



# OHIO ASSOCIATION OF BLOOD BANKS



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## *From The OABB President*

Dear OABB members,

I am pleased to take this opportunity to update you on the Association's activities.

On September 23<sup>rd</sup>, the 2008 Fall Workshop was held at the Fawcett Center in Columbus. There were 91 attendees who gave the speakers and topics very good evaluations. Thank you to the Chair, Sandi Gerhan, and the Education Committee for their hard work in making this workshop a success! OABB did not have a Fall Workshop the previous two years, so it is wonderful this popular event returned.

The OABB Board began planning the 2009 Annual Meeting. It will be in Columbus on April 30 at the Concourse Hotel near the Columbus airport. The topics and speakers are being finalized, blood bank vendors have committed to come, and great prizes are planned for a drawing at the business meeting. You'll hear more about the 2009 Annual Meeting in the February issue of the Newsletter. Mark your calendars now for this event!

Proficiency samples are mailed four times a year to OABB institutional

members. The 2009 schedule will be January, April, July, and October. Suzie Davisson, who is the Proficiency Coordinator, oversees sending out these samples and providing results to the members. For faster turn-around-time of the intended results, the results are emailed to participants if an email address is provided. Results are also in the OABB Newsletter and on the OABB website, [www.OABB4U.org](http://www.OABB4U.org).

The OABB Newsletter provides a continuing education (CE) opportunity in each issue. Each is worth 0.5 contact hours (CH). You can complete the CE, hand it in to your supervisor, and compare your responses to the answers provided in the next Newsletter. It is an inexpensive and fun way to earn CE credits!

The Board is also pleased that the OABB website is back without the previous difficulties. You can renew your membership on line, read current and past newsletters, and find results of proficiency samples. So take some time and visit [www.OABB4U.org](http://www.OABB4U.org)!

Mary Schumacher  
OABB President

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## Should We Use This Blood?

Recently, there have been discussions about using blood collected by therapeutic phlebotomy from patients with hereditary hemochromatosis (HH). Hereditary hemochromatosis is a disease where excessive iron accumulates in the body due to a genetic iron absorption abnormality and requires regular frequent phlebotomy.

Iron gets into the body by two transport pathways, infusion (blood transfusion) and absorption (food and dietary supplements in the gastrointestinal tract). Normally, the body absorbs iron from the small intestine, and the surplus iron is either excreted in the urine or sloughed in epithelial cells. However, when iron coming into the body exceeds daily capacity of excretion, iron accumulates in the body organs such as the liver, pancreas, heart, and skin. Accumulation of iron in the liver can induce cirrhosis, and in the pancreas can provoke diabetes mellitus.

HH patients absorb an excessive amount of iron and cannot fully excrete the surplus. The extra iron accumulates in the body in the form of storage iron, ferritin. The major organ of iron accumulation is the liver, and liver biopsy is commonly used as a confirmatory test for hemochromatosis.

HH is surprisingly high in prevalence, 0.24-0.5% in Caucasians, which is approximately 1 in 300 people. However, this disease is not easily detected at an early stage since there are no specific symptoms. When HH is detected early, patients are properly treated and live a normal life expectancy.

Therapeutic phlebotomy is the best treatment for HH. When blood is removed from the circulation, it stimulates the bone marrow to make more red blood cells. As a result, more iron is needed for red blood cell production, and iron comes out of storage for incorporation into hemoglobin. With regular therapeutic phlebotomy, the amount of iron in the body can decrease below a toxic level. This is the reason why early detection is very important. However, even physicians are not well acquainted with the fact that HH is a highly prevalent disease entity. Therefore, it is recommended to screen iron levels in asymptomatic adults if they have predisposing factors such as family history.

The level of iron in the body can be measured through various tests. Among them, transferrin saturation is the most commonly used screening test. It measures the saturation status of the iron binding protein, transferrin. When saturation is over 40%, more screening or a confirmatory test is recommended. The ferritin level is an additional screening test. Liver biopsy or quantitative phlebotomy is used as a confirmatory test. Genetic tests looking for the abnormal hemochromatosis gene are also performed. The hemochromatosis gene, called HFE gene, regulates the absorption of iron by modulating the interaction between transferrin and its receptors. In HH patients, HFE gene is mutated. The most common mutation is C282Y.

HH patients need regular therapeutic phlebotomy, and their blood is regularly collected. Can we use this blood? Think about the nature of HH. It is the disease of iron metabolism, not the disease of blood. However, many people have a misunderstanding of this concept which leads to misunderstanding in dealing with this special, unspecial blood.

Countries using blood from HH patients for transfusion reported no difference between blood from HH patients and normal healthy donors. There is no evidence genetic defects are transferred through blood transfusion.

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In the US, the Food and Drug Agency (FDA) requires labeling blood from HH patients, if it is used for transfusion, with their disease. This labeling was a barrier to general use of HH blood since physicians were reluctant to use labeled "diseased" blood. In 1999, FDA approved variances to remove labeling as long as the following are met:

- ◆ All HH donors meet the same suitability requirements as other donors.
- ◆ HH donors are educated that there is no cost for therapeutic phlebotomy.
- ◆ HH donors are informed therapeutic phlebotomy is free of charge even if they are ineligible by allogeneic donor criteria.
- ◆ HH donors need a physician's prescription or a physician's examination at the donor center to certify they are in good health on the day of donation if they donate more than once in 8 weeks.

Blood donation without labeling with HH must be preapproved by FDA and variance request procedures followed. The guidelines to variance requests are well explained in the FDA publication (<http://www.fda.gov/cber/gdlns/hemchrom.pdf>).

Let's go back to the original question. Should we use this blood? Based upon the facts described above, it is reasonable to think blood from HH patients is safe for transfusion. It would expand the donor pool and better supply the public's constant need.

A list of establishments granted approval for a variance to 21CFR640.3(d) and 21CFR640.3(f) in order to collect blood and blood products from patients with hemochromatosis can be found at <http://www.fda.gov/cber/blood/hemochromvar.htm>.

You can learn more about hemochromatosis from the site [www.irondisorders.org](http://www.irondisorders.org).

Submitted by Byeong Keun Ha, M.D., Ph.D.  
Transfusion Medicine Fellow  
The Ohio State University

References:

[Phatak PD](#), [Sham RL](#), [Raubertas RF](#), [Dunnigan K](#), [O'Leary MT](#), [Braggins C](#), [Cappuccio JD](#). Prevalence of hereditary hemochromatosis in 16031 primary care patients. [Ann Intern Med](#). 1998 Dec 1;129(11):954-61

[Fields AC](#), [Grindon AJ](#). Hemochromatosis, iron, and blood donation: a short review. [Immunohematology](#). 1999;15(3):108-12

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[Allen KJ](#), [Nisselle AE](#), [Collins VR](#), [Williamson R](#), [Delatycki MB](#) Asymptomatic individuals at genetic risk of haemochromatosis take appropriate steps to prevent disease related to iron overload. [Liver Int](#). 2008 Mar;28(3):363-9

## OABB Continuing Education Activity

After reading this Continuing Education article, the participant shall be able to:

- ◆ State the purpose of antibody detection methods
- ◆ Define the prevalence of a low-incidence antigen
- ◆ State how an antibody to a low-incidence antibody is detected
- ◆ Name at least three low-incidence antigens
- ◆ Select methods to provide blood for patients with antibodies to low-incidence antigens.

### **Antibody Detection**

Prior to the mid-1980s, the antibody detection test (antibody screen) and antiglobulin (AHG) crossmatch were required as a screening method for potential patient-donor incompatibility. Since then, transfusion services rely on antibody detection tests to detect non-ABO clinically-significant antibodies in a patient sample and abbreviate the crossmatch to an immediate spin (IS) phase, or use an electronic crossmatch, to detect ABO incompatibilities. This practice, some would argue, may miss clinically-significant alloantibodies that could cause a transfusion reaction. The missed antibodies are directed against low-incidence (or low-prevalence) antigens. Standard antibody screens do not detect these antibodies because commercially available antibody detection cells in the USA usually do not possess low-incidence antigens, such as C<sup>w</sup>, Kp<sup>a</sup>, Js<sup>a</sup>, V, or Lu<sup>a</sup>.

### **Defining low-incidence antigens**

Low-incidence antigens are defined as antigens present in less than 1% of the population, making antigen-negative donor units easy to find when needed. However, antigen frequencies can vary by ethnic or geographical populations. For example, V and Js<sup>a</sup> are considered low-incidence antigens in the general population, usually characterized by Caucasian donors, but in African American donors the frequency is much higher.

Although antibodies to low-incidence antigens can be clinically significant, many are IgM and/or do not react at 37 C, and the clinical significance is

questionable<sup>1</sup>. In his 2003 Transfusion editorial, Garratty<sup>1</sup> referenced a study in which Shulman investigated the frequency of hemolytic transfusion reactions (HTR) when pretransfusion compatibility was determined by a negative antibody screen and an IS crossmatch. The HTR risk due to antibodies to low-incidence antigens was 1 in 650,000 crossmatches. Other studies also produced similar frequencies.

### **Detecting antibodies to low-incidence antigens**

Since the AHG crossmatch is used much more infrequently when the antibody screen is negative, how are antibodies to low-incidence antigens detected? An unexpected reaction during the problem-solving process may suggest an antibody to a low-incidence antigen. For example, there might be a single unexplained reactive panel cell during antibody identification. The technologist should evaluate if there is a low-incidence antigen on the cell to explain the reaction. Similarly, a positive AHG crossmatch with antigen-negative donor cells in a patient with other antibodies may suggest an antibody to a low-incidence antigen. Of course, if a patient develops a positive direct antiglobulin test (DAT) post transfusion, and the eluate is non-reactive and there is no other explanation, the investigation may include evaluating the presence of an antibody to a low-incidence antigen.

Lastly, an antibody to a low-incidence antigen could be possible when detecting a positive DAT in a newborn sample. If the evaluation rules out ABO antibodies, and the maternal sample has a negative antibody screen, testing the eluate with paternal cells is a good way to determine if the mother's antibody is due to a low-incidence antigen stimulated by a previous pregnancy.

Identifying antibodies to low-incidence antigens can be challenging to the standard hospital laboratory. If the reactive cell is known to possess a low incidence antigen (according to the panel antigen profile), test at least one or two additional antigen-positive cells with the serum. Positive reactions with the additional cells provides the standard statistical probability of identification (2+2 or 3+3 rule)<sup>2</sup>. One caution when selecting additional cells from expired panels, be sure they are from different donors: The donor reference number of the cells must be different.

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If the antigen profile of the unexpected single reactive cell is unknown, i.e. a donor cell or a panel without any low-incidence antigen notations, other approaches must be used. If the reaction is with a panel cell, contact the panel manufacturer. Not all antigen specificities are listed on the panel profile worksheet. If the reaction was observed against a donor cell, the serum can be tested against reagent cells with low incidence antigens (a "low" panel), hoping one of the cells is reactive. Alternatively, the initially reactive donor cell can be tested with known antibodies to low-incidence antigens, if available, to attempt identifying the low incidence antigen present on the cell. Then the identification with known cells may be easier to determine. The technologist must be aware, though, that sera with antibodies to low-incidence antigens often contain multiple specificities.<sup>2</sup>

### **Selecting Units For Transfusion**

Once the antibody is identified and reactivity appears it is clinically-significant, antigen-negative blood should be provided if available. The lack of commercially available antisera presents a difficult situation for most laboratories. If reagent is available, only a few units need testing, since more than 99% will be negative. More units need testing when the antigen frequency is higher in certain ethnic groups. For example, if searching for V- or Js(a-) cells, more units are needed when searching in the African-American population.

If no reagent is available and the antibody is reacting, the best alternative is to use the patient serum to provide AHG crossmatch-compatible units. It is also strongly suggested to collect all serum/plasma from the patient (check in Chemistry), and freeze it in small aliquots for future testing. Patient's antibodies can diminish in reactivity. If the antibody is no longer demonstrating, using the serum to detect antigen-positive units is not possible. When using the stored serum/plasma, testing positive and negative controls is important to ensure the antibody survived the storage process.

After all this, there is still a question about whether it is even necessary to rule out and/or identify antibodies to low-incidence antigens. It is

an accepted practice to "not rule out" antibodies to low-incidence antigens during routine antibody identification unless there is a clear reason to suspect one. Judd<sup>3</sup> clearly states, when speaking of low-incidence antigens, that it is not necessary to "run additional cells positive for these antigens" if they are the only antibodies not ruled out. If, however, there is a suspicion of an antibody to a low-incidence antigen, the facility must have a policy regarding the lengths to which identification will be pursued. The AABB Technical Manual states, and every blood banker would agree, "transfusion should not be delayed while identification studies are performed"<sup>2</sup>.

Facilities must have established policies to provide units of Red Blood Cells to patients with antibodies to low-incidence antigens. The facility must, in conjunction with their blood provider, determine if and when labeled antigen-negative products will be provided. If no licensed reagent or stored serum is available, and the patient antibody is no longer demonstrating, the blood provider may be able (and willing) to provide historically antigen-negative red cells. Sometimes, however, that is not even a possibility, in which case crossmatch-compatible random products must be provided.

Prepared by: Sandra Gehran, M.Ed, MT(ASCP)SBB

### References:

1. Garratty G. How concerned should we be about missing antibodies to low incidence antigens? *Transfusion* 2003;43:844-847
2. Roback JD, Combs MR, Grossman BJ et al, eds. Technical manual, 16<sup>th</sup> ed. Bethesda, Maryland: AABB. 2008.
3. Judd WJ, Johnson ST, Storry JR. Judd's methods in immunohematology. Bethesda, MD: AABB. 2008.

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Answers for this CE will be posted in December to the OABB web site and appear in the next issue of the OABB newsletter.

### Questions

1. Performing the immediate-spin crossmatch allows detection of:
  - a. ABO antibodies
  - b. Clinically-significant antibodies to common antigens
  - c. Antibodies to low-incidence antigens not found on screening cells
  - d. Eliminate less sensitive AHG methods
2. The prevalence of a low-incidence antigen is defined as equal to or less than:
  - a. 1%
  - b. 3%
  - c. 5%
  - d. 7%
3. Detection of an antibody to a low-incidence antigen is most likely found when
  - a. the donor cells have a positive DAT
  - b. anti-A is eluted from cord cells
  - c. antigen-negative units selected for the patient are incompatible
  - d. the antibody screen is positive
4. The following are low-incidence antigens
  - a. C<sup>w</sup>, Kp<sup>b</sup>, Lu<sup>a</sup>
  - b. C<sup>w</sup>, Kp<sup>a</sup>, Lu<sup>b</sup>
  - c. C<sup>w</sup>, Kp<sup>a</sup>, Lu<sup>a</sup>,
  - d. V, Js<sup>a</sup>, Lu<sup>b</sup>
5. Selection of appropriate units for transfusion when a patient has an antibody to a low-incidence antigen is to:
  - a. request units from the blood supplier
  - b. use the patient's reactive sample to screen units
  - c. purchase the antisera from a vendor
  - d. request the physician to sign for incompatible units

### *Answers to August CE Activity: Neonatal Exchange Transfusion (0.5 CH)*

1. The percentage of infant mortality due to exchange transfusion is
  - a. **1%**
  - b. 5%
  - c. 7%
  - d. 10%
2. A one volume exchange would be:
  - a. 50-60 mL/kg
  - b. 60-70 mL/kg
  - c. 70-80 mL/kg
  - d. **80-90 mL/kg**
3. FFP rather than 24 hour plasma is used for exchange transfusion because
  - a. it is more readily available
  - b. it has a longer shelf life
  - c. **the newborn has an immature liver**
  - d. it has a higher concentration of proteins
4. Fresh blood for exchange transfusion is considered as units less than \_\_\_ days old.
  - a. 3
  - b. 5
  - c. **7**
  - d. 10
5. A unit of CPD blood weighs 300 gm. You need to prepare a RWB with a hematocrit of 55%. How much plasma must you add to the unit of RBCs?
  - a. 40 mL
  - b. 60 mL
  - c. **80 mL**
  - d. 100 mL

### **OABB Newsletter** **Submissions**

Letters, articles, and announcements of upcoming events may be submitted at any time.

Classified advertisements will be accepted from any member institution and printed at no charge.

**Teleconferences Sponsored By  
American Red Cross Central Ohio Region**

Date	Teleconference Title
Nov 19 2:00 – 3:30 PM	Platelet Refractoriness: Causes and Treatments  Contact numbers of Sponsors: Central Ohio Blood Services: 614-253-2740, ext. 2215 Northern Ohio Blood Services: 216-431-3118 Community Blood Center/Community Tissue Services™: 937-461-3580
Dec 10 2:00 – 3:30 PM	Differential Diagnosis of Suspected Pulmonary Transfusion Reactions  Contact numbers of Sponsors: Central Ohio Blood Services: 614-253-2740, ext. 2215 Community Blood Center/Community Tissue Services™: 937-461-3580

**Education Opportunities**

Masters level lectures in Blood Transfusion Medicine and Cellular Therapy are ongoing at Hoxworth Blood Center and open to anyone who wants to attend. Please contact Pam English at [pamela.english@uc.edu](mailto:pamela.english@uc.edu) for more information.

**Attention AABB Assessors!**

Assessors with even membership numbers are required to submit CE reports by November 30, 2008.

Assessors with odd membership numbers are required to submit CE reports by March 30, 2009.

If you are on a team for AABB-CAP coordinated assessments, you are required to perform the on-line self-study every 2 years by going to [www.cap.org](http://www.cap.org) > Education Programs > LAP Education Activities.

**News from the Proficiency Coordinator:**

Results of the October proficiency will appear in the February Newsletter. The results will be emailed to those who provided an email address. You may also find the results on the OABB website: [www.OABB4U.org](http://www.OABB4U.org). Next year's samples will be shipped January, April, July, and October.

Suzanne M. Davisson, BS SBB(ASCP)<sup>CM</sup>