Challenges in Blood Group Alloantibody Detection: the Antibody Screen

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Non-ABO alloimmunization: clinical significance

Alloimmunization to non-ABO blood group antigens is a highly relevant issue in laboratory medicine

- About 1-3% of general patients possess such antibodies
- Higher rates (upwards of 40%) reported in chronically-transfused groups

Alloantibodies create issues for transfusion practice

- Delay timely provision of compatible red blood cells (RBCs)
- Increase risks for hemolysis
Transfusion fatalities reported to the FDA, FY2005-13

- Abs associated with fatalities: anti-Jk<sup>a</sup>, -Jk<sup>b</sup>, -K, -E, -c, -C, -Fy<sup>a</sup>, -Fy<sup>b</sup>, -Js<sup>a</sup>, -Js<sup>b</sup>, -S, -N, -V, -Co<sup>a</sup>, -I, HTLA, and others

Chart created with data from (11).
Morbidity & mortality related to challenges in antibody detection

One of the major causes for the high rates of morbidity/mortality observed with non-ABO antibodies is difficulties in their detection.

Three fundamental challenges in antibody detection:
- Alloantibody evanescence
- Transfusion record fragmentation
- Missed opportunities for antibody detection

We will also briefly discuss some strategies to overcome these challenges.
Alloantibody Evanescence

• The disappearance (evanescence) of blood group antibodies over time is a well-known phenomenon to most blood bankers

• A few smaller studies estimated that about one-quarter to one-third of antibodies become undetectable over time

• A more recent investigation was done to better quantify evanescence rates
  • The strategy involved examining only antibodies developed after a transfusion at the study facility
Alloantibody Evanescence

- Nearly half (48.6%, 108/222) of hospital-acquired antibodies disappeared from detection over time
- The more follow-up testing performed, the higher the evanescence rates
- Evanescence was antibody specific
  - Highest rates seen with anti-Jk$^a$

Chart created with data from (5).
Evanescence: A Function of Assay Sensitivity?

- Antibody detection, in large part, can be dependent on the method of testing/screening used

- In general:
  - Tube methods = lowest sensitivity
Evanescence: A Function of Assay Sensitivity

- More recently developed platforms offer greater sensitivity
- Acrylamide gel & solid phase = moderate-high sensitivity

- ELISA & flow cytometry = highest sensitivity
  - These platforms not routinely available in most lab settings
Transfusion Record Fragmentation

- It is not uncommon for patients to be treated at multiple medical facilities

- Patient movement from facility to facility can create risks for alloimmunized patients
  - No robust system for communication of alloantibody info
  - Because of evanescence, this can create ‘fragmentation’ of the transfusion/antibody record
How often do patients seek transfusion at >1 Facility?

23% of patients reported receiving a transfusion at another facility

Charts created with data from (7).
Alloantibody Discrepancies

- 200 alloimmunized patients at Hospital A were extracted from an antibody database.
- Antibody information for these patients was investigated at nearby Hospital B.
- 21% (42/200) underwent a screen at Hospital B.
- 64% (27/42) of these had a discrepancy in records.

Lack of antibody detection was the most common discrepancy.

Chart created with data from (7).
Missed Alloimmunization

- Historical data indicate that it takes about one month before even the most immunogenic antigens (e.g., D, K) can induce a detectable antibody response.

- How often do patients undergo follow-up testing after transfusion?
  - Is this testing adequately timed to detect non-ABO antibodies?
Missed Alloimmunization

- We performed a pilot study examining >550 consecutive transfusions to determine if follow-up testing was done.
- For these RBC transfusions, about a quarter had no follow-up testing.
- Another quarter had follow-up <30 days after transfusion.

Chart created with data from (8).
Conclusions About Challenges to Alloantibody Detection

• Antibodies evanesce (disappear from detection) at rates approaching 65% >5 years after initial development

• Upwards of 25-30% of patients will seek care at multiple facilities, resulting in fragmentation of their records
  • This causes significant antibody record discrepancies

• Real-world blood bank testing is not designed to optimally detect many blood group antibodies
  • Half of RBC transfusions have inadequate follow-up testing
How to overcome antibody detection challenges

• **Evanescence**
  - Provide patients with wallet cards or alert bracelets re: antibody history
  - Develop/utilize higher sensitivity tests

• **Record fragmentation**
  - Obtain transfusion history from patients; contact other hospitals for that history
  - Enroll in (or create) local or regional antibody registries

• **Missed alloimmunization**
  - Promote routine / regular follow-up for transfused patients

• **Prevention of alloimmunization**
  - Provide pheno- or genotyped matched RBCs for transfusion, especially for chronically-transfused groups
References


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