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Hemolytic Transfusion Reactions

Part 1: Biological Product Deviations
 (Errors and Accidents)

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Introduction. Acute hemolytic transfusion reactions (AHTRs) are a potentially fatal complication of incompatible blood transfusion. Delayed HTRs (DHTRs) generally are milder and characterized by anemia and hyperbilirubinemia following red cell transfusion. Errors (which the Food and Drug Administration [FDA] now calls biological product deviations) in sample and patient identification account for the majority of both reactions. FDA defines a biological product deviation as a deviation from the agency's current good manufacturing practices, applicable standards, or established specifications that may affect the safety, purity, or potency of a blood product.

The Problem. Hemolytic transfusion reactions (HTRs) typically occur when immunologic incompatibility between transfused donor red blood cells (RBCs) and recipient alloantibodies produces accelerated destruction of transfused cells. Transfusion of ABO-incompatible RBCs to a recipient with the corresponding preformed antibodies is the most common etiology. Complement-mediated intravascular hemolysis is associated with AHTRs and extravascular RBC destruction with DHTRs. AHTRs are the most severe and are a medical emergency requiring rapid identification of the event,

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discontinuation of the transfusion, hydration, and intensive patient monitoring.¹ Clinical symptoms and signs of AHTR vary in severity and may include fever, chills, nausea, vomiting, flank or back pain, dyspnea, hypotension, renal failure, and disseminated intravascular coagulation (DIC). Laboratory findings include hemoglobinemia, hemoglobinuria, and decreased haptoglobin.

Incidence. Blood product deviations in transfusion medicine are not uncommon. Fortunately, most do not produce a clinically unfavorable outcome.² Approximately two-thirds of incorrectly transfused units will be ABO-compatible by chance alone. In one study, only half of the patients known to have received ABO-incompatible RBCs had clinical AHTR.^{3,4}

The true frequency of blood product deviations leading to HTRs is unknown. Underreporting, failure to make the diagnosis, and lack of regulatory requirements to report nonfatal events, or so-called near misses, limit the accuracy of estimates.

Previously, FDA required only transfusion errors associated with a fatality to be reported. However, effective May 7, 2001, FDA will require blood banks and transfusion services that have control over a product when a deviation occurs and the product is distributed to report the deviation.⁵

Hemolytic Transfusion Reactions and Error

- 1 in 19,000 red cell units are administered erroneously; 1 in 1.8 million result in fatality.
- Most result from administration of properly labeled blood to an unintended recipient.
- As little as 30 mL of incompatible blood can be fatal.

Early studies estimated the risk of erroneous administration of blood at 1 in 12,000 units, with resultant fatal AHTR at approximately 1 in 600,000 to 1 in 800,000 units transfused.^{6,7} According to a report from the New York State Department of Health (which requires reporting of transfusion errors), from 1990 to 1999, 1 in 19,000 RBC units were administered erroneously and 1 in 1,800,000 resulted in fatality.⁴

Alternatives to allogeneic RBC transfusion are no less prone to human error. Autologous blood programs, which aim at curtailing negative effects of transfusion (e. g., virus transmission, alloimmunization, and immunomodulation), also are subject to process errors that may result in transfusion of a blood product to other than the intended recipient.^{3,8}

Causes of HTRs. There are multiple causes of AHTRs. Process error - often clerical-associated with ABO - incompatible RBC transfusion is the most common. Sample or patient misidentification at any step in the transfusion process - from phlebotomy, through laboratory handling and testing, to blood issuance and administration - can result in the inadvertent transfusion of incompatible blood. The most commonly reported error is the administration of properly labeled blood to an unintended recipient as a result of failure to accurately identify the blood unit and recipient.^{3,4,6} See Table 1 for other deviations. Of note, administration of as little as 30 mL of incompatible blood can result in fatality.⁴

Accidents, in which no process deviation is identified, also may lead to HTRs. Infrequently, laboratory antibody identification techniques may fail to detect clinically significant antibodies, resulting in an incompatible blood transfusion.⁹⁻¹⁰ Additionally, deliberate transfusion of ABO-incompatible plasma-containing products,

such as plasma and platelets, may occasionally result in HTRs.⁶ Approximately 1 in 6,600 to 1 in 9,000 apheresis platelet preparations derived from group O donors have been associated with acute intravascular hemolysis. Of note, the increasing popularity of apheresis platelets may contribute to such reactions.¹¹ In apheresis platelets, plasma with high titers of anti-A or anti-B is not diluted as it is by the pooling of random donor platelet preparations. Apheresis products often are transfused to patients with a minor ABO compatibility mismatch.

Table 1: Product Deviations Associated with HTRs¹

- Collection of blood from the incorrect patient
- Incorrect labeling of blood samples
- Misidentification of the sample at the blood bank
- Issuance of the wrong unit from the blood bank
- Transfusion of blood to the incorrect patient

Contributing Factors

- Failure to follow SOPs
- Preprinted sample labels
- Patients with similar or identical names
- Sequential patient identifiers
- Verbal and stat orders
- Simultaneous specimen processing from more than one patient
- Manual issuance of blood
- Overriding computer error messages

- Insufficient segregation of units in refrigerators

Product Deviation Investigation. Human error is inevitable. Careful investigation of deviations is necessary to identify process weaknesses and reduce the potential for future error. Identification of the root cause of the deviation is critical in all investigations. For example, determining that a phlebotomist incorrectly labeled a patient's hospital admission blood sample explains how ABO mismatched blood was erroneously transfused during surgery, but serves little to prevent future incidents. The root cause of the mislabeling must be identified. Possible root causes of the mislabeling include: training adequacy; availability, clarity, and comprehensibility of standard operating procedures (SOPs); and situation-specific vs. systemic factors contributing to the deviation. Many transfusion deviations occur as a result of multiple factors.³ Contributing factors commonly associated with transfusion deviations are summarized in Table 1.⁴

Deviation Prevention. Humans will make errors at low levels despite their best efforts to avoid them. Repetitive or mentally unchallenging activities, such as sample and patient identification, are particularly prone to error. Therefore, systems to prevent transfusion deviations must be designed to reduce errors and provide safeguards to handle low levels of expected human error.¹² Many systems incorporate second checks to address these issues, e. g., requiring two individuals to verify unit and patient identification. However, not all second checks are successful - suggesting that the primary approach must be designed carefully.

In the laboratory, process control - a systematic effort to achieve standardization and maintain operational control - is used to limit unintended variation. This is achieved by defining how a process is to be performed in an SOP, validating the

process, providing effective training to individuals involved in the process, and monitoring the process through audits and variance investigation. As most transfusion-related errors occur outside the blood bank, process controls should be extended to include the sample collection and administration arms of the transfusion process.³

Certain system changes appear to be successful. Computerization of patient and sample labeling activities - including on-demand labels, preferably computer-generated and preferably including a bar code - can result in decreased transcription errors.¹³ Preprinted labels are to be avoided.

Future Directions. Fortunately, the incidence of fatal HTRs has declined over time, perhaps due to increased understanding of immunohematology, better antibody identification techniques, improved recognition and treatment of reactions, enhanced quality assurance initiatives, and increased use of automated identification leading to decreased errors.^{13,14} However, errors and accidents resulting in HTRs remain the largest risk to transfusion safety.

The breadth and quantity of transfusion product deviations leading to HTR needs to be better determined. Development of a non-punitive centralized data collection system that could compile and analyze anonymous deviation reports and periodically publish data for the benefit of the transfusion community has been proposed.¹² Such a program could be used to identify common system errors and make transfusion safer.

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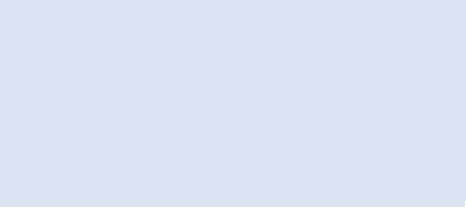


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