North Tees and Hartlepool
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Fetal Maternal Haemorrhage – An Ethical Dilemma

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Aims of the session

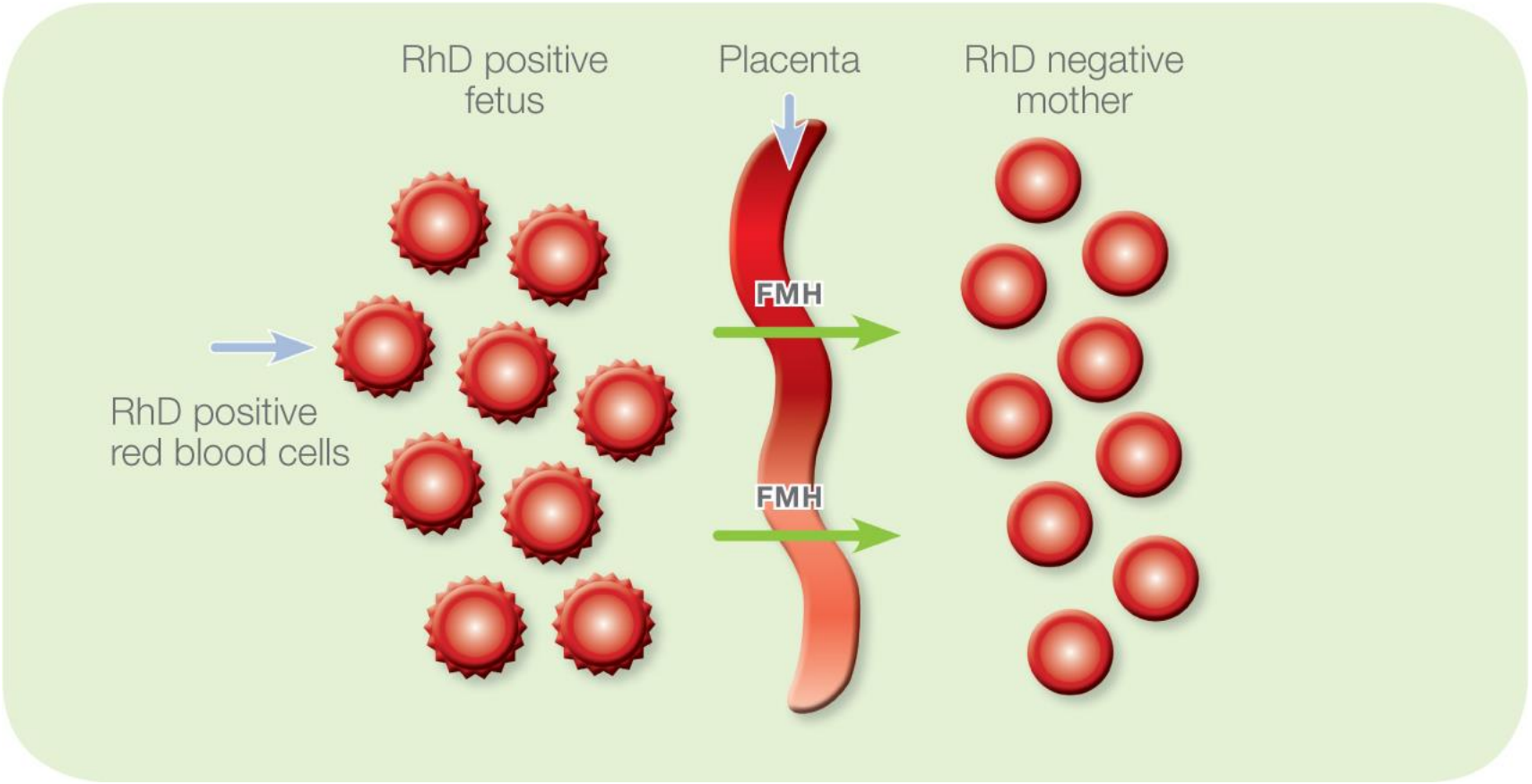
- Overview of a FMH
- Haemolytic Disease of the Newborn (HDN)
- The Kleihauer Test
- Flow Cytometry
- Anti-D
- Case Study
- Resulting Dilemma

Fetal Maternal Haemorrhage

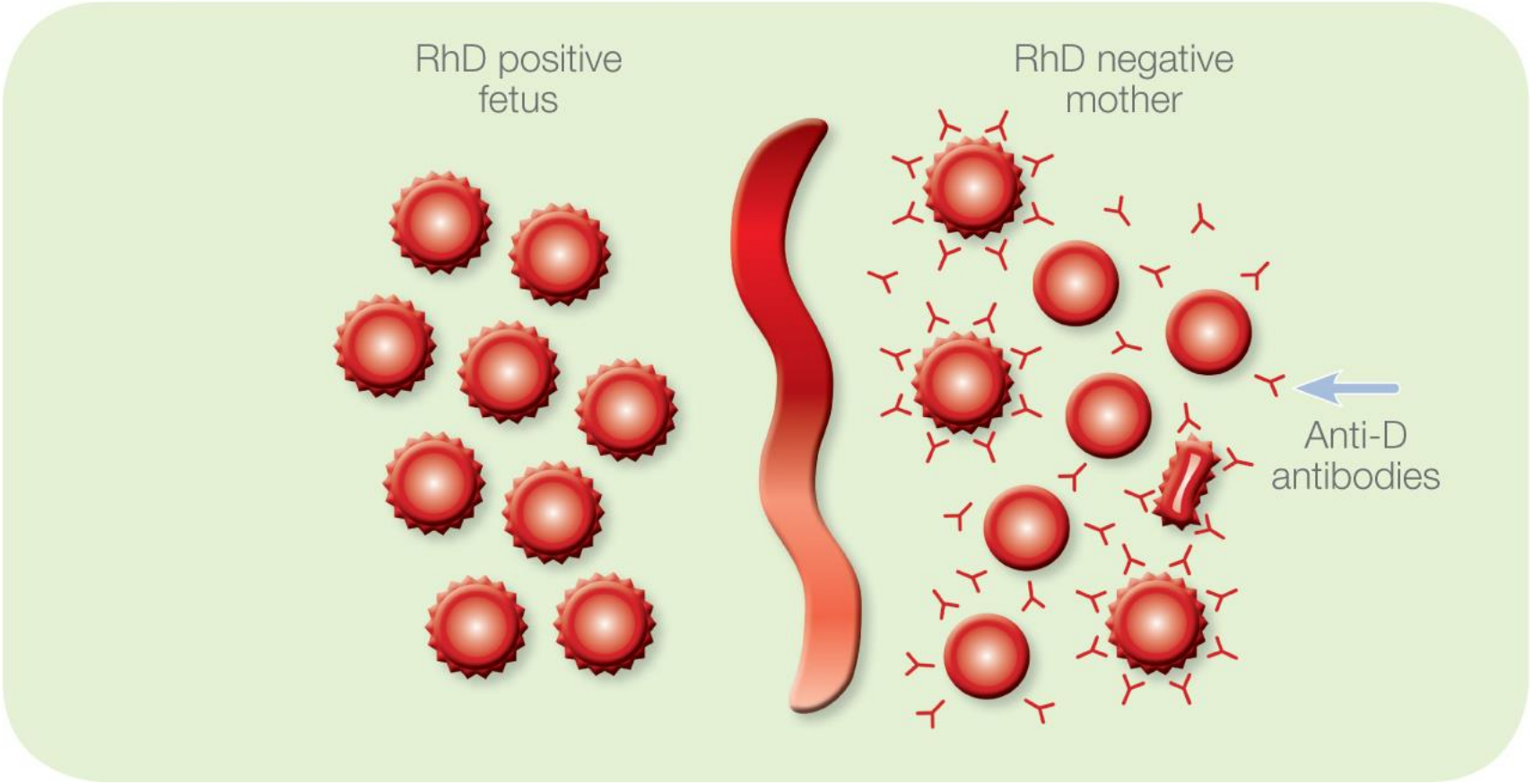
- Caused by a range of potentially sensitising events:
  - PV bleed, abdominal trauma, miscarriage, termination, IUD diagnosis, stillbirth, external cephalic version, invasive antenatal procedures, delivery
- Sensitising event during pregnancy leads to red blood cells from the fetus crossing into the mother's circulation (TPH or FMH)
- If mother is RhD Negative she can then produce antibodies against the antigen on fetal red cells if fetus is RhD Positive – IgG antibodies
- Can result in HDN – usually in second pregnancy

RhD Positive fetal cells can cross the placenta

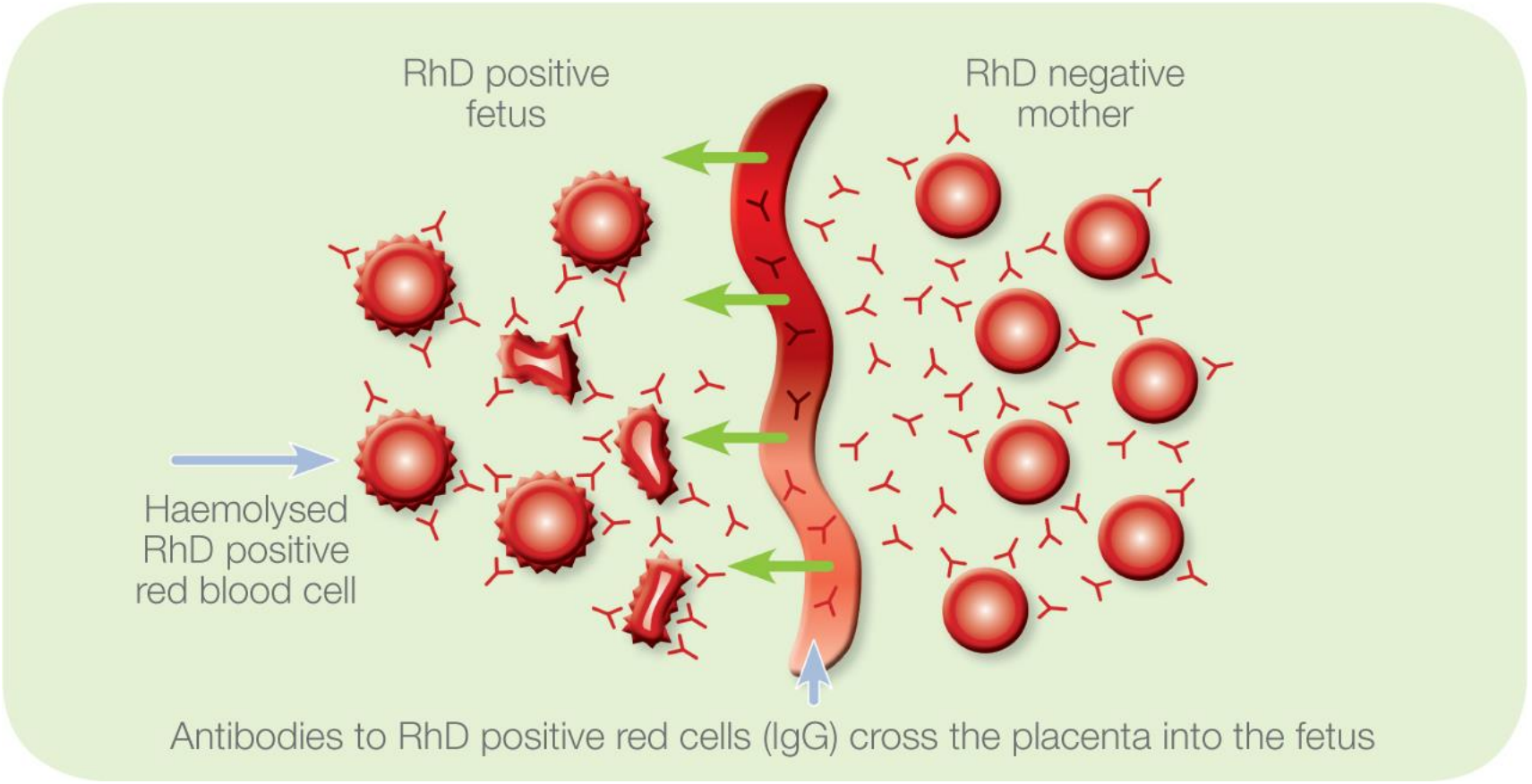
First pregnancy



RhD Negative mother develops Anti-D in immune response

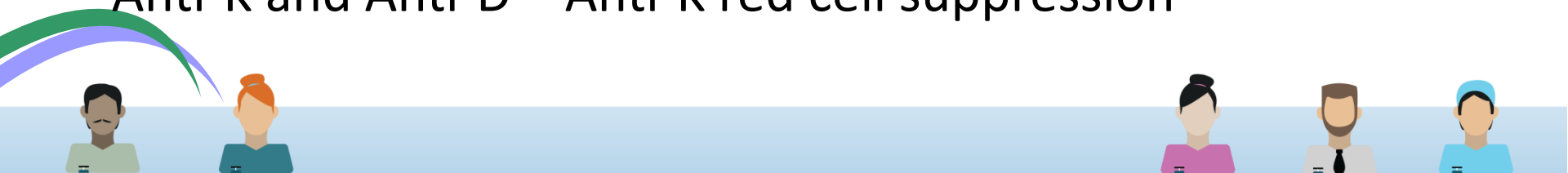


IgG crosses placenta - antibody attaches to fetal red cells and causes haemolysis in the fetal circulation



Haemolytic Disease of the Newborn

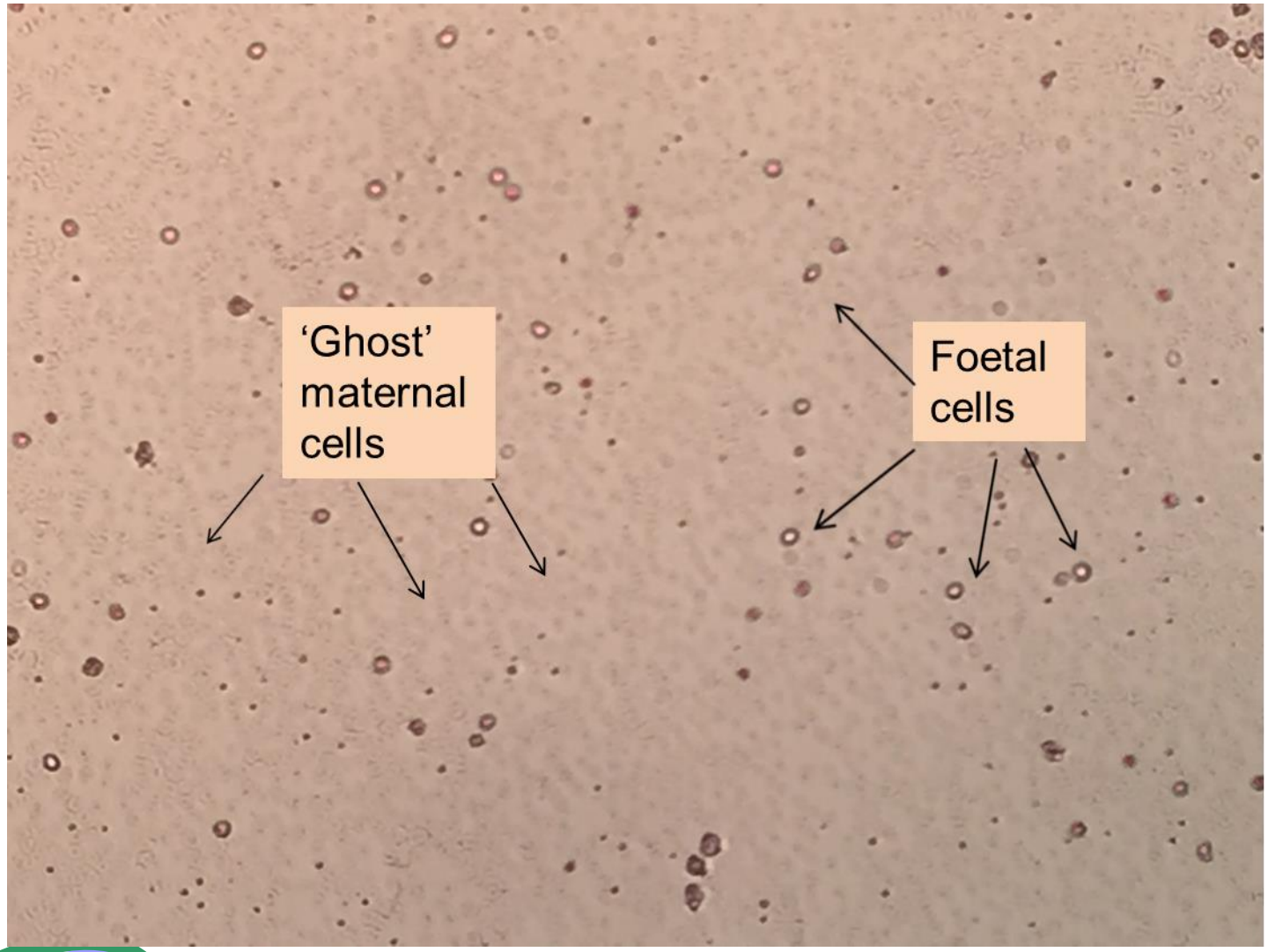
- IgG crosses placenta - antibody attaches to fetal red cells and causes haemolysis in the fetal circulation
- Fall in haemoglobin, increase in serum bilirubin
- High bilirubin can result in brain damage
- If affected prior to birth the result is usually intrauterine death from hydrops fetalis
- Post natal - can range between mild, moderate and severe
- Main antibodies responsible for HDN are Anti-c, Anti-K and Anti-D – Anti-K red cell suppression



The Kleihauer-Betke Test

- Test used to screen for FMH after 20 weeks gestation
- Acid elution test – HbF resistant to elution in an acid environment, HbA removed
- Film is stained with eosin
- Maternal cells appear as ‘ghost’ cells, fetal cells stain deep pink
- Can be counted under a microscope – time consuming
- UHNT screen only – number determined via Flow Cytometry

The Kleihauer-Betke Test



Positive Kleihauer film representing a bleed of approximately 12ml

Flow Cytometry

- More accurate
- Based on detection and quantification of fluorescent markers bound to RhD positive fetal cells
- Fetal bleed calculated within 90 minutes
- Samples sent to Leeds for testing
- If the mother is RhD positive this test cannot be used
- Necessary treatment with Anti-D immunoglobulin is then calculated

Anti-D Immunoglobulin

- 125 IU covers a 1ml bleed
- We issue 1500 IU as a minimum – 12ml bleed
- Prophylaxis a major success story – HDN deaths in England and Wales in 1977 : 106, in 1990 : 11
- Prevents mother from producing immune Anti-D
- Informed choice – paternal genotyping?
- Most effective if given within 72 hours
- Efficacy tails off over 10 days

*** The 72 hour window of opportunity ***

Case Study

- 21 year old
- Gravida 4

  2 early miscarriages
- Parity 1

  NVD in 2016
- Rh negative

- Previous safeguarding issues but case now closed
- Declined screening
- No concerns regarding fetal growth during pregnancy

Antenatal History

At 16w Gestation

- Fall onto abdomen at work
- Abdominal pain but no vaginal bleeding
- Treatment

  Anti-D 1500 IU IM

At 19w Gestation

- Unprovoked minimal vaginal bleeding
- Patient could not wait for Anti-D and did not attend follow up for Anti-D administration
- 20 week scan normal

Antenatal History

At 33w Gestation

- Had a fall onto abdomen
- Kleihauer <8ml
- Anti-D 1500 IU IM administered

At 40w Gestation

- Reduced Fetal Movements
- CTG and Ultrasound normal
- Declined induction of labour as preferred home birth

Labour

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<u>At 40+5w Gestation</u>

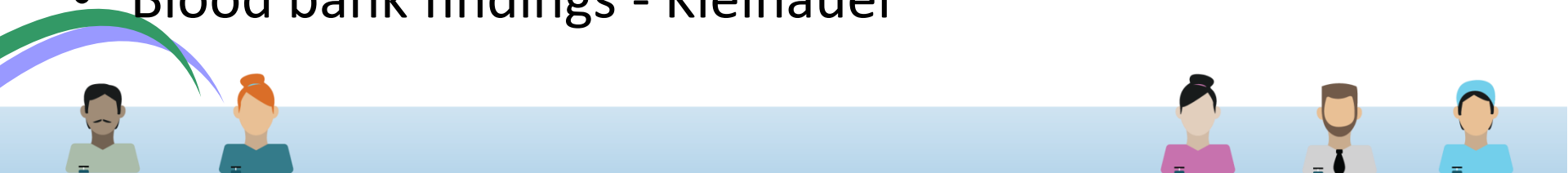
Patient attends Maternity Assessment Unit with Spontaneous Rupture of Membranes (SROM) with tightening

On further questioning, patient stated SROM occurred approximately 2 days earlier……..

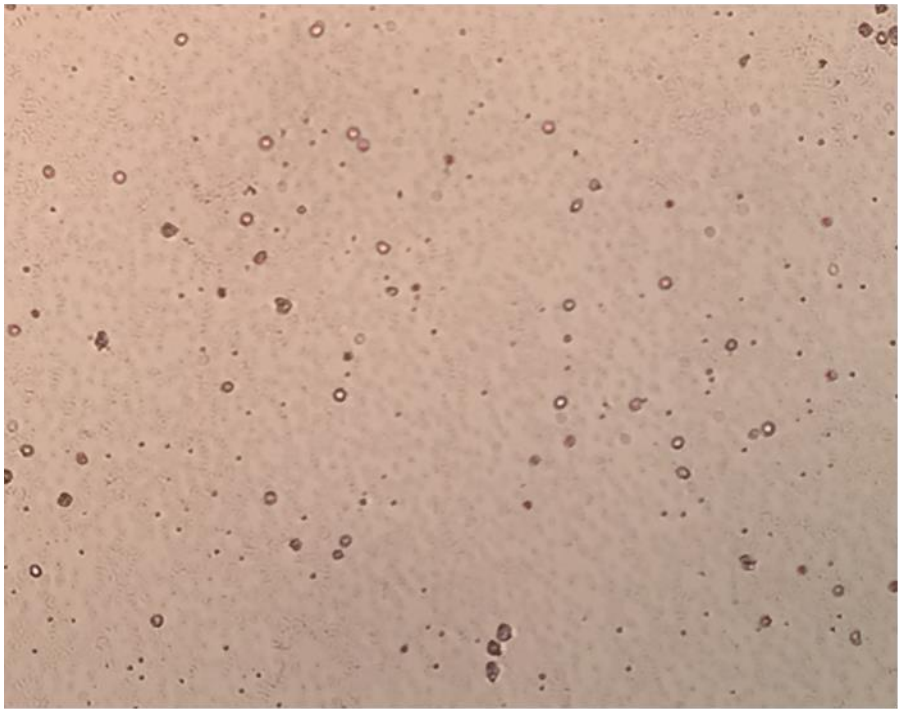
As had another fall

Labour

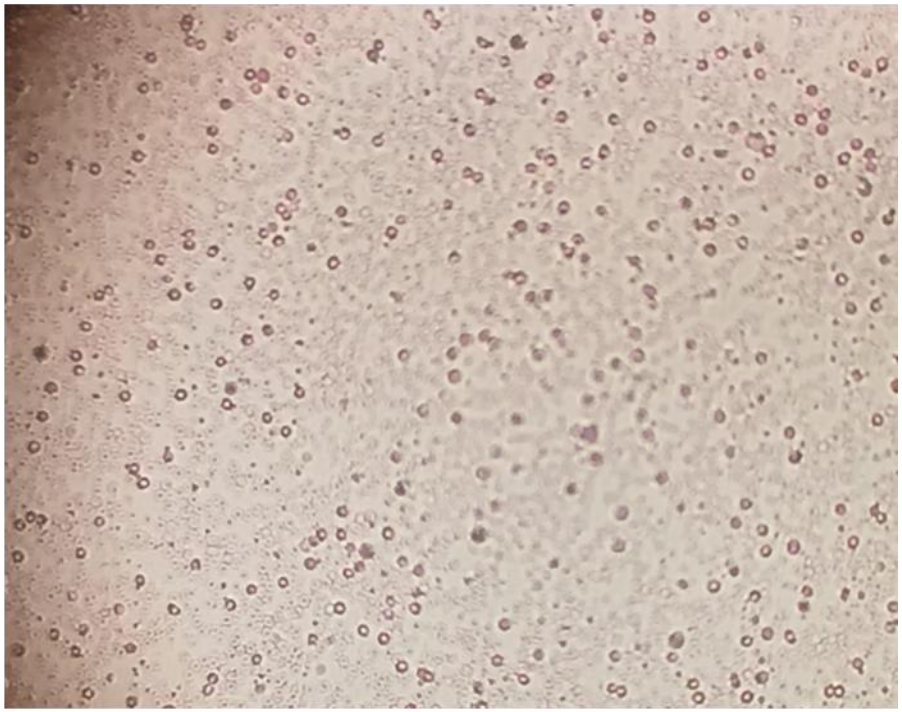
- Vaginal examination confirmed rupture of membranes and light meconium was noted
- IV antibiotics commenced
- Abnormal CTG in the first stage of labour
- Class 1 Emergency Caesarean Section
- Baby born white, floppy with significant meconium
- Cord blood gases suggestive of Metabolic Acidaemia
- Blood results for baby: Hb 40g/L, RBC 1.20 x 10^{12}/L, Total Bilirubin 16 umol/L, DCT Negative
- Requested HPLC, G6PD – assumption of haemolysis
- Blood bank findings - Kleihauer



Kleihaeur test results



12 ml bleed



Larger bleed

Post Natal Management of Mother

- Kleihauer results assessed by Haematology Consultant at Leeds
- Kleihauer 173ml (very high)
- Patient required Anti-D 15000 IU via IV (maximum dose IV) given slowly over a minimum period of 10 minutes
- This was to be followed by a further 4500 IU via IM
- Anti-D needed to be administered ASAP to maximise effectiveness as patient had fell 2 days earlier and had not received Anti-D

Initial Decision Making Issues

1. Patient required an unusually high dose of Anti-D
2. This scenario occurred in early hours of morning and staff unsure if they should delay giving dose until morning
3. Time pressure
4. The Trust Anti-D Guidelines appeared to be insufficient to cover this unusual scenario
5. Both Doctors and Midwives believed the other should prepare and administer the Anti-D

Midwifery Concerns

1. The Anti-D dosage was very high, 15000 IU not 1500 IU
2. The Anti-D administration route for the 15000 IU was IV, not IM: Midwives Exemptions Cover Midwives to administer 1500 IU IM
3. Anaphylaxis
4. Midwives Scope of practice and professional accountability (loss of registration if complications arisen after administration)

Specialist Lead Midwife liaised with Trust Patient Services Manager for guidance around drug administration. Joint decision was made: Midwifery staff to support medical staff to administer

Doctors Concerns

- The prescription was valid as it was the instructions given by the Consultant Haematologist at Leeds to On-Call medical staff
- The dosage had been double checked by blood bank as it was unusually high
- The Midwives had received training to prepare and administer single dose Anti-D 1500 IU via IM
- Doctor had never given Anti-D either via IM or IV previously

How would this scenario be currently managed at your hospital?

1. Who would prepare and administer the Anti-D?

2. Where would you administer the Anti-D?

Ethical Decision Making (1)

<u>The Principle of Beneficence</u> - i.e. patients best interests

- We agreed that administrating the Anti-D ASAP would reduce the patients chances of developing Anti-D antibodies and subsequently reduce the risk of HDN in future pregnancies (if the foetus was Rh positive).

Ethical Decision Making (1)

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Principle of Non Maleficence – ie avoiding patient harm

- We agreed that if we DID NOT give the Anti-D quickly, the patient was more likely to suffer from future HDN (if foetus was Rh positive).

- Therefore we would be causing patient and any future foetus potential harm by NOT administrating the drug

Management of Mother

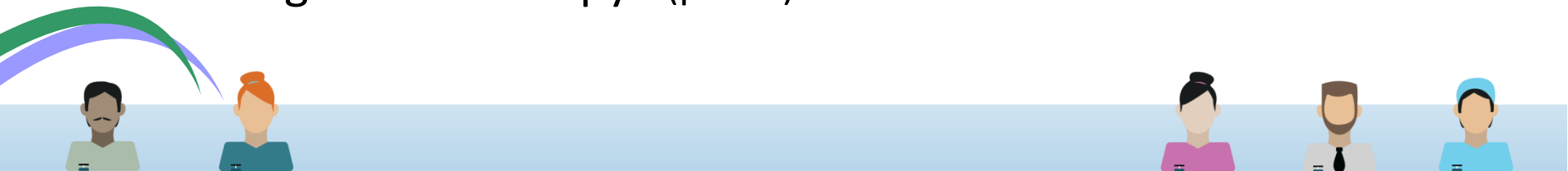
- The preparation and administration of the Anti-D was completed by a doctor under the supervision of the senior midwife in charge
- After drug administration, 15 minute observations were completed by the midwife in charge in the patients side room on the post natal ward to monitor for anaphylaxis
- The crash trolley was checked and placed outside the patients side room prior to administration
- The patient received Anti-D 15000 IU IV over 10 minutes followed by a further 4500 IU IM

Management of Mother

- Kleihauer repeated 48 hours after initial dose
- Kleihauer result still showed 20ml of fetal blood
- The patient required a further 3000 IU Anti-D to be given via IM
- Follow up Kleihauer was performed after 72 hours
- Kleihauer result indicated negative for foetal blood
- Baby was transfused 5 units of blood
- The patient did not attend follow up appointment
- The case was discussed at Risk Management

Updated Trust Guidelines (2)

- **"Intravenous** Anti-D Immunoglobulin must be prescribed by the medical staff" (p9).
- "NMC: Midwives Exemptions state registered midwives can administer **intramuscula**r Anti-D Immunoglobulin to an adult, for antenatal/postnatal use - the midwife cannot administer **intravenous** Anti-D Immunoglobulin unless it is prescribed by a medical practitioner" (p9).
- "The woman should be cared for in a high dependency clinical area, such as the Delivery Suite, with communication between the medical staff and the senior specialist lead midwife" (p9).
- "The woman should remain in the high dependency clinical area for a minimum of one hour following completion of the Anti-D Immunoglobulin therapy" (p9-10).



References

1 Hope T Medical Ethics A Very Short Introduction (2004) United States Oxford University Press.

2 North Tees and Hartlepool NHSfT Issuing and Tracing Anti-D Immunoglobulin 2018

Thank you

Debbie Cox – Transfusion Practitioner
Carole Smales – Transfusion Laboratory Manager
Ellie Todd – Specialist Biomedical Scientist
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