BIOCHEMISTRY

Lec:6 : 2nd stage Dr. Shaimaa S.Mutlak

METABOLISM OF LIPIDS

PATHOLOGICAL VARIATIONS OF SERUM CHOLESTEROL

1. **Normal value:** Normal serum total cholesterol varies widely, though different values by different methods, have been given by different workers. Normal range

in young adults: 150 to 240 mg/100 ml.

2. **Increase:** Increase of serum cholesterol level above normal is called hypercholesterolaemia which is found most characteristically in:

1. **nephrotic syndrome** (Type II nephritis): In earlier stages when associated with oedema, values up to 600 to 700 mg are common. Sometimes it may reach up to 1000 mg or more.
2. **Diabetes mellitus:** Values up to 400 to 550 mg% are commonly found when treatment is inadequate.
3. **Obstructive jaundice:** Increase is found most commonly. Increases parallel with increase in serum bilirubin.
4. **Myxoedema:** High values are obtained usually ranging from 500 to 700 mg%. Helps in diagnosis.
5. **xanthomatous biliary cirrhosis**: Very high values are seen.
6. **hypopituitarism:** Small increases ranging from 250 to 350 mg may be seen.

7. **Xanthomatosis:** Frequently found to be associated with high cholesterol values.
8. **In coronary thrombosis and in angina pectoris:** Value between 300 to 400 mg is rather of frequent finding.
9. Idiopathic hypercholesterolaemia has also been described.

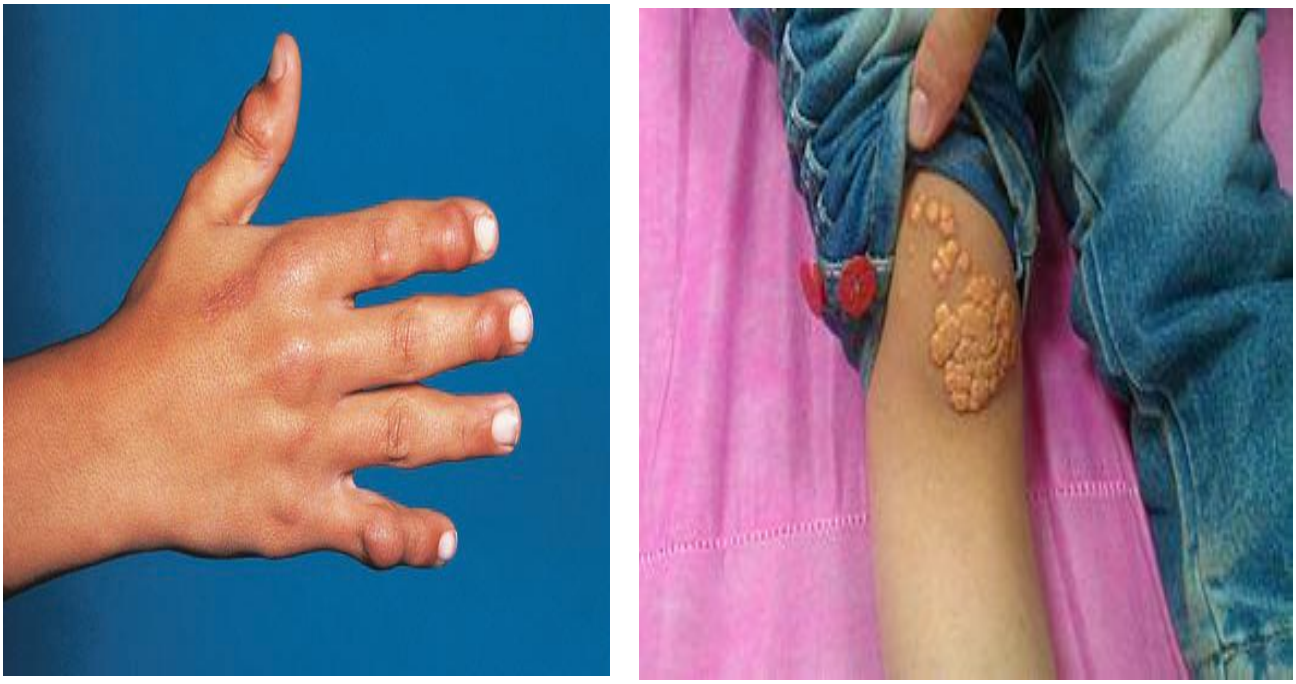

Figure 1;2: xanthomas in familial hypercholesterolaemia.

3. **Decrease:** Decrease in blood cholesterol below normal is called hypocholesterolaemia.

Hypocholesterolaemia is characteristically seen in:

1. **thyrotoxicosis**: Values as low as 80 to 100 mg% may be seen. But quite a number of hyperthyroidism cases may have a serum cholesterol within normal range.
2. Pernicious anaemia and in other anaemias.

3. haemolytic jaundice.
4. Malabsorption syndrome.
5. Wasting diseases.
6. In acute infections and in a number of terminal states.

Fredrickson's classification of hyperlipidaemias

type	electrophoretic	Increased lipoprotein
I hyperlipidaemia	Increased chylomicrons	Chylomicrons
IIa hyperlipidaemia	Increased β-lipoproteins	LDL
IIb hyperlipidaemia	Increased β and pre- β-lipoproteins	LDL and VLDL
III hyperlipidaemia	Broad β -lipoproteins	IDL
IV hyperlipidaemia	Increased pre- β-lipoproteins	VLDL
V hyperlipidaemia	Increased chylomicrons and pre- β lipoproteins	Chylomicrons and VLDL

RELATION OF CHOLESTEROL AND OTHER LIPIDS AS RISK FACTOR IN CORONARY HEART DISEASE (CHD)

Of the serum lipids, cholesterol has been the one most often incriminated as the risk factor. However, other parameters such as serum TG, VLDL and LDL have been incriminated. Patients with CHD can have any one of following abnormalities:

• Elevated concentrations of VLDL with normal concentrations of LDL
• Elevated LDL with normal VLDL
• Elevation of both VLDL and LDL.

1. Role of Cholesterol

An elevation of the total cholesterol in plasma is considered to be a 'Prime risk factor' for CHD. The Framingham Study has demonstrated a linear increase in coronary "risk" with increment of total plasma cholesterol level from 180 mg upwards.

The Lipid Research Clinics Coronary Primary Prevention Trial had presented firm proof that in humans, a lowering of plasma cholesterol level reduces the coronary thrombosis and myocardial infarction and mortality. One conclusion deduced from this pioneering work is: A 1 per cent fall in cholesterol predicts a 2 per cent reduction in CHD risk.

2. Role of LDL and HDL

Recent studies have shown that atherogenic significance of the total cholesterol concentration must be viewed with restrictions. From many studies, it is now concluded that LDL is the carrier of 70 per cent of total cholesterol and it transports cholesterol to tissues and thus is most potential atherogenic agent. On the other hand, an increase of second cholesterol rich class HDL is not associated with 'risk' at all. An inverse relation between CHD and HDL concentration has been found. A raised HDL concentration is beneficial and protective against CHD. This protective mechanism is explained by the following two mechanisms operating in parallel:

1. Mechanisms 1: “Reverse transport” of cholesterol from peripheral tissues into the Liver by way of HDL which thus reduces the intracellular cholesterol content (scavenging action of HDL).
2. Mechanisms 2: Control of catabolism of TG rich lipoproteins. High HDL concentrations are associated with a faster elimination from the plasma of TG rich lipoproteins and their atherogenic intermediate.

3. Role of TG and VLDL

Elevated VLDL and hypertriglyceridaemia may also be considered a primary ‘risk’ factor because it is associated in specific cases, with an increased atherogenic risk.

• A low blood TG level is suggestive of efficient intravascular lipolysis and thus of enhanced formation of HDL by this route.

• Hypertriglyceridaemia, on the other hand, indicates less effective intravascular lipolysis and hence a reduced formation of HDL which is in turns associated with a higher atherogenic risk.

Atherogenic index (AI): is a logarithmically transformed ratio of molar concentrations of triglycerides to HDL-cholesterol was categorized as low **risk** (<0.1), intermediate **risk** (0.1–0.24), and high **risk** (>0.24).