LDL pathway: LDL is mainly contained cholesterol and the one form of apoLP; apo B100. It is the carrier LP of cholesterol from liver and S.I to peripheral tissues so it is an important LP for development and growth ??.

The control of blood LDL level is by to ways:
1. Hepatic tissue receptors; the hepatic LDL receptor which account for 2/3 removal of blood LDL and is regulable and saturable mechanism.
2. Scavenger receptor 1/3 of blood LDL and is found in many cell of tissues but predominant in Macrophage cells(the native of them are Monocyte cells) and it is nonsaturable and not regulated by blood LDL.
1. Downregulate HMG CoA Reductase
2. Upregulate ACAT
3. Downregulate LDL Receptors

LDL Binding → Internalization → Lysosomal Hydrolysis → Regulatory Actions
Hyperlipidaemiaes are important disorders because of their relation with (atherosclerosis): CHD, CVD, peripheral atherosclerosis, pancreatitis, hepatosplenomegaly.

One of classification of dyslipidaemiaes is Fredricson and co-workers which dependent on which LP is elevated in blood. However, now classification is dependent on results of laboratory analysis and defined as:

**Primary** and **Secondary**

Each of the which is subdivided into:
1. Hypertriglyceridaema,
2. Hypercholesterolemia,
3. Combined hyperlipidaemia (CHL)
1. Hypertriglyceridaemia: The primary type is:

A. Hyperchylomicronemia (Type I Fredrickson): is genetic (primary) disorder of lipid metabolism and characterized by significant increased of chylomicrone (and the contained TG) in fasting state due to absence or mutant form of LPL enzyme or apo CII (less severe). Clinical presentation are: abdominal pain, acute pancreatitis, hepatosplenomegaly (if LPL) and eruptive xanthoma (if LPL); TG $\geq 1000$ mg/dl. It occurs during childhood period; less than 10 year of age.

B. HyperVLDLaeemia (Type IV): is genetic disorder characterized by increase of blood TG and is due to genetic increase in production of apo B100 and VLDL.
In this disorder S.TG is more than 900 mg/dl.

C. Increased of VLDL and chylomicron: It is characterized by increased of blood TG due to increase both of VLDL and chylomicron. It is genetic abnormalities in which there is either increased production or decreased degradation of these two LPs. The secondary hypertriglyceridaemia is due to:

1. Diabetes Mellitus D M
2. Chronic alcoholic abuse
and some time the Nephrotic syndrome NS

Eureptive xanthoma
2. **Hypercholesterolemia**: The primary form is due to genetic defect:

**A. Familial hypercholesterolemia (FH), Type II Fredrickson**: It is due to defect in LDL-receptor, either absence or mutant, and may be homozygous (complete absence of LDL receptor): serum cholesterol 500-1200 mg/dl, in childhood (during the first 10 year of age) there is CHD complication and tendon xanthoma and death during the third decade. In heterozygous (50 % absence of LDL receptor), CHD during the fourth decade and xanthoma the third decade and it is less severe than homozygous: The homozygous incidence is 1/million, heterozygous 1/500.
FH is the most common form of lipid disorder that is associated with high incidence of CHD. FH is also associated with tendon xanthoma (Achillus xanthoma), xanthelesma (before 40 years of age) and arcus xanthoma. Similar clinical characteristics observed in Familial defective of apo B100 (FDAB).  

**Polygeneic hypercholesterolemia:** This type is the most common causes of hypercholesterolemia and is due to multigeneic abnormalities and the associated environmental factor; such as infection.

The secondary hypercholesterolemia is:
1. Hypothyroidism
2. Nephroteic syndrome (NS)
Dysbetalipoproteinemia; Type III Fredrickson which associated with Palmar xanthoma.

Apo E, mainly apo E3 is essential for hepatic uptake of chylomicrone and VLDL remnants, in variant form of apo E, such as apo E2, there is increased of these blood remnants concentrations, hypertriglyceridaemia, hypercholesterolemia and increased the risk of CHD.
3. **Combined Hyperlipidaemia (CHL)**: It is familial and referred to FCHL and implied in affected family; the increased of blood cholesterol in member (IIa Fredrickson), the TG in anther member (IV Fredrickson) and the cholesterol and TG in third member (IIb Fredrickson) of same family. The increased of lipid parameters is not significant (Serum cholesterol: 240-360 mg/dl, S.TG: 180-540 mg/dl). Xanthomata is usually not present, but there is often family history of CHD.
Hypolipidaemia: 1.

**Hypoalphalipoproteinemia (↓HDL):** It is characterized by low level of HDL-C, and in severe form, the Tangier’s disease the HDL is severely low due to apo A deficiency and the clinical features include large, yellow tonsils and hepatomegaly.

2. **Abetalipoproteinemia:** It is characterized by absence of apo B100 and apo B48 with resultant deficiency or lack of LDL-C, VLDL and chylomicone. The clinical features are steatorrhea, impaired transport of fat-soluble vitamins and acanthocytosis. Failure to growth in infants and children.