Donath-Landsteiner antibody-associated hemolytic anemia after
*Haemophilus influenzae* infection in a child

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A 6-year-old male developed jaundice and pallor after an infection (fever and respiratory symptoms). He had not received childhood immunizations due to parental preference. Laboratory studies showed a Hb level of 5.8 g per dL, bilirubin 6.5 mg per dL (direct, 2.2 mg/dL), absent haptoglobin, and reticulocytes 3.7 percent. A throat culture grew *Haemophilus influenzae*; all other cultures were negative. Peripheral blood smear showed microspherocytes and polychromasia.

Immunohematologic evaluation showed negative antibody screen, and DAT positive for C3d and negative for IgG. Cold agglutinin titer was normal. A Donath-Landsteiner (DL) test was performed. In each set (A-C), tubes labeled “1” contain 10 mL of patient serum, tubes labeled “2” contain 5 mL of patient serum and 5 mL of fresh normal serum, and tubes labeled “3” contain 10 mL of fresh normal serum. Each tube also contains one volume of a 50-percent suspension of Group O RBCs. Tubes A1 through A3 were placed in an ice bath for 30 minutes, followed by a 1-hour incubation at 37°C. Tubes B1 through B3 were maintained in an ice bath for 90 minutes. Tubes C1 through C3 were maintained at 37°C for 90 minutes. Hemolysis occurred only in tubes A1 and A2. Given that the DL antibody most frequently shows specificity for the P antigen, testing against P-antigen-negative RBCs was performed and showed no hemolysis. These findings are consistent with a positive DL test, demonstrating the biphasic nature of the P antibody.
The patient was diagnosed with DL hemolytic anemia secondary to *H. influenzae*. He received a 5-day course of Zithromax, but did not receive RBC transfusions or steroids and was discharged, against medical advice, with a Hb level of 5.7 g per dL, 5 days after admission.

In the past, a positive DL test was characteristic of the chronic disorder known as paroxysmal cold hemoglobinuria, usually secondary to syphilis. Currently, most cases of DL antibody-associated hemolysis occur as acute transient episodes in children after or concurrent with a variety of viral infections, including measles, mumps, CMV, EBV, varicella, adenovirus type 2, influenza A, *Klebsiella*, *H. influenzae*, *Mycoplasma*, and *E. coli*. Given that these episodes are usually neither recurrent nor related to exposure to cold, the condition is now referred to as DL hemolytic anemia (DL-HA).

DL-HA is a rare condition with a reported incidence ranging from 1.6 percent to 5.1 percent in children with hemolytic anemia. It is usually self-limiting with rapid and complete recovery within a few days. When treatment is necessary, it focuses on rest and warmth; the use of steroids is controversial, and RBC transfusion is usually not required.

In summary, this is a case of DL-HA secondary to *H. influenzae* in an unvaccinated child. Receipt of the recommended childhood vaccination for *H. influenzae* most likely would have prevented this rare complication.