

RHOCLONE

# Rh Incompatibility

The Role of Rho(D) Immune Globin (RhIG)



# Rhesus Factor

- The term **Rhesus (Rh) blood group system** refers to the 5 main Rhesus antigens (C, c, D, E and e) as well as the many other less frequent Rhesus antigens.
- The terms **Rhesus factor** and **Rh factor** are equivalent and refer to the **Rh D antigen** only.
- Individuals either have, or do not have, the **Rhesus factor** (or Rh D antigen) on the surface of their red blood cells.

# Basics Of Rh Factor

Mother  
Rh-ve

Father  
Rh+ve

Child  
50% chances of  
Rh+ve



## Facts behind Rh Factor .....

- When Mother is Rh-ve, Father is Rh+ve and Baby is Rh+ve
- The fetal RBCs are separated from the mother's circulation by the layer of cells in the placenta called trophoblast.
- However during late pregnancy and especially during childbirth the fetal RBCs may escape into mother's circulation
- Once these cells reach the mother's circulation, they are perceived as an antigen and thus can provoke an antibody response





# Rh factor causes HDN

- Antibodies to fetal RBCs are not usually made before first childbirth
- Repeated pregnancies provoke high antibody levels in the mother
- Maternal IgG antibodies can cross the placenta and reach the fetal circulation
- They react with fetal RBCs and cause their destruction and eventually death





# DANGERS OF HDN

## **BEFORE BIRTH**

- Antibodies cause destruction of the red cells
- Anemia – reduction in number of RBCs
- Heart failure
- Fetal death

# DANGERS OF HDN

## AFTER BIRTH

- Antibodies cause destruction of the red cells
- Anemia – reduction in number of RBCs
- Build up of bilirubin – yellowish pigment in bile
- Jaundice
- Hepatomegaly – enlargement of liver
- Splenomegaly- enlargement of spleen
- Kernicterus – parts of brain and spinal cord are infiltrated with bilirubin
- Severe retardation
- Heart failure



# WHAT IS FMH?

- FMH is fetomaternal hemorrhage
- FMH means the amount of blood passing from the fetus to the mother
- FMH can be calculated by the Kleihauer Betke test





# How Does FMH take place???

A reduction in red blood cells leads to anemia, a condition marked by weakness and fatigue. Severe anemia can lead to heart failure and death. The breakdown of red blood cells also causes the formation of bilirubin, the build up of which can lead to jaundice and possibly brain damage.



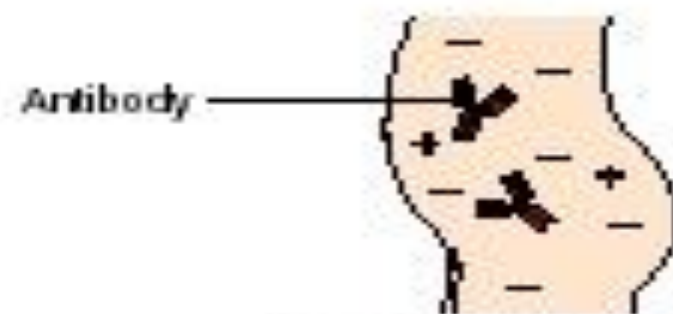
An Rh positive father and Rh negative mother may conceive an Rh positive baby.



In a subsequent pregnancy with an Rh positive baby there is the risk that it will develop Rh disease. Even though the blood circulation of the mother is separate from that of the child, the antibodies in her system can cross the placenta, enter the bloodstream of the baby, and cause its red blood cells to be killed.



This usually isn't a problem if it's the mother's first pregnancy with an Rh positive child, because her blood circulation is separate from that of the baby.



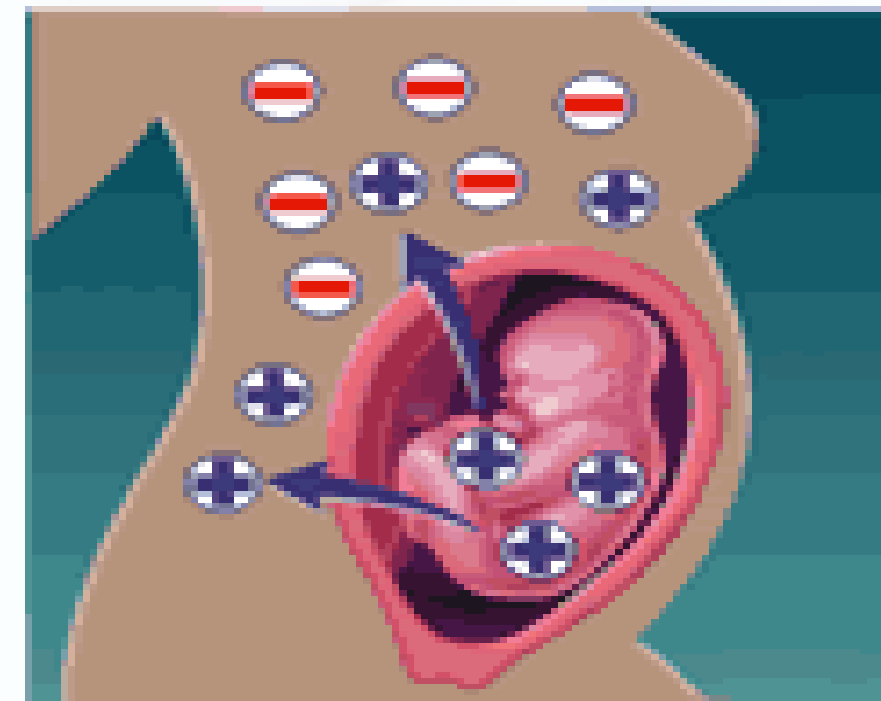
The mother's immune system recognizes the cells as foreign and develops antibodies against them.



At birth, or after an abortion or miscarriage, Rh positive blood cells from the baby enter the mother's bloodstream.

# What is FMH

- Fetomaternal hemorrhage (FMH) is a common occurrence most often associated with small volumes of blood transferred across the placenta.
- Fetomaternal hemorrhage leads to sensitization of Rh D-negative mothers, resulting in an increased risk of hemolytic disease of the newborn.
- FMH can be calculated by the Kleihauer Betke test



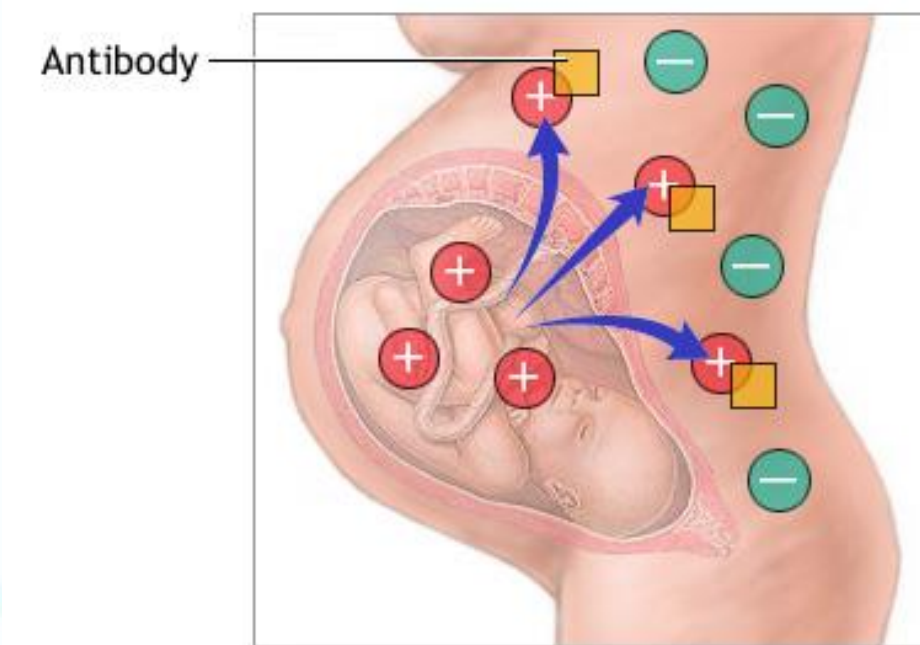
## IS POSTPARTUM IMMUNIZATION ENOUGH?

- 1.6-1.9% of Rh negative women become immunized inspite of postpartum administration of anti D
- This is due to a large amount of FMH at delivery or during pregnancy
- The FMH during pregnancy is called as silent bleed.
- This could happen due to abdominal trauma, injury etc during pregnancy
- 3% of pregnant women have FMH in the first trimester, 12% in the second and 45% in the third



## HOW TO TAKE CARE OF SILENT FMH?

- A single injection of 300 mcg of anti D at 28 weeks gestation provides protection for 12 weeks
- A further injection of 300 mcg within 72 hrs of delivery of Rh positive infant will protect most non immunized Rh negative mothers
- This is known as antepartum prophylaxis
- 300 mcg of anti D neutralizes ml of positive red cells or 30 ml blood





# What Is Anti-D?

- Anti- D is an antibody against D Epitope present on fetal RBC, so as to prevent the Rh –ve women from sensitization.







# What Is Monoclonal Antibody???

- Highly specific antibodies against single antigenic epitope produced by the clone of a single hybrid cell formed in the laboratory by the fusion



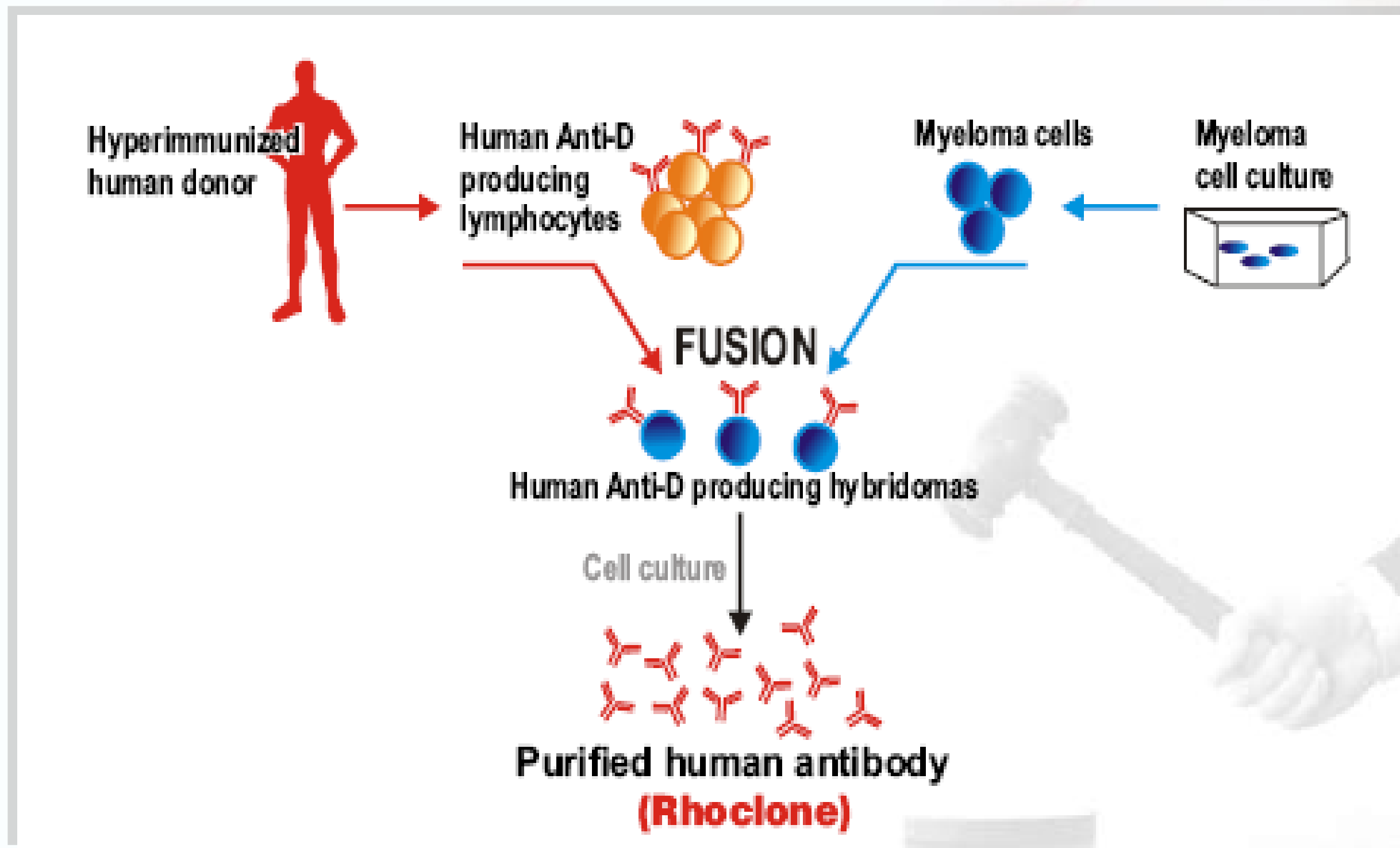


# What Is Rhoclone???

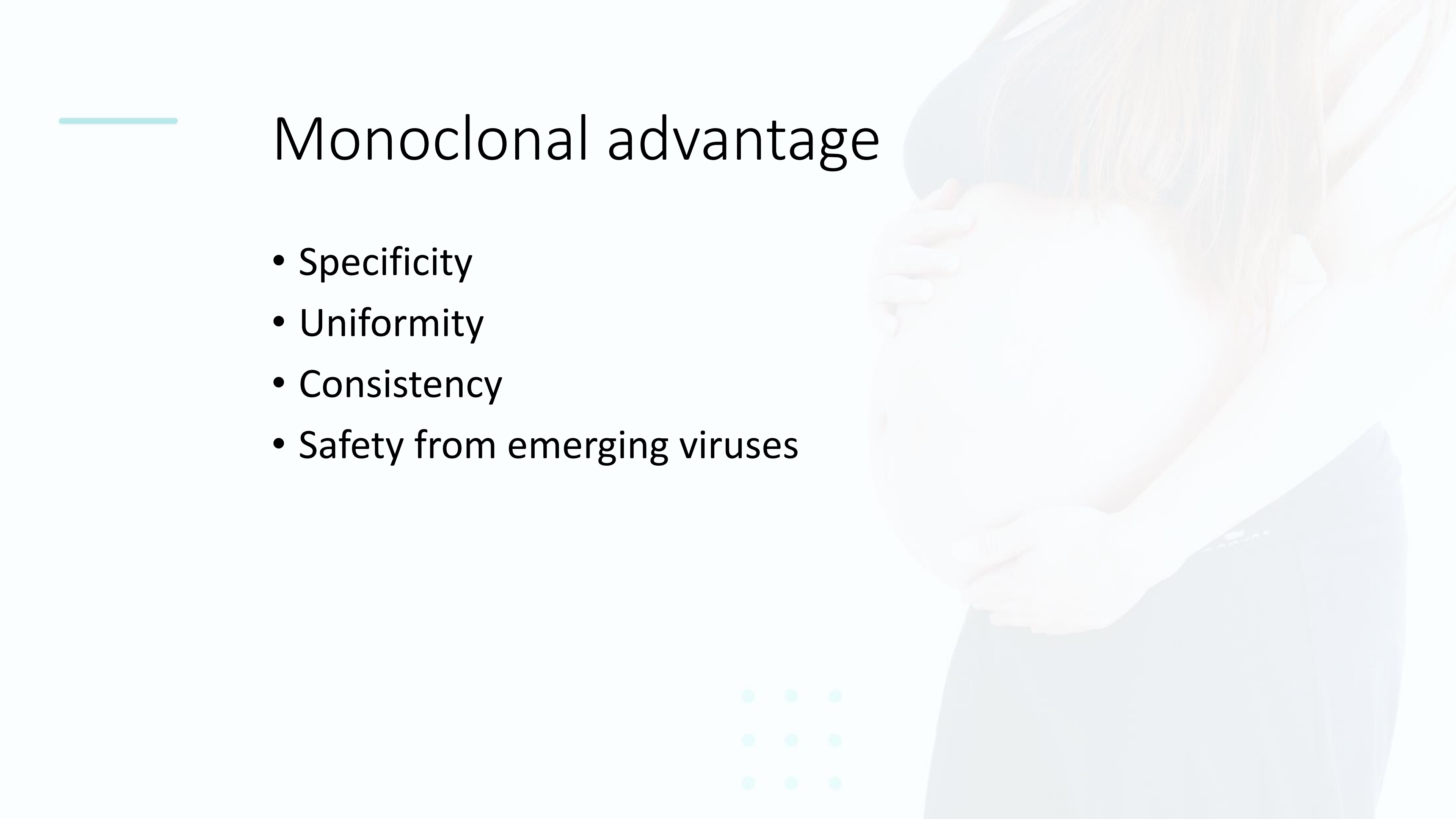
- MONOCLONAL Anti- D Immunoglobulin highly specific against D epitope on Fetal RBC



# Manufacturing Process







# Monoclonal advantage

- Specificity
- Uniformity
- Consistency
- Safety from emerging viruses





## Efficacy

- Rate of red cell clearance – The ability of Rhoclone to clear the D positive RBCs through the spleen.
- The study proves that specificity for RHOCLONE is only for sensitized cells and not for non sensitized RBCs. There is complete clearance of sensitized RBCs from spleen within 3 hrs of administration of RHOCLONE





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## USPs

- No donor pool involved
- No risk of emerging viruses
- No lot to lot variation
- Unlimited supply
- Consistency & uniformity assured



# INDICATIONS



- Prevention of HDN
- Antenatal prophylaxis of HDN
- Termination of pregnancy
- Miscarriage
- Abdominal trauma
- External cephalic version
- Ectopic pregnancy

*20 mcg of anti D neutralizes 1 ml of Rh positive cells or 2 ml of positive blood*

# Guidelines





# FIGO/ICM guidelines for preventing Rhesus disease: A call to action

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## Abstract

The introduction of anti-Rh(D) immunoglobulin more than 50 years ago has resulted in only a 50% decrease in Rhesus disease globally owing to a low uptake of this prophylactic approach. The International Federation of Gynecology and Obstetrics, International Confederation of Midwives, and Worldwide Initiative for Rhesus Disease Eradication have reviewed current evidence regarding the utility of anti-Rh(D) immunoglobulin. Taking into account the effectiveness anti-Rh(D), the new guidelines propose adjusting the dose for different indications and prioritizing its administration by indication.

## KEYWORDS

Anti-D immunoglobulin, FIGO, Guidelines, International Confederation of Midwives, Prophylaxis, Rhesus disease, Worldwide Initiative for Rhesus Disease Eradication

# FIGO/ICM guidelines for preventing Rhesus disease: A call to action

## HIGH PRIORITY

- Determine the maternal Rh factor, preferably in early pregnancy.
- For Rh(D)-negative women, determine the Rh factor of the newborn from umbilical cord blood.
- Administer anti-Rh(D) immunoglobulin within 72 hours of delivery to women with a Rh(D)-positive newborn, unless already sensitized.
- Use a dose of 500 IU (100 µg) of anti-Rh(D) immunoglobulin; if affordable and with sufficient supply, 1500 IU (300 µg) may be given, as is common in high-income countries. The intramuscular route is as effective as the intravenous route.



- Visser GHA, Thommesen T, Di Renzo GC, Nassar AH, Spitalnik SL; FIGO Committee for Safe Motherhood, Newborn Health. FIGO/ICM guidelines for preventing Rhesus disease: A call to action. Int J Gynaecol Obstet. 2021;152(2):144-147. doi:10.1002/ijgo.13459



# FIGO/ICM guidelines for preventing Rhesus disease: A call to action

## MIDDLE PRIORITY

- Routine anti-Rh(D) prophylaxis during pregnancy: 1500 IU (300 µg) at 28-34 weeks.
- Anti-Rh(D) immunoglobulin prophylaxis (500 IU; 100 µg) after a surgical abortion or ectopic pregnancy (all gestational ages), or after spontaneous or medical abortion/miscarriage after 10 weeks.
- Anti-Rh(D) prophylaxis after bleeding, abdominal trauma in pregnancy, and/or fetal death (500 or 1500 IU; 100 or 300 µg) during the second or third trimester. Kleihauer-Betke test can be used to estimate the optimal dose.

## LOW PRIORITY

- Anti-Rh(D) prophylaxis after amniocentesis, chorionic villus sampling, or external cephalic version (500 IU; 100 µg).

- Visser GHA, Thommesen T, Di Renzo GC, Nassar AH, Spitalnik SL; FIGO Committee for Safe Motherhood, Newborn Health. FIGO/ICM guidelines for preventing Rhesus disease: A call to action. Int J Gynaecol Obstet. 2021;152(2):144-147. doi:10.1002/ijgo.13459



## Rhesus isoimmunization: An underappreciated reproductive risk

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Leaders in obstetrics practice from various African countries met towards the end of last year to discuss the unmet need to address the burden of Rhesus disease. They noted that, despite being entirely preventable, Rhesus disease was identified as one of the roadblocks to achieving maternal universal health coverage. The team recommended all stakeholders to facilitate access to anti-D immunoglobulin and screening tools for widespread screening and treatment.

# Latest Tanzania MOH recommendations on Rh disease - 2021

MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT,  
GENDER, ELDERLY AND CHILDREN

## STANDARD TREATMENT GUIDELINES AND NATIONAL ESSENTIAL MEDICINES LIST FOR TANZANIA MAINLAND



THE UNITED REPUBLIC OF TANZANIA

### Investigations

- Maternal Blood group+ Rhesus factor
- Paternal blood group+ Rhesus factor
- Infant Cord blood at delivery for grouping, FBC, Coombs test to detect maternal antibodies and Total Billirubin

### Prevention of Rhesus isoimmunisation

If the mother is Rhesus negative give

**C:** anti D immunoglobulin 300microgram within 72hours of delivery

#### Antepartum

**C:** anti D immunoglobulin (IM)at 28-32weeks of gestation

#### Abortion in Rhesus negative mother give

**C:** anti D immunoglobulin 100microgram (IM) within 72hours of abortion

# Latest Uganda MOH recommendations on Rh disease - 2022

## Essential Maternal and Newborn Clinical Care Guidelines for Uganda

May 2022



### Investigations to Ensure the mother is “Fit for Labour”

- Blood haemoglobin level
- Blood grouping and cross-matching and Rhesus factor (for high-risk mothers)
- Urinalysis: protein, sugar and acetone

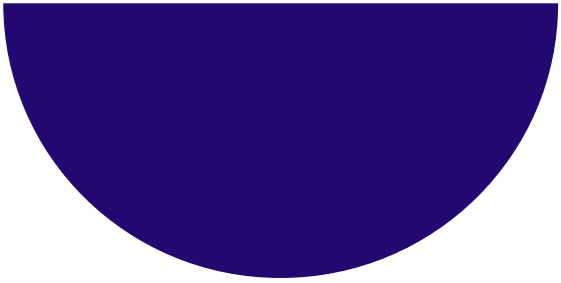
### Gestational age 26-37 weeks

- Rhesus negative mothers should receive anti-D immunoglobulin 300mg

# Conclusion

- Rh isoimmunization is a real problem and real efforts need to be made to mitigate its impact
- Although its incidence has decreased dramatically, yet the consequences of haemolytic disease of the newborn remain.
- Every woman of childbearing age should have her ABO and Rh types done at first contact
- Obtain the ABO/Rh types for husbands of women found to be Rh-negative.
- Even today a larger number of women, who should be protected against Rh immunization, are not receiving Anti- D.





THANK

YOU