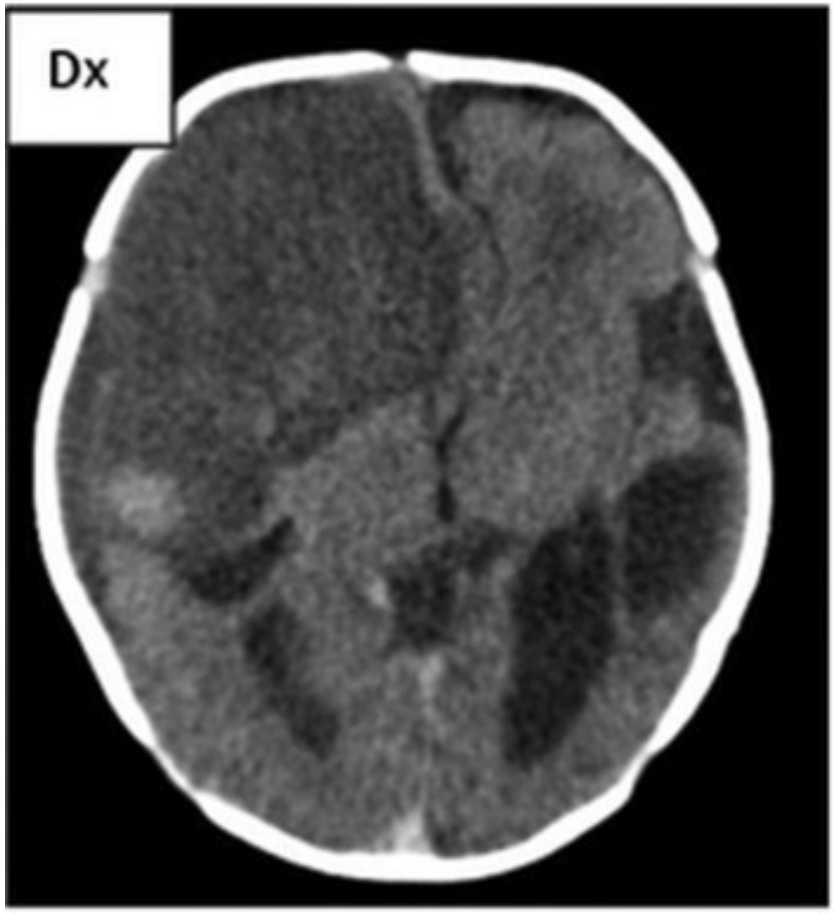
AntiNAITal Care



Tom Latham
Consultant Haematologist NHSBT Filton

The patient's story

- Our NAIT story began with the words “Something is wrong with your baby.”
- "I think we both knew at that point that something wasn’t quite right. Our son was covered in bruises and little tiny bright red spots "
- "The doctors were rather vague. They weren’t sure why he had a low platelet count, and they began to do more tests "

The patient's story

- "...we also knew that this incompatibility could affect our ability to have healthy children in the future. It was also difficult being told that the antibodies in my blood and attacked the platelets in my baby, and nearly killed him"
- "We had always hoped for a big family but once NAIT became a part of it things were not so straight forward anymore. We would spend the next 2 years agonizing over a third baby "
- "At 30 weeks we were really struggling to hold it together without knowing if the treatment was working or if the counts were dropping and so opted for the fetal blood sampling "

NAIT - introduction

- Neonatal alloimmune thrombocytopenia
- 21 known platelet blood groups
- Immunisation of mother against paternal-inherited platelet groups (HPA antigens)

- Differences from red cell HDN
  -commonly occurs in 1st pregnancy
  -no primary prophylaxis (anti D)
  -antibody levels do not predict risk

HPA-1	HPA-1a HPA-1b	Zw^{a}, PL^{A1} Zw^{B}, PL^{A2}	97.9 28.8
HPA-2	HPA-2a HPA-2b	Ko^{b} Ko^{a}, Sib^{a}	>99 13.2
HPA-3	HPA-3a HPA-3b	Bak^{a}, Lek^{a} Bak^{b}	80.95 69.8
HPA-4	HPA-4a HPA-4b	Yuk^{b}, Pen^{a} Yuk^{a}, Pen^{b}	>99.9 <0.1
HPA-5	HPA-5a HPA-5b	Br^{b}, Zav^{b} Br^{a}, Zav^{a}, Hc^{a},	99.0 19.7
	HPA-6bw	Ca^{a}, Tu^{a}	0.7
	HPA-7bw	Mo	0.2
	HPA-8bw	Sr^{a}	<0.01
	HPA-9bw	Max^{a}	0.6
	HPA-10bw	La^{a}	<1.6
	HPA-11bw	Gro^{a}	<0.25
	HPA-12bw	ly^{a}	0.4
	HPA-13bw	Sit^{a}	0.25
	HPA-14bw	Oe^{a}	<0.17
HPA-15	HPA-15a HPA-15b	Gov^{b} Gov^{a}	74 81
	HPA-16bw	Duv^{a}	<1
	Va^{a}	<0.4	
	Mou^{a}	26	
Note: *Frequencies are based on studies in Caucasians.			

NAIT introduction

- 80% of cases due to anti HPA 1a
- 15% due to anti HPA 5b
- Other antibodies rare

- Antibodies not detected in ~30% of suspected NAIT:
  -alternative cause for thrombocytopenia
  -early antibody formation
  -low affinity antibody
  -private antigens

How common is NAIT ?

UK retrospective data

12·4 cases per 100 000 total births

30% were known at the start of pregnancy.

Unknown cases were more likely to experience
-haemorrhagic complication (67% vs. 5%)
-intracranial haemorrhage (20% vs. 4%)

How common is NAIT

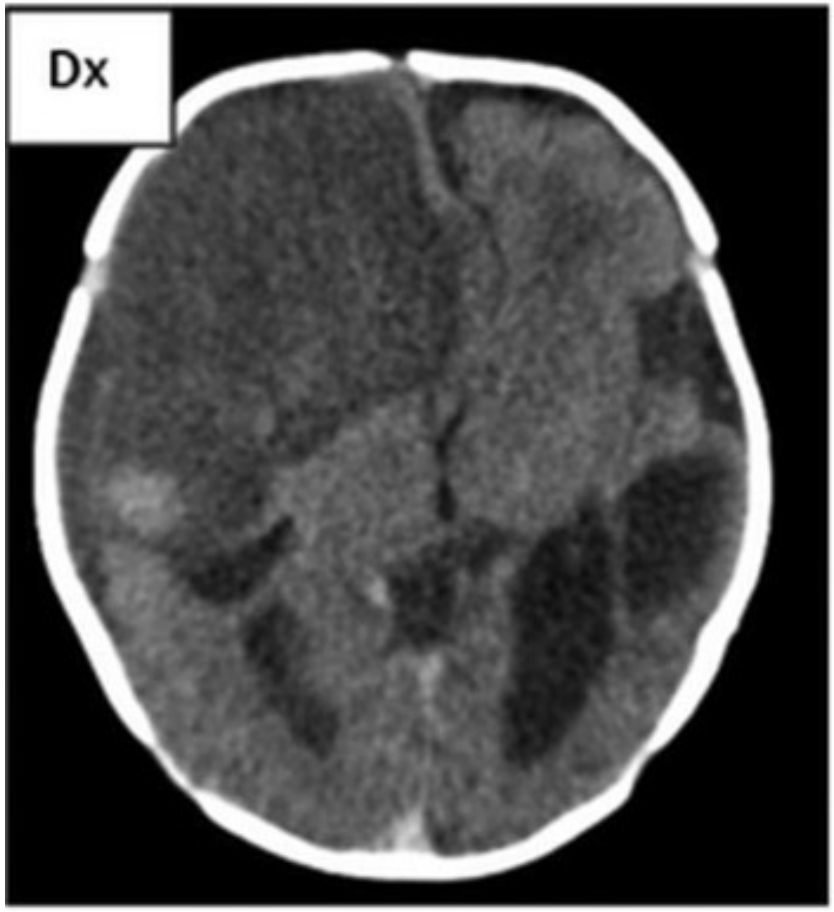
Norwegian screening study (2007)
100448 pregnant women.
2.1% HPA 1a negative
anti–HPA 1a 10.6% of these

170 pregnancies were managed
161 HPA 1a–positive children
55 had severe thrombocytopenia (< 50 × 109/L)
2 intracranial hemorrhage (ICH).

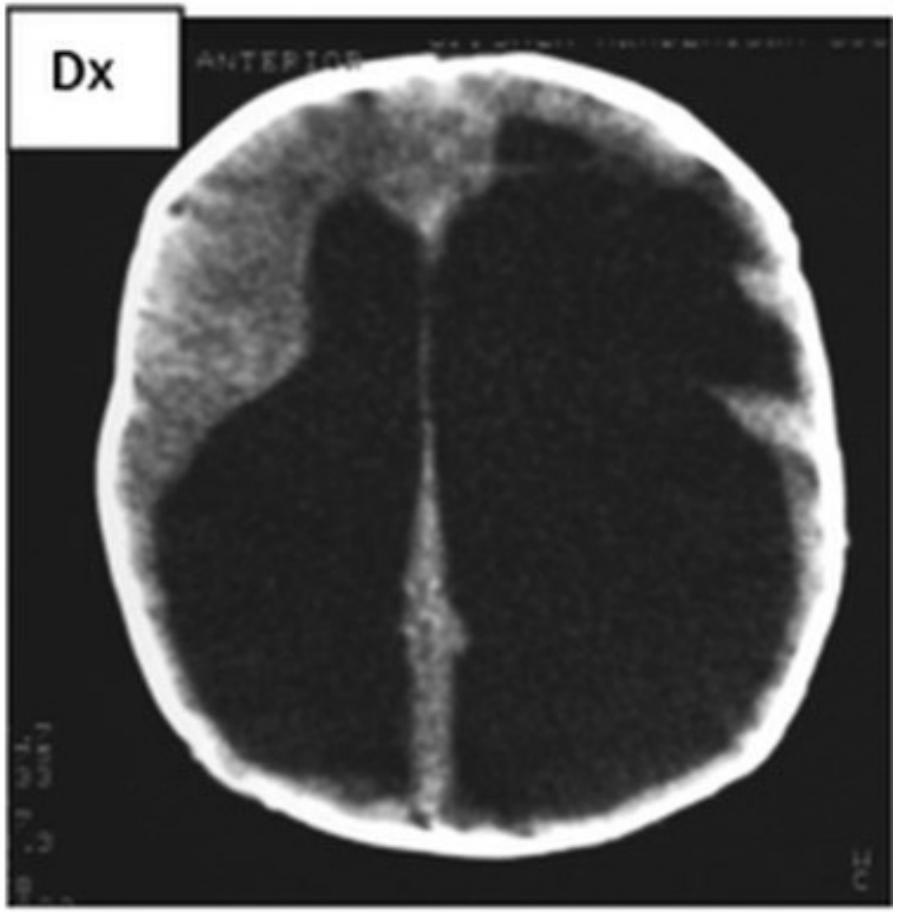
How common is NAIT

- Retrospective testing underestimates incidence
- 1/2 to 1/3 cases unrecognised

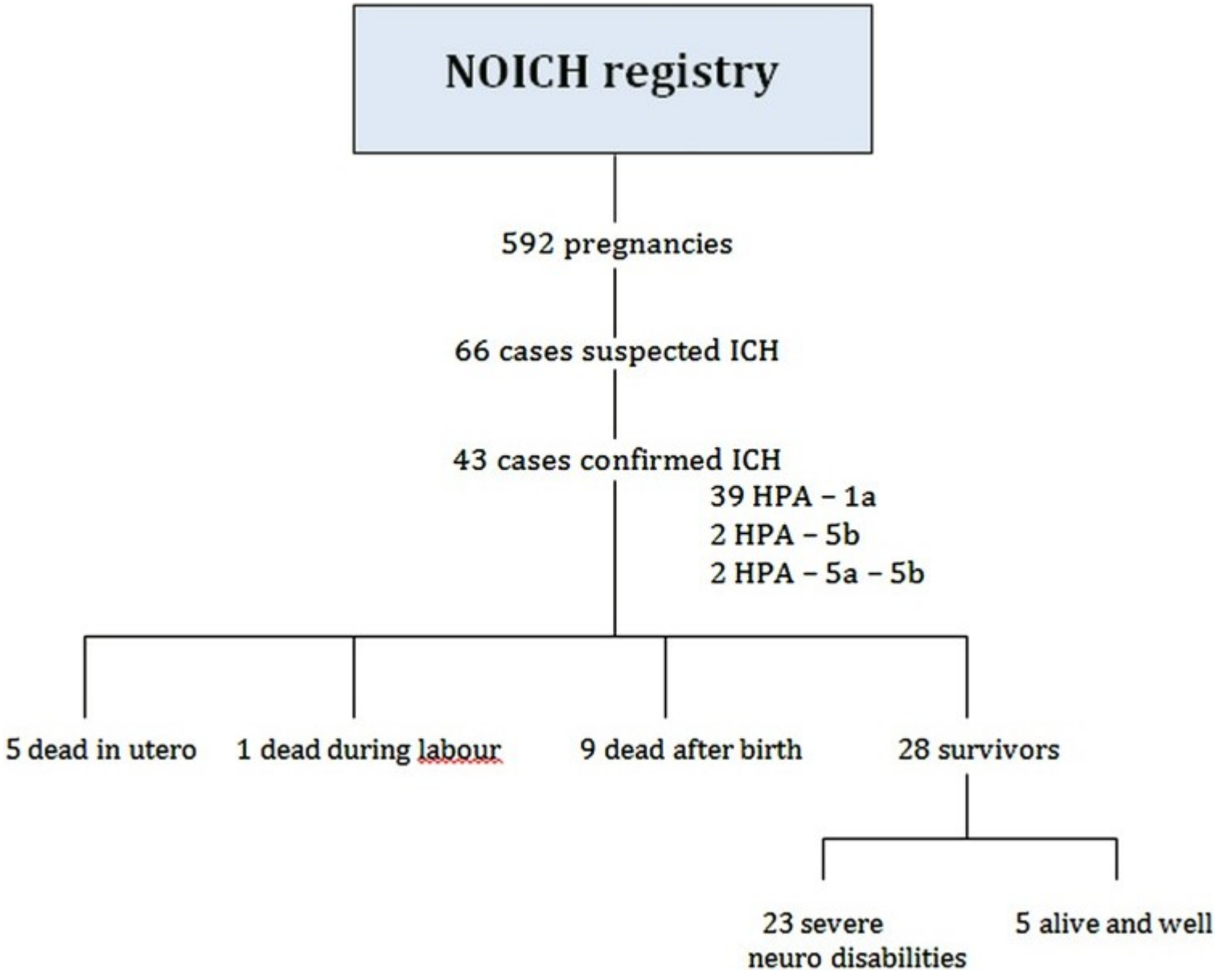
(a) **Intraparenchymal hemorrhage**



(b) **Intraventricular hemorrhage**



Outcomes from NAIT



Testing for NAIT-antenatal

- Fetal ICH, hydrocephalus or ventriculomegaly or cerebral cysts
- Family history of NAIT
- Unexplained fetal anaemia
- Unexplained, recurrent miscarriages after the first trimester
- Incidental discovery (e.g of fetal thrombocytopenia or HPA 1b/1b)

Testing for NAIT- postnatal

- Incidental finding of neonatal thrombocytopenia
- Family history of NAIT
- Signs or symptoms of bleeding with thrombocytopenia

Testing for NAIT

- Mother and father (baby) genotype
  -HPA 1,2,3,5,15
- Mother- test for platelet antibodies
  -PIFT: detects presence of antibodies
  -MAIPA: determines specificity

Testing for NAIT- limitations

- 30% of anti HPA1a may not be detected -repeat after 6 weeks if mother HPA1a negative
- <1/2500 cases due to private antigens -consider platelet crossmatch if high clinical suspicion and testing negative

Testing for NAIT- practicalities

- 6ml EDTA and 6ml serum -mother
- 6ml EDTA- father (+1ml baby)
- Send to NHSBT Filton via your blood bank
- Please include clinical details (not just ?NAIT)
- Please include name of hospital and name of clinician to contact.

How do we treat NAIT-postnatal

- Transfuse platelets if <30
- Request HPA 1a negative 5b negative platelets if suspicious of NAIT
- HPA1a-5b- platelets
  -available "off shelf" Filton, Colindale, Sheffield
- Antigen negative once results back
- If emergency transfuse random platelets while waiting for platelets to arrive

How do we treat NAIT-postnatal

- Nadir platelet count usually ~d4
- Most babies only need 1-2 transfusions but can be prolonged
- Send samples for investigation in routine working time
- Ultrasound to look for ICH

How do we treat NAIT-postnatal

- Persistent thrombocytopenia
  -consider treatment with IVIG
  -alternative diagnosis
  Infection (bacterial, TORCH)
  congenital thrombocytopenia

How do we treat NAIT-antenatal

- Discuss with fetal medicine unit
- Consider
  -outcome of previous pregnancies (platelet counts/ bleeding)
  -specificity of antibody
  -paternal genotype
- Baby can be typed by amniocentesis if father is heterozygous

General measures

- Usual advice for pregnancies with possible bleeding risk
  -avoid aspirin/ NSAID
  -avoid ventouse/ scalp electrodes
- Arrange for antigen negative platelets to be at blood centre for time of delivery (if antibodies other than HPA1a or 5b this will need special arrangement)

Intravenous immunoglobulin

- First line treatment if previously affected pregnancy
- 1g/kg weekly
- Typical start 20 weeks (can be from 12 weeks if bad history)
- About 2/3 respond
- May also decrease risk of ICH independent of effect on platelets
- Little evidence to recommend steroids

Intravenous immunoglobulin

- Landmark study -van den Akker (2007)
- 98 pregnancies
- IVIG treatment only
- No intracranial haemorrhage

- 3 emergency CS after fetal blood sampling
- Standard approach is becoming to avoid FBS in first line treatment

Role for fetal blood sampling

- Strategy of regular platelet sampling
  -6-10% risk of loss over whole pregnancy
- Some units offer FBS at 28 weeks to check response to IVIG
- Has a place in pregnancies which have failed previous IVIG treatment

Transfusion advice

- Fetus
  -Hyperconcentrate for IUT
  -prepared specially
  -ideally 7 days notice
- Mother
  -If possible give HPA negative products (risk of boosting antibody/ PTP)
  -do not delay giving standard products in an emergency
  -give an antibody card

Should we screen for NAIT?

	Detection	Treat?	
Downs	1/1000	N	
HIV	2/1000	Y	
HBV	5/1000	Y	
Syphilis	2/1000	Y	Rising prevalence
Rubella	50/1000 susceptible	Y	~1 affected birth/ yr in UK
Sickle cell	0.4/1000	N	
USS	20/1000	?N	

NAIT	0.5/1000	part	~10% poor outcome

Should we screen for NAIT?

Norwegian screening study (2007)
100448 pregnant women.
-All screened for HPA1a
-HPA1a negative mothers tested for antibodies
-Women with antibodies delivered 2-4 weeks early
-55 had severe thrombocytopenia (< 50 × 109/L), 2 with ICH

Previous prospective studies
136 814 women
-51 cases of severe NAIT (3 intrauterine deaths and 7 with ICH).

i.e. programme might decrease death/ICH by 2/3
UK - might prevent about 12 cases ICH/ death per year

Can we prevent NAIT?

PROFNAIT

An EU-funded, collaborative project aiming to develop a safe, prophylatic treatment of FNAIT

What is FNAIT? | Donate plasma | PROFNAIT project | Contact and links

PROFNAIT Project

- Consortium members
- Sounding Board
- Project Funding

Consortium members

PROFNAIT is a collaborative project with participation of eleven Northern European hospitals, blood banks and companies with key expertises in FNAIT and drug development and manufacturing.

All project participants comply with the highest safety standards. The clinical studies will be approved by the national ethical committees and follow the European Medicines Agency's guidelines.

Together we strive to develop and prove the safety and efficacy of this novel treatment of FNAIT and to bring it to the mothers at risk of having a baby/newborn with FNAIT.

"...NAIT changed our lives, but it couldn’t take away our greatest joy"

Resources

- hospital.blood.co.uk
  then search for "nait"
  -NHSBT information sheet
  -Patient information leaflet
  -Request forms + user info for lab
- Naitbabies.org
  -patient support group (international)