Lipoproteins

Wednesday, November 19, 2014
10:11 PM

Lecture Outline:
- Lipos a clive problem of moving fat through blood
- Apos confer structure & function to Lipos
- receptors & Apos mediate uptake of Lipo content
- blood lipid levels reflect net secretion/removal of circulating particles
- HYPERLIPIDEMIA: due to ↑Lipo secretion & ↓Lipo removal

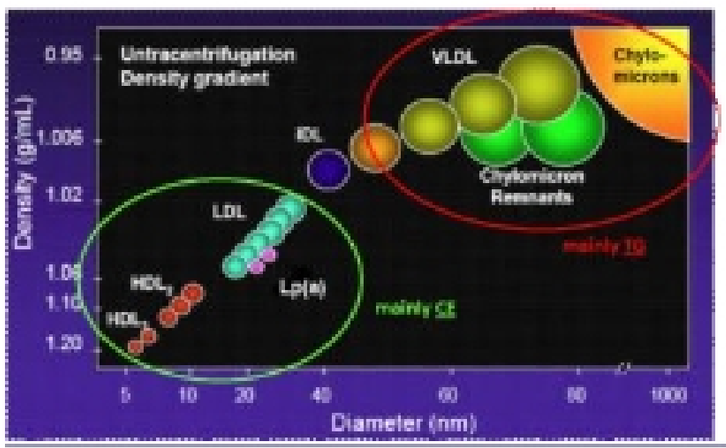


TABLE 21-2 Major Classes of Human Plasma Lipoproteins: Some Properties

		Composition (wt %)				
Lipoprotein	Density (g/mL)	Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
Chylomicrons	<1.006	2	9	1	3	85
VLDL	0.95–1.006	10	18	7	12	50
LDL	1.006–1.063	20	20	8	37	10
HDL	1.063–1.210	55	24	2	15	4

Source: Modified from Kritchevsky D. (1988) Atherosclerosis and nutrition. Alaric Inc. 3, 299–317.

*some ppl can have a ton of blood Cholesterol, even after Fasting

VLDL = TG/5

LDL = TC - (VLDL + HDL)

LIPOPROTEIN - lipids + proteins ≥1)
- Apoproteins
- Other proteins (structure/function)
- Cholesterol
- CEs
- TGs
- Phospholipids

Lipoprotein

Lipoprotein	Apo	Main Lipids	Present in Fasting Blood
Chylo	B-48, C, E	TG	NO
VLDL	B-100, C, E	TG	YES
IDL	B-100, C, E		YES
LDL	B-100	Cholesterol	YES
HDL	A, C, E	Cholesterol	YES

*C,E: acquired in circulation
*B-48 is part of B-100... B-48 doesn't contain LDLR binding site

Apo	Receptor	Function
A-I	LCAT	Cholesterol --> CE
A-I	SR-B1	load/unload Cholesterol from HDL into cell
C-II	LPL	hydrolyzes TG (lipolysis)
E	LDLR, LRP	removal from blood
B-100	LDLR	removal from blood

Removal of Lipoproteins:

LDLR	E, B-100
LRP *(major in brain)*	E
HSPG	non-specific
SR-B1	A
Macrophages (other SRs)	non-specific

*LDL Removal = LDLR only

HDL - starts out as lipid-poor A-I & grows; gets most lipids from ABC Transport (Efflux) Proteins
- LCAT - Cholesterol --> CE; allow HDL to turn from discs to spheres (activated by A-I)
- SR-B1 - scavenger receptor on cell that binds A-I & allows cell to load/unload cholesterol

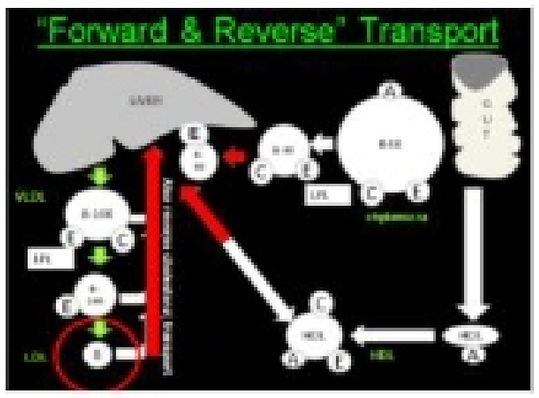
LDL - main cholesterol-containing particle in fasting & fed; simplest lipoprotein
- *accumulates bc it is only removed via LDLR
- *oxidation of B-100 impairs LDLR uptake

"HDL=Good" Hypothesis
1) reflects cholesterol removed
2) antioxidant/anti-inflammatory
3) REVERSE CHOLESTEROL TRANSPORT - macrophage donates Cholesterol to HDL (which takes it back to Liver)
   - ABC TRANSPORT (EFFLUX) PROTEINS - transfer cholesterol out of macrophages into A-I/HDL

Drugs

↑ HDL	no change in heart attacks (some block Reverse Cholesterol Transport)
↓ LDL	↓ heart attacks (remove LDL via Reverse Cholesterol Transport)

Drug	↓ LDL-C
Statins	30%
PCSK9 Ab	70%
Statin + PCSK9 Ab	70%



STATINS - ↓HMG-CoAR, ↓cellular Cholesterol, ↑LDLR & PCSK9 expression
PCSK9 Ab (SAR236553) - ↓PCSK9, ↑LDLR
PHYTOSTEROLS/EZETIMIBE - ↓NPC1-L1
FIBRATES/BILE ACID BINDERS - ↓Bile Acid reabsorption
NIACIN - ↓free FA delivery to Liver
FISH OIL - ↓VLDL synth

*↓LDLR, ↓cellular Cholesterol, ↑Cholesterol synthesis
*can live w/o LDLR
*CANNOT live w/o cellular Cholesterol metabolism

XANTHOMA - cholesterol buildup in the blood (seen in vessels, hands, feet, etc)

MACROPHAGE - expressed LDLR if low cholesterol levels
- FOAM CELL - macrophage that takes up a bunch of oxLDL; leads to atherosclerosis
  - *unregulated uptake overcomes efflux capacity

Drugs of the Future: liposome packaging