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Challenges in Blood Group Alloantibody Detection: the Antibody Screen

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Non-ABO alloimmunization: clinical significance

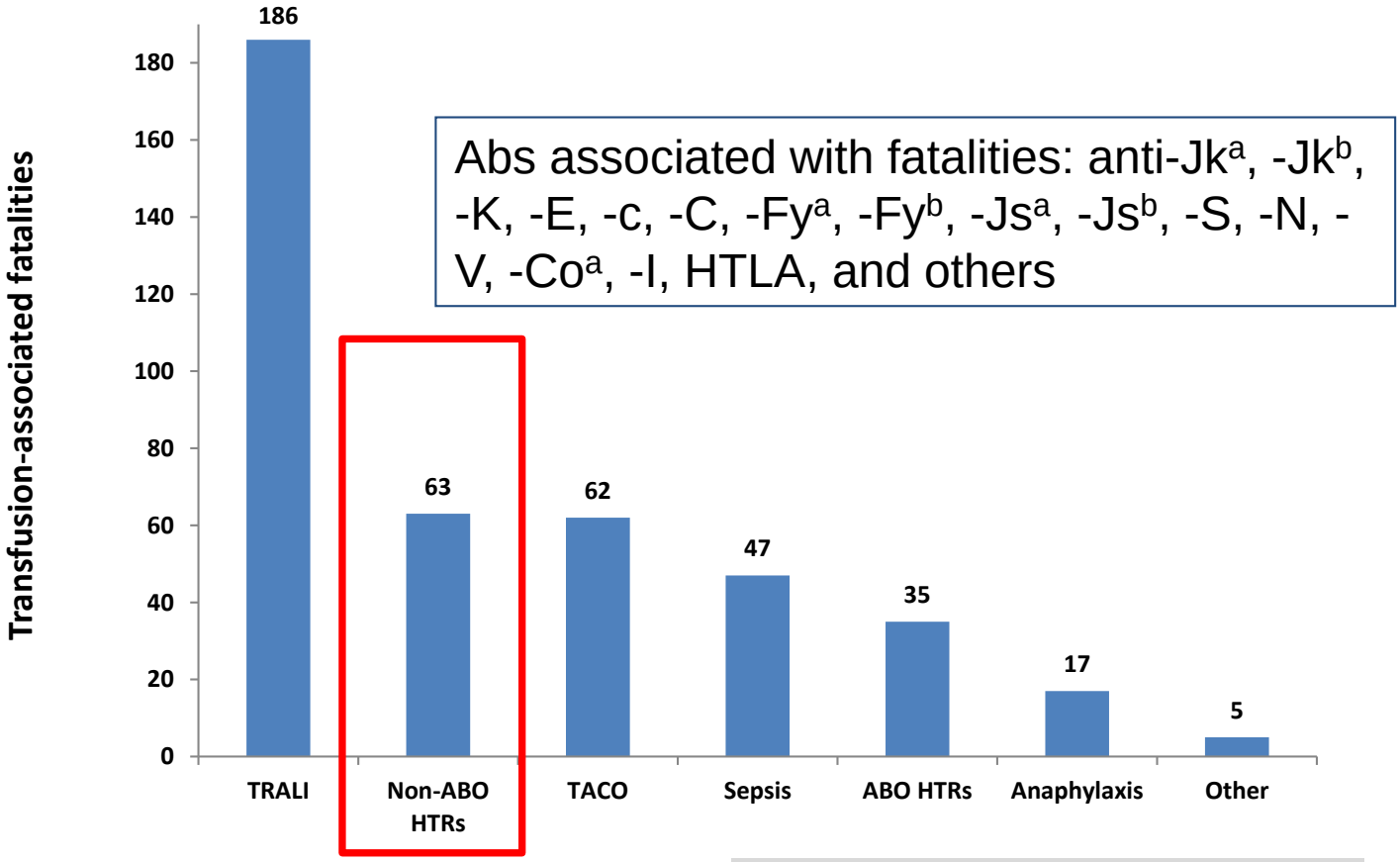
Alloimmunization to non-ABO blood group antigens is a highly relevant issue in laboratory medicine

- 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



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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

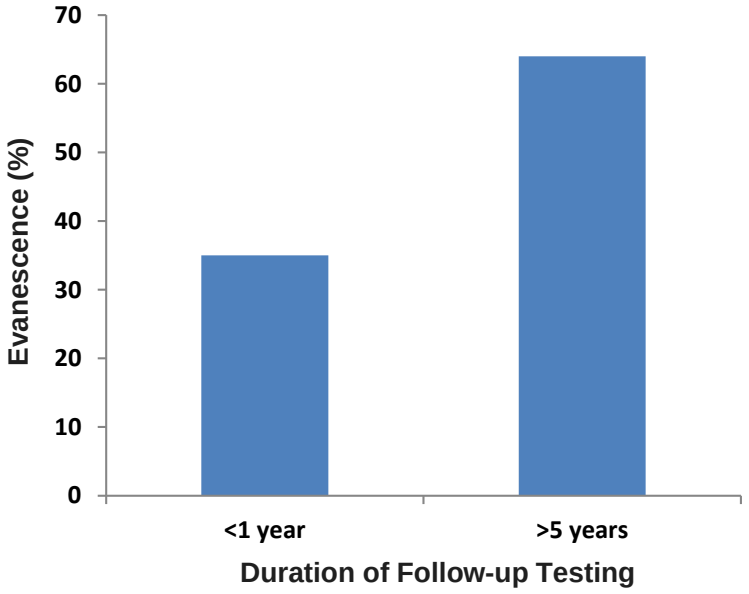
We will also briefly discuss some strategies to overcome these challenges.

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}



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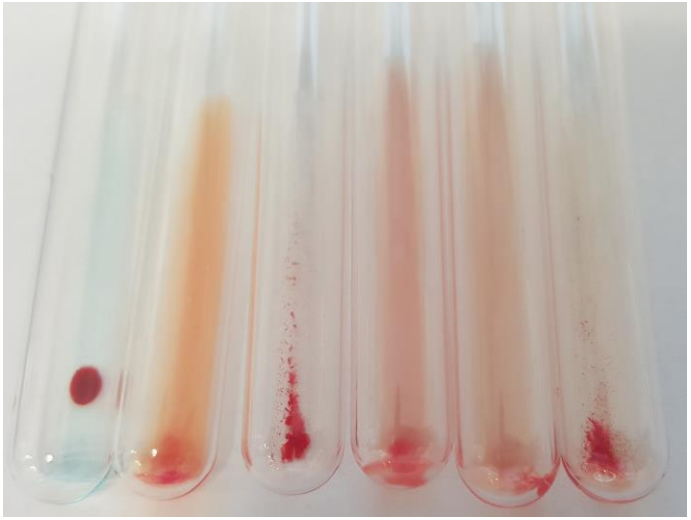
Evanescence: A Function of Assay Sensitivity?

- 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

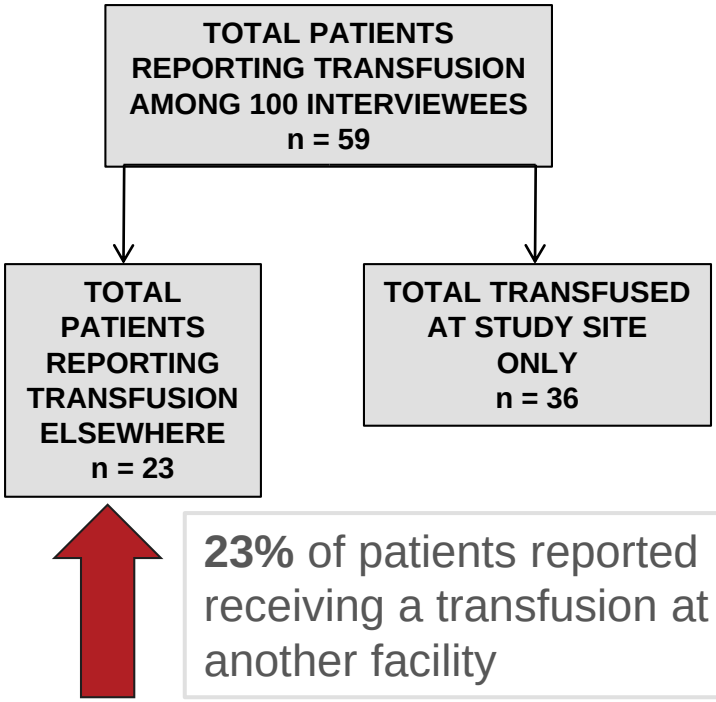
- More recently developed platforms offer greater sensitivity
- Acrylamide gel & solid phase = moderate-high sensitivity

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

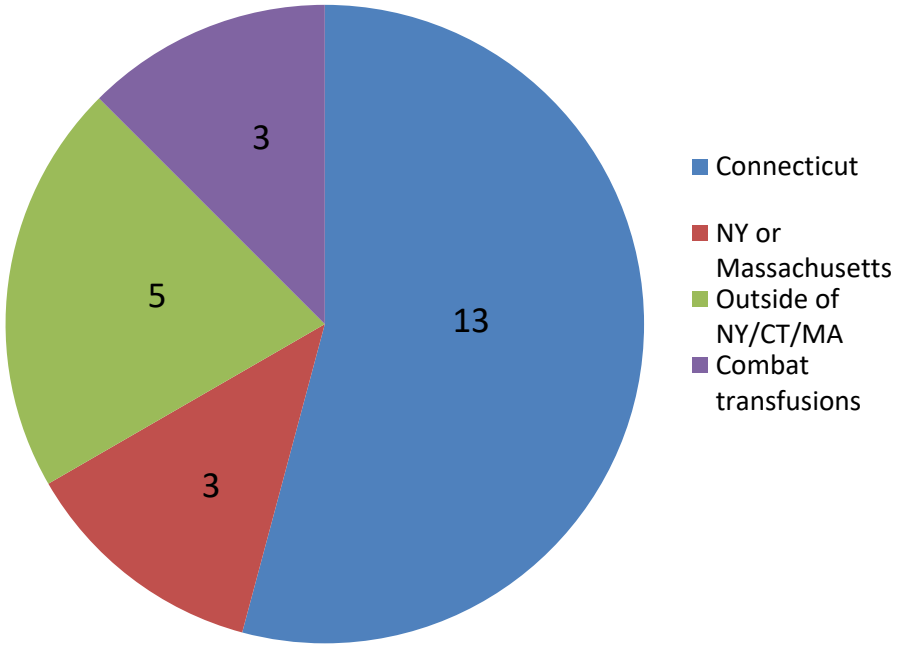
Transfusion Record Fragmentation

- 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?



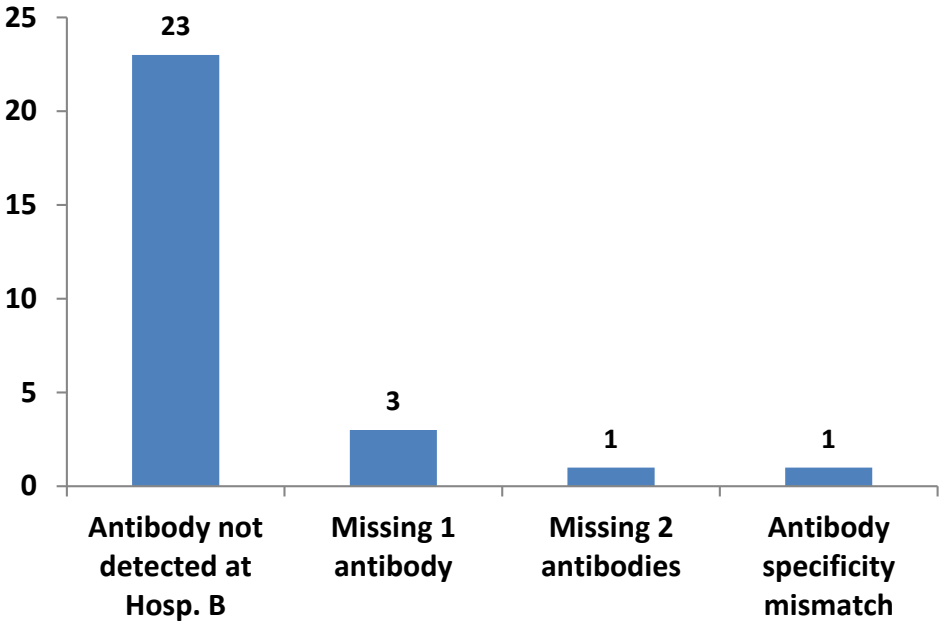
23% of patients reported receiving a transfusion at another facility



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

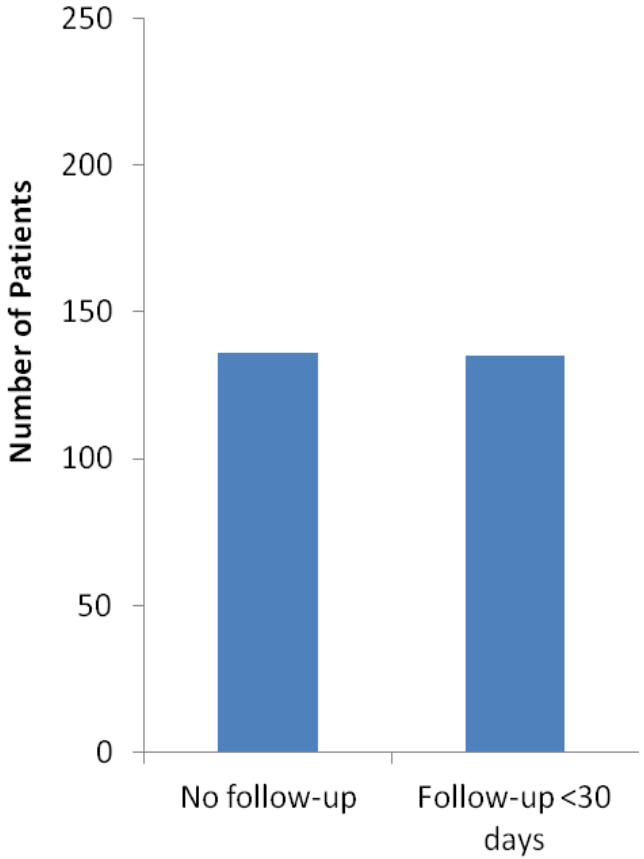


Chart created with data from *(8)*.

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

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Disclosures/Potential Conflicts of Interest

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