

# Blood Bank IV

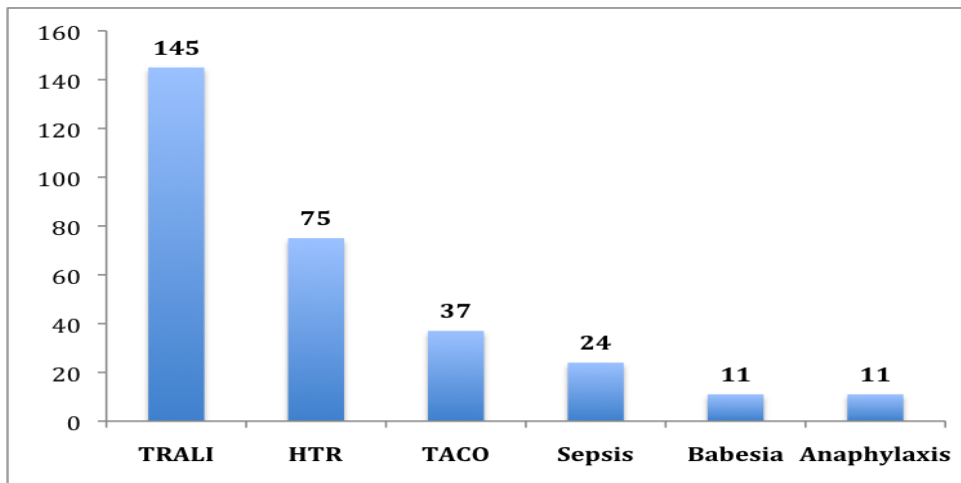
D. Joe Chaffin, MD  
Bonfils Blood Center, Denver, CO

## Transfusion Complications

### I. Transfusion Reactions

#### A. Scope of the issue

1. Transfusions still harm people, despite great improvements in infectious disease screening
2. FDA Transfusion Fatalities FY 2005-2010:



#### B. Suspected reaction workup

1. General philosophy: Assume all reactions are hemolytic, and work to disprove your assumption.
2. **Stop the transfusion!**
  - a. Don't disconnect the unit (though that will eventually happen); at least stop the flow of blood.
  - b. Main indicator of survival of an acute HTR: amount of incompatible blood infused.
  - c. Leave a line open with saline.
3. Necessary parts of workup (things everyone should do).
  - a. **Clerical check**
    - 1) Bedside paperwork and bag check to ensure right unit went to right patient
    - 2) Blood bank check to answer same question
  - b. **Visible hemoglobinemia check**
    - 1) Spin a post-transfusion sample.
    - 2) Compare to pretransfusion sample if abnormal.
    - 3) Detects as little as 2.5 to 5 ml of hemolysis
    - 4) Most sensitive way to detect intravascular hemolysis; not specific, though (bad sticks)
  - c. **Direct antiglobulin (Coombs) test (DAT)**
    - 1) Discussed in BB I
    - 2) Compare to pretransfusion if positive.

- d. **Repeat ABO testing**
  - 1) Another check for right patient, right blood
- 4. Other things often done (but not required)
  - a. Additional serologic testing.
    - 1) Repeat antibody screen (both pre- and post); consider enhancement if suspicious
    - 2) Elution studies if DAT is +
    - 3) Repeat crossmatch with pre- and post samples
  - b. Indirect bilirubin
    - 1) Really more useful to *confirm*, not *make* diagnosis
    - 2) Rises quickly, peaks in less than 10 hours, may be normal within 24 hours (if liver is OK)
  - c. Haptoglobin
    - 1) Levels decrease in acute intravascular hemolysis.
    - 2) Turnaround time and acute phase reaction make for limited usefulness in acute setting.
      - a) If you must use, compare pre- and post levels.
  - d. Urine hemoglobin
    - 1) Not as sensitive or as fast as hemoglobinemia
    - 2) Remember that hematuria does not equal hemoglobinuria!

**C. Classification of reactions**

- 1. Organization (see chart below)
  - a. Febrile vs afebrile
  - b. Acute vs delayed
    - 1) Acute = reaction occurs during or within 24 hours after transfusion.

<b>Presenting With Fever</b>	
<p><b><u>Acute</u></b>            Acute Hemolytic            Febrile Nonhemolytic            Transfusion-related Sepsis            TRALI</p>	<p><b><u>Delayed</u></b>            Delayed Hemolytic            TA-GVHD</p>
<b>Presenting Without Fever</b>	
<p><b><u>Acute</u></b>            Urticarial            Anaphylactic            Anaphylactoid            TACO            Acute Pain Reaction</p>	<p><b><u>Delayed</u></b>            Post-transfusion Purpura            Iron Overload</p>

**D. Acute reactions presenting with fever**

- 1. **Acute hemolytic transfusion reactions (AHTRs)**
  - a. Disastrous, may be fatal
  - b. Clerical errors (both in BB and at bedside)
  - c. May be intravascular or extravascular
    - 1) Fatalities are often ABO-related and intravascular.

- 2) 2009-10: More US non-ABO than ABO fatal HTRs
- d. Signs/symptoms
- 1) Fever and chills
    - a) Most common presenting symptom (> 80%)
  - 2) Back or infusion site pain
  - 3) Hypotension/shock
  - 4) DIC/increased bleeding (important in anesthetized patients)
  - 5) Hemoglobinuria
  - 6) Sense of “impending doom”
- e. Lab findings
- 1) Hemoglobinemia (pink or red serum/plasma)
  - 2) Positive DAT (unless all donor cells destroyed)
  - 3) Elevated indirect bilirubin
  - 4) Lab findings of DIC
  - 5) Hemoglobinuria
  - 6) RBC abnormalities
    - a) Schistocytes: intravascular hemolysis
    - b) Spherocytes: extravascular hemolysis



- f. Pathophysiology
- 1) Classically ABO-related
    - a) Group O recipients getting blood from group A donor most common (and most commonly fatal).
    - b) ABO antibodies are largely IgM (also IgG in group O) and are great complement-fixers.
    - c) Also seen with incompatible donor plasma transfusion (platelet transfusions)
  - 2) Rapid destruction of transfused red cells by complement fixation (with resultant C3a/C5a)
  - 3) Antigen-antibody complexes activate factor XII (Hageman factor) and numerous cytokines (IL-1, TNF, etc), and activates bradykinin.
    - a) Coagulation consequences:
      - Direct intrinsic path activation by factor XII and indirect activation of extrinsic path by tissue factor
      - Combination leads to DIC in 10% of patients.
    - b) Circulatory consequences:
      - Increased bradykinin and anaphylatoxins leads to systemic hypotension, which leads to sympathetic activation.
      - Alpha-adrenergic receptors lead to renal vasoconstriction and acute tubular necrosis.
      - Oliguric renal failure in about 1/3 of confirmed acute HTRs
      - Aggressive hydration; pulmonary edema risk

- g. Treatment
  - 1) Support volume and blood pressure carefully
  - 2) Maintain urine output > 1 mL/Kg/hr
    - a) Low-dose dopamine controversial
  - 3) Watch for DIC; some consider heparin
  - 4) Consider exchange transfusion, especially for high-volume incompatible transfusion
- h. Prevention
  - 1) Training and careful attention to phlebotomy, labeling, issue, and administration processes
  - 2) Requiring two separate ABO/Rh types before transfusion
  - 3) Advanced methods (RFID, bar codes, etc)
- 2. **Febrile nonhemolytic transfusion reactions**
  - a. Most frequently reported reaction (about 1%)
  - b. Unexplained increase in temperature of 1C or 2°F
    - 1) Don't get too hung up on this definition, though; an increase of less than this has the same physiology.
  - c. Cause: Increased pyrogenic substances (e.g., tumor necrosis factor, IL-1 $\beta$ , soluble CD4ligand [PLT derived])
    - 1) Where do the cytokines come from?
      - a) Cytokines produced before transfusion
        - Donor WBCs secrete while in the storage bag.
        - More common in platelet transfusions
      - b) Cytokines produced after transfusion
        - Recipient anti-HLA/HNA antibodies attack donor WBCs, or (less commonly) donor antibodies attack recipient WBCs
        - This action leads to cytokine release in recipient
        - More common with RBC transfusions
  - d. Signs/symptoms
    - 1) Transient fever and chills (+/- rigors?) during or up to 2 hours after transfusion
    - 2) Symptoms tend to occur later in transfusion; if very early, be suspicious of transfusion-related sepsis
    - 3) Note that chills may be first; fever may be delayed up to one hour or more after transfusion
    - 4) Variant versions in premedicated or head injury patients may never have fever
  - e. Lab findings
    - 1) None; negative hemolysis workup
  - f. Treatment
    - 1) Antipyretics (acetaminophen)
    - 2) Meperidine (Demerol) for rigors; be careful!
  - g. Prevention
    - 1) Acetaminophen premedication will sometimes prevent febrile manifestations, but is not reliable

- 2) **Preventing FNH during RBC transfusions**
  - a) Most occur due to post-transfusion production of pyrogenic cytokines, as above.
  - b) Pre-storage leukocyte reduction prevents most of these reactions (still occurs in 0.2% or so).
- 3) **Preventing FNH during platelet transfusions**
  - a) Most due to pre-transfusion cytokine production
  - b) Pretransfusion leukoreduction ineffective because substances are already in the bag!
  - c) Prestorage leukoreduction works best, but still see reactions in ~1% of platelet transfusions
  - d) Soluble CD40 ligand is PLT-derived, not WBC, so LR wouldn't prevent that group of reactions
3. **Transfusion-related sepsis (septic transfusion reaction)**
  - a. General statements
    - 1) Bacterial contamination is the #1 infectious risk from transfusion, much more common than viruses
    - 2) Some sources: As many as 1 in 3000 platelet units are contaminated (many fewer reactions, however)
    - 3) Most contaminated products that cause reactions are older (gives bacteria time to proliferate)
  - b. Organisms depend on product.
    - 1) Red cells
      - a) Gram-negative rods (endotoxin-makers):
        - *Yersinia enterocolitica* (60%)
        - *E. coli*
        - *Enterobacter/Pantoea sp*
        - *Serratia marcescens* and *S. liquifaciens*
        - *Pseudomonas* species
      - b) Gram-positive cocci
        - *Staph. epidermidis*
    - 2) Platelets
      - a) Most are gram positive cocci (skin contaminants); majority give mild reactions
      - b) Gram negs can also contaminate and cause fatalities.
  - c. Signs/symptoms
    - 1) Rapid onset high fever
    - 2) Rigors
    - 3) Abdominal cramping, nausea/vomiting
    - 4) Shock
    - 5) DIC
  - d. Lab findings
    - 1) Discolored RBC product (+/-)
    - 2) May have hemoglobinemia/uria (non-immune)
    - 3) Patient DAT negative
    - 4) Gram stain + in only **half** of proven cases!
    - 5) Culture positive (from both unit and recipient)

- e. Know your source
  - 1) In my opinion, the source of the gram stain and culture is very important.
  - 2) Culturing or staining a segment to me is useless (unless nothing else is available); false negatives when culturing segs only have been described
  - 3) Remember to culture associated IV fluids
- f. Treatment
  - 1) Immediate IV antibiotics
  - 2) Pressure support
- g. Prevention
  - 1) Careful donor history
  - 2) Proper phlebotomy technique
  - 3) Leukocyte reduction filters may decrease risk
  - 4) *AABB Standard* (2004) discussed earlier; platelet products must have methods to limit and detect bacterial contamination.
  - 5) Despite detection methods, false negatives occur, and pathogen reduction may be the ultimate answer
- 4. **Transfusion-related acute lung injury (TRALI)**
  - a. Though underdiagnosed, currently the **#1 cause of transfusion-related fatality in the US!** (see pg 1)
  - b. Two almost identical standard definitions:
    - 1) National Heart, Lung, and Blood Institute (NHLBI) Working Group and Canadian Consensus Conference Panel
      - a) New acute lung injury within 6 hours of a transfusion; ALI defined:
        - Hypoxemia with  $\text{PaO}_2/\text{FiO}_2 \leq 300$  mm Hg (or  $\text{O}_2$  sat  $<90\%$ ) and bilat CXR infiltrates
      - b) Lack of other risk factors for pulmonary edema
      - c) No pre-existing acute lung injury
    - 2) Usually also with fever, chills, possibly hypotension
    - 3) Most common with platelets and plasma transfusions
  - c. Clinical differential diagnosis:
    - 1) **ARDS**: TRALI may look exactly like ARDS, but usually resolves in 24-48 hours.
    - 2) **Circulatory overload (TACO)**: Again, may be very similar clinically, complete with a “wet” chest x-ray, but TRALI does not respond to diuretics.
    - 3) Anaphylactic reactions (generally afebrile)
    - 4) Acute pulmonary and myocardial disorders
  - d. Pathophysiology: Two currently accepted pathways that are very closely intertwined
    - 1) **Immune (“Donor antibody”) pathway**
      - a) Anti-HLA or anti-neutrophil antibodies **from the donor** attack the recipient white cells (neutrophils in particular).

- b) Antibody-WBC complexes deposit in and damage pulmonary vasculature.
- c) Sequence leads to damage to capillaries with leakage and resultant edema.
- d) This mechanism may also occur with **recipient** antibodies against donor WBCs, but this is less common.
- 2) **Non-immune (“Two-event”) pathway**
  - a) First event: Pre-transfusion condition that activates lung endothelial cells and PMNs
    - Examples include sepsis, major surgery, massive transfusion
  - b) Second event: Transfusion of stored blood product (+/- antibodies)
    - Stored blood products accumulate substances that can prime/activate destructive neutrophils (lipids, soluble CD40 ligand).
    - Substances are called “biologic response modifiers” (BRMs).
    - Either BRMs or antibodies mentioned in the immune hypothesis may induce capillary damage by activating the primed PMNs
  - c) Combination of these events leads to capillary damage and subsequent pulmonary edema.
- e. Diagnosis
  - 1) Difficult, as it is often confused for something else
  - 2) Typical early findings: bilateral CXR infiltrates, oxygen saturation less than 90%, no evidence of volume overload (no jugular venous distention, normal wedge pressure, normal BNP levels)
  - 3) Lab findings may include demonstration of anti-HLA and/or anti-neutrophil antibodies, and possibly increased biologic response modifiers in the bag.
    - a) Remember, this is a clinical and radiographic diagnosis; confirming the presence of donor antibodies may take days or weeks!
- f. Treat with respiratory support (oxygen, maybe intubation).
  - 1) Mortality reported between 5 and 25%
  - 2) 80% recover quickly
- g. Prevention
  - 1) Current AABB mandate for transfusion centers to reduce TRALI risk
  - 2) Implicated donors should usually be deferred (if antibodies outlined above are found).
  - 3) Use of all (or mostly) male plasma has been shown to decrease the risk of TRALI (females have higher incidence of anti-HLA and anti-neutrophil antibodies because of pregnancy).

- 4) Some centers have begun testing parous female PLT donors for anti-HLA +/- neutrophil antibodies and deferring those who with antibodies

## **E. Acute reactions presenting without fever**

### **1. Hypersensitivity-type reactions**

#### **a. Mild allergic (urticarial) transfusion reactions**

- 1) Second most frequently reported reaction
- 2) Usually just localized hives, but may have respiratory symptoms and laryngeal edema
- 3) Mechanism
  - a) Type I hypersensitivity to donor plasma proteins
- 4) Prevention and treatment
  - a) Diphenhydramine (Benadryl) IV 50 mg (may not be effective as prophylaxis in patients without a history of reaction)
  - b) Transfusion **may be restarted** after localized urticarial reactions clear.

#### **b. Severe allergic (anaphylactic) transfusion reactions**

- 1) Opposite end of hypersensitivity reaction spectrum
- 2) Uncommon (thankfully)
- 3) Classic history: IgA deficient recipient (discussed in BB III); haptoglobin, latex, drugs, foods too
- 4) Anaphylactic shock **very early in** the transfusion
  - a) Classic presentation: acute hypotension, lower airway obstruction, abdominal distress, systemic crash!
  - b) **Don't rely on** a progression from mild to severe symptoms to make the diagnosis
- 5) Prevention
  - a) Washed products (or IgA deficient products)
  - b) Benadryl is insufficient for prevention and for treatment!
- 6) Treatment
  - a) Epinephrine immediately
  - b) SQ or IM preferred, but may give IV if already crashed.

### **2. Anaphylactoid reactions**

#### **a. Term used for two main situations:**

- 1) Reactions associated with **ACE inhibitors**
  - a) Rapid onset of flushing and hypotension in transfused patients who are on ACE inhibitors (e.g., Vasotec, Lotensin, Zestril, Capoten).
  - b) Seen historically with bedside leukoreduction filters; also seen in plasma exchange
  - c) Possibly caused by accumulation of increased bradykinin from contact with filter or equipment
    - ACE inhibitors prevent metabolism of bradykinin.
    - Bradykinin causes marked hypotension.

- 2) **Allergic reaction of intermediate severity**
  - a) These patients may not completely lack IgA, and may have milder symptoms and consequences from IgA exposure.
  - b) Still, hypotension and dyspnea occur and can be alarming
- b. These reactions managed with same principles as with anaphylactic reactions
3. **Transfusion-associated circulatory overload (TACO)**
  - a. Main differential diagnosis: TRALI
  - b. Acute onset of congestive heart failure as a direct result of blood transfusion
    - 1) Dyspnea, orthopnea
    - 2) Systolic hypertension (widened pulse pressure), tachycardia, bilateral rales, jugular venous distension
    - 3) Often have headache
    - 4) Usually afebrile
  - c. Radiographs similar to TRALI
  - d. Patients most at risk
    - 1) Patients with pre-existing CHF
    - 2) Very young and very old patients
    - 3) Renal failure patients
    - 4) Patients with chronic anemias, e.g., sickle cell, thalassemias (due to compensation for anemia with increased plasma volume)
  - e. Distinguishing from TRALI
    - 1) Clinical (response to diuretics in TACO, fever in TRALI but not in TACO)
    - 2) Lab: elevated brain natriuretic peptide (BNP) suggests TACO, antibodies as above
  - f. Treatment
    - 1) Discontinue transfusion, evaluate, sit patient up
    - 2) Diuretics +/- oxygen
  - g. Prevention in at-risk patients
    - 1) Control infusion rates (1 mL/Kg/hour).
    - 2) Split units when possible.
    - 3) Consider lower volume units (using CPD-RBCs rather than AS-RBCs, for example) or volume reduction of certain products.
4. **Acute Pain Reactions**
  - a. Sudden onset pain in trunk and extremities during transfusion
  - b. No predictable risk factors, no way to prevent
  - c. Lab workup is negative, and symptoms resolve shortly after transfusion
  - d. May require narcotics to relieve pain

**F. Delayed reactions presenting with fever**

**1. Delayed hemolytic transfusion reactions (DHTR)**

- a. Hemolysis occurring several days to 2 weeks after transfusion (rare reports up to 6 weeks).
- b. Pathophysiologic possibilities
  - 1) Anamnestic response
    - a) A previously formed but currently undetectable antibody comes roaring back after re-exposure.
    - b) Typical for Kidd, Duffy, Kell antibodies
  - 2) Primary response
    - a) New antibody formed as foreign RBC is still circulating.
    - b) MUCH less common
- c. Classically extravascular hemolysis
  - 1) Delayed HTRs due to Kidd antibodies may be intravascular and severe (IgM component).
- d. Signs/symptoms
  - 1) Often none
    - a) If asymptomatic and without lab findings other than newly positive antibody screen, may be called “**delayed serologic reaction (DSTR)**”
  - 2) Fever and anemia of unknown origin
  - 3) Mild jaundice may be seen
- e. Lab findings
  - 1) Icteric serum
  - 2) DAT positive (classically “mixed field”)
  - 3) Anemia
  - 4) Positive antibody screen (may change from previously negative).
  - 5) Spherocytes on peripheral smear
- f. Treatment
  - 1) As for AHTR if severe and intravascular
  - 2) Often no treatment necessary

**2. Transfusion-associated graft-vs-host disease**

- a. Discussed in BB III.

**G. Delayed reactions presenting without fever**

**1. Post-transfusion purpura**

- a. Marked thrombocytopenia about ten days following transfusion (may be below 10,000/ $\mu$ L)
  - 1) Triggering transfusion can be platelets **or** RBCs.
- b. Multiparous females especially at risk (5:1 female-male ratio)
- c. Anti-HPA-1A (PL<sup>A1</sup>) most common (70%)
  - 1) Almost everyone is HPA-1A positive.
  - 2) HPA-1A negative patients are exposed through pregnancy or transfusion.
  - 3) Transfusion after antibody is formed leads to devastating destruction of platelets.

- 4) **HPA-1A-positive transfused platelets and HPA-1a-negative patient platelets are both destroyed**
  - a) Several possible explanations, including passive adsorption of antigen/antibody complexes, autoantibody formation, adsorption of soluble platelet antigens, etc.
  - d. IVIG is successful in reversing the process and dramatically increasing the platelet count.
    - 1) Due to this success, plasma exchange is used much less often today.
    - 2) Mortality is about 10% or so without treatment; near 0% with treatment.
  - e. Platelets should not be given acutely if possible.
  - f. Future platelet transfusions should be antigen matched
- 2. **Iron overload**
  - a. Each unit of RBCs: 200-250 mg iron
  - b. Lifetime load of ~100 transfusions in 70 Kg person = risk for overload.
  - c. Deferoxamine treatment is painful and awful!

## H. Consequences of significant reactions

- 1. FDA requirements
  - a. If there is **suspicion** that a death is transfusion-related, FDA requires notification within 24 hours by phone.
    - 1) Official rule says “confirmed”, but FDA cites for not reporting “suspicions.”
  - b. Phone report must be followed up by a full investigation and written report within 7 days.
  - c. FDA is aggressively enforcing this rule.
- 2. JCAHO
  - a. Acute hemolytic transfusion reactions are “sentinel events” and require intensive investigation (Root Cause Analysis) and reporting to JCAHO.

## II. Transfusion-transmitted Diseases (See April 2011 Podcast on iTunes)

### A. Current risk of disease transmission

Organism	Current Risk Estimate
<b>HIV-1</b>	1 in 1,467,000 (2010)
<b>Hepatitis B</b>	1 in 355,000-357,000 (2009)
<b>Hepatitis C</b>	1 in 1,149,000 (2010)
<b>HTLV-I</b>	1 in 3,000,000
<b>HIV-2</b>	Remote
<b>WNV</b>	Remote
<b>Syphilis</b>	Remote
<b>T. cruzi</b>	Unknown, likely remote
<b>Bacteria</b>	1 in 75,000 platelet transfusions 1 in 500,000 RBC transfusions

1. For perspective, risk of acute hemolytic reaction stated as 1 in 25,000 transfusions
2. Risk of dying in the hospital from something other than transfusion problem: 6 per 1000!

## **B. Hepatitis viruses**

### **1. Hepatitis A virus**

- a. Fecal-oral transmission (30 day incubation)
- b. Generally not a big blood banking problem (not tested)
- c. Some concern in pooled products
  - 1) Solvent-detergent treatment doesn't deactivate HAV (nonenveloped).
  - 2) Transmission documented in pooled factor concentrates
- d. Not prone to chronicity like HBV and especially HCV

### **2. Hepatitis B virus**

- a. DNA virus (*Hepadnavirus*)
- b. Blood transmission, intimate contact transmission possible but less likely
- c. Both cellular and plasma components transmit.
- d. Incubation period: approximately 8-12 weeks (but can range from approximately 5 to 25 weeks)
- e. Clinical
  - 1) Primary infection may be subclinical (65%) or only mild (jaundice, nausea, fatigue, dark urine).
  - 2) Fulminant presentation rare
  - 3) Chronic infection ("carrier state") much less likely than with HCV (< 5% of adult infections)
    - a) Greatly decreased carriers since routine vaccination
    - b) 400 million worldwide carriers, per WHO
- f. Current testing (see appendix from BB II)
  - 1) Anti-HBc EIA/ChLIA and HBsAg EIA/ChLIA
    - a) Confirmatory test for HBsAg: neutralization
    - b) No confirmatory test for anti-HBc
  - 2) No anti-HBsAg testing (vaccinated donors would be positive).
  - 3) HBV NAT in use in many centers now; will likely be required eventually (like HCV testing).
  - 4) With improvements in HIV and HCV testing, HBV is currently the most likely of the major viruses to be transmitted via transfusion!
  - 5) See appendix in BBII for deferral guidelines
- g. Serology patterns (general); see next page

HBV DNA	HBsAg	ANTI-HBc (TOTAL)	ANTI-HBc (IGM)	ANTI-HBsAg	INTERPRETATION
—	—	—	—	—	Incubation
+	+	+	+	—	Acute infection
—	—	+	—	+	Recovered infection
+/-	+	+	—	—	Carrier
—	—	—	—	+	Vaccinated
—	—	+	—	—	Probable false positive, but possible early infection

**3. Hepatitis C virus**

- a. RNA virus
- b. 0.5-1.0% of US blood donors
- c. Both cellular and plasma components transmit.
- d. Strong association with chronic hepatitis (75%), cirrhosis, and hepatocellular carcinoma (even stronger association than HBV)
  - 1) HCV infection is currently the number one reason for hepatic transplant in the US.
  - 2) Initial presentation tends to be quite mild or asymptomatic.
- e. Donor testing (see appendix from BB II)
  - 1) Antibody test is **anti-HCV (EIA/ChLIA)**
    - a) Reactive anti-HCV is confirmed by Recombinant ImmunoBlot Assay (RIBA)
  - 2) Approximately 70-80 days from infection until anti-HCV positivity
    - a) During much of this time, HCV RNA is detectable by PCR testing, and the virus is transmissible by transfusion (see below).
  - 3) Also must test using PCR for HCV RNA (**HCV NAT**)
    - a) Reduces window period from 70-80 days to 10 to 30 days
  - 4) See appendix in BBII for deferral guidelines

**4. Hepatitis D virus**

- a. Formerly known as “delta agent”
- b. Blood transmission
- c. “Defective” virus (requires coating with HBsAg in order to cause disease).
- d. No screening for HDV in blood donors (HBV screening takes care of it), though antibody and RNA testing are available.

**5. Hepatitis E virus**

- a. Fecal-oral transmission
- b. Epidemics in India and Asia; rare transfusion transmission

c. No testing required, but antibody and RNA testing are available.

6. **GBV-C (a.k.a. hepatitis G virus)**

- a. 1-3% prevalence in US donors, with higher antibody rate
- b. Readily transmitted through transfusion
- c. 10-20% of HCV-infected patients are co-infected.
- d. Despite transmission, not associated with actual disease!
- e. Screening not yet available (or necessary)

7. **Others**

- a. **TTV**: no disease association as of yet, but is definitely transfusion-transmissible.
- b. **SEN-V**: related to TTV but no definite disease association

**C. Retroviruses**

1. **HIV-1 and HIV-2**

- a. RNA retrovirus identified in 1984
  - 1) Hemophiliacs and homosexual men first
  - 2) Transmitted via transfusion, sexual contact, breast-feeding, blood exposure
- b. Clinical/pathophysiology
  - 1) Symptoms in acute infection: “flu-like”
  - 2) Followed by LONG asymptomatic period (often over ten years), then rapid immune compromise
  - 3) Damage caused by attack on CD4+ lymphocytes (“helper” T cells)
  - 4) Ultimately, death is secondary to opportunistic infections or unusual malignancies such as Kaposi’s sarcoma or CNS lymphoma
- c. Testing
  - 1) Antibody testing
    - a) Required since 1985
    - b) Window period = 20-22 days
  - 2) Organism testing
    - a) HIV-1 antigen (p24) testing introduced March 1996
      - Reduced window period to about 16 days
    - b) p24 testing replaced in 1999-2000 by PCR testing for HIV RNA (HIV NAT)
      - Reduction of window period to 10 days
- d. Both cellular and plasma products can transmit HIV-1
- e. See appendix in BBII for deferral guidelines
- f. **HIV-2**
  - 1) Related virus found originally in West Africa
  - 2) Really, really rare (per *AABB Tech Manual*, only three true HIV-2 infected donors found in the US since 1992).

- 3) It appears that HIV-2 is less readily transmitted than HIV-1, and that fewer infections progress to AIDS.
  - 4) No licensed confirmatory test
2. **HTLV I/II**
- a. Transmission through cellular products only
  - b. HTLV-I disease associations
    - 1) Adult T-cell leukemia/lymphoma (ATLL)
    - 2) HTLV-associated myelopathy (HAM; formerly called “tropical spastic paraparesis”)
  - c. HTLV-II: no clear-cut disease associations
  - d. Both viruses are *transmitted* readily, but actual post-transfusion *disease* is not likely.
  - e. See testing discussion in appendix of BB II.

## D. Other organisms

1. **West Nile virus (WNV)**
  - a. Became huge issue in summer 2002 as infection spread across the US; currently uncommon.
  - b. Testing done via NAT; pooled until high risk of disease in area, then single donor
  - c. Deferrals:
    - 1) Confirmed or suspected WNV infection: 28 days from symptom onset or 14 days after symptoms resolved (whichever is later)
    - 2) Positive WNV test only: 120 days from date of positive test
2. ***Trypanosoma cruzii* (Chagas’ disease)**
  - a. Transmitted through bite of reduviid bug (“kissing bug”) in Central/South America
  - b. Potentially growing problem with immigration (roughly 1 in 20,000 donors, but much higher in immigrant-rich populations)
  - c. Specific question on donor questionnaire (permanent deferral for history of Chagas’ disease); the problem is that many are asymptomatic.
  - d. Screening test approved (EIA); required to be implemented by December 2011
    - 1) Testing allowed to be one time per lifetime of donor
3. ***Treponema pallidum***
  - a. Organism doesn’t survive well in refrigerated storage (48-96 hours); not considered a large transfusion medicine problem.
  - b. Surrogate marker for high-risk behavior
  - c. See testing discussion in appendix of BB II
4. **Cytomegalovirus (CMV)**
  - a. Extremely common DNA virus (approximately 50% are exposed) that lives in WBCs only (monocytes).
  - b. Causes severe infections in immunocompromised adults and neonates, but minimal disease in healthy people (may have cold-like symptoms)

- c. Prevent with seronegative donors and leukocyte reduced products (see discussion in BB 3)
  - d. Testing not required but available.
5. **Parvovirus B19**
- a. Primarily infects RBCs
    - 1) Entry through P antigen receptor
  - b. Causes “fifth disease” in children and can cause red cell aplasia in adults
  - c. Nonenveloped, so not destroyed by solvent-detergent treatment (concern in pooled treated products)
  - d. Due to this concern, source and recovered plasma intended for plasma derivative manufacture are tested for Parvovirus via NAT
6. **Prion disease**
- a. Prion: probably an infectious protein particle
  - b. Creutzfeldt-Jakob disease (CJD) and variant Creutzfeldt-Jakob disease (vCJD)
    - 1) Research (early 2007) suggests the possibility that prions in CJD may be secondary to a viral infection.
  - c. CJD
    - 1) Mostly sporadic (occasionally familial) spongiform encephalopathy, nearly universally fatal
    - 2) Found in older patients
    - 3) Long disease course
    - 4) Transmission via transfusion theoretical only
  - d. vCJD
    - 1) Emerging syndrome in the United Kingdom
    - 2) Caused by prion that causes bovine spongiform encephalopathy (“mad cow” disease)
    - 3) Distinct from CJD (younger, more rapid course)
    - 4) Transfusion transmission proven (at least 4 cases)
    - 5) Has led to US deferral of many donors who lived in UK or Europe since 1980 (see earlier) and universal leukoreduction in Europe and Canada
7. ***Plasmodium* species**
- a. Malaria is readily transmissible through transfusion.
  - b. No effective screening except by history.
  - c. See BB II for deferral guidelines
8. ***Babesia* species**
- a. Tick-borne intraerythrocytic parasite infection
  - b. Huge concern in endemic areas in East currently; pilot studies to test donors
  - c. Caused 11 cases of transfusion fatality between 2005 and 2010
  - d. Screen via history (permanent deferral)