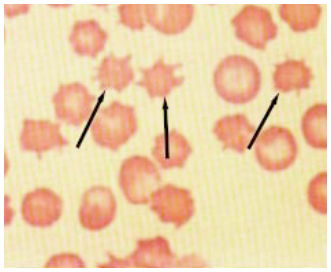
Model Case Study #2: Young Patient, "Old" Liver
BC362, Medical Biochemistry

Case Background:

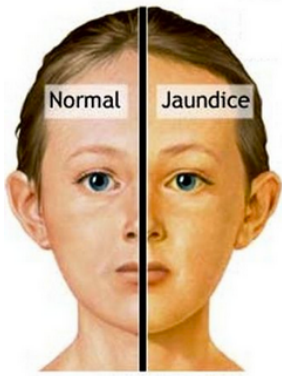
A 4-year-old Caucasian girl is admitted to your hospital for evaluation of anemia. She had first been admitted at 18 months of age for progressive jaundice, enlarged spleen, and failure to thrive, but symptomatic therapy kept her condition stable. Recently, she has developed increasing lethargy and anorexia (loss of appetite). You notice a distinct yellow color of her skin and eyes, and her spleen is palpable. Family history reveals that a maternal cousin had died of liver failure at the age of 3. You decide to run further tests.

Clinical Findings:



Significant findings in the CBC (complete blood count) panel include a very low red blood cell count and hemoglobin = 5.8 g/100 mL (normal is about 12). A blood smear reveals bizarre "spur" red cells with unusual thorny projections (see adjacent). A liver panel reveals elevation of certain molecular markers of liver damage.

Biochemistry:



jaundice

Jaundice is a term used to describe yellowing of the skin or whites of the eyes, arising from hyperbilirubinemia (too much of the pigment bilirubin in the blood). Bilirubin, the breakdown product of the molecule heme, is made in the liver during the body's destruction of aged red blood cells. (In the time it takes you to read this sentence aloud, roughly 20 million of your red blood cells have died, and roughly 5 x 10^{15} molecules of heme are in need of disposal.) Normally, the liver converts bilirubin to bile, which is delivered to the small intestine for excretion. Several factors can result in hyperbilirubinemia, including obstruction of the bile duct, liver disease, and excessive breakdown of red blood cells. Your goal is to determine the cause in your patient in the hopes of providing an effective treatment.

Vocabulary:

Anemia, jaundice, anorexia, CBC, hyperbilirubinemia, bilirubin

Analysis:

Q1. You ask the lab to check the lipid composition of the patient's red cells (Table 1). What is most striking about these data? What do the fluorescence polarization results reveal about the fluidity of the patient's red cells?

TABLE 1. Morphology and Composition of Fresh Red Cells from Normal Subjects and from Patient

	Normal Subjects		Patient	
Morphology	Normal		Spur cells	
Cholesterol ($\mu g/10^8$ cells)	14.0 + 0.5	(10)	22.3	(3)
Phospholipid ($\mu g/10^8$ cells)	31.0 + 1.0	(10)	33.0	(3)
Cholesterol/phospholipid (mole/mole)	0.92 + 0.03	(10)	1.35	(3)
Fluorescence polarization (P)	0.272 + 0.002	(10)	0.308	(3)

* Values are means ± SD; values in parentheses are number of subjects tested or number of determinations in patient.

Q2. Red cells need to deform to traverse small channels in the body without lysing. Because of the shape and rigidity of the patient's red cells, which arises from their unusual lipid composition, they are prematurely lysing. What symptoms does this information explain?

Q3. Reading the literature, you find that your patient's disorder is called spur cell anemia. Usually, this syndrome is found in adults with advanced alcoholic liver disease, which can result in defective synthesis of enzymes that control the cholesterol content of red cells. Your patient is clearly not an alcoholic. How can you explain this case?

References:

Balistreri, W. F.; Leslie, M. H.; Cooper, R. A. (1981) *Pediatrics 67*, 461- 466.
Privitera G.; Meli G. (2016) *Gastroenterol Hepatol Bed Bench*. *9*, 335-339.

Solutions:

1. The data show that the patient has elevated cholesterol content of her membranes. Fluorescence polarization data reveal a higher degree of gel-like character, or less fluidity, as would result from increased cholesterol disrupting the mobility of the fatty acid tails.

2. Premature red cell lysis (hemolysis) results in increased bilirubin, which is causing her jaundice. Fewer red cells leads to anemia and reduced oxygen delivery, which causes lethargy. Red cells are filtered in the spleen, so it becomes enlarged. Increased bilirubin processing is stressful on the liver, which is resulting in liver damage.

3. The family history suggests a genetic mutation leading to a defective enzyme…the enzyme must play a role in overseeing the correct cholesterol content in membranes.