Title: Cold Agglutinins in Children Undergoing Repair of Congenital Heart Defects with Cardiopulmonary Bypass

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ABSTRACT BODY:
Introduction: Hypothermic cardiopulmonary bypass and cold cardioplegia solutions are regularly used during repair of congenital heart defects. The result is that the blood is exposed to a cooling process. Blood may contain auto antibodies which at cold temperatures cause an agglutination process to occur. The purpose of this abstract is to report the incidence of this problem at our institution and discuss possible solutions to dealing with the problem.

Methods: Children presenting for cardiac surgery with cardiopulmonary bypass were screened for the presence of cold agglutinins. Blood samples were drawn in EDTA and patient plasma was tested for agglutinins using 3 screening red cells (Panoscreen I, II, and III, Immucor, Norcross GA). Cold agglutinin screening was performed by mixing, 1 drop of each screening cell with 2 drops patient plasma. Samples were incubated for 30 minutes at both room temperature (RT) and 4 degrees C, centrifuged, and visualized for agglutination. When the cold agglutinin screen was positive, additional studies were performed by incubating samples at 4, 12, room temperature, 30, and 37 degrees for 1 hour. All agglutination reactions were graded from 0 (no agglutination) to 4 (strong agglutination) after centrifugation.

Results: During a six month period (April to September 2009) 56 children were screened for cold agglutinins of who 11 (19.6%) were found to have positive screens requiring further study. Of these, 2/11(18%) had 3-4+ reactivity at 4C. The remainder (9/11) had weaker (1-2+) reactivity at 4C. At 12 degrees 8 of 11 showed reactivity, but only 1 had stronger than a 2+ reaction. None of these samples reacted at room temperature or higher. No patients had antibodies with RBC specificity (e.g. anti-M, P1, etc.).

Discussion: Cold agglutinins react reversibly and can become clinically relevant when red cells are cooled below the thermal amplitude for agglutination. This can result in increased blood viscosity and red cell clumping, compromising organ perfusion. The etiology of cold agglutinins is often related to infections. Mycoplasma is well known to stimulate IgM autoagglutinins. The cold agglutinins develop early in the disease (7 -10 days), peak at 2-3 weeks, and can persist for 2 to 3 months. The only symptom the patient may have is a dry persistent cough. Our cold agglutinin screening strategy resulted in patients being postponed or the cardioplegia technique being modified. Prior to delivery of the cardioplegia to the patient, blood was added to the cardioplegia/heat exchanger and examined at 5-15 degrees for signs of agglutination. Two patients underwent acute normovolemic hemodilution after induction of anesthesia prior to bypass to lower the circulating agglutinins. Dilution on bypass also had an effect on decreasing the cold agglutination titer. Patients with cold agglutinins appeared to wake and become extubated slower. The literature contains regular reports of morbidity and mortality from this uncommon problem. We documented an incidence close to 20% in 2009. In 2004, Madershahianm, examined 2294 patients and documented an incidence of only 1.6%. They reported 1 death in an unscreened patient with cold agglutinins who developed intracoronary RBC clumping, myocardial ischemia, and hemolysis that underwent moderate (31 degree) hypothermia. In the rest of their 37 patients, strategies were used to minimize the effects of the cold agglutinin. Cold agglutinins are commonly detected pre-surgically in pediatric cardiac patients, and some of these react at temperatures used during bypass. The impact of these agglutinins is unclear, but may be relevant in certain patients. Strategies are needed to determine how to identify and manage patients at risk from cold agglutinins.