

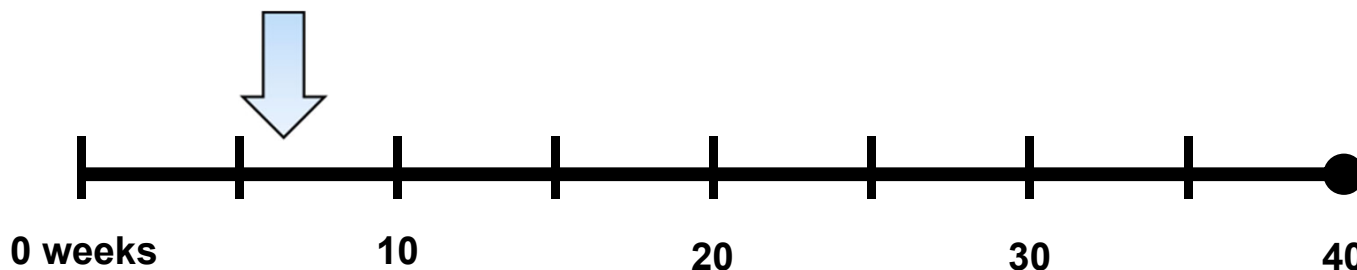
What are the Odds? The $< 1\%$ Failure

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Case Presentation

- 28 year old female
- G1P0
- Presented on 13-Nov-2017
- PV bleeding at 6/40
- O Rh(D) Negative
- No antibodies detected (BioVue CAT)
- **250 IU** Rh(D) immunoglobulin (RhDIg) was administered



Case Presentation

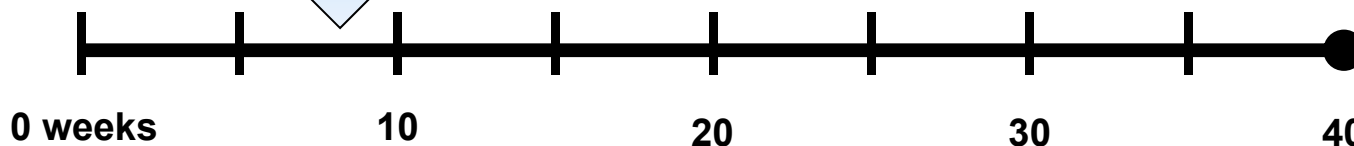
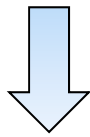
- Further unprovoked PV bleeding
- < 5 mL, mostly mixed with mucous
- No abdominal pain, no testing done

Guidelines for the use of Rh(D)
Immunoglobulin (Anti-D) in obstetrics
in Australia



The Royal Australian
and New Zealand
College of Obstetricians
and Gynaecologists
Excellence in Women's Health

There is insufficient evidence to suggest that a threatened miscarriage before 12 weeks gestation necessitates Anti-D.



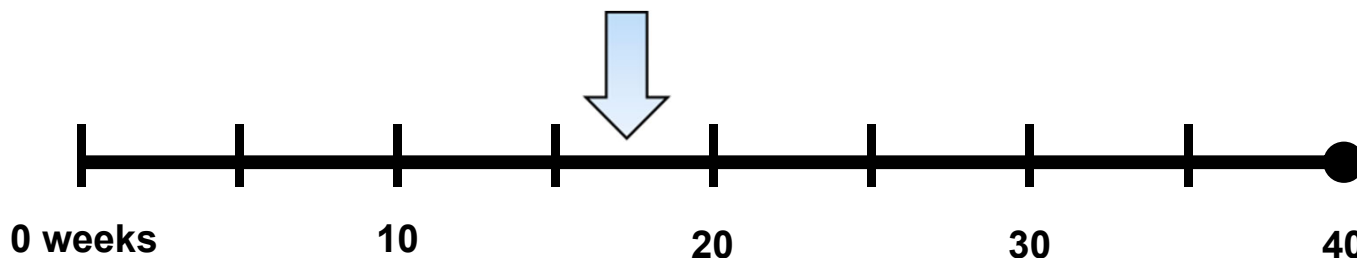
MonashPathology
MonashHealth

Case Presentation

- Small retro placental haemorrhage
- O Rh(D) Negative.
- **No antibodies** detected (BioVue CAT)
- **625 IU RhDIg** was administered
- Kleihauer testing not indicated

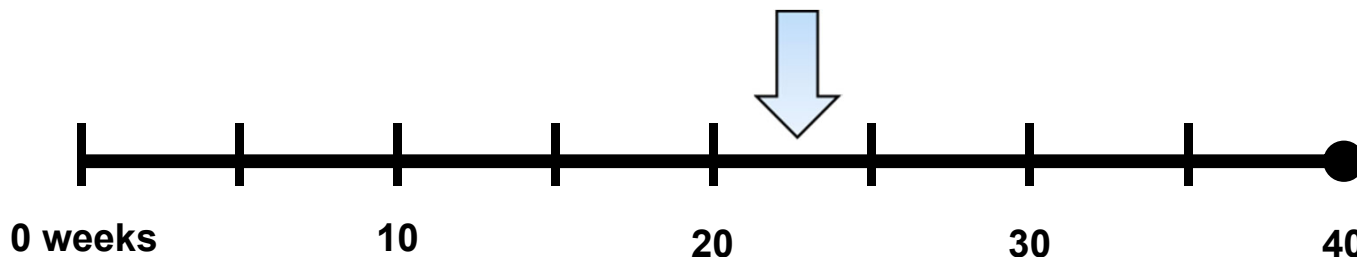


① Before 20 weeks, the fetomaternal blood volume is sufficiently small to be covered by the standard dose of RhD-Ig; therefore, quantitation of FMH volume is unnecessary.



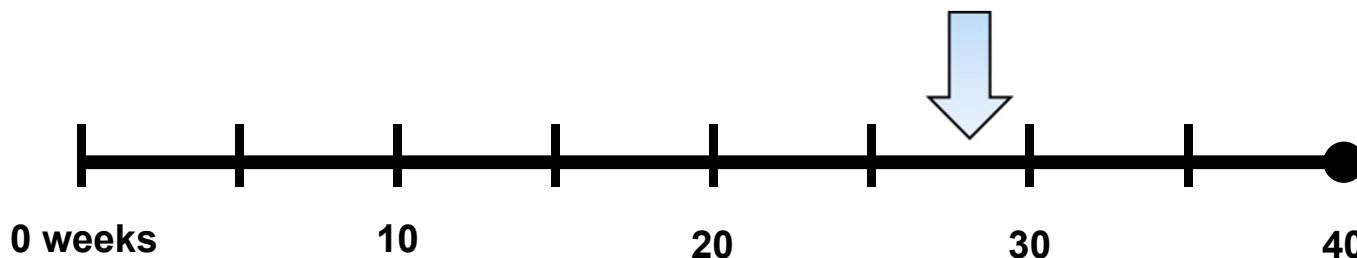
Case Presentation

- Presented to Emergency Department
- Abdominal pain
- Vomiting, diarrhoea, fevers for 2 days
- ? Appendicitis. Normal pelvic ultrasound
- Has eaten rockmelon. ? Listeria. Given antibiotics
- Sent home ? Gastroenteritis



Case Presentation

- Routine antenatal appointment at 28/40
- Routine blood tests collected
- 625 IU RhD Ig given
- Results :
 - Rh(D) Negative
 - Anti-D** detected
 - ? Due to RhD administration 11 weeks ago
 - ? Did they take the specimen after giving RhD Ig



? Passive or Immune

7.4.1 *Distinguishing between passive and immune anti-D*

- 7.4.1.2 At present, passively acquired anti-D (due to RhD-Ig) cannot be serologically differentiated from immune anti-D otherwise stimulated by pregnancy or transfusion, and differentiation based on antibody screening reaction strengths is not reliable.

	BioVue CAT
SC I (R_1R_1)	4
SC II (R_2R_2)	4
SC III (rr)	0

Anti-D Titre = 32 (R_2R_2 cell. BioVue CAT)

? Passive or Immune

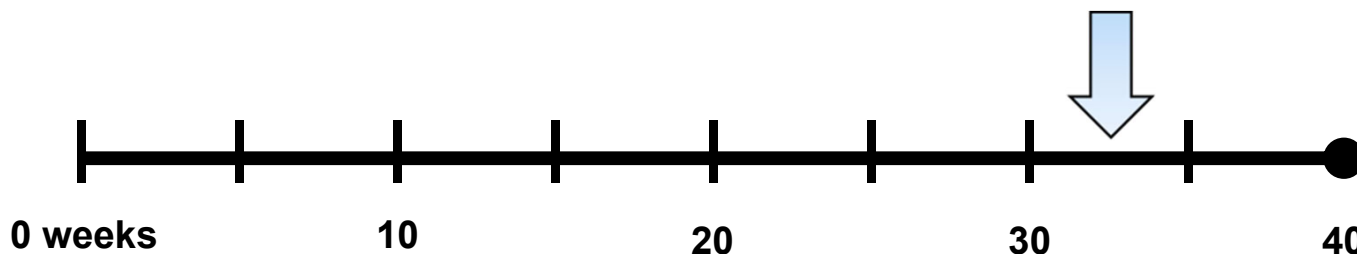
- Presumed iso immunisation
- Clinical team notified
- Referral to specialist unit recommended
- Recommended titres every two weeks and / or Doppler ultrasound assessment of fetal middle cerebral artery peak systolic velocity (MCA PSV)

Case Presentation

- Presented after a fall
- Anti-D but also **anti-C and anti-E** now detected
 - Anti-D + E titre (R_2R_2 cells) = 512
 - Anti-D + C titre (R_1R_1 cells) = 512
 - Anti-C titre ($r'r$ cells) = 1
 - Anti-E titre ($r''r$ cells) = 8

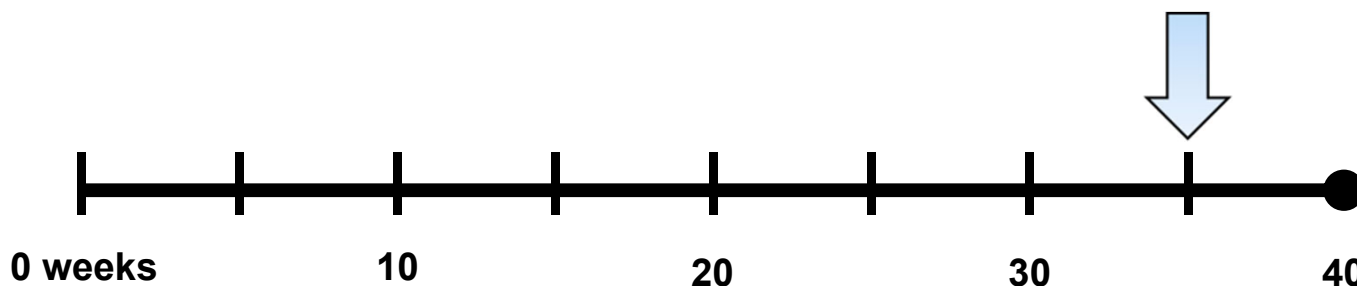
Kleihauer :

- 0.03% of fetal cells seen and estimated fetal red cell bleed of 0.72 mL



Case Presentation

- O Rh(D) Negative
- Anti-D, Anti-C and Anti-E detected
 - Anti-D + E titre (R_2R_2 cells) = **2048**
 - Anti-D + C titre (R_1R_1 cells) = 1024
 - Anti-C titre ($r'r$ cells) = 1
 - Anti-E titre ($r''r$ cells) = 8
- Kleihauer test – No fetal cells seen



Management

- Monitor titre
- Monitor by Doppler for MCA-PSV
- Extended maternal phenotype, in case of requirement for an IUT
- Extended phenotype performed on mother
- C-, c+, E-, e+, K-, Kp(a-) Fy(a-b+), Jk(a+b-), M+N+, S+s+

Prevention of Rh D alloimmunisation

- Routine antenatal prophylaxis at 28/40 & 34/40
- Any sensitising events
- Post delivery
- Kleihauer test to ensure that the dose of RhD Ig is sufficient after any sensitising event
- In our patient :
Appropriate treatment of sensitising events.

Isoimmunisation has still occurred



Failure to Prevent Isoimmunisation

- Prophylaxis is **not** 100% effective
- Failure rate is $< 1\%$ ⁽¹⁾
- American Guidelines
 - Failure Rate 0.14 - 0.2% ⁽²⁾
- United Kingdom review
 - Failure Rate 0.35% ⁽³⁾

1. RhD Immunoglobulin-VF AU Package Insert 12.00 December 2014

2. Prevention of RhD Alloimmunisation. ACOG Practice Bulletin. Clinical Management Guidelines for Obstetrician-Gynecologists. Number 181, August 2017

3. Routine antenatal anti-D prophylaxis for women who are Rhesus D Neg. NICE Technology Appraisal Guidance. 27 Aug 2008. nice.org/guidance/ta156

Failure to Prevent Isoimmunisation

- Reasons for failure
 - Not administering correct antenatal prophylaxis
 - Insufficient dosage after a known sensitising event
 - Not administered in a timely fashion - should be within 72 hours of a known sensitising event
 - Obese mother (BMI ≥ 30)
 - No obvious reason for failure. ? Unrecognised fetomaternal haemorrhage

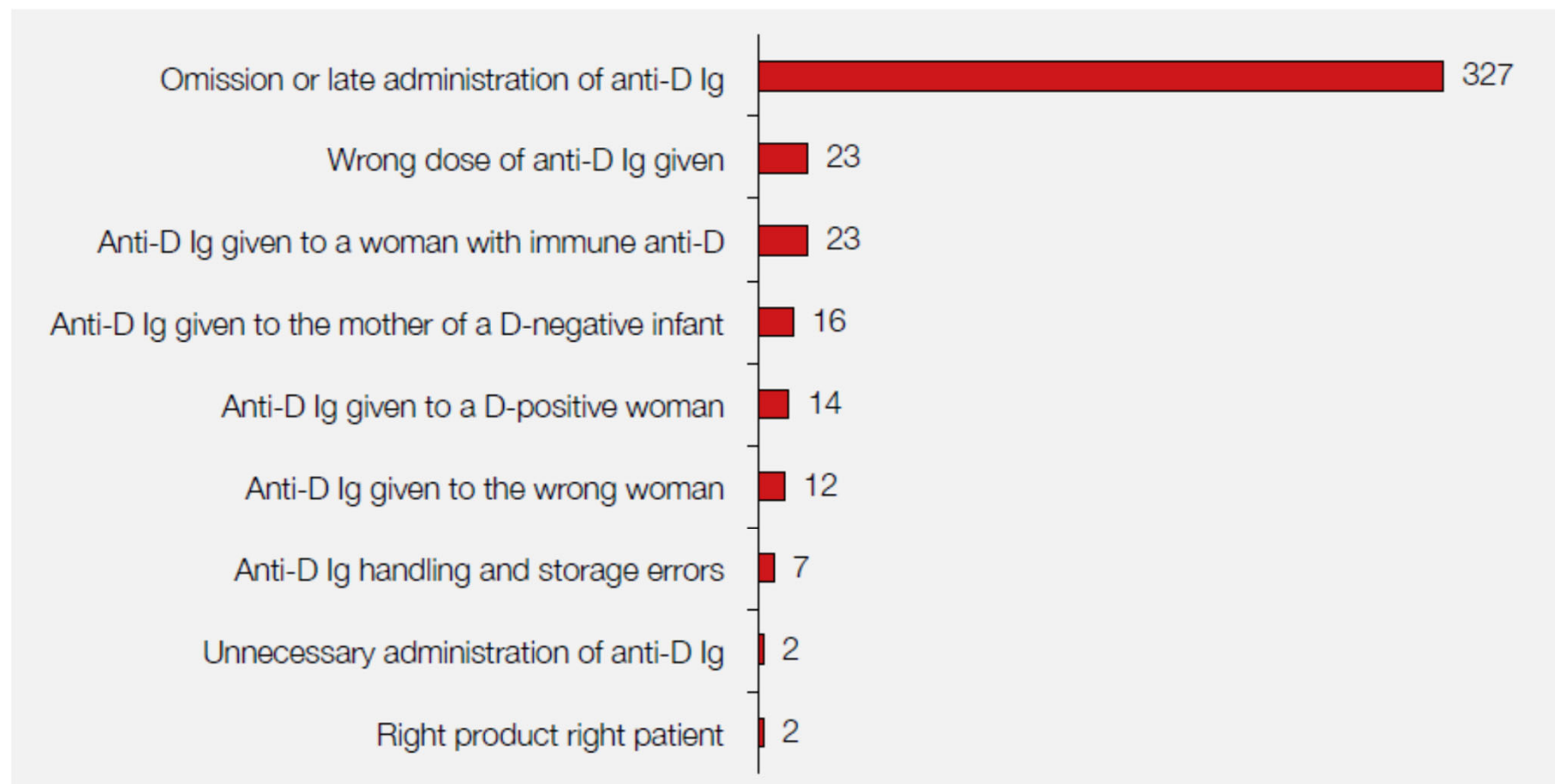
Prevention of Rh D Alloimmunisation. ACOG Practice Bulletin. Clinical Management Guidelines for Obstetrician-Gynecologists. Number 181, August 2017

STIR Report 2015 / 2016

- 14 errors reported
- 5 administered not required
 - 2 with Rh(D) Negative baby
 - 2 Rh(D) Positive women
 - 1 woman with immune anti-D
- 2 RhD dose omitted
- 7 released / administered to the wrong patient

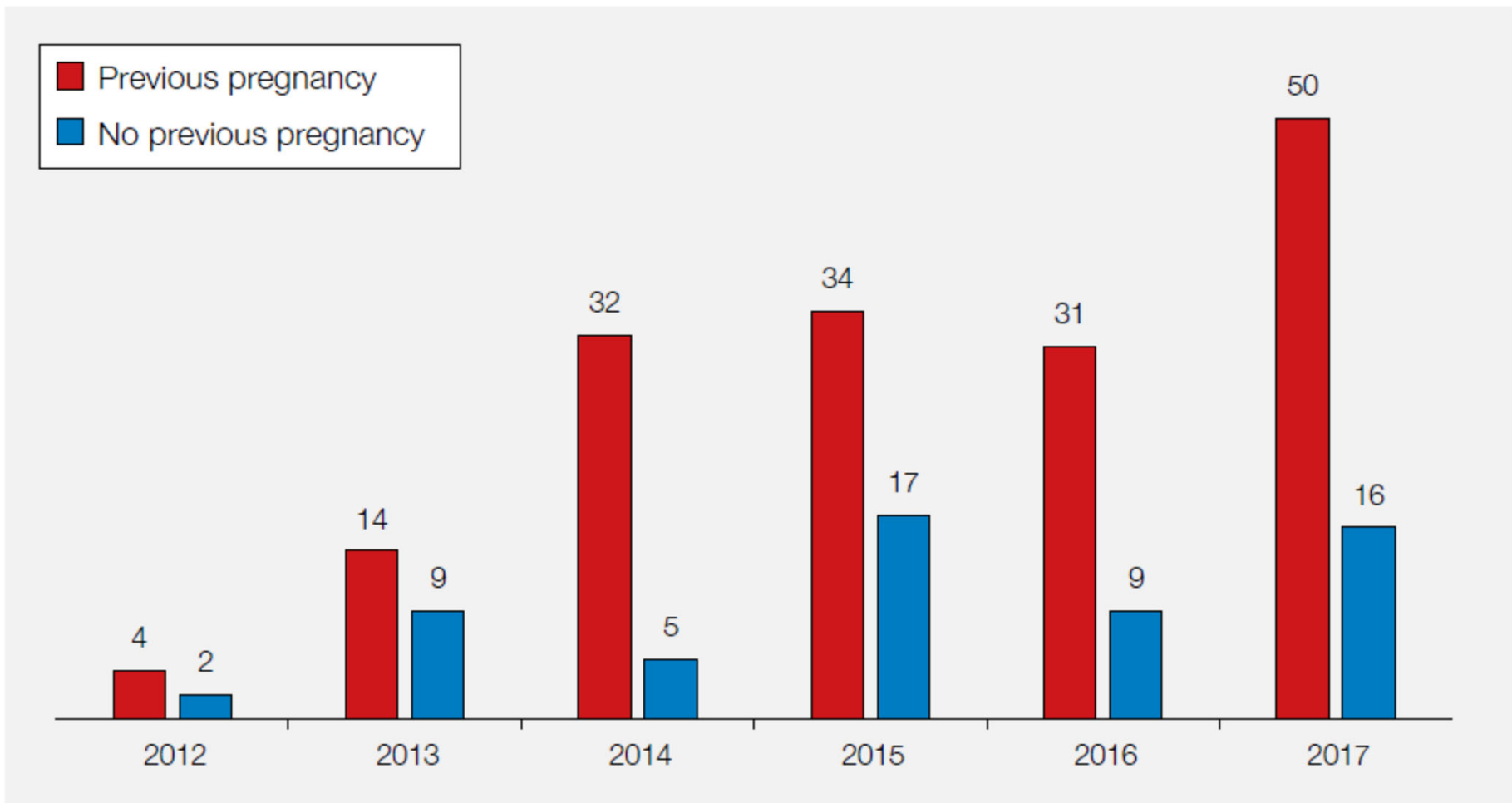


Anti-D Ig Related Errors



SHOT Report 2017. Chapter 14. Adverse Events Related to Anti-D immunoglobulin (Ig)
N =426

Failure to Prevent Isoimmunisation



Number of Reports of Anti-D immunisation in pregnancy by year, 2012 – 2017

SHOT Report 2017. Immune Anti-D in Pregnancy : Cases Reported up to the end of 2017

Failure to Prevent Isoimmunisation

	Number of new cases 2017	Number of cases cumulative to 2017
Before 28 weeks	2	6
At or after 28 weeks, before delivery	4	15
At delivery	10	35
Other	0	1*
No information	0	1
Total	16	58

No Previous Pregnancy. Details of Time of Detection of Alloimmune anti-D

SHOT Report 2017. Immune Anti-D in Pregnancy : Cases Reported up to the end of 2017

Failure to Prevent Isoimmunisation

PSE	Number of cases
None	44
7 antepartum haemorrhage (APH) 2 interventions (chorionic villous sample, amniocentesis) 2 falls 1 large FMH at delivery 1 twin pregnancy	Some women had more than one PSE

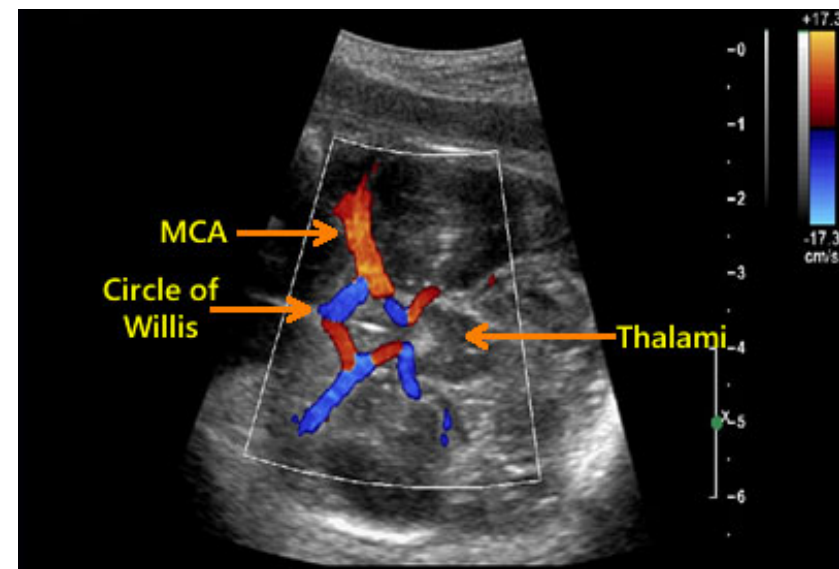
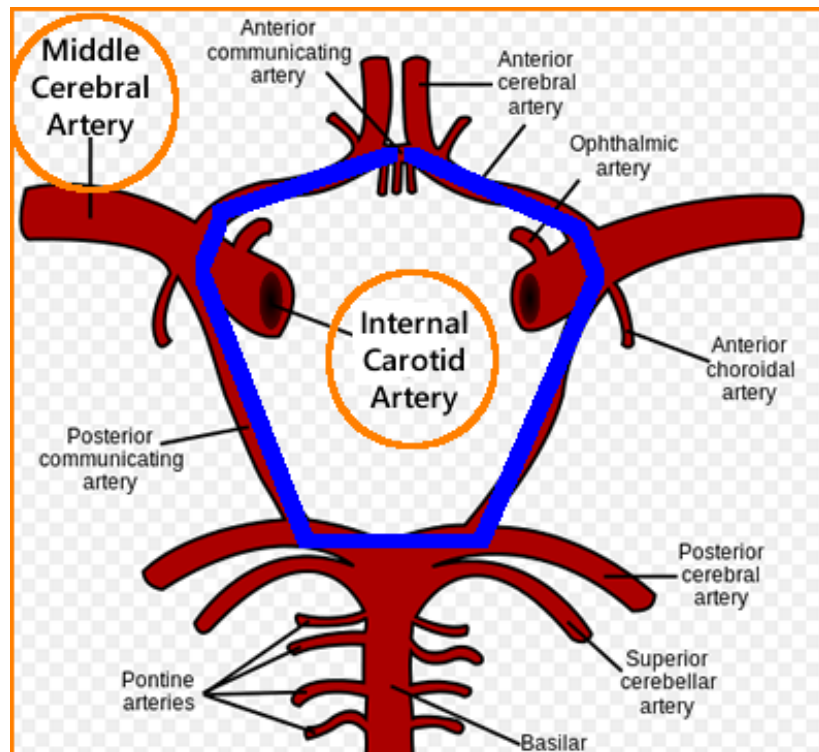
No Previous Pregnancy. Details of Previous Sensitising Events

SHOT Report 2017. Immune Anti-D in Pregnancy : Cases Reported up to the end of 2017

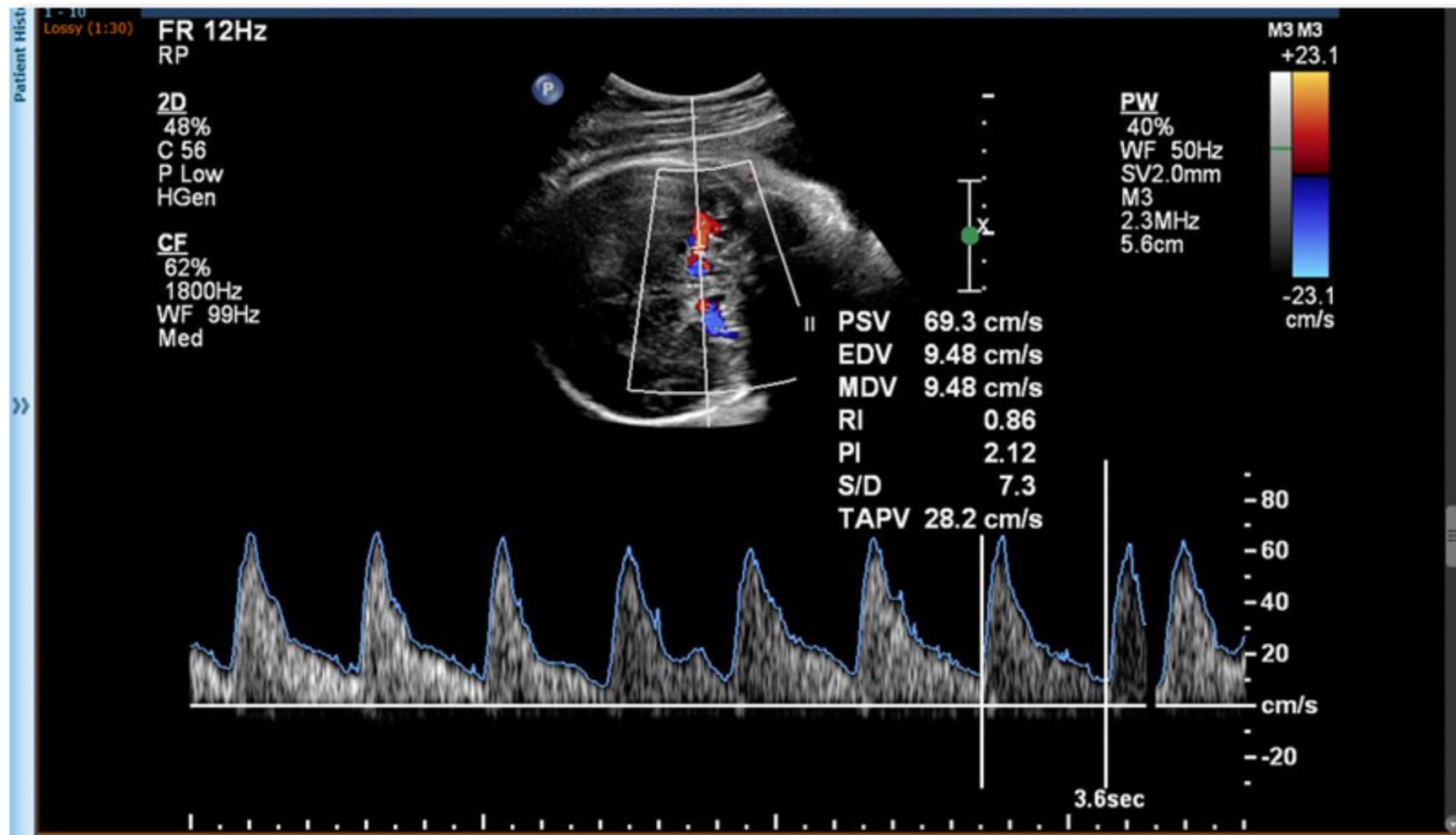
Failure to Prevent Isoimmunisation

- The cause of failure to prevent isoimmunisation in this patient is not known.
- Probable cause is clinically silent unrecognised bleeding episodes.
- Her BMI was normal (29).
- Isoimmunisation has occurred despite adherence to published guidelines.
- Cases such as this should be reviewed to monitor the effectiveness of clinical practice guidelines

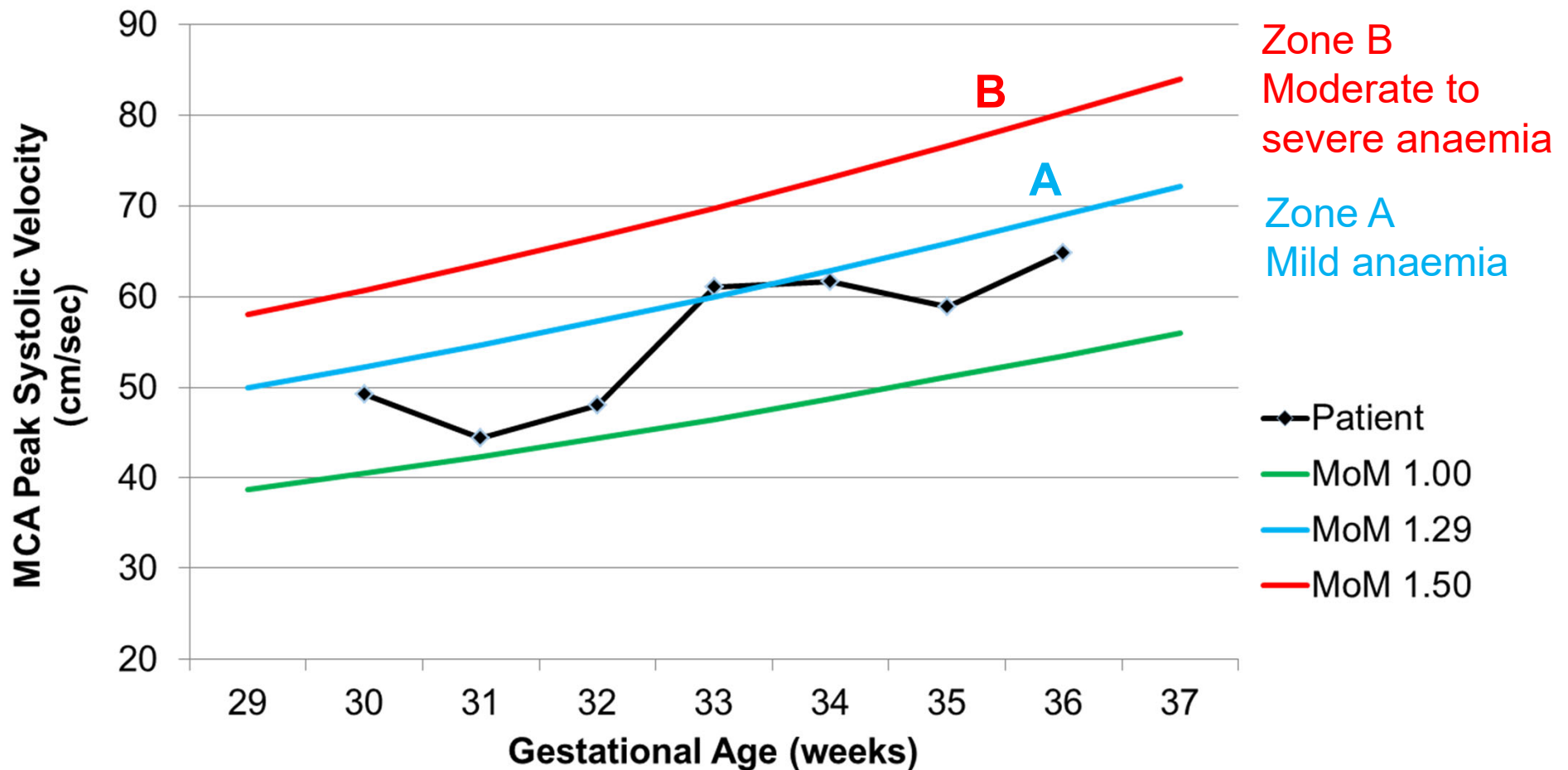
Fetal Doppler MCA-PSV



Fetal Doppler MCA-PSV



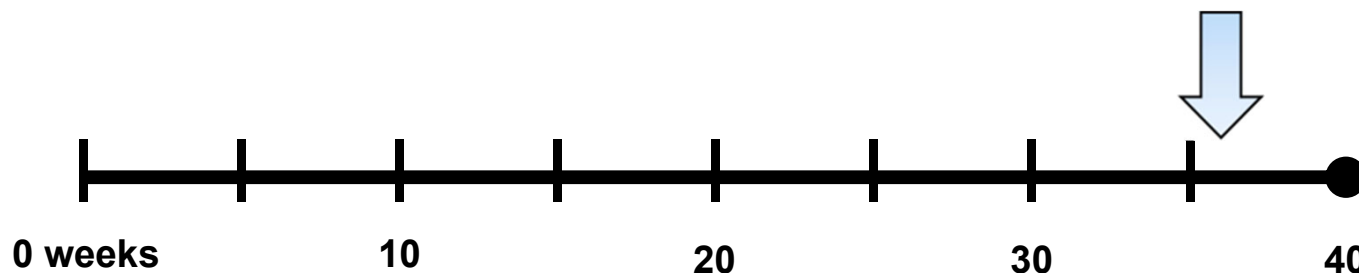
Doppler Results MCA-PSV MoM



Mari G. Noninvasive Diagnosis by Doppler Ultrasonography of Fetal Anaemia Due to Red Cell Alloimmunization. *N Eng J Med* 2000. 342 : 9 - 14

Delivery

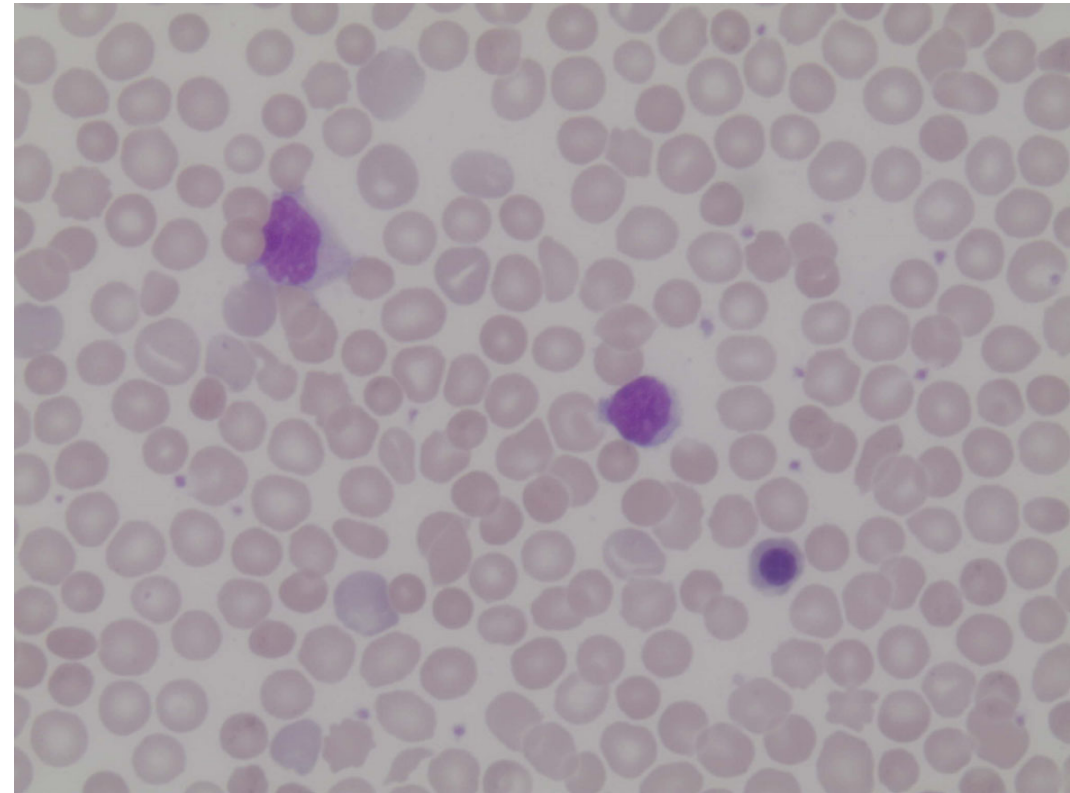
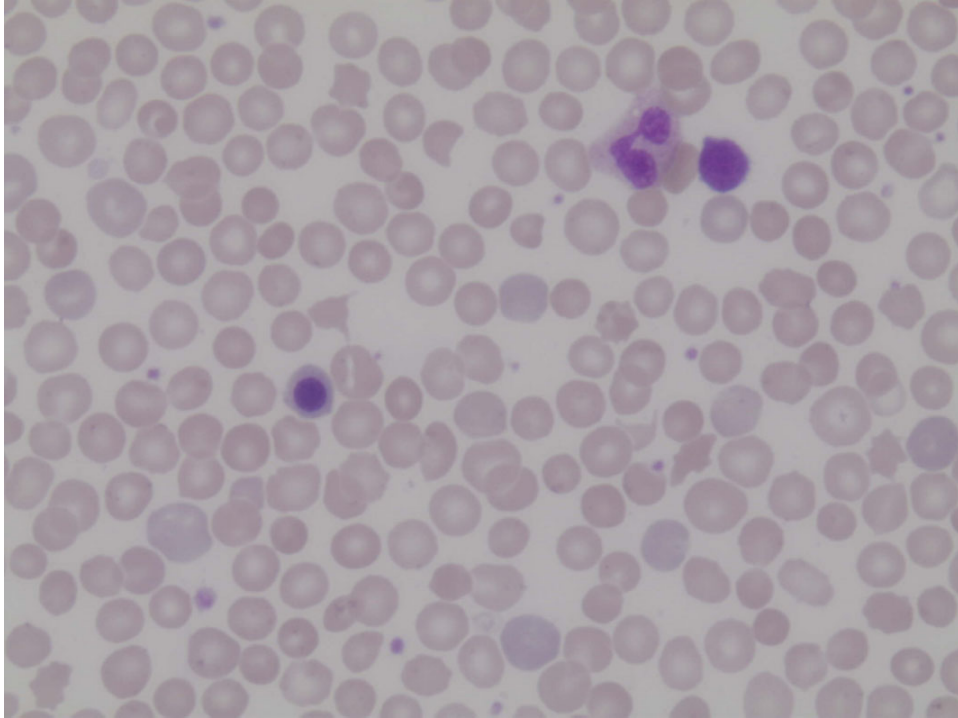
- 16-June-2018
- Induction of Labour for reduced fetal movements
- NVD
- 400 mL blood loss
- No complications



Baby Results

- Prematurity (36/40)
- At Birth, Jaundice
 - Hb 145 g/L (RR 135 - 230)
 - WCC $18.8 \times 10^9/L$ (RR 13.0 - 37.0)
 - Platelet Count $265 \times 10^9/L$ (RR 100 - 500)
 - Some NRBCs 17 / 100 WBCs
 - Mild polychromasia. Occasional spherocytes.
 - Bilirubin = $65 \mu\text{mol/L}$

Blood Film



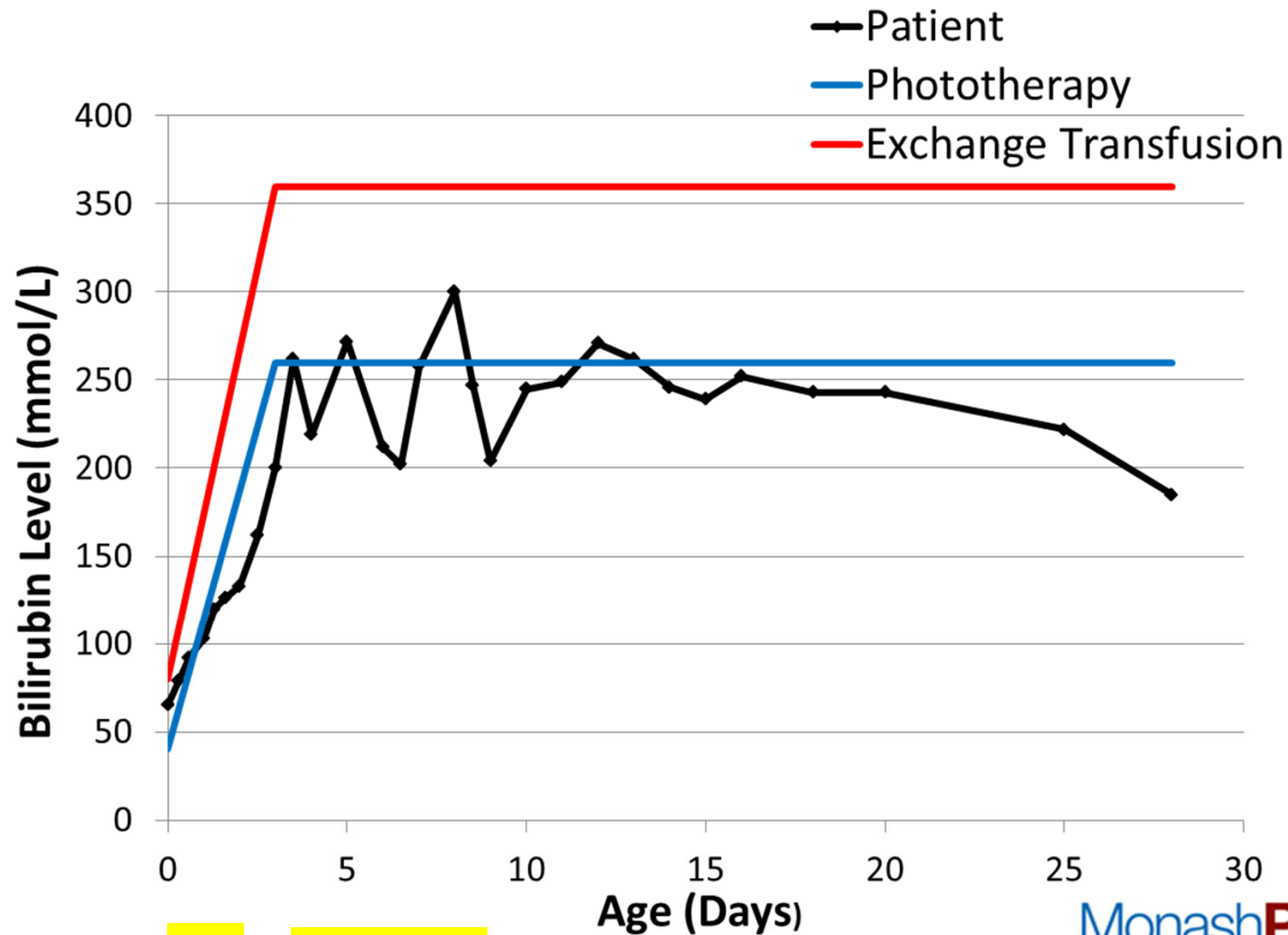
Baby Results

- O Rh(D) Positive
- DAT Positive
- Anti-D and anti-E eluted (DiaCidel elution)
- Phenotype
 - C Neg, c Pos, E Pos, e Pos - R₂r
 - Note that the maternal anti-C was presumably actually anti-G
- Phototherapy for jaundice

Treatment



Neonatal Bilirubin Levels



Outcome

- Neonate sent to Casey Hospital on Day 4
 - Continued monitoring of jaundice and Hb
- Discharged home on Day 19
- Back to ED on Day 28 with gastroenteritis
- Home again next day



Questions?

