



Detecting Anti-D Due to Prophylactic Rhlg Administration Using a Gel-based Antibody Screen: A Quality Issue with Clinical Implications



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Case History:

- A 31 year old RhD negative, pregnant female presented to UC-Davis Medical Center in December 2014 for delivery at full term gestational age
- She received a 300ug Rhlg immune prophylaxis injection in September 2014 at 28 weeks gestational age
- However, her pre-delivery antibody screen was negative (Figure 1E)

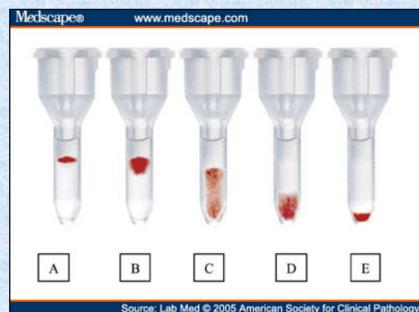


Fig. 1: Graded reactivity on a gel-based antibody screen (uncoated cells fall to the bottom of the gel): A) 4+; B) 3+; C) 2+; D) 1+; E) 0

Measurement of Improvement:

- Cohorts were collected (Table 1) with inclusion criteria:
 - RhD negative women with singleton pregnancies
 - Documented Rhlg administration in the UCDHS
 - No pregnancy complications requiring additional Rhlg
 - Presented to UCDMC at full term gestational age for delivery

Rh negative Mothers Carrying Rh positive babies		N = 87
Negative Antibody Screen at Delivery - Number (percent)	40 (46)	
Average Days between 28 week Rhlg and Delivery (weeks)	85.5 (12.2)	
Follow up Antibody Screens Available - Number (percent)	9 (23)	
Evidence of RhD sensitization on follow up testing (percent)	0 (0)	
Positive Antibody Screen at Delivery - Number (percent)		47 (54)
Average Days between 28 week Rhlg and Delivery (weeks)	77.1 (11.1)	
Follow up Antibody Screens Available - Number (percent)	8 (17)	
Evidence of RhD sensitization on follow up testing (percent)	0 (0)	
Rh negative Mothers Carrying Rh negative Babies		N = 28
Negative Antibody Screen at Delivery - Number (percent)	15 (53.5)	
Average Days between 28 week Rhlg and Delivery (weeks)	87.4 (12.5)	
Positive Antibody Screen at Delivery - Number (percent)		13 (46.5)
Average Days between 28 week Rhlg and Delivery (weeks)	79.6 (11.4)	

Table 1: Characteristics of UCDHS Cohorts Analyzed

Fig. 2: Pre-Delivery Antibody Screen Results in RhD Negative Mothers Carrying RhD Positive (A) and RhD Negative (B) Babies

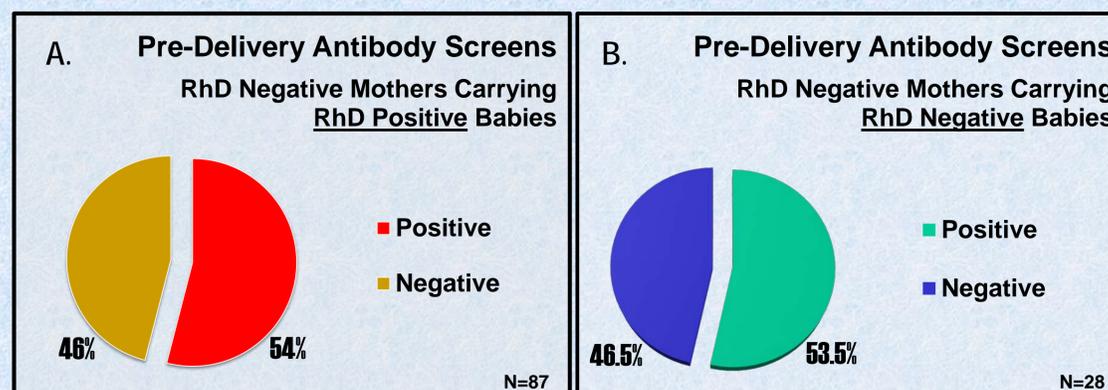


Fig. 3: Estimated Rhlg Detection Durations with Different Testing Methods and Formularies†

Rhlg Formulary	Half-life	Duration with Solid Phase	Duration with Gel Testing	Duration with Tube Testing
RhoGAM	31 days	~159 days	~97 days	~97 days
Rhophylac	20 days	~121 days	~81 days	~61 days
WinRho	24 days	~120 days	~120 days	~72-96 days
HyperRHO	30 days	~150 days	~120 days	~90-120 days

† Unpublished Personal Correspondence from Kael Mikesell, MD

National Guidelines

- ACOG¹
 - The RhD negative woman who is not RhD-alloimmunized should receive anti-D immune globulin at approximately 28 weeks of gestation
- AABB Standard 5.30.2²
 - Women who are pregnant should be considered for Rh immune globulin administration when all of the following apply:
 - The woman's test for D antigen is negative
 - The woman is not known to be actively immunized to the D antigen
 - The RhD type of the fetus/infant is unknown

Lessons Learned:

- Testing methods vary in sensitivity and formularies vary in average duration (Figure 3)
- Duration of Rhlg detection by gel testing is indirectly related to BMI (Figure 4)

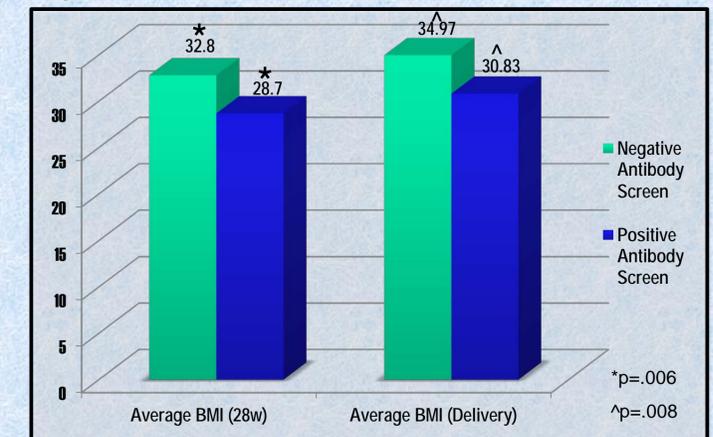


Fig. 4: Duration of anti-D detection due to Rhlg immune prophylaxis correlates indirectly to BMI

Problem:

A Negative Antibody Screen Logically Indicates Prophylactic Rhlg is No Longer Present in the Patient's Plasma

DOES THIS PATIENT REQUIRE ADDITIONAL RHlg ADMINISTRATION PRE-DELIVERY?

Strategy for Change:

- Collect relevant data
- Ask pertinent questions
- Search published literature
- Consult national guidelines



Conclusions:

- Women with an elevated BMI may require a higher dose of Rhlg
 - National guidelines do not currently recommend Rhlg dosing by weight
- A negative antibody screen pre-delivery does not definitively indicate lack of protection by the 28 week Rhlg dose
 - 23% of women delivering Rh positive babies with negative antibody screens pre-delivery had follow up blood bank testing available
 - None were sensitized to RhD

REFERENCES

- ACOG Practice Bulletin: Prevention of RhD alloimmunization. 1999;66(4):63-70.
- Standards for Blood Banks and Transfusion Services 29th Edition. Effective April 2014. AABB Press.