Sanquin

Hyper immunisation of Anti D Donors: The Dutch Experience

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For Life.

Dutch anti-D donors (program stopped in 2020)

- Majority: Women immunised during pregnancy
- A few blood donors with naturally occurring anti-D detected during IEA screening
- Small group of male volunteers, voluntarily immunised in the past

Women immunised during pregnancy

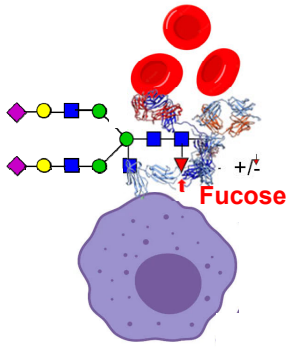
- Below 45 years of age: no hyperimmunization, plasmapheresis for low titer anti-D until >45 years
- > 45 years: If women agree => hyperimmunization program
- Selection of D+ RBCs compatible for other RBC antigens
- Hyperimmunization with small volumes of RBCs 3-4X

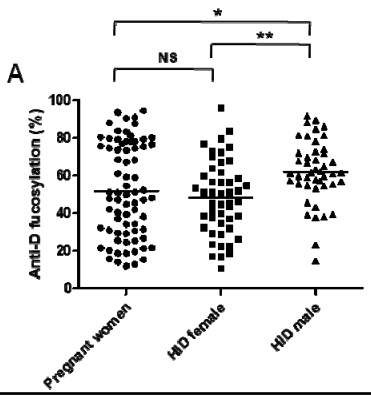
  If titer ≥ 1:512 => high titer donor program
  If titer < 1:512 => low titer donor program

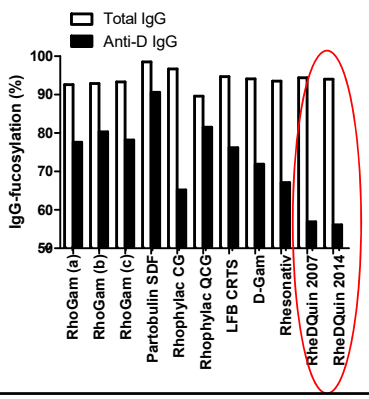
- If titer drops 2 steps or each year: boost with same RBCs

Pregnancy induced anti-D IgG display optimal Fc-fucosylation profile

Kapur R et al. Prophylactic anti-D preparations display variable decreases in Fc-fucosylation of anti-D. Transfusion. 2015;55:553-62



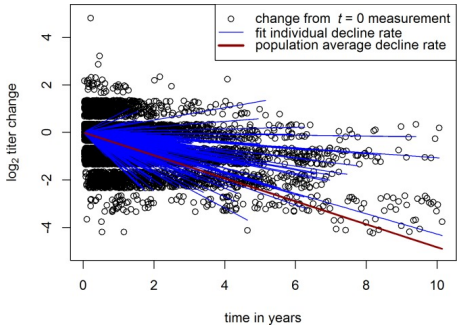




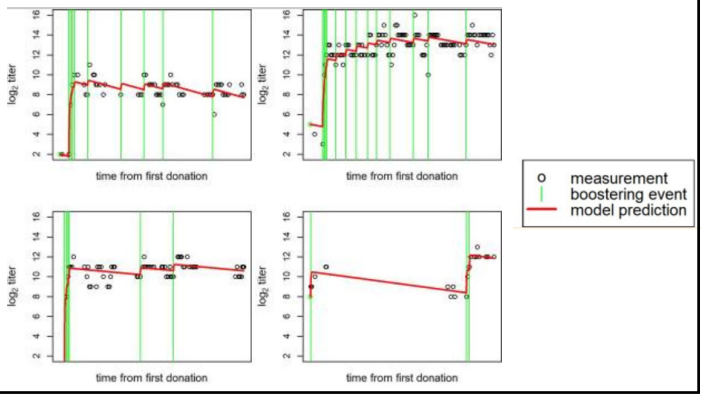
Predicting anti-RhD titers in donors: Boostering response and decline rates are personal

(de Vos A et al. Plos One 2018; 13(4): e0196382)

Naturally antibody decline in the absence of boosts (random effects model)



Four examples of model fits to individual donor titers observed over time



Self sufficiency for the Netherlands?

- 16.000 D negative pregnant women

=> 32.000 vials

- With current immunization program:

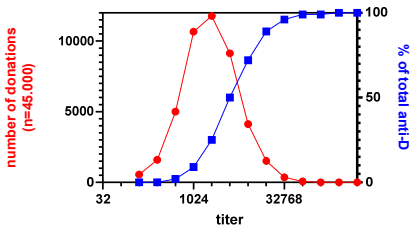
  One plasma donation => 10 vials of 300ug/1000 IU

  => 3200 donations
  average number of donations is 5 / donor

` 640 donors needed

Potential improvements to increase yield

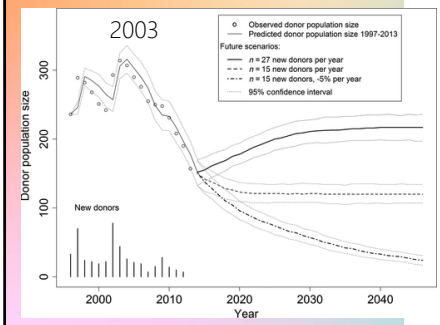
- Donation frequency has not been guided by titers!



60% of donations
titers ≤ 2000
only 25% of total anti-D

  - More frequent plasmapheresis of only donors with highest titers will increase the yield and might even decrease the total number of fereses
- Optimization of hyperimmunization protocol (not evidence based)
- Better timing of plasmapheresis in relation to boost immunization
- Pre-selection of HLA-DRB1*15*01 positive donors

How to sustain anti-D donor pool size?



- Success of immunoprophylaxis => decline in (potential) donors

  (Donors immunized before introduction immunoprophylaxis are now >75 yr)
- Modelling showed that in the Netherlands 27 new donors/year are needed to sustain the donor pool (*van der Hoeven L et al. Prediction of the anti-RhD donor population size for managerial decision-making. Vox Sang 2016 ;111:171-7)*

(57 new immunisations / year in the Netherlands because of failure of prophylaxis)

Facilitators and barriers for RhD-immunized women to become and remain anti-D donors

(Slootweg YM et al. Transfusion 2018;58:960-968

- Questionnaire to women (43-65 yrs) with anti-D antibodies
  - 93 of 134 women (~ **70%) w**ould have considered **to become donors** if they had known about the possibility
- Motivators of being anti-D donors (n=174)
  - Anti-D donors are needed
  - It does not cost me much trouble, and it helps others
  - I want to do something in return
- Negative factors of anti-D donorship (n=174)
  - Time (36%)
  - Travel time (21%)
  - **No negative factor (50%)**

Present situation at Sanquin

- 2020: Decision to stop collection of anti-D plasma because
  - Sanquin Plasma Products did not continue specific IgG plasmaproducts
  - Extra costs for optimization of program
  - No market for relatively small batch of Dutch anti-D plasma

Summary

- For long time the Netherlands have been self-sufficient in collection of anti-D plasma
- Polyclonal anti-D IgG from naturally immunised women might be more effective
- Success of immunoprophylaxis results in decline of potential anti-D donors, BUT:
  - Optimization of hyperimmunization and collection is possible
  - More efforts needed to include highly motivated potential donors