

It's just an M How bad can it be?

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Background - Baby R

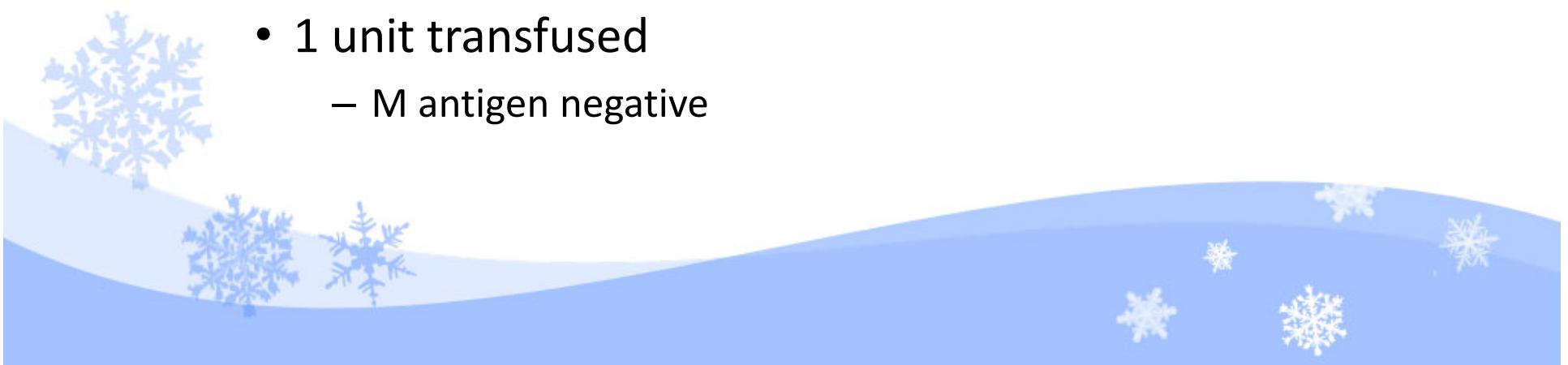
Baby R - 1st Presentation 2014

- Presented to ED at 3 weeks of age
 - FBC
 - Hb 41 g/L
 - » Macroscopic red cell agglutination
 - » Marked reticulocytosis
 - » Normal WCC and platelets
 - Group and Screen
 - Pre-warming required
 - » B RhD positive
 - » Antibody screen – negative
 - » DAT – negative
 - 1 unit transfused and baby discharged

Background - Baby R

Baby R - 2nd Presentation

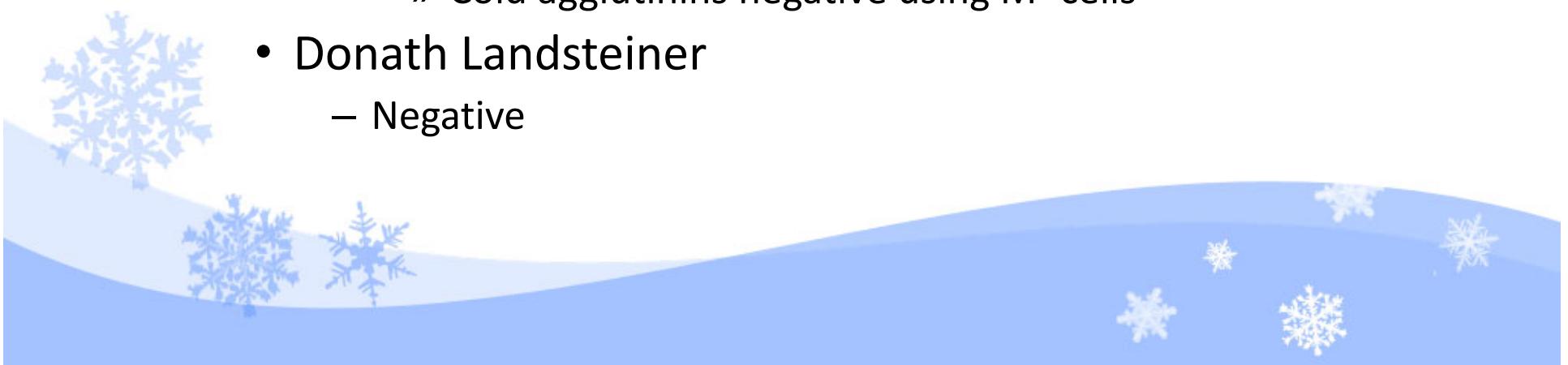
- Re-presented at 6 weeks of age
 - FBC
 - Hb 59 g/L
 - Group and Screen
 - Anti-M weakly detected
 - DAT – negative
 - 1 unit transfused
 - M antigen negative



Background - Baby R

Investigations

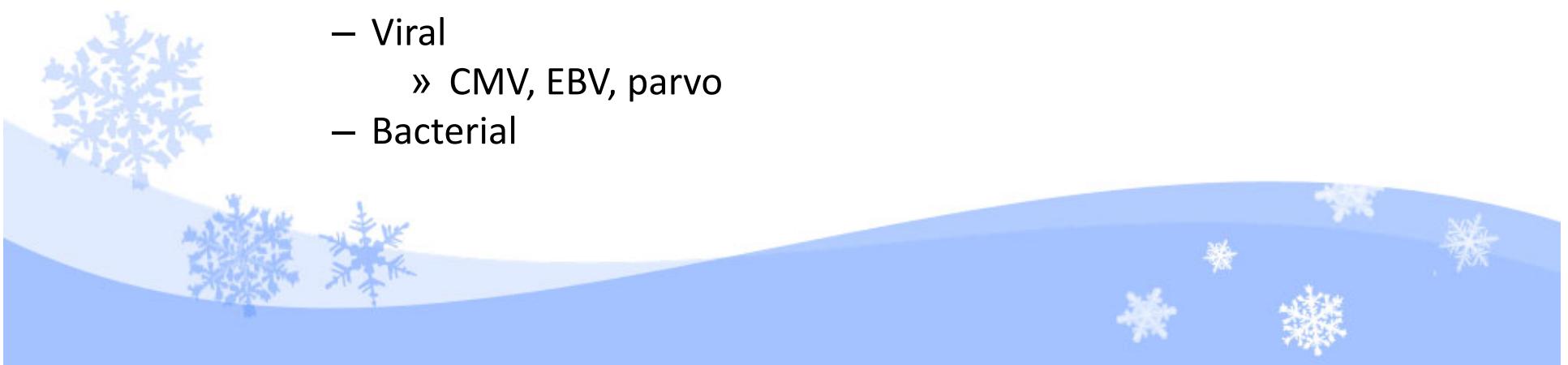
- Maternal sample
 - Anti-M confirmed
 - Titre <2 at time of delivery
 - Prophylactic anti-D administered
 - Positive cold agglutinins
 - M+ adult and cord cells
 - » Cold agglutinins negative using M- cells
 - Donath Landsteiner
 - Negative



Background - Baby R

Investigations

- Neonatal sample
 - Positive cold agglutinins
 - M+ adult and cord cells
 - » Cold agglutinins negative using M- cells
 - Inherited causes
 - Thalassemia
 - » No abnormalities detected
 - No evidence of infection
 - Viral
 - » CMV, EBV, parvo
 - Bacterial



Background - Baby R

Diagnosis

- Baby R's Hb continued to drop
- IVIG was administered
 - 2 x 6g Intragam P
 - Indication: Auto-immune haemolysis of unknown cause
- Transferred to a specialised children's hospital
 - FBC films also sent for review
- Paroxysmal Cold Haemoglobinuria (PCH)
 - Morphological features
 - Very occasional erythrophagocytosis noted on film

2nd Pregnancy

Mother - 2nd Pregnancy 2017

Gestation	37°C IAT	37°C Saline		30°C saline		RT Saline		4°C Saline	
	M+M+ cells	Adult	Cord	Adult	Cord	Adult	Cord	Adult	Cord
26 weeks	8	<2	8	<2	64	<2	128	32	256
30 weeks	8	NP	NP	NP	NP	NP	NP	NP	NP
32 weeks	8	<2	<2	<2	<2	<2	<2	<2	<2
35 weeks	16	<2	<2	<2	<2	8	16	32	32
Delivery	NP	<2	<2	<2	16	16	32	32	32
1 week post delivery	NP	<2	16	<2	16	2	16	256	64

*NP – not performed **Saline testing performed using M+N+ cells

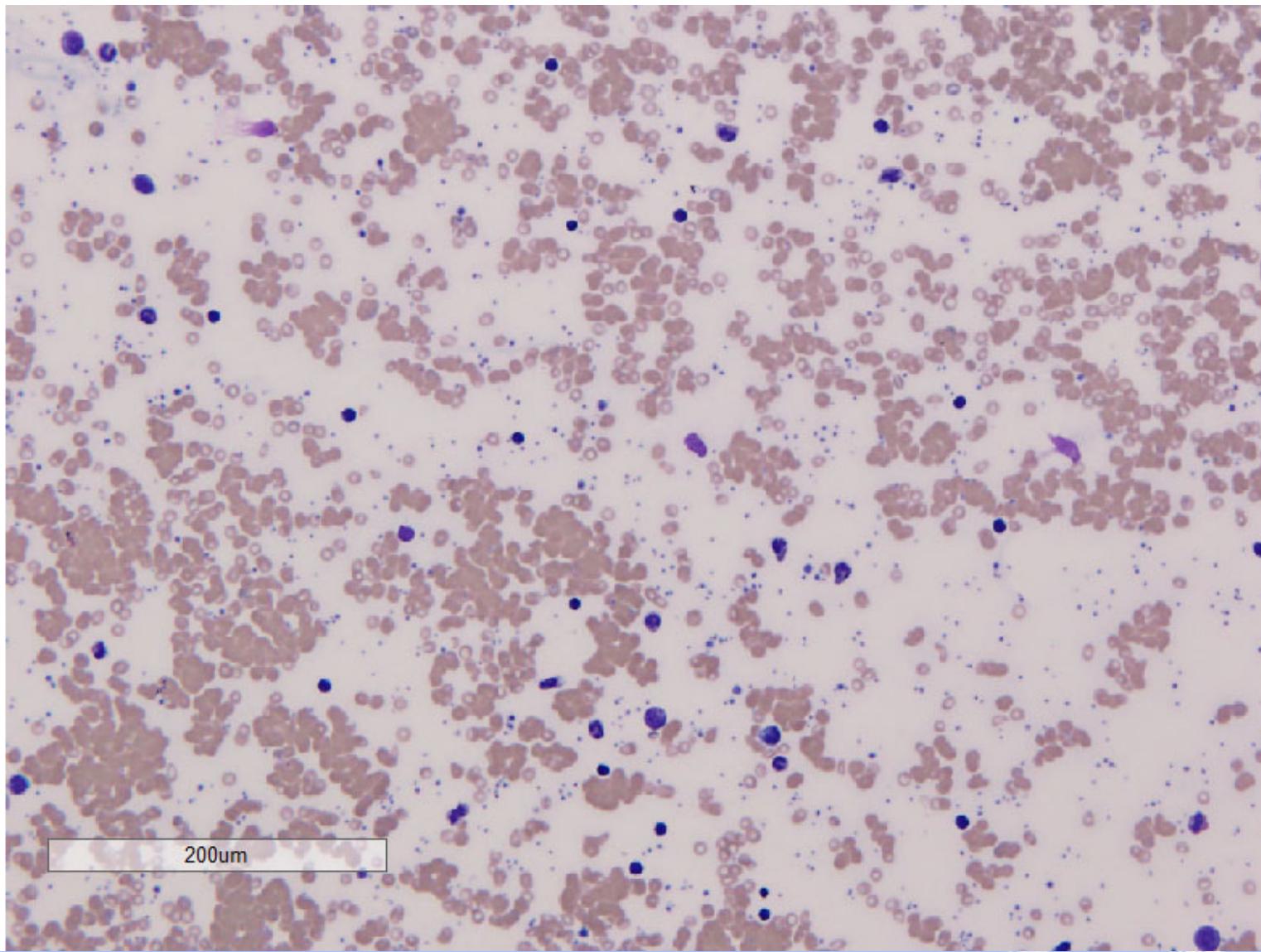


Baby A

At Delivery

- Caesarean delivery at 39 weeks
- Cord blood and FBC samples
 - Showed marked macroscopic red cell agglutination
- FBC
 - 167 g/L
 - Retics 5.04%
 - Normal WCC and platelets
- Chemistry
 - Total bilirubin 46 μ mol/L (ref. range <87 μ mol/L)

Baby A - Red Cell Agglutination on Film



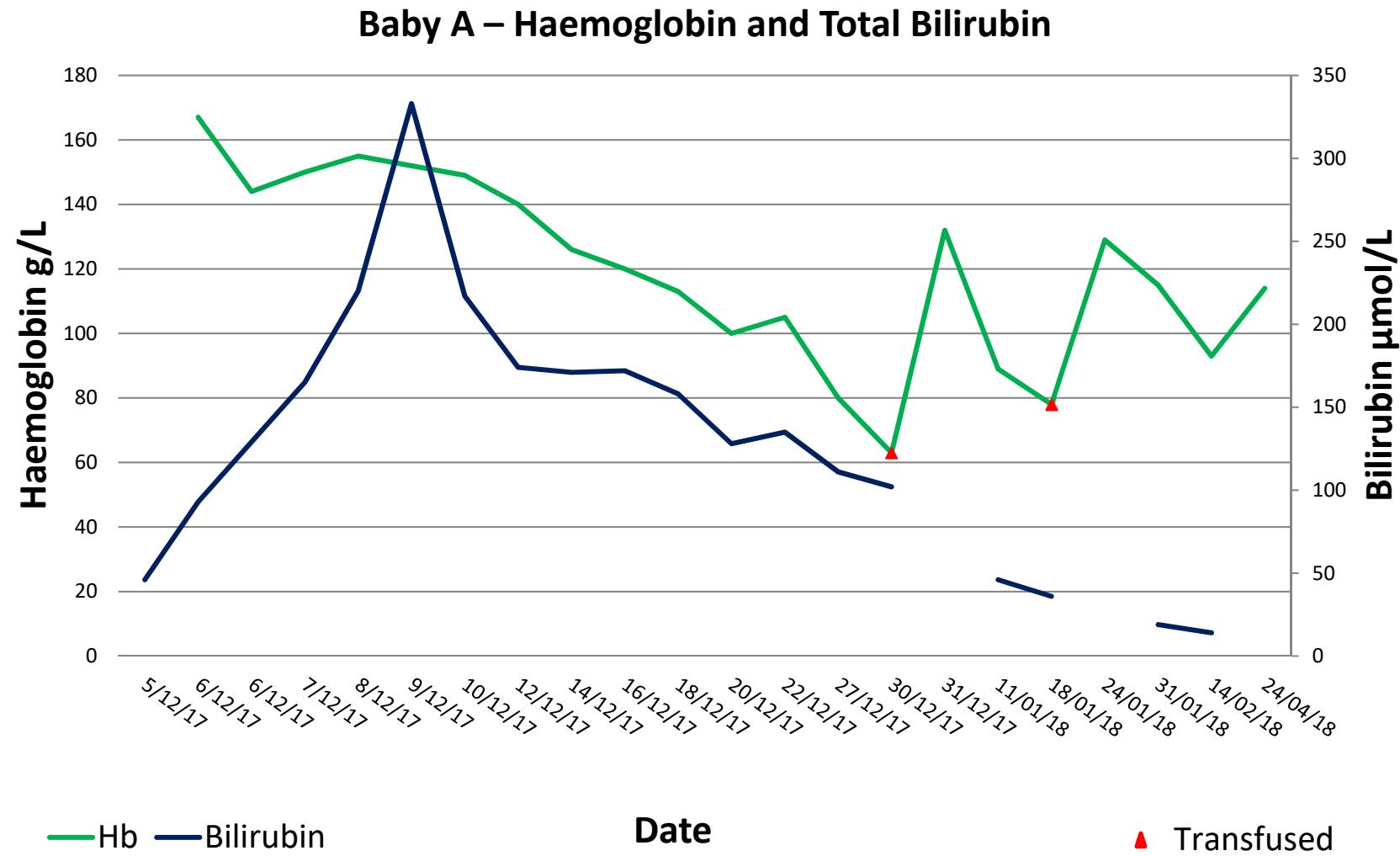
Baby A

At Delivery

- Group and Screen
 - Pre-warming required
 - O Rh D positive
 - DAT positive – grade 2
 - » Anti-M and anti-D (prophylactic) eluted
 - Additional phenotyping
 - » M+N+
- Over the next 4 days
 - Hb started dropping
 - Bilirubin started to rise
 - Peaking at 333 μ mol/L



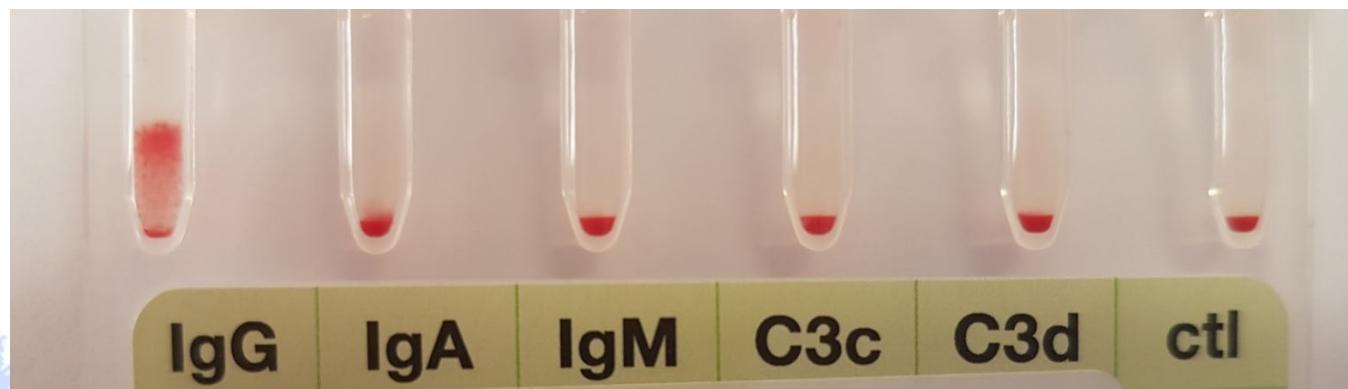
Baby A



Baby A

Diagnosis and Treatment

- DAT remained negative
- Anti-M demonstrated in the plasma
 - Antibody class – IgG

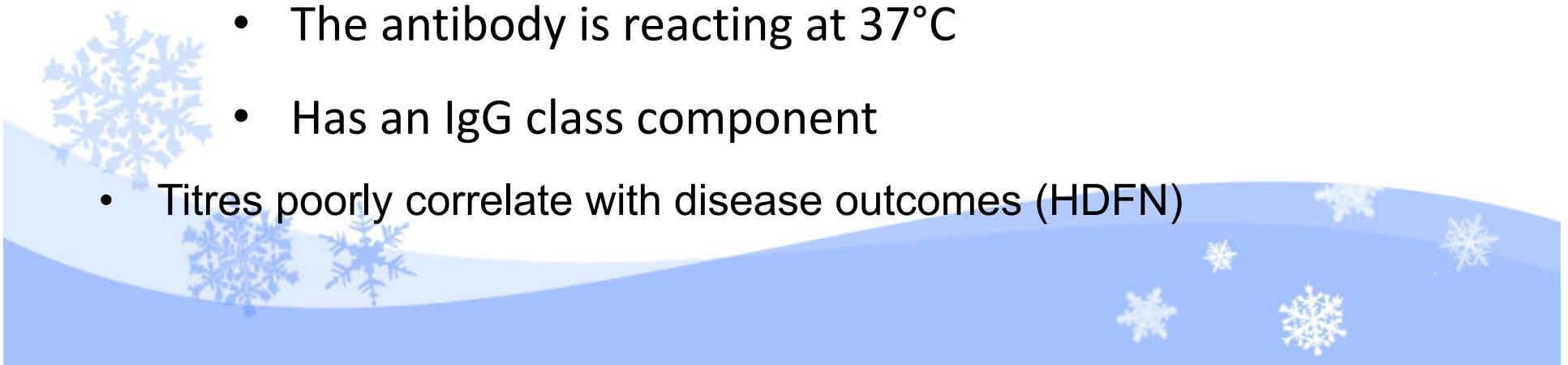


- 10 weeks of age
 - Hb recovered
 - Bilirubin within normal range

Discussion - A little bit on Anti-M

Anti-M Antibodies

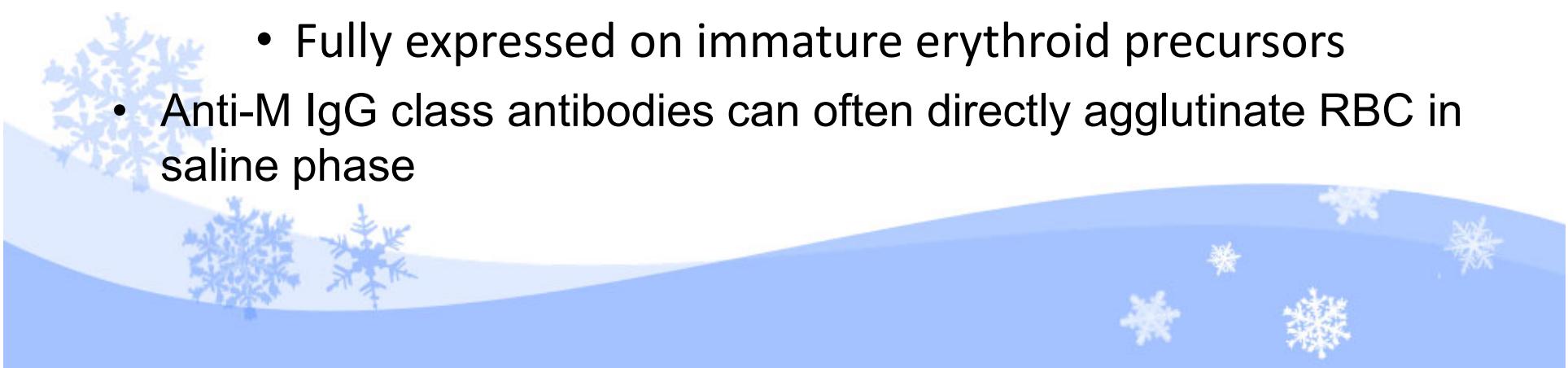
- Can be naturally occurring
- Predominantly IgM class
 - Low thermal reactivity
- Generally not considered to be clinically significant or associated with HDFN or HTR
- **Unless...**
 - The antibody is reacting at 37°C
 - Has an IgG class component
 - Titres poorly correlate with disease outcomes (HDFN)



Discussion - A little bit on Anti-M

M Antigen Expression

- M/N antigens are located on the terminal end of Glycophorin A
 - Fully developed on foetal RBC
 - Detected from 9 weeks gestation
 - Glycophorin A expression
 - Abundantly expressed on RBC
 - About a million copies / cell
 - Fully expressed on immature erythroid precursors
 - Anti-M IgG class antibodies can often directly agglutinate RBC in saline phase



Conclusion

HDFN - Due to Low Thermal Amplitude Anti-M

- Baby A's DAT remained negative (with exception of cord blood sample)
 - Continued to show signs of haemolysis
- Mechanism for haemolysis
 - Destruction of erythroid progenitors
 - Intravascular haemolysis
- This case demonstrates an atypical presentation of a maternal Anti-M antibody causing severe HDFD
 - Low thermal amplitude IgG class anti-M
- HDFN is probably the likely cause of the first Baby's anaemia

Thank you

- Dr Philip Crispin
 - Sam Lennard
 - Marianne de Souza
 - Dr Farah Sethna
 - Dr Carolyn Wilson
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- Mohd Nazri, H, *et al.* Anti-M induced severe haemolytic disease of foetus and newborn in Malay woman with recurrent pregnancy loss. Malaysian Journal Pathology 2017; 39(1) 73-76.
 - Daniels, Geoff. Human Blood Groups, 2nd Ed, Blackwell Science, 2007.
 - Gardner, B, *et al.* Epitopes on Sialoglycoprotein alpha: evidence for heterogeneity in the molecule. Immunology 1989; 68(2) 283-9.

