LIPIDS CASE STUDIES

CASE STUDY 1

An infant girl was hospitalised because of respiratory difficulty, myopathy, brain damage and poor growth. When she was fed a high carbohydrate diet, the urine contained large quantities of short chain fatty acids. A liver biopsy revealed that almost no acetyl CoA carboxylase activity was present, whereas propionyl CoA carboxylase activity was in the normal range. Analysis of cultured skin fibroblasts confirmed this finding.

What does AcCoA carboxylase do?

Regulation?

What metabolic processes would be defective in this child as a result of the deficiency?

What associated deficiencies could be associated with loss of acetyl CoA carboxylase activity?

Why does a high carbohydrate diet accentuate excretion of short-chain fatty acids such as acetic acid?

What lipid abnormality might be related to the neonatal respiratory difficulties?

CASE STUDY 2

A 13-year old was referred to a Medical Center because of muscle pain and poor exercise tolerance. Careful neurological examination revealed some muscle weakness in her extremities. Increased amounts of two muscle enzymes, creatine kinase and lactate dehydrogenase, were found in her plasma. She was given an exercise test that had to be stopped because of severe pain in the arms and legs. Several muscle biopsies were performed. Microscopic examination indicated muscle cells filled with vacuoles containing lipid. Chemical measurement indicated increased triacylglycerol and severely decreased carnitine.

What is the main intracellular function of carnitine?

What is the function of Carnitine Palmitoyl Transferase?

What are the consequences for fatty acid β-oxidation?

Would you expect the oxidation of pyruvate to be impaired in this patient?

How might carnitine deficiency account for TAG accumulation in the muscle?

CASE STUDY 3

A 3-year-old boy was referred to the paediatric service because of repeated episodes of vomiting, lethargy and coma. The parents were told to bring him back to the clinic in the morning without giving him breakfast, in order to obtain a fasting blood sample. Because of a very busy patient schedule including several emergencies, the child was not seen until noon. The nurse noted that he was lethargic and asked for blood glucose to be measured. The plasma glucose concentration was 2mmol/l, indicating hypoglycaemia. Subsequent analysis indicated normal level of ketone bodies, but high concentrations of dicarboxylic acids were present in the urine. Hexanoylglycine, a metabolite formed from a six-carbon fatty acid, was also present in the urine.

Diagnosis?

Which organelles carry out β–oxidation?

Does this disease affect the β–oxidation process in each of these organelles?

Why did the patient become hypoglycaemic on fasting?

What is ketosis, and why did this patient not produce ketone bodies if he was hypoglycaemic?

How were the dicarboxylic acids produced?

Would you expect hexanoylglycine to be formed if the genetic defect in this case involved long-chain acyl CoA dehydrogenase instead of the medium-chain enzyme?

CASE STUDY 4

A 34-year-old woman was admitted to the hospital because of easy bruising and excessive bleeding. Examination revealed a large spleen and liver, as well as pancytopaenia, a decrease of all blood cells. Coagulation tests that a prolonged bleeding time was the only abnormality. Bone marrow analysis demonstrated the presence of Gaucher's cells.

What is a lipidosis?

What are Gaucher's cells, and how is finding them in the bone marrow related to the metabolic defect in this disease?

Describe the pathophysiology of the pantocytopaenia and the prolonged coagulation time.

What biochemical tests can be performed to identify individuals with a form of lipidosis? Can these tests detect the carrier state as well as the patient with overt disease?

How is Gaucher's disease treated?

CASE STUDY 5

A 9-month-old girl was admitted to the paediatric unit of a hospital because of poor weight gain and psychomotor retardation. Although the child appeared well at birth, she developed these problems at 5-months of age and became progressively worse. Physical examination confirmed the nutritional failure and psychomotor retardation. Subcutaneous nodules, hepatomegaly and splenomegaly were observed. Despite vigorous supportive therapy, she deteriorated rapidly and died 3 weeks after admission. Tissue specimens were obtained for histological and chemical analysis during the post-mortem examination. Large quantities of lipid-staining material were observed in many tissues, and this was demonstrated chemically to be ceramide.

Diagnosis??

How is ceramide synthesised? What types of lipid can be formed from ceramide?

Based on current knowledge of lipid storage disease, would you expect this problem to be caused by excessive synthesis of ceramide?

What therapeutic approaches might be effective?

CASE STUDY 6

A 33-Year-old man was referred to a cardiologist because of severe intermittent chest pains. He had these pains for about two years, and they were gradually becoming worse. They typically occurred after mild exertion such as brisk walking, carrying a bag of groceries up a flight of stairs, or mowing the lawn. A coronary artery angiogram revealed coronary artery atherosclerosis, and the patient was treated by angioplasty. Subsequently, his plasma cholesterol concentration was found to be 385mg/dl (10.0 mmol/L), and most of the elevation was present in LDL. The patient was placed on a diet low in cholesterol and saturated fat, and treatment was started with lovastatin, HMGCoA reductase inhibitor.

What is hypercholesterolaemia?

How is hypercholesterolaemia thought to be related to the development of atherosclerosis, myocardial infarction and tendon xanthomas?

What is the purpose of treating the hypercholesterolemia in this patient?

How is dietary cholesterol absorbed? Is it possible for a patient to have high plasma cholesterol after being on a cholesterol free diet for 3 months?

What is a reductase inhibitor?

Why was HMGCoA reductase targeted for treatment in this patient?
Why was the patient maintained on a low cholesterol diet while he was being treated with a reductase inhibitor?

What are the potential dangers of therapy with reductase inhibitors?

CASE STUDY 7

A 39-year-old woman consulted her physician because of intermittent abdominal distress. The discomfort usually followed the ingestion of a large meal, often one that contained greasy or fried foods. The pain was located in the upper abdomen and sometimes radiated to her chest. The patient felt bloated during these episodes and thought that she obtained some relief from belching. Occasionally she become severely nauseated and vomited during one of these acute episodes. She had not experienced any previous episodes of jaundice or gastrointestinal bleeding. Initially a diagnosis of irritable bowel syndrome was entertained, and her physician prescribed antacids and a bland diet. This treatment produced no relief. A cholecystrogram demonstrated the presence of numerous gallstones in the gallbladder. A cholecystectomy was performed, and the gallstones were found to be composed predominantly of cholesterol.

What are the components of bile?

What is the function of bile in digestion?

What is the metabolic relationship between cholesterol and bile acids?

How is cholesterol kept in the soluble state in normal human bile?

What physical-chemical factors cause the formation of cholesterol gallstones?

Can gallstones be dissolved by feeding certain bile acids?

What other alternatives to surgery are presently available?

CASE STUDY 8

A 33-year-old female was admitted to the hospital because of proteinuria. Further examination revealed that she was anaemic and had diffuse, grayish corneal opacities. She also had hyperlipidaemia. Analysis of her plasma lipid levels revealed an elevated amount of cholesterol and almost no measurable cholesteryl esters; normally about 65% of cholesterol is in the form of cholesteryl esters. No lecithin-cholesterol acyltransferase activity was detected in the patients' plasma.

What are cholesteryl esters?

Where does the LCAT reaction occur, and what is the role of phospatidylcholine in this reaction?

How does the synthesis of cholesteryl esters in the tissues differ from the LCAT reaction?

Can severe liver disease produce LCAT deficiency?

Does the hydrolysis of cholesteryl esters occur through the reverse of the LCAT reaction?

CASE STUDY 9

A middle-aged man was referred to a dermatologist because of extensive yellowish papules, with erythematous bases, on his buttocks and elbows. The dermatologist recognised these as eruptive xanthomas 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 slightly turbid.

Investigations:

Serum cholesterol 8.5 mmol/l

Serum triglyceride 6.4 mmol/l

ApoE phenotyping indicated that the patient was homozygous for apoE2.

What do the results of the investigation indicate? Diagnosis?

LDL levels for this disorder are usually low. Why?

CASE STUDY 10

A 19-year old woman sought medical help because she was 30 kg overweight. Most of her excess weight was in the form of adipose tissue triacylglycerol. A dietary history revealed that her diet was extremely poor. Much of her caloric intake was carbohydrate – candy, cookies, cake, soft drinks and beer. Her dietary fat intake was actually quite moderate.

How is it possible to form excess triacylglycerol in the body if a diet contains predominantly carbohydrate?

How does acetyl CoA generated inside the mitochondria reach the cytoplasm for use by the fatty acid de novo biosynthetic pathway?

Why is bicarbonate required for fatty acid synthesis?

What is the rate-limiting enzyme in fatty acid synthesis?

How might carbohydrate ingested by this patient supply the reducing equivalents needed for fatty acid synthesis?

Devise a test that would indicate whether this patient could mobilise the triacylglycerol that is stored in her adipose tissue.