Lipids, lipoproteins and cardiovascular disease

Presented by

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The requirements for the Clinical Chemistry
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Cardiovascular disease

Plasma enzymes have been used in the diagnosis of myocardial infarction:

1) **Creatine kinase (CK-MB)**; regarded as gold standard.
2) **Troponin**; regarded as gold standard.
3) Aspartate aminotransferase
4) Lactate dehydrogenase
Cardiovascular disease

1) Creatine kinase (CK-MB); regarded as gold standard.

- **CK-MB increased** as a result of heart injury and rarely skeletal muscle damage.

- **CK and LDH isoenzymes** provides a definitive diagnosis of acute myocardial infarction (MI).

Note: **CK** begins **rise** within 4–8 hours following onset of chest pain, reaches a **peak of activity at 24 hours**, and **returns to baseline after 48–72 hours**.
Cardiovascular disease

2. Troponin; regarded as gold standard.
   ✓ Troponin is very specific for myocardial infarction.
   ✓ Troponin I are regulatory proteins for myocardial contractility.
   ✓ They are released into the plasma and elevated in response to cardiac damage.
   ✓ Troponin appears in plasma within 4–6 hours after an MI, peaks in 8–28 hours, and remains elevated for 10 days.

3. Myoglobin
   ✓ Myoglobin is an oxygen binding protein that is released from myocardial cell when they are injured.
   ✓ It can detected 1-4 hours after the insult.
   ✓ Myoglobin level peaks at 4-12 hours.
   ✓ It is cleared from the circulation within 24 hours.
Cardiovascular disease

4. Aspartate aminotransferase
   ✓ AST (GOT) increased 4-8 hours following a myocardial infarction (MI).
   ✓ AST is not a specific or sensitive enough marker for the diagnosis of myocardial infarction so cardiac troponins is much used.

5. Lactate dehydrogenase (LDH or LD)
   Increased levels of LDH-1 and LDH-2, are associated with myocardial infarction (MI).
Functions of Lipids

• Energy storage as triglyceride
• Building block included structure components of cells (cholesterol and phospholipids)
• Thermal Insulator
• Specialized functions
  – Messenger/Signaling
  – Bone strength
  – precursor of steroid hormones and bile salts Antioxidant
  – Electron Transport Chain
Plasma lipids

The major lipids present in the plasma are:

1. Fatty acids
2. Triglyceride
3. Cholesterol
4. phospholipids
Plasma lipids

The major lipids present in the plasma are:

1. Fatty acids
   - Long chain and have general formula R-COOH
   - Saturated fatty acid don't contain C-C double bond.
   - Unsaturated fatty acid, contain C-C double bond.

2. Triglyceride
   - Consist of glycerol esterified with three fatty acids.
   - Synthesized in the liver & adipose tissue.
   - Source of storage energy.
Plasma lipids

The major lipids present in the **plasma** are:

3. **Cholesterol**
   - Cholesterol production occurs in the **liver** & **intestines**.
   - Source: 70% synthesized in body, 30% from food (animal source as meat, eggs and dairy products)
   - The rate-limiting step being catalysed by HMG-CoA reductase.
   - Important in cell membrane structure and is the precursor of steroid hormones in adrenal & gonades and precursor bile acids.
   - Cholesterol is oxidized by the liver into a variety of **bile acids** then excreted.

4. **phospholipids**
   - The simplest Glycerophospholipids (phosphatidates), consist of **two fatty acyl groups esterified to C-1 and C-2 of glycerol C3 phosphate** to glycerol
   - production occurs in the **liver** & **intestines**.
   - Present in the cell membrane.
Lipoproteins

- Lipids are **not water soluble** so lipids **transported** in the plasma in **association with proteins**.

- **Apolipoproteins** are the protein components of the lipoproteins and divided four groups (**apo A, B, C and E**)

Apolipoproteins important in:

1. Maintaining the structure integrity of the lipoproteins
2. Promote and control lipid transport through the circulation and lipid uptake into tissues
3. Regulating certain enzymes that act on lipoproteins.

- **Albumin** is the **carrier** of free **fatty acids**.
Lipoproteins consist of triglyceride and cholesteryl esters surrounded by a surface layer of phospholipids.

Lipoproteins are classified on the basis of their densities to:

1. Chylomicrons
2. Very low density Lipoproteins (VLDL)
3. Low density Lipoproteins (LDL)
4. High density Lipoproteins (HDL)
Figure 14.4 Composition of lipoproteins; although the composition in each class is similar, the particles are heterogeneous, so the percentages given are approximate. Figures shown for HDL are for HDL3; HDL2 contains less protein and more lipid. Only the principal apolipoproteins are shown.
Lipoprotein Nomenclature and Composition

CM: chylomicron  
VLDL: very low density lipoprotein  
IDL: intermediate density lipoprotein  
LDL: low density lipoprotein  
HDL: high density lipoprotein

CM= chylomicron  
VLDL= very low density lipoprotein  
IDL= intermediate density lipoprotein  
LDL= low density lipoprotein  
HDL= high density lipoprotein

Major Protein:  
apoB-48  
apoB-100  
apoB-100  
apoB-100  
apoA-I

Major Lipid:  
TG  
TG  
CE  
CE  
CE

TG= triglyceride  
CE= cholesteryl ester

Apo = apolipoprotein
## Functions of the major apolipoproteins

<table>
<thead>
<tr>
<th>Apolipoprotein</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-I</td>
<td>activates LCAT structural (in HDL)</td>
</tr>
<tr>
<td>A-II</td>
<td>inhibits HTGL at high concentration structural (in HDL)</td>
</tr>
<tr>
<td>B-100</td>
<td>structural (in LDL and VLDL) receptor binding</td>
</tr>
<tr>
<td>B-48</td>
<td>structural (in chylomicrons)</td>
</tr>
<tr>
<td>C-II</td>
<td>activator of LPL</td>
</tr>
<tr>
<td>C-III</td>
<td>inhibits LPL inhibits clearance of CM and VLDL remnant particles</td>
</tr>
<tr>
<td>E</td>
<td>binding to LDL and remnant receptors</td>
</tr>
</tbody>
</table>

**Apolipoproteins**
- A-I
- A-II
- B-100
- B-45
- C-II
- E

*Figure 14.2 Functions of the major apolipoproteins. Abbreviations are explained in the text.*
### Classification and characteristics of lipoproteins

<table>
<thead>
<tr>
<th>Lipoprotein</th>
<th>Density (g/mL)</th>
<th>Mean diameter (nm)</th>
<th>Electrophoretic mobility</th>
<th>Source</th>
<th>Principal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CM</td>
<td>&lt;0.95</td>
<td>500</td>
<td>remains at origin</td>
<td>intestine</td>
<td>transport of exogenous triglyceride</td>
</tr>
<tr>
<td>VLDL</td>
<td>0.96–1.006</td>
<td>43</td>
<td>pre-β</td>
<td>liver</td>
<td>transport of endogenous triglyceride</td>
</tr>
<tr>
<td>IDL</td>
<td>1.007–1.019</td>
<td>27</td>
<td>‘broad β’</td>
<td>catabolism of VLDL</td>
<td>precursor of LDL</td>
</tr>
<tr>
<td>LDL</td>
<td>1.02–1.063</td>
<td>22</td>
<td>β</td>
<td>catabolism of VLDL, via IDL</td>
<td>cholesterol transport</td>
</tr>
<tr>
<td>HDL</td>
<td>1.064–1.21</td>
<td>8</td>
<td>α</td>
<td>liver, intestine; catabolism of CM and VLDL</td>
<td>reverse cholesterol transport</td>
</tr>
</tbody>
</table>

Figure 14.3 Classification and characteristics of lipoproteins.
Classification and characteristics of lipoproteins

- Lipoprotein (a), or LP(a), is unknown function, large and more dense than LDL but has similar composition except in addition one molecule of apo (a) for every molecule of apo B-100.
- Apoa homology with plasminogen.
- Range of Lp(a) concentrated in plasma from 0-1000mg/L.
- Elevated Lp(a) independent risk factor for cardia heart disease (CHD).
- Drugs that lower LDL have little effect on Lp(a) concentration.
Lipoproteins

- **Chylomicrons**
  - Triglycerides (90%), cholesterol (5%), phospholipids (4%), and proteins (1%).
  - **Largest** lipoprotein
  - **Not present in normal fasting plasma**
  - Apo A and apo-48 are synthesized in the gut and present in chylomicrons.
  - Apo CII and apoE are transferred to chylomicrons from HDL.

**Metabolism of Chylomicrons see the figure in the next slide**

1. **Chylomicrons** synthesized by the gut.
2. **Chylomicrons** transport **exogeneous** triglyceride to other tissues and transport cholesterol and fat soluble vitamin to the liver.
3. **Triglyceride in Chylomicrons** removed by lipoprotein lipase (LPL) which converted it to fatty acids which activated by apoCII from HDL. **(Note: LPL activated by apo CII)**.

**So the Metabolism of Chylomicrons take it two pathways:**

**First pathway:** Remnant particles of **Chylomicrons** removed from the blood by the liver which bind to **remnant receptor in liver and recognized by apo E)**. **(NOTE: remnant receptor recognized by ApoE).**

**Second pathway:**
- **HDL take it** triglyceride witch removed from chylomicrons and also apoA, apoCII, cholesterol & phospholipids. Then esterified cholesterol.
- cholesterol ester exchange by cholesteryl ester transfer protein (CETP) and exchange cholesterol ester by triglyceride.
Figure 14.5 Chylomicrons transport dietary triglycerides to tissue where they are removed by the action of lipoprotein lipase. The resulting remnant particles are removed from the bloodstream by the liver. They bind to remnant receptors (which recognize apo E) and LDL receptors (not shown) on hepatic cells, are internalized and catabolized. Apolipoproteins A and B-48 are synthesized in intestinal cells; apo C and apo E are acquired, together with cholesteryl esters (CE), from HDL. Apolipoprotein C-II activates lipoprotein lipase. As triglycerides (TRIG) are removed from chylomicrons, apo A, apo C, cholesterol (CHOL) and phospholipids are released from their surfaces and transferred to HDL where the cholesterol is esterified. Cholesteryl esters are transferred back to the remnant particles in exchange for triglycerides by cholesteryl ester transport protein (CETP).
Very Low Density Lipoproteins (VLDL), see figure in the next slide

- VLDL synthesized by the liver.

**Metabolism of VLDL**

1. VLDL in synthesized in liver and transport **endogenous** triglyceride from liver to other tissue.

2. VLDL triglyceride removed by lipoprotein lipase (LPL).

3. At the same time, cholesterol, phospholipids, apo C, apo E transferred to HDL. SO **VLDL convert to IDL**.

4. Cholesterol esterified by (CETP) in HDL and exchange it with triglyceride in IDL.

5. Some **IDL** removed by liver by LDL receptor in the liver.

6. Most **IDL** removed by hepatic triglyceride lipase and converted to LDL.
Figure 14.6 VLDLs are synthesized in the liver and transport endogenous triglyceride from the liver to other tissues where they are removed by the action of lipoprotein lipase. At the same time, cholesterol, phospholipids and apo C and apo E are released and transferred to HDL. By this process, VLDL are converted to IDL. Cholesterol is esterified in HDL and cholesteryl esters are transferred to IDL by cholesteryl ester transfer protein. Some IDL is removed by the liver, but most has more triglyceride removed by hepatic triglyceride lipase and is thereby converted into LDL. Thus the triglyceride-rich VLDL are precursors of LDL, which comprise mainly cholesteryl esters and apo B-100.
Lipoproteins

3. Low density Lipoproteins (LDL) or bad cholesterol

- LDL cholesterol is easy to **stick to the walls of blood vessels**.
- High LDL in blood associated with **atherosclerosis, heart disease** and **myocardial infarction**
- Because high LDL in blood will **deposited in blood artery and trigger clot formation**.
Low density Lipoproteins (LDL)

- Generated from VLDL in the circulation.
- Rich in cholesterol.
- Main carrier of cholesterol from liver to peripheral tissues.

Metabolism of LDL

1. LDL uptake by liver and other tissue by recognition of apoB-100 in LDL by the LDL receptor.
2. LDL hydrolysed by lysosomal enzymes releasing free cholesterol.

So Free cholesterol results:

a. Inhibit HMG-COA reductase which cause decease cholesterol synthesis.

b. Inhibit LDL receptor synthesis.

c. Stimulates cholesterol esterification by the enzyme acyl CoA: cholesterol acyl transferase (ACAT).
Figure 14.7 LDL uptake and catabolism. LDL are derived from VLDL, via IDL. They are removed by the liver and other tissues by a receptor-dependent process involving the recognition of apo B-100 by the LDL receptor. The LDL particles are hydrolysed by lysosomal enzymes, releasing free cholesterol which (i) inhibits HMG-CoA reductase, the rate-limiting step in cholesterol synthesis, (ii) inhibits LDL receptor synthesis and (iii) stimulates cholesterol esterification by augmenting the activity of the enzyme acyl CoA:cholesterol acyl transferase (ACAT).
Lipoproteins

4. High density Lipoproteins (HDL) or good cholesterol
   - Smallest lipoproteins.
   - Synthesized in liver and intestinal.
   - It contains the highest proportion of protein to lipids.
   - Protective function against arterial disease.

HDL has two Functions:
1. Source of apoproteins for chylomicrons and VLDL.
2. Revers cholesterol transport, taking cholesterol from tissues to the liver.
HDL metabolism and reverse cholesterol transport (see the next figure in the next slide)

1. Nascent HDL synthesis in liver and gut acquires free cholesterol from extrahepatic cells, chylomicrons and VLDL, SO nasent HDL convert to HDL3.

2. Cholesterol in HDL3 is esterified by the enzyme Lecithin cholesterol acytransferase (LCAT).
   
   **Note:** LCAT activated by apo A1.

3. Then, cholesterol esters in HDL3 exchange with triglyceride in remnant chylomicrons and IDL by (CETP).

4. remnant chylomicrons and IDL removed from circulation by the liver, whence the cholesterol excreted in bile or bile acids.

5. Much HDL2 recycled, but some removed from the circulation through scavenger receptor type B1 receptor (SRB1) in the liver which recognize by apoA1 OR by hepatic triglyceride lipoprotein lipase (HTGL).
Figure 14.8 HDL metabolism and reverse cholesterol transport. Nascent HDL acquires free cholesterol from extrahepatic cells, chylomicrons and VLDL, and is thereby converted to HDL3. The cholesterol is esterified by the enzyme LCAT and cholesteryl esters are transferred to remnant lipoproteins by CETP in exchange for triglyceride. Remnant particles are removed from the circulation by the liver, whence the cholesterol is excreted in bile both per se and as bile acids. Much HDL is recycled, although some is probably taken up by the liver and steroidogenic tissues. Apoprotein transfers have been omitted for clarity.
Lipoprotein metabolism

Fig 66.2 Lipoprotein metabolism.
Investigation of plasma lipid abnormalities

Standard lipid profile consists of the following:

- Total cholesterol
- HDL-cholesterol
- Triglyceride

If quantity expressed in (mmol/L)

\[ \text{VLDL} = \frac{\text{TRIG}}{2.2} \]

\[ \text{LDL CHOL} = \text{TOTAL CHOL} - \left( \text{HDL CHOL} + \frac{\text{TRIG}}{2.2} \right) \]

If quantity expressed in (mg/dl)

\[ \text{LDL-cholesterol} = \text{total cholesterol} - (\text{HDL} + \text{VLDL}) \]

Where \( \text{VLDL} = \frac{\text{Triglyceride}}{5} \)
<table>
<thead>
<tr>
<th>Variable</th>
<th>HDL cholesterol</th>
<th>LDL cholesterol</th>
<th>Triglyceride</th>
</tr>
</thead>
<tbody>
<tr>
<td>sex</td>
<td>F &gt; M</td>
<td>M = F</td>
<td>F &lt; M</td>
</tr>
<tr>
<td>age</td>
<td>slight ↑ in F</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>high P/S ratio</td>
<td>N or ↓</td>
<td>↓</td>
<td>N or ↓</td>
</tr>
<tr>
<td>exercise</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>obesity</td>
<td>↓</td>
<td>N</td>
<td>↑</td>
</tr>
<tr>
<td>alcohol</td>
<td>↑</td>
<td>N</td>
<td>↑</td>
</tr>
<tr>
<td>exogenous oestrogens</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Condition</td>
<td>HDL cholesterol</td>
<td>LDL cholesterol</td>
<td>Triglyceride</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-----------------</td>
<td>-----------------</td>
<td>--------------</td>
</tr>
<tr>
<td>obesity</td>
<td>↓</td>
<td>N</td>
<td>↑</td>
</tr>
<tr>
<td>excessive alcohol intake</td>
<td>↑</td>
<td>N</td>
<td>↑</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>N/s ↓</td>
<td>N</td>
<td>↑↑</td>
</tr>
<tr>
<td>hypothyroidism</td>
<td>N</td>
<td>↑↑</td>
<td>N/↑</td>
</tr>
<tr>
<td>nephrotic syndrome</td>
<td>↓</td>
<td>↑↑</td>
<td>↑↑</td>
</tr>
<tr>
<td>chronic renal failure</td>
<td>↓</td>
<td>N/↑</td>
<td>↑</td>
</tr>
<tr>
<td>cholestasis</td>
<td>N</td>
<td>↑</td>
<td>N</td>
</tr>
</tbody>
</table>
1. Familial hypercholesterolemia (FH):
   a. Inherited disease due to mutation can affect LDL receptor synthesis or defective apo B-100.
   b. High plasma total cholesterol (specifically high LDL).
   c. **yellow deposits of cholesterol-rich fat may be seen in various places** on the body such as around the eyelids (known as **xanthelasma palpebrarum**), the outer margin of the **iris** (known as **arcus senilis corneae**), and in the **tendons** of the hands, elbows, knees and feet, particularly the **Achilles tendon** (known as a **tendon xanthoma**).

2. Familial dysbetaalipoproteinaemia (hyperlipoproteinaemia):
   a. Elevated level of IDL and chylomicron.
   b. fat deposits in the **palmar creases** and by **tuberous xanthomata**
   c. Increase cholesterol and triglyceride.
Primary hyperlipidemia

3. Familial chylomicronaemia:
   a. Elevated chylomicron.
   b. Inherited disease because deficiency of lipoprotein lipase, and in the other a deficiency of apo C-II, which is required for activation of this enzyme.
   c. Presentation is usually in childhood, with eruptive xanthomata, recurrent abdominal pain due to pancreatitis and sometimes hepatosplenomegaly. Lipaemia retinalis may also be present.
   c. Management involves giving a low fat diet

4. Familial hypertriglyceridaemia:
   a. It is usually not manifest until adulthood.
   b. Inherited disease; there is increased hepatic synthesis of VLDL.
   c. High level of triglyceride and low level of HDL.
   c. Physical signs (e.g. eruptive xanthomata and lipaemia retinalis) usually present.

5. Familial combined hyperlipidaemia
   a. This is due to hepatic overproduction of apo B, leading to increased VLDL secretion and increased production of LDL from VLDL.
   b. Either plasma cholesterol or triglyceride, or both, may be elevated;
Several drugs can also cause hyperlipidaemia, including thiazides, β-blockers lacking intrinsic sympathomimetic activity (ISA), corticosteroids, immunosuppressants and antiretroviral drugs.

Ideally, calcium antagonists, angiotensin-converting enzyme (ACE) inhibitors or angiotensin antagonists, β-blockers with ISA or α-blockers should be used for treating hypertension in patients with hyperlipidaemia.

Oestrogens, especially when given to postmenopausal women, may lower plasma cholesterol concentrations but may cause, or exacerbate, hypertriglyceridaemia. Certain progestogens used in oral contraceptives also have a small adverse effect on plasma lipids.
<table>
<thead>
<tr>
<th>Investigation</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>urine analysis</td>
<td>for protein (renal disease) and glucose (diabetes, a cardiovascular risk factor)</td>
</tr>
<tr>
<td>plasma creatinine</td>
<td>renal disease</td>
</tr>
<tr>
<td>plasma potassium</td>
<td>mineralocorticoid excess (primary or secondary)</td>
</tr>
<tr>
<td>plasma calcium</td>
<td>hyperparathyroidism</td>
</tr>
<tr>
<td>plasma cholesterol and triglycerides</td>
<td>cardiovascular risk assessment</td>
</tr>
<tr>
<td>plasma renin and aldosterone</td>
<td>Conn’s syndrome</td>
</tr>
<tr>
<td>overnight dexamethasone suppression test</td>
<td>Cushing’s syndrome</td>
</tr>
<tr>
<td>urinary catecholamines/metabolites</td>
<td>phaeochromocytoma</td>
</tr>
</tbody>
</table>
A 55-year-old man presented with a history of lethargy, loss of concentration and constipation. He had suffered from angina for two years, but this had become less of a problem recently, as he had become much less active. On examination, he appeared myxoedematous.

<table>
<thead>
<tr>
<th>Serum: TSH</th>
<th>&gt;100 mU/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>cholesterol</td>
<td>12.2 mmol/L</td>
</tr>
<tr>
<td>triglyceride</td>
<td>1.5 mmol/L</td>
</tr>
</tbody>
</table>

The patient was treated cautiously with thyroxine, starting with a low dose; his angina was controlled effectively with nitrates and a calcium channel blocker. His serum cholesterol fell to 8.2 mmol/L on treatment, with an LDL cholesterol of 6.4 mmol/L.

Comment
1. Hypothyroidism causes hypercholesterolaemia
2. LDL increase
3. HDL normal
4. Triglyceride normal
Comment

1. Alcohol causes hypertriglyceridaemia by increasing triglyceride synthesis.
2. Obesity cause insulin resistance by secretion resistin hormone.
3. HDL Increase, LDL normal so total cholesterol increase.
An obese 44-year-old woman with type 1 diabetes was found to have a blood glucose concentration of 32 mmol/L at the outpatient clinic and was admitted to hospital. Blood was taken for further biochemical analysis and the serum was seen to be grossly lipaemic.

<table>
<thead>
<tr>
<th>Serum: cholesterol</th>
<th>53 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>triglyceride</td>
<td>150 mmol/L</td>
</tr>
</tbody>
</table>

The sample was inspected after standing overnight and had a creamy, supernatant layer, although the infranatant remained lipaemic.

**Comment**

1. Hyperlipidemia can be complicated by uncontrolled diabetes.
2. Diabetes cause extremely elevated in triglyceride.
3. Because diabetes inhibit lipoprotein lipase and increase hepatic triglyceride.
A 36-year-old man consulted an optician to obtain a prescription for reading glasses. The optician noticed that the patient had bilateral corneal arcus, and recommended that he consult his GP. The GP found that he also had tendon xanthomata arising from the Achilles tendons. Blood pressure was normal; he was a non-smoker and not overweight. His father had died of a heart attack at the age of 40. An ECG taken at rest was normal, but ischaemic changes developed on exercise. Analysis of fasting blood for lipids showed the following.

<table>
<thead>
<tr>
<th>Serum: cholesterol</th>
<th>13.2 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>triglyceride</td>
<td>1.3 mmol/L</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>11.4 mmol/L</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>1.2 mmol/L</td>
</tr>
</tbody>
</table>

Comment
1. Familial hypercholesterolemia
2. Increase cholesterol, LDL increased
3. Normal triglyceride.
4. See symptom of Familial hypercholesterolemia in the case such as tendon xanthomata.
A middle-aged man was referred by his family doctor to a dermatologist because of extensive yellowish papules, with erythematous bases, on his buttocks and elbows. The dermatologist recognized these as eruptive xanthomata and noticed that there were yellow, fatty streaks in the palmar creases. Blood was drawn after an overnight fast for lipid analysis, and the serum was seen to be slightly turbid.

<table>
<thead>
<tr>
<th>Serum: cholesterol</th>
<th>8.5 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>triglyceride</td>
<td>6.4 mmol/L</td>
</tr>
</tbody>
</table>

Comment
1. Familial dysbetalipoproteinaemia (palmar creases, xanthomata)
2. Increase cholesterol, LDL increased
3. Increase triglyceride.
Remember in familial hypertriglyceridaemia

Comment

1. Cholesterol increase or normal.
2. Extremely elevated in triglyceride.
3. Because increased hepatic synthesis of VLDL and inhibition of LPL due to defect on apolipoprotein CII
Cases for Disorder of carbohydrate metabolism
An 18-year-old woman consulted her family doctor because of tiredness and weight loss. On questioning, she admitted to feeling thirsty and had noticed that she had been passing more urine than normal. The doctor tested her urine and found glycosuria. He arranged for her to be seen at the hospital’s diabetic clinic the next day. By then, however, she felt too ill to get out of bed, had started vomiting and had become drowsy. Her doctor visited her at home and arranged for immediate admission to hospital. On examination, she was found to have a blood pressure of 96/60 mmHg with a pulse rate of 112/min and cold extremities. She had deep, sighing respiration (Kussmaul respiration) and her breath smelt of acetone.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum sodium</td>
<td>130 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>5.8 mmol/L</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>5 mmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>18 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>140 μmol/L (eGFR 45 mL/min/1.73 m²)</td>
</tr>
<tr>
<td>Blood glucose</td>
<td>32 mmol/L</td>
</tr>
<tr>
<td>Arterial blood pH</td>
<td>7.05</td>
</tr>
<tr>
<td>Arterial blood H⁺</td>
<td>89 nmol/L</td>
</tr>
<tr>
<td>Arterial blood PCO₂</td>
<td>2.0 kPa (15 mmHg)</td>
</tr>
</tbody>
</table>

**Comment:**
1. Type 1 diabetes, Diabetic ketoacidosis due to urea less than 25, decrease Na, increase K, increase H+, decrease bicarbonate, increase in glucose level.
A middle-aged widow, who lived alone, was admitted to hospital after her son found her semiconscious at home. He had not seen her for a week but she had seemed well at their last meeting. On examination, she was extremely dehydrated but not ketotic. Her breathing was normal.

<table>
<thead>
<tr>
<th>Serum: sodium</th>
<th>149 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>potassium</td>
<td>4.7 mmol/L</td>
</tr>
<tr>
<td>bicarbonate</td>
<td>18 mmol/L</td>
</tr>
<tr>
<td>urea</td>
<td>35 mmol/L</td>
</tr>
<tr>
<td>creatinine</td>
<td>180 μmol/L (eGFR 27 mL/min)</td>
</tr>
<tr>
<td>total protein</td>
<td>90 g/L</td>
</tr>
<tr>
<td>osmolality</td>
<td>370 mmol/kg</td>
</tr>
<tr>
<td>Blood glucose:</td>
<td>54 mmol/L</td>
</tr>
</tbody>
</table>

Comment:
1. Patient had NIDDM (type II) due to, urea more than 25, increase Na, increase serum osmolality more than 330 mmol/kg due to hyperglycemia
Thinking of your kindness and sending you many thanks.