Fetal and Neonatal Alloimmune Thrombocytopenia

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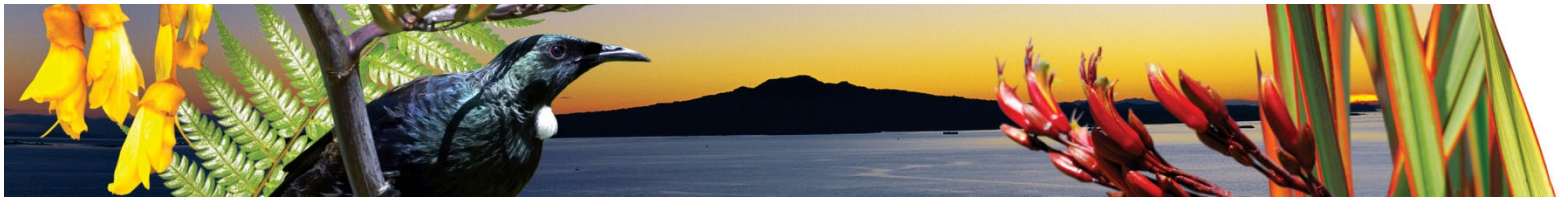

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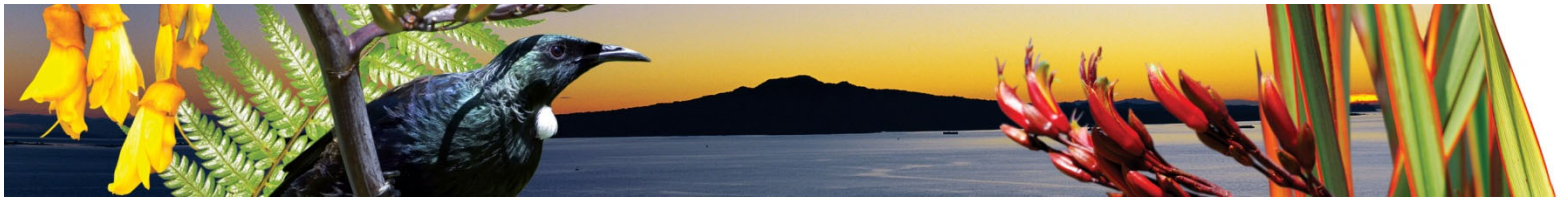
Outline

- Case Study
- Description of FNAIT
- Comparison of FNAIT and HDFN
- Review of IV Ig (Intragam-P) in FNAIT
- Prediction of severity of FNAIT
- Prophylaxis against FNAIT



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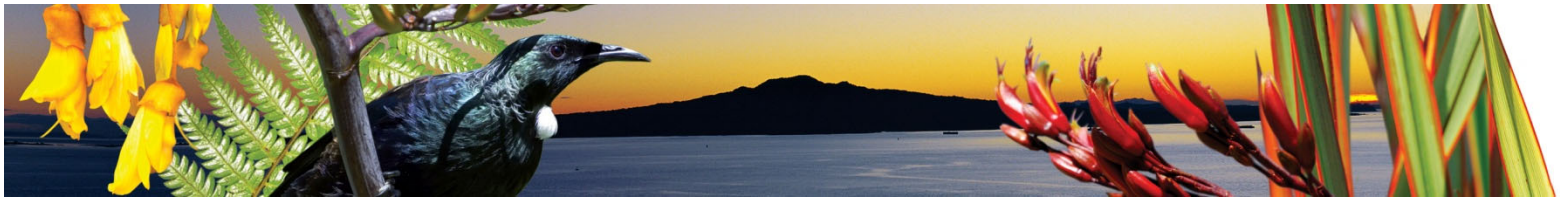
Case Study MC

- Patient MC in West Auckland
- 2014 - First baby born at 2480 g
- Petechiae noticed on day 1



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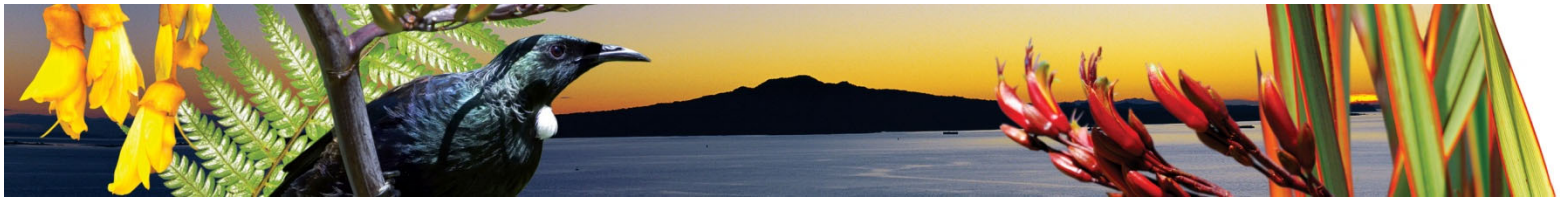
Petechiae



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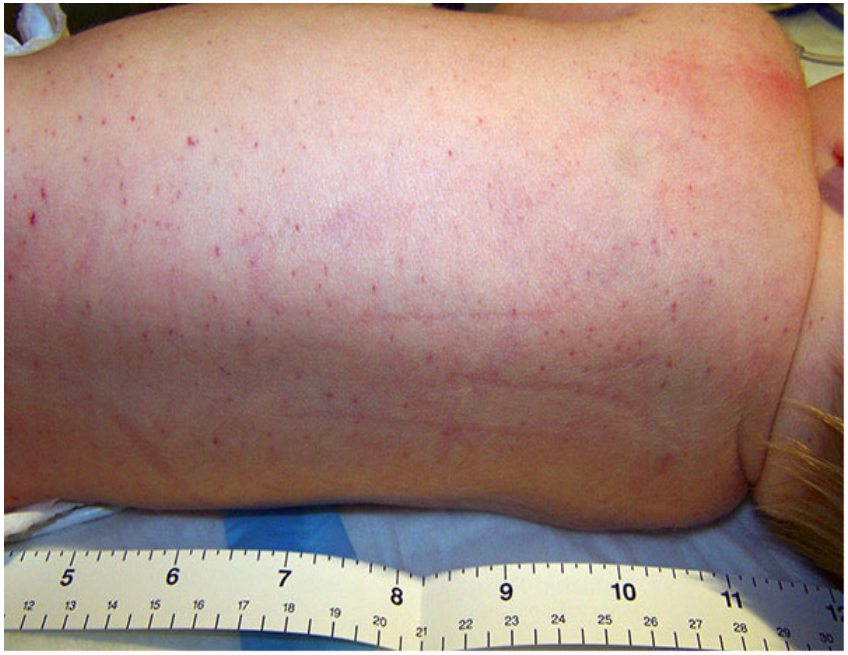
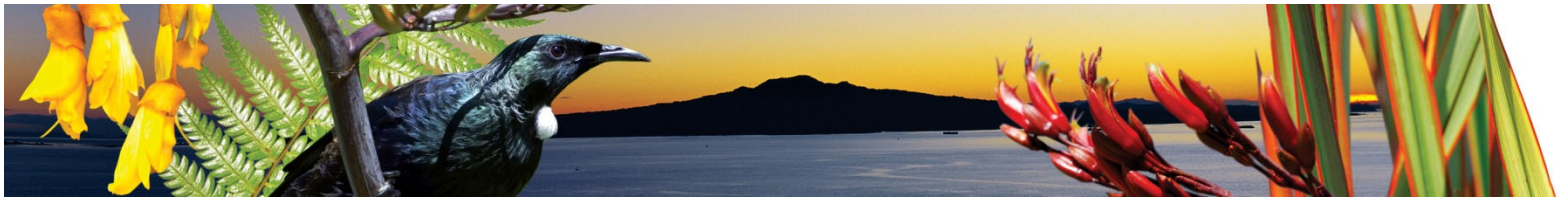
Petechiae





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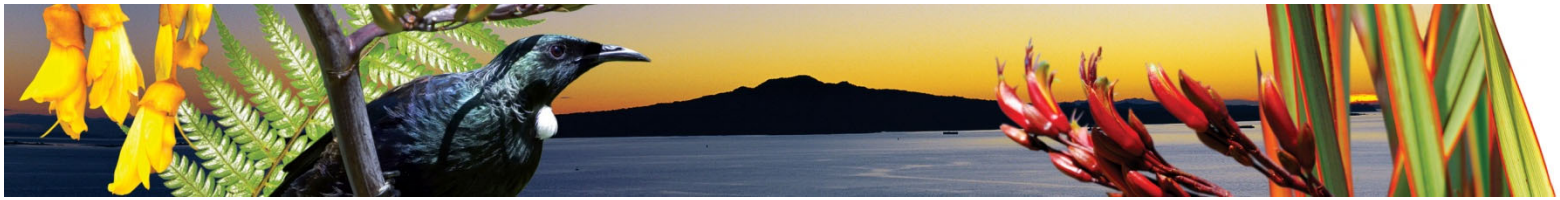
Case Study MC

- Platelet count < 10×10^9 / L (150-400)
- Platelet transfusions (random?)
- Discharged with Plt 29×10^9 / L



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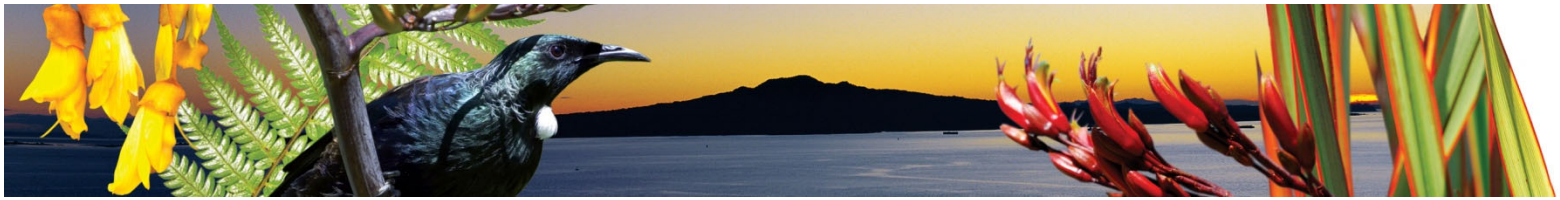
Case Study MC

- November 2013
- Patient MC and husband plan next pregnancy
- MC plasma contains Anti-HPA1a
- MC genotype is HPA 1b1b
- Husband's genotype HPA 1a1a
- Diagnosis FNAIT
- Obstetrician recommends IV Ig



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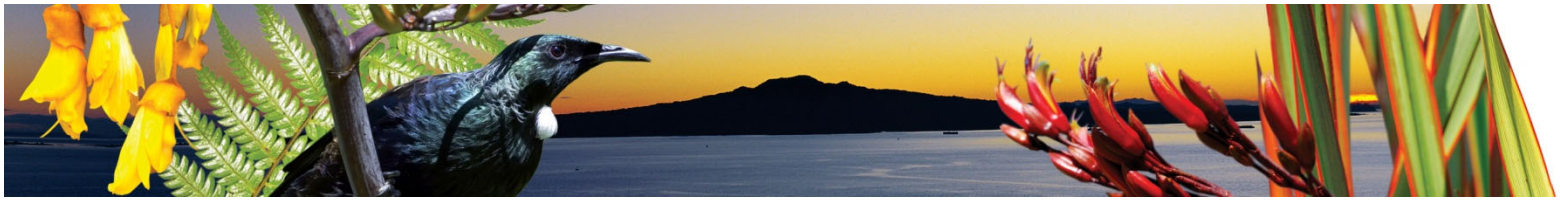
Case Study MC

- September 2015 MC pregnant
- Intragam-P 0.5 g/kg/week from 28/40
- 3 x 12g (36g) per week for 9 weeks
- 27 x $1,038 = $28,626
- Caesarean at 37/40



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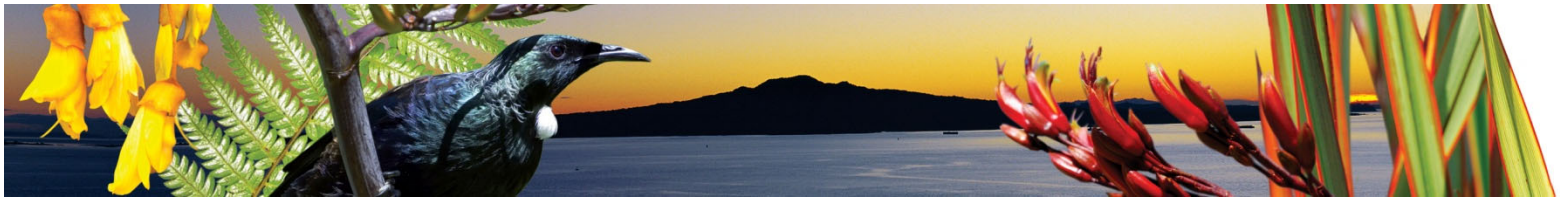
Case Study MC

- 13 May 2016
- MC delivers girl 2,420g
- Apgar 8/10/
- Cord blood 0900 hrs
- Platelet count ???? x 10^9 / L
- Marked thrombocytopenia on film



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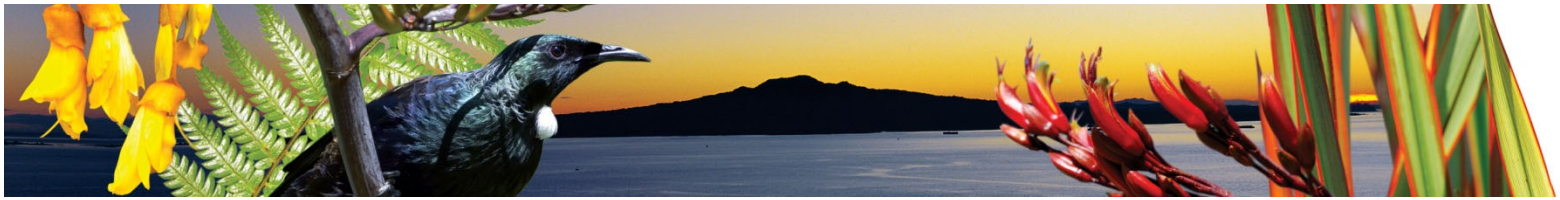
Case Study MC

- Repeat (venous) sample 1120 hrs
- Platelets 205 x 10^9 / L
- 16/05/2017 1445 hrs
- Platelet count ??? x 10^9 / L
- Repeat at 1545 hrs
- Platelets 196 x 10^9 / L
- Success!



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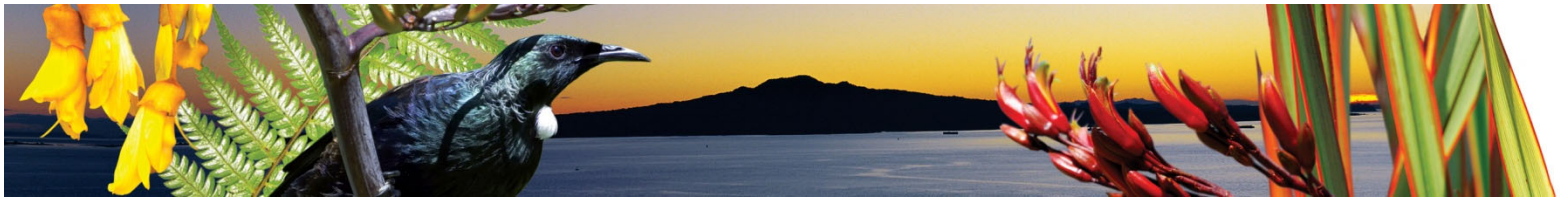
Fetal and Neonatal Alloimmune Thrombocytopenia

- Similar to Haemolytic Disease of the Fetus and Newborn.
- During pregnancy or childbirth the mother becomes immunised to paternally derived platelet antigens
- Anti-Platelet Antibody crosses placenta



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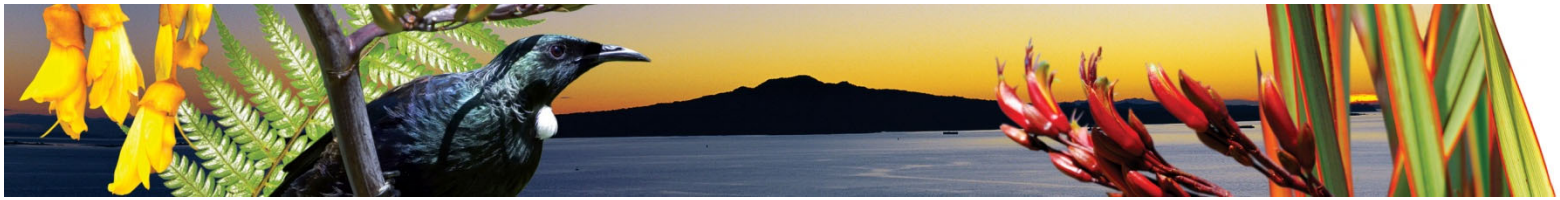
Fetal and Neonatal Alloimmune Thrombocytopenia

- 86 per 100,000 births
- NZ has ~ 60,000 births per annum
- Expect 50 cases in NZ p.a.
- Expect 6 or 7 cases in WDHB p.a.
- ? Under-diagnosed / reported



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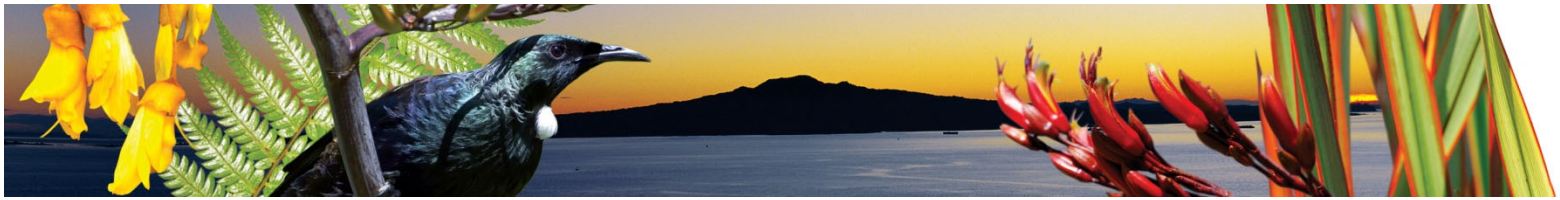
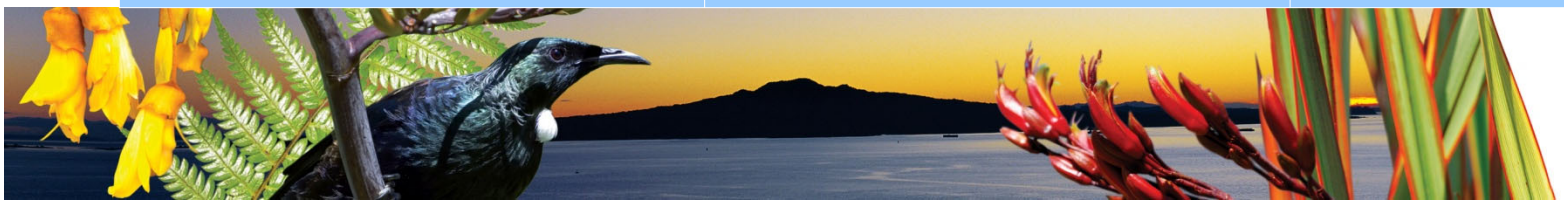
Factor	FNAIT / Anti HPA 1a	HDFN/ Anti-D
Percentage at risk	2% of women HPA1a neg	10% to 15% of women Rh(D) neg
Occurrence	First pregnancy (42%)	Mostly 2nd and subsequent pregnancies
Transfusion	Rare	Anti-D was common before prophylaxis
Effect	Thrombocytopenia	Anaemia / Haemolysis
Causes of fetal death	Intra-cranial haemorrhage	Heart failure. Hydrops
Causes of neonatal death	Intra-cranial haemorrhage	Kernicterus



Factor	FNAIT / Anti HPA 1a	HDFN/ Anti-D
HLA association	HLA DRB 3*0101 HLA DQB 1*0201	None
Routine Screening	None	First trimester. Rh(D) phenotype Antibody Screen
Antibody detection	Post natal after thrombocytopenic baby	First & third trimester
Fetal diagnosis	None	Doppler ultrasound Fetal Haematocrit via PUBS
Treatment of alloimmunised women	IV Ig +/- steroids	None
Treatment of baby	Fetal IUT. Neonatal Transfusion	Fetal IUT. Neonatal exchange. Phototherapy



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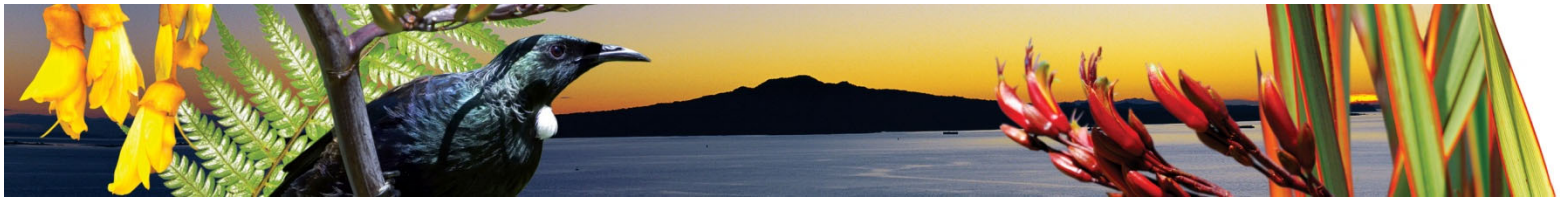
Factor	FNAIT / Anti HPA 1a	HDFN/ Anti-D
Prevention of immunisation	None yet (2018)	Antenatal and Postnatal Rh (D) Ig (since 1970s)



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Review of IV Ig (Intragam-P) in FNAIT

- Intravenous Immunoglobulin (IV Ig)
- Intragam® P
- Primary Immune Deficiency (1952)
- Symptomatic Hypogammaglobulinaemia
- ITP (1981)
- Kawasaki Disease
- Guillain-Barré Syndrome
- FNAIT (? Late 1980s)

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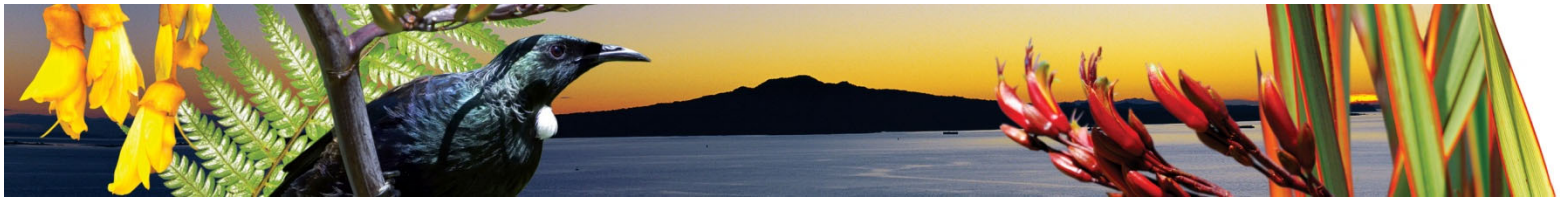
Mechanism of action of IV Immunoglobulin

- Replacement of deficient IgG
- Immune modulation



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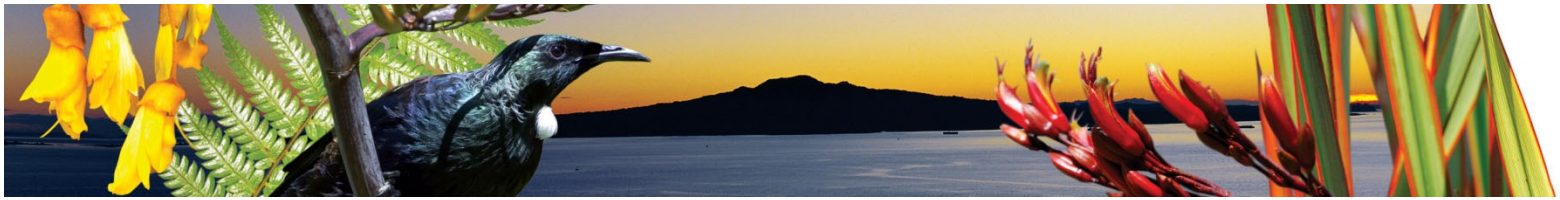
Mechanism of action of IV Immunoglobulin in Immunomodulatory therapy

- Dilution of IgG / competition
- Anti-idiotype F(ab')2 mechanisms
- Fcγ receptor saturation
- T cell modulation
- B cell modulation



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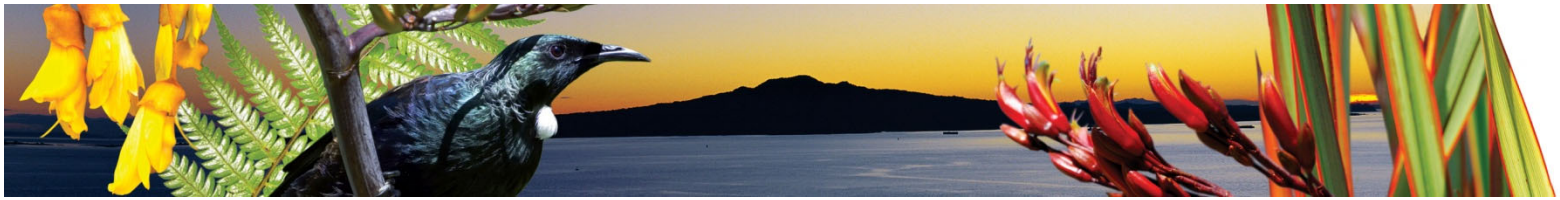
Prediction of severity of FNAIT

- Anti-Hpa1a titre by MAIPA
- PUBS (invasive)



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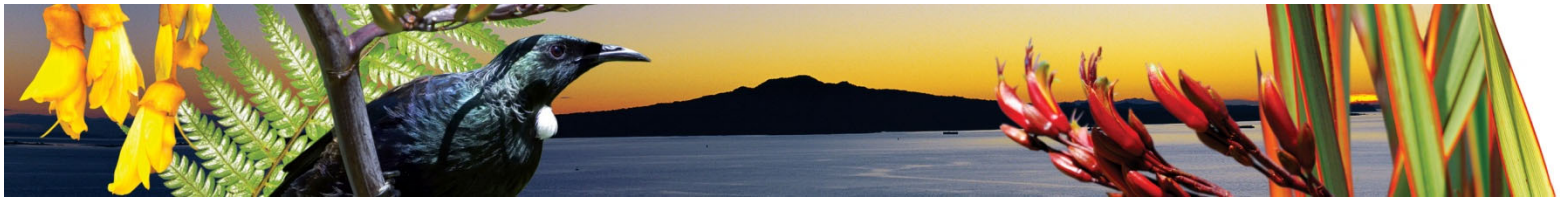
Prophylaxis against FNAIT

- Similar model to prevention of HDFN
- But Anti-HPA1a is uncommon
- Scandinavian trial
- Mouse model (Tiller et al 2012)
- Need to identify women at risk
- Considerable investment required (Kumpel 2012)



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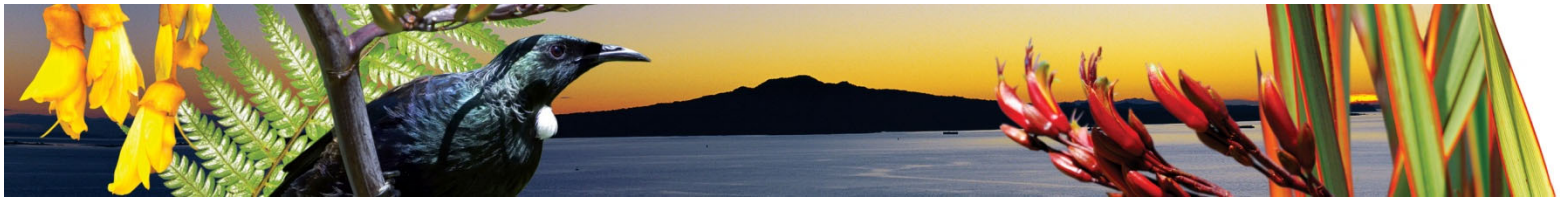

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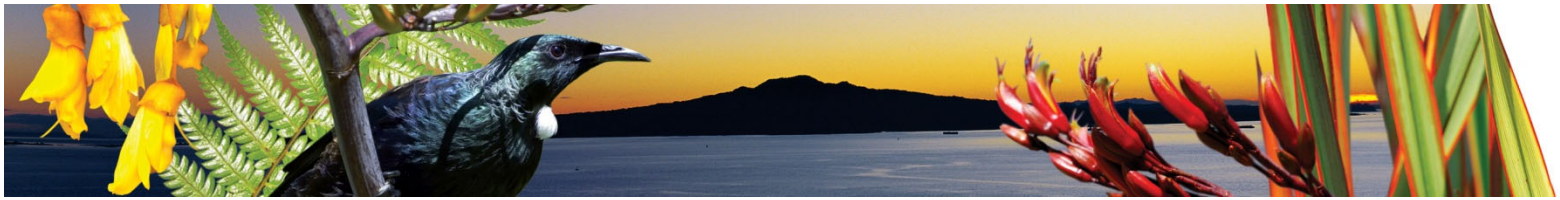

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