Fetal Anaemia and Intrauterine Transfusion

Mr William Dennes PhD FRCOG

Consultant Obstetrician, Specialist in Fetal Medicine

Queen Charlotte's and Chelsea Hospital

London W12 0HS

South East Coast Regional Transfusion Committee Education Symposium

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Imperial College Healthcare NHS
NHS Trust

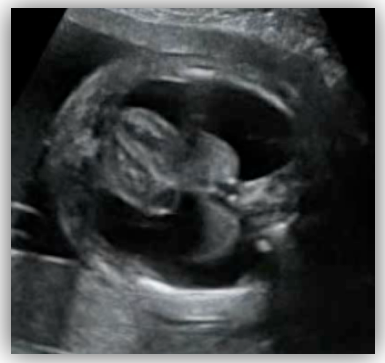
Fetal Anaemia

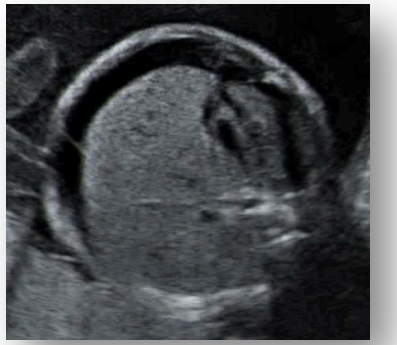
- Clinical presentation:
  - Immune Fetal Hydrops
  - (Non-immune Fetal Hydrops)
- Management Fetal anaemia
  - MCA assessment
  - Fetal Blood sampling / Intrauterine Transfusion
- Case Studies

Clinical presentation – Fetal anaemia:

Fetal Hydrops:

- Immune and non-immune Fetal hydrops
- Abnormal fluid collection in at least two different fetal compartments:
  - Pericardial effusion
  - Pleural effusion
  - Ascites
  - Skin oedema (>5 mm)
  - Polyhydramnios
  - Thickened placenta (>6cm)
  - Cardiac failure
  - IUD





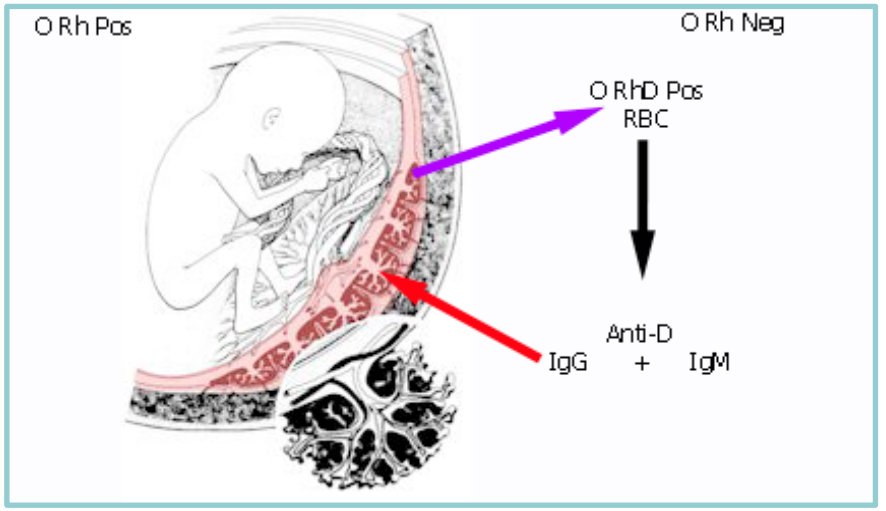
Immune Fetal Hydrops:

Result of circulating maternal AB against (fetal) red cell antigens (Red cell isoimmunization)

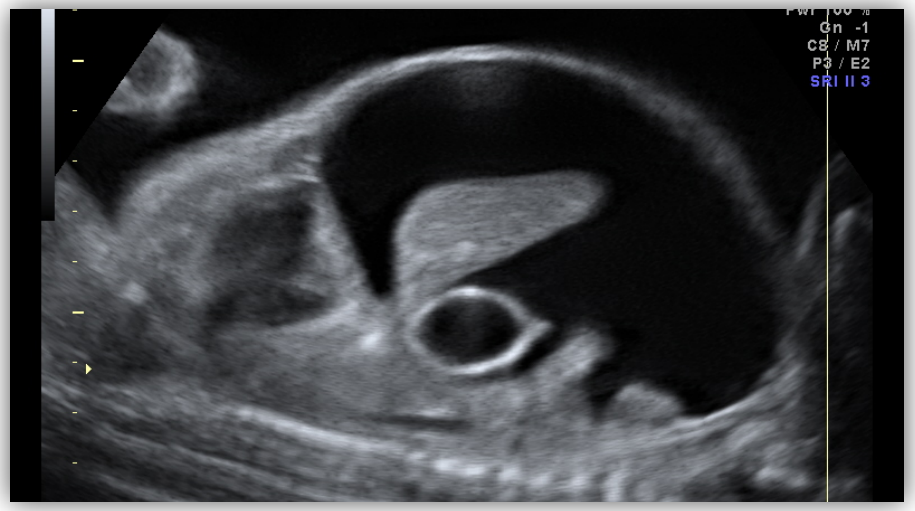
- >100 Red cell antigens, but isoimmunization associated with <30:
  - Typically:
    - anti-D, anti-C, anti-Kell, anti-E
  - Rarely:
    - anti-M, anti-N, anti-S

Red cell iso-immunization:

- 15% of Antenatal population Rh Negative
- Routine pregnancy AB screen – 12 and 28 week
- Rh negative patient – cfDNA for fetal genotype (IBGRL Bristol)
- If Rh positive fetus: Anti-D prophylaxis at 28 weeks (and after any sensitising event)
- cfDNA now available for Kell, C, e and C



Red cell iso-immunization: Assessment



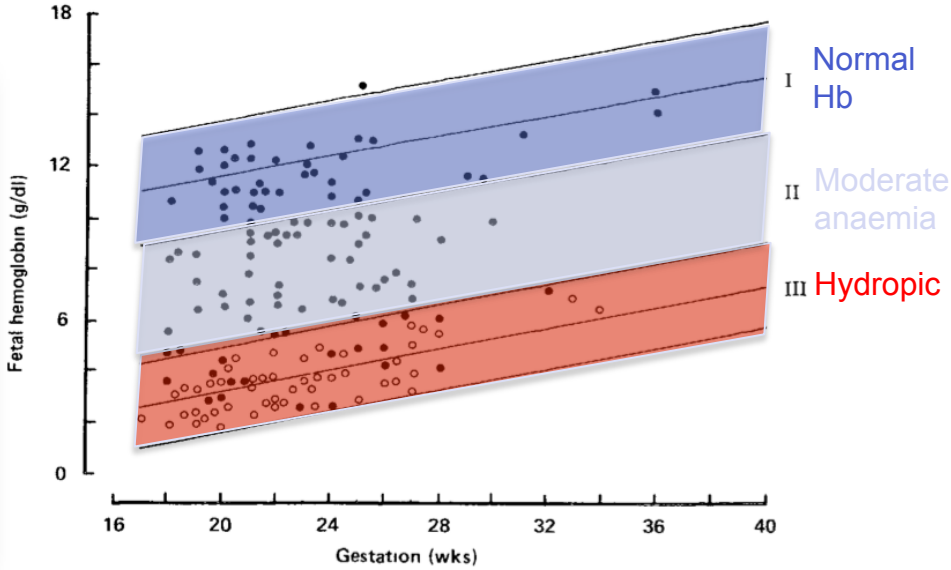
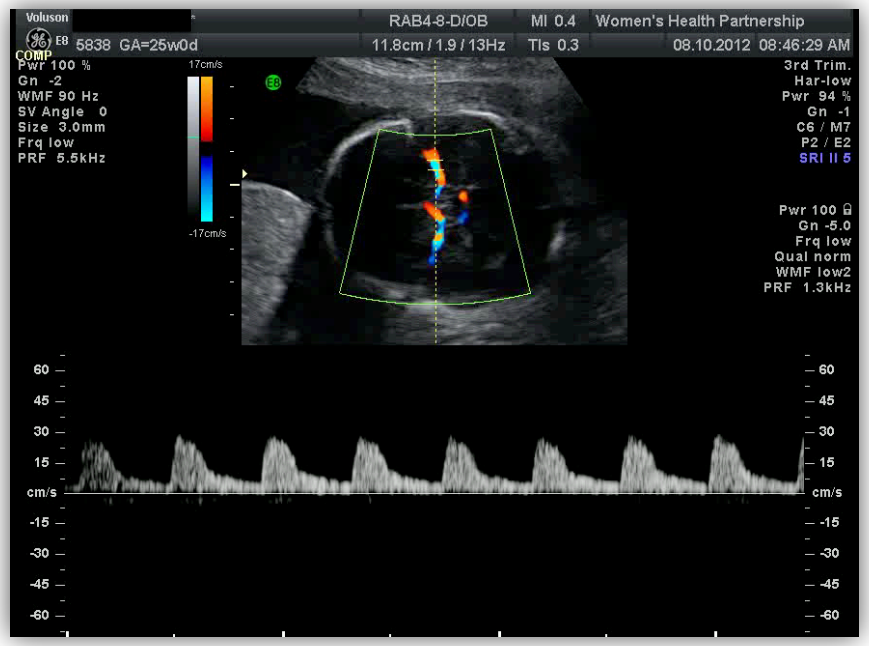


Fig 1—Fetal haemoglobin concentration of 48 hydropic (○) and 106 non-hydropic (●) fetuses from red cell isoimmunised pregnancies at time of first fetal blood sampling.

Red cell iso-immunization: Assessment



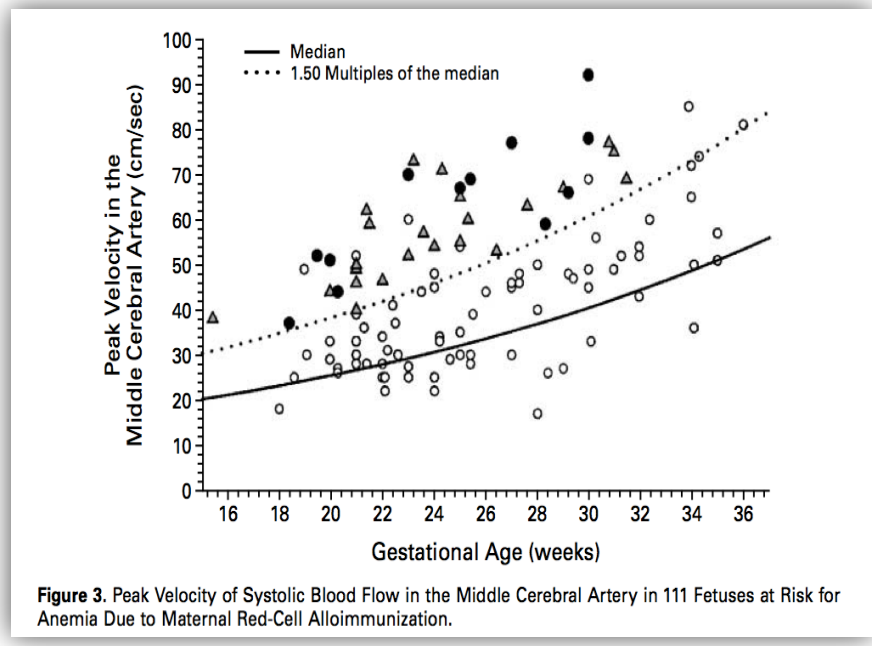
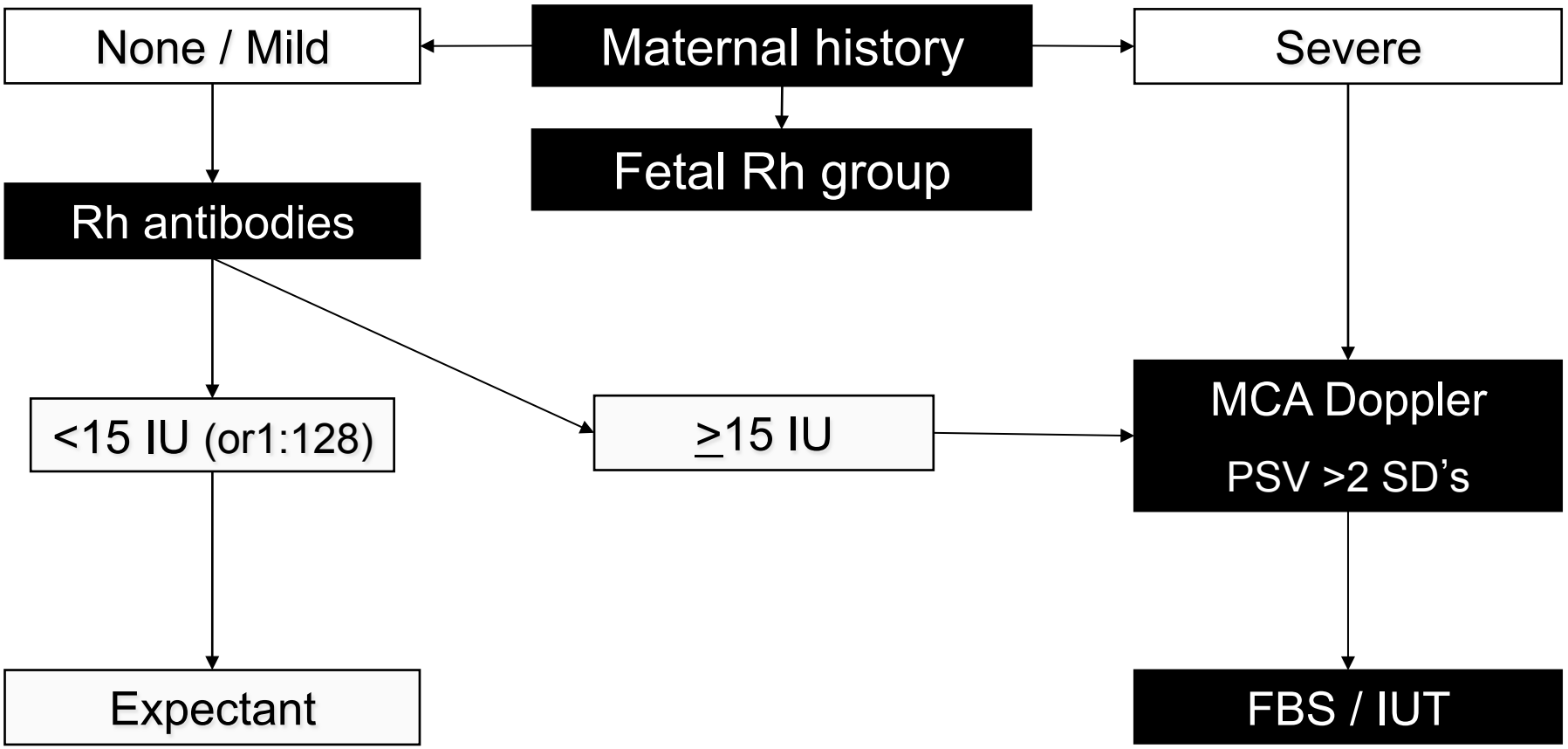


Figure 3. Peak Velocity of Systolic Blood Flow in the Middle Cerebral Artery in 111 Fetuses at Risk for Anemia Due to Maternal Red-Cell Alloimmunization.

- Fetal Anaemia - decreased blood viscosity
- Increased venous return + preload – increased cardiac output
- Increased arterial + venous blood flow velocities
- MCA-PSV useful method to assess anaemia
- Low false positive rate

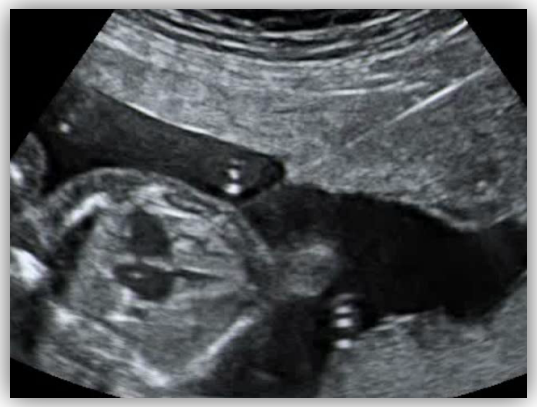
Mari G. Non-invasive diagnosis by Doppler ultrasonography of fetal anemia due to maternal red-cell alloinmunization. N Eng J Med 2000;342:9-14.

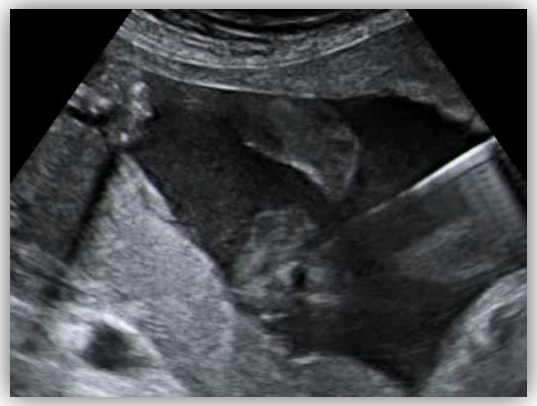
Red cell isoimmunization: management

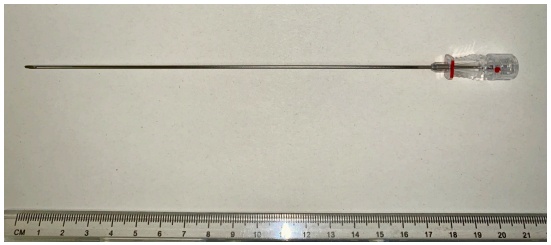


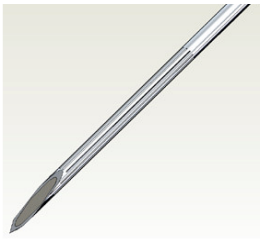
Red cell isoimmunization: management

- **Fetal Blood sampling / Intra-uterine Transfusion:**
  - Cordocentesis, Intrahepatic vein, intracardiac
  - Outpatient procedure – Fetal Medicine Unit
  - Consent - 1-2% procedure – related loss (PPROM/Fetal bradycardia)
  - Preoperative IV AB
  - Ultrasound guidance
  - Aseptic technique
  - Local Anaesthetic infiltration
  - 17 Gauge needle (1.4 mm diameter)



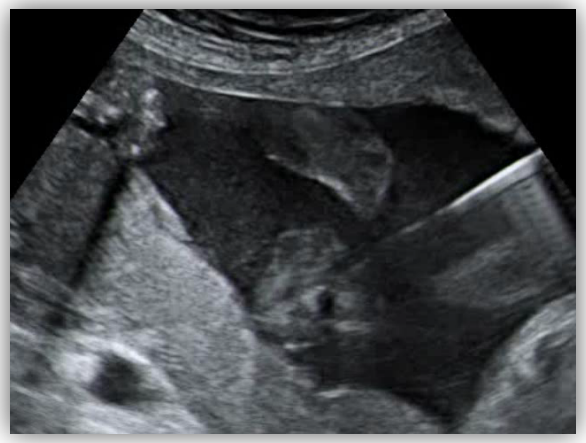






Red cell isoimmunization: management

- **Intra-uterine Fetal Blood sample:**
  - From 16 weeks of pregnancy
  - Transplacental or transamniotic
  - Sample site:
    - Intrahepatic vein
    - Umbilical Cord insertion
    - Free loop
    - Intracardiac
  - 1mL sample –immediate result in Fetal Medicine unit by Haematology team or Haemacue.

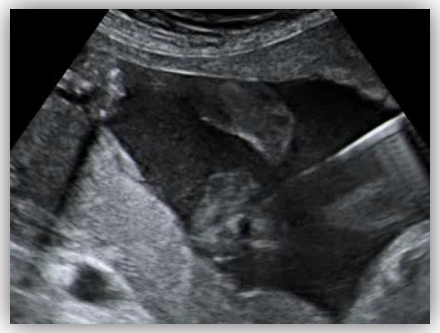


Red cell isoimmunization: management

- **Intrauterine Transfusion:**
  - Transfuse O Rh Negative, packed cells (HCT >85%), irradiated, CMV negative, Kell Negative
  - Rate – 10-15 ml/min
  - Monitor FH
  - Volume – dependent on HCT and fetal Hb:

Gestational age:	Volume to transfuse:
16-18 weeks	5ml
20 weeks	20ml
> 20 weeks	20mL + 10ml/week of gestation to a max of 100ml

  - Repeat FBS post transfusion
  - Paired samples to Haematology department for formal FBC.



Red cell isoimmunization: timing of subsequent transfusions

- Initial decision for IUT based on:
  - Hydrops
  - MCA PSV
- Timing of Subsequent IUT:
  - MCA predictive of severe anaemia for 2nd (but not the 3rd transfusion (for a DR of 95%, MCA PSV): FPR
    - 1st Transfusion 14%
    - 2nd Transfusion 37%
    - 3rd Transfusion 90%
  - Anticipate rate of decrease of 0.4 g/dL/day
  - Empirically IUT every 2-3 weeks

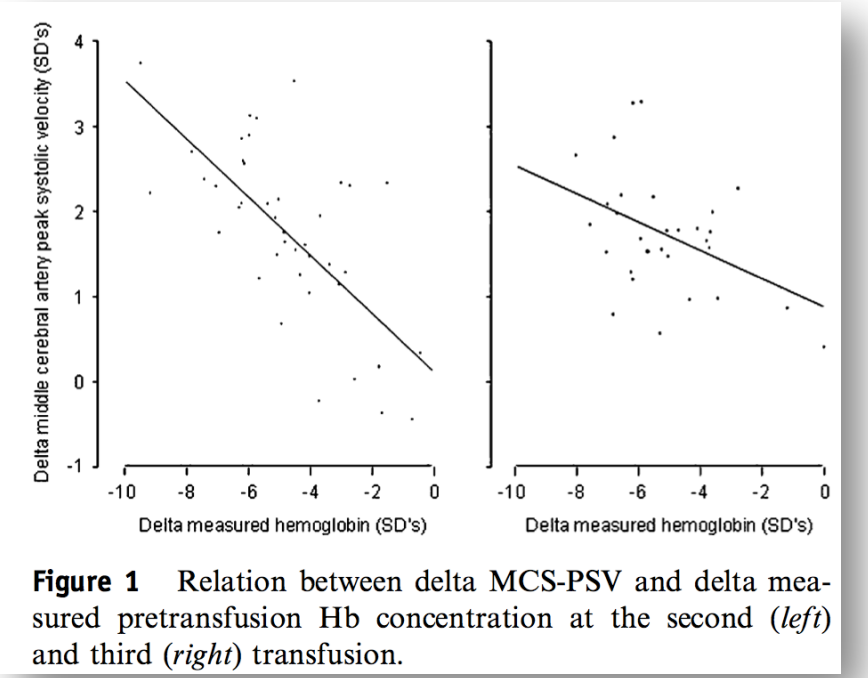


Figure 1 Relation between delta MCS-PSV and delta measured pretransfusion Hb concentration at the second (*left*) and third (*right*) transfusion.

Nicolaides et al. Prediction of severe fetal anemia in red blood cell alloimmunization after previous intrauterine transfusions
Am Journal of Obstetrics and Gynecology (2006) 195, 1550–6

Red cell isoimmunization: timing and mode of delivery

- Aim to manage / resolve hydrops prior to delivery
- No contraindication to vaginal delivery (deliver on standard obstetric indications)
- Aim for delivery 34-36 weeks (based on good neonatal outcomes / limitations of MCA data)

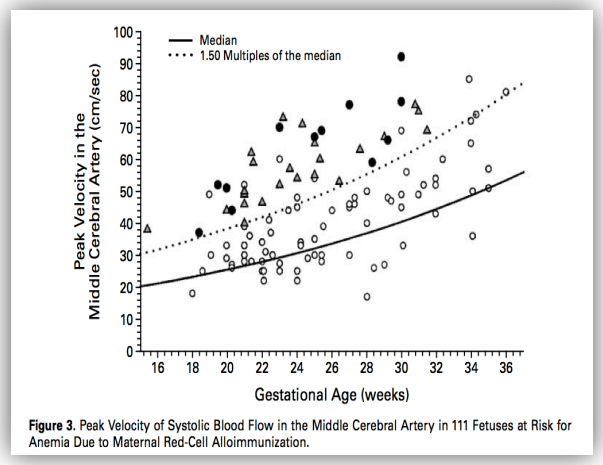


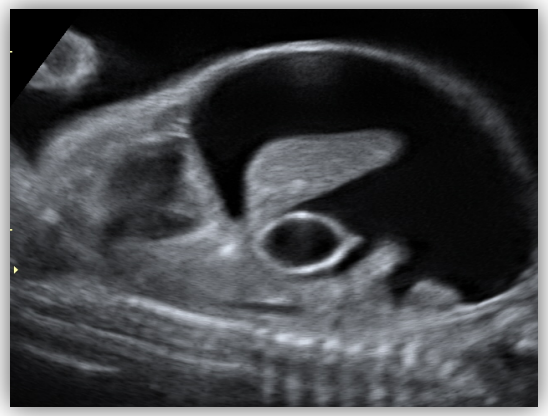
Figure 3. Peak Velocity of Systolic Blood Flow in the Middle Cerebral Artery in 111 Fetuses at Risk for Anemia Due to Maternal Red-Cell Alloimmunization.

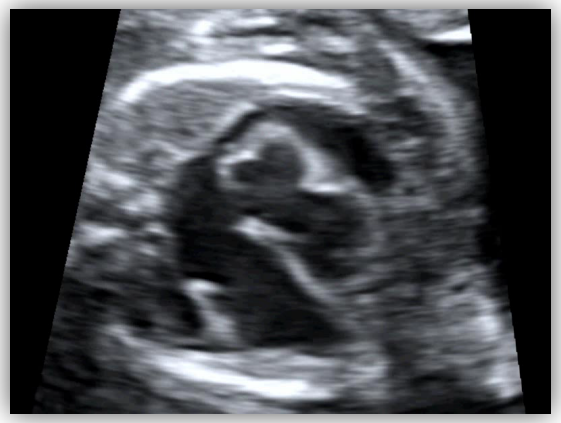
Non-Immune Fetal Hydrops:

- Structural abnormalities:
  - Cardiac - HLHS, PA, arrhythmia (SVT, WPW)
  - Pulmonary – CCAM, CDH
- Chromosomal abnormalities (X-, T13, T18, T21)
- Genetic syndromes
  - Arthrogryposis, TS
- Haematological disorders:
  - Failure to manufacture Hb (a-thalassaemia)
  - Fetal haemorrhage (ICH)
  - Haemolysis (G6PD)
- Infection:
  - Bone marrow destruction (Parvovirus B19 , CMV, Toxoplasmosis)
- MCDA Twins - TTTS

Non-Immune Fetal Hydrops:

- History:
  - FH of Metabolic disorders
  - Recent infection / exposure
- Investigations:
  - Maternal Blood:
    - Blood Group , Kleihauer and AB
    - FBC and electrophoresis
    - Viral screen – Toxoplasma, CMV, Rubella, Parvovirus
  - US/S (tertiary referral):
    - Detailed ultrasound scan
    - Fetal Echo
    - MCA Doppler
    - FBS (Fetal - FBC, Blood Group, karyotype, Viral screen)
  - Offer karyotype (10-20% risk of aneuploidy)



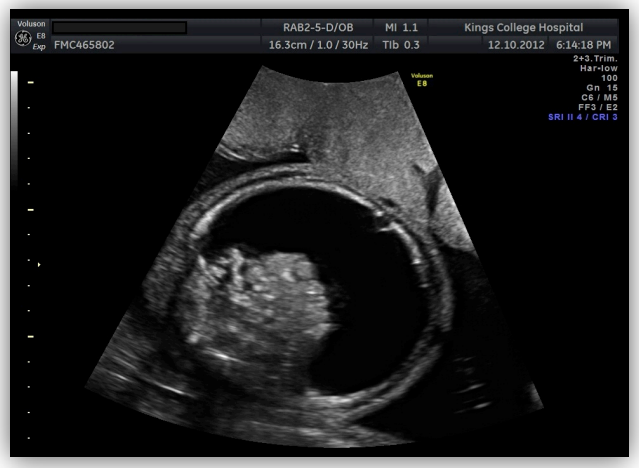


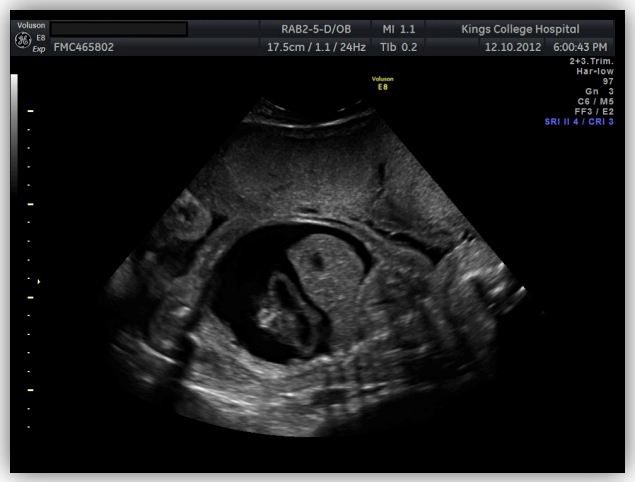
Non-Immune Fetal Hydrops:

- Management:
  - Dependent on aetiology
  - Cardiac malformation: very poor prognosis if hydrops secondary to structural (cardiac malformation). Offer TOP.
  - Cardiac arrhythmia: maternal therapy (Digoxin/Flecainide)
  - Fetal anaemia - IUT
  - Termination of pregnancy
  - Timing of delivery – may be associated with preterm delivery (secondary to polyhydramnios, or iatrogenic – PET).
  - Mode of delivery – optimal mode remains unclear. Aim for SVD.
  - Perinatal mortality rate – 40-90%

Case study #1:

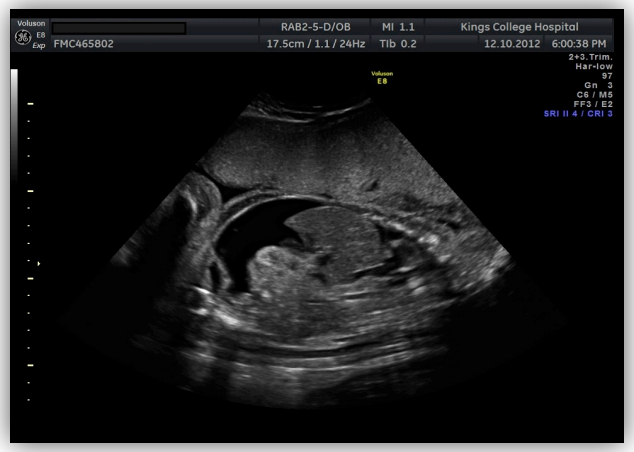
- 36 year old
- G3 P2+0
- Admitted to DGH 29+6/40:
  - Oedema, hypertension, proteinuria – "feeling unwell"
  - Investigations:
    - Normal FBC, LFT and renal function
    - AB Rh positive – no atypical AB (at 28 weeks)
  - Management:
    - Admitted, routine Obs, CTG
    - US/S: Widespread hydrops, placentamegaly, pleural and pericardial effusions, skin oedema.
    - MCA 95 cm/s (≥ 1.5 MoM)

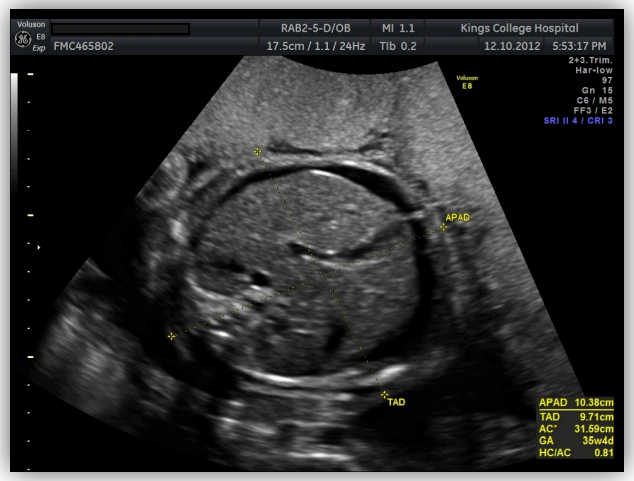




Case study #1:

- Further history – recent viral infection
- Diagnosis – **Parvovirus B19 infection with maternal PET**
- Management:
  - FBS/IUT
  - Initial Hb – 3.8 g/dL (Blood sent for TORCH, Karyotype)
  - Transfusion – 120 ml. Post procedure Hb – 9.5 g/dL
  - Planned repeat IUT
  - Returned to referring hospital
  - Abnormal CTG – Emergency LSCS. Neonatal admission
  - Confirmed Parvovirus
  - BW – 1980g.



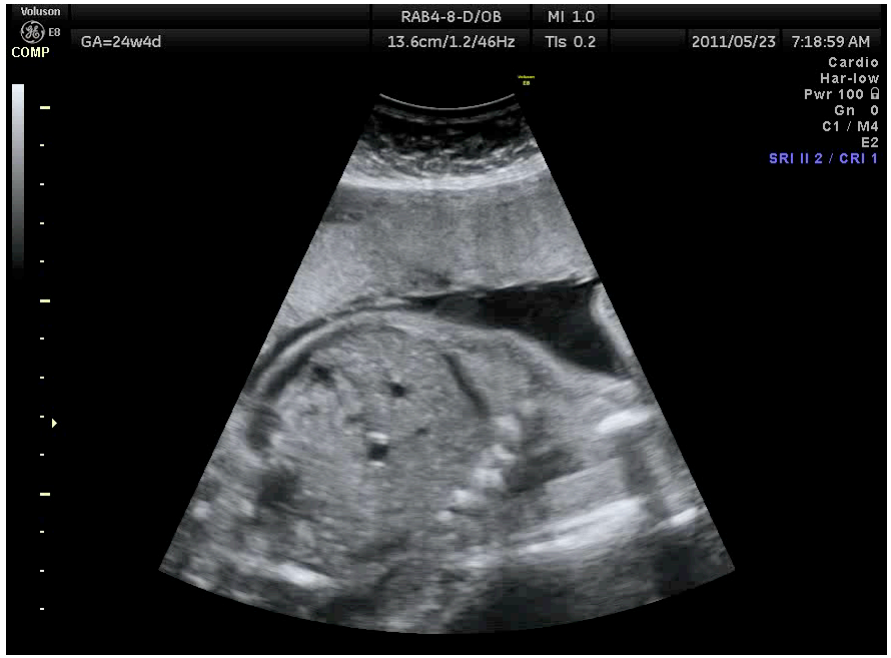


Case study #2:

- 34 year old
- G1 P0
- Low risk first trimester Combined screening
- Routine anomaly scan (22 weeks):
  - Fetal Supraventricular Tachycardia
  - No evidence of hydrops
- Management:
  - Fetal Echo
  - Maternal ECG
  - Commenced on Digoxin 250µg TDS

Case study #2:

- Follow up scan – 24 weeks
  - Persistent SVT
  - Moderate Hydrops
  - (Normal MCA)
- Follow up scan – 27 weeks
  - Hydrops resolved
  - Normal SR (Rate 140 bpm)
- Continued on Maternal Digoxin
- Outcome:
  - IOL at 40 weeks (Maternal PET)
  - Normal SVD – Female infant 3572g (~50th centile)
  - Neonatal – Propranolol to 6 months of age.



Any Questions?

Fetal Anaemia Summary:

- Immune Hydrops:
  - Assess History, Maternal AB screen, Detailed US/S + MCA
  - FBS / IUT if MCA >1.5 MoM
  - FU: IUT 2 weeks
- Non-immune Hydrops:
  - Infection: Parvovirus B19 , CMV, Toxoplasmosis.
  - MCDA Twins – TTTS
  - FBS / IUT if MCA >1.5 MoM

The Fetal Medicine Foundation

william.dennes@nhs.net