433 Teams

MEDICINE

13|Dyslipidemia

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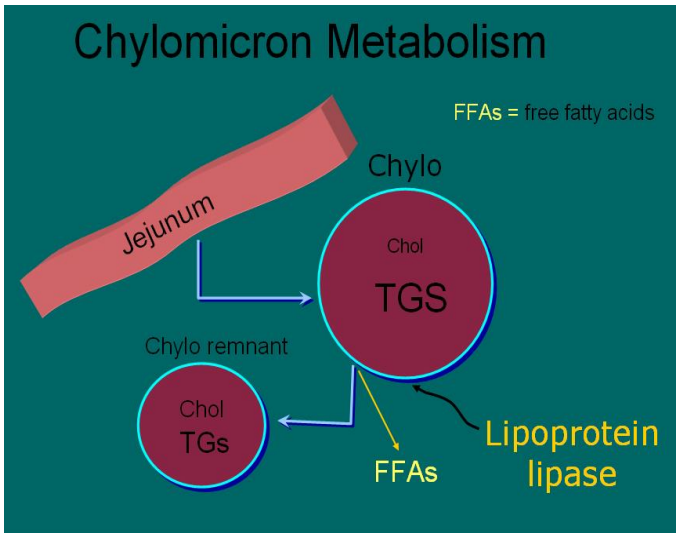
Slides - Step-Up medicine - Kaplan Notes - Extre explanation - Doctor Notes

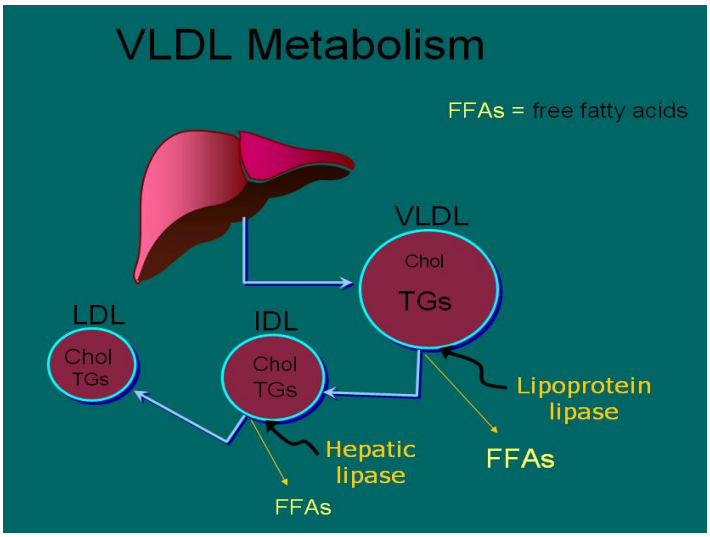
Objectives:

1) Know the Physiology of lipid and lipoprotein cycles.
2) Know the most important hereditary diseases related to lipid.
3) Know the 2ry causes of hyperlipidemia.
4) Approach the patient with hyperlipidemia.
5) Discussion around the therapy.

Lipid Transport:

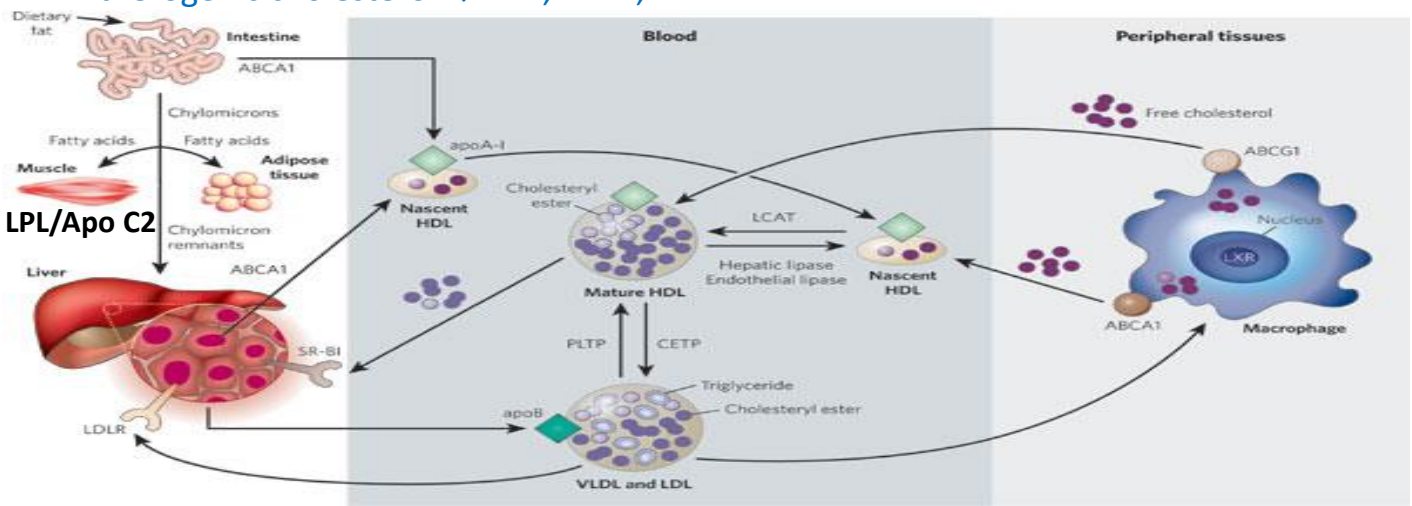
Lipoprotein metabolism has a key role in atherogenesis. It involves the transport of lipids, particularly cholesterol and triglycerides in the blood. The intestine(jejunum) absorbs dietary fat and packages it into chylomicrons (large triglyceride-rich lipoproteins) , which are transported to peripheral tissues through the blood. In muscle and adipose tissues, the enzyme lipoprotein lipase breaks down chylomicrons and fatty acids enter these tissues. The chylomicron remnants are subsequently taken up by the liver. The liver loads lipids onto apoB and secretes very-low-density lipoproteins (VLDLs), which undergo lipolysis by lipoprotein lipase to form low-density lipoproteins (LDLs). LDLs are then taken up by the liver through binding to the LDL receptor (LDLR), as well as through other pathways. By contrast, high-density lipoproteins (HDLs) are generated by the intestine and the liver through the secretion of lipid-free apoA-I. ApoA-I then recruits cholesterol from these organs through the actions of the transporter ABCA1, forming nascent HDLs, and this protects apoA-I from being rapidly degraded in the kidneys. In the peripheral tissues, nascent HDLs promote the efflux of cholesterol from tissues, including from macrophages, through the actions of ABCA1. Mature HDLs also promote this efflux but through the actions of ABCG1. (In macrophages, the nuclear receptor LXR upregulates the production of both ABCA1 and ABCG1.) The free (unesterified) cholesterol in nascent HDLs is esterified to cholesteryl ester by the enzyme lecithin cholesterol acyltransferase (LCAT), creating mature HDLs. The cholesterol in HDLs is returned to the liver both directly, through uptake by the receptor SR-BI, and indirectly, by transfer to LDLs and VLDLs through the cholesteryl ester transfer protein (CETP). The lipid content of HDLs is altered by the enzymes hepatic lipase and endothelial lipase and by the transfer proteins CETP and phospholipid transfer protein (PLTP), affecting HDL catabolism.





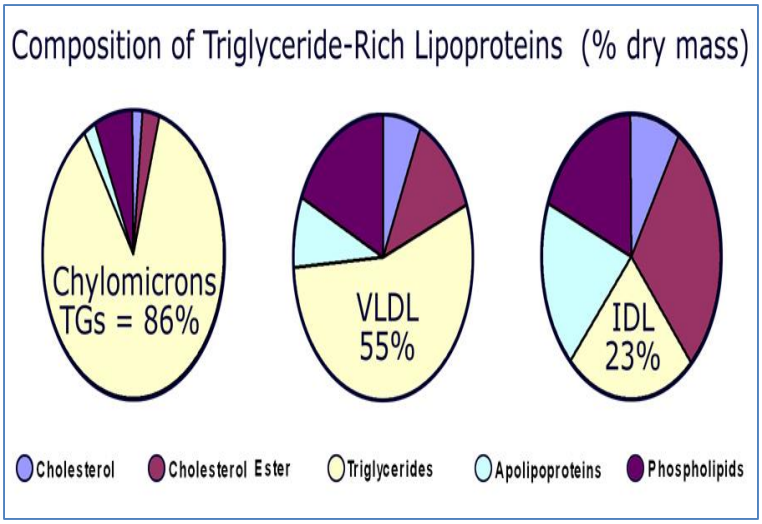
The story of lipids

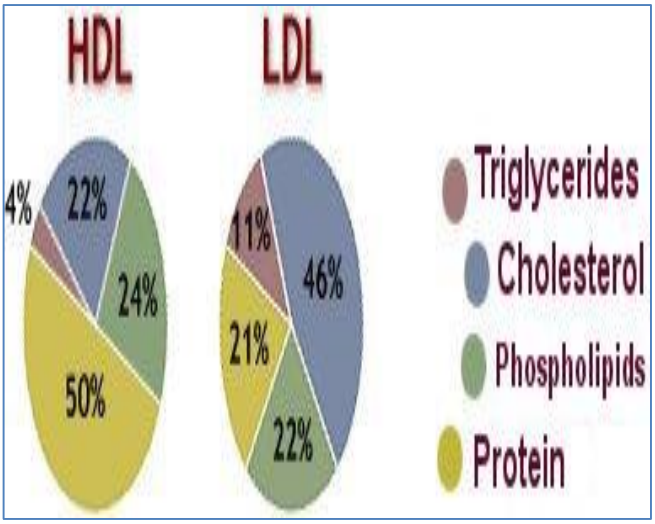
- Chylomicrons transport fats from the intestinal mucosa to the liver.
- In the liver, the chylomicrons release triglycerides and some cholesterol and become low-density lipoproteins (LDL).
- LDL then carries fat and cholesterol to the body's cells.
- High-density lipoproteins (HDL) carry fat and cholesterol back to the liver for excretion.
- When oxidized LDL cholesterol gets high, atheroma formation in the walls of arteries occurs, which causes atherosclerosis. (The most atherogenic lipoprotein is LDL because the concentration of cholesterol is high on it)
- HDL cholesterol is able to go and remove cholesterol from the atheroma.
- Atherogenic cholesterol → LDL, VLDL, IDL.



Atherogenic particles

Not only LDL-Cholesterol is a risk factor for cardiovascular disease, but triglyceride-rich lipoproteins—very low density lipoprotein (VLDL), VLDL remnants, and intermediate-density lipoprotein (IDL)—may also increase the risk of heart disease.
The NCEP ATP III uses non-HDL-C principally as a surrogate for these atherogenic particles.





General characteristics

1. Hyperlipidemia is one of the most important (and modifiable) risk factors for CAD. It causes accelerated atherosclerosis.
2. Hyperlipidemia may be a primary disorder such as a familial dyslipidemia syndrome or secondary to another cause.
3. Classification of dyslipidemia syndromes: Types IIA, IIB, and IV account for over 80% of all of familial dyslipidemias .
4. Secondary causes of hyperlipidemia:

a. Endocrine disorders: hypothyroidism, DM, Cushing's syndrome.
b. Renal disorders: Nephrotic syndrome, uremia , dialysis.
c. Chronic liver disease, Obstructive liver disease. Acute hepatitis.
d. Autoimmune disease : Systemic lupus erythematousus.
e. Medications: glucocorticoids, estrogen, thiazide diuretics, β-blockers, AIDS (protease inhibitors).
F. Pregnancy
g. Anorexia nervosa, Obesity
h. Alcohol

Plasma lipoproteins

Type	Source	Major lipid	Apoproteins	ELFO	Athero-genicity
Chylomicrons	Gut	Dietary TGs	A-I, B-48, C-I, C-III, E	no mobility	– (pancreatitis)
VLDL	Liver	Endogenous TGs	B-100, E, C-II, C-III,	Pre-β	+
IDL	VLDL remnant	Ch esters, TGs	B-100, C-III, E	Slow pre- β	+
LDL	VLDL, IDL	Ch esters	B-100	β	+++
HDL	Gut, liver	Ch esters, PLs	A-I, A-II, C-II, C-III, D, E	α	anti-atherogenic

Fredrickson classification of hyperlipidemias

Phenotype	Lipoprotein(s) elevated	Plasma cholesterol	Plasma TGs	Athero-genicity	Rel. freq.	Treatment
I	Chylomicrons	Norm. to ↑	↑↑↑↑	– pancreatitis	<1%	Diet control
IIa	LDL	↑↑	Norm.	+++	10%	Bile acid sequestrants, statins, niacin
IIb	LDL and VLDL	↑↑	↑↑	+++	40%	Statins, niacin, fibrates
III	IDL	↑↑	↑↑↑	+++	<1%	Fibrates
IV	VLDL	Norm. to ↑	↑↑	+	45%	Niacin, fibrates
V	VLDL and chylomicrons	↑ to ↑↑	↑↑↑↑	+ pancreatitis	5%	Niacin, fibrates

Hereditary Causes of Hyperlipidemia

❖ **Familial Hypercholesterolemia (autosomal dominant):**

- Co-dominant genetic disorder occurs in heterozygous form.
- Occurs in 1 in 500 individuals.
- Mutation in LDL receptor , resulting in elevated levels of LDL at birth and throughout life.
- High risk for atherosclerosis, tendon xanthomas (75% of patients), tuberous xanthomas and xanthelasmas of eyes.

It has two types:

1. Heterozygous Familial Hypercholesterolemia: Autosomal dominant disorder present in 1 in 500 of normal population (common) one allele affected, the genetic defect is underproduction or malproduction of the LDL receptor in the liver.

2. Homozygous Familial Hypercholesterolemia: Its very rare (one in a million) two alleles affected, affect children have no LDL receptor in the liver , the LDL here is sky-high and they suffer from myocardial infarction since the childhood (12 – 14 age) even younger .

❖ **Familial Combined Hyperlipidemia**

Autosomal dominant Increased secretions of VLDLs

❖ **Dysbetalipoproteinemia**

Affects 1 in 10,000
Results in apo E2, a binding-defective form of apoE (which usually plays important role in catabolism of chylomicron and VLDL)
Increased risk for atherosclerosis, peripheral vascular disease
Tuberous xanthomas, striae palmaris

Primary hypercholesterolemias

Disorder	Genetic defect	Inheritance	Prevalence	Clinical features
Familial hyper-cholesterolemia	LDL receptor	dominant	heteroz.:1/500 5% of MIs <60 yr homoz.: 1/1 million	premature CAD (ages 30–50) TC: 7-13 mM CAD before age 18 TC > 13 mM
Familial defective apo B-100	apo B-100	dominant	1/700	premature CAD TC: 7-13 mM
Polygenic hypercholesterolemia	multiple defects and mechanisms	variable	common 10% of MIs <60 yr	premature CAD TC: 6.5-9 mM
Familial hyper-alphalipoproteinemia	unknown	variable	rare	less CHD, longer life elevated HDL

Primary hypertriglyceridemias

Disorder	Genetic defect	Inheritance	Prevalence	Clinical features
LPL deficiency	endothelial LPL	recessive	rare 1/1 million	hepatosplenomegaly abd. cramps, pancreatitis TG: > 8.5 mM
Apo C-II deficiency	Apo C-II	recessive	rare 1/1 million	abd. cramps, pancreatitis TG: > 8.5 mM
Familial hyper-triglyceridemia	unknown enhanced hepatic TG-production	dominant	1/100	abd. cramps, pancreatitis TG: 2.3-6 mM

Primary mixed hyperlipidemias

Disorder	Genetic defect	Inheritance	Prevalence	Clinical features
Familial dysbeta-lipoproteinemia	Apo E high VLDL, chylo.	recessive rarely dominant	1/5000	premature CAD TC: 6.5 -13 mM TG: 2.8 – 5.6 mM
Familial combined	unknown high Apo B-100	dominant	1/50 – 1/100 15% of MIs <60 yr	premature CAD TC: 6.5 -13 mM TG: 2.8 – 8.5 mM

Secondary hyperlipidemias

Disorder	VLDL	LDL	HDL	Mechanism
Diabetes mellitus	↑ ↑ ↑	↑	↓	VLDL production ↑, LPL ↓, altered LDL
Hypothyroidism	↑	↑ ↑ ↑	↓	LDL-rec.↓, LPL ↓
Obesity	↑ ↑	↑	↓	VLDL production ↑
Anorexia	-	↑ ↑	-	bile secretion ↓, LDL catab. ↓
Nephrotic syndrome	↑ ↑	↑ ↑ ↑	↓	Apo B-100 ↑ LPL ↓ LDL-rec. ↓
Uremia, dialysis	↑ ↑ ↑	-	↓	LPL ↓, HTGL ↓ (inhibitors ↑)
Pregnancy	↑ ↑	↑ ↑	↑	oestrogen ↑ VLDL production ↑, LPL ↓
Biliary obstruction PBC	-	-	↓	Lp-X ↑ ↑ no CAD; xanthomas
Alcohol	↑ ↑ chylomicr. ↑	-	↑	dep. on dose, diet, genetics

Risk factors

Diet

- Saturated fatty acids and cholesterol cause elevation in LDL and total cholesterol.
- High-calorie diets do not increase LDL or cholesterol levels (are “neutral”) but do increase triglyceride (TG) levels.
- Alcohol increases TG levels and HDL levels but does not affect total cholesterol levels.

Age:

Cholesterol levels increase with age until approximately age 65.The increase is greatest during early adulthood about 2 mg/dL per year.

Inactive lifestyle, abdominal obesity

Family history of hyperlipidemia

Gender:

Men generally have higher cholesterol levels than do women; when women reach menopause, cholesterol levels then equalize and may even be higher in women than in men.

Medications

- Thiazides:increase LDL, total cholesterol, TG (VLDL) levels.
- β-blockers (propranolol):increase TGs (VLDL) and lower HDL levels
- Estrogens:TG levels may further increase in patients with hypertriglyceridemia.
- Corticosteroids and HIV protease inhibitors can elevate serum lipids.

Genetic mutations that predispose to the most severe hyperlipidemias

Secondary causes of dyslipidemia.

Clinical features

1. Most patients are asymptomatic.
2. The following may be manifestations of severe hyperlipidemia:
a. Xanthelasma—yellow plaques on eyelids
b. Xanthoma—hard, yellowish masses found on tendons (finger extensors, Achilles tendon, plantar tendons).
3. Pancreatitis can occur with severe hypertriglyceridemia.

Diagnosis

1. Lipid screening (see Health Maintenance section)—Measure total cholesterol and HDL levels (nonfasting is acceptable). If either is abnormal, then order a full fasting lipid profile.
2. A full fasting lipid profile includes TG levels and calculation of LDL levels.
3. Consider checking laboratory tests to exclude secondary causes of hyperlipidemia.
a. TSH (hypothyroidism)
b. LFTs (chronic liver disease)
c. BUN and Cr, urinary proteins (nephrotic syndrome)
d. Glucose levels (diabetes)

Checking lipids

- Nonfasting lipid panel
  - measures HDL and total cholesterol
- Fasting lipid panel
  - Measures HDL, total cholesterol and triglycerides
  - LDL cholesterol is calculated:
    - LDL cholesterol = total cholesterol – (HDL + triglycerides/5)

When to check lipid panel

- Different Recommendations:
  - Adult Treatment Panel (ATP III) of the National Cholesterol Education Program (NCEP)
    - Beginning at age 20: obtain a fasting (9 to 12 hour) serum lipid profile consisting of total cholesterol, LDL, HDL and triglycerides
    - Repeat testing every 5 years for acceptable values
  - United States Preventative Services Task Force
    - Women aged 45 years and older, and men ages 35 years and older undergo screening with a total and HDL cholesterol every 5 years.
    - If total cholesterol > 200 or HDL <40, then a fasting panel should be obtained
    - Cholesterol screening should begin at 20 years in patients with a history of multiple cardiovascular risk factors, diabetes, or family history of either elevated cholesteral levels or premature cardiovascular disease.

Treatment Targets

- LDL: To prevent coronary heart disease outcomes (myocardial infarction and coronary death)
- Non LDL(TC/HDL): To prevent coronary heart disease outcomes (myocardial infarction and coronary death)
- Triglyceride: To prevent pancreatitis and may be coronary heart disease outcomes (myocardial infarction and coronary death)

Canadian New Guideline

Risk categories

Risk level	10-year CAD risk	Recommendations
High	≥20%	*Treatment targets:* Primary target: LDL-C <2.0 mmol/L Secondary target: TC/HDL-C <4.0
Moderate	10% - 19%	*Treat when:* LDL-C ≥3.5 mmol/L *or* TC/HDL-C ≥5.0
Low	<10%	*Treat when:* LDL-C ≥5.0 mmol/L *or* TC/HDL-C ≥6.0

High risk includes coronary artery disease (CAD), peripheral artery disease, cerebrovascular disease and most patients with diabetes.

To remember ;
LDL target: 2 , 3.5 , 5
TC/HDL target : 4 ,5 ,6

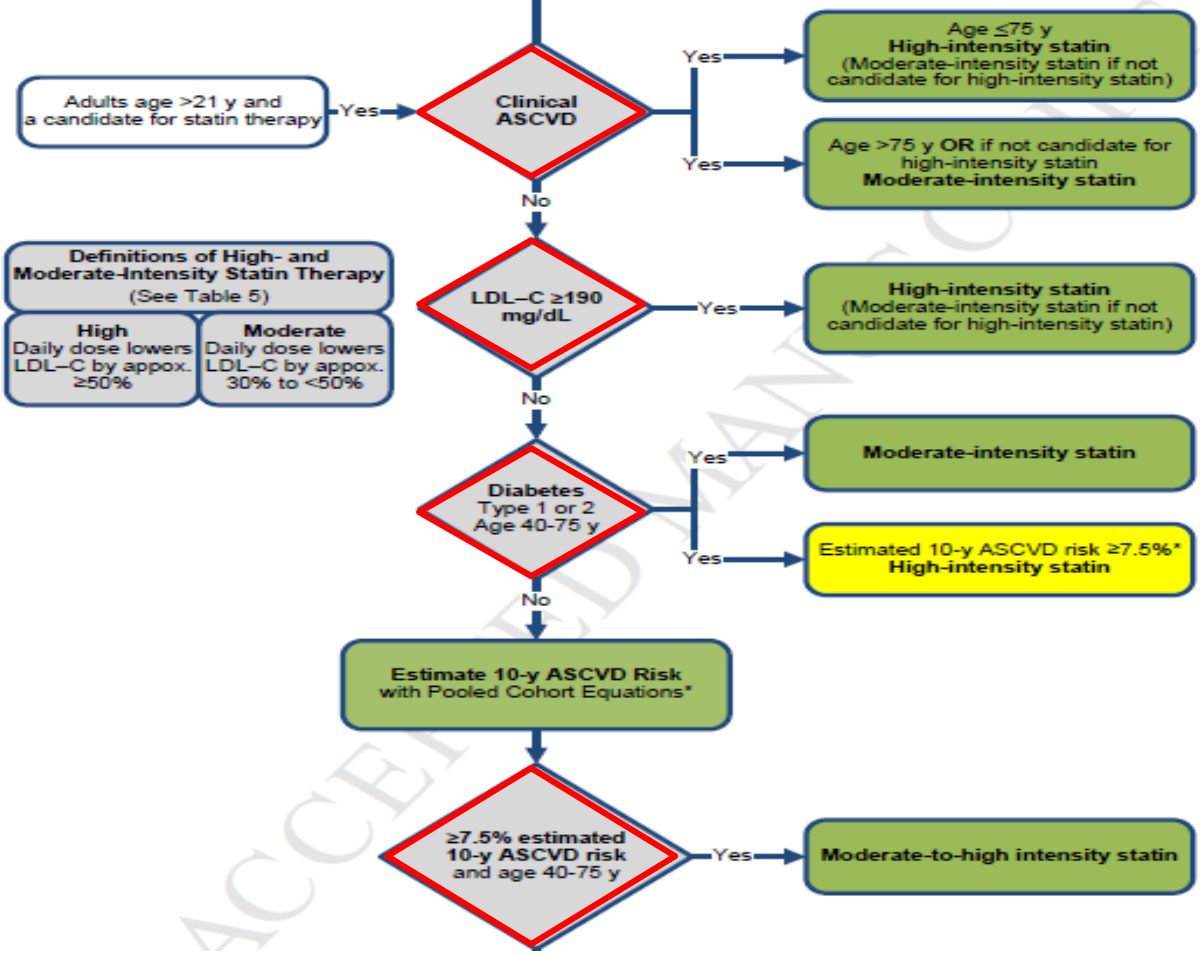
Risk Assessment Tool for Estimating 10-year Risk of Developing Hard CHD (Myocardial Infarction and Coronary Death)
Framingham Heart Study to estimate 10-year risk for coronary heart disease outcomes

- ✓ Age
- ✓ LDL-C
- ✓ T. Chol
- ✓ HDL-C
- ✓ Blood Pressure
- ✓ Diabetes
- ✓ Smoking

CLINICAL PEARL 12-1

Risk Factors for Coronary Artery Disease (CAD) in Evaluation of Patients with Hyperlipidemia

- Current cigarette smoking (dose-dependent risk)
- Hypertension
- Diabetes mellitus
- Low HDL cholesterol (<35 mg/dL); high HDL (>60 mg/dL) is a negative risk factor (subtract 1 from total)
- Age
  - Male: >45 years of age
  - Female: >55 years of age
- Male gender—if you count as a risk factor, do not count age
- Family history of **premature** CAD
  - MI/sudden death in male first-degree relative <55 years of age
  - MI/sudden death in female first-degree relative <65 years of age



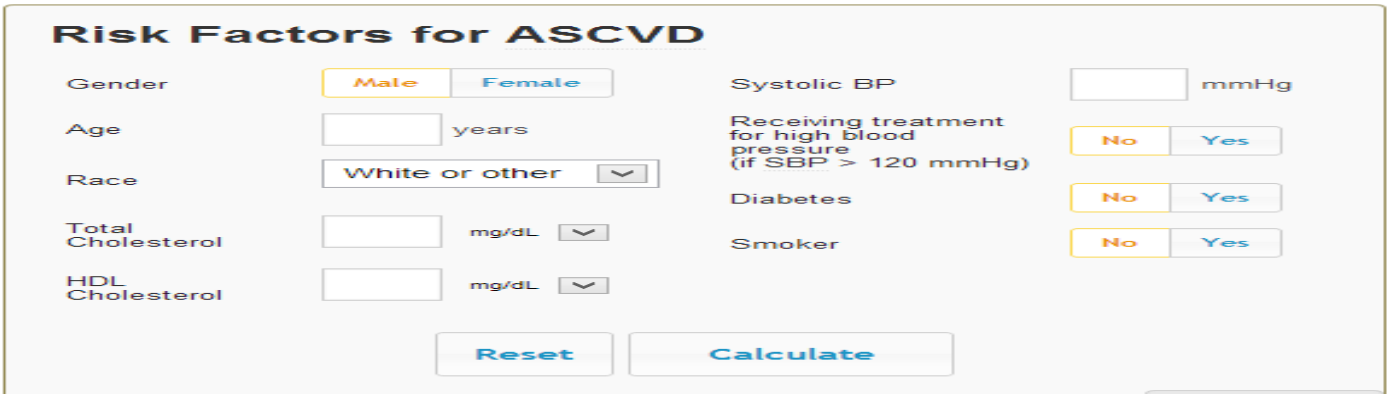
- You see the 4 statin benefit groups in the middle: on top, you see the patient's group with clinical ASCVD, below that you see the group with LDL >190, below that you see the patient's with history of DM 40-75 years old, and in the bottom, you see patients who don't have the characteristics of the first 3 groups but their 10 year ASCD risk is greater than 7.5%
- For the first group: based on the guidline, if you have clinical ASCD, are younger than 75 and don't have any history of intolerance to statin, you should be started on high intensity statin. On the other hand, if you are older than 75, or not a candidate for high intensity statin due to lets say intolerance to statins, you are a candidate for moderate-intensity statin
- For the second group, if your LDL is greater than 190, you need to be started on high-intensity statin, unless you have contra-indication to high dose →start on moderate dose
- For the third group, individuals with diabetes with above mentioned group age, you need to calculate the 10 year ASCVD risk using a new equation/calculater called "pooled Cohort Equations" →if the 10 year risk is greater than 7.5%, start them on high-intensity, otherwise, you can start them on moderate-intensity statin
- For the last group, you need to calculate patient's risk factor and start them on moderate-to-high intensity statin if their estimated 10-y ASCVD risk is greater than 7.5%
- Keep that in mind that what we mean by "high intensity" statin, is the daily dose of statin that lowers the LDL by appox greater than 50%, and what we mean by moderate intensity statin, is the daily dose of statin that lowers the LDL by appox 30-50%.

This is the new equation, the pooled cohort risk assessment equation.

- As you can see, there are different parameters that you need to plug in to the equation to calculate the risk: gender, age, race, total cholesterol, HDL, systolic BP, whether or not you are on any anti-HTN meds, any history of DM or being a smoker

Pooled Cohort Risk Assessment Equations

Predicts 10-year risk for a first atherosclerotic cardiovascular disease (ASCVD) event



Intensity of Statin Therapy in primary and secondary prevention

Table 5. High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)*

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL–C on average, by approximately ≥50%	Daily dose lowers LDL–C on average, by approximately 30% to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin (40†)–80 mg **Rosuvastatin 20 *(40)* mg**	**Atorvastatin 10 *(20)* mg** **Rosuvastatin *(5)* 10 mg** **Simvastatin 20–40 mg‡** **Pravastatin 40 *(80)* mg** **Lovastatin 40 mg** ***Fluvastatin XL 80 mg*** **Fluvastatin 40 mg bid** ***Pitavastatin 2–4 mg***	***Simvastatin 10 mg*** **Pravastatin 10–20 mg** **Lovastatin 20 mg** ***Fluvastatin 20–40 mg*** ***Pitavastatin 1 mg***

- ✓ The risk to have MI in diabetic patient is equal the risk to have another MI in a patient who had a previous MI (DM equivalent to pre-existing MI).
- ✓ Diabetic patients who is more than 75 years old we don't give them high dose of statins because the side affects will be more prominent on them and they are old already there is no need for prevention.

Table 8.1—Recommendations for statin treatment in people with diabetes

Age	Risk factors	Recommended statin dose*	Monitoring with lipid panel
<40 years	None	None	Annually or as needed to monitor for adherence
	CVD risk factor(s)**	Moderate or high	
	Overt CVD***	High	
40–75 years	None	Moderate	As needed to monitor adherence
	CVD risk factors	High	
	Overt CVD	High	
>75 years	None	Moderate	As needed to monitor adherence
	CVD risk factors	Moderate or high	
	Overt CVD	High	

*In addition to lifestyle therapy.
**CVD risk factors include LDL cholesterol ≥100 mg/dL (2.6 mmol/L), high blood pressure, smoking, and overweight and obesity.
***Overt CVD includes those with previous cardiovascular events or acute coronary syndromes.

Treatment of Hyperlipidemia

- ✓ Lifestyle modification
  - Low-cholesterol diet
  - Exercise

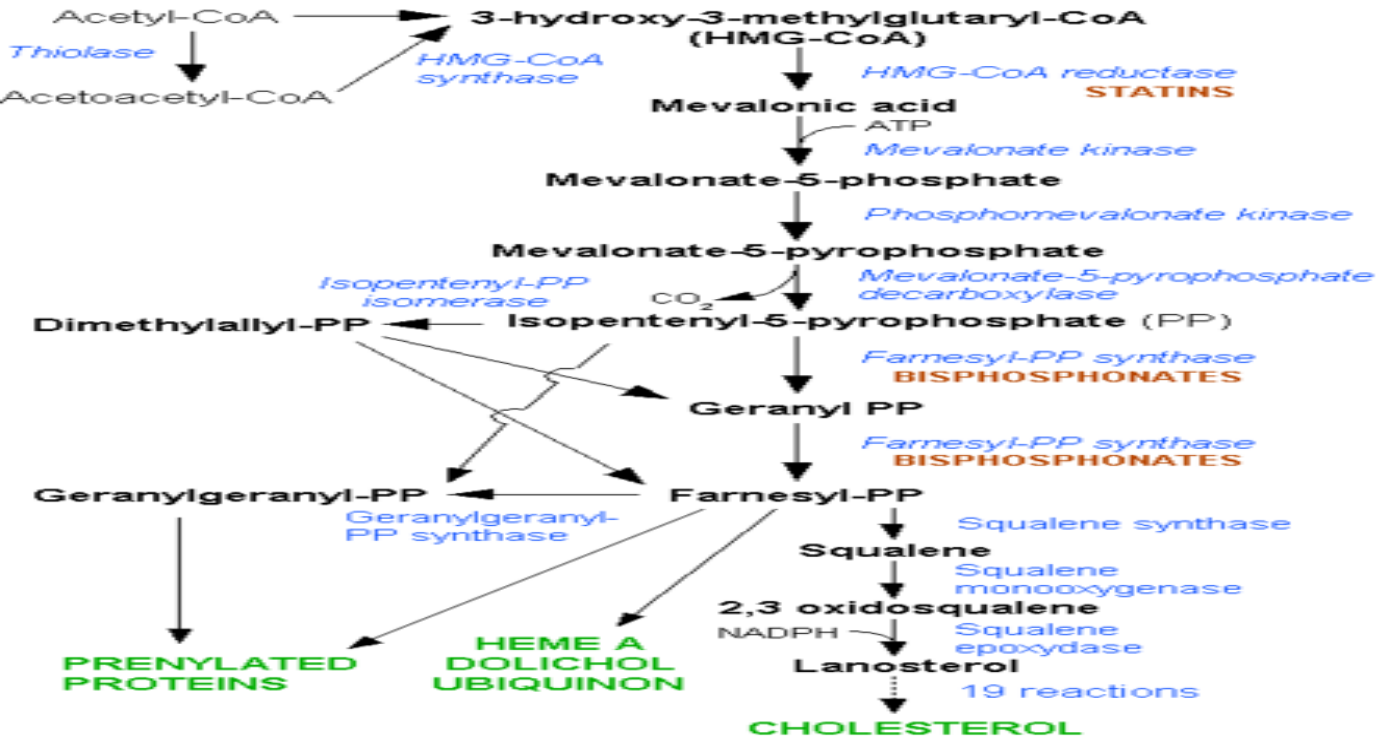
Medications for Hyperlipidemia

Drug Class	Agents	Effects (% change)	Side Effects
HMG CoA reductase inhibitors	Statins	↓LDL (18-55),↑ HDL (5-15) ↓ Triglycerides (7-30)	Myopathy, increased liver enzymes
Cholesterol absorption inhibitor	Ezetimibe	↓ LDL(14-18), ↑ HDL (1-3) ↓Triglyceride (2)	Headache, GI distress
Nicotinic Acid		↓LDL (15-30), ↑ HDL (15-35) ↓ Triglyceride (20-50)	Flushing, Hyperglycemia, Hyperuricemia, GI distress, hepatotoxicity
Fibric Acids	Gemfibrozil Fenofibrate	↓LDL (5-20), ↑HDL (10-20) ↓Triglyceride (20-50)	Dyspepsia, gallstones, myopathy
Bile Acid sequestrants	Cholestyramine	↓ LDL ↑ HDL No change in triglycerides	GI distress, constipation, decreased absorption of other drugs

- ✓ The only drug that reduce mortality and increase survival from ischemic heart diseases is statin.
- ✓ TG< 5.6 = no risk of pancreatitis only risk of MI > give statin.
- ✓ TG> 5.6 = Risk of pancreatitis = give fibrate .

The mechanism of action of statins

1) Inhibition of HMG CoA reductase (reduce the cholesterol in the hepatocyte)
2) Up-regulation of the LDL receptor.



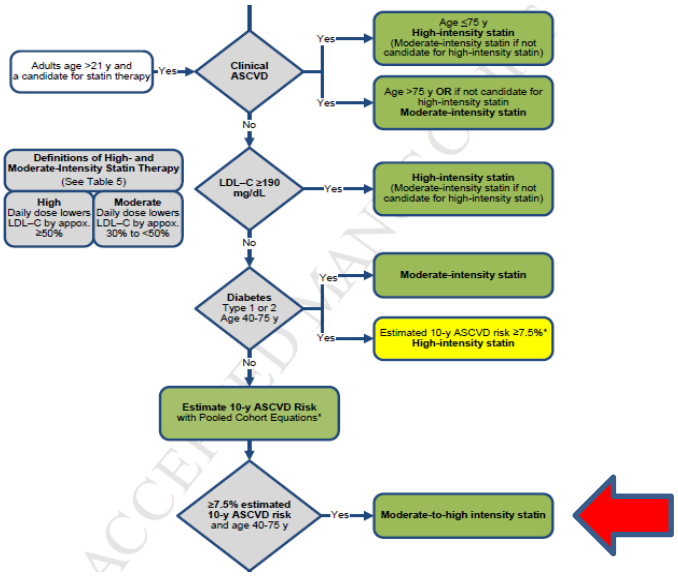
STATIN Safety recommendations

- Conditions that could predispose pts to statin side effect:
  - Impaired renal or hepatic function
  - History of previous statin intolerance or muscle disorder
  - Age >75y
  - Unexplained ALT elevation > 3x ULN
  - History of hemorrhagic stroke
  - Asian ancestry
- Check baseline ALT prior initiating the statin (Grade B)
- Check LFTs if patient develops Symptoms of hepatic dysfunction (Grade E)
- If 2 consecutive LDL <40, Consider decreasing the statin dose (Grade C, weak recommendation)
- It may be harmful to initiate simvastatin 80mg, or increase the dose of simvastatin to 80mg (Grade B)

(Symptoms of hepatic dysfunction: unusual fatigue or weakness, loss of appetite, abdominal pain, dark colored urine, Jaundice)

Case 1

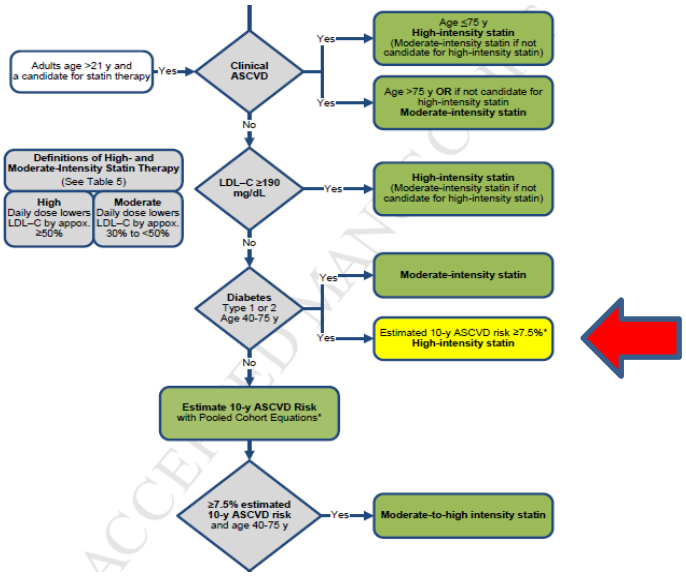
62 year old AA male
Total cholesterol: 140
Low HDL: 35
SBP: 130 mmHg
Not taking anti-hypertensive medicati
Non-diabetic
Non-smoker
Calculated 10 yr risk of ASCVD : 9.1%



Ans:
Mention that patient belongs to the fourth group meeting the criteria for moderate to high intensity statin given the 10 year risk of ASCVD is greater than 7.5%

Case 2

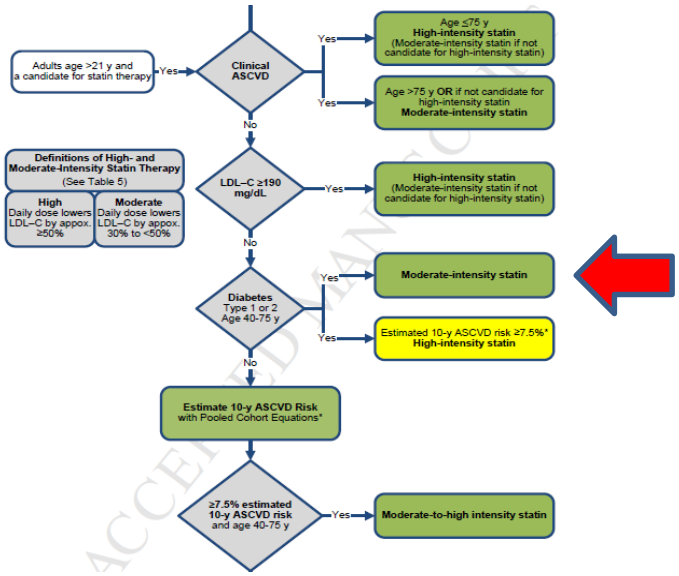
50 year old white female
Total cholesterol 180
HDL: 50
SBP: 130
taking anti-hTN meds
+diabetic
+smoker
Calculated 10 yr ASCVD: 9.8%



Ans:Mention that patient is a diabetic with 10 yr risk is greater than 7.5% so he or she is candidate for high intensity statin

Case 3

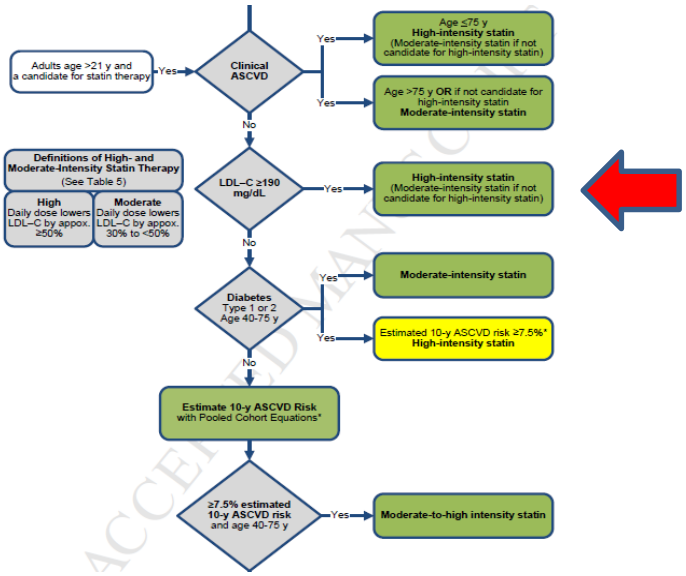
48 yo white female
Total cholesterol 180
HDL: 55
SBP: 130
Not taking anti-hTN meds
+diabetic
Non-smoker
Calculated 10 yr risk ASCVD : 1.8%



Ans:Mention that patient is a diabetic but since his or her ASCVD is less than 7.5%, he or she is a candidate for moderate intensity statin

Case 4

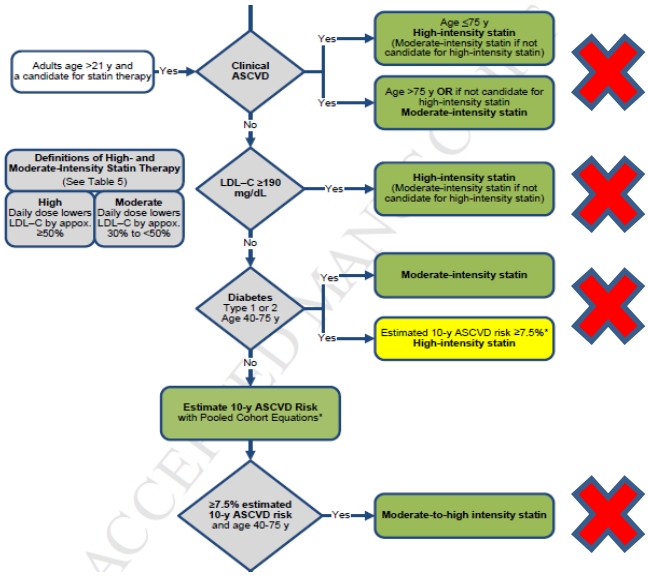
22 yo white male
LDL: 195
SBP: 120
Not taking anti-hTN meds
Non-diabetic
Non-smoker



Ans:Ask the learner whether or not you need to calculate the 10 yr risk for developing the ASCVD in a patient with LDL>195. The answer is NO. This patient belongs to the second statin benefit group and is a candidate for high intesntity Statin regardless of 10 year risk

Case 5

66 yo white female
High Total cholesterol: 230
HDL: 55
SBP: 150
taking anti-hTN meds
Non-diabetic
Non-smoker
Calculated 10 yr risk of ASCVD : 2.0 %



Ans:Mention that despite the fact that the total cholesterol is high, since the LDL is less than 195, and patient doesn't meet any other statin benefit group, there is no indication for statin therapy

Take home massage

1.Rather than LDL–C or non-HDL– C targets, new guideline uses the intensity of statin therapy as the goal of treatment.
2.Know the 4 Statin Benefit Groups:

I. Individuals with clinical ASCVD
II. Individuals with primary elevations of LDL–C ≥190 mg/dL
III. Individuals 40 to 75 years of age with diabetes and LDL–C 70 to189 mg/dL without clinical ASCVD
IV. Individuals without clinical ASCVD or diabetes who are 40 to 75 years of age with LDL–C 70 to 189 mg/dL and have an estimated 10-year ASCVD risk of 7.5% or higher. (**using the Pooled Cohort Equations for ASCVD risk prediction**)

MCQ's

Q1. 39-year-old man with a prior history of myocardial infarction complains of yellow bumps on his elbows and buttocks. Yellow-colored cutaneous plaques are noted in those areas. The lesions occur in crops and have a surrounding reddish halo. Which of the following is the best next step in evaluation of this patient?

a. Biopsy of skin lesions
b. Lipid profile
c. Uric acid level d. Chest x-ray
e. Liver enzymes

Q2. A 58-year-old man who smokes cigarettes has a history of hypertension and asks about reducing his risk for myocardial infarction. A lipid profile shows low HDL cholesterol at 32 mg/dL. Which of the following is an important recommendation in attempting to raise the HDL?

a. Aspirin, 325 mg each day
b. Low-cholesterol diet
c. Vitamin E, 400 units each day
d. DHEA (dehydroepiandrosterone) supplementation
e. Exercise and smoking cessation

Q3. A 60-year-old white man has just moved to town and needs to establish care. He had a “heart attack” last year. Preferring a “natural” approach, he has been very conscientious about low-fat, low-cholesterol eating habits and a significant exercise program. He has gradually eliminated a number of prescription medications (he does not recall their names) that he was on at the time of hospital discharge. Past history is negative for hypertension, diabetes, or smoking. The lipid profile you obtain shows the following:
Total cholesterol: 194 mg/dL
Triglycerides: 140 mg/dL
HDL: 42 mg/dL LDL (calculated): 124 mg/dL
ECG shows Q waves in leads II, II, and aVF consistent with an old inferior MI
Which of the following recommendations would most optimally treat his lipid status?

a. Continue current dietary efforts and exercise.
b. Add an HMG-CoA reductase inhibitor (statin drug) to reduce LDL cholesterol to less than 100 mg/dL with an ideal goal of 70 mg/dL if achievable.
c. Add a fibric acid derivative such as gemfibrozil or fenofibrate.
d. Review previous medications and resume an angiotensin-converting enzyme inhibitor.
e. Have the patient buy over-the-counter fish oil tablets and take 2 g in the morning and 2 g in the evening.

Q4 A 32-year-old, overweight, diabetic woman is found to have a triglyceride level greater than 1000 mg/dL. Family history is positive for diabetes, pancreatitis, and premature coronary artery disease. TSH is normal. You advise the patient to follow a low-fat diabetic diet, to exercise regularly and to avoid alcohol. What medication would be most appropriate to start at this time?

a. High-dose rosuvastatin
b. Nicotinic acid
c. Low-dose atorvastatin
d. High-dose fenofibrate
e. Over-the-counter fish oil

Answer: 1.b 2.e 3.b 4.d

Explanations

A1. The description and location of these lesions are suggestive of eruptive xanthomas. Eruptive xanthomas occur primarily on buttocks or extensor surfaces and are associated with elevated triglycerides. Tophaceous gout can result in deposits of monosodium urate, usually in the skin around joints of the hands and feet. Tophi are usually white and may discharge a chalky material. Skin biopsy is not usually necessary to distinguish these lesions. The cutaneous lesions of sarcoidosis (which would usually show disease on CXR) are reddish-brown waxy papules, usually on the face. Obstructive liver disease can occasionally cause palmar xanthomas, which are seen as yellow plaques along the palmar creases.
Xanthomas can be important cutaneous clues for underlying lipid disorders. Xanthelasmas, yellowish plaques on the inner aspect of the upper eyelids, are nonspecific but are associated with hyperlipidemia 50% of the time. Tendon xanthomas are important clues for familial hypercholesterolemia. Tuberous xanthomas, which often present as plaques or even polypoid nodules over pressure points, usually signify hypercholesterolemia. Eruptive xanthomas, again, are associated with triglyceride levels above 1000 mg/dL. Treatment of the hypertriglyceridemia usually results in resolution of lesions. Biopsy of a xanthoma would show lipid-containing macrophages, but is usually not necessary for diagnosis.

A2. Within this group of choices, only exercise and smoking cessation have been shown to raise HDL. A low-cholesterol diet actually lowers HDL. Among current lipid-lowering medications, nicotinic acid has the most potent HDL- increasing effect at 15% to 35%, followed by fibric acids and then statins. Alcohol also increases the HDL level (HDL2 and HDL3 subfractions), thereby imparting some cardioprotective effect, but at the risk of cardiomyopathy, sudden death, hemorrhagic stroke, and other noncardiovascular problems among heavy drinkers. The cardiovascular system may benefit from aspirin (because of antiplatelet effects), but it has no effect on HDL. After initial enthusiasm for vitamin E, more recent studies have not shown consistent cardiovascular benefit from antioxidant vitamins. None of these raise HDL. DHEA supplements lower HDL values.

A3. The National Cholesterol Education Program Adult Treatment Panel III recommendations include lowering the LDL cholesterol to less than 100 mg/dL in those with known coronary heart disease (secondary prevention). The 2004 update to these guidelines adds an optional goal of LDL less than 70 mg/dL in very high-risk patients. In this case, with dietary efforts and exercise already well established, it is unlikely that the LDL will be further reduced hence a statin drug is indicated. Statins typically lower LDL by 20% to 50%. Gemfibrozil is used primarily for hypertriglyceridemia; this patient's triglyceride level is normal (< 150 mg/dL). ACE inhibitors have no significant effect on lipids. While high-dose fish oil does lower triglyceride levels, it is not effective at lowering LDL cholesterol levels. Lowering LDL cholesterol is of prime importance in the prevention of coronary heart disease of coronary heart disease prevention

A4. A normal triglyceride (TG) level is below 150 mg/dL. A moderate to high triglyceride level is between 150 to 499 mg/dL, and over 500 is considered very high. Obesity increases TG levels by causing increased hepatic VLDL production. In diabetes, insulin insufficiency leads to decreased lipoprotein lipase activity and impairment of VLDL catabolism. In addition, this patient may have familial hypertriglyceridemia or familial combined hyperlipidemia. All such patients should be advised to follow a low-fat diet. Because of the risk of acute pancreatitis with such high levels of TG, medication should be instituted as well. Patients with levels over 500 should be started on a fibrate such as fenofibrate or gemfibrozil.
While potent statins such as rosuvastatin and atorvastatin decrease TG modestly, they are second-line agents in this situation. Nicotinic acid also reduces TG levels but often elevates the blood glucose level in diabetics. Fish oil in high doses can lower the TG level but not as effectively as fenofibrate or gemfibrozil.

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