

Blood Bank IV

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Transfusion Complications

I. Transfusion Reactions

A. Suspected reaction workup

1. General philosophy: Assume all reactions are hemolytic, and work to disprove your assumption.
2. **Stop the transfusion!**
 - a. This doesn't necessarily mean to disconnect the unit (though in most cases 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 paperwork check to answer the 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) Fastest and best way to detect acute intravascular hemolysis
 - c. **Direct antiglobulin (Coombs) test (DAT)**
 - 1) Discussed in BB I
 - 2) Compare to pretransfusion if positive.
 - d. **Repeat ABO testing**
4. Other things often done (but not required)
 - a. Repeat additional serologic testing.
 - 1) Repeat antibody screen.
 - 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) Scavenger of free hemoglobin, so 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, be sure to compare pre and posttransfusion levels.

- d. Urine hemoglobin
 - 1) Not as good or as early as hemoglobinemia
 - 2) Remember that hematuria does not equal hemoglobinuria!

B. 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.

Presenting With Fever	
<u>Acute</u> Acute Hemolytic Febrile Nonhemolytic Bacterial Contamination TRALI	<u>Delayed</u> Delayed Hemolytic TA-GVHD
Presenting Without Fever	
<u>Acute</u> Urticarial Anaphylactic Anaphylactoid Circulatory Overload Medicated Febrile	<u>Delayed</u> Post-transfusion Purpura Iron Overload

C. 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) Fatal ones are usually ABO-related and are usually intravascular.
 - 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) Most commonly ABO-related
 - a) Group O recipients getting blood from a group A donor is most common (and most commonly fatal).
 - b) ABO antibodies are mostly IgM and are great complement-fixers.
- 2) Rapid destruction of transfused red cells by IgM antibodies
- 3) Antigen-antibody complexes activate factor XII (Hageman factor) and numerous cytokines (IL-1, TNF, etc), and activates bradykinin.
 - a) Coagulation consequences:
 - Direct intrinsic pathway activation by factor XII and indirect activation of intrinsic pathway by tissue factor
 - This combination leads to DIC in 10% of patients.
 - b) Circulatory consequences:
 - Increased bradykinin leads to systemic hypotension, which leads to sympathetic activation.
 - Alpha-adrenergic receptors in kidney lead to renal vasoconstriction and eventual acute tubular necrosis.
 - Renal failure in about 1/3 of confirmed acute HTRs

g. Treatment

- 1) Support volume and blood pressure
- 2) Maintain urine output
- 3) Watch for DIC

2. **Febrile nonhemolytic transfusion reactions**

- a. Most frequently reported reaction (about 1%)
- b. Increase in temperature of 1 C or 2 F with no other explanation.
 - 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 cytokines (eg, tumor necrosis factor, IL-1 β)
 - 1) Where do the cytokines come from?
 - a) Cytokines secreted before transfusion
 - Donor WBCs may secrete cytokines while in the storage bag.
 - More common in platelets

- b) Cytokines secreted after transfusion
 - Recipient anti-WBC antibodies stimulate donor (transfused) WBCs to secrete cytokines.
 - Recipient's WBCs secrete cytokines secondary to interaction with donor WBCs.
 - More common with RBC transfusions
- d. Signs/symptoms
 - 1) Fever and chills (generally no rigors)
- e. Lab findings
 - 1) None
- f. Treatment
 - 1) Antipyretics (acetaminophen)
- g. Prevention
 - 1) Acetaminophen premedication will often prevent febrile manifestations.
 - 2) **Preventing FNH during RBC transfusions**
 - a) Most occur due to post-transfusion secretion of pyrogenic cytokines, as above.
 - b) Leukocyte reduction usually prevents these reactions.
 - Timing of leukoreduction is not critical; bedside works fine, prestorage works fine.
 - 3) **Preventing FNH during platelet transfusions**
 - a) Most due to pre-transfusion cytokine secretion
 - b) Bedside (or other "pretransfusion") leukoreduction often ineffective because the cytokines are already in the bag!
 - c) "Prestorage" leukoreduction works best.
- 3. **Bacterial contamination (septic reaction)**
 - a. Bacteria may proliferate in storage.
 - 1) Bacterial contamination is the #1 infectious risk from transfusion.
 - 2) Some sources: as many as 1 in 3000 platelet units are contaminated.
 - b. Organisms depend on product.
 - 1) Red cells
 - a) *Yersinia enterocolitica*
 - b) *Citrobacter freundii*
 - c) *E. coli*
 - d) *Pseudomonas* species
 - 2) Platelets
 - a) Gram positive cocci
 - b) *Y. enterocolitica* has been reported.
 - c. Signs/symptoms
 - 1) Rapid onset high fever
 - 2) Rigors
 - 3) Abdominal cramping
 - 4) Nausea/vomiting
 - 5) Shock

- d. Lab findings
 - 1) Discolored product (+/-)
 - 2) May have hemoglobinemia/uria
 - 3) DAT negative
 - 4) Gram stain + in only *half* of proven cases!
 - 5) Culture positive (both from the unit and the 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); the product in the bag is what actually went into the patient!
- f. Treatment
 - 1) Immediate IV antibiotics
 - 2) Pressure support
- g. Prevention
 - 1) Careful donor history (many just report extremely mild symptoms).
 - 2) Proper phlebotomy technique
 - 3) Some evidence that leukocyte reduction filters may decrease risk.
 - 4) *AABB Standard* (March 2004) discussed earlier; platelet products must have methods to limit and detect bacterial contamination.
- 4. **Transfusion-related acute lung injury (TRALI)**
 - a. Though underdiagnosed, currently the **#1 cause of transfusion-related fatality in the US!**
 - 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 completed transfusion
 - b) Hypoxemia
 - c) Bilateral infiltrates on chest radiograph
 - d) Lack of other risk factors for pulmonary edema
 - 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) Acute pulmonary and myocardial disorders
 - d. Pathophysiology: Two currently accepted mechanisms that are very closely intertwined

- 1) **Immune (“Donor antibody”) hypothesis (original hypothesis)**
 - 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”) hypothesis**
 - a) First event: pre-existing condition that activates (“primes”) neutrophils (makes them susceptible to stimuli).
 - Examples include sepsis, major surgery, massive transfusion
 - b) Second event: transfusion of stored blood product
 - Stored blood products accumulate lipids that can further activate the primed neutrophils.
 - These lipids are called “biologic response modifiers” (BRMs).
 - Either the BRMs or the antibodies mentioned in the immune hypothesis may induce capillary damage
 - c) The combination of these events leads to capillary damage and subsequent pulmonary edema.
- e. Diagnosis
 - 1) May be 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 blood 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%.

- 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 multiparous female donors for anti-HLA/neutrophil antibodies and deferring those who have the antibodies

D. Acute reactions presenting without fever

1. Hypersensitivity-type reactions

a. Urticarial transfusion reactions

- 1) Second most frequently reported reaction
- 2) Usually just localized hives
- 3) Mechanism
 - a) Type I hypersensitivity to donor plasma proteins
- 4) Prevention and treatment
 - a) Diphenhydramine (Benadryl)
 - b) Transfusion **may be restarted** after localized urticarial reactions clear.

b. Anaphylactic transfusion reactions

- 1) The opposite end of the hypersensitivity reaction spectrum
- 2) Uncommon (thankfully)
- 3) Classic history: IgA deficient recipient (discussed previously)
- 4) Anaphylactic shock **within the first few drops** of the transfusion
 - a) Classic presentation: acute hypotension, abdominal distress, systemic crash!
 - b) **Don't rely on** wheezing, gradual dyspnea, etc. to make the diagnosis (though they may occur).
- 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 types:
 - 1) Reactions associated with **ACE inhibitors**
 - a) Rapid onset of flushing and hypotension in transfused patients who are on ACE inhibitors

- (drugs such as Vasotec, Lotensin, Zestril, Capoten).
- b) Famous in association with bedside leukoreduction filters (negatively charged)
- c) Possibly caused by accumulation of increased bradykinin from contact with filter
 - ACE inhibitors prevent metabolism of bradykinin.
 - Bradykinin causes hypotension.
- 2) **Milder forms of IgA deficiency**
 - a) These patients may not completely lack IgA, and may have milder symptoms and consequences from IgA exposure.
 - b. 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, eg, 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
 - 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. **Premedicated FNH**
 - a. A fabulous oxymoron!

- b. Premedicated patients may only have chills without fever.

E. Delayed reactions presenting with fever

1. Delayed hemolytic transfusion reactions

- a. Hemolysis occurring several days to weeks after transfusion.
- b. Pathophysiologic possibilities
 - 1) Anamnestic response
 - a) A previously formed antibody comes roaring back after re-exposure.
 - b) Typical for Kidd, Duffy
 - 2) Primary response
 - a) New antibody is formed while foreign RBC is still circulating.
 - b) Less common
- c. Classically extravascular
 - 1) Delayed HTRs due to Kidd antibodies may be intravascular and severe.
- 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.**”
 - 2) Fever of unknown origin
 - 3) Mild jaundice
- 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.

F. Delayed reactions presenting without fever

1. Post-transfusion purpura

- a. Marked thrombocytopenia about one week following transfusion (may be below 10,000/ μ L)
 - 1) The triggering transfusion does not have to be platelets: platelets **or** RBCs can start the reaction.
- b. Multiparous females especially at risk (5:1 female-male ratio)
- c. Anti-PL^{A1} (HPA-1A) most common (~70%)
 - 1) Almost everyone is PL^{A1} positive.
 - 2) PL^{A1} negative patients are exposed through pregnancy or transfusion.

- 3) Transfusion after antibody is formed leads to devastating destruction of platelets.
- 4) **PL^{A1} positive transfused platelets and PL^{A1} negative patient platelets are both destroyed**
 - a) Several possible explanations, including passive adsorption of antigen/antibody complexes, autoantibody formation, alteration of self 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.
- 2. **Iron overload**
 - a. Each unit of RBCs: 200-250 mg iron
 - b. Lifetime load of ~150 transfusions in 70 Kg person = risk for overload.
 - c. Deferoxamine treatment is painful and awful!

G. 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) This may seem too restrictive, and the official rule says “confirmed”, but I have seen numerous FDA citations for not reporting “suspicions.”
 - b. This phone report must be followed up by a full investigation and written report within 7 days.
 - c. FDA is aggressively enforcing this rule during recent site visits.
- 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

A. Current risk of viral disease transmission

- 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!
- 3. Our current best guesses (from AABB Tech Manual, 16th ed, 2008):

Virus	Current Risk Estimate
HIV-1	1 in 2,300,000
Hepatitis B	1 in 220,000

Hepatitis C	1 in 1,800,000
HTLV-I	1 in 2,993,000
HIV-2	Remote
WNV	Remote
Syphilis	Remote
<i>T. cruzi</i>	Unknown, likely remote
Bacteria	1 in 75,000 platelet transfusions 1 in 500,000 RBC transfusions

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 6 weeks (but can range from approximately 5 to 25 weeks)
- e. Clinical
 - 1) Primary infection may be subclinical or only mild (jaundice, nausea, fatigue, dark urine).
 - 2) Fulminant presentation possible
 - 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. Serology patterns (general)

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

- g. Current testing (see appendix from BB II)
 - 1) Anti-HBc and HBsAg
 - 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 DNA testing 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!

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, per some sources.
 - 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)**
 - 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. Hepatitis D virus

- a. Formerly known as “delta agent”
- b. Blood transmission
- c. “Defective” virus (requires HBV 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
- c. No testing required, but antibody and RNA testing are available.

6. **GBV-C (a.k.a. hepatitis G virus)**
 - a. 1% prevalence in US blood donors
 - b. Readily transmitted through transfusion
 - c. 10-20% of HCV-infected patients are co-infected with HGV.
 - d. Despite transmission, not associated with actual hepatitis!
 - 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 discovered 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” (time from infection until antibody formation) = 22 days
 - 2) Antigen testing
 - a) HIV-1 antigen (p24) testing introduced March 1996
 - Reduced window period to about 16 days
 - b) Currently, p24 testing replaced by PCR testing for HIV RNA (called “Nucleic Acid Testing”, or NAT)
 - Further reduction of window period to 10 days
 - d. Both cellular and plasma products can transmit HIV-1, but current testing has nearly eliminated the risk.
 - e. **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) Western blot and IFA for confirmation
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; 2003 was even worse.
 - b. Transmission via transfusion proved (testing required)
 - 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. **Cytomegalovirus (CMV)**
 - a. Extremely common DNA virus (approximately 50% are exposed) that lives in WBCs only (may be 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
 - d. Testing not required but available.
3. **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. Some product manufacturers are testing via NAT (PCR).
4. **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) Apparently caused by prion that causes bovine spongiform encephalopathy (“mad cow” disease)
 - 3) Clinically distinct from CJD (younger patients, more rapid course)
 - 4) Presence of prion in lymphoid tissue raises possibility of transfusion transmission, but not yet proven.
 - 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
5. ***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
6. ***Trypanosoma cruzi* (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 but not yet required (EIA)
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 parasite infection
 - b. Organisms related to *Plasmodium*
 - c. Screen via history (permanent deferral)