Hemolytic Disease of Newborn (HDN) in Uganda

Aggrey Dhabangi, MD PhD; On behalf of the study team

SECA Fellowship_Dissemination Workshop

Date: Jan 12, 2023

Outline

- Background to the problem (Hemolytic Dz of the Newborn)
- The HDN study; Aim, Methods, and Findings
- Other Project outputs

Relevant disclosures

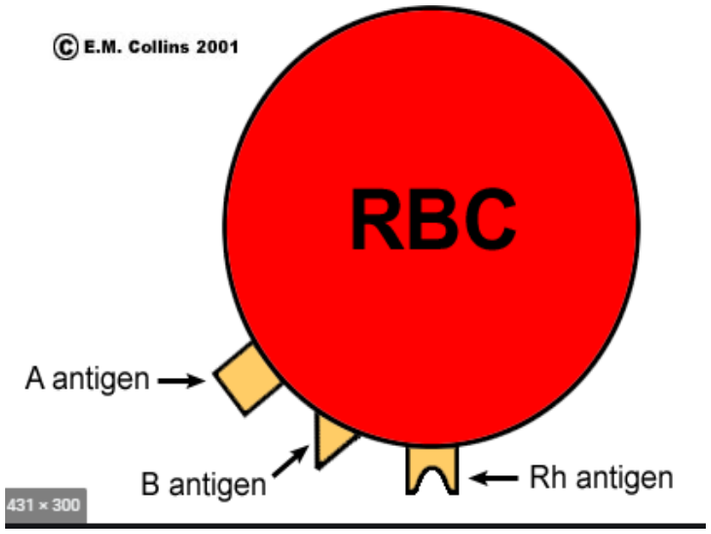
- Commercial: None

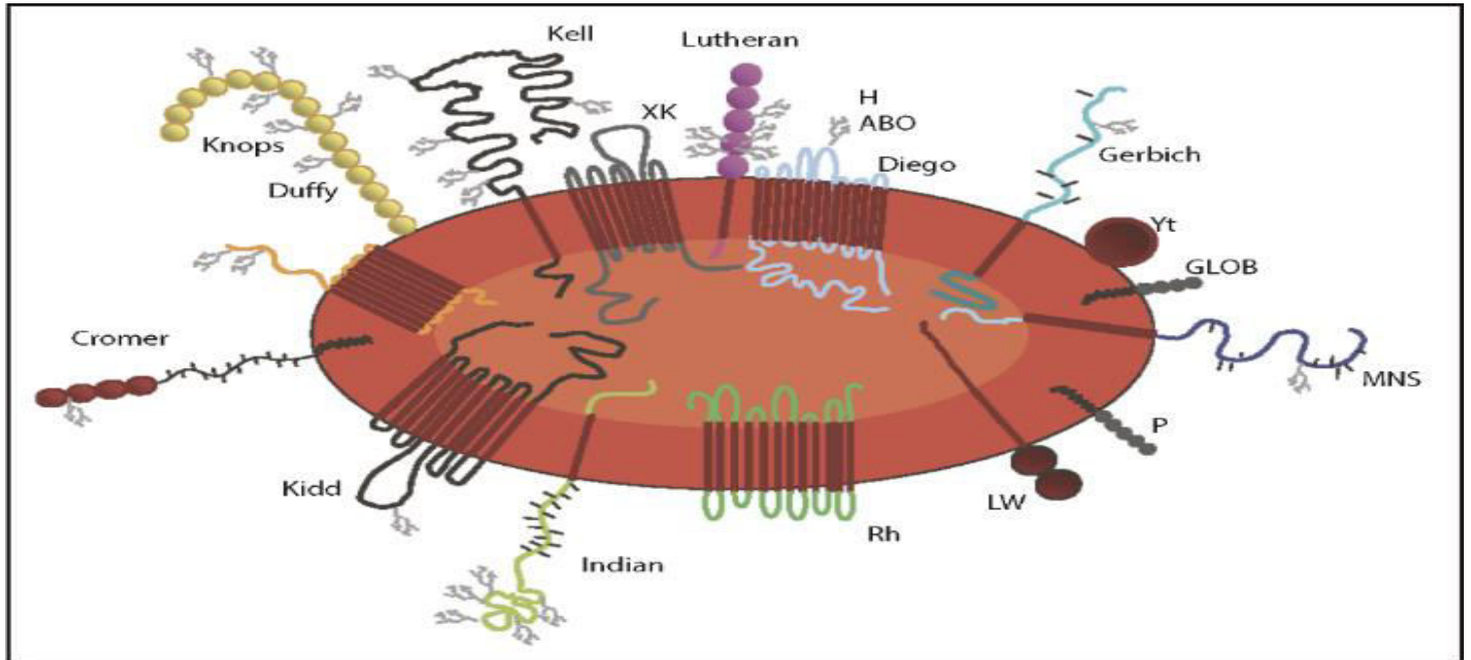
- Non-commercial: Motivation from personal experience

(RhD-incompatible couple)

Common terms

- Red Blood Cells (RBCs)
- RBCs Antigen
- Blood groups
- Alloimmunization
- Antibody





What is HDN

- HDN is an immune hemolytic anemia resulting from destruction of newborn RBCs by maternal antibodies (Abs)

➢ Antibodies; **Only IgG iso-type** ..... (can cross the placenta)

- Severe HDN disease mostly from **RhD antibodies**; (among **RhD+** babies born to **RhD- mothers**).

- Other RBC antibodies of the IgG class also cause HDN, eg. ABO

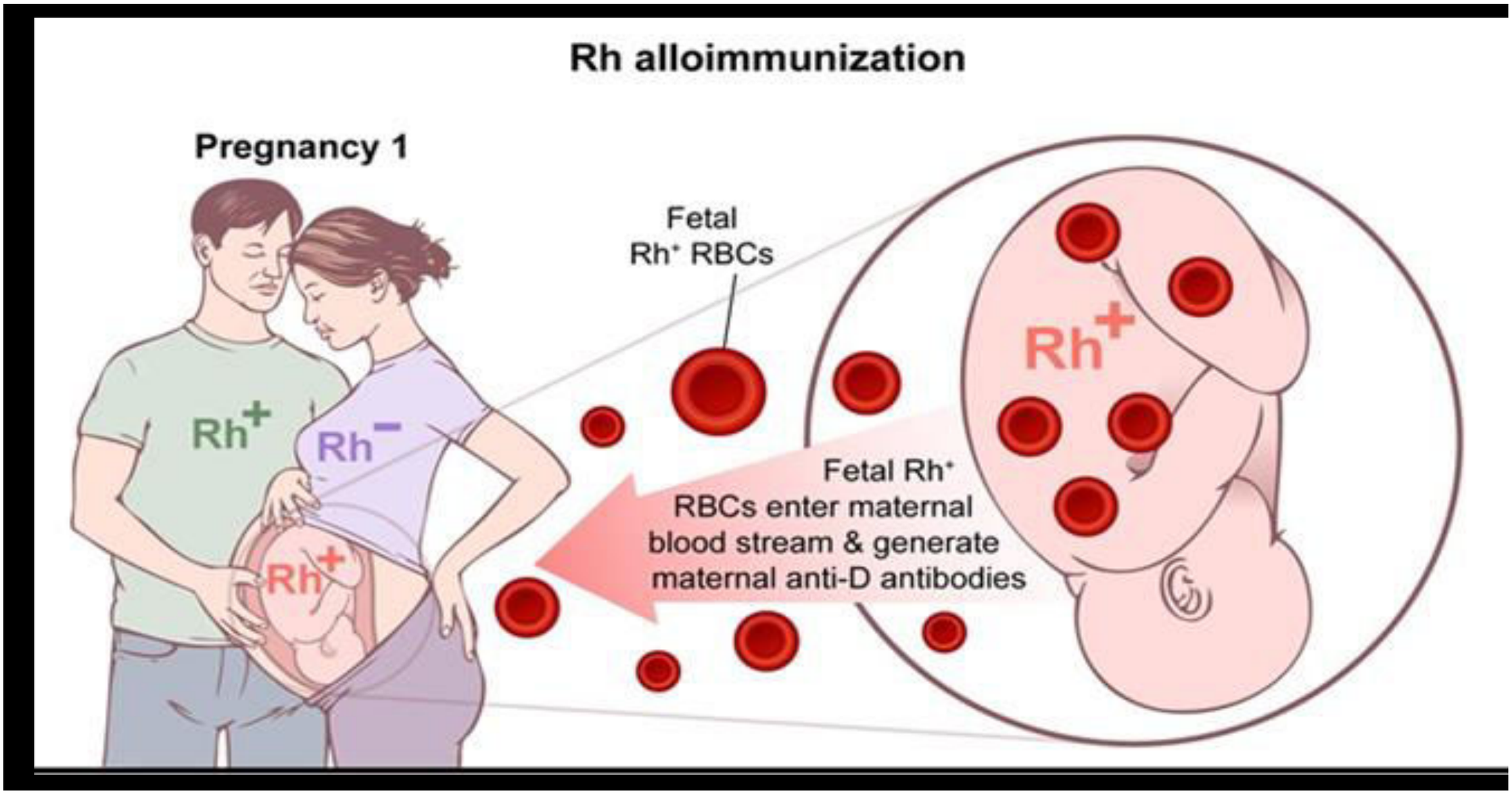
Harmening DM. Modern blood banking and Transfusion practice, 6th Ed. p428-436

Mellissa MS. Perinatal issues in transfusion practice. In AABB technical manual, 13th Ed, p625-636

Main problem: RhD-Antibodies

Rh
incompatibility

RhD Alloimmunization/Sensitization



Feto-maternal Hemorrhage: Alloimmunizing events

- **Timing:**

➢ **During birth:**

✓ Greatest risk of F-M bleeding

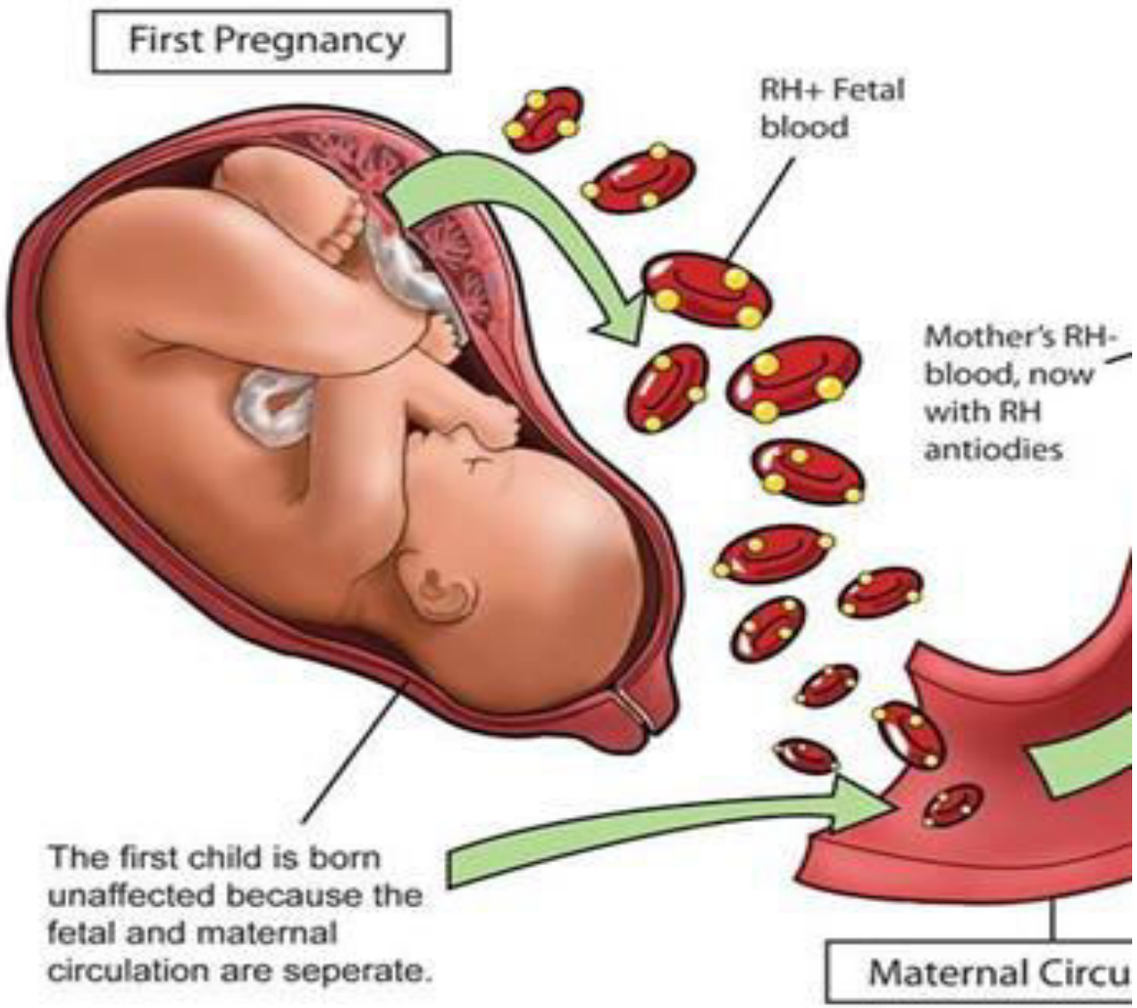
➢ **Others:**

✓ Abortion/Miscarriages/Ectopics

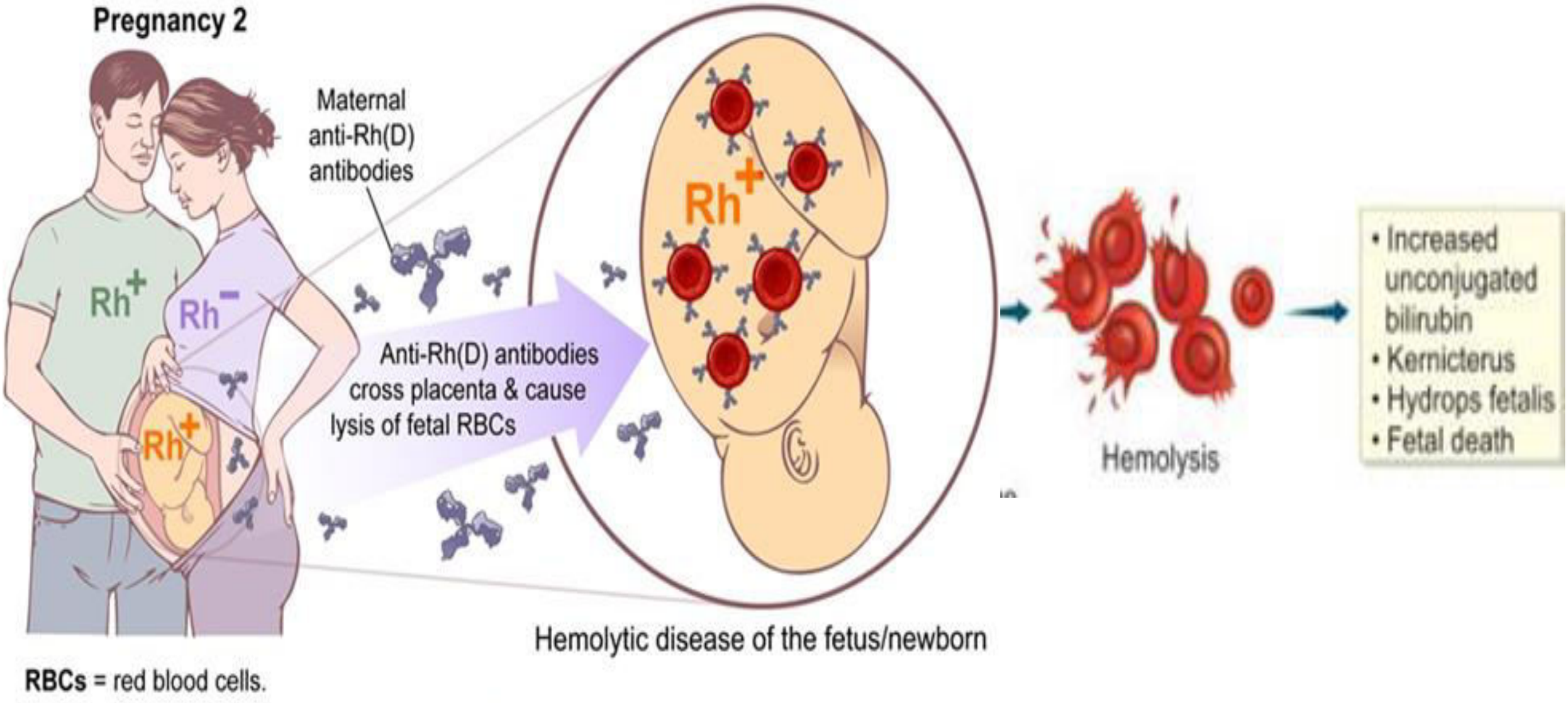
✓ Pre-natal procedures (Amniocentesis

✓ Blunt trauma to the abdomen

✓ Blood transfusion

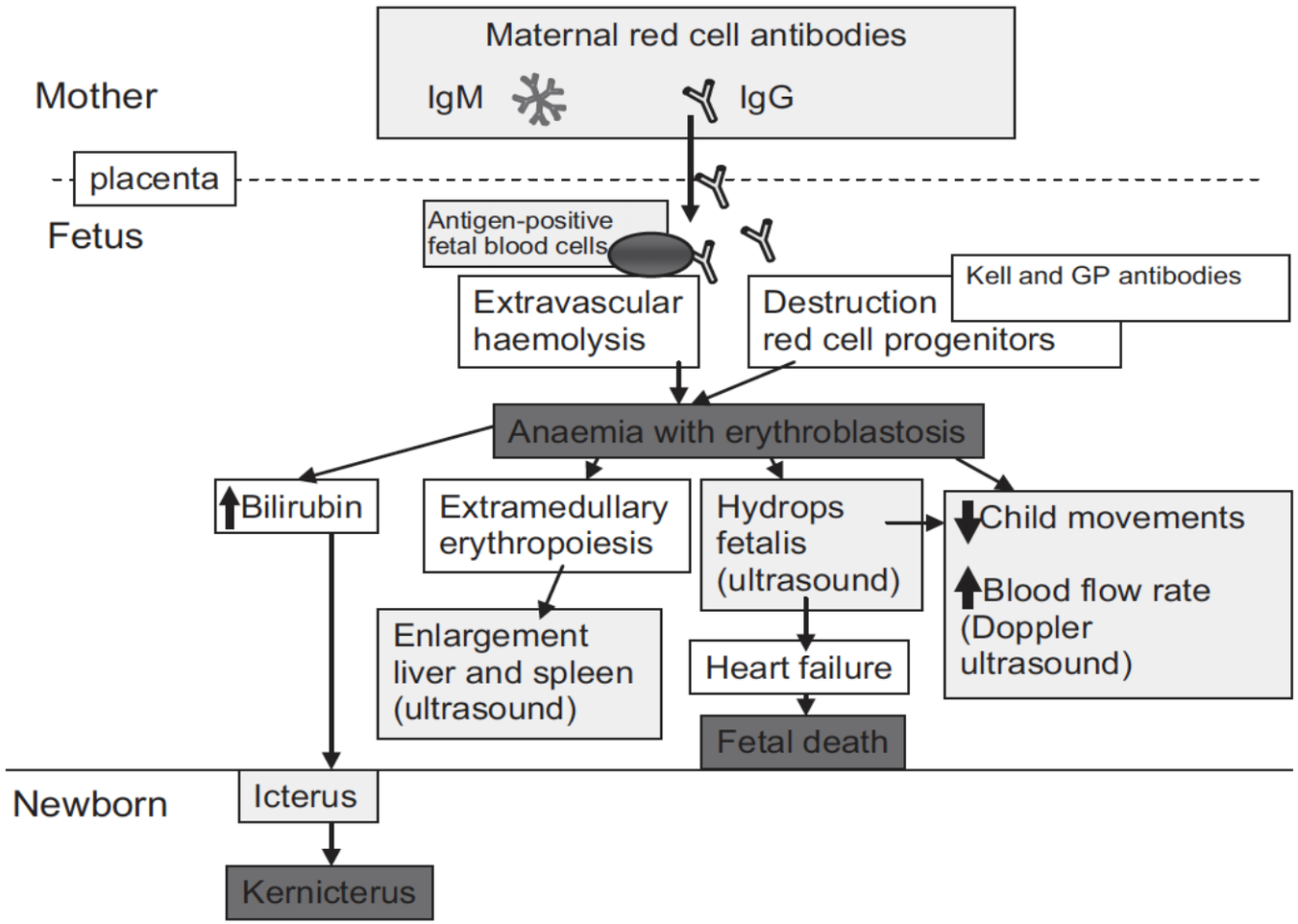


HDN



RBCs = red blood cells.

HDN Pathophysiology



de Haas M et al. Vox Sang 2015

Hydropic newborns

Burden of HDN

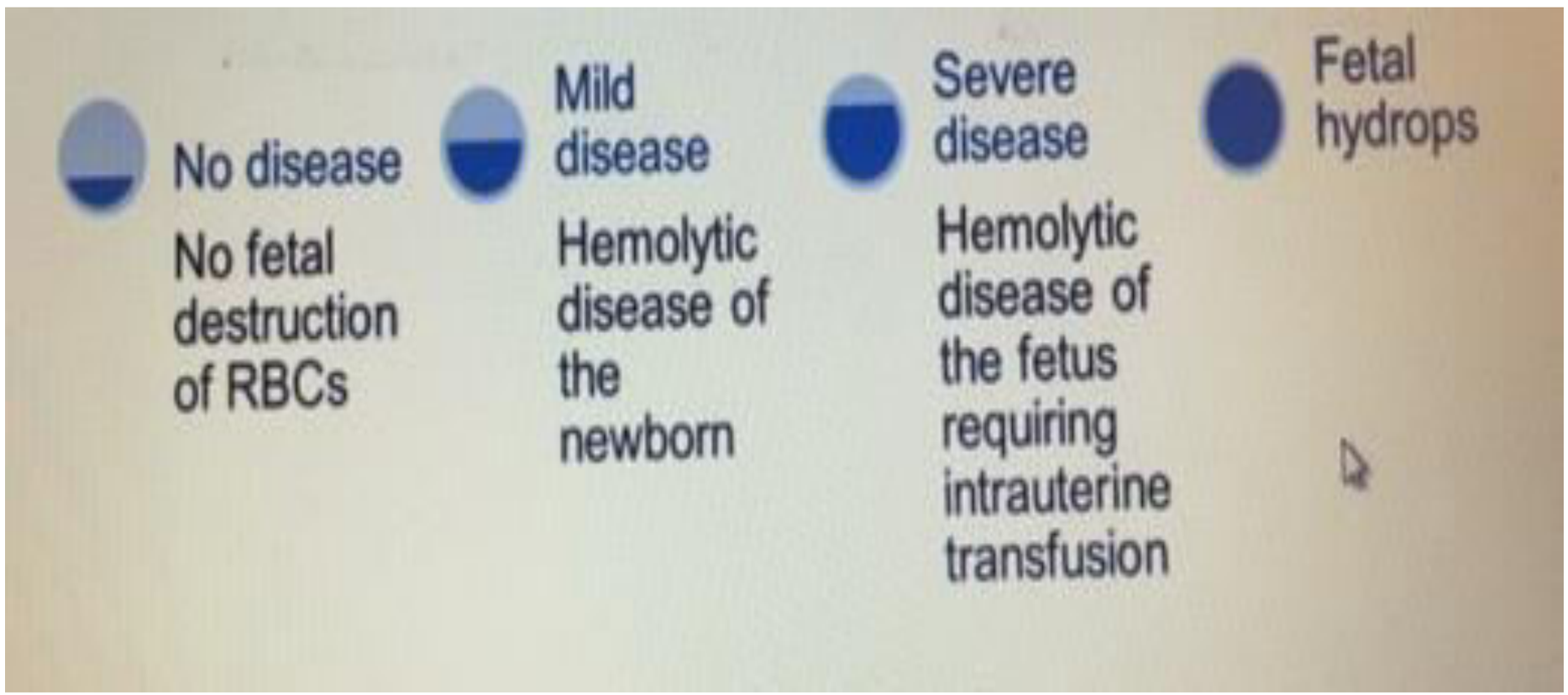
- Burden **varies in difference settings**; Determined by:
  - Population **distribution of RBC** Antigens (blood groups)
  - Prenatal care p**olicies; have changed** over the years; since **1960s** through **2017**.

- **Generally:** Anti-D HDN most problematic.
- **HDN, in Rh-D neg Women:**
  - Previously at **16%**; now reduced to as **low as 0.1%** (**de Haas M et al. 2015**)

- **Overall burden**:
  - Recent study in **Canada**: **0.6/1,000** **Lieberman L et al. Transfusion2020**
  - **In Uganda**: No data

Clinical presentation

- **Spectrum** of HDN:
- Generally: **½ = mild dz**, ¼ = anemia (requiring Tx), ¼ severe Dz



(*slide Courtesy; Dr. Shehata*)

Prevention of HDN – *from Anti-RhD*

- Main strategy: Antenatal **Rh Immune globulin** (RhIg) prophylaxis to RhD-neg women. .....[First Introduced-**1969**]

➢ Routine Antenatal screening .....(**blood grouping** & Ab screening),

➢ RhIg prophylaxis

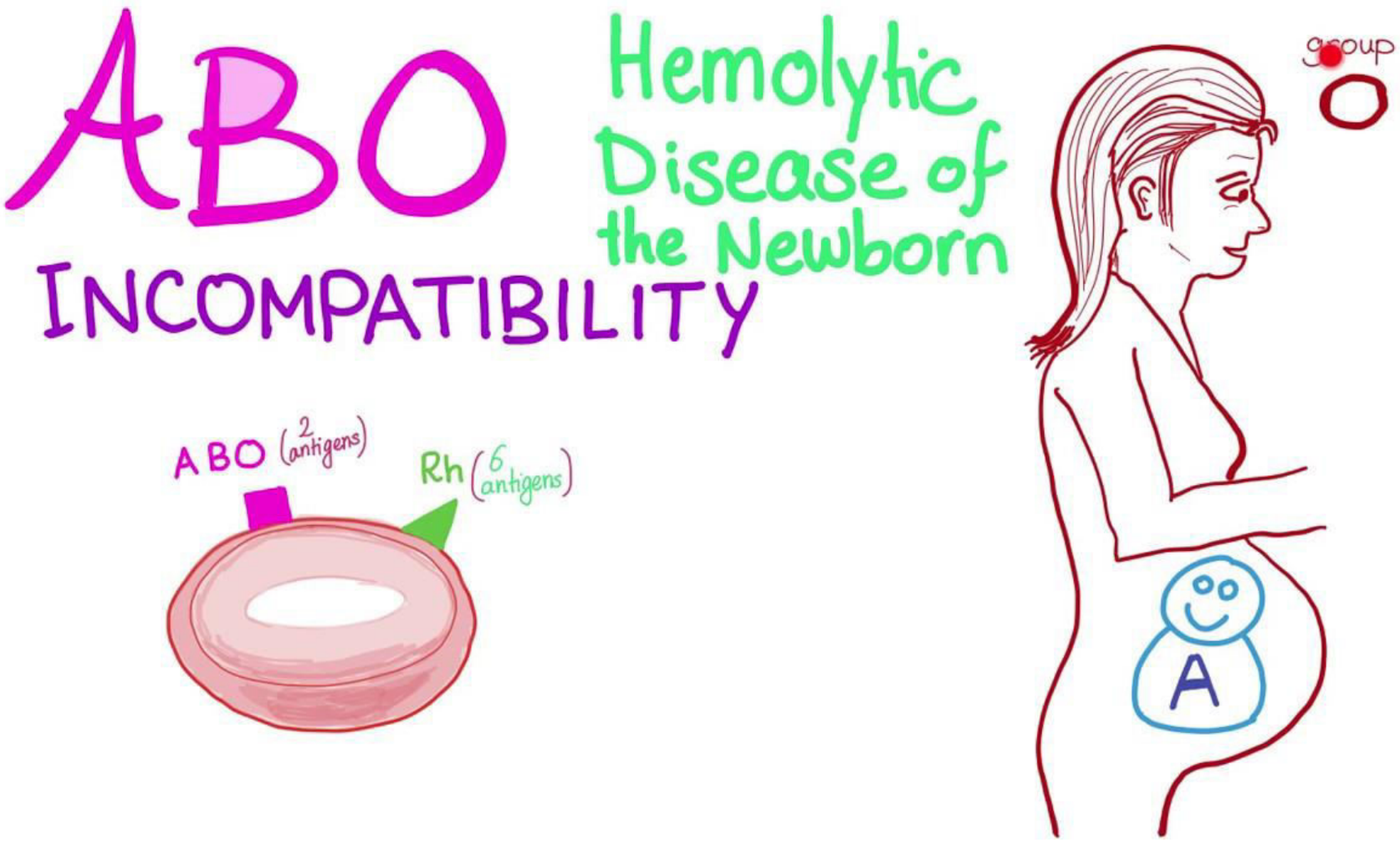
✓ 1st dose: at **28 wks,** &

✓ 2nd dose; **within 72hrs post-delivery** ..... of a RhD+ baby

- Universal RhIg prophylaxis in high-income nations has reduced the risk of HDN among Rh-neg women from **16% to as low as 0.1%**

(de Haas M et al)

HDN from ABO-Incompatibility

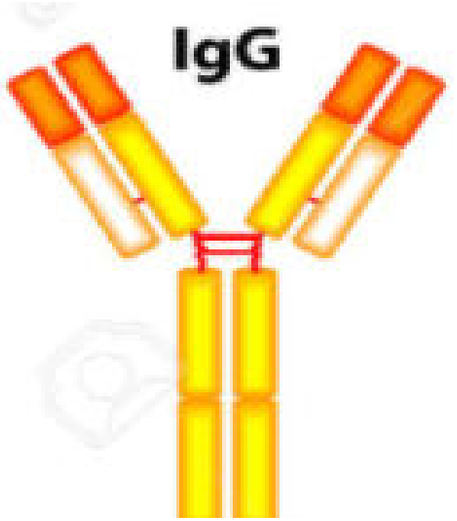


ABO-HDN -2

- **Antibodies:**

➢ We know about the ABO blood groups, and their Abs

➢ In **group-O** individuals,….majority of **Anti-A/B are IgG**



- **ABO- HDN disease**

➢ Affects ABO Incompatible Mum-Baby pairs (e.g: **Mum-O, Baby-A or B**)

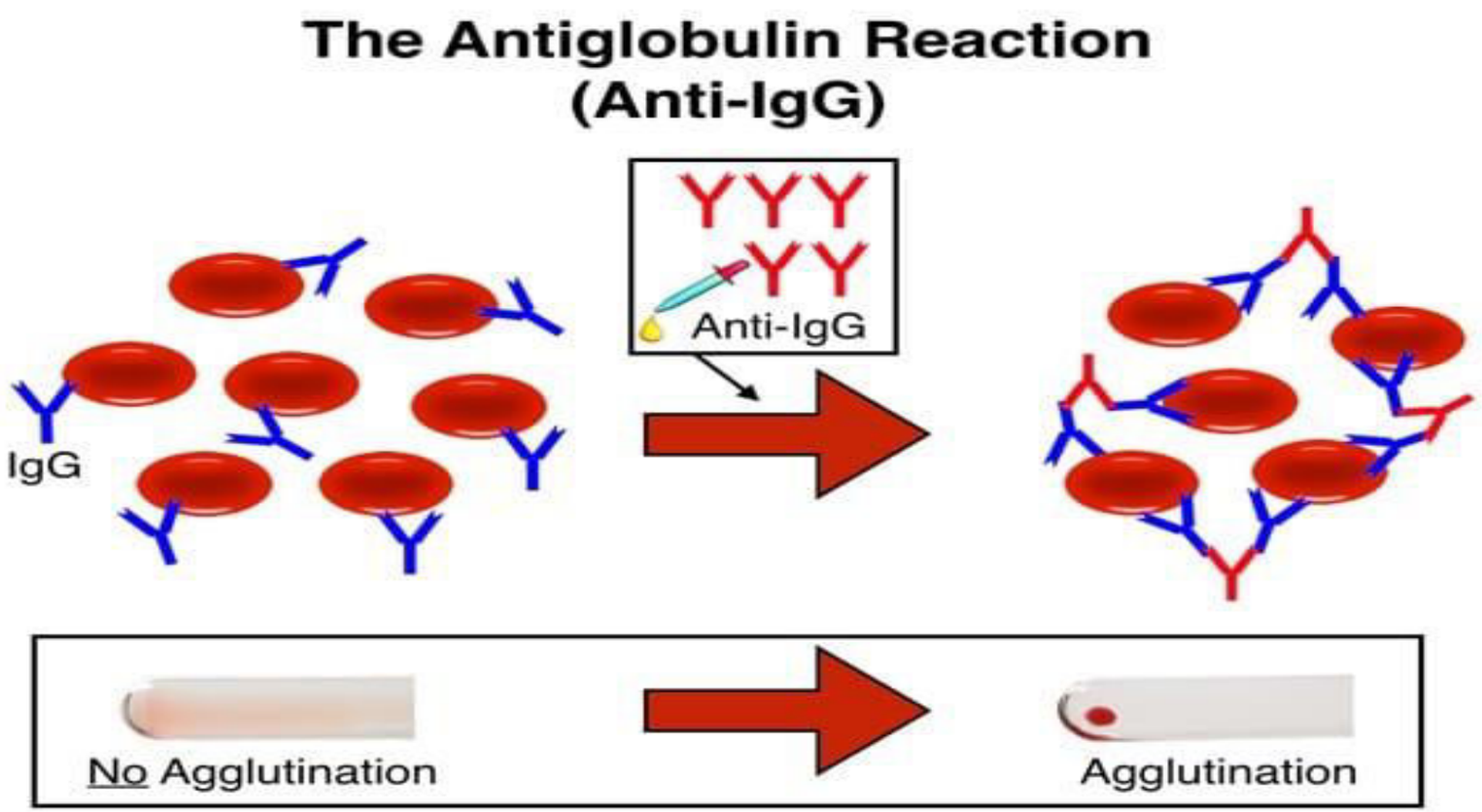
➢ **Often Mild**….(as such, PT alone usually successful in Rx), but common

➢ Burden:

✓ About **15**-25% of ABO incompatible mum-baby pairs

HDN Diagnosis

1. Direct Antiglobulin Test (DAT) / ……*a.k.a Direct Coombs Test*



DAT – is the **most vital test** in dx of HDN

- Detects antibodies –non-agglutinating coating RBCs

What we did

Hemolytic Disease of Newborn (HDN) in Ugandan

An Observational Study of HDN in Uganda

SOMREC #: 2020-214

UNST #: HS-1089ES

Background and Objectives

- **Rationale:**

➢ Although Anti-D HDN disease is preventable through prenatal **RhIg prophylaxis to RhD-negative women**, such interventions are **not universally available in Uganda**, putting many newborns at risk.

➢ The burden and characteristics of HDN in Uganda have not been described before.

- **Primary Objective**: To determine the prevalence of **HDN** among newborn infants with jaundice admitted to Kawempe National Referral hospital in Uganda.

Methods

- **Study design**: Cross-sectional
- **Study site:** Kawempe National Referral hospital, Kampala.

- **Inclusion:**

✓ Newborns aged 0-14 days, with:

➢ Clinical diagnosis of neonatal **jaundice** (or total bilirubin > 50 µmol/L) and,

➢ A positive Antiglobulin Test (**DAT**)

Clinical Assessment

- **Baby**:

➢ Date, type of birth, age, gender, Symptoms; e.g. jaundice, physical examination, clinical diagnoses, treatment provided, hospitalization outcome.

➢ TcB (using a *Bilirubinometer*)

- **Mother**:

➢ Prenatal history, past obstetric history, past medical history and social history

Laboratory tests

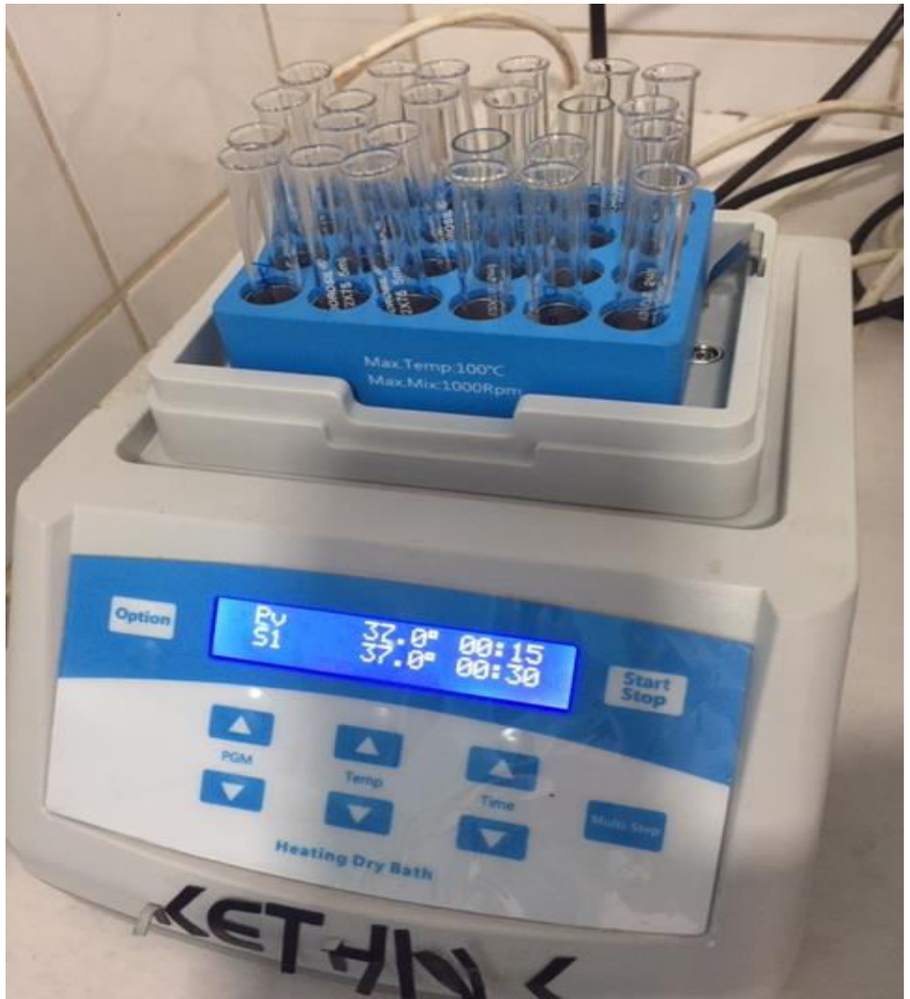
- **Blood draws:**

➢ 2mL of EDTA tube - Baby; Screening (DAT)

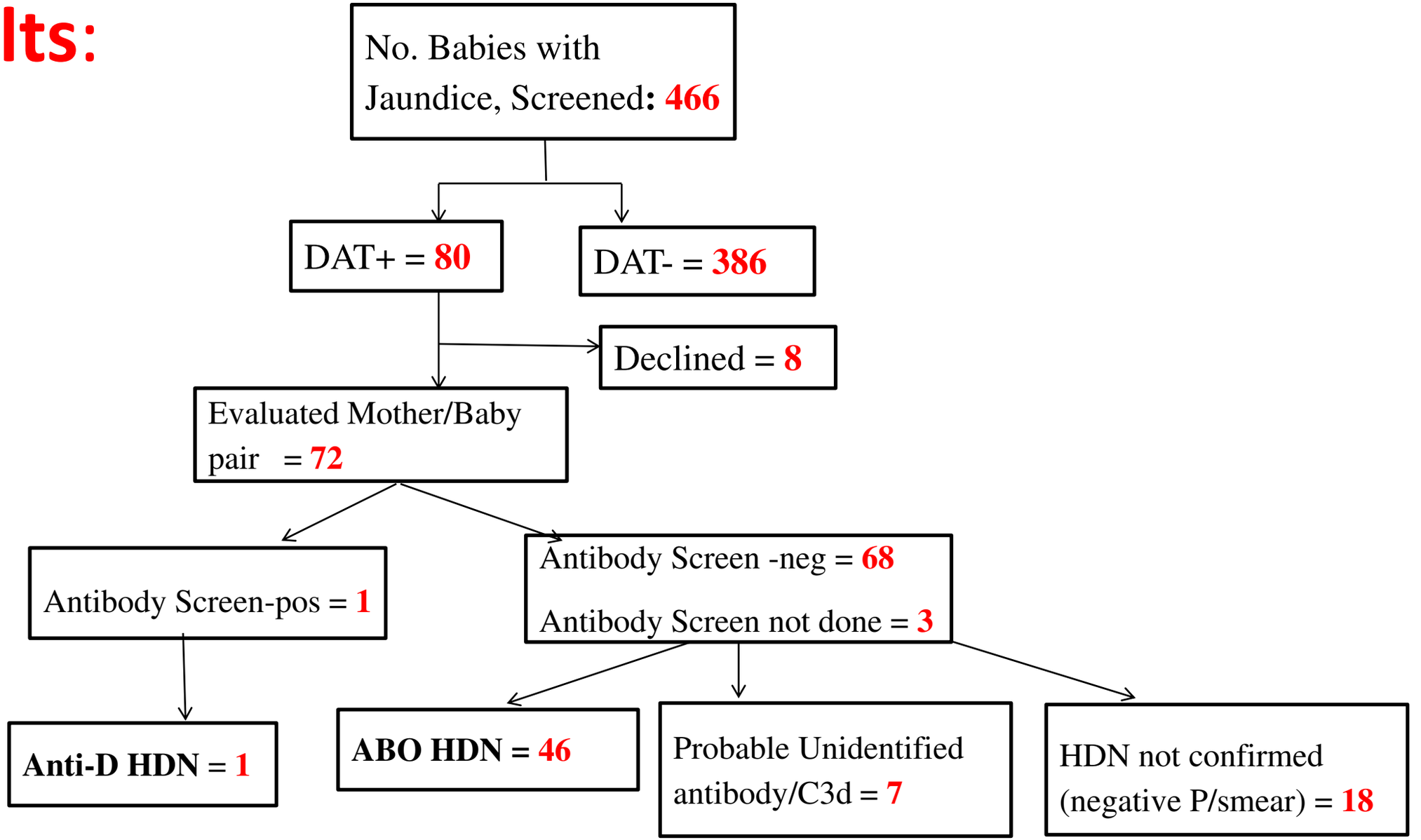
➢ 6mL of EDTA tube from mother; if enrolled

Test	Mother	Baby
1. Hb		x
2. Total bilirubin (TcB); Bilirubinometer		x
3. Direct Antiglobulin Test (DAT) – Polyspecific		x
4. Peripheral blood smear – (for spherocytes)		x
5. ABO and Rh typing (tube method)	x	x
6. 3-cell Antibody screen (IAT)	x	
7. Antibody identification; if (6) above is positive	x	

- **Lab Equipment,** set up at Stanfield ward – Mulago, MakCHS



Results:


No. Babies with Jaundice, Screened: 466
DAT+ = 80
DAT- = 386
Declined = 8
Evaluated Mother/Baby pair = 72
Antibody Screen-pos = 1
Antibody Screen -neg = 68
Antibody Screen not done = 3
Anti-D HDN = 1
ABO HDN = 46
Probable Unidentified antibody/C3d = 7
HDN not confirmed (negative P/smear) = 18

Results

- **Primary outcome:**

- DAT Test results = **17.2%** DAT Positive

✓ **Prev. of HDN among Newborns with jaundice**

Results – 2

- One baby [**1/466**] (*or 2 in 1000*) babies, had **Anti-D HDN** disease, while
- **46/466** (or 1 in 10) had **ABO HDN**

- **82%** of babies with HDN also had **neonatal sepsis or birth asphyxia**.

- **79.2%** **(**57/72) of Mums of affected intants did not have their ABO/D blood groups performed during antenatal (despite attending antenatal)

- One infant (*with ABO HDN)* died during hospitalization (rest recovered fully and were discharged)

Baby with Anti-D HDN: ….Counseling

- **Baby**:

✓ Male term, B/wt –3.8kg, C/section birth

✓ Admitted 2 DOL: **jaundice and HIE**,

✓ Blood group = **O+,**

- **Mother**:

✓ 26 yrs, P–3, all babies are alive,

✓ None of the past two had N/jaundice.

✓ ABO/RhD typing never beenperformed

✓ Blood group = **B-**

✓ Antibody screen: **Positive for Anti-D**

Conclusions

- Among babies with NJ in Uganda, HDN is not rare– the majority being **ABO Incompatibility** disease.

- **Prompt identification** and mgt babies with HDN– including phototherapy may result in favorable outcomes.

- HDN commonly presents with other comorbid conditions namely; **neonatal sepsis and HIE** (risks: misdiagnosis, increases M&M, etc).

Policy Recommendations

- There is need to strengthen the implementation of **routine ABO/Rh** grouping during antenatal, and……

- Improve access to RhIg prophylaxis for **RhD negative** women

Local Dissemination: Two meetings

Published Article

Received: 4 July 2022 | Revised: 4 October 2022 | Accepted: 19 October 2022

DOI: 10.1111/vox.13376

Vox Sanguinis ISBT International Society of Blood Transfusion

ORIGINAL ARTICLE

A cross-sectional study of haemolytic disease of the newborn in Uganda

Aggrey Dhabangi[1] | Jolly Nankunda[2,3] | Violet Okaba[3] | Sarah Nakubulwa[4] | Heather A. Hume[5] | Walter H. Dzik[6] | Nancy M. Heddle[7]

[1]Child Health and Development Centre, Makerere University College of Health Sciences, Kampala, Uganda

[2]Department of Critical Care, Mulago Specialized Women and Neonatal Hospital, Kampala, Uganda

[3]Department of Pediatric and Child Health, Makerere University College of Health Sciences, Kampala, Uganda

[4]Department of Obstetrics and Gynecology,

Abstract

Background and Objectives: Haemolytic disease of the newborn (HDN) is an immune haemolytic anaemia from maternal alloantibodies. Rh immunoglobulin (RhIg) prophylaxis can prevent alloimmunization to the D antigen. However, RhIg is not universally available in Uganda. ABO incompatibility also causes HDN. We determined the prevalence of HDN among newborn infants with jaundice in Uganda.

Materials and Methods: We conducted a prospective cross-sectional study at Kawempe

Seminars in TM w Med. Postgraduates x 4

- Trained a total **140 of graduate students.**

- Department of Pediatrics; **52**
- Department of Obstetrics; **27**
- Department of Surgery; **42**
- Department of Internal Medicine; **19**

TM Exam taken by Med. graduate students

- Respondents: **124/140**

- Scores: **Poor** (Average = **30%**)

- **Manuscript,** *title: "Transfusion medicine knowledge among Physicians in graduate training in a resource-poor setting: A pilot study from Uganda "* [.....*Under reviwe: Transfusion Medicine Journal*]

Dep’t Grant to CHDC

- **Equipment** : Video Teleconferencing device

- **Research Capacity dep’t**:

✓CHDC Organized into Research Programs (6)

✓Ten (10) seminars

Acknowledgements

- **The study participants**
- **The Research teams**

- **Funding support**:
  - **Carnegie Corporation**
  - Makerere univeristy, DRGT,

- **Mentors:** Drs: J. Nankunda, WH. Dzik, CM Scerti, N.Heddle, H.Hume

Thank you