

- cholesterol
- It is not a metabolic fuel like fatty acids and triglycerides.
- But cholesterol is very important to the body for plasma membrane ,bile salts steroid hormones.

- Sources of cholesterol:
- 1. dietary cholesterol: it comes from animal sources e.g egg yolk for example a single egg contain 250mg of cholesterol. Not all ingested cholesterol is absorbed into the blood much of it simply passes through the length of the gastro-intestinal tract and is excreted in the feces.

- 2. cholesterol synthesis within the body:
- Almost all cells can synthesize some of the cholesterol required for their plasma membranes but most can not do so in adequate amounts and depend upon receiving cholesterol from the blood this is true for the endocrine cells that produce steroid hormones from cholesterol .thus most cells remove cholesterol from the blood.

- In contrast the liver and cells lining the gastrointestinal tract can produce large amounts of cholesterol most of which enters the blood.
- The liver cells is the center of the cholesterol universe because it can add newly synthesized cholesterol to the blood or it can remove cholesterol from the blood secreting it into the bile or metabolizing it to bile salts.

- The homeostatic control mechanism that keep plasma cholesterol relatively constant operate on all of these hepatic process. But the single most important response involves cholesterol production.
- The synthesis of cholesterol by the liver is inhibited whenever dietary cholesterol is increased this is because cholesterol inhibits the enzyme critical for cholesterol synthesis by the liver.

- Thus as soon as the plasma cholesterol level starts rising because of increased cholesterol ingestion hepatic synthesis is inhibited and the plasma concentration remains close to its original value.
- Conversely when dietary cholesterol is reduced and plasma cholesterol begins to fall hepatic synthesis is stimulated [release from inhibition] and this increased production opposes any further fall .

- This is called negative –feedback control of cholesterol synthesis.
- The sensitivity of this negative-feedback control system differs greatly from person to person for example a documented case of a man who due to a compulsion had been eating 25 eggs a day for 15 years and yet had a relatively low plasma cholesterol his intestinal

- Absorption and hepatic synthesis of cholesterol were markedly below normal and his conversion of cholesterol to bile salts was markedly elevated.
- So we have the following processes for cholesterol homeostasis:1. absorption.2.synthesis.3.secretion.4. excretion

- Diet can have influence on plasma cholesterol for example ingesting saturated fatty acids of animal origin [red meat, most cheeses and whole milk] raises plasma cholesterol.
- In contrast eating either polyunsaturated fatty acids or monosaturated fatty acids such as those in olive or peanut oil lower plasma cholesterol .
- The various fatty acids exert their effects by altering cholesterol synthesis, excretion and metabolism to bile salts .there is no cholesterol of plant origin.

- Cholesterol is insoluble in water so it is carried in plasma by lipoproteins[lipoprotein is lipid plus protein].
- Types of lipoproteins:
 - 1.chylomicrons contain
 - Phospholipids 4%
 - Triglycerides 90%
 - Cholesterol 5% and protein1%

- 2. very low density lipoprotein[VLDL] contains:
 - Phospholipids 18%
 - Triglycerides 60%
 - Cholesterol 14%
 - Protein 8%
- 3. low density lipoprotein[LDL] contain:
 - Phospholipids 20%.triglycerides 10%,cholesterol 45% and protein 25%

- Like most other lipids cholesterol is not water soluble and to circulate in plasma it must be carried by lipoproteins .
- LDL are the main cholesterol carriers and deliver cholesterol to cells which has LDL receptor in their cell membrane after this binding there will be endocytosis of the receptor complex and cholesterol will be released in cytosol to be used by cells.

- HDL serve as acceptor of cholesterol from various tissues . They promote the removal of cholesterol from cells and its secretion into the bile by the liver.
- LDL-cholesterol is often designated of bad cholesterol since high levels of it in the plasma are associated with increased deposition of cholesterol in arterial walls and higher incidence of heart attacks using the same

- Criteria HDL –cholesterol has been designated good cholesterol .
- The designation bad should not obscure the fact that LDL are essential for supplying cells with the cholesterol they require to synthesize cell membranes and in the case of the gonads and adrenal glands to synthesize hormones.

- There is some evidence that severely reducing plasma cholesterol levels below about 180mg\ dl may be harmful in adults . Cholesterol is required for normal membrane structure in cells and abnormally low cholesterol levels may lead to weakened blood vessel and increased risk for cerebral haemorrhage.

- The American heart association recommends that cholesterol should be limited to 300 mg[the amount in an egg yolk] or less per day in adults of course in children higher level is required for growth.

- The best single indicator of the likelihood of developing atherosclerotic heart disease is therefore not total plasma cholesterol but rather the ratio of plasma LDL-cholesterol to plasma HDL-cholesterol the lower the ratio the lower the risk.
- Another complexity in evaluating plasma cholesterol involves a substance called lipoprotein[a] which when present in large quantities accounts for much of the risk for coronary artery disease.

- This molecule is very similar in structure to LDL except that it contains one additional large protein dubbed apolipoprotein[a].
- Almost all people have some lipoprotein[a] in their blood but its concentration varies on a genetic basis nearly 1000 –fold among individuals.