THE HYPER IMMUNIZATION OF ANTI D DONORS IN THE US - FROM KEDRION PERSPECTIVE

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KEDRION
BIOPHARMA

Keep Life *Flowing*

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MEETING AGENDA

KEDPLASMA
UNITED STATES
a Kedrion Biopharma company

1. INTRODUCTION
2. UNDERSTANDING ANTI-D PLASMA & DONOR IMMUNIZATION
3. RISKS & BENEFITS
4. CURRENT PRACTICES AND REGULATIONS
5. IMMUNIZATION PROTOCOLS AND PROCEDURES
6. SUCCESS STORIES
7. MAIN TAKEAWAYS

THE SPEAKER

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CINDY HORTON
Manager, Specialty Programs

Industry experience

- More than 40 years

Discover of Anti-D impact

- As Center Manager, from a donor's story

Motivation

- Save lives

SUPPLY-DEMAND BALANCE FOR ANTI-D PLASMA AND THE GROWING NEED OF DONOR PARTICIPATIONS

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Plasma containing the Anti-D antibody is the only source for manufacturing the medications

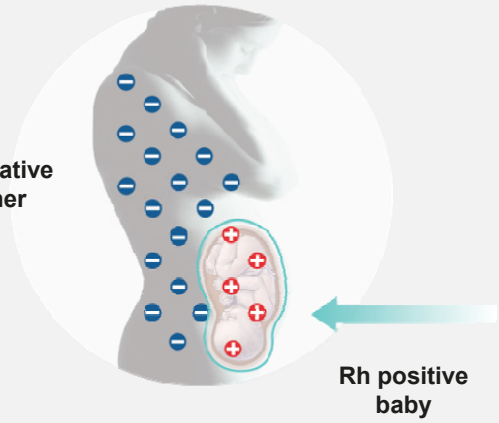
The **medications are doing their job** by preventing mothers from developing the Anti-D antibody

With more volume of medications, more women can have access to the **Anti-D prophylaxis**

Wider prophylaxis leads to **less availability of naturally sensitized donors**

Immunization of Rh- males or sterile females with Rh positive cells in hopes of developing the D antibody and ultimately collecting their plasma to sustain the Anti-D plasma demand.

WHAT IS RH-SENSITIZATION



Rh-sensitization
Occurs when an Rh negative mother's immune system reacts to her Rh-positive baby's red blood cells

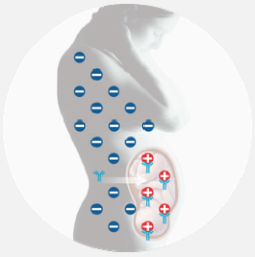
RH-SENSITIZATION AND HDFN

HDFN: hemolytic disease of the fetus and newborn

The baby's Rh positive red blood cells enter the mother's bloodstream

The mother produces antibodies against the baby's red blood cells

These antibodies do not typically affect the first baby



If a future baby is Rh positive, the mother's antibodies will try to destroy the baby's red blood cells, **putting the baby at risk for HDFN**

THE IMPACT OF HDFN

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HDFN is a serious and often fatal condition

1968
Introduction of anti-D

Prior to 1968

1%
As many as 1% of babies were **born with HDFN**

40%
Up to 40% of HDFN cases **were fatal**

THE ANTI-D BREAKTHROUGH

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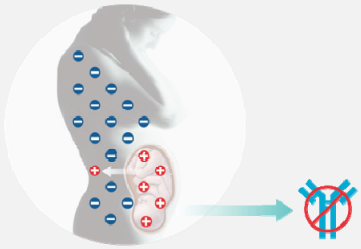
1968: RhoGAM becomes the **first and only** anti-D product available to **prevent Rh-sensitization**

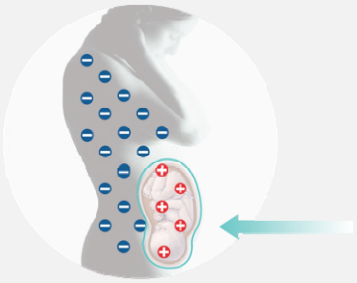
Dr. John Gorman
Columbia University
Blood Bank Director

Dr. Vincent Freda
Columbia University
Obstetrician

HOW ANTI-D MEDICATIONS WORKS

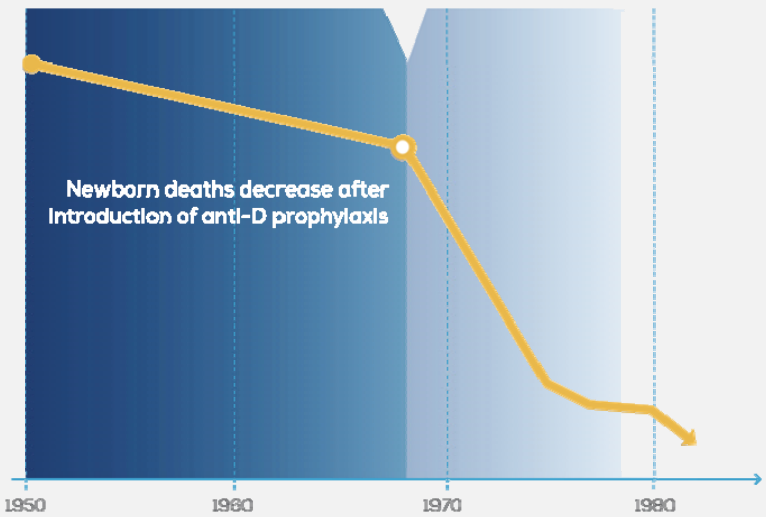


Anti-D medications prevent the mother from making antibodies against her Rh positive baby's blood cells



As long as the Rh negative mother receives Anti-D medications appropriately during every pregnancy, her babies are at very low risk of developing HDFN

A REVOLUTION IN OBSTETRICAL CARE



KEDRION'S PERSPECTIVE ON ANTI-D

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Plasma supply in US (KEDPLASMA)

70 centers in US

5 centers in New York, Alabama, Florida, Ohio and Georgia **collecting anti-D plasma**

3 centers in New York, Alabama and Florida actively immunizing donors through the **DENOVO Program**

Production of Medications

- **RhoGAM** is produced in a US facility
- **IMMUNORHO** is produced in IT facility

DEVELOPMENT PLAN

Extend the **Immunization Program (DENOVO)** and the collection of anti-D to other US centers of the KEDPLASMA fleet

Extend the list of Countries in which the IMMUNORHO is registered

THREATS FOR THE ANTI-D SUPPLY-DEMAND

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To sustain the demand of Anti-D medications the Program is facing several challenges:

Covid-19 hit the Anti-D Donor Base → reduction greater that 25%

Subject enrollment in the immunization program is possible only if meeting several requirements, of which the more stringent are:

- the **Rh-negative blood type** → about 15% of the population [*]
- **age** between **18y and 66y old** (people over the age of 66 require physician approval)
- **women** must be **no longer of child bearing age** or are surgically **no longer able to bear children**

Immunization response is an individual characteristic. Some recipients of red cells produce high antibody levels without excessive immunization and others may not produce antibodies at all.
→ historical conversion rate 30-35%

Once converted, the process of donor potency stabilization could take up to 12 months

OPPORTUNITY FOR THE PEOPLE TO CONTRIBUTE BY ENROLLING IN THE IMMUNIZATION PROGRAM

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BENEFIT FOR ANTI-D DONOR

Minimized risks of immunization and boosting through a continued optimization of **safety measures** and **protocols**

Provide visibility to the donor of the immunization process and the Red Blood cells used for the injections

When **qualified a donor** can :

- donate up to 2 times per week → 104 times per year
- be compensated for the time
- *enable moms to helps their babies*

FREQUENTLY ASKED QUESTIONS

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1. **Is it safe?**

   Yes, all equipment used is sterile and disposed of after each use. Several Rho (D) Immune Globulin donors have been participating in the anti-D donor program for more than 35 years.

2. **Will I need more injections after the antibody is made?**

   Yes, in order to keep your antibody at an acceptable level to donate recurring injections are necessary.

3. **Is the antibody harmful to my body?**

   No, the Anti-D antibody will not harm your body. However, if you were to be given an Rh positive blood transfusion the antibody could cause a transfusion reaction. This occurrence is highly unlikely since all donor blood is typed for presence of Rho (D) antigen and all patients are screened for the presence of the antibody.

   If you decide to participate, we congratulate you for your commitment to help produce this very valuable and increasingly needed product known as Rho (D) Immune Globulin. As you can imagine, fewer Rh-negative women have problems with Rh disease, because of donors like you.

CURRENT PRACTICES AND REGULATION FOR ANTI-D IMMUNIZATION IN US

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FDA Regulation regarding the Immunization process:

Test for prospective recipients: ABO; Rh (D) blood groups and phenotypes for 13 Red Cell antigens.

Red Cells used for immunization will be compatible with the recipient's red blood cells as possible, except for the antigen (D) necessary to elicit the intended antibody response. Antigens considered essential for compatibility are A, B, D, C, E, c, e, K and Fya .

For the immunization of person without Anti-D antibodies (DENOVO), the **maximum volume** of packed red cells to be used for immunization for Anti-D (Rho) shall not exceed **50ml within four months period**

To person with pre-existing antibodies (boosting procedure to stabilize donor potency) the **maximum volume** of packed red cells to be administered is **4.0ml in a single injection**. This volume may be administered **up to 5 times in a single month** but may **NOT exceed 40ml of packed red cells within any 6-month period**.

Over +40 years of experience, KEDPLASMA has developed **best practices** to tailor the immunizations and boosting procedure around the **individual response** while meeting all requirements from FDA Regulation

IMMUNIZATION PROTOCOLS AND PROCEDURES

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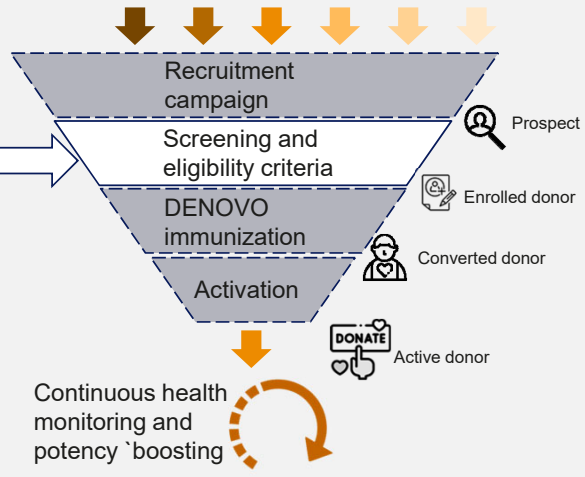
FULL LIST OF REQUIREMENTS

- Rh- negative blood type
- Cannot donate whole blood or plasma at another facility while on the Program
- Meet the requirements to be a Source Plasma donor
- Women must be **post-menopausal or sterile**
- Have a commitment to the program and plan to stay in the area as this is not a short term or temporary process

FUNNELING FOR DONOR RECRUITMENT



MAIN TAKEAWAYS

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- •Anti-D medications are the key for prophylaxis and prevention of Rh-sensitization which can lead to HDFN
- Plasma with Anti-D antibodies is the only source for producing these medications
- Immunization of donors is the only way to sustain the supply of Anti-D plasma
- The immunization of donors is a stringent process due to the requirements and the individual response
- With many years of experience, procedures and best practices have been developed to minimize the risks
- Donating Anti-D plasma is personally rewarding and a powerful way to impact the life of people in needs

How can you can help?
'Share knowledge and help recruit donors for participation.
Together, we can make a life-saving impact!"