HYPERLIPIDEMIA.

- abnormally elevated levels of any or all lipids and/or lipoproteins in the blood but Plasma cholesterol and triglyceride are clinically important because they are major modifiable risk factors for cardiovascular disease, whilist severe hypertriglyceridaemia also predisposes to acute pancreatitis.

THE STORY OF LIPIDS.

- ***Chylomicrons---***
- Transport fats from the intestinal mucosa to the liver.
- ***LDL---***
- In the liver chylomicrons release triglycerides and some cholesterol and become low density lipoprotein. Then carries fat and cholesterol the body's cells. Oxidized LDL cholesterol---Atheroma formation.
- HDL---Carry fat and cholesterol back to the liver for excretion.
- Atherogenic cholesterol---LDL, VLDL, IDL.

Type	Lipoprotein Fraction elevated	*Cholesterol level*	TAG level
Type I	Chylomicrons	N	↑ ↑
Type IIA	LDL	↑↑	N
Type IIB	LDL and VLDL	↑↑	↑
Type III	Broad beta-VLDL and Chylomicrons	↑ ↑	↑
Type IV	VLDL	↑	↑ ↑
Type V	VLDL Chylomicrons	N	↑ ↑

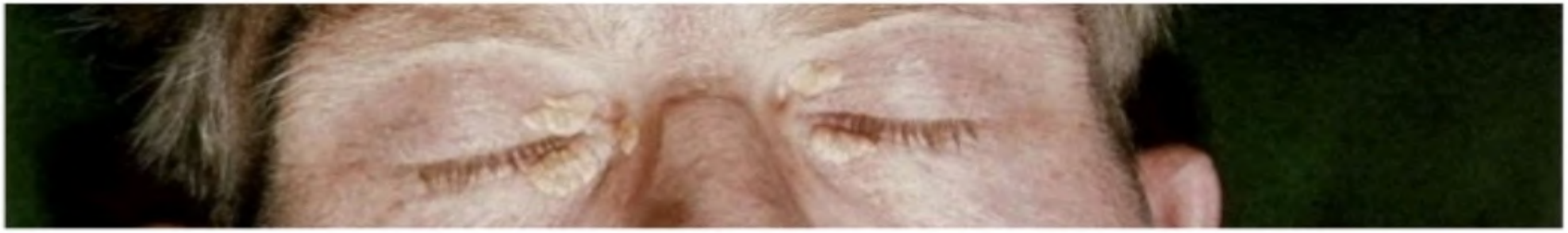
Causes of Hyperlipidemia

- Diet
- Hypothyroidism
- Nephrotic syndrome
- Anorexia nervosa
- Obstructive liver disease
- Obesity
- Diabetes mellitus
- Pregnancy

- ***Diabetes Mellitus—***Acetyl CoA pool is increased and more molecules are channeled to cholesterol'
- ***Obstructive jaundice---***
- Excretion of cholesterol through bile is blocked.
- ***Hypothyroidism—***The receptor for HDL on liver cells are decreased and so excretion is not effective.
- ***Nephrotic syndrome—***ALBUMIN is lost through urine (globulin and lipoprotein) are increased as a compensatory machanism.

- ***ATHERSCLEROSIS-***The elevation of lipids in plasma leads to the deposition of cholesterol on arterial wall.

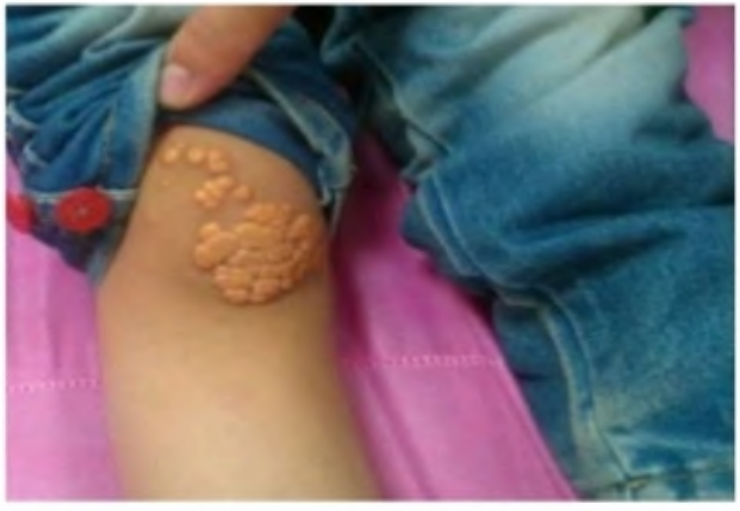
- ***IHD and CVA—***Thromboembolic episodes in coronary and cerebral vessels leads to myocardial infarction and stroke.



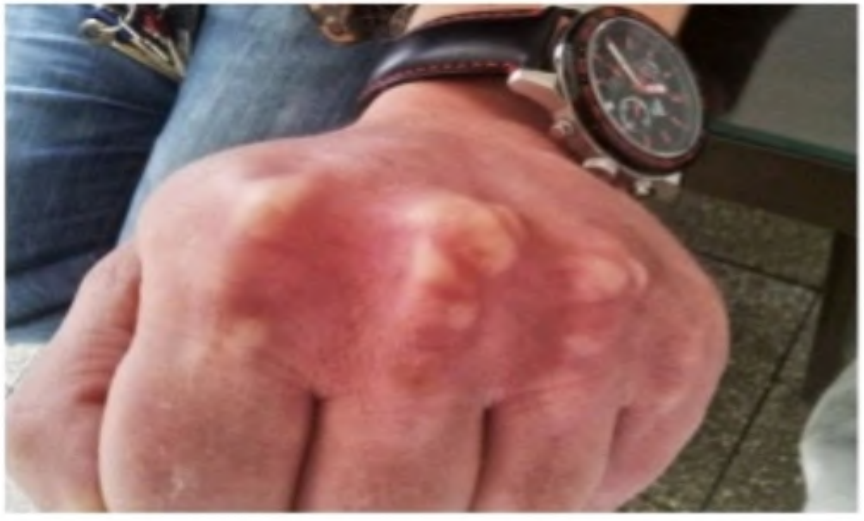
1. **Xanthelasmas:** nodular lipid deposits around the eyelids
2. Typically bilateral, yellow, flat plaques on the upper eyelids (nasal side)
3. Occurrence: primary or hypercholesterolemia (e.g., primary biliary cholangitis), hyperapobetalipoproteinemia, ↑ LDL level

- **XANTHOMA-**The deposition of lipid in subcutaneouas tissue.

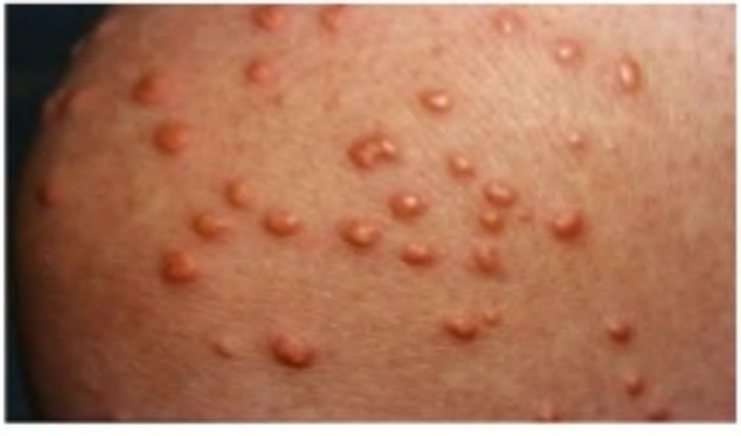
- **CORNEAL ARCUS-** Deposits of lipids in cornea, indicating hypercholestremia.
- Hyperlipidemia, in order to highest to lowest incidence are Type IIA, Type IIB, IV, I, III and V.



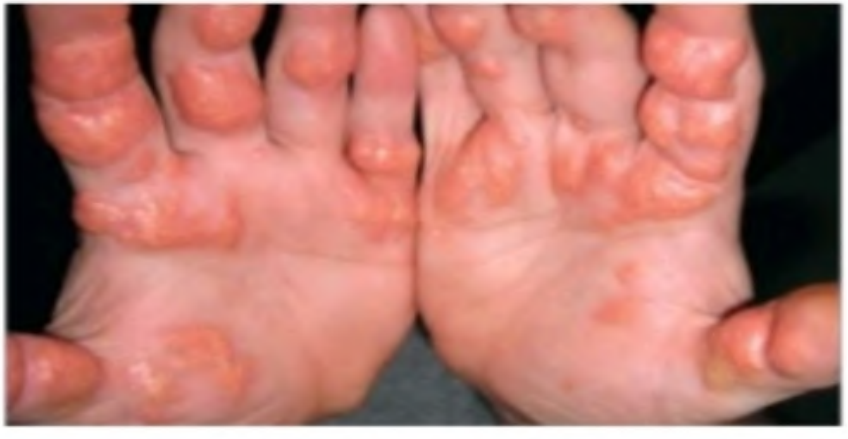
Xanthomas : nodular lipid deposits in the skin and tendons



Tendinous xanthomas



Eruptive Xanthomas



Palmar Crease Xanthomas

HYPOLIPOPROTEINSMIAS

- Familial hypobetalipoproteinemia:
- It is an inherited disorder.
- Due to an impairment in the synthesis of apo B.
- The plasma LDL concentration in the affected individuals is between 10 to 50 of normal values.
- This disorder is harmless & the individuals have healthy and long life.

ABETALIPOPROTEINEMIA

- This is a rare disorder due to a defect in the synthesis of apoprotein B.
- It is characterized by a total absence of B-lipoprotein (LDL) in plasma.
- Triacylglycerols are not found in plasma, but they accumulate in liver & intestine.
- Serum cholesterol level is low.
- Impairment in physical growth & mental retardation.

FAMILIAL ALPHA-LIPOPROTEIN DEFICIENCY (TANGIER DISEASE)

- The plasma HDL particles are almost absent.
- The plasma TG are elevated.
- Increased risk of atherosclerosis.

TYPE II A.(PIMARY FAMILIAL HYPERCHOLESTREMIA)

- There is elevation of LDL.
- Patients seldom survive the second decade of life due to ischemic heart disease.
- The cause is **LDL receptor** defect.

TYPE IIA(PRIMARY FAMILIAL HYPERCHOLESTREMIA).

- Receptor deficiency in liver and peripheral tissues will result in the elevation of LDL levels in plasma, leading to hypercholesterolemia.

- The LDL receptor defect may be due to the following reasons.

1. **LDL receptor deficiency.**

2. **Defective binding** of B-100 to the LDL receptors.

- This defect is known as B-3500 or **familial defective apo B.**

3. Receptor-LDL complex is not internalized.

- Secondary type II hyperlipopteinemia is seen in hypothyroidism, diabetes mellitus, nephrotic syndrome and cholestasis.

Goals of Lipids.

- LDL
- <100----------optimal.
- 100—129------Near optimal.
- 130---159------Borderline.
- 160—189--------High.
- ≥ 190----------Very high.

- TOTAL CHOLESTEROL
- <200----------Desirable.
- 200----239----Borderline.
- ≥ 240------------Very High.
- HDL
- <40------Low
- ≥ 60----High

- SERUM TRIGLYCERIDES
- < 150—NORMAL
- 150—199—BORDERLINE.
- 200—499----HIGH
- ≥ 500– VERY HIGH.

Non-pharmacologic

Management of hyperlipidemia.

Diet

Weight Loss and Exercise

PREVENTIONSION OF ATHEROSCLEROSIS.

Reduce dietary cholesterol.
Vegetables oil and PUFA
Green leafy vegetables
Exercise
Hypolipidemic drug.

HYPERLIPIDEMIA

TREATMENT.

Pharmacologic Treatment

- HMG-CoA reductase inhibitors (statins)
- Cholesterol absorption inhibitors
- Bile acid sequestrants
- Nicotinic acid
- Fibric acid derivatives
- Omega 3 fatty acids
- Novel Agents-*PCSK9 Inhibitors*

Medication for Hyperlipidemia.

Drug class	Agent
HMG COA Reductase inhibitor	LOVASTATIN.
Cholesterol absorption inhibitor	Ezetimibe
Nicotinic acid	
Fibric acid	Fenofibrate
Bile acid sequestrant	Cholesttyramine.

Risk factor cardiovascular Disease.

modifiable	Non-modifiable
Dyslipidemia--LOW HDL, High LDL, ↑Triglycerides	age
smoking	gender
Raised blood pressure.	Family history of CHD.
Diabetes mellitus	
Diet	