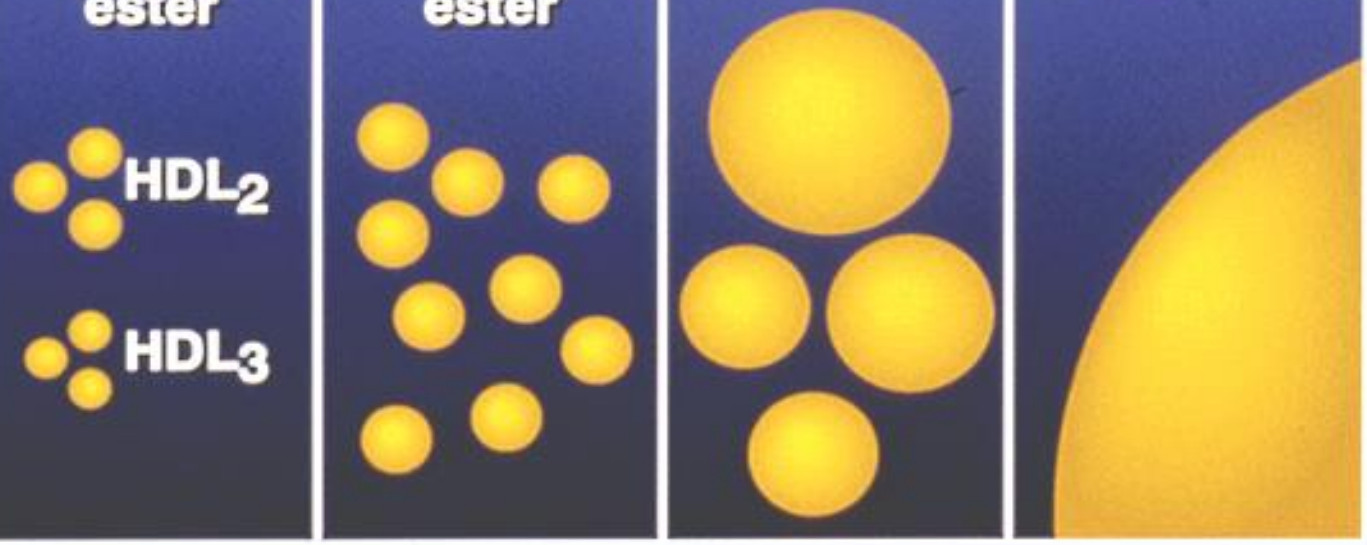
- Total cholesterol measures the combination of LDL, HDL, and VLDL (very low density lipoprotein) in your bloodstream. VLDL is a precursor of LDL, the bad cholesterol.
- A total cholesterol score of under 200 is considered healthy in most cases.


LIPOPROTEIN STRUCTURE
Apoprotein
Core
Triglyceride
Cholesteryl ester
Phospholipid
Cholesterol


FUN IN THE ULTRACENTRIFUGE
Fat Floats
Chylomicrons & VLDL
are triglyceride-rich
Cholesterol In-between
LDL is cholesterol-rich
Protein Sinks
HDL is protein-rich
Jan Reeden
© Baylor College of Medicine 1990

FOUR MAJOR LIPOPROTEIN CLASSES

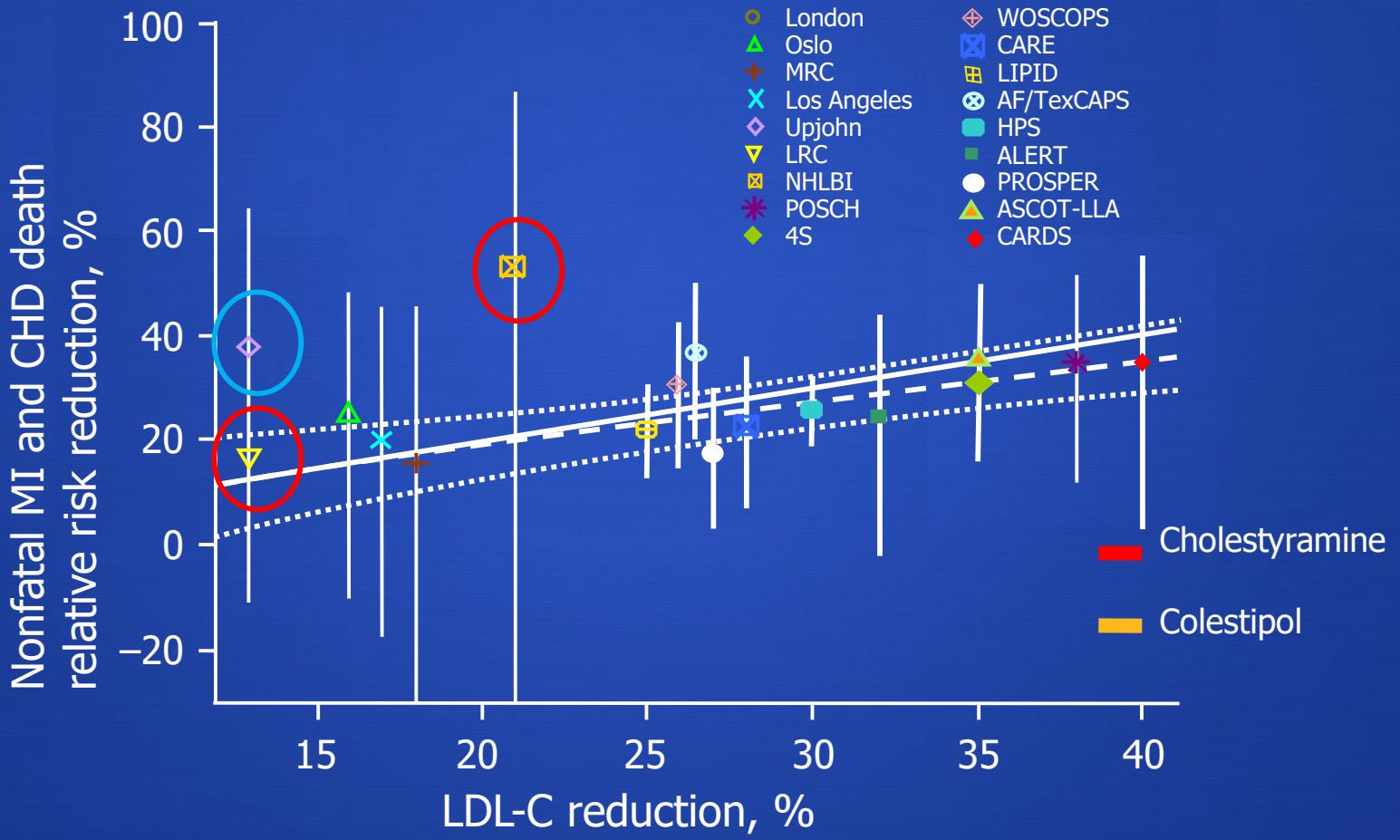
	High Density	Low Density	Very Low Density	Chylo-microns
Apolipo-proteins	A-I, A-II E, Cs	B-100	B-100, Cs, E	B-48, Cs, E, A-I, A-II
Major core lipids	Cholesteryl ester	Cholesteryl ester	Triglyceride	Triglyceride
Relative sizes	HDL_2 HDL_3			



Low Density Lipoproteins

- Most of the cholesterol in the blood is carried by proteins called low density lipoproteins or LDL or the bad cholesterol
- LDL combines with other substances to clog the arteries.
- A diet high in saturated fats and trans fats tends to raise the level of LDL cholesterol.
- For most people, an LDL score below 100 is healthy, but people with heart disease may need to aim even lower

Consistent relationship between LDL-C reduction and CHD relative risk for all LDL-lowering treatments



Robinson JG et al. *J Am Coll Cardiol.* 2005;46:1855–1862.

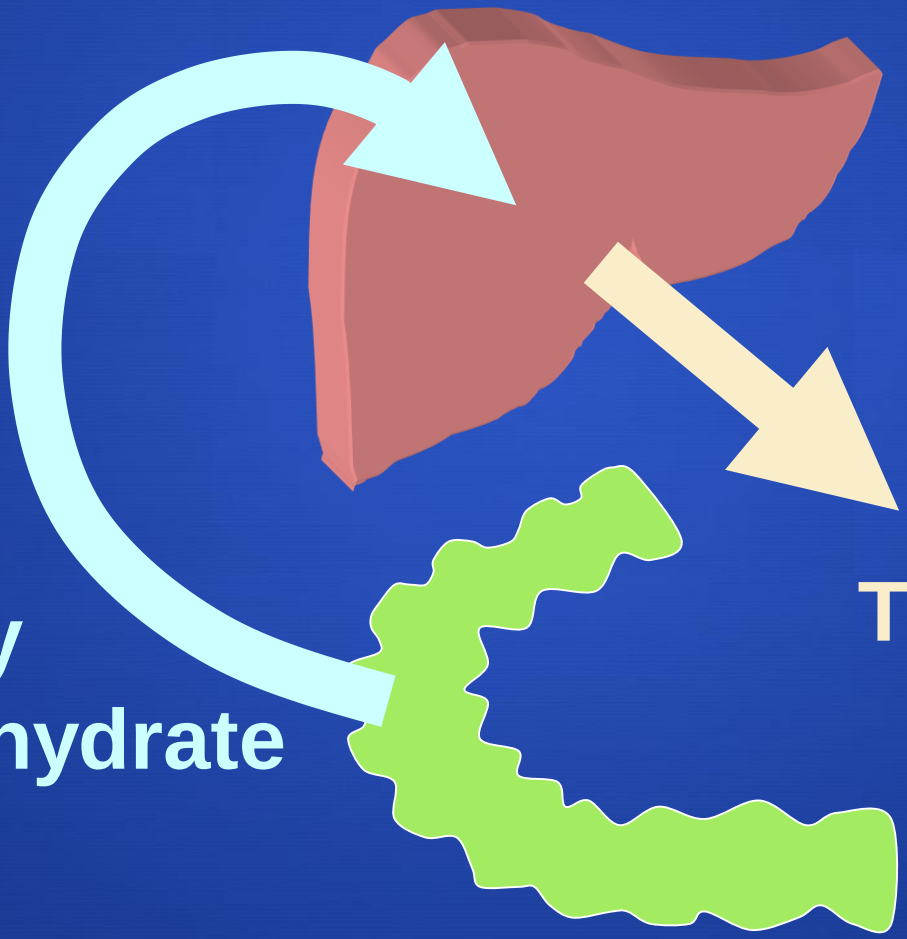
High-Density Lipoproteins

- Up to a third of blood cholesterol is carried by high-density lipoproteins or HDL or the good cholesterol.
- HDL helps remove bad cholesterol, preventing it from building up inside the arteries.
- The higher the level of HDL cholesterol, the better. People with too little are more likely to develop heart disease.

Triglycerides

- The body converts excess calories, sugar, and alcohol into triglycerides, a type of fat that is carried in the blood and stored in fat cells throughout the body.
- People who are overweight, inactive, smokers, or heavy drinkers and those who eat a very high carbohydrate diet tend to have high triglycerides
- A triglycerides score of 150 or higher puts you at risk for metabolic syndrome, which is linked to heart disease and diabetes.

Dietary Carbohydrate Increases VLDL Production



Dietary Carbohydrate

Plasma Triglyceride (VLDL)

Triglycerides

Causes of high triglycerides in the general population

- Overweight and obesity
- Physical inactivity
- Cigarette smoking
- Excess alcohol intake
- Very high carbohydrate diets (>60% of energy)
- Other disease (diabetes, renal failure, nephrosis)
- Drugs: steroids, protease inhibitors, estrogen, etc
- Genetic factors

NCEP JAMA 2001;285:2486 Final Report Circulation 2002;106:3143-3421

Triglycerides

Risk Classification of Serum Triglycerides

Normal <150 mg/dL

Borderline high 150–199 mg/dL

High 200–499 mg/dL

Very high ≥500 mg/dL

NCEP JAMA 2001;285:2486 Final Report Circulation 2002;106:3143-3421

Triglycerides

- Publication of meta-analyses have shown that elevated triglycerides are in fact an ***independent risk factor*** for CHD

- This suggests that some triglyceride-rich lipoproteins (TGRLP) are atherogenic.

NCEP JAMA 2001;285:2486 Final Report Circulation 2002;106:3143-3421

Triglycerides

- When triglyceride levels are ≥200 mg/dL, the presence of increased quantities of atherogenic remnant lipoproteins can heighten CHD risk substantially beyond that predicted by LDL cholesterol alone.
- For these reasons, ATP III modified the triglyceride classification to give more attention to moderate elevations.

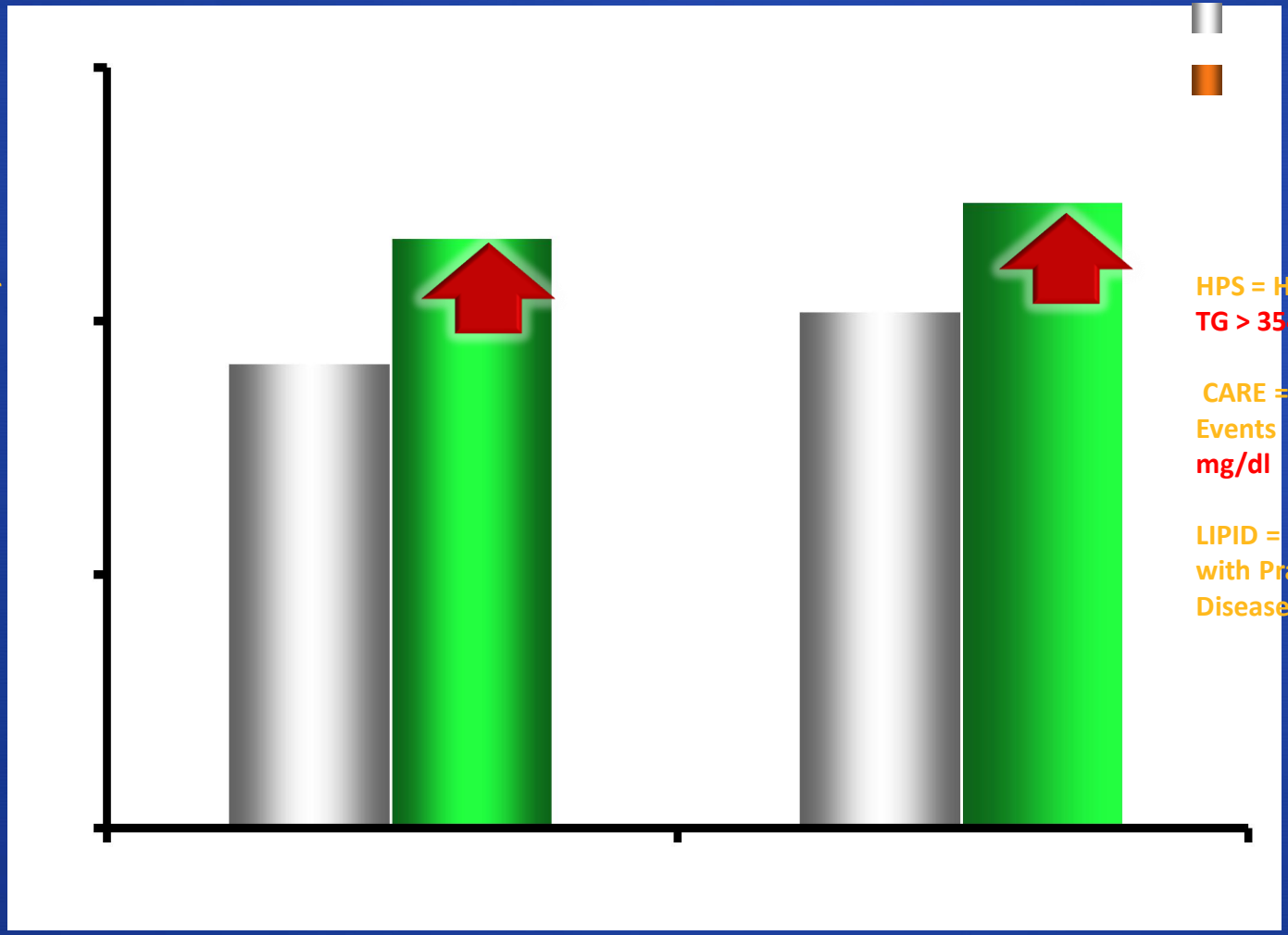
NCEP ATP III Chapter II Circulation December 2002 pp3169

Triglycerides

- If triglycerides are very high (≥500 mg/dL), attention turns first to prevention of acute pancreatitis, which is more likely to occur when triglycerides are >1000 mg/dL.
- Triglyceride-lowering drugs (fibrate or nicotinic acid) become first line therapy; although statins can be used to lower LDL cholesterol to reach the LDL goal, in these patients

NCEP ATPIII. Chapter IV *Circulation December 2002 pp 3247*

Statin Therapy Does Not Eliminate CV Risk Associated With High TG Level



HPS = Heart Protection Study: High TG > 354 mg/dL

CARE = Cholesterol & recurrent Events High TG > 207 mg/dl

LIPID = Long Term Intervention with Pravastatin in Ischemic Disease High TG > 207 mg/dL

HPS Collaborative Group. Lancet. 2002;360:7-22 Sacks FM et al. Circulation. 2000;102:1893-1900

Metabolic Syndrome

- Clinical diagnosis requires more than 3 of the following risk factors:
  - Abdominal Obesity (waist circumference): men ≥ 102 cm (40 in) women ≥ 88 cm (35 in)
  - Elevated Triglycerides ≥ 150 mg/dL
  - Reduced HDL cholesterol: men < 40 mg/dL women < 50 mg/dL
  - Hypertension ≥ 130/85
  - Impaired fasting glucose ≥ 100 mg/dL

Enlarged Waist Combined With Elevated Triglyceride (EWET) Editorial

- There is a growing consensus about the importance of triglycerides, particularly in women, and it has been shown in the same national US sample that triglyceride level was the single most predictive component of the MS-NCEP for CVD in multivariate analysis.
- *Conclusions:* The combined presence of EWET may be the best indicator of cardiovascular risk in postmenopausal women.
  - The TG value of concern is 128 mg/dL

Michael Criqui Editorial *Circulation*.2005;111:1869-1870

What Increases Your Risk?

- Several factors can make you more likely to develop high cholesterol:
  - A diet high in saturated fats and cholesterol
  - A family history of high cholesterol
  - Being overweight or obese
  - Getting older

Ways to Lower Cholesterol

- Dietary Modifications
- Lifestyle Modifications
- Medications/Drugs
  - Statins
  - Non-Statins

Dietary Modifications

- Eat more fiber
- Know your fats
- Smart protein
- Low-carb diet

Eat More Fiber

- Good sources of soluble fiber include whole-grain breads and cereals, oatmeal, fruits, dried fruits, vegetables, and legumes such as kidney beans.

Dietary Modifications

- Eat more fiber
- Know your fats

Know Your Fats

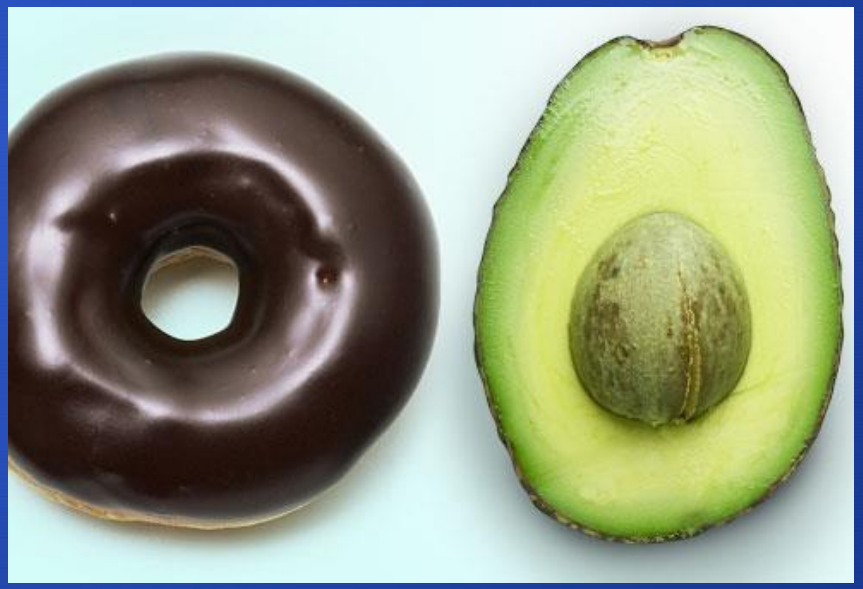
- No more than 35% of your daily calories should come from fat.
- But not all fats are equal
  - Saturated Fats
  - Trans Fats
  - Unsaturated Fats

Know Your Fats

- Saturated fats -- from animal products and tropical oils -- raise LDL cholesterol.
- Trans fats increase bad cholesterol and lowers the good cholesterol
- These two bad fats are found in many baked goods, fried foods (doughnuts, french fries, chips), stick margarine, and cookies.

Know Your Fats

- Unsaturated fats may lower LDL when combined with other healthy diet changes. They're found in avocados, olive oil, and peanut oil.



Dietary Modifications

- Eat more fiber
- Know your fats
- Smart protein

Smart Protein

- Meat and full-fat milk are protein but they are also major sources of cholesterol.
- Switch to soy protein, such as tofu.
- Fish is rich in omega-3 fatty acids, which can improve cholesterol levels.
- The AHA recommends eating fish at least twice a week.

Dietary Modifications

- Eat more fiber
- Know your fats
- Smart protein
- Low-carb diet

Low-Carb Diet

- There's growing evidence that low-carb diets may be better than low-fat diets for improving cholesterol levels.
- In a two-year study funded by the National Institutes of Health, people who followed a low-carb plan had significantly better HDL (good cholesterol) levels than those who followed a low-fat plan.

Lifestyle Modifications

- Lose weight
- Quit smoking
- Exercise

Lose Weight

- If you're overweight, talk to your doctor about beginning a weight loss program.
- Losing weight can help you reduce your levels of triglycerides, LDL, and total cholesterol.
- Good cholesterol level tends to go up 1 point for every 6 pounds you lose.

A couple were talking, and the wife says, “It’s my birthday tomorrow.”

Her husband responds with, “What do you want for your birthday?”

The wife says, “I want something that goes very fast.”

The next day, the husband comes home and says, “I have a gift for you, which goes from 0 to 300 in 3 seconds.”

The wife asks, “Is it a Ferrari? Or a Lamborghini?”

The husband says, “No, it’s a weighing scale!!!”

…The husband’s funeral is tomorrow.

Lifestyle Modifications

- Lose weight
- Quit smoking

Quit Smoking

- Tobacco use is one of the most important risk factors for CHD
- It is the most preventable cause of death in the US
- 440,000 deaths each year are attributable to tobacco use
- When you stop smoking, your good cholesterol is likely to improve

Lifestyle Modifications

- Lose weight
- Quit smoking
- Exercise

Exercise

- If you're healthy but not very active, starting an aerobic exercise program could increase your good cholesterol by 5% in the first two months.
- Regular exercise also lowers bad cholesterol. Choose an activity that boosts your heart rate, such as running, swimming, or walking briskly
- Aim for at least 30 minutes on most days of the week. It doesn't have to be 30 continuous minutes; two 15-minute walks works just as well.

Medications

- Statins
- Non-Statins
  - Cholesterol Absorption Inhibitor (Ezetimibe)
  - Nicotinic Acid (Niacin)
  - Bile Acid Sequestrants
  - Fibric Acid Derivatives
  - Omega-3 Fatty Acids

Statins

- Atorvastatin
- Fluvastatin
- Lovastatin
- Pravastatin
- Rosuvastatin
- Simvastatin

Statins

- Decrease LDL by 18 – 55 %
- Increase HDL by 5 – 15 %
- Decrease TG by 7 – 30 %

Statins

- The drug of choice for elevated LDL levels
- Prevents cardiovascular and cerebrovascular events
- Contraindicated in active or chronic liver disease, pregnancy and lactation
- Adverse effects include myopathy and increase in liver transaminases

Statin Safety: Key Conclusions and Recommendations of the NLA

Conclusions of the NLA Safety Task Force for Muscle Safety

- Myopathy and rhabdomyolysis are associated with statin therapy, as a class effect
- Elevated creatine kinase (CK) levels may indicate statin-induced muscle damage
- Muscle weakness or pain without CK elevation may indicate statin-induced muscle damage
- Myopathy and rhabdomyolysis risk increases with increased statin dose and serum levels
- Myopathy and rhabdomyolysis risk increases with drug-drug interactions that retard statin metabolism
- Drugs that can interact to amplify statin related myopathy include gemfibrozil and CYP-3A4 inhibitors

Thompson PD et al. *Am J Cardiol.* 2006;97:69C-76C

Conclusions of the NLA Safety Task Force on Liver Function

- Statin use is associated with elevated serum aminotransferase levels, but it is unclear whether this is a causal link
- Statin-associated serum aminotransferase elevation is not predictive of liver damage
- Very rare case reports of liver failure have occurred in patients receiving statin therapy
- Patients on statin therapy do not require routine liver function testing
- Statin therapy is not contraindicated in any hepatic conditions, with the exception of decompensated cirrhosis and acute liver failure

Cohen DE et al. *Am J Cardiol.* 2006;97:77C-81C

Conclusions of the NLA Safety Task Force on Renal Issues

- Marketed doses of statins do not produce clinically meaningful proteinuria
- There is no association between statin use and renal tubular damage
- There is no evidence that statin use leads to renal glomerular damage
- There is no convincing link between statin use and hematuria
- Some evidence indicates statins may provide some kidney protection

Kasiske BL et al. *Am J Cardiol.* 2006;97:82C-85C

Conclusions of the NLA Safety Task Force on Neurology

- There is no association between statin use and clinically meaningful peripheral neuropathy
- There is no convincing evidence that statins cause impaired memory or cognitive dysfunction
- Clinical trial data indicate that lowering lipids with statins does not increase risk of cerebral hemorrhage

Brass LM et al. *Am J Cardiol.* 2006;97:86C-88C

Recommendations Regarding Patient Monitoring

- Monitoring CK levels is recommended only for symptomatic patients
- Patients on statin therapy do not require routine monitoring of liver function, renal function, or cognitive function

Messages for Patients

- Statins can produce muscle pain and weakness, which can very rarely become an important medical problem
- Serious liver damage due to statins is extremely rare
- Marketed doses of statins do not have any direct adverse effects on the kidney
- Statins do not cause peripheral neuropathy and do not impair memory or cognition

Non-Statins: Cholesterol Absorption Inhibitor

- Decrease LDL by 18 – 20%
- Increase HDL by 1 – 5%
- Decrease TG by 5 – 11%

Non-Statins: Cholesterol Absorption Inhibitor

- Ezetimibe
- Safe and effective adjunct to statins when further LDL lowering is required
- Contraindicated in patients with active liver disease or unexplained persistent transaminase elevations
- Adverse effects include GI complaints

Non-Statins: Niacin

- Decrease LDL by 5 – 25 %
- Increase HDL by 15 – 35 %
- Decrease TG by 20 – 50%

Non-Statins: Niacin

- Uniquely effective in atherogenic dyslipidemia
- Useful in nearly all dyslipidemias and adjunctive therapy for mixed dyslipidemias
- Contraindicated in chronic liver disease, severe gout, active peptic ulcer disease
- Adverse effects include flushing, hyperglycemia, hyperuricemia, hepatotoxicity


PHUKET ISLANDS ONLINE

Safety Considerations with Niacin Therapy

Recommendations to healthcare professionals regarding niacin safety

- Healthcare professionals may expect that 5%–10% of patients will not tolerate niacin in long-term use because of flushing.
- Skin rashes associated with niacin therapy are generally not allergic but are likely related to dermal prostaglandin release and to dry skin.
- Serious hepatic toxicity can occur with niacin therapy, but it is almost entirely associated with the use of slow-release formulations. IR (regular or crystalline) niacin or ER niacin generally should be used rather than SR niacin.

CK creatine kinase; **ER** extended release; **HDL** high-density lipoprotein; **IR** immediate release; **PCP** phencyclidine; **SR** sustained release; **ULN** upper limit of normal

Recommendations to healthcare professionals regarding niacin safety

- Hepatic transaminase levels should be monitored every 6–12 week during the first 6–12 month of treatment with niacin and periodically thereafter (eg, at 6-mo intervals).
- Niacin is useful for the treatment of the dyslipidemia of diabetes mellitus, especially low HDL cholesterol. Minor increases (4%–5% on average) in glucose levels result from niacin-induced insulin resistance, but these increases are often clinically insignificant.
- The onset of type 2 diabetes (multiple fasting glucose levels 125 mg/dL or postprandial glucose levels 200 mg/dL) in a patient taking niacin should prompt consideration of niacin withdrawal or dosage reduction.

Recommendations to healthcare professionals regarding niacin safety

- On the basis of almost 2 decades of clinical evidence, niacin coadministration with a statin does not potentiate statin-related myopathic reactions.
- Niacin should not be used in the presence of active peptic ulcer disease, but a remote history of peptic ulcer is not a contraindication to niacin use. Gastroesophageal reflux disease is generally not affected by niacin.

Recommendations to healthcare professionals regarding niacin safety

- Palpitations and tachycardia are potential adverse experiences with niacin. In rare cases, this may relate to the increased incidence of "definite or suspected" atrial fibrillation.
- Active gout is a relative contraindication to niacin use, because niacin (nicotinic acid) competes with uric acid for secretion by kidney tubules and raises serum uric acid levels by 5%–15%.

Guyton G, Bays H. Report of the National Lipid Association's Safety Task Force: The Nonstatins. *Am J Cardiol* 2007;99(suppl):22C-31C

Non-Statins:
Bile Acid Sequestrants

- Decrease LDL by 15 – 30 %
- Increase HDL by 3 -5 %
- TG is usually not affected but may increase

Non-Statins:
Bile Acid Sequestrants

- Include Colesevelam, Cholestyramine , Colestipol
- Indicated for moderate hypercholesterolemia, in younger patients with elevated LDL and women with elevated LDL who are considering pregnancy
- Adverse effects include constipation, flatulence and decreased absorption of other drugs like digoxin, warfarin, HCTZ, beta blockers, thyroxine and penicillin G

Non-Statins: Fibrates

- Decrease LDL by 5 – 20 %
- Increase HDL by 10 – 35 %
- Decrease TG by 20 – 50 %

Non-Statins: Fibrates

- Includes Gemfibrozil, Fenofibrate and Clofibrate
- Indicated in hypertriglyceridemia and atherogenic dyslipidemia
- Contraindicated in severe hepatic or renal dysfunction, primary biliary cirrhosis and gall bladder disease
- Adverse effects include dyspepsia, upper GI complaints, cholesterol gallstones, myopathy

Recommendations to healthcare professionals regarding fibrate safety

- Before the initiation of fibrate therapy, a measurement of serum creatinine should be determined. If impaired renal function is present, the patient should be prescribed gemfibrozil (unless taking a statin), or a lower starting dose of fenofibrate (48 mg is most commonly available) should be considered.
- Routine monitoring of creatinine is not required.
- Creatinine monitoring may be advisable if a patient is taking another medication, such as metformin, which may need to be discontinued for creatinine elevations 1.4 mg/dL in women and 1.5 mg/dL in men, or a statin, which may require downward dosage adjustment.

CK creatine kinase; **HDL** high-density lipoprotein; **INR** international normalized ratio; **IV** intravenous; **PT** prothrombin time; **ULN** upper limit of normal

Recommendations to healthcare professionals regarding fibrate safety

- Clinicians should still use caution when prescribing the highest doses of statins used in combination with fibrate therapy, because both classes of drugs are independently associated with an increased risk for myopathy. In combination with a statin, fenofibrate is the preferred option, and gemfibrozil should be avoided.
- Gemfibrozil has less effect than fenofibrate on creatinine and therefore is the National Kidney Foundation's (NKF) fibrate of choice for renal insufficiency. It does seem reasonable to discourage the administration of fenofibrate to kidney transplant patients and those on dialysis, because fenofibrate is nondialysable.

Recommendations to healthcare professionals regarding fibrate safety

- Clinicians should warn patients about the possibility of myopathy on fibrate therapy and advise the reporting of side effects of diffuse muscle pain or weakness as soon as possible.
- It is not necessary to measure CK levels in asymptomatic patients during the course of fibrate therapy, because marked, clinically important CK elevations are relatively rare.

Recommendations to healthcare professionals regarding fibrate safety

- Clinicians should be aware that fibrates have not been demonstrated to significantly reduce total and cardiovascular mortality.
- Fibrate therapy elevates homocysteine, however, routine monitoring of plasma homocysteine levels on fibrate is not necesary unless further research ascertains that this elevation is clinically relevant.

Recommendations to healthcare professionals regarding fibrate safety

- Caution should be exercised when anticoagulants are given in conjunction with both fenofibrate and gemfibrozil because of the potentiation of coumarin-type anticoagulants in prolonging PT and the INR.
- All fibrates have the potential to increase the cholesterol saturation index and increase the risk for cholelithiasis; however, cases of gallbladder disease and cholecystectomies appear to be uncommon with gemfibrozil and fenofibrate.

Davidson M, Armani A, McKenney JM, Jacobson T. Report of the National Lipid Association's Safety Task Force: The Nonstatins. *Am J Cardiol* 2007;99(suppl):3C-18C

Non-Statins: Omega-3 Fatty Acids

- Decrease TG by 45 %
- Increase HDL by 9 %
- Increase LDL by 44 %

Non-Statins: Omega-3 Fatty Acids

- Fish Oils
- Its major use is in hypertriglyceridemia greater than 500mg/dL
- Contraindicated in patients with known hypersensitivity to fish and in women who are pregnant or breastfeeding
- Adverse effects include eructation, dyspepsia, and taste perversion

Safety Considerations with Omega-3 Fatty Acid Therapy

Recommendations to healthcare professionals regarding fish oil therapy safety

- The clinical trial evidence does not support an increased bleeding risk with fish oil therapy, even when used in combination with other agents that may increase bleeding (such as aspirin and warfarin).
- It is reasonable to monitor patients treated with fish oils and anticoagulants for potential bleeding adverse experiences.
- Fish oils should probably be discontinued during acute bleeding episodes, such as hemorrhagic stroke.

Recommendations to healthcare professionals regarding fish oil therapy safety

- The decision to discontinue fish oils days before an invasive procedure at high risk for bleeding complications should be based on weighing the unproved potential increase in bleeding risk versus the potential reduction in atrial fibrillation before certain procedures, such as coronary artery bypass surgery.
- Rigorous purification processes involved in fish oil manufacturing reduce the risk of fatty acid oxidation, hypervitaminosis, and exposure to environmental toxins.

Recommendations to healthcare professionals regarding fish oil therapy safety

- Clinicians and patients should be aware of the variance in the purification processes among different fish oil manufacturers.
- Because fish oil supplements are generally regarded as safe, they are not subject to FDA premarket and approval requirements.
- If a product has the "USP-Verified" mark on its label, the manufacturer has met voluntary USP standards, which include initial and ongoing determinations to ensure that (1) what is on the label is in fact in the bottle (all the listed ingredients in the declared amounts), (2) the supplement does not contain harmful levels of contaminants, (3) the supplement will break down and release ingredients in the body, and (4) the supplement has been made under current good manufacturing practices.

Recommendations to healthcare professionals regarding fish oil therapy safety

- Claims of a fish oil supplement being "pharmaceutical grade" have little meaning regarding safety and have even less meaning with regard to efficacy, unless the fish oil preparation has been approved by the FDA as a prescription pharmaceutical.
- Prescription fish oil preparations undergo the same rigorous FDA regulatory requirements as other prescription pharmaceuticals, with regard to both efficacy and safety.

Recommendations to healthcare professionals regarding fish oil therapy safety

- One of the most common pitfalls in the day-to-day, clinical use of fish oil therapy is the sense among patients that all fish oil therapies are the same. Clinicians need to educate patients of the wide variance in fish oil therapies regarding efficacy, tolerability, and perhaps even safety. For example, the efficacy of fish oil therapy is most dependent on the amount of omega-3 fatty acids (such as EPA and DHA) in each capsule, not the total amount of fish oil concentrate. Thus, to achieve the same level of omega-3 fatty acid intake, patients may have to take as many as 11 capsules of some fish oil supplements to match the same amount of omega-3 fatty acid intake as 4 fish oil capsules of prescription fish oil.

Bays H. Report of the National Lipid Association's Safety Task Force: The Nonstatins. *Am J Cardiol* 2007;99(suppl):35C-43C

Take Home Points

- In the treatment of dyslipidemia:
  - Statins are the most effective and safe first line of treatment.
  - Non-statins, which include cholesterol absorption inhibitors, niacin, bile acid sequestrants, fibrates, and omega-3 fatty acids, probably help improve the outcomes of patients with CHD, although strong evidence remains lacking.
- Triglycerides are now considered as an independent risk factor for CHD.

ANY QUESTIONS ???