# Where Did the Blood Go? Anchoring Bias on the Assurance of Haptoglobin.

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## INTRODUCTION

- G6PD deficiency is an X-linked inherited condition in which exposure to oxidative stress can cause both intravascular and extravascular hemolysis.
- Diagnosis relies on clinical context:
  - Patient demographics
  - Predisposing exposures
  - Supportive laboratory tests
- Accurate diagnosis can be confounded by multiple acute illnesses and conflicting data.

## BACKGROUND

**ID**

- A 31-year-old **African American** woman with history of IVDU presented to the Ob/Gyn service with PPROM and delivered a 22-week-old stillborn.

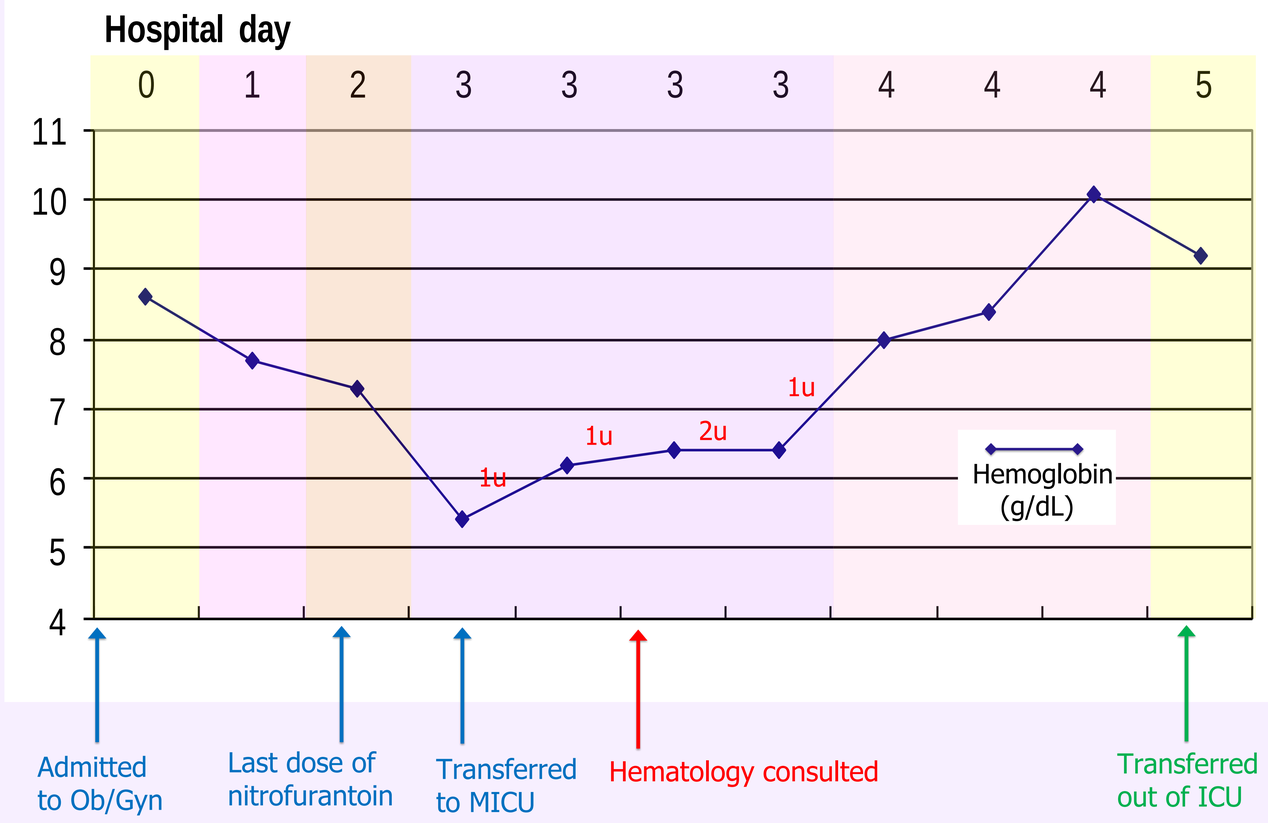
**Recent History**

- One day prior to admission, pt had been seen at OSH ED for back pain and began a course of **nitrofurantoin** for incidental finding of **MRSA UTI.**
- Quickly after admission, developed fever and hypoxemia requiring transfer to MICU.
- Found to have **MRSA bacteremia** and tricuspid valve **endocarditis** with pulmonary emboli.
- Started on broad-spectrum antibiotics, later narrowed to vancomycin.

## PRESENTATION

- Hospital course complicated by acute-on-chronic anemia, which worsened from Hgb of **8.6** g/dL on admission to **5.4** g/dL on hospital day 3.
- Anemia persisted, despite multiple transfusions and no clinically apparent source of bleeding.
- Hematology was consulted; initially concluded acute bleed was still the most likely cause despite lack of an obvious source. Reasoning against hemolysis was her normal haptoglobin.

## TREATMENT COURSE




## COURSE OF WORKUP

- Thorough skin exam, rectal exam, vaginal exam, and abdominal ultrasound
  -> all negative for bleeding
- Hemolysis labs on hospital day 3 showed:
  - LDH 347 (ref <250 U/L)
  - **Haptoglobin 126**
  - Bilirubin 4.5 total (3.1 direct); was 1.2 total on admission
  - Negative coombs tests
  - No schistocytes on smear
- Hematology felt that labs were not consistent with hemolysis; recommended CT abd/pelvis for further bleeding workup.
- CT abdomen/pelvis with contrast showed no peritoneal or retroperitoneal bleed.
- Peripheral smear was reviewed by hematology attending – found bite cells:

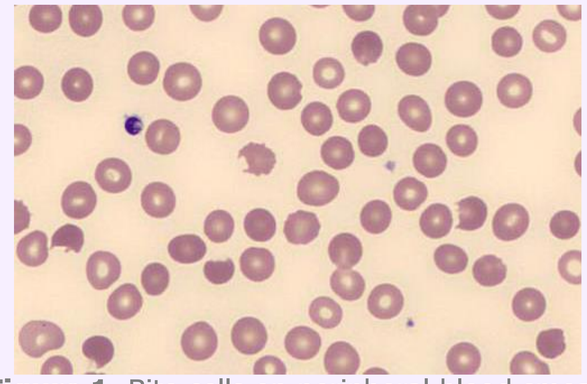


**Figure 1.** Bite cells on peripheral blood smear

- Repeat hemolysis labs on hospital day 4:
  - Haptoglobin <1
  - LDH rose from 347 → 625 → 712
  - Total bili rose to max of 9.3 (5.6 direct)
- Subsequent G6PD assay showed **reduced activity of 9.4** (ref: 9.9-16.6)
- A special stain showed **Heinz bodies**

## OVERVIEW: G6PD DEFICIENCY

- Glucose-6-phosphate dehydrogenase (G6PD) is the only source of NADPH (a reducing agent) in red blood cells.
- Low G6PD activity predisposes RBCs to oxidative damage from free radicals.
- Metabolic stress states (toxins, infection, **medications** [e.g. dapsone, **nitrofurantoin**], hypoxemia, shock) can lead to hemolysis in individuals with low G6PD activity.
- Hemolysis is **both intravascular** (RBC fragility) and **extravascular** (destruction by spleen) and tends to occur **1-4 days after** medication exposure.
  - Low serum **haptoglobin** is 83% sensitive and 96% specific for hemolysis[1]
- **Heinz bodies** and **bite cells** are classic features of oxidative RBC damage.
- G6PD enzyme level can be **deceptively normal** during acute hemolysis.

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- G6PD deficiency is the most common inborn error of metabolism.
  - X-linked recessive transmission
  - Most common in patients of **African** & **Mediterranean** descent
- Affects ~10% of African-American men[2]
  - Rare in women; unclear prevalence

## LEARNING POINTS

- Suspect hemolysis in patients with risk factors and otherwise unexplained anemia.
- Medication exposures are more easily overlooked after multiple transitions of care.
- No single lab test can definitively rule out hemolysis.[1]
  - Haptoglobin is an acute phase reactant; and the level was deceptively normal in this septic patient.

## REFERENCES

1. Marchand A, Galen RS, Van lente F. The predictive value of serum haptoglobin in hemolytic disease. JAMA. 1980;243(19):1909-11.

2. Heller P, Best WR, Nelson RB, Becktel J. Clinical implications of sickle-cell trait and glucose-6-phosphate dehydrogenase deficiency in hospitalized black male patients. N Engl J Med. 1979;300:1001–5.