THE GLOBAL BURDEN OF Rh DISEASE

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CENTRE OF PERINATAL AND REPRODUCTIVE MEDICINE
UNIVERSITY OF PERUGIA, PERUGIA ITALY

International Federation of Gynecology and Obstetrics

FIGO Mission

- The International Federation of Gynecology and Obstetrics (FIGO) is a unique organization, being the only international professional body that brings together **135 obstetrical and gynecological associations** from all over the world.

- FIGO is dedicated to the improvement of women's health and rights and to the reduction of disparities in health care available to women and newborns as well as to advancing the science and practice of obstetrics and gynecology. The organization pursues its mission through advocacy, programmatic activities, capacity strengthening of member associations and **education and training**.

FIGO Committees and their Chairpersons

- Capacity Building in Education and Training (Ernesto Castelazo Morales, Mexico)
- Ethical Aspects of Women´s Health (Frank A Chervenak, USA)
- Fistula and Genital Trauma (Ajay Rane, Australia)
- Gynecologic Oncology (Neerja Bathla, India)
- Menstrual Disorders (Rohana Hathtootuwa, Sri Lanka)
- Reproductive Medicine, Endocrinology and Infertility (Edgar Mocanu, Ireland)
- **Safe Motherhood and Newborn Health (Gerald H A Visser, the Netherlands)**
- Urogynecology and pelvic Floor (Tsung-Hsien Su, Taiwan)
- Women´s Health and Human Rights, WHHR (Chiara Benedetto, Italy)
- **NCDs and Maternal Offspring Health (Moshe Hod, Israel; Mark Hanson, UK)**

FIGO Working Groups and their Chairpersons

- Adolescent, Pre-conception and Maternal Nutrition (Mark Hanson, UK)
- Breast Disease (Sven Becker, Germany)
- **Challenges in the Care of Mothers and Infants During Labour and Delivery (Roberto Romero, USA)**
- Contraception (Jill Sheffield, USA)
- **Good Clinical Practice in Maternal-Foetal Medicine (Gian Carlo Di Renzo, Italy)**
- Hyperglycemia in Pregnancy (Moshe Hos, Israel)
- **Preterm Birth (Joe Leigh Simpson, USA)**
- Reproductive and Developmental Environmental Health (Linda Giudice, USA),
- Violence against Women (Diana Galimberti, Argentina)

FIGO

International Federation of Gynecology and Obstetrics

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FIGO Committees

FIGO's Committees reflect a continued deter
the health and wellbeing of women worldwide
obstetrics.

This section is in the process of being upd

- Capacity Building in Education and Training
- Ethical Aspects of Human Reproduction and
- Fistula
- Gynecologic Oncology
- Menstrual Disorders
- Reproductive Medicine
- Safe Motherhood and Newborn Health
- Women's Sexual and Reproductive Rights

Inaugural meeting:
May 3-4 2016
London

Chair: Gerard H.A.Visser (Nls)
Past Chair: Will Stones (UK/Keynia)
Diogo Ayres-de-Campos (Port)

Gerhard Theron (SA)

Middle & Far East:
Answar Nassar (Lib)
P.K.Shah (India)
Luming Sun (China)

America's:
Eytan Barnea (USA)
Maria F.Escobar (Col)
Isabel Lloyd (Pan)
Wanda Nicholson (USA)

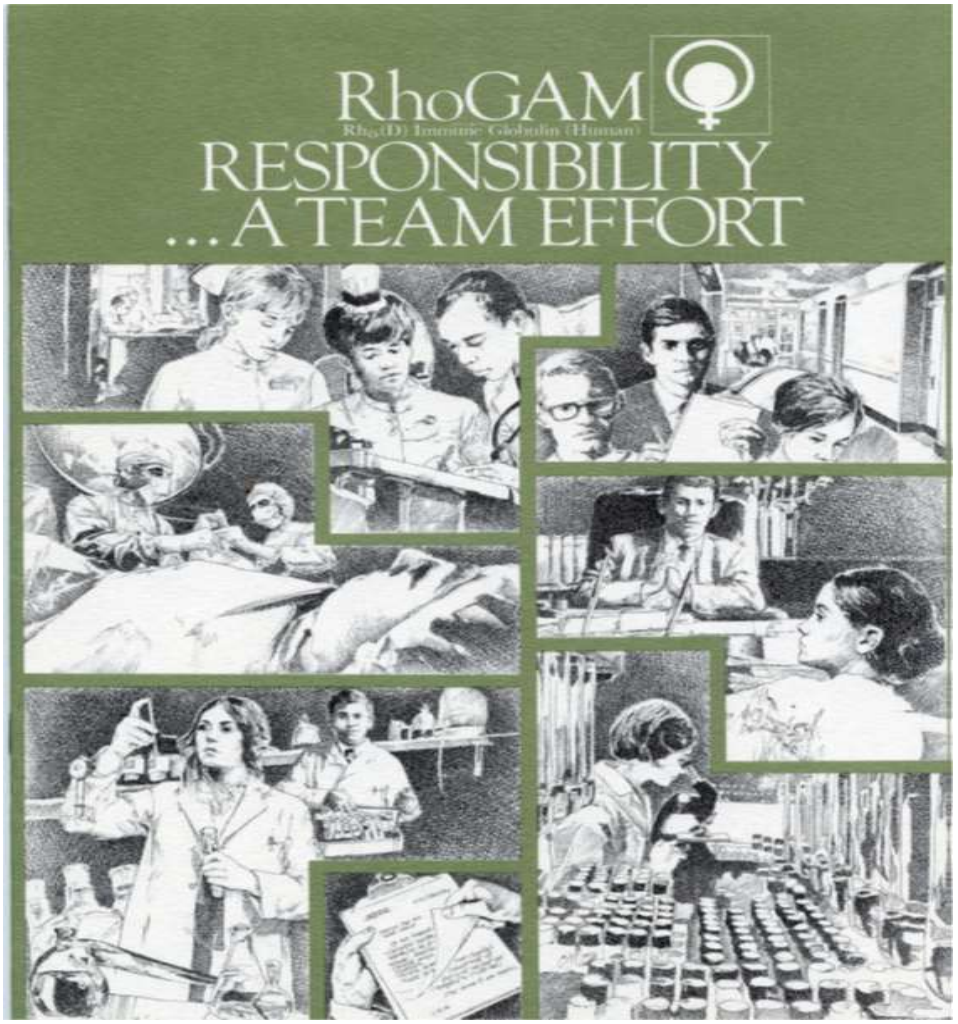
International Federation of Gynecology and Obstetrics
Working Group on Good Practice in Maternal-Fetal Medicine

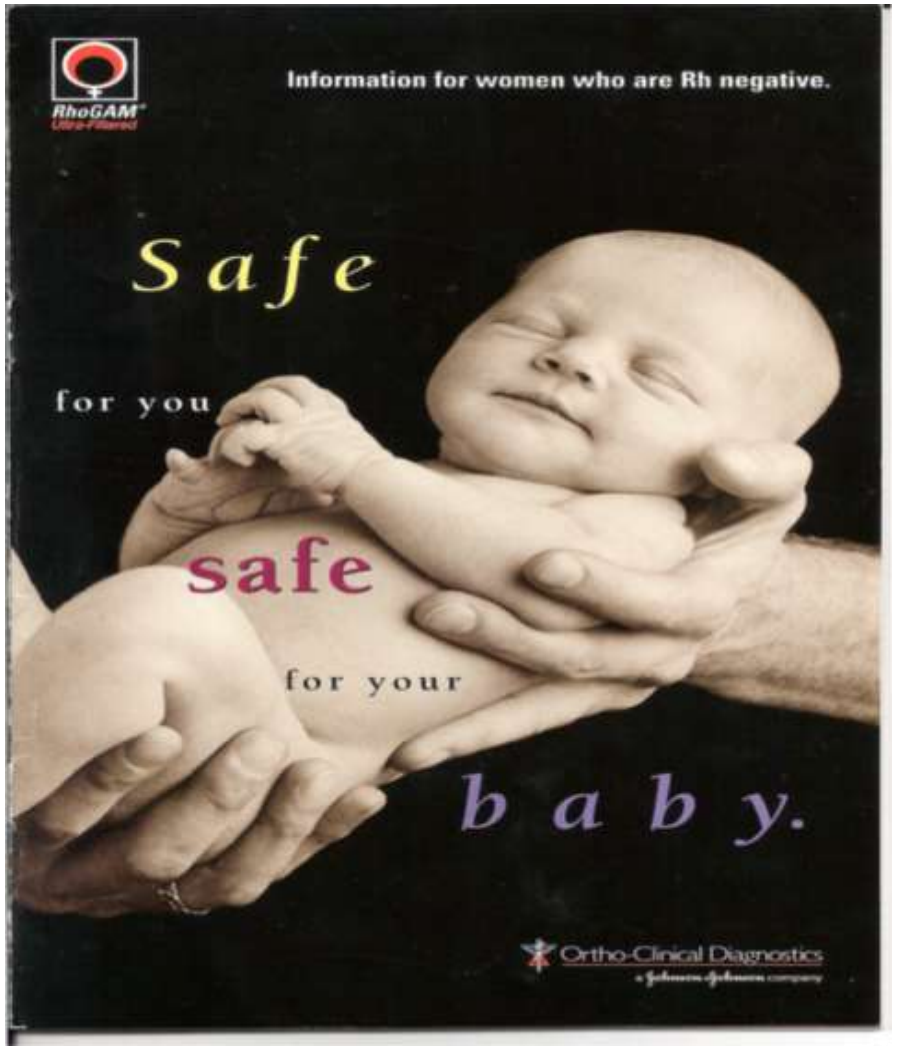
Chair: G C Di Renzo

Expert members:
E Fonseca, Brasil
E Gratacos, Spain
S Hassan, USA
M Kurtser, Russia
F Malone, Ireland
S Nambiar, Malaysia
M Sierra, Mexico
K Nicolaides, UK
H Yang, China

Expert members ex officio:
C Fuchtner, FIGO
M Hod, EAPM
GH Visser, SM Committee
E Castelazo, CBET Committee
L Cabero, GDM WG
V Berghella, SMFM
Y Ville, ISUOG
M Hanson, DOHaD
PP Mastroiacovo, Clearinghouse
JL Simpson, March of Dimes
D Bloomer, GLOWM

Rh DISEASE: the burden





APRIL 19, 1968
RHOGAM is APPROVED THE first anti-D IN HISTORY

Anti-D introduction changed the fate of millions of newborns, BUT …

200.000 NEWBORNS EVERY YEAR PERISH OR ARE SEVERELY DAMAGED BY HEMOLYTIC DISEASE OF NEWBORN (HDN)

114.000 Newborn deaths

55.000 Brain damage

26.900 Deaths in utero

HDN Global figures

Neonatal hyperbilirubinemia and Rhesus disease of the newborn: incidence and impairment estimates for 2010 at regional and global levels

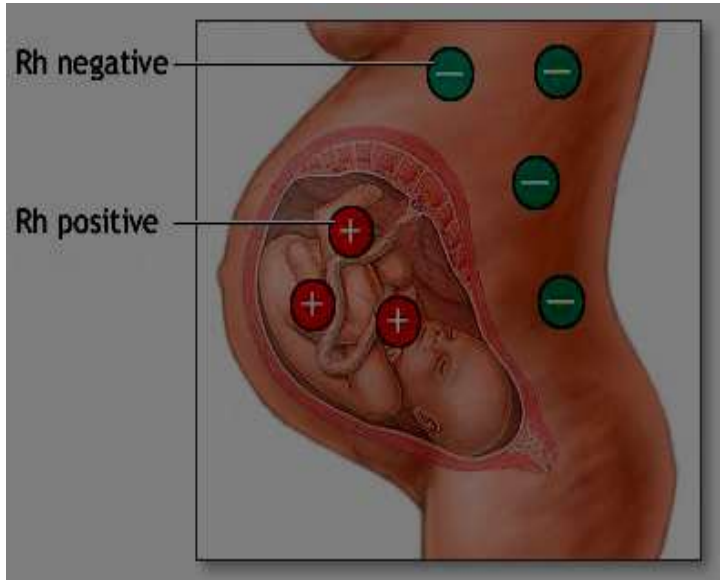
Vinod K. Bhutani[1,2], Alvin Zipursky[1], Hannah Blencowe[3], Rajesh Khanna[4], Michael Sgro[5], Finn Ebbesen[6], Jennifer Bell[1], Rintaro Mori[7], Tina M. Slusher[1,8], Nahed Fahmy[9], Vinod K. Paul[10], Lizhong Du[11], Angela A. Okolo[12], Maria-Fernanda de Almeida[13], Bolajoko O. Olusanya[14], Praveen Kumar[15], Simon Cousens[4] and Joy E. Lawn[16,17]

Geographic differences exist about

access, coverage, awareness

Sensitizing events

- **First trimester bleeding or miscarriage**
- **Medical o surgical termination of first trimester pregnancy**
- Ectopic pregnancy
- Vescicular mole
- Second trimester bleeding
- **Diagnostic invasive procedures (villus sampling, amniocentesis, cordocentesis)**
- **Antepartum haemorrhage**
- External cephalic version
- **Closed abdominal injury**
- Intrauterine death
- **Manual removal of placenta**
- **Twin deliveries**
- **Mismatched platelet or blood transfusion**



Rh disease prevention

The risk of sensitization is directly proportional to the gestational age and the volume of fetal-maternal hemorrhage (FMH)

Gestational age	Fetal-maternal hemorrhage	Volume (ml)
FIRST TRIM	6.7%	0.07
SECOND TRIM	13.9%	0.08
THIRD TRIM	29%	0.13
DELIVERY	76%	0.19

TESTS FOR THE SIZE OF FMH:

KLEIHAUER-BETKE TES
FLOW CYTOMETRY
ROSETTING TECHNIQUE

Volume of FMH	Risk of sensitization
0.1 ml	1%
0.5-1 ml	25%
> 5 ml	65%

Rh disease prevention

Routine antenal anti-D prophylaxis (RAADP)

- Anti-D Ig 300 microg should be routinely given to all Rh-negative nonsentisitized women at **28 weeks' gestation** when the fetal blood type is unknown or known to be Rh+
- (recommended by the American College of Obstetricians and Gynecologists and the US Preventive Services Task Force)

- Alternatively, 2 doses of 100-200 microg may be given one at 28 weeks and one at 34 weeks or a single dose of 300 microg at 28 weeks

Rh disease prevention

Routine antenal anti-D prophylaxis (RAADP)

- There is no evidence that the efficacy of the single-dose or two dose regimens differs, and the chosen regimen depends on local organisational factors
- Informed consent should be obtained and recorded in the case notes

Rh disease prevention

Routine post-partum prophylaxis

- If Rh- mothers don't receive postpartum anti-D Ig prophylaxis after an Rh+ baby, the incidence of sensitization is 12-16%, compared to 1.6% to 1.9% in mothers receiving postpartum prophylaxis.
- Anti-D Ig 300 microg Ig should be given within 72 hours of delivery to a nonsensitized Rh- woman delivering a Rh+ baby

Rh disease prevention

- **Routine post-partum prophylaxis**

- If anti-D is not given within 72 hours of delivery or other potentially sensitizing events, anti-D should be given as soon as the need is recognised, for up to 28 days after delivery or other potentially sensitizing event (III-B)

NIPT

What is the role of non-invasive assessment of fetal blood type?

At present RAADP is recommended to all Rh-D negative pregnant women

"The disadvantage" of this is that about 40% of Rh-D negative women receive unnecessary antenal anti-D Ig ...

NIPT

What is the role of non-invasive assessment of fetal blood type?

"Circulating Cell-Free DNA to determine the fetal RhD status in all three trimester of pregnancy" Moise et al. Obstet Gynecol, 2016

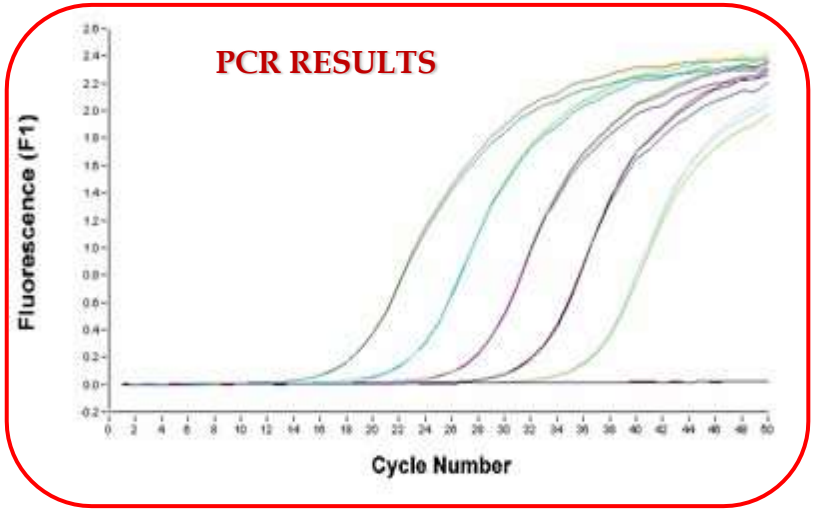
Circulating Cell-free fetal DNA can accurately predict the fetal RhD status in all three trimester of pregnancy

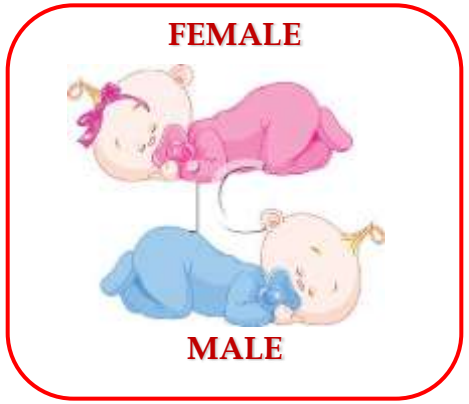
Di Renzo et al Transf Med Hemoth 2015

Di Renzo et al Pren Diag 2016

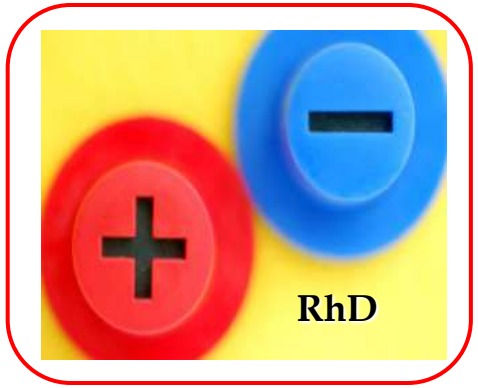
CELL-FREE FETAL DNA

Fetal gender determination
Diagnostic accuracy: 99,8%





Fetal RhD genotyping
Diagnostic accuracy: 98,5%



PRENATAL ASSESSMENT OF FETAL RhD STATUS

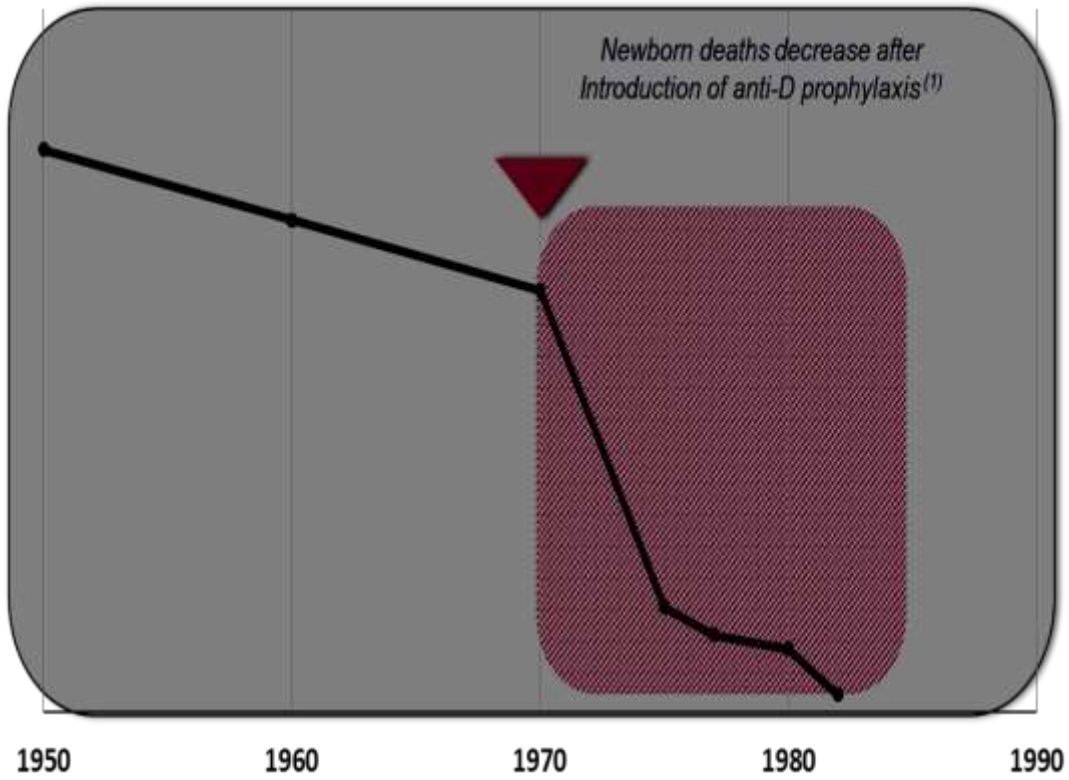
1. The test has been performed on 316 pregnant women

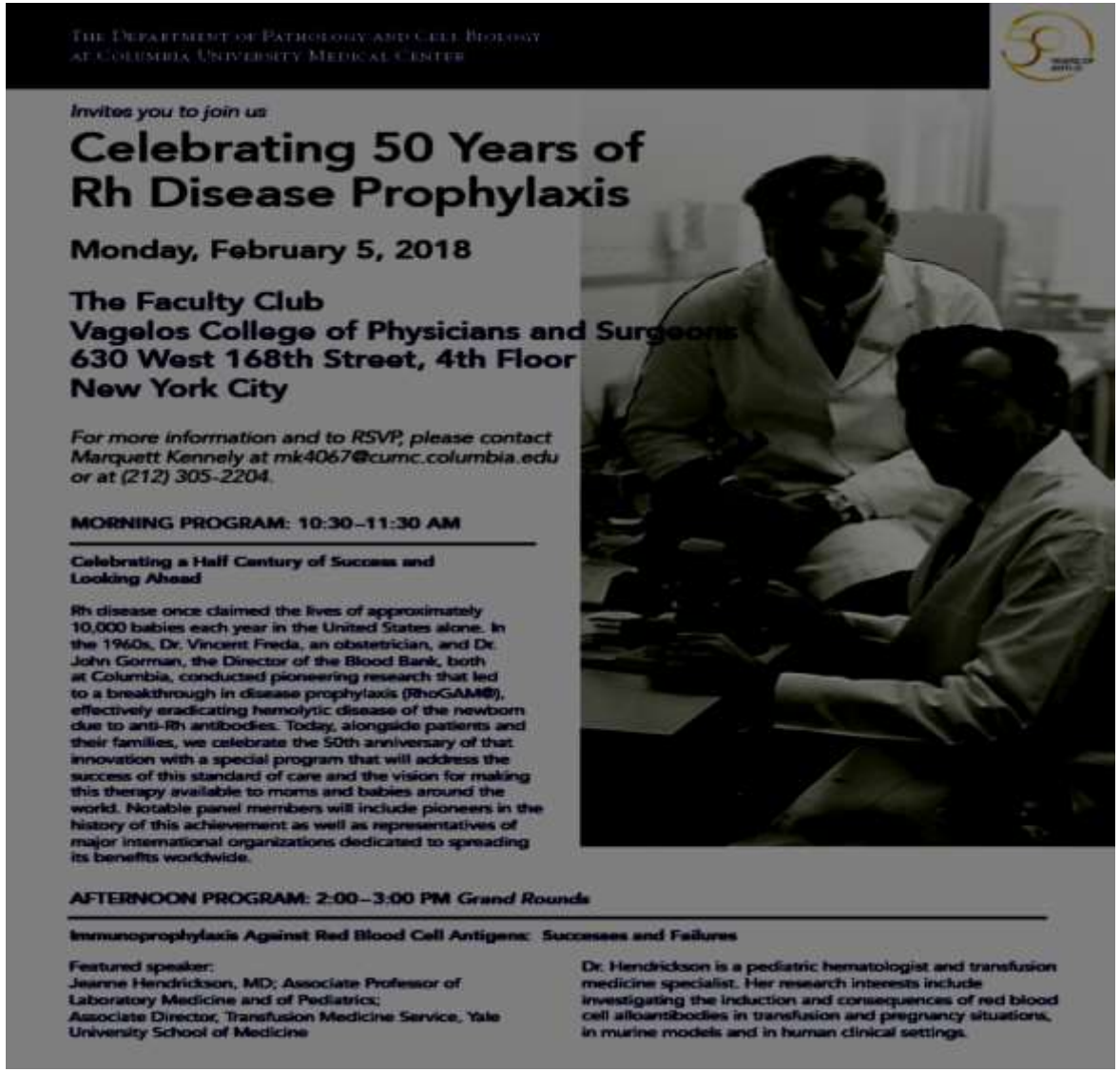
2. The test is functional in clinical routine practice of non invasive prenatal diagnosis since it is easy, rapid and automated. After about 4 hours from the blood sampling it is possible to obtain the results of 20 samples simultaneously.

SENSITIVITY (%)	98.7
SPECIFICITY (%)	100
VPP (%)	100
VPN (%)	98.3
EFFICIENCY (%)	99.9

50 YEARS LATER....

Columbia 50 years celebration






Panelists
Marianne Cummins
Mary E. D'Alton, M.D.
Alvin Zipursky, M.D.
Vinny Bhutani, M.D.
Funmi Banire, M.B.A.
Gerard Visser, M.D., Ph.D.
Columbia University
Irving Medical Center

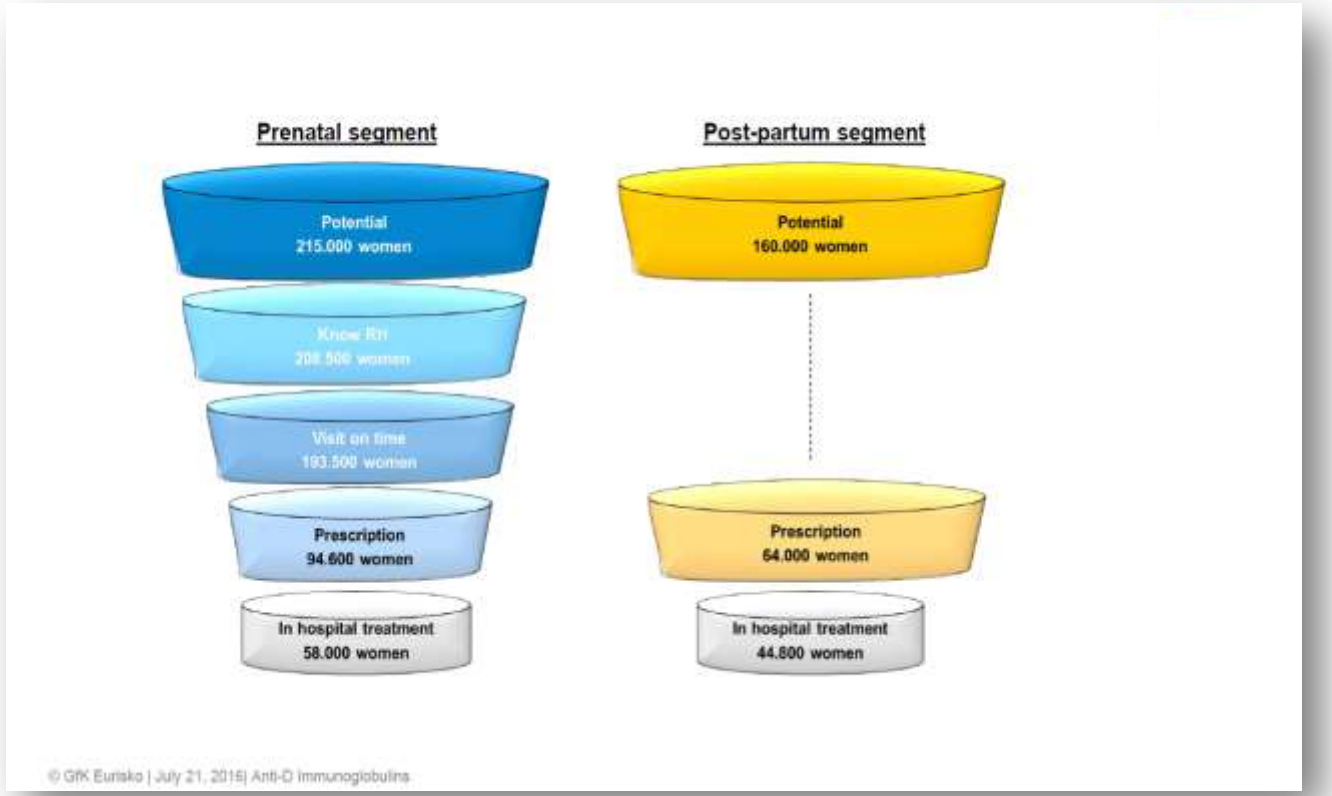
STATUS QUO

- Globally about **50% of Rh-women still do not receive** care when pregnant.
- 81% pregnant women in Africa do not receive anti-D … about 66% in Asia … 72% in Russia and ex CIS Countries
- MAIN REASONS : **inadeguate assistance, restricted drug access, low disease awareness …**

Recommendations in different countries depend on the relative availability and costs of anti-D, and the costs of laboratory assessments of the volume of feto-maternal hemorrhage.

RUSSIA
Quantitative analysis to estimate sources of gap and magnitude. Pregnancy segment

90 % of pregnant women know Rh at first visit



28% of women only receive postpartum prophylaxis in hospital

STRATEGIES

Health professionals have been at the forefront of social changes, such as those that have gradually made smoking increasingly unacceptable, driving down smoking rates—and saving many lives

- **Awareness** of the relevance of the problem both for ObGyns and for women
- **Resolve** the geographical disparities about Rh disease prevention
- Actually a large shared approach is the **antenatal plus postnatal prophylaxis** in Rh- women with Rh+ baby
- Global and national leadership is needed to mobilize action and improve system approaches, policies and programs … **ideally shared guidelines!**

TRIPLE A

IS PATIENT RECEIVING HEALTH COVERAGE?

ADVOCACY

IS DRUG REIMBURSED OR MADE AVAILABLE?

ACCESS

IS THE ISSUE KNOWN AND TAKEN INTO CONSIDERATION?

AWARENESS

STRATEGIES

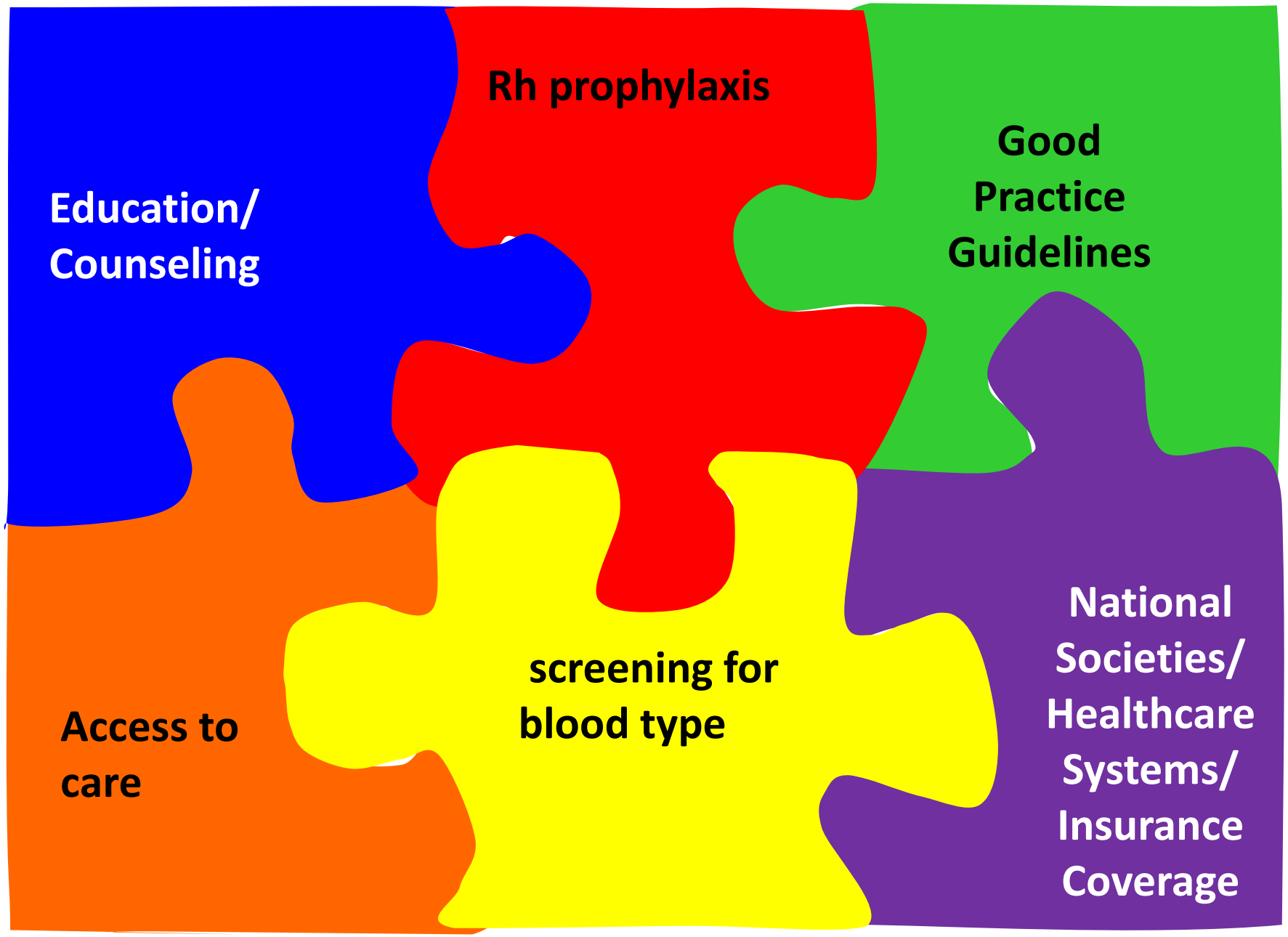
- Integrate women and children's health into all strategic discussions
- Develop a global focus on effective access
- Building education and sustaining resiliency
- Investing in Public Health
- "One Health" Approach with global collaboration across disciplines
- EMPOWER WOMEN

How Can We Lead?

- Support legislation with **guidelines**
- Create **educational** opportunities at all levels
- Share **information** with our patients
- Address the **needs** of the underserved throughout the world
- **Collaborate** with colleagues in backing a "**Rh agenda**" in our homes, workplace and communities
- Apply evaluation of research so that Medical organizations can **advocate** on behalf of women to reduce undertreatment

We share a common goal: we want healthy mothers, healthy infants, and a healthy future.
IF there was no doubt about research, if there was no cost impact for implementing change, if there was a uniformity of agreement in all the discussions, we would have no work.

So finding points of agreement has got to be where we start, **educating our clinicians, the public and the governing bodies then is the ideal next step so that finally we see that we *have* implemented changes**


Education/
Counseling
Rh prophylaxis
Good
Practice
Guidelines
Access to
care
screening for
blood type
National
Societies/
Healthcare
Systems/
Insurance
Coverage

‘Alone we can do so little;

together we can do so much.’

Helen Adams Keller (1880-1968)

BIRTHCONGRESS.EU

POWERED BY MCA scientific events

14-17 November | 2018

GRAZIE

merci

gracias

thank you

谢谢

DZIĘKUJEMY

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Баярлалаа

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