EDUCATIONAL COMMENTARY – TESTING BLOOD DONORS FOR COMMUNICABLE DISEASES

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Learning Outcomes
Upon completion of this exercise, the participant will be able to:

- List the communicable diseases and define the regulatory authority under which allogeneic blood donations must be tested.
- List the communicable diseases and define the regulatory authority under which autologous blood donations must be tested.
- Define the risk versus benefit of storing and transfusing autologous blood that is known to be reactive/confirmed positive for a communicable disease test.
- Define the risk versus benefit of storing and transfusing autologous blood that is untested for evidence of communicable diseases.

The AABB estimates that approximately 8,000,000 individuals volunteer to donate blood each year. According to the National Blood Data Resource Center (NBDRC)\(^1\) about 15 million units of allogeneic whole blood and red blood cells were donated in the United States in 2001.\(^2\) The minority of transfused blood products are “autologous” units, which are collected from individuals (patients) for their own use, usually in advance of a scheduled surgery, or during the peri-operative period using various blood conservation techniques.\(^3,4,5\)

After an allogeneic blood donation has been collected, it is tested for ABO group and Rh type, as well as for any unexpected red blood cell antibodies that may cause problems in a recipient. Screening tests also are performed for evidence of donor infection with hepatitis B and C viruses, human immunodeficiency viruses HIV-1 and HIV-2, human T-lymphotropic viruses HTLV-I and HTLV-II, and syphilis. The FDA has licensed nucleic acid amplification tests (NAT) to detect HIV-1 and HCV and has recently licensed one of two investigational NAT assays to screen blood for West Nile virus (WNV) genetic material.

The specific tests currently performed include:

- Hepatitis B surface antigen (HBsAg)
- Hepatitis B core antibody (anti-HBc)
- Hepatitis C virus antibody (anti-HCV)
- HIV-1 and HIV-2 antibody (anti-HIV-1 and anti-HIV-2)
- HTLV-I and HTLV-II antibody (anti-HTLV-I and anti-HTLV-II)
- Serologic test for syphilis
- Nucleic acid amplification testing (NAT) for HIV-1 and HCV
- NAT for West Nile virus
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Depending on local practice, blood donations (such as those used for low birth weight babies or CMV sero-negative recipients of bone marrow, stem cells, or solid organs) are tested for antibodies to CMV. Plateletpheresis donations are routinely tested for evidence of bacterial contamination, usually by culture. Some centers test donated platelets for evidence of bacterial contamination either by culture or by looking for a drop in the pH or glucose level of the product.

Allogeneic blood products are not used for transfusion if the product is reactive for evidence of hepatitis B, hepatitis C, HIV-1, HIV-2, HTLV-I, HTLV-II, syphilis, West Nile Virus, or bacterial contamination. Such a policy has helped to reduce the risk of transfusion-transmitted HIV-1 or HCV to about 1 in 2,000,000 and transfusion-transmitted HBV to about 1 in 200,000.6

Regulatory Authority for the Testing of Allogeneic Blood Donations

The Code of Federal Regulations, Title 21 CFR 610.40 (et seq), requires testing schemes to reduce adequately and appropriately the risk of transmission of communicable disease through blood products. Title 21 CFR 610.40(a)7 requires each donation of human blood or blood component to be tested for HIV 1 and 2, Hepatitis B virus, Hepatitis C virus, HTLV I, and HTLV II. Title 21 CFR 610.40(i)8 requires each donation of human blood or blood component also to be tested for syphilis. Title 21 CFR 610.40(b)9 requires that the testing methods used employ one or more FDA-approved screening tests. Title 21 CFR 610.40(e)10 requires that each donation of human blood or blood component that has a reactive screening test be tested further by a supplemental (additional, more specific) test, if one is available and approved by the FDA. The FDA has published guidance documents describing how blood establishments can comply with the federal regulations.11 For example, the HIV-1 NAT and HCV NAT guidance explains that FDA considers the licensed tests as necessary to adequately and appropriately reduce the risk of transmitting HIV-1 and HCV for donations that are not reactive on a donor-screening test for the detection of antibodies to HIV or HCV, respectively.12

Although most (if not all) donor collection centers are testing for evidence of infection with West Nile virus (WNV), there is no FDA required test yet. However, at the time of this writing there is one licensed test. Once there is a licensed test on the market, unlicensed tests should not be used. The FDA policy on WNV is currently described in a guidance document.13 However, the FDA recommends donor screening for the presence of WNV nucleic acid.

NAT for HBV is currently under consideration.14 15 However, in a pooled sample format the test sensitivity is not significantly different than newer ultra-sensitive versions of HBsAg tests. Furthermore, it might be more cost-effective to sponsor HBV vaccination programs to prevent disease rather than test blood donations with HBV NAT to try and detect those with the infection.16 17
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(cont.)

Testing for anti-HBc and/or for evidence of syphilis is controversial. Many consider a positive result for anti-HBc and/or syphilis serology to be a surrogate marker of life style behaviors that make blood donation undesirable, while others argue that anti-HBc is a specific marker of HBV infection. It is arguable whether or not syphilis is transmitted by transfusion of stored blood products.

There is no regulatory requirement at present to test donated blood products for antibodies to CMV. There is also no regulatory requirement that requires platelets be tested for evidence of bacterial contamination, although both the AABB and CAP have made such testing a condition of accreditation.

Regulatory Authority for the Testing of Autologous Blood Donations

Federal regulations require all blood donations to be tested for communicable diseases; however, testing of autologous donors is exempted in certain situations. Title 21 CFR 610.40(d) requires autologous units to be tested for communicable diseases, including supplemental testing, unless the unit is only to be used within the facility that collected it, and the facility does not “cross-over” the autologous units for allogeneic transfusion. Furthermore, if an autologous unit is reactive in a communicable disease-screening test, the product may still be transfused (unlike an allogeneic blood product). The AABB Standards require that if an autologous unit is to be shipped to another facility and the unit tests positive for any marker of transfusion-transmitted disease, the shipping facility shall notify the receiving transfusion service.

Additional Information on the Use of Autologous Units

The majority of transfusion services store and transfuse autologous units that are confirmed positive for HIV, HBV, or HCV. Furthermore, transfusion services that collect but do not test autologous units for communicable diseases may unknowingly store and transfuse autologous units from infected donors. As the Table below shows, at least 1% of autologous blood donors whose blood is collected by the American Red Cross are infected with HIV-1, HBV, or HCV, with HCV being the most common infection.

Table: Prevalence of Donors Confirmed Positive for Transfusion-Transmitted Disease (per 10,000 donors)

<table>
<thead>
<tr>
<th>Confirmed Infection</th>
<th>Autologous 23</th>
<th>Allogeneic 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1</td>
<td>3.38</td>
<td>0.38</td>
</tr>
<tr>
<td>HCV</td>
<td>110.08</td>
<td>8.32</td>
</tr>
<tr>
<td>HBV</td>
<td>13.64</td>
<td>3.62</td>
</tr>
</tbody>
</table>
While the transfusion of units from infected autologous donors may not present a risk to the
donor/patient from whom the blood was collected, accidental needle stick and splatters put blood
handlers at risk. Furthermore, accidental mis-transfusion of an infected autologous unit to the wrong
recipient is possible and could likely have disastrous consequences, since about 1% of such units may
transmit HCV. The actual risk of mis-transfusing an autologous blood product that has been collected
days in advance of a scheduled surgery to the wrong person is unknown, but in this author’s opinion, it
is probably in the range of 1 in every 10,000 to 25,000 transfusions. For example, in 1992, the
College of American Pathologists (CAP) did a survey of 3852 hospital transfusion services and found
that 34 (0.9%) had issued one or more autologous blood products to the wrong patient during the
previous year and that 20 of these units were actually transfused. An analysis of 256 licensed
transfusion services by The New York State Department of Health, from 1990 through 1998, indicated
that 1 in 19,000 RBC units were transfused to the wrong patient or were of incorrect ABO group or Rh
type. Even the mis-transfusion of an autologous unit that tested negative for communicable
diseases can present a potential risk to a recipient. Many collection sites only ask autologous donors
the screening questions that pertain to minimizing the risk of a reaction to the donation process
(vasovagal, etc.), and not the questions that pertain to the safety of the recipient from acquiring an
infection, such as malaria, Babesia, T. cruzi, etc. Thus, the risk of mis-transfusing ANY autologous
unit (including the tested ones) is greater than that for allogeneic units, although this increased risk
has not been well quantified.

One possible reason why many hospitals store and transfuse infected autologous units is over fear of
non-compliance with the Americans with Disabilities Act (ADA), which affords to asymptomatic
individuals infected with HIV a protected class status under the ADA. There is a concern
that not offering autologous services to these donor/patients might be interpreted as a violation of this
act. This situation is ironic in that it is unlikely that the ADA ever intended to increase the risk of
transfusion-transmitted disease for the general public. In fact, since disabled individuals may require
blood transfusions, mis-transfusion of virus-positive autologous blood might increase the risk of
transfusion-transmitted communicable disease (especially HCV) for the very people who are to be
protected by the ADA. It is interesting that in her editorial “Managing Infectious or Untested
Autologous Blood Components: The Ethical Dilemma of Private Rights Versus Public Safety”, Dr.
Kathleen Sazama points out that if safety for all transfused patients were the sole consideration (which
of course it isn’t), then the safest practice (or the least risk alternative) would be to store only
allogeneic units, and to exclude ALL autologous units from inventory, whether tested negative,
reactive/confirmed, or untested.

Summary
Recognition and reduction of transfusion transmitted communicable diseases has decreased
significantly the risk that a unit of blood will contain an infectious agent that the donor can transmit to
the recipient. Thus, the relative importance of other risks of transfusion (such as ABO incompatible
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hemolytic reactions, Transfusion Related Acute Lung Injury (TRALI), and bacterial sepsis from platelet transfusions) has risen such that these other risks of transfusion now far exceed the risk of transfusion transmitted communicable diseases. Other risks of transfusion include cardiopulmonary toxicity, transfusion associated Graft versus Host disease, and metabolic/coagulopathic derangements in massive transfusions. Obviously, a lot more work needs to be done to make transfusion therapy even safer.

GLOSSARY OF TERMS:

**Allogeneic:** Taken from different individuals of the same species. Two or more individuals are said to be allogeneic to one another when the genes at one or more loci are not identical. In blood transfusion and transplantation, a situation in which the donor and recipient are different people.

**Autologous:** In blood transfusion and transplantation, a situation in which the donor and recipient are the same person. Patients scheduled for non-emergency surgery may be autologous donors by donating blood for themselves that will be stored until the surgery.

**Pooled sample format:** When testing blood donations for communicable diseases, it has been customary to test each donation separately. However, recently for certain tests (such as nucleic acid amplification tests (NAT)), laboratories have been allowed to combine (or pool) the samples of individual donations, and then test the pool of samples for evidence of infection.

**Cross-over:** In blood transfusion, cross-over refers to the use in the general blood supply of unutilized blood that was donated for autologous transfusion.

REFERENCES:

1. [http://www.aabb.org/About_the_AABB/Nbdrc/index.htm](http://www.aabb.org/About_the_AABB/Nbdrc/index.htm) (last accessed January 3, 2006)

2. [http://www.aabb.org/All_About_Blood/FAQs/1](http://www.aabb.org/All_About_Blood/FAQs/1) (last accessed January 3, 2006)


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