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Case Study #8: Chylomicron Craziness
BC362, Medical Biochemistry

Case Background:
Billy, a 19-month-old boy born to consanguineous parents, presented with **failure to thrive**, chronic **steatorrhea**, vomiting, and stomach protrusion. His symptoms began in early infancy and included persistent fatty diarrhea and inadequate weight gain despite sufficient caloric intake. Physical examination revealed abdominal swelling and growth parameters below the 10th percentile for age.

Lipid Profile (fasted)

	Patient (mg/dL)	**Desirable (mg/dL)**	**Borderline (mg/dL)**	**High Risk (mg/dL)**
Cholesterol	**87**	<200	200-239	240
Triglycerides	**144**	<150	150-199	200-499
HDL cholesterol	**23**	60	35-45	<35
LDL cholesterol	**31**	60-130	130-159	160-189

Discussion Question 1: Discuss with your group any notable findings in the case background and lipid panel.

Biochemistry:
In normal physiology, dietary fats and cholesterol are absorbed by **enterocytes** in the small and large intestines, packaged into chylomicrons, and secreted into the lymphatic system before entering the bloodstream. Chylomicrons deliver triglycerides and cholesterol to tissues, and their remnants are cleared by the liver, contributing to the body's cholesterol pool.

Chylomicron retention disease (CMRD) differs from normal cholesterol metabolism because enterocytes cannot secrete chylomicrons. **Biallelic mutations** in the SAR1B gene, which encodes a GTPase essential for the COPII coat complex in enterocytes, disrupt the transport of chylomicrons from the endoplasmic reticulum to the Golgi apparatus. As a result, chylomicrons accumulate within enterocytes and never reach circulation.

Apolipoproteins are protein "wrappers" that are a component of the outer shell of lipoprotein complexes along with phospholipids and free cholesterol. Apolipoprotein B48 is a specific marker of intestinal chylomicrons.

Key words:
Steatorrhea, Failure to thrive, Biallelic mutations, Enterocytes

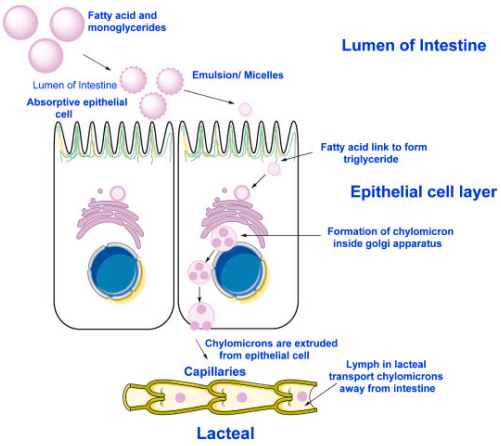

Figure 1. Chylomicron synthesis

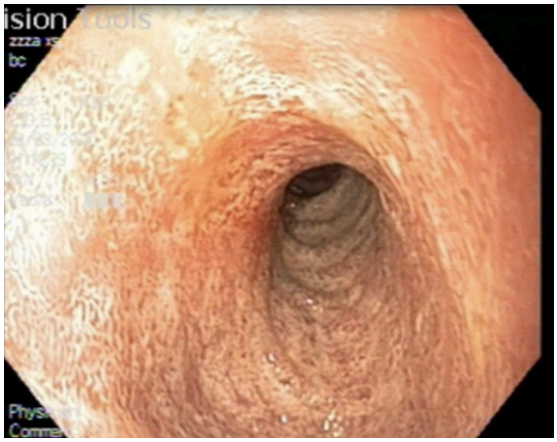

Figure 2. Upper endoscopy reveals a white duodenal mucosa in CMRD

Discussion Question 2: If a patient had a mutation to the SAR1B gene (chylomicrons are not secreted) what effects might be seen? Is this a primary or secondary disorder?

Disease Background:
Endoscopic evaluation of the small intestine revealed a white, frosted-appearing duodenal mucosa (Figure 2). This corresponds to the presence of lipid-laden enterocytes, a hallmark finding in CMRD.

CMRD leads to markedly reduced plasma cholesterol and apolipoprotein B-48 levels, normal-to-low triglycerides, an absence of intestinal chylomicrons, and presents as malabsorption of fat and cholesterol, hypocholesterolemia, and fat-soluble vitamin deficiencies.

Discussion Question 3: What types of tests could enable a physician to diagnose CMRD?

Discussion Question 4: What treatment options should be considered to manage this disorder?

References:

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OpenEvidence. https://www.openevidence.com/ask

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Key words:
Steatorrhea - Pale, bulky, foul-smelling stool as a result of excess fat

Failure to thrive - inadequate physical growth or inability to maintain growth in children

Biallelic mutations - mutations that occur in both copies of a gene (one inherited from each parent)

Enterocytes - epithelial cells that line the small and large intestines and are responsible to absorbing nutrients

Answer Key:

1. Low cholesterol, low LDL cholesterol, low HDL cholesterol, and normal to low triglycerides
2. Since chylomicrons are not secreted from the endoplasmic reticulum, they do not enter the bloodstream and tissues. Triglycerides therefore remain in enterocytes and are not biologically available for the body to use. This results in low cholesterol, LDL, and HDL.
3. Genetic testing for SAR1B gene, test blood concentration of apolipoprotein B-48 (since apoB48 is a marker for intestinal chylomicrons), and endoscopic evaluation similar to the case study.This is a primary disorder because there is a genetic mutation in a protein in fat metabolism.
4. The patient needs calories and vitamins to survive, but has difficulty processing fats. Therefore, a low-fat, calorie dense diet supplemented by vitamins and essential fatty acids should partially relieve symptoms. Despite this, the patient may have difficulty maintaining fat stores and adequate weight.

Notes:

- A COPII vesicle is a type of transport vesicle that moves newly made proteins and lipids from the endoplasmic reticulum (ER) to the Golgi apparatus, the first major step in the secretory pathway.