HDL

A Look into the Role of HDL and Heart Disease for All Ages

- TheFatNurse
The message of cholesterol often boils down to HDL = GOOD LDL = BAD. However, the process is a lot more complex than this and it would be a disservice in healthcare for this simple message to continue perpetuating.

This comic is designed to help introduce more complex aspects of HDL that many of us may not have read. It is simplified and largely based on the more detailed Lecturepad series by Dr. Thomas Dayspring MD who is the director of cardiovascular education at The Foundation for Health Improvement and Technology. If anything in this comic piques your interest please look up Dr. Dayspring's work. You may also find the works of Peter Attia MD, Tara Dall MD, Bill Cromwell MD and Ronald Krauss MD fascinating as well on cholesterol.

- TheFatNurse R.N
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You know TheFatNurse (TFN), all this talk of heart disease and LDL stuff leaves me wondering...

TFN: I think I know-

MAKE ROOM LOZERS!!! He's HERE! HE IS REALLY HERE!!!!!

TFN: You were gonna ask about HDL right?

"OMG! look at him go!"
"He's so dreamy!"
"He's the best!"

"I love a man who cleans ups!"
"I love how he protects my heart!"
"He's definitely got my heart!"

"I want more of him!"
"I want him inside me...circulating inside me that is!"

TFN: See this mass love affair we have to deal with?

No no, I'm just saying we should really understand how HDL works before going on this mass love affair!

Wait...are you saying HDL is not good?
Are you telling me HDL doesn't just simply come in and clean our arteries?

TFN: the story is a lot more complex than that...for example do you know what HDL is?

Oh yea of course, I get it checked on by my doc to see if I am in good health!

TFN: That's HDL-C. Measuring the Cholesterol in HDL. Like LDL-P, we want to view HDL in particles (HDL-P)

Alright let's start from the very beginning. Remember that HDL is a lipoprotein which means it will be composed of apoproteins with a cholesterol triglyceride core and surrounded by phospholipids:

- Apolipoproteins
- Cholesteryl Esters (CE)
- Triglycerides (TG)
- Apolipoprotein A1 (Apo-A1)
- Phospholipids
- Unesterified Cholesterol (UC)

Hey that is like the Lipoprotein from the first comic...but why is Apo-A1 bolded?

TFN: Glad you caught that! Apo-A1 is associated with HDLs that's why!

0... kinda like how Apo-B is associated mostly with LDLS?

TFN: Yes! Except 1 HDL particle can have multiple Apo-A1s. Remember, that there is only 1 Apo-B for every 1 LDL particle

HDL brings home multiple As and is #1 (Apo A-1) in his class!

TFN: Again, I'm stressing Apo-A1 because its so crucial to HDL. One can even say it gives birth to HDL!

Congrats on your Apo-A1!

Thanks! I've always wanted more HDLs!
1) Apo-Al basically comes from three places: Hepatic Cells (Liver), jejunal enterocytes (small intestine) and Chylomicrons:

2) Cells from both organs can secrete Apo-Al into the plasma. This new Apo-Al is known as unlipidated Apo-Al.

3) Another way the body can create Apo-Al is through Chylomicrons. As it turns out, Chylomicrons carry some Apo-Als on them. Chylomicrons, as you may recall, are TG rich and carry TGs from the gut to muscles for energy or fat for storage.

4) When they give up their TGs to fat or muscle, they shrink and release some of their Apo-Als and phospholipids. The shrunken Chylomicron is called a remnant chylomicron and is recycled in the liver. Some Apo-Als then combine with the phospholipids to form phospholipidated Apo-Al.

Both unlipidated and phospholipidated Apo-Als love cholesterol!
That's interesting, but how do these Apo-Als actually get cholesterol in them?

TFN: Glad you asked! It's quite amazing!

Getting cholesterol into these Apo-Als to become HDLs is known as Apo-A1 mediated Cholesterol Transport.

This occurs through sterol efflux transporters. I like to think of these as pumps.

There are three main pumps (below) that exist in multiple kinds of cells in our body to get rid of excess cholesterol. Too much in the cell crystalizes them and causes cell death. Therefore, these pumps pump out cholesterol from cells to Apo-A1 along with Phospholipids.

ATP binding cassette transporter A1 (ABCA1)

Transporter G1 (ABCG1)

Scavenger Receptor B1 (B1)

TheFatNurse, you keep adding more acronyms and details! This is getting complicated! BAH!

Don't worry too much about the details! It's just for those who want it! This will all make sense in the end I promise!

ABCA1: pumps out free cholesterol to unlipidated apo-A1. Exists in virtually every cell.

ABCG1: pumps out free cholesterol to larger HDL species

Eh? What the heck is a larger HDL?

TFN: No worries! It'll all make sense soon!

B1: Can pump in or out cholesterol ester! Will not allow free cholesterol through. Free cholesterol? Ester? What the heck are you talking about!?
Think of our plasma like water. Since CE is scared of water it avoids it by hiding inside things like cells or lipoproteins. UC is okay with water so it stays in contact with the plasma.

Alright you've been talking about pumps and now different kinds of cholesterol...Get to the part about HDL already!

TFN: I'm setting the stage! Here have some bacon and calm down!

Now let's get back to explaining how Apo-A1s get cholesterol in them. I like to think of HDLs as ballons and the Apo-A1s as the lip of the balloon (where air is pumped into the ballon). Except instead of using air to expand, HDL expands with cholesterol through Apo-A1!

1) So here's an Apo A-1 on the prowl for cholesterol

2) Apo-A1 gets "pumped" with UC cholesterol from the ABCA1 pump mentioned earlier this creates a Pre-Beta HDL

3) To get UC from the surface of the HDL to the inside, the Apo-A1 turns the UC into CE*. CE is afraid of water/plasma so hides inside the HDL making a disc shape called alpha 4 HDL

4) As Alpha 4s get bigger, they need a different pump and ABCG1 comes in to pump even more cholesterol to HDL which is now alpha 3.

5) Alpha 3s continue to mature by getting bigger from more pumping and eventually becomes Alpha 2s in size.

6) B1 pumps CE into the alpha 2 and creates the ultimate alpha 1 size HDL

*UC is turned to CE with the help of Lechthin Cholesterol acyl transferase (LCAT)

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Ah...I think I'm starting to understand this balloon and pump analogy...
TFN: Good! You can see this system of "pumps" getting rid of excess cholesterol by inflating HDL balloons (HDL-P) in a lot of cells!

Just dump them in the ABCA1 pumps and let the HDLs take care of it! If there's more just put them back in the gut!

We see it in the cells of the gut which use the ABCA1 pumps after making those huge chylomicrons:
Enterocyte: Hey boss I've spent all day making Apo-A1 and chylomicrons with TGs and cholesterol. What you wanna do with the left over cholesterol?

This same mechanism exists in adipocytes which are the cells of fat:

TFN: Now that you understand how cells pump out cholesterol to the Apo-A1s on HDLs...we'll go over how these pumps can protect your heart through macrophage reverse cholesterol transport

With cholesterol stuck in our artery wall from the crash, this catches the attention from macrophages
Cholesterol: Get me outta here!
Macrophage: Sure!

Remember when we talked about how LDL-P (the cars) carrying cholesterol (the passengers) actually causes heart disease when they crash into our artery walls in the first comic? If not go read it!

Cholesterol:
Oui...when did they build an artery wall here?

So what does the macrophage do?
TFN: It eats it!

It eats the cholesterol...
TFN: Yes! It becomes a foam cell when this happens!
Foam cells use all three pumps to get the cholesterol they swallowed out of themselves (thus out of your artery wall) by pumping the cholesterol out into the plasma and into your circulation!

1) Apo-A1 goes into artery cell wall towards foam cell

3) Apo-A1 goes back out to circulation where UC turns into CE and thus inflating and creating small HDL ballons

4) These small HDL ballons will go back inside the artery wall to get pumped by ABCG1s which pump larger sized HDLs

5) Like before, these HDL ballons will go back out to circulation to turn more UC into CE and thus become even bigger HDLs

6) Bigger HDL ballons can then utilize the B1 pumps to pump CE into the HDL to become the biggest Alpha 1 HDLs!

TFN: Pretty amazing stuff right? By utilizing different pumps for different size HDL particles (the ballons), our foam cells try to spit out as much cholesterol from our artery walls and into our circulation to be disposed of as possible!

I think I get it now! This must be why my doc wants my HDL cholesterols level high...because it means I am pulling out a lot of cholesterol from my arteries and into my circulation!

TFN: I like your thinking! But...brace yourself...

Uh oh...

TFN: Even in people with severe atherosclerosis, the amount of cholesterol pulled from their arteries probably amounts to 0.5% of their total cholesterol...
So similar to how LDL-C doesn't give you a complete picture of what's happening with LDL-P, the HDL-C doesn't give you a complete picture of what's going on with HDL-Ps!

Additionally, foam cells can alter mature HDLs to make them release some Apo-A1s!

- Foam Cell
  - modulating enzymes
  - Released Apo-A1 on the hunt again
- HDL release some of its ApoA1
  - starts a new cycle collecting cholesterol

* Don't confuse foam cells as being "healthy" tho! They contribute to atherosclerosis too! See glossary.

Whoa so our bodies have a lot of ways to utilize HDLs

TFN: Yea pretty amazing right!

But... what do these HDL particles/balloons do once they are full of cholesterol?

Oh I know this one! The HDLs get rid of it through the liver!

TFN: Happy for your enthusiasm, but once again its not quite that simple!

Good Question! This brings us to...

DELIPIDATION OF HDLs!!!

HDLs can empty their cholesterol in three ways:

1) HDL mediated cholesterol transport

2) Direct Reverse Cholesterol Transport

3) Indirect Reverse Cholesterol Transport

*Reverse Cholesterol Transport (RCT) is the sum of both indirect and direct RCT...you'll learn what indirect/direct RCT is in a bit!

It's not too complicated tho! Just remember the analogy of HDLs inflating and deflating like baloons using cholesterol instead of helium and it'll be easy!

MOTHER OF GOD...

HDL Mediated Cholesterol Transport AKA "Forward Cholesterol Transport Via Dr. Dayspring"

"Forward Cholesterol," a term by Dr. Dayspring, is a good way to describe this process because HDLs are "forwarding" their cholesterol to much needed parts of the body.
The steroidogenic tissues in our body such as the adrenals, testes and ovaries need cholesterol to function. These cells can produce their own but they need additional cholesterol to operate at optimal levels. This is where the HDLs "forward" the cholesterol!

These Tissues use the B1 scavenger to influx (remember that B1 can also efflux as well) the cholesterol from the HDL into themselves!

Wait So what happens to the HDL after giving up their cholesterol?
TFN: That's the beauty of it! The HDL shrinks/deflates back to a smaller size or even prebeta levels!

Then the cycle with cells "pumping" out cholesterol to HDL-Ps starts again! Smaller "deflated" HDL

Steroidogenic tissue

Large "inflated" HDL

This process of pumping out cholesterol and inflating HDL-Ps which "forward" these cholesterol to cells and leaving a deflated HDL-P to begin the process all over again can be found in adipocytes as well!

Hah! All This time I thought it was the liver that got rid of the cholesterol!
TFN: No the liver is involved! When HDLs and their cholesterol "reverse" back towards the liver and gut its called...
Direct Reverse Cholesterol Transport

1) We start out in a very similar process with a large mature HDL-P inflated from the pumps with cholesterol. It approaches the cells of the liver (instead of steroidogenic cells this time) and uses B1 influx pumps to get the cholesterol into the liver cells.

2) After the liver gets the cholesterol, it can either use it as a bile salt or convert it to unesterified cholesterol. Either way, both end up in the biliary system. If the body decides not to absorb the cholesterol to use again its excreted! So the cholesterol is pooped out!

TFN: This is just one of many different way of direct reverse cholesterol transport tho!

Alright, the HDL story is definitely a lot more complex than I imagined!

Holoparticle receptor (ATP synthase B chain)

Hepatocyte

Another method uses a holoparticle receptor on a hepatocyte that takes in the entire HDL-P instead of sucking out it's contents! *Requires Hepatic lipase to do this

Another method is with LDL receptors located on the liver. This process takes the cholesterol from mature HDLs and sends it to the liver but the HDL is destroyed in this process

Well thanks! I feel like I know a little bit more HDLs now- TFN: Wait! We're not done yet! What!!! Still more!? TFN: Yeap it's called indirect reverse cholesterol transport and uses Apo B particles like LDL!
Indirect Reverse Cholesterol Transport

"Hey wanna trade for a cholesterol?"

"Sure I'll give ya a Triglyceride"

The indirect mechanism of cholesterol transport occurs when a Large Mature HDL encounters an Apo B particle (LDL or VLDL). There is a 1 to 1 exchange were 1 cholesterol from HDL is exchanged with 1 triglyceride from the Apo B particle. This is called hetero exchange

This leaves HDLs cholesterol poor and Apo B's cholesterol rich

Wait...so is it a bad or good thing that HDL gives its cholesterol to Apo B particles like LDL?

TFN: It's both!

It's good if the LDLs are carrying the cholesterol where they can eventually be carried to the liver where it may be converted to bile or unesterified cholesterol to be excreted or reabsorbed.

...But remember our first comic about LDL and heart disease?

These LDL-Ps can also crash into the artery walls and deposit their cholesterol...and thus triggering a cascade that can lead to plaque formation

No matter where the cholesterol from LDL particles ends up...what we just covered means lots of the cholesterol carried by LDLs originated from HDLs!

Again...lots of the cholesterol in LDL particles originated from HDL particles...MIND = BLOWN

What about the HDLs which are carrying the TGs they got from the LDLs?

Oh those TG rich HDLs drop off their TGs to the liver with hepatic lipase...this shrinks/deflates the HDLs back to prebeta or small HDL where they can start the cycle of collecting cholesterol again! Or they may be dumped
Eh? Dumped?

TFN: Through a process called HDL catabolism, small HDLs (of 7-8 nm) and Apo-Als can be removed from our bodies through the kidneys.

A receptor called cubillin may bind to megalin which binds to HDL particles. Since this process occurs with small HDLs, the hetero exchange with LDL that we mentioned earlier can increase the likely hood of peeing out HDLs!

But I thought HDLs shrinking to a smaller size was a normal process? The whole inflating deflating cycle you've been talking about!

TFN: Yes! This process may be a normal way to get rid of Apo-A1 and small HDL particles. After all, the half life is 5 days, so they can get old! However, remember in hetero LDL-HDL exchange that triglycerides play a part as well! Therefore, in conditions traditionally with high triglycerides, such as Insulin resistance, it may explain why their is usually high Triglycerides and low HDLs!

However, hetero exchange isn't the only place where TGs are swapped. Large HDLs may swap TGs with smaller TGs for their Cholesterol as well! This is known as homotypic exchange.

These smaller HDLs can then use hepatic lipase to give their TGs to the liver and shrink to even smaller HDLs or prebeta HDLs and start the inflation deflation cycle again!

Congrats! You now know the gist of HDL!

TFN: uh...you ok?
Dude...that was a lot of info...I barely remember anything...something like HDL inflates and deflates with cholesterol like a ballon?
TFN: Alright one last review!
Putting It All Together

1) It all starts with Apo-Als made in the liver, small intestine or from Chylomicrons!

2) These Apo-Als then get cholesterol into them from different kinds of pumps located in different kinds of cells in our body.

3) As Apo-A1 is being pumped with cholesterol and phospholipids, it forms HDLs of different sizes like balloons getting bigger from being pumped with helium.

4) This system of cells pumping and inflating HDLs is very important, especially with Foam cells which use these pumps for cholesterol in your artery walls.

5) Inflated HDLs then deliver their cholesterol by "forward cholesterol transport" or get rid of them by direct reverse cholesterol transport or indirect reverse cholesterol transport. In some of these mechanisms, the HDLs will shrink once they deflate and give off their cholesterol... which allows some HDLs to be reused in the previously covered steps.

6) "Forward cholesterol transport" means the HDLs are "forwarding" the cholesterol to tissues in the body that need cholesterol like our adrenals.

7) Direct Reverse Cholesterol Transport involves the HDLs "reversing" back to the liver and gut. Cholesterol is basically converted to bile salt or UC cholesterol and excreted or absorbed.

8) Indirect Reverse Cholesterol Transport involves Apo-B particles swapping their TGs with Cholesterol from HDL particles. This leaves HDLs cholesterol poor and LDLs cholesterol rich. The LDLs then "reverse" back to the liver. We see these sort of swaps occurring with larger HDLs giving their TGs for the cholesterol of smaller HDLs as well.

9) The body gets rid of some old Apo-Als or small HDLs by excreting them! This may be normal, but when their is a lot of smaller HDLs such as the swaps of TG & cholesterol with LDLs, this may cause the body to excrete more HDLs than normal which may be why individuals who are insulin resistant have high TGs and low HDLs.

Oh man... HDL is definitely not as simple as I thought it was.

TFN: Right! This is why we need to know more than the usual "HDL is good!"
What you have read is just a part of the emerging knowledge about HDL and may change with time. Every other month there seems to be fascinating new discoveries about Lipoproteins. Some of these discoveries often contradict conventional wisdom as well! Lots of things are going on in Lipidology right now so keep your eyes/ears open and enjoy this exciting ride.

-TheFatNurse
Glossary For TheFatNurse’s For All Ages Series

**Adipocytes**, also known as lipocytes and fat cells, are the cells that primarily compose adipose tissue, specialized in storing energy as fat.

**Apolipoprotein A-I** is a protein that in humans is encoded by the *APOA1* gene. It has a specific role in lipid metabolism. **Apolipoprotein A-I** is the major protein component of high density lipoprotein (HDL) in plasma. Chylomicrons secreted from the intestinal enterocyte also contain ApoA1 but it is quickly transferred to HDL in the bloodstream. The protein promotes cholesterol efflux from tissues to the liver for excretion. It is a cofactor for lecithin cholesterolacyltransferase (LCAT) which is responsible for the formation of most plasma cholesteryl esters.

**Apolipoprotein B** (APOB or ApoB) are the primary apolipoproteins of chylomicrons and low-density lipoproteins (LDL - known commonly by the misnomer "bad cholesterol" when in reference to heart disease), which is responsible for carrying cholesterol to tissues. While it is unclear exactly what functional role APOB plays in LDL, it is the primary apolipoprotein component and is absolutely required for its formation.

**Atherosclerosis** (also known as **arteriosclerotic vascular disease** or **ASVD**) is a condition in which an artery wall thickens as a result of the accumulation of fatty materials such as cholesterol. It is a syndrome affecting arterial blood vessels, a chronic inflammatory response in the walls of arteries, caused largely by the accumulation of macrophage white blood cells and promoted by low-density lipoproteins.

**ATP-binding cassette transporter ABCA1 (member 1 of human transporter sub-family ABCA)**, also known as the cholesterol efflux regulatory protein (CERP) is a protein which in humans is encoded by the *ABCA1* gene. This transporter is a major regulator of cellular cholesterol and phospholipid homeostasis.

**ATP-binding cassette sub-family G member 1** is a protein that in humans is encoded by the *ABCG1* gene. It is involved in macrophage cholesterol and phospholipids transport, and may regulate cellular lipid homeostasis in other cell types.

**Cholesteryl ester** is, as its name would imply, an ester of cholesterol. The ester bond is formed between the carboxylate group of a fatty acid and the hydroxyl group of cholesterol. Cholesteryl esters have a lower solubility in water than cholesterol and, in other words, are more hydrophobic.

**Chylomicrons** are lipoprotein particles that consist of triglycerides (85-92%), phospholipids (6-12%), cholesterol (1-3%) and proteins (1-2%). They transport dietary lipids from the intestines to other locations in the body. Chylomicrons are one of the five major groups of lipoproteins (chylomicrons, VLDL, IDL, LDL, HDL) that enable fats and cholesterol to move within the water-based solution of the bloodstream.
**Concordance:** similar with respect to one or more particular characters.

**C-reactive protein (CRP)** is a protein found in the blood, the levels of which rise in response to inflammation (i.e. C-reactive protein is an acute-phase protein). Its physiological role is to bind to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system via the C1Q complex.

**Cytokines** are small cell-signaling protein molecules that are secreted by numerous cells and are a category of signaling molecules used extensively in intercellular communication.

**Discordance:** dissimilar with respect to one or more particular characters—compare concordant.

**Foam cells** are cells in an atheroma derived from both macrophages and smooth muscle. In chronic hyperlipidemia, lipoproteins aggregate within the intima of blood vessels and become oxidized by the action of oxygen free radicals generated either by macrophages or endothelial cells. The macrophages engulf oxidized low-density lipoproteins (LDLs) by endocytosis via scavenger receptors, which are distinct from LDL receptors. The oxidized LDL accumulates in the phagocytes, which are then known as foam cells. Foam cells form the fatty streaks of the plaques of atheroma in the tunica intima of arteries. Foam cells are not dangerous as such, but can become a problem when they accumulate at particular foci thus creating a necrotic centre of atherosclerosis. If the fibrous cap that prevents the necrotic centre from spilling into the lumen of a vessel ruptures, a thrombus can form which can lead to emboli occluding smaller vessels. The occlusion of small vessels results in ischemia, and contributes to stroke and myocardial infarction, two of the leading causes of cardiovascular-related death.

**HDL-C:** Blood tests typically report HDL-C level, i.e. the amount of cholesterol contained in HDL particles

**Intermediate-density lipoproteins (IDL)** belong to the lipoprotein particle family and are formed from the degradation of very low-density lipoproteins. IDL is one of the five major groups of lipoproteins (chylomicrons, VLDL, IDL, LDL, HDL) that enable fats and cholesterol to move within the water-based solution of the bloodstream. Each native IDL particle consists of protein that encircles various fatty acids, enabling, as a water-soluble particle, these fatty acids to travel in the aqueous blood environment as part of the fat transport system within the body. Their size is, in general, 25 to 35 nm in diameter, and they contain primarily a range of triacylglycerols and cholesterol esters. They are cleared from the plasma into the liver by receptor-mediated endocytosis, or further degraded to form LDL particles.

**Insulin resistance (IR)** is a physiological condition where the natural hormone insulin becomes less effective at lowering blood sugars. The resulting increase in blood glucose may raise levels outside the normal range and cause adverse health effects.
**LDL-C**: low-density-lipoprotein cholesterol (passenger).

**LDL-P**: Low-density lipoprotein particle (Car).

**Lp-PLA₂** is involved in the development of atherosclerosis. In human atherosclerotic lesions, 2 main sources of Lp-PLA₂ can be identified, including that which is brought into the intima bound to LDL (from the circulation), and that which is synthesized de novo by plaque inflammatory cells (macrophages, T cells, mast cells)." It is used as a marker for cardiac disease.

A meta-analysis involving a total of 79,036 participants in 32 prospective studies found that Lp-PLA₂ levels are positively correlated with increased risk of developing coronary heart disease and stroke.

**Lipoprotein(a)** (also called Lp(a)) is a lipoprotein subclass. Genetic studies and numerous epidemiologic studies have identified Lp(a) as a risk factor for atherosclerotic diseases such as coronary heart disease and stroke.

**Macrophages** function in both non-specific defense (innate immunity) as well as help initiate specific defense mechanisms (adaptive immunity) of vertebrate animals. Their role is to phagocytose (engulf and then digest) cellular debris and pathogens, either as stationary or as mobile cells.

**Macrophage reverse cholesterol transport**: Important to cardiovascular health and transports cholesterol from macrophages/foam cells in artery wall. Hardly any effect on total HDL-C.

**Monocytes** are a type of white blood cell and are part of the innate immune system of vertebrates including all mammals (including humans), birds, reptiles, and fish. Monocytes play multiple roles in immune function.

**Phosphocoline**: one of the binding targets of C-reactive protein (CRP). Thus when a cell is damaged, CRP binds to phosphocholine beginning the recognition and phagocytotic immunologic response.

**Phospholipids** are a class of lipids that are a major component of all cell membranes as they can form lipid bilayers. The 'head' is hydrophilic (attracted to water), while the hydrophobic 'tails' are repelled by water and are forced to aggregate.

**Plasminogen**: Precursor to Plasmin.

**Plasmin** is an important enzyme present in blood that degrades many blood plasma proteins, most notably, fibrin clots. The degradation of fibrin is termed fibrinolysis.

**Reverse cholesterol transport** is a multi-step process resulting in the net movement of
cholesterol from peripheral tissues back to the liver via the plasma.

Cholesterol from non-hepatic peripheral tissues is transferred to HDL by the ABCA1 (ATP-binding cassette transporter). ApoA-1 acts as an acceptor, and the phospholipid component of HDL acts as a sink for the mobilised cholesterol. The cholesterol is converted to cholesteryl esters by the enzyme LCAT (lecithin-cholesterol acyltransferase). The cholesteryl esters can be transferred, with the help of the cholesterol-ester transfer protein (CETP) in exchange for triglycerides, to other lipoproteins (such as LDL and VLDL), and these lipoproteins can be taken up by the liver through its LDL receptors.

However, the receptor SR-B1 (scavenger receptor class B1) present on the liver cells’ plasma membranes mediates most of the liver’s uptake of cholesteryl esters from HDL in the absence of uptake of apolipoproteins. The overall process by which HDL removes cholesterol from extrahepatic tissues and returns it to the liver is called reverse cholesterol transport. Once in the liver, the cholesteryl esters are converted to cholesterol and enter the general pool. Therefore, the liver can eliminate cholesterol from the body by secreting unesterified cholesterol into the bile or by converting cholesterol to bile acids.

**Scavenger receptor class B, type I (SR-B1)** is an integral membrane protein found in numerous cell types/tissues, including the liver and adrenal. It is best known for its role in facilitating the uptake of cholesteryl esters from high-density lipoproteins in the liver. This process drives the movement of cholesterol from peripheral tissues towards the liver for excretion. This movement of cholesterol is known as reverse cholesterol transport and is a protective mechanism against the development of atherosclerosis, which is the principal cause of heart disease and stroke.

**Triglycerides** are the main constituents of vegetable oil (typically more unsaturated) and animal fats (typically more saturated). In humans, triglycerides are a mechanism for storing unused calories, and their high concentration in blood correlates with the consumption of starchy and other high carbohydrate foods.

**Very-low-density lipoprotein (VLDL)** is a type of lipoprotein made by the liver. VLDL is one of the five major groups of lipoproteins (chylomicrons, VLDL, low-density lipoprotein, intermediate-density lipoprotein, high-density lipoprotein) that enable fats and cholesterol to move within the water-based solution of the bloodstream. VLDL is assembled in the liver from triglycerides, cholesterol, and apolipoproteins. VLDL is converted in the bloodstream to low-density lipoprotein (LDL). VLDL particles have a diameter of 30-80 nm. VLDL transports endogenous products, whereas chylomicrons transport exogenous (dietary) products.

***Relevent parts of definitions extracted from Wiki***