



# e-Network Forum

## CALIFORNIA BLOOD BANK SOCIETY

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### ***Should we worry about cold-reacting antibodies in patients undergoing hypothermia for cardiac surgery? (revisited, AGAIN)***

Once again the importance (or non-importance) of cold-reacting antibodies in patients undergoing total body chilling (hypothermia) is being raised. The following two inquiries are representative of the questions and confusion in the field. Evidence-based responses would be very much appreciated. Although this issue was discussed before (see e-Network Forum archives of [March, 1999](#)), a new discussion is appropriate, given newer testing schemes such as those employing Gel and solid phase methods.

**Query #1. A blood banker reports that in Quebec** some hospitals have a policy that a patient undergoing cardiac surgery who may have their body temperature lowered during surgery, are tested with an antibody screening method that includes testing for room temperature reactive antibodies. The Quebec blood banker wonders what the evidence-based data are to compel laboratories to employ a room temperature phase when screening such patients, and if such evidence exists, if references could be produced.

**Query #2. A blood banker reports that in Iowa** her hospital has policies and procedures for transfusion of patients with cold antibodies undergoing surgical procedures with hypothermia (especially CABG). She wonders if institutions are performing special testing to determine the range of the temperatures at which certain antibodies react (or no longer react), so that the surgeon will know to what temperature they can safely cool a patient. If special testing is done, do all patients with cold antibodies reacting at any strength have this additional testing completed, and if not, what criteria is used for additional testing. Also, with new technology such as gel and solid phase tests, how do cold reacting antibodies get detected, especially for patients who are undergoing hypothermia? The above questions are important to the inquiring blood banker, since a couple of cardiac surgeons at her hospital are under the impression that any cold agglutinin is of great concern when performing procedures on patients undergoing hypothermia. The blood bank's impression is that only strong cold agglutinins causing hemolytic anemia should be of concern in these situations. The hospital pathologist would like to know how other institutions handle reporting of cold reacting antibodies. At this time they attempt to determine the specificity of each antibody that reacts at any phase of testing, and they report findings, such as non-specific cold agglutinins etc., even though they consider these antibodies not to be clinically significant.

Do other institutions report such antibodies or only the clinically significant antibodies?

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The following responses have been received.

1. **A transfusion medicine physician in New York** (who is a credible academic physician) reports that his hospital laboratory **does NOT do screening for cold antibodies for patients undergoing hypothermia**. As far as he is aware, there is no evidence in the literature that antibodies that cannot be detected at 37 degrees C and/or the indirect antiglobulin phase can mediate problems at room temperature during hypothermic perfusion. All clinically significant cold agglutinins that his laboratory has seen or that he has read about are detectable by standard methods at body temperature OR the indirect antiglobulin test due to their wide thermal amplitude. If they do discover an antibody that is ONLY cold-reactive through the back typing or workup of a warm reactive antibody, AT THE EXPRESS REQUEST OF THE PERFUSION TEAM, the blood bank has BEEN NOTIFYING the perfusion team and that team has stated that they DO NOT use **severe** hypothermia or cold cardioplegia in such patients as a precaution. Likewise if there is any history of a cold reactive antibody. According to the New Yorker, one of the unappreciated aspects of these issues is that one is really interested only in spontaneous agglutination caused by cold-reactive antibodies, not those that react in serologic testing only. Antibodies that react at 25 degrees with 180g centrifugation, but do not cause spontaneous agglutination on mixing are unlikely, it seems to the responding physician, to do anything bad to a patient, unless that patient is also centrifuged (:-)]. The aforementioned scheme is PREDICATED ON WIDESPREAD AND LONGSTANDING ACCEPTANCE OF THE FACT THAT ALLO-ANTIBODIES THAT REACT ONLY AT ROOM TEMPERATURE OR BELOW WILL NOT MEDIATE SIGNIFICANT RED CELL REMOVAL OR LYSIS. The New Yorker stresses

that "PATIENTS WITH COLD AUTOIMMUNE HEMOLYTIC ANEMIA ARE TREATED AS A **SPECIAL CASE** AND COLD CARDIOPLEGIA AND HYPOTHERMIA ARE AVOIDED AS A MATTER OF COURSE".

**ADDENDA** Nov. 21, 2002

2. **A blood banker at Duke University** (in North Carolina; attribution used with permission) wrote that due to recent interest at the AABB and on the [CBBS web site](#) regarding the management of cold agglutinins in patients undergoing bypass, she contacted the chief perfusionist at Duke for information on the approach at that institution. She reports that for the last 23 years at that center, they **do not routinely perform pre-surgical screening for cold agglutinins in these patients**. Rather, these patients are successfully managed in the OR if agglutination is noted during the procedure. From the responding blood banker's understanding, this essentially involves switching to crystalloid cardioplegia. She provided the following articles that describe the general approach. Apparently, the article by Dake is the one that the Duke perfusionist references most often.

- [Dake et al.](#) Detection of cold hemagglutination in a blood cardioplegia unit before systemic cooling of a patient with unsuspected cold agglutinin disease. *Ann Thorac Surg* 1989;47:914-5.
- Fischer, et al. Increased pressures in the retrograde blood cardioplegia line an unusual presentation of cold agglutinins during cardiopulmonary bypass. *Anesthesia and Analgesia* 1997;84(2):454-6.
- [Izzat MB, Rajesh PB, Smith GH.](#) Use of retrograde cold crystalloid cardioplegia in a patient with unexpected cold agglutination. *Ann Thorac Surg* 1993 Dec;56(6):1395-7

**Other colleagues are encouraged to share their local experiences.**

**ADDENDA** Nov. 26, 2002

3. **A physician from the National Blood Service in London** (UK) agrees completely with the transfusion Medicine specialist from New York, and they do not undertake any special testing below 37C on patients undergoing hypothermia. If however, cold-reactive autoantibodies are present, the surgeons are cautioned about the level of hypothermia.

**ADDENDA** Dec. 15, 2002

4. **An esteemed colleague with 'three generations' of experience in blood banking** continues to be amazed at the truth of an old observation that everything gets redone in every generation - every 15 years. Quote "Having been around for three 15 year cycles I can swear to it. One of the delights of research before computers was that you went to the literature yourself. The answer to your discussion can be found in the title of an article entitled "Cold antibody and persistent intravascular hemolysis after surgery under hypothermia" by Wertlake PT, McGinniss MH and Schmidt PJ. *Transfusion* 1969;9:70-73."

According to Dr. Schmidt, this was a patient they had at the NIH Clinical Center in 1964, which was more than two cycles ago. But read more than the title, read (and print) the article the way we used to do, for reasons of serendipity (each link is a page of the article).

- [Transfusion MarApr 1969, page 70.pdf](#)
- [Transfusion MarApr 1969, page 71.pdf](#)
- [Transfusion MarApr 1969, page 72.pdf](#)
- [Transfusion MarApr 1969, page 73.pdf](#)

**ADDENDA** May 22, 2003

5. **A colleague in Denver would like to resurrect the discussion** about whether to supply antigen-negative blood to patients undergoing cardiac surgery procedures with hypothermia. Her pediatric institution has had a policy to supply antigen-negative blood to children demonstrating antibodies against P1 and M antigens because they felt it was a conservative, prudent and relatively simple thing to do for such patients as 6 month-old babies undergoing heart transplant. These antibodies occur quite infrequently. They have begun to disagree among themselves, but they do not feel it appropriate to change their current policy without the involvement of the Cardiothoracic Surgery Service. She would like to know how other colleagues deal with such situations **in children** and on what basis they support their decisions to regard or disregard these antibodies.

**ADDENDA** June 2, 2003

6. **Dr. Larry Petz** (attribution used with permission) has provided the following input to this discussion for consideration by the e-network. (Reprinted as a [PDF file](#) from "Immune Hemolytic Anemias", 2nd edition, 2003. Petz LD, Garratty G. In Press, with permission from Elsevier.)

**ADDENDA** Sept. 22, 2003

7. **The blood banker in Iowa (Query #2 above) asks again for further feedback from the e-Network Forum.** They have had an ongoing problem with their cardiac surgeons. Recently the

**cardiac surgeons became furious when they were doing cold cardioplegia and the blood became "sludgy"**. They had not been notified that the patient had a cold antibody and were under the impression that every patient was screened by the laboratory for cold agglutinins. Upon discovering that this screening was not being done, the **cardiac surgeons were adamant that the screening be done** and that cold agglutinin titers and thermal amplitude testing be done on any patient with a positive screen at 4C.

The blood bank technical experts tried to explain that many normal people have low-titered cold agglutinins reactive at 4C that have no clinical significance. The cardiac surgeons were given literature including the results of a CBBS e-Network Forum discussion. Since they were not dissuaded it was agreed that the laboratory would perform the requested cold agglutinin screening and followup testing, **if** the testing was specifically ordered prior to admission. Of note, **most of the surgical patients are admitted the same day as surgery and orders for blood are processed that same morning**. Thus, from an operational standpoint, the workup of discovered cold agglutinins at the time of a 'same day surgery' would be nearly impossible for the technologists, who were already not happy with this increased work for something that the laboratory leadership considered clinically insignificant. After a few weeks of experience with the above protocol, during which **over 60 percent of the patients screened were positive for a cold agglutinins**, the cardiac surgeons have dropped their requests for routine cold agglutinin testing of their patients.

**ADDENDA** Sept. 30, 2004

8. **A transfusion medicine physician in Australia** reports that she is interested to learn of what preoperative testing, if any, is currently done to detect cold agglutinins prior to cardiac surgery. She is aware of a variety of methods used for cardiothoracic patients, from 'off pump' to whole body cooling and injection of ice cold cardioplegia. Surgeons at her hospital want to know if a patient has cold reacting antibodies that can agglutinate red cells during a heart surgery case, **since the presence of such antibodies would alter their approach to surgery**. She acknowledges that a number of laboratories in her city have ceased to perform preop cold antibody testing and have not reported any clinical problems. In her unit they currently perform testing at room temperature, 4C and 15C degrees if requested (mostly for major procedures ). She would be interested to hear what practices and protocols others follow, including testing performed, rate of cold antibody detection (if testing is performed) and what the clinical experience has been.

**ADDENDA** May 26, 2005

9. **The Medical Director of a blood bank at a hospital in Orlando, Florida** reports that his laboratory does **NOT routinely screen** cardiovascular surgery patients for cold autoantibodies/agglutinins. However, a cardiovascular surgeon has **begun ordering screens for cold agglutinins** on his patients. The Florida blood banker's understanding of the literature is that **cold agglutinin titers are not helpful in predicting risk of intra-operative agglutination/hemolysis** in patient's undergoing cardiac surgery with hypothermia. He has communicated this to the cardiovascular surgeon, but the surgeon is intent on ordering cold agglutinin screens. The Florida blood banker wonders **if there is new information** to compel the routine screening for cold agglutinins in the setting of cardiac surgery.
10. **The education coordinator of a transfusion service in Wisconsin** wonders what are other hospitals' **policies regarding providing antigen negative blood or performing thermal amplitude testing** on cardiac bypass patients with cold agglutinins.

Please submit comments to the [e-Network Forum](#).



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**Addenda:** Nov. 21 & 26, Dec. 15, 2002; May 22, June 2 & Sept. 22, 2003; Sept. 30, 2004; May 26, 2005

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