

XII. Adverse Effects of Blood Transfusion

A. Introduction

1. Transfusion of blood and components is ordinarily a safe and effective way to correct hematologic deficits, but untoward results may occur.
2. Many of these adverse effects are commonly called "transfusion reactions", but the deleterious results of administering blood include a range of events and problems broader than this term.
3. Some adverse effects can be prevented; others cannot.
4. Healthcare providers should know the risks of blood transfusion and evaluate them against potential therapeutic benefits in light of these risks.
5. Transfusion reactions are broken down into two categories.
 - a. Immediate adverse effects occur during or shortly after the transfusion of blood or blood components.
 - b. Delayed adverse affects occur weeks or months after transfusion of blood or blood components.

B. Evaluation of Suspected Hemolytic Transfusion Reactions

1. The time between suspicion of a transfusion reaction and the investigation and initiation of appropriate therapy **should be as short as possible**.
2. Responsibility for recognizing a reaction rests with the transfusionist, who may be a nurse, physician or other member of the clinical team.
3. The following lists details what the transfusionist should look for as an adverse effect that would be cause for immediate action. The presenting of fever and chills may be the same for life-threatening hemolytic transfusion reactions and less serious febrile reactions.
 - a. fever
 - b. chills
 - c. chest pain
 - d. hypotension
 - e. nausea
 - f. flushing
 - g. dyspnea
 - h. hemoglobinuria
 - I. shock
 - j. generalized bleeding (DIC)
 - k. oliguria or anuria
 - l. back pain
 - m. pain or burning at infusion site
4. Any adverse symptom or physical sign occurring during transfusion of blood or its components should be considered as a potentially life-threatening reaction.

5. **Nursing personnel** must take the following actions:
 - a. **Stop the transfusion immediately** to limit the amount of blood infused **and** notify a responsible physician.
 - b. Keep the IV line open with infusion of normal saline.
 - c. **At the patient's bedside check all labels, forms and patient identification** to determine if the patient received the intended component.
 - d. Report the suspected transfusion reaction to blood bank personnel **immediately**.
 - e. **Send required blood samples**, carefully drawn to avoid mechanical hemolysis, to the blood bank **as soon as possible**, together with discontinued bag of blood, the administration set **without** the IV needle, attached IV solutions and all the related forms and labels.
 - f. Send other blood samples for evaluation of acute hemolysis as directed by the blood bank director or patient's physician.

6. **Laboratory investigation** of a suspected hemolytic transfusion reaction should include the following:
 - a. Check identification of patient blood sample and donor blood.
 - 1) If there is a discrepancy, **immediately** notify the patient's physician or other responsible health-care professional and search appropriate records to find if **other patient samples or donor units have been misidentified or incorrectly issued**.
 - 2) After ascertaining if other patients are at risk, and after performing appropriate diagnostic procedures, trace each step of the transfusion process to find the error.
 - b. **Compare the patient's pretransfusion and postransfusion specimen for color of serum or plasma.**
 - 1) *Pink or red discoloration* present in the postransfusion specimen but not in the pretransfusion specimen may indicate the presence of free hemoglobin from destruction of donor red cells.
 - 2) *Intravascular hemolysis* of as little as 5 mL of RBCs can produce **visible** hemoglobinemia.
 - 3) *Mechanical hemolysis* occurring during blood sample collection can also produce pink or red-tinged serum.
 - 4) If faulty sampling is suspected, a second specimen should be requested but a slightly hemolyzed sample is acceptable for the DAT.
 - 5) Yellow or brown discoloration from hemoglobin breakdown products such as bilirubin may indicate recent hemolysis in samples drawn 5-7 hours after transfusion.
 - c. **Perform a DAT on the postransfusion specimen.**
 - 1) If incompatible transfused cells are not immediately destroyed, *the DAT from the postransfusion specimen will be positive, with a mixed-field appearance.*

- 2) Since circulating antibody- or complement coated cells may be very rapidly destroyed, the DAT may be negative if the specimen was drawn several hours after the suspected reaction.
 - 3) Nonimmune hemolysis, e.g., from thermal damage or mechanical trauma, as from the roller pumps used in cardiac bypass systems, can produce hemoglobinemia **without** a positive DAT.
7. If the clerical check reveals no errors in patient identification, if the plasma has no hemolysis and the DAT is negative **nothing further needs to be done.**

C. Investigation for Possible Alloantibodies

1. *If the DAT is positive or hemolysis is evident* or if the physician truly suspects a hemolytic transfusion reaction additional testing is required.
2. *Repeat ABO and D on the pre- and postransfusion specimens as well as the sprigs used in the crossmatch procedure.*
 - a. A mixed-field pattern with microscopic reading of the DAT suggests the presence of incompatible donor cells.
 - b. If ABO and D typing on the **patient's** two samples do not agree, there has been an error in either patient identification, typing or blood drawing. **Another patient's blood may have been drawn at the same time and may have been incorrectly labeled, making it especially important to check records of all specimens received at approximately the same time.**
 - c. If the donor blood specimen is not of the ABO group noted on the bag label, there has been an error in labeling and, almost certainly, an error in the crossmatch as well.
3. *Repeat the antibody detection tests on the pre- and postransfusion samples and on the donor blood.* If any tests are positive, identify the antibody.
 - a. Test donor units for the presence of the corresponding antigen.
 - b. If the patient's pretransfusion sample or the donor blood has an unexpected antibody not previously reported, check records to see how the discrepancy occurred.
 - c. If the donor blood has a previously overlooked antibody, do a minor crossmatch against the patient's pretransfusion sample or type the patient for the suspected antigen.
 - d. If the postransfusion specimen has an antibody not present before transfusion, suspect an anamnestic reaction or passive administration of antibody in a transfusion component recently infused.
 - e. If antibody is identified, phenotype the patient's pretransfusion RBCs to be sure that the patient lacks the corresponding antigen. Check the patient's records to make sure that the patient has not been recently transfused.
4. *Repeat the crossmatch including an AHG phase, testing both the pre- and postransfusion sample against the RBCs from the donor unit*
 - a. If results are incompatible with both the pre- and postransfusion specimens, an error was made during pretransfusion testing. The donor specimen used for the crossmatch may have been taken from a different unit or the patient antibody screen was incorrectly read as negative.

- b. The crossmatch should be repeated against cells from the segment actually used in the initial crossmatch (original segment).
- c. If the crossmatch is incompatible with the postransfusion specimen but compatible with the pretransfusion sample, suspect an anamnestic antibody response.
 - 1) This is most likely if the reaction has occurred, or if the postransfusion sample was drawn, several days after transfusion.
 - 2) If only a short time has elapsed since transfusion, check the patient's previous transfusion history. It is possible that an antibody has developed to RBCs transfused in the preceding few days.
 - 3) Less likely, an antibody might have been present in a transfused blood component.
- d. If both crossmatches are compatible and there is strong clinical reason to believe an acute immune hemolytic reaction has occurred, further testing is necessary.

D. Investigation for Nonimmune Hemolysis

1. *Consider bacterial contamination of the donor unit if:*
 - a. The cells or plasma have *brownish or purple* discoloration.
 - b. There are *clots or abnormal masses* in the liquid blood or segments closest to primary bag appear hemolyzed.
 - c. The plasma is *opaque or muddy*.
 - d. There is a *peculiar odor*.
 - e. If any of these are notated set up cultures at 4 C, 20-24 C and 35-37 C and perform a gram stain on the unit.
2. *Examine the supernatant **plasma** from the **donor blood** container for presence of **free hemoglobin**.*
 - a. The unit may have been damaged by improper temperatures in shipping or storage or at the time of administration.
 - b. Drugs or hypotonic solutions may have been added to the blood.
 - c. Bacterial contamination may be present.
3. *Examine the blood remaining in the administration tubing for presence of free hemoglobin.*
 - a. If the administration set had previously been used for hypotonic solutions or dextrose solutions, there could be hemolysis in the **tubing** but not in the bag.
 - b. Excessive heat from a faulty in-line blood warmer could also damage the infused blood without causing abnormalities within the blood container.
4. *Consider the possibility that the patient or donor has an intrinsic RBC defect.*
 - a. Patients with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency or sickle cell anemia may experience **intravascular** hemolysis because of medical problems not necessarily related to the transfusion.
 - b. Paroxysmal nocturnal hemoglobinuria (PNH) is a rare problem but, when present, may produce severe hemoglobinemia and hemoglobinuria.
5. *Consider the possibility of mechanical hemolysis.* Mechanical RBC lysis can occur with the use of roller pumps such as those used in cardiac bypass surgery, pressure infusion pumps, pressure cuffs or small bore needles.

6. *Consider osmotic hemolysis* due to inadvertent entry into the circulation of hypotonic fluids, such as distilled water used for post-prostatectomy bladder irrigation.
- E. Clinical evaluation *once hemolysis is proven or strongly suspected* includes the following:
1. Examine *postransfusion* urine specimens for the presence of free **hemoglobin**.
 2. Test *postransfusion* serum samples for unconjugated **bilirubin**, carefully recording the timing of sample collection. Peak levels occur at 5-7 hours and disappear within 24 hours.
 3. Measure serum **haptoglobin** in *pre- and postransfusion* specimens. Haptoglobin is a protein that binds to hemoglobin, decreased levels are seen in conjunction with hemolysis.
- F. Special tests to diagnose red cell incompatibility *when routine tests are uninformative and if immune hemolysis continues to be strongly suspected*.
1. Perform antibody detection tests and compatibility tests with more sensitive techniques.
 2. Perform DAT and IAT on several postransfusion specimens at daily or other frequent intervals.
 3. Measure hematocrit or hemoglobin at frequent intervals postransfusion to document whether the transfused cells have or have not produced the expected therapeutic rise, or to demonstrate that a drop in hematocrit has occurred after an initial rise.
 4. Type the cells of the recipient and of the donor unit under suspicion to find antigens present in the donor and absent in the recipient.
 5. In patients with a hemoglobinopathy such as sickle cell anemia, hemoglobin electrophoresis can be used to determine if transfused cells containing hemoglobin A have survived.
 6. Rare cases have documented the occurrence of hemolytic transfusion reaction in the absence of any detectable alloantibody.
- G. Acute Hemolytic Transfusion Reaction
1. *Triggered by an antigen-antibody reaction, which activates the complement and coagulation systems and endocrine responses.*
 2. **Catastrophic** clinical events that may occur include shock, disseminated intravascular coagulation (DIC), and acute renal failure.
 3. *Life threatening HTRs are **almost always due to ABO mismatch attributable to an identification error that results in the recipient receiving the wrong blood group.***
 4. Incompatibility in other blood groups may also cause acute hemolysis in a recipient with alloantibodies stimulated by previous transfusions or pregnancies. These reactions are rarely as severe as those involving ABO incompatibility.
 5. Diagnosis
 - a. *The most common initial sign noted in recipients is **fever**, frequently accompanied by symptomatic chills.*

- b. Reactions may occur when as little as *10-15 mL of incompatible blood* have been infused.
 - c. The onset of symptoms may be misleadingly mild, such as vague uneasiness or an aching back.
 - d. *The first sign the patient observes is **red urine***, which may be accompanied by **back pain** or may be completely painless.
 - e. *The severity of initial symptoms is **often related to the amount of blood transfused*** and may presage the severity of the ensuing clinical problems.
 - f. In the *unconscious or anesthetized recipients* the only manifestations of an acute HTR may be bleeding at the surgical site (due to DIC), hypotension or the presence of hemoglobinuria.
 - g. *Whenever an HTR is suspected, the **transfusion must be stopped immediately***, keeping the IV line open for therapeutic interventions that may be required.
 - h. Follow the guidelines for working up a transfusion reaction, starting with the clerical check at the bedside, since identification errors could mean another patient could be in danger also.
6. Therapy involves vigorous treatment of hypotension and promotion of adequate renal blood flow.
- a. Fluid therapy should be directed at *maintaining urine flow rates above 100 mL/hour* in adults for at least 18-24 hours. Diuretics are also helpful.
 - b. DIC with resultant bleeding is the predominant clinical problem in some HTRs and may be the initial presenting finding in anesthetized patients. It is largely due to hypotension and shock.
 - c. A physician experienced in intensive care medicine should be involved in the treatment of patients with renal failure or shock since the medical management may be very complicated and require aggressive intervention to prevent serious morbidity or mortality.
7. *Total prevention of HTRs is impossible* because hemolysis may occur even when the crossmatch is compatible.
- a. Errors in identifying samples, donor units or recipients are the most common causes of severe, acute HTRs.
 - b. Human error of this sort is difficult to prevent, but opportunities for error can be minimized through careful delineation of every step in transfusion procedure in a readily available SOP manual, and careful adherence to detail by **every member** of the transfusion service and clinical team, from phlebotomist to medical technicians/technologists to transfusionist.
8. **Fatalities** resulting directly from transfusion complications (eg, hemolytic reactions or viral hepatitis) *must be reported* to the Director, Office of Compliance, Center for Biologics Evaluation and Research, Food and Drug Administration, within 24 hours.

H. Other **Immediate** Adverse Effects

1. Febrile Non-hemolytic Reactions (FNH)- **are the most common type of transfusion reaction.**
 - a. *Defined as a temperature rise of 1 C (2 F) or more occurring in association with transfusion and without any other explanation.*

- b. Due to cytotoxic or agglutinating antibodies directed against transfused lymphocytes, granulocytes or platelets.
 - c. FNH reactions tend to occur in recipients who have been repeatedly transfused or who have had multiple pregnancies.
 - d. Fever may be the initial manifestation of several types of transfusion reactions, some of which are potentially fatal.
 - e. **The transfusion must be stopped and the work up initiated.**
 - f. If a patient has 2 or more febrile transfusion reactions it is best to give leukocyte poor products and pre-medicate the patient with antipyretics (not aspirin).
2. Bacterial Contamination
- a. *Bacteria may enter the blood or component containers or contaminate the port of the bag during phlebotomy or component preparation. With sterile disposable equipment, bacterial contamination of refrigerated blood and components is very rare.*
 - b. Although fortunately very rare, bacteria present in blood or blood components can cause a devastating *septic transfusion reaction characterized by high fever, shock, hemoglobinuria, DIC and renal failure.*
 - c. A purple color, clots in the bag or hemolysis suggest contamination, but the appearance of the blood bag is often unremarkable.
 - d. The patient's blood, the suspect component and all IV solutions used should be cultured for aerobic and anaerobic organisms at 4 C, 22 C and 37 C.
 - e. Bacterial contamination is very rare **but such reactions may be fatal.**
 - f. Yersinia enterocolitica has recently been involved, healthy person donates, later becomes ill with a self-limiting diarrheal illness.
 - f. **The transfusion must be stopped and a work up ordered.**
3. Anaphylactic Reactions.
- a. *Features that distinguish anaphylactic reactions from other immediate adverse reactions are that they occur after the infusion of only a few milliliters of blood or plasma and the absence of fever.*
 - b. The onset may be characterized by the following symptoms: coughing, broncho spasm, respiratory distress, vascular instability, nausea, abdominal cramps, vomiting, diarrhea, shock and loss of consciousness.
 - c. Some of these reactions occur in **IgA deficient patients who have developed anti-IgA antibodies** after immunization by previous transfusion or pregnancy.
 - d. **The transfusion must be stopped** and, once anaphylaxis is diagnosed, immediate treatment with epinephrine. A work up must be ordered.

- e. **Sensitized IgA-deficient patients must be transfused with blood and blood components that lack IgA.** Washed or deglycerolized RBCs can be used for replacement of RBCs. The AABB Rare Donor File would need to be contacted about components (plasma, platelets) for the patient. *Approximately 1 in 700 individuals is IgA deficient.*
4. Urticaria (Cutaneous Hypersensitivity Reaction)
- a. This is a commonly encountered transfusion reaction, **second only to febrile nonhemolytic reactions.**
 - b. *Characterized by local erythema, hives and itching, usually without fever or other adverse effects.*
 - c. **If localized urticaria is the only manifestation, it is usually not necessary to discontinue the transfusion.**
 - d. Etiology is unknown but thought to be an allergy to a soluble product in donor plasma. Transfusion of washed or deglycerolized RBCs prevents urticarial reactions but is rarely necessary unless the patient has repeated, severe urticarial reactions.
 - e. Recipients with frequent urticarial reactions may be pre-treated with antihistamine.
5. Circulatory Overload
- a. **Hypervolemia** must be considered if dyspnea, severe headache, peripheral edema or other signs of congestive heart failure occur during or soon after transfusion.
 - b. Rapid increases in blood volume are poorly tolerated by patients with compromised cardiac or pulmonary status and/or chronic anemia with expanded plasma volume. Elderly and pediatric patients at highest risk. **Transfusion must be stopped and a work up ordered.**
 - c. Symptoms include coughing, cyanosis, orthopnea and difficulty in breathing.
 - d. Patients susceptible to circulatory overload should receive RBCs, not WB in **small volumes**, infused slowly.
6. Transfusion Related Acute Lung Injury - TRALI (Noncardiogenic Pulmonary Reactions)
- a. Transfusion recipients rarely experience clinically apparent pulmonary edema without concurrent changes in cardiac pressures. Chest x-ray is typical of acute pulmonary edema, and there is acute respiratory insufficiency but no evidence of heart failure.
 - b. *Symptoms of respiratory distress occur after infusion of volumes too small to produce hypervolemia, and may be accompanied by chills, fever, cyanosis and hypotension.*
 - c. *Two mechanisms postulated.*
 - 1) Reaction between **donor** leukocyte **antibodies** and **recipient** leukocytes, which produces white cell aggregates that are trapped in the pulmonary micro-circulation where they produce changes in vascular permeability. Fluid enters the alveolar air spaces causing problems with adequate gas exchange.
 - 2) During the transfusion of granulocyte concentrates the reverse is possible, leukocyte antibodies in the recipient aggregate the transfused granulocytes.

- d. **The transfusion should be stopped** immediately and a work up ordered.
- e. Treatment includes IV steroids and respiratory support as required.
- f. Washed RBCs may prevent such reactions.

7. Metabolic Reactions

- a. Citrate toxicity
- b. Hypothermia
- c. Hyperkalemia and hypokalemia
- d. Air embolism

I. Delayed Adverse Effects

1. Delayed Hemolytic Transfusion Reactions - **Primary Immune Response.**

- a. The first of delayed hemolytic transfusion reaction is mild, occurs **several weeks** after transfusion and is the result of primary alloimmunization. Antibody production after the stimulating transfusion begins **no earlier than 7-10 days after transfusion and usually several weeks or months later.**
- b. As the antibody increases in titer and avidity, it can react with antigen positive transfused RBCs that are still circulating.
- c. The degree of hemolysis depends on the **quantity of antibody produced and the quantity of transfused cell remaining.**
- d. Primary immunization rarely causes hemolysis of transfused RBCs, and such delayed hemolysis is usually **unsuspected clinically.**
- e. Diagnosis might be suggested by an unexplained fall in hemoglobin coupled with a positive DAT and/or the appearance in the serum on a new RBC alloantibody.
- f. The blood bank will make the diagnosis if additional crossmatches are ordered within the appropriate time frame (ie, when antibody is detectable in patient serum).

2. Delayed hemolytic transfusion reaction - **Secondary (anamnestic) Immune Response.**

- a. The second type of delayed HTR occurs in a **previously immunized recipient** who experiences an anamnestic, or secondary, response to transfused red cell antigens.
- b. some alloantibodies formed after primary immunization may diminish to levels undetectable in serum. Antibodies in the Kidd system (anti-Jk^a and anti-Jk^b) typically behave in this manner.
- c. Pretransfusion testing **reveals no unexpected antibodies and no serologic incompatibility.**
- d. **Within 3-7 days after transfusion,** an anamnestic response leads to increasing levels of **IgG antibodies** that react with the transfused cells.
- e. **The combination of high antibody levels and large numbers of transfused cells in the circulation may produce readily apparent manifestations.**

- f. The **most common presenting signs are fever, an unexplained fall in the patient's hemoglobin and mild jaundice**, but associated clinical problems are infrequent.
 - g. Hemoglobinuria may occur; acute renal failure is a rare complication. Treatment is rarely necessary, but the patient's urine output and renal function should be followed.
3. Detection of delayed transfusion reactions.
- a. The blood bank may detect a DTR, through serologic findings in patients with no clinical symptoms if more transfusions are ordered.
 - b. The current blood specimen **may have a positive DAT**.
 - c. Positive antibody detection tests and crossmatch incompatibilities might be noted if the antibody has risen to levels which are now detectable in the serum.
 - d. The specimen used for compatibility testing **must be no more than 72 hours old at the time of transfusion if the patient has been transfused or pregnant within the past 3 months**. This practice will detect rapidly developing antibodies that, if missed, might cause **acute HTR** upon subsequent transfusion.
 - e. If a DAT is performed at this time, or is part of a routinely performed autologous control, the presence of antibody-coated transfused cells may be detected even though antibody in the serum is not yet detectable.
 - f. *Elution and identification of the antibody is critical* when the DAT becomes positive in a patient who has been transfused within the previous 2-3 weeks.
 - g. In cases where the DAT is positive but results on testing the patient's serum are negative or equivocal, crossmatching with the RBC eluate may be useful.

J. Delayed Adverse Affects- **Infectious Complications of Blood Transfusions.**

1. Viral Hepatitis

- a. Transfusion-associated hepatitis remains the most frequent serious infectious complication of blood transfusion.
- b. Transmission of hepatitis A virus by transfusion is **extremely rare**.
- c. Hepatitis B transmission has been markedly reduced by mandatory testing for Hepatitis B surface antigen (HBsAg) in donor blood and by eliminating the use of paid blood donors.
- d. For at least 90% of the cases of postransfusion hepatitis, no known virus can be identified as the etiologic agent and these cases have been termed non-A, non-B, non-C (NANBNC) hepatitis.
- e. Many patient will have a mild case of the disease and recover, but 50% may have abnormal liver function tests for *6-12 months after transfusion*.
- f. These liver abnormalities are thought to indicate chronic persistent hepatitis or chronic active hepatitis, which in some cases may progress to cirrhosis and death.

- g. Since there is no reliable test to detect NANBNC hepatitis, prevention depends upon careful screening of donors and **careful follow up of recipients who become infected with hepatitis due to blood transfusion.**
 - h. The blood bank should be given the names of all patients who develop viral hepatitis posttransfusion, “look back”.
 - 1) The blood bank records all donors transfused to the patient and sends this information to the blood supplier.
 - 2) The blood supplier documents all donors as having been involved in a case of posttransfusion hepatitis and will permanently defer donors if it is statistically proven that they are carriers.
2. Cytomegalovirus
- a. Immunosuppressed patients have been recognized to be at high risk for more severe forms of transfusion-induced CMV infections.
 - b. Patients who have undergone bone marrow transplantation may develop fatal CMV interstitial pneumonia.
 - c. CMV is known to be **transmissible by viable leukocytes** in the peripheral blood.
 - d. Significant morbidity and mortality attributable to CMV infection may occur in low birth weight *premature infants born of CMV-seronegative mothers.*
 - e. Many blood centers have developed programs to provide CMV-seronegative units to patients at high risk for CMV infection by blood transfusion.
3. Malaria
- a. There are no practical laboratory screening tests for malaria.
 - b. Although still very rare, the number of cases of transfusion-associated malaria has increased to the highest level in the past 25 years.
 - c. Travel and immigration are among the factors responsible for this increase.
 - d. *Exclusion of donors at high risk* of harboring parasites is the only effective preventive measure.
 - e. All cases of posttransfusion malaria must be reported to the blood bank and blood provider.
4. Babesiosis
- a. Caused by *Babesia* species, ticks are the definitive hosts, and occasional tick-borne human infections have been reported.
 - b. In humans, the organisms multiply in RBCs. Clinical signs following the bite of an infected tick resemble symptoms of malaria. On examination of blood smears one must be careful not to confuse the morphology with malaria.
 - c. *Donors are permanently deferred.*

5. Syphilis

- a. Transmission by transfusion is possible but requires blood be drawn during the brief period of spirochetemia **and** that organisms are viable at the time of transfusion.
- b. Treponemes may survive for 72 hours at 4 C, so transmission can be through components stored at RT or transfused shortly after collection.
- c. Performance of the STS does not prevent transmission because the test is characteristically negative in primary syphilis and most positive STS are due to biologic false positive.
- d. AABB Standards requires STS of donors since a positive test may reflect high risk life style activities.

6. Chagas' Disease

- a. Caused by Trypanosoma cruzi.
- b. Transmitted by the bite of the reduviid bug. The parasite uses the blood stream in life cycle to get to the tissues.
- c. Disease found primarily in Mexico, Central and South America. It is the cause of 30% of adult deaths in Brazil. there have been a few cases reported in Texas and California.

7. Toxoplasmosis

- a. Has been reported as an unusual transfusion complication of immunosuppressed patients.
- b. Clinical illness reported in granulocyte recipients, but is not a problem in routine transfusion practice.

8. Lyme Disease

- a. Caused by the spirochete *Borrelia burgdorferi*, transmitted by ticks.
- b. May be a potential transfusion problem, transfusion related cases have not been reported.
- c. Donors with a history of Lyme disease should be asymptomatic and have completed a full course of antibiotic therapy prior to donating blood.

9. Human Immunodeficiency Virus (HIV)

- a. Initially recognized in late 1979. Most cases have been associated with sexual contact among gay males, IV drug abuse or heterosexual contact with high risk groups.
- b. Initially it was felt that HIV could not be transmitted by blood transfusion, unfortunately this was not the case. The largest population hit by transfusion transmitted HIV has been the hemophiliacs who contracted it through commercially prepared Factor VIII concentrates.

- c. Attempts to prevent transfusion transmitted HIV by the blood providers is based on a *four-point program*:
 - 1) voluntary blood donation
 - 2) careful medical history and physical examination to eliminate high risk donors.
 - 3) a sensitive test for anti-HIV
 - 4) a confidential self-exclusion
- d. Recommendations to reduce the potential spread of HIV through blood transfusion include the following:
 - 1) transfusion of blood and blood components should be given **only for clear medical indications**.
 - 2) blood donors should be carefully screened and individuals in high risk groups should be educated to abstain from donation.
 - 3) autologous transfusion should be employed as widely as possible.

K. Other Delayed Adverse Effects of Transfusion

1. Transfusion Associated Graft-vs-Host Disease (TA-GVHD)

- a. TA-GVHD is a rare, usually fatal, complication following transfusion to patients who are severely immunosuppressed, such as those being intensively treated with chemotherapy and irradiation.
- b. *TA-GVHD occurs if immunocompetent donor lymphocytes engraft and multiply in the bone marrow of a severely immunodeficient recipient. These engrafted donor cells react against the "foreign" tissues of the host-recipient.*
- c. The clinical syndrome of TA-GVHD may include fever, skin rash, hepatitis, diarrhea, bone marrow suppression and infection usually progressing to a fatal outcome.
- d. ***Pretransfusion irradiation of all blood components containing lymphocytes will prevent TA-GVHD.*** The function of RBCs, granulocytes and platelets is not affected by such irradiation. Situations include:
 - 1) cellular components for intrauterine transfusions
 - 2) patients identified as being at risk for TA-GVHD
 - 3) cellular directed donations from relatives
 - 4) transfusion of HLA selected products

2. Posttransfusion Purpura

- a. Posttransfusion thrombocytopenic purpura (PTP) is a rare event, occurring almost exclusively in multiparous women.
- b. A precipitous fall in platelet count produces generalized purpura about a week after a blood transfusion.
- c. Some patients have been shown to have developed a platelet-specific alloantibody, **anti-HPA-1^a** (formerly **anti-Pla¹**). this antigen has a prevalence of 98.3% in the population, so only 1.7% of recipients are at risk of developing the alloantibody.
- d. The antibody destroys not only the transfused HPA-1^a platelets but also the patient's HPA-1^a negative platelets. the mechanism for the destruction of autologous platelets remains the subject of intense investigation.

- e. The thrombocytopenia is usually severe, and if treatment is needed exchange plasmapheresis has been suggested as possible therapy.
- f. The thrombocytopenia is usually *self-limiting* and platelet transfusions are **usually not beneficial**.

3. Iron Overload (Transfusion Hemosiderosis)

- a. Every unit of RBCs contains approximately 200 mg of iron. For chronically transfused patients, such as thalassemics with persistent hemolysis, progressive and continual accumulation of iron in the mitochondria of cells can be dangerous.
- b. *When patients have received more than 100 transfusion, iron deposition may interfere with function of the heart, liver or endocrine glands.*
- c. Treatment is directed at removing iron without unduly reducing the patient's circulating hemoglobin.
- d. Use of neocytes is being investigated, these young RBCs should remain longer in the circulation and thereby decrease the number of transfusions needed.

4. Immunomodulation by Transfusion

- a. Transfusion has been known to modulate immune system responses and have been implicated in other clinical settings, including:
 - 1) Improved renal allograft survival in transfused patients.
 - 2) increased rates of solid tumor recurrences
 - 3) and increased rates of postoperative bacterial infections.
- b. Effects are somewhat controversial and have not been confirmed, but suggests that the relationship between transfusion and the immune system is more complex than previously considered.

L. Records of Transfusion Complications

- 1. Records must be kept of all reports of transfusion complications.
- 2. Patient records should indicate the need for “special” components such as leukopoor, irradiated, CMV negative, antigen negative, etc..
- 3. Cases of transfusion-associated disease (including but not confined to hepatitis B, NANB hepatitis and transfusion associated AIDS) must be reported to the center that drew the blood.
- 4. **Fatalities** resulting directly from transfusion complications (eg, hemolytic reactions or viral hepatitis) must be reported to the FDA within 24 hours followed by written report within 7 days.