Lecture 50

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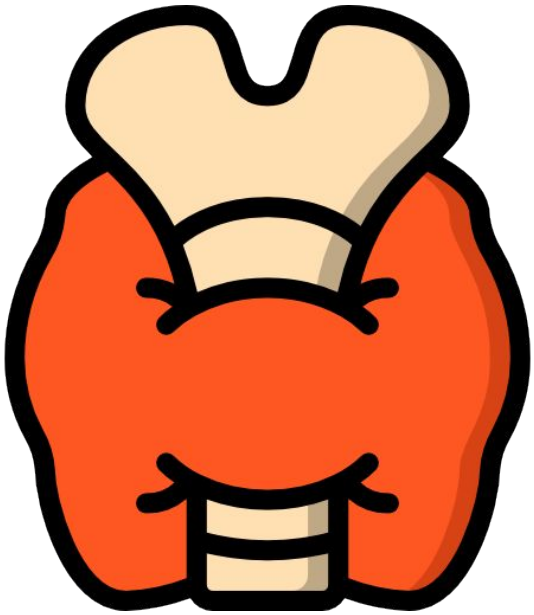

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Dyslipidemia

Objectives:

- ★ Know the Physiology of lipid and lipoprotein cycles
- ★ Know the most important hereditary diseases related to lipid
- ★ Know the 2ndary causes of hyperlipidemia
- ★ Approach the patient with hyperlipidemia
- ★ Discussion around the therapy

Color index:

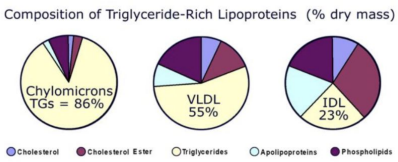
Original text Females slides Males slides
Doctor's notes Textbook Important Golden notes Extra

Introduction

Definition

Lipids are insoluble in water, and are **transported in the bloodstream as lipoprotein** particles composed of:

- **Lipids:**
  - Mainly triglycerides, cholesterol and cholesterol esters
  - surrounded by a coat of phospholipids.
- **Proteins:**
  - Called apo- proteins
  - Embedded into the phospholipid coating exert a stabilizing function and allow the particles to be recognized by receptors in the liver and peripheral tissues.



◄ Plasma lipoproteins:

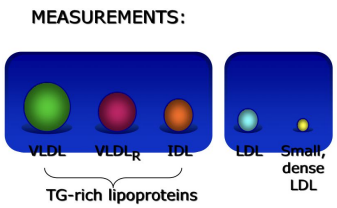
Type	Source	Major lipid	Apoproteins	ELFO	Atherogenicity
Chylomicron	• **Function:** transport the digestion products of dietary fat to the liver and peripheral tissues.				
	Gut	Dietary TGs and a small amount of cholesterol and its ester	A-I, B-48, C-I, C-III, E	no mobility	**Not atherogenic** (doesn't cause MI) **but causes pancreatitis**
VLDL	• Contain **most of the body's endogenous triglyceride** and a smaller quantity of cholesterols • Very raised triglyceride concentrations (>6 mmol/L) cause a greatly increased risk of acute pancreatitis and retinal vein thrombosis. Hypertriglyceridemia tends to occur in association with a reduced HDL concentration.				
	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	• The main carrier of cholesterol, and deliver it both to the liver and to peripheral cells. And can deposit lipid into the walls of the peripheral vasculature				
	VLDL, IDL	Ch esters	B-100 and E	β	+++
HDL ★	• Nascent HDL become mature particles by the acquisition of phospholipids, and the E and C apoproteins from chylomicrons and VLDL in the circulation • **Function:** transports cholesterol away from the periphery either indirectly to other particles such as VLDL in the circulation or directly to the liver and steroid-synthetic tissues (ovaries, testes, adrenal cortex)				
	Gut, liver	Ch esters, PLs	A-I, A-II, C-II, C-III, D, E	α	**Anti-atherogenic**

Introduction *(cont.)*

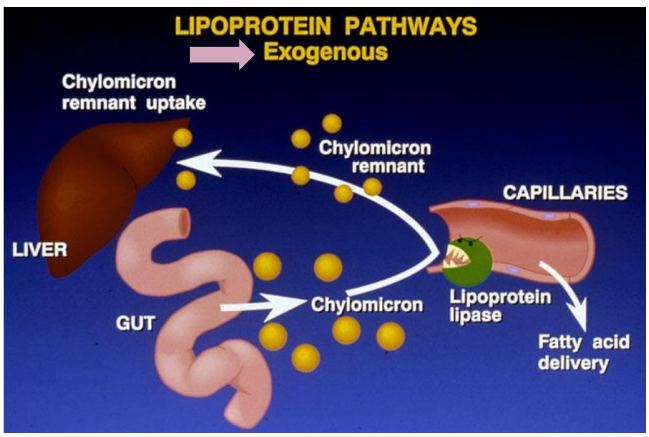
◄ Atherogenic particles

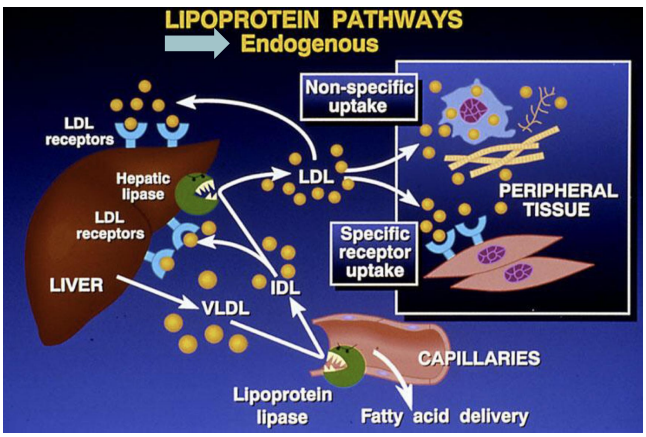
Atherogenic cholesterol → LDL, VLDL, IDL

- When oxidized LDL cholesterol gets high → atheroma formation in the walls of arteries occurs → atherosclerosis.
- **HDL** cholesterol is able to go and **remove cholesterol from the atheroma.**
- ★ **Which one has the most atherogenic effect? Small dense LDL.** Because it's very small and can easily penetrate the intima of the blood vessels, can easily concentrate there and easily taken by macrophages. Even though it has the least amount of cholesterol!



◄ lipoprotein pathway





IMP to know the enzymes & their functions

Exogenous pathway (post-prandial):

Chylomicrons transport fats **from the intestinal mucosa** to the **liver** through the portal vein:

- Chylomicrons acquire apoproteins C-II and E from HDL particles in the bloodstream. Apoprotein C-II binds to specific receptors in adipose tissue and skeletal muscle and the liver, where the endothelial enzyme, **intestinal lipoprotein lipase** hydrolyses chylomicron and form chylomicron remnants and free fatty acid into blood stream. chylomicron remnant particle is then taken up by the liver through LDLRs (Low-Density Lipoprotein receptors) which recognizes Apoprotein E.

Endogenous pathway of (VLDL → IDL):

- In the **liver**, **VLDL** released **to blood stream** to form LDL, IDL and LDL, how? contains Apoprotein B-100. And acquires apoproteins C-II and E from HDL particles in the bloodstream. apoprotein C-II allows triglyceride to be removed by lipoprotein lipase in the capillary endothelium. leaves a particle depleted of triglyceride and apoprotein C-II, called IDL (**Endothelial lipoprotein lipase** breakdown VLDL to form IDL and FFA)

Endogenous pathway of (IDL → LDL):

- Most IDL particles bind to liver LDL receptors through apoprotein E molecule and are then catabolized by **hepatic lipase (which breakdown IDL to form LDL).** Some of the IDL is taken up by LDL receptor (it has some affinity to IDL). **LDL** then carries fat and cholesterol **to the body's cells**. After that, LDL has two pathways to be taken up. Either through LDL receptors s in Liver take the LDL to Liver. Or to the peripheral tissue (main way) by two means: specific receptor uptake (by muscles) and non-specific uptake (by WBCs).

Reverse cholesterol transport (HDL):

- **Nascent HDL** released from **intestine** and **liver** and **carry fat and cholesterol from blood vessels (Periphery) to the liver**. There are two forms of HDL: Mature HDL (Already contains cholesterol) and Nascent HDL (Empty of cholesterol, carries nothing). So, if you want to inject HDL, **you inject nascent HDL NOT** mature HDL because mature HDL is already saturated with cholesterol)

Hyperlipidemia

◀ Dietary sources of cholesterol

Type of fat	Main source	Effect on Cholesterol levels
Monounsaturated (the best type)	Olives, olive oil, canola oil, peanut oil, cashews, almonds, peanuts and most other nuts; avocados	Lowers LDL, Raises HDL
Polyunsaturated	Corn, soybean, safflower and cottonseed oil; fish	Lowers LDL, Raises HDL
Saturated	Whole milk, butter, cheese, and ice cream; red meat; chocolate; coconuts, coconut milk, coconut oil , egg yolks, chicken skin	Raises both LDL and HDL
Trans (the worst type)	Most margarines; vegetable shortening; partially hydrogenated vegetable oil; deep-fried chips; many fast foods; most commercial baked goods	Raises LDL

◀ Classification of hyperlipidemias

Skipped by the dr " i hated it when i was young so i won't give to you"

Fredrickson classification of hyperlipidemias

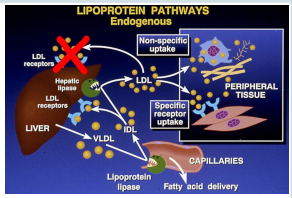
Phenotype	Lipoprotein(s) elevated	Plasma cholesterol	Plasma TGs	Athero-genicity	Rel. freq.	Treatment
I	Chylomicrons	Norm. to ↑	↑↑↑↑	– pancreatitis	<1%	Diet control
IIa	LDL	↑↑	Norm.	+++	10%	Bile acid sequestrants, statins, niacin
IIb	LDL and VLDL	↑↑	↑↑	+++	40%	Statins, niacin, fibrates
III	IDL	↑↑	↑↑↑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

An area for your notes

Hyperlipidemia *(cont.)*

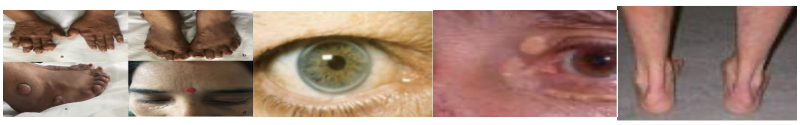
◄ Hereditary causes of hyperlipidemia :

Familial Hypercholesterolemia



Mutation in LDL receptor (normally take up LDL from blood stream), resulting in elevated levels of LDL at birth and throughout life

- **Heterozygous:**
  - Co-dominant genetic disorder, cooccurs in heterozygous form. needs only one allele
  - Occurs in 1 in 500 individuals
  - High risk for atherosclerosis, tendon xanthomas (75% of patients) especially in the extensors of the fingers + achilles tendon, tuberous xanthomas, xanthelasmas of eyes and arcus senilis (In younger ppl, it's called arcus juvenilis)
- **Homozygous:**
  - **Total absence** of LDL receptors
  - Death from ischaemic heart disease in late childhood or adolescence.
  - Repeated plasmapheresis has been used to remove LDL cholesterol. But Liver transplantation is the 'cure'.



Treatment:

- Individuals often require treatment with **diet** and more than one cholesterol-lowering drug.
- The cholesterol absorption inhibitor **ezetimibe** is a logical addition to a statin.
  - Bile acid sequestrants are an alternative to ezetimibe, but there are problems with tolerability.
- Concurrent therapy with **statins and fibrates**, particularly **fenofibrate**, can be used in severe cases.

Familial Combined Hyperlipidemia

- Autosomal dominant.
- Prevalence: 1/50 – 1/100 dominant (15% of MIs <60)
- **diagnosis**: by finding **raised cholesterol AND triglyceride** concentrations in association with a typical family history. There are no typical physical signs.
- Increased secretions of VLDLs
- Genetic defect: unknown → high Apo B-100
- Clinical features:
  - premature CAD
  - TC: 6.5 -13 mM
  - TG: 2.8 – 8.5 mM.

Treatment: is the same for all varieties of combined hyperlipidaemia.

- For any given cholesterol concentration the hypertriglyceridaemia found in the combined hyperlipidaemias **increases the cardiovascular risk considerably**.
- **Treatment aim:** reducing serum cholesterol below 4.0 mmol/L and triglycerides below 2.0 mmol/L.
- Therapy is with **diet**
- Add drugs if an adequate response has not occurred:
  - **Fibrates** are the treatment of choice since these reduce both cholesterol and triglyceride concentrations, and also have the benefit of raising cardioprotective HDL concentrations. Combination with other agents is often needed

◀ Hereditary causes of hyperlipidemia *(cont.)*:

Dysbetalipoproteinemia

- Rare cause of combined hyperlipidemia
- Recessive but rarely can be dominant, affects 1 in 10,000 (1/5000)
- Almost always due to the inheritance of a variant of the apoprotein E allele. Results in apo E2, a binding-defective form of apoE (which usually plays important role in metabolism of chylomicron and VLDL → High VLDL and chylomicrons)
- It is due to accumulation of LDL remnant particles
- Increased risk for atherosclerosis, peripheral vascular disease
- Clinical features:
  - premature CAD
  - TC: 6.5 -13 mM
  - TG: 2.8 – 5.6 mM
  - Tuberous xanthomas: typically over the knees and elbows
  - Xanthomas in the palmar creases (diagnostic)
  - striae palmaris

◀ other causes of hyperlipidemia :

Disorders of HDL

Very low HDL, low total cholesterol.

1. **Tangier disease**
   - **a.** autosomal recessive disorder characterized by a low HDL cholesterol concentration.
   - **b.** due to mutation in ABC1 which normally promotes cholesterol uptake from cells by HDL particles.
   - **c.** Cholesterol accumulates in reticuloendothelial tissue and arteries causing enlarged orange-coloured tonsils and hepatosplenomegaly. Cardiovascular disease, corneal opacities and a polyneuropathy.

An area for your notes

Hyperlipidemia *(cont.)*

◀ Primary hypercholesterolemia :

Disorder	Genetic defect	inheritance	Prevalence	Clinical features
★ **Familial hypercholesterolemia**	**LDL receptor**	**Dominant**	**heterozygous:** 1/500 (5% of MIs<60 yr) **homozygous:** 1/1 million[1]	• **Heterozygous:** Premature CAD (ages 30-50) TC:7-13 mM • **Homozygous:** CAD (before age 18) TC>13 mM
Familial defective apo B-100	apo B-100[2]	dominant	1/700	(same as heterozygous familial hypercholesterolemia) • premature CAD • TC: 7-13 mM
Familial alphalipoproteinemia	unknown	Variable	common (10% of MIs<60yrs)	• abd. cramps • pancreatitis • retinal vein thrombosis • TG: 2.3-6 mM
Familial hyperalphalipoproteinemia	unknown	Variable	Rare	• Less CHD • longer life • elevated HDL

◀ Primary hypertriglyceridemia :

Disorder	Genetic defect	inheritance	Prevalence	Clinical features
LPL deficiency[3]	**Endothelial LPL**	**Recessive**	Rare (1/1 million)	• hepatosplenomegaly • abd. cramps • **pancreatitis at young age** • TG: > 8.5 mM
Apo C-II deficiency[4]	**Apo C-II** (the only cofactor that helps LDL to work)			• abd. cramps • pancreatitis • TG: > 8.5 mM
Familial hypertriglyceridemia	unknown enhanced hepatic TG-production	dominant	1/100	• abd. cramps • pancreatitis • retinal vein thrombosis • TG: 2.3-6 mM

1: no LDL receptor, cause massive MI, scenario is usually a young (30s) family member who died of MI.

2: Mutations in the apoprotein B-100 gene: LDL particles bind to their receptor in the liver through apoprotein B-100, defect in it results in high LDL concentrations, its clinical picture resembles heterozygous familial hypercholesterolaemia. Treatment approach is the same.

3: result in very high level of chylomicron and VLDL= ↑TGs

4: Lipoprotein lipase deficiency and apoprotein C-II deficiency: rare diseases produce greatly elevated triglyceride concentrations due to the persistence of chylomicrons (not VLDL particles). Patients present in childhood with eruptive xanthomas, lipaemia retinalis and retinal vein thrombosis, pancreatitis and hepatosplenomegaly.

Hyperlipidemia *(cont.)*

◀ Secondary hyperlipidemias

Disorder	VLDL	LDL	HDL	Mechanism
Secondary hypercholesterolemia				
Hypothyroidism[3]	↑	↑↑↑	↓	LDL-rec.↓, LPL ↓
Anorexia nervosa	-	↑↑	-	bile secretion ↓, LDL catab. ↓
Nephrotic syndrome	↑↑	↑↑↑	↓	Apo B-100 ↑ LPL ↓ LDL-rec. ↓
Pregnancy Everything will increase	↑↑	↑↑	↑	oestrogen ↑ VLDL production ↑, LPL ↓
Biliary obstruction PBC	-	-	↓	Lp-X ↑↑ no CAD; xanthomas
Other causes	• drugs: Diuretics, ciclosporin, glucocorticoids, androgens, ART agents (protease inhibitors).			
Secondary hypertriglyceridaemia				
Diabetes mellitus[1]	↑↑↑	↑	↓	VLDL production ↑, LPL ↓, altered LDL[2]
Obesity	↑↑	↑	↓	VLDL production ↑
Uremia, dialysis	↑↑↑	-	↓	LPL ↓, HTGL ↓ (inhibitors ↑)
Alcohol	↑↑↑ chylomicron. Risk of pancreatitis	-	↑	dep. on dose, diet, genetics
Other causes	• Hepatocellular disease (Acute hepatitis), SLE, diet. • drugs: B-blockers, retinoids, glucocorticoids, ART agents (protease inhibitors).			

◀ When to check lipid panel?

Different Recommendations:

1. **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
2. **US preventive services task force:**

- **Women ≥ 45** years
- **Men ≥ 35** years

undergo screening with a **total** and **HDL** cholesterol **every 5 years.**

If total **cholesterol > 200** or **HDL<40** → a fasting panel should be obtained

Cholesterol screening should begin **at 20 years in patients with a history** of:

- Multiple cardiovascular risk factors
- Diabetes
- Family history of:
  - Elevated cholesterol levels
  - Premature cardiovascular disease.

1: most important and most common
2: very bad combination.
3: affect hepatic lipase

Hyperlipidemia: treatment

◀ Treatment of hyperlipidemia

Click here for a drugs summary table

1 Lifestyle modification, Low-cholesterol diet, Exercise, Alcohol and Smoking cessation.

2 Medication

➔ **Goal of treatment[1]:**

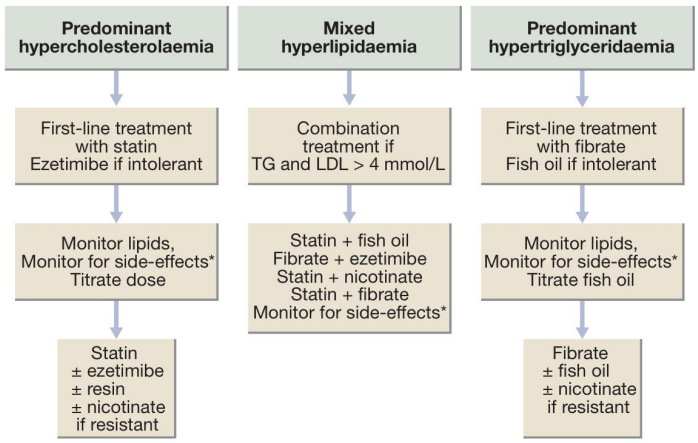
- **LDL**: To **prevent coronary heart disease outcomes** (myocardial infarction and coronary death)
- **Non LDL(Total Cholesterol/HDL)[2]:** To prevent coronary heart disease outcomes (myocardial infarction and coronary death)
- **Triglyceride:** To **prevent pancreatitis** and may be coronary heart disease outcomes (myocardial infarction and coronary death)

Drug class	Agents[3]	Effects (% change)	Side Effects
HMG CoA reductase inhibitors*	Statins	↓LDL (18-55), ↑HDL (5-15) Triglycerides (7-30)	• Myopathy (High CK level) • increased liver enzymes
Fibric Acids[4]	Gemfibrozil Fenofibrate	↓LDL (5-20), ↑HDL (10-20) ↓Triglyceride (20-50)	• Dyspepsia • gallstones • myopathy
Cholesterol absorption inhibitor	Ezetimibe[5]	↓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
Bile Acid sequestrants	Cholestyramine	↓LDL, ↑HDL No change in triglycerides	• GI distress • constipation • decreased absorption of other drugs
PCSK9 inhibitors[6]	Evolocumab Alirocumab	↓LDL (50-60%)	• injection-site reactions • muscle pain • neurocognitive adverse events → include memory impairment and confusion

1: normal range of lipoproteins depend on pt plus his medical condition.
2: all lipoproteins except HDL
3: most used classes are: statins, ezetimibe and PCSK9
4: stimulate peroxisome proliferator-activated receptor (PPAR) alpha, which controls the expression of gene products that mediate the metabolism of TG and HDL (work mainly on TGs). As a result, it will decrease synthesis of fatty acids, TG and VLDL, while increase lipoprotein lipase, which catabolises TG. In addition, production of Apo A1 and ABC A1 is up-regulated, leading to increased HDL. usually well tolerated but share a similar side-effect profile to statins (discussed in the next slide). In addition, they may increase the risk of cholelithiasis and prolong the action of anticoagulants.
5. Ezetimibe + statins for synergistic effect
6: Monoclonal antibodies that neutralise PCSK9, an enzyme that degrades the LDLR. This causes levels of LDLR to increase, which markedly reduces LDL-C. administered by subcutaneous injection every 2–4 weeks, well tolerated and highly effective. **Treats Hypercholesterolemia**

Hyperlipidemia: treatment *(cont.)*

◀ Flow chart for the drug treatment of hyperlipidemia



◀ Statin therapy

- Reduce cholesterol synthesis by **inhibiting the HMG CoA reductase enzyme. Low** levels of intracellular cholesterol → **up-regulates** production of the **LDL receptor** → increases clearance of LDL & its precursor.
- Generally well tolerated and serious side-effects are rare.
  - Liver function test abnormalities and muscle problems, such as myalgia, asymptomatic increase in creatine kinase (CK), myositis and, infrequently, rhabdomyolysis, are the most common.
- **Atorvastatin** and particularly **rosuvastatin** have the **most potent cholesterol-lowering effects**
- There is clear evidence of **protection against total and coronary mortality**, stroke and cardiovascular events across the spectrum of cardiovascular disease risk.

Low intensity statin therapy

Daily dose lowers LDL-C, on average **by <30%**

- Simvastatin 10 mg
- Pravastatin 10–20 mg
- Lovastatin 20 mg
- Fluvastatin 20–40 mg
- Pitavastatin 1 mg

Medium intensity statin therapy

Daily dose lowers LDL-C, on average, by approximately **30% to <50%**

- 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

High intensity statin therapy

Daily dose lowers LDL-C, on average by approximately **≥50%**

- Atorvastatin (40†)–80 mg
- Rosuvastatin 20 (40) mg

An area for your notes

Hyperlipidemia: treatment *(cont.)*

◀ ASCVD prevention

Stepwise approach:

1) The first question you ask yourself: **does the patient have clinical cardiovascular disease?** (= always treat)

- **if Yes**, what is his age?
  - **Age ≤75 = HIGH-Intensity statins.**
  - **Age >75 = Moderate-Intensity statins.**

2) If the patient has **NO** clinical cardiovascular disease, **is the level of LDL ≥ 190?** (High even for healthy individuals)

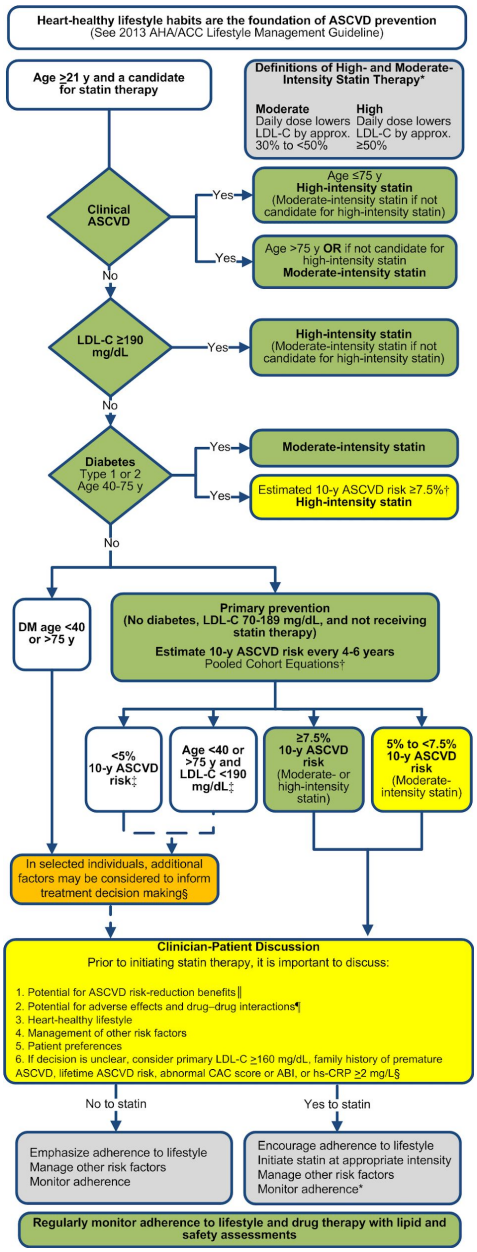
- Yes? Give **HIGH-Intensity statins**. Regardless of the age.

3) If the patient has **NO** clinical cardiovascular disease & the LDL level is **NOT ≥ 190,** the next question is: **does this patient have diabetes**?

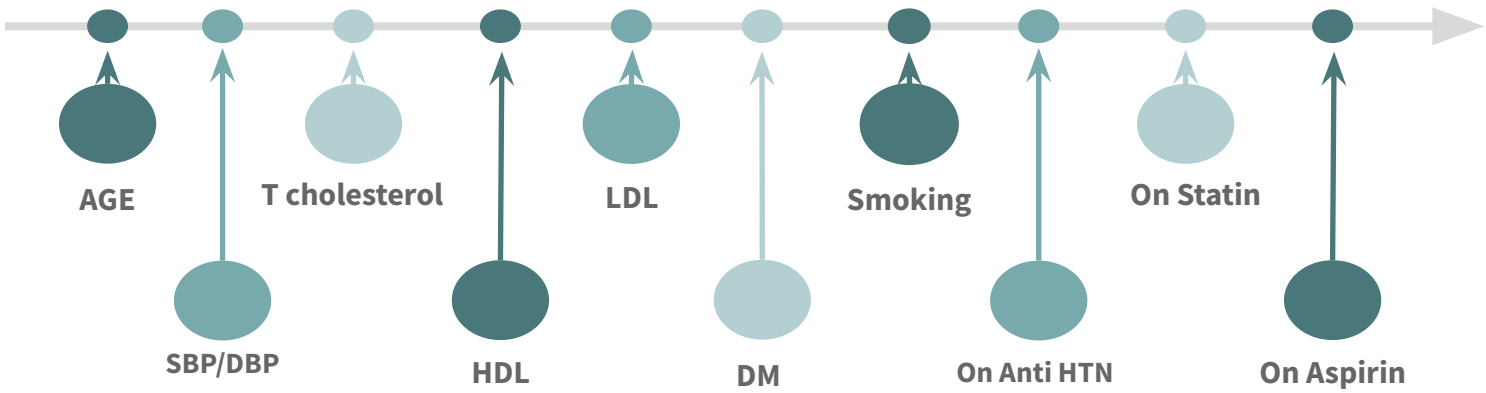
- **if yes,** what is his age <40 or >40?
  - **if the Age is <40** and has **no** IHD **nor** its risk factors = **NO NEED** for treatment
  - **if the Age is <40** and has **no** IHD **but has** its risk factors = **Moderate or high intensity statins**
  - **if the Age is <40** and **has IHD** = **HIGH-Intensity statins**.
  - **if the Age is >40** = Start statins.

4) If the patient has **NO** clinical cardiovascular disease & the LDL level is **NOT ≥ 190 & has NO** diabetes. you calculate the 10-y ASCVD risk.

- **<5% =** No need for treatment
- **≥ 7.5 =** Moderate or high intensity statins
- **5% to <7.5% =** Moderate-intensity statins



◀ Parameters used to estimate 10-year risk for ASCVD:



Hyperlipidemia: treatment *(cont.)*

◀ Guideline of therapy

Patient	Risk Factors	Statin Intensity*
>29 Age	ASCVD[1]	High
>29 years	LDL >190 mg/dl (4.9 mmol/l)	High
NO DM LDL <190	estimate 10-year risk for ASCVD <5%	No
	estimate 10-year risk for ASCVD 5-7.5%	Moderate
	estimate 10-year risk for ASCVD >7.5%	High

◀ Recommendations in DM:

Age	Risk Factors	Statin Intensity*
<40 years	None[2]	None
	ASCVD risk factor(s)	Moderate or high
	ASCVD	High
40–75 years	None	Moderate
	ASCVD risk factors	High
	ACS & LDL ≥50 or in patients with history of ASCVD who can't tolerate high dose statin	Moderate + ezetimibe
>75 years	None	Moderate
	ASCVD risk factors	Moderate or high
	ASCVD	High
	ACS & LDL ≥50 or in patients with history of ASCVD who can't tolerate high dose statin	Moderate + ezetimibe

1: any pt with cvd risk it's recommended to use high intensity statin
2: the only condition where diabetic pt won't take statin is if the pt is <40 years old and has no risk factors

Hyperlipidemia: treatment *(cont.)*

◀ Treating Hypertriglyceridemia: ★

Table 1: Assessment and action strategies for elevated plasma triglyceride concentrations [TG]

[TG], mmol/L	Step	Action and comments	interval, mo*
< 2		Continue current management • Reassess lipid profile regularly, to ensure that [LDL-C] is at target	6-12
≥ 2, < 5	1. Therapeutic lifestyle measures	• Weight control • Reduce dietary fat, simple sugars • Reduce alcohol intake • Increase physical activity Reassess lipid profile regularly, to ensure that [LDL-C] is at target	3-6
	2. Manage other secondary factors	• Control glycemia, if diabetic • Reassess medications; consider lipid-neutral alternatives	
	3. Consider pharmacologic treatment	• Intensify LDL-lowering (e.g., statin therapy) • Fish oil (omega-3 fatty acid) • Niacin (e.g., extended release)	
≥ 5, < 10	4. Intensify steps 1-3, above	• [LDL-C] cannot be estimated when [triglycerides] > 5 mmol/L • Apolipoprotein B determination might be helpful	2-3
	5. Consider fibrate therapy, e.g.,	• Bezafibrate (Bezalip) 400 mg/d • Fenofibrate — Lipidil micro 200 mg/d — Lipidil supra 160 mg/d — Lipidil EZ 145 mg/d • Gemfibrozil (Lopid) 600-1200 mg/d	
≥ 10	6. Further intensify steps 1-3	With acute pancreatitis: • Very-low-fat diet (10%-15% of energy intake) • Cessation of alcohol • Insulin, if indicated for glycemic control • Admit patient to hospital — Nothing by mouth: IV fluid replacement — Plasma exchange is unhelpful	1-2
	7. Initiate fibrate therapy	• Monitor serum [creatinine]	
	8. Consider specialist referral		

- **TG = <2:** No risk for anything, no treatment required.
  - Just advise lifestyle modification
- **TG = ≥2 to <5:** At this level, the goal is to **prevent CVS complications**. "CVS protection".
  - **Use statins. You can add omega-3 also**
- **TG = ≥5 to <10:** At this level, the goal is **to prevent pancreatitis**, need something stronger than statins.
  - **Use fibrate therapy**. in this case fibrate is enough unless pt has CVD risk.

An area for your notes

Summary

Primary hyperlipidemia	
Primary hypercholesterolemia	- Familial hypercholesterolemia : LDL receptor mutation -> Elevated LDL + Family history of premature CVD death
	- High risk for atherosclerosis, tendon xanthomas, tuberous xanthomas and xanthelasmas of eyes.
Primary hypertriglyceridemia	• LPL deficiency • Familial hypertriglyceridemia: enhanced hepatic TG-production • Apo-CII deficiency (**All can lead to pancreatitis**)
Secondary hyperlipidemia	
Diabetes Mellitus	VLDL increased production
Obesity	VLDL increased production
Hypothyroidism	Mainly LDL increased production
Anorexia	Increased LDL ONLY
Aims of dyslipidemia treatment (first, life style modification)	
LDL	prevent coronary heart disease (statins)
Non LDL (TC/HDL)	prevent coronary heart disease
Triglyceride	prevent pancreatitis and may be coronary heart disease outcomes (fibrates)

Guidelines of Therapy

1- Life style modification.
2- Does this patient have established coronary artery disease? (Had MI...)
✓ If yes? High intensity statin! except if pt is old >75.
3- Is his LDL more than 190?
✓ If yes? High intensity statin! No need for further questions
4- Has DM? More than 40 years?
✓ If yes? High intensity statin!
5- Anything other than that (2,3,4), we apply the 10 year risk assessment (done by websites & applications):-

- If its less than 5% > No need for meds.
- between 5%-7.5% > needs moderate intensity statin.
- More than 7.5% > needs High intensity statin.

- **Best to prevent CAD/MI : Statins (reduce LDL)**
- **Best to prevent Pancreatitis: Fibrate (reduce TGs)**

Lecture Quiz

Q1: 40 year old gentleman presented to you after doing lipid profile after an advice by his cardiologist. His brother died 3 months ago after a massive myocardial infarction (MI) at age of 32. His BP: 118/72, BMI: 27, LDL-Cholesterol: 305 mg/dl (8mmol/l), HDL-Cholesterol: 45 mg/dl (1.2mmol/l), Triglyceride: 144 mg/dl (1.63mmol/l). Which is the most likely cause of this disorder?

A. Lipoprotein lipase (LPL) deficiency
B. Apo C-11 coenzyme deficiency
C. Familial hypercholesterolemia
D. Nascent HDL deficiency

Q2: 25 years old male, not hypertensive and does not have DM and not a smoker. his brother dies from a cardiovascular disease at age 32.His lipid profile is: LDL: 6.1 mmol/L (=~196), HDL 0.1 and a 10 y risk of AVCAD .0,1%. What is the best management for him?

A. high sustained statin therapy.
B. low sustained statin therapy.
C. moderate sustained statin therapy.
D. don't give him anything.

Q3: 32 years old female presented to you after a routine blood work done for the new employment application. Her BP: 118/72, BMI: 27, LDL-Cholesterol:105 mg/dl (2.7mmol/l), Triglyceride:1444 mg/dl (16.3mmol/l). Which one of the following is your best treatment option to prevent pancreatitis?

A. Nicotinic acid
B. High intensity statin therapy
C. Low intensity statin therapy
D. Fenofibrate

Q4: Which one of the following found to be an important protective factor against coronary artery disease?

A. Low triglyceride level
B. High LDL-Cholesterol
C. High HDL-Cholesterol
D. Low VLDL-Cholesterol

Q5: Which of the following is the most common adverse effect of statin medications?

A. Liver dysfunction.
B. Renal failure.
C. Encephalopathy.
D. Hyperkalemia.

Answers: Q1:C | Q2:A | Q3:D | Q4:C | Q5:A

THANKS!!

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Send us your feedback:
We are all ears!