

## Lipoprotein lipase

### Background information.

The enzyme that hydrolyses the triglycerides contained in the circulating chylomicrons and VLDL is lipoprotein lipase (LPL). It possesses also phospholipase A1 activity (approximately 20-fold lower than its triacylglycerol hydrolase activity), which is necessary for the access to the hydrophobic core of the lipoprotein particles. It acts at the surface of the capillary endothelial cell. The enzyme is activated by apolipoprotein C-II, one of the low molecular weight proteins present in VLDL, CHY and HDL. Lipoprotein lipase is present in many tissues, including adipose tissue, striated muscle, mammary gland and heart. In the adipose tissue the activity of LPL is increased by administration of the hormone insulin. The enzyme is formed within the tissue and then secreted. It passes through the capillary endothelium and binds firmly to the heparan sulfate carbohydrate chains of glyocalix present at the surface of endothelial cells. The enzyme acts on lipoprotein triglycerides while it remains firmly bound to the endothelial cell surface. LPL has the specificity for fatty acids esterified at positions sn-1 and sn-3 of the triglycerides.

Hepatic lipase is a lipid hydrolase with properties somewhat similar to lipoprotein lipase, which is present in the liver sinusoids. This enzyme acts on IDL and HDL<sub>2</sub>. It hydrolyses the triglycerides contained in these lipoproteins, as well as phosphoglycerides present in their surface coat. In this way, hepatic lipase probably is involved in the processing of IDL, either for uptake by the liver or for conversion to LDL. Likewise, hepatic lipase is also involved in HDL<sub>2</sub> conversion back to HDL<sub>3</sub>.

Effect of heparin. When heparin is given intravenously, lipoprotein lipase activity is released into the blood plasma. This is a pharmacologic action of heparin, and heparin is not a physiologic cofactor for the enzyme. The lipolytic activity that is released represents two different enzymes that hydrolyze triglycerides. One of the lipases is derived from the liver and is resistant to inactivation by protamine or 1 M NaCl. This is hepatic lipase. The second enzyme, which is of extrahepatic origin and is inhibited by protamine or 1 M NaCl is lipoprotein lipase. After heparin injection a major part of lipolytic activity that appears in the blood plasma is protamine and salt resistant, that is, it is the hepatic lipase.

### Case report. Hyperchylomicronemia

A 15-year-old boy had a long history of abdominal complaints, including bouts of abdominal pain so severe that narcotics were required for relief. These episodes were intermittent, occurring every 6 months on average. On one occasion abdominal surgery (an exploratory laparotomy was performed, and the patient's appendix was removed. However, this did not correct the problem. The patient had recently felt well until he suddenly developed another episode of abdominal pain. His mother stated that the illness came on 4 hr after he had eaten a meal consisting of pork chops, fried potatoes, milk, ice cream topped with generous serving of whipped cream. No one else in the family had been made ill by this meal. Examination of the patient indicated an acute abdominal emergency. The patient was brought to the hospital at 8:00 AM. 14 hr after his last meal. On arrival

a blood specimen was drawn. Within 15 min the laboratory technician reported that valid results could not be obtained from the blood plasma because it was cloudy. The plasma was "milky" but on centrifugation for 30 min at 15,000 rpm, it cleared considerably and there was a thick band of "cream" located at the top of the specimen

Careful physical examination revealed cutaneous xanthomatosis (white to yellow cutaneous nodules raised on erythematous base). The enlargement of liver and spleen was also detected.

#### Biochemical questions

1. What kind of lipid abnormality would you suspect in this patient?
2. What chemical and electrophoretic studies should be obtained on the plasma sample to aid the diagnosis?
3. What kind of a diet would be helpful to treat this disease?
4. Would you recommend to supplement this boy's diet by medium chain triglycerides?
5. Give an explanation for the xanthomatosis and for the hepato- and splenomegaly.

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