

### Background

Zieve's syndrome is a complication of alcohol-induced liver injury that presents with the clinical triad of jaundice, hyperlipidemia, and hemolytic anemia. The syndrome is underreported in patients with alcohol use disorder with an estimated incidence of 1 in 1600 admissions. Symptomatic presentation may be vague with symptoms including abdominal pain, nausea, vomiting, malaise, weakness, and low-grade fever. Workup may reveal hyperbilirubinemia (secondary to hemolysis, cholestasis, and hepatocellular injury), hyperlipidemia (impaired lipid production secondary to advanced liver dysfunction), hemolytic anemia, and vitamin deficiency.

Though the syndrome is not fully understood, there are three proposed mechanisms for this hemolysis pattern: (1) hyperlipidemia and the presence of abnormal lipids such as lysolecithin disrupt the RBC membrane, (2) vitamin E deficiency secondary to alcohol use results in pyruvate kinase instability and disrupted RBC metabolism, and (3) vitamin E deficiency and hypophosphatemia lead to decreased ATP production in RBCs. Whether through abnormal membrane composition or dysfunctional intracellular metabolism, previous studies have demonstrated hemolysis of both native and transfused RBCs, meaning the trigger lies within the cell's environment (i.e., extrinsic hemolysis) rather than with an abnormally-produced RBC.

Interventions such as supportive care, blood transfusions, and alcohol cessation can fully reverse the syndrome in many cases. Without intervention, the syndrome may be complicated by myalgias, acute renal failure, and intracranial hemorrhage.

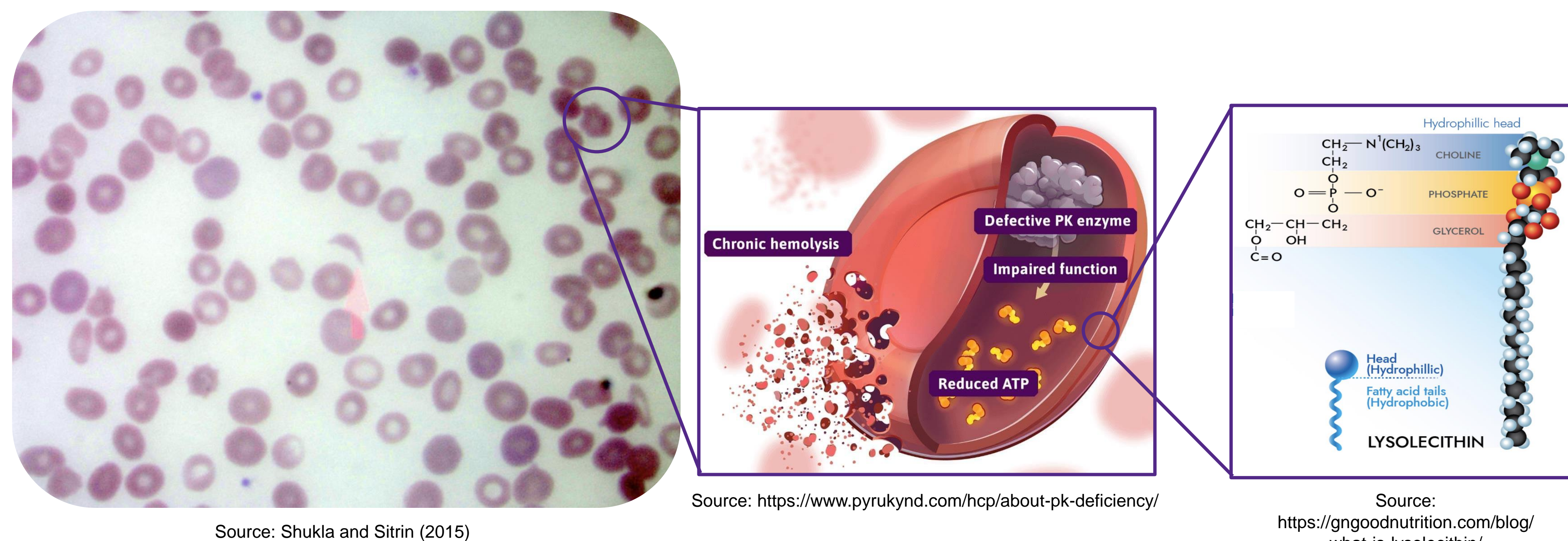


Figure 1: Peripheral Blood Smear and Proposed Hemolysis Mechanism

### Case Presentation: Subjective

A 50-year-old male presented to the ED with complaints of acute shortness of breath, hematemesis, hallucinations, and worsening fatigue

<b>Past Medical History</b> <ul style="list-style-type: none"> <li>Alcoholic cirrhosis complicated by grade I esophageal varices and recurrent ascites s/p TIPS procedure</li> <li>Chronic HCV</li> <li>Tobacco use</li> </ul>	<b>Surgical History</b> <ul style="list-style-type: none"> <li>Hernia repair</li> <li>EGD</li> <li>Colonoscopy</li> <li>Multiple paracenteses</li> <li>TIPS insertion</li> </ul>	<b>Family History</b> <ul style="list-style-type: none"> <li>No pertinent family history noted</li> </ul>	<b>Social History</b> <ul style="list-style-type: none"> <li>Tobacco: Smokes 2 cigarettes per day for 35 years</li> <li>Alcohol: Sober for over a year, but relapsed and drinks 1 – 1.5 pints of vodka daily</li> <li>Drugs: Denies substance abuse currently but has a history of amphetamine use.</li> </ul>	<b>Home Medications</b> <ul style="list-style-type: none"> <li>Folic acid 1 mg daily</li> <li>Spironolactone 50 mg daily</li> <li>Thiamine 100 mg daily</li> <li>Pantoprazole 40mg BID</li> <li>Lactulose 20g PRN</li> <li>Hydroxyzine 25mg nightly PRN</li> </ul>
--	--	---	--	--

### Case Presentation: Objective

#### Vital Signs

- T<sub>max</sub>**: 99.5° F
- Blood pressure**: 95/62
- Pulse**: 138
- Respiratory rate**: 20
- SpO<sub>2</sub>**: 98% on room air

#### Physical Exam

- General**: Patient drowsy but in no acute distress
- HEENT**: Scleral icterus
- Pulmonary**: Clear to auscultation bilaterally, normal work of breathing on room air
- Cardiology**: Tachycardic, regular rhythm. No murmurs.
- Abdominal**: Distended, shifting dullness, diffusely tender to palpation. No guarding or rebound tenderness. Normal bowel sounds.
- Skin**: Jaundiced. Scabs present on forehead and forearms.
- Extremities**: No edema
- Neurologic**: Alert and oriented x 3

### Workup and Findings

#### Trending Hemoglobin and Hematocrit

- Day 1: 9.6/26.5
- Day 2: 8.1/22.8
- Day 3: 7.1/19.7
- Day 4 AM: 6.1/16.8
- Day 4 PM: 7.7/21.4
- Day 5 AM: 8.1/22.8
- Day 5 PM: 8.2/23.2
- Day 6 AM: 7.9/22.1
- Day 6 PM: 7.5/21.3
- Day 7: 7.1/19.4

#### Hemolysis Workup

- Low haptoglobin and fibrinogen
- Elevated LDH and reticulocyte count
- Negative for immune-mediated hemolysis
- Peripheral Blood Smear: Severe normocytic anemia and thrombocytopenia with red cell fragments, suggestive of a microangiopathic hemolytic anemia; neutrophilic leukocytosis with no abnormal white blood cells

#### Investigating GI Blood Loss

- EGD: Mild portal gastropathy but no source of blood loss seen
- Colonoscopy: No significant findings

#### Vitamin Deficiency Workup

- Vitamin E (alpha and gamma) within normal limits
- Cobalamin within normal limits
- Folate within normal limits

#### Lipid Panel

- Cholesterol, triglycerides, and LDL within normal limits
- Low HDL

### Patient Outcome and Summary

Supportive care measures including blood transfusions and symptomatic management were provided, resulting in intermittent improvement. By discharge, the patient was transitioned to comfort care with hospice.

Though much of the clinical and laboratory findings hinted towards GI blood loss as the cause of this patient's anemia, it is important to consider Zieve's syndrome as a cause of hemolytic anemia in patients with alcohol use disorder. Due to low awareness about this syndrome in the medical community, it is not often considered as a differential diagnosis though the workup for this syndrome is easily incorporated into an anemia workup. Early consideration may lead to an earlier diagnosis and more efficient management. With more awareness of this syndrome and making the clinical diagnosis, there is likely to be improvement in the future management of this syndrome and the research surrounding pathophysiology and treatment.