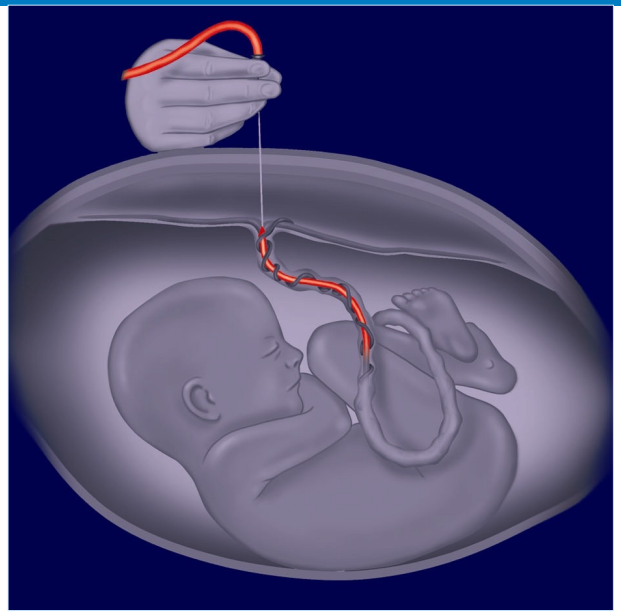
Leids Universitair Medisch Centrum

Sanquin

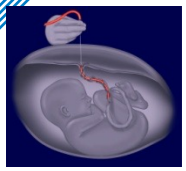
Over rode antistoffen, witte foetussen en gele babies



Annemieke Middeldorp
perinatoloog-foetaal behandelaar

Enrico Lopriore
neonatoloog

Waar gaan we het over hebben?



'Rhesusziekte'

HZFP

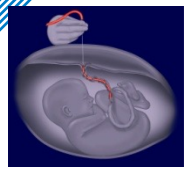
hemolytische ziekte van de foetus en pasgebore

HDFN

Hemolytic disease of the fetus and the newborn

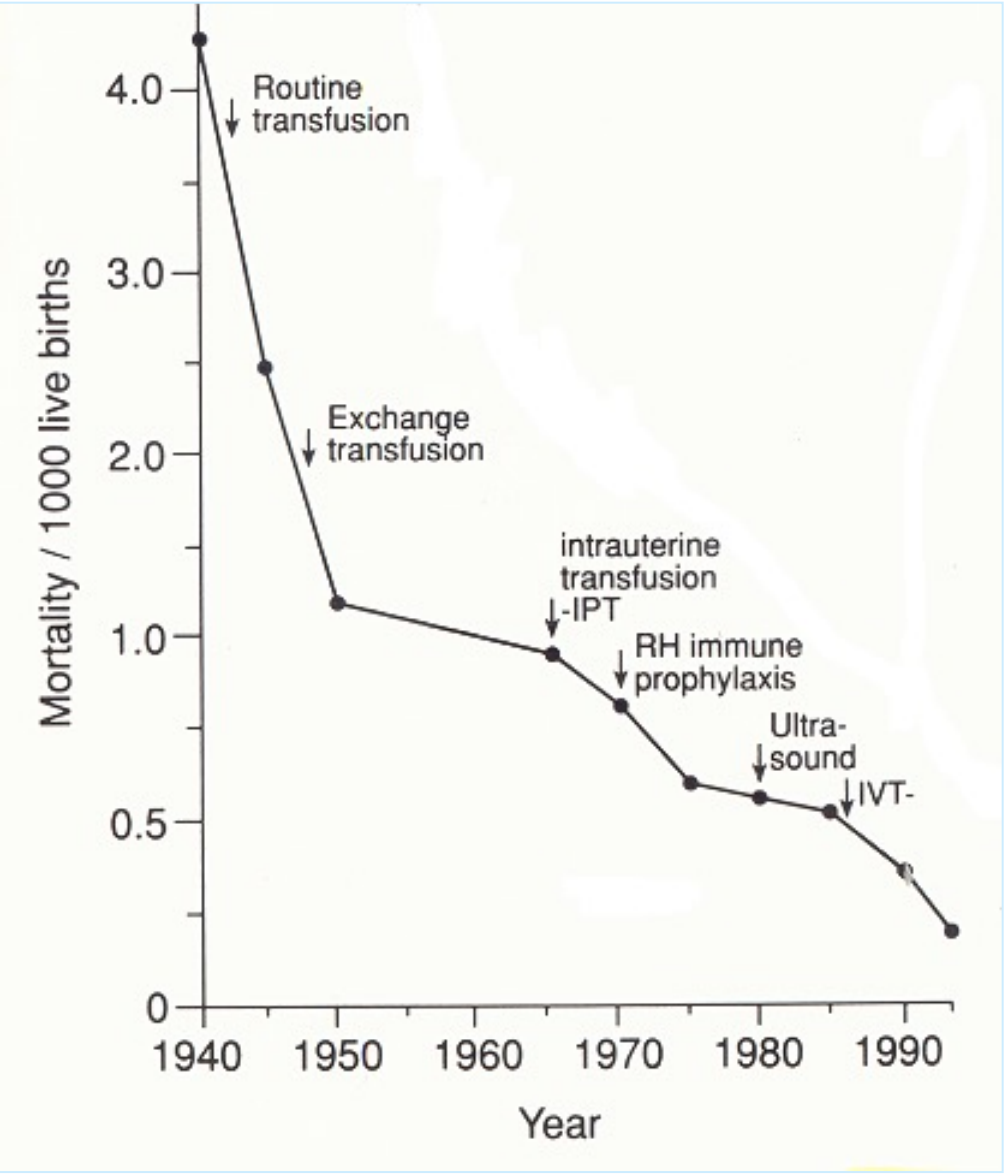
tot 1940 belangrijkste oorzaak van perinatale sterfte

De puzzel compleet circa 1940



- bloedgroep-incompatibiliteit
- (foeto)maternale transfusie
- sensibilisatie (immunisatie)
- foetale hemolyse
- foetale anemie
- foetale hydrops
- neonatale icterus
- sterfte

Milestones



1940: Rh factor (*Macaca-rhesus*)

1946: wisseltranfusie*(Wallerstein)*

1958: fototherapie

1961: bilirubine in vruchtwater(*Liley*)

1963: intraperitoneale transfusie (*Liley*)

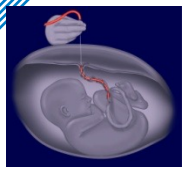
1965: Anti-D (*Clarke/Freda*)

1983: intra-vasculaire transfusie (*Daffos*)

1997: foetaal DNA maternaal plasma (*Lo*)

2000: MCA-Doppler *(Mari)*

Waar gaan we het over hebben?



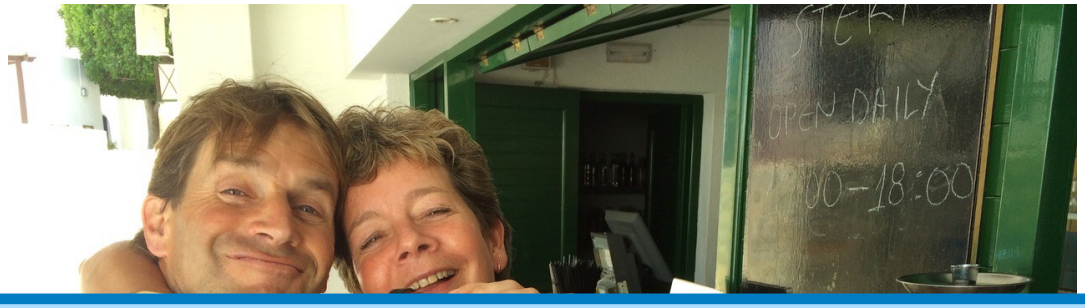
Antenataal:

- introductie
- screening en preventie
- identificatie risicozwangerschap
- diagnostiek foetale anemie
- behandeling foetale anemie
- toekomstperspectieven

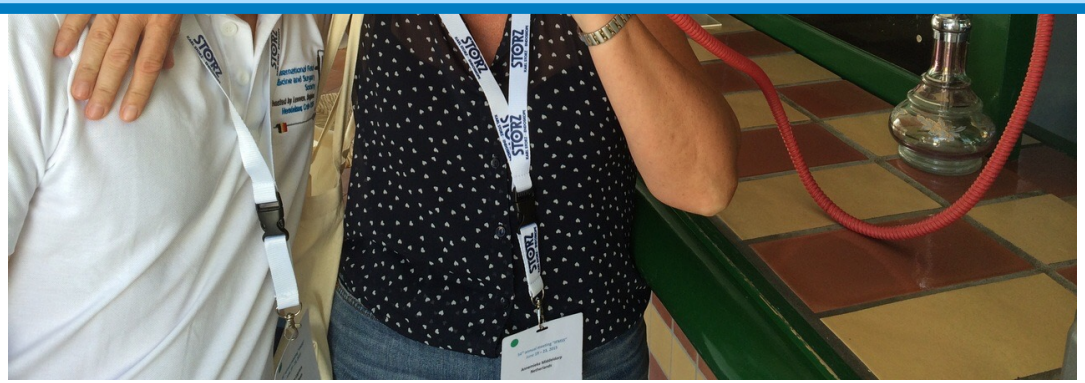
Neonataal:

- opvang en behandeling
- korte- en lange termijn uitkomsten

Innige samenwerking..

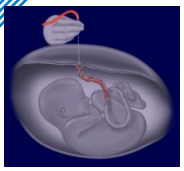


GEEN BELANGENVERSTRENGELING!!!



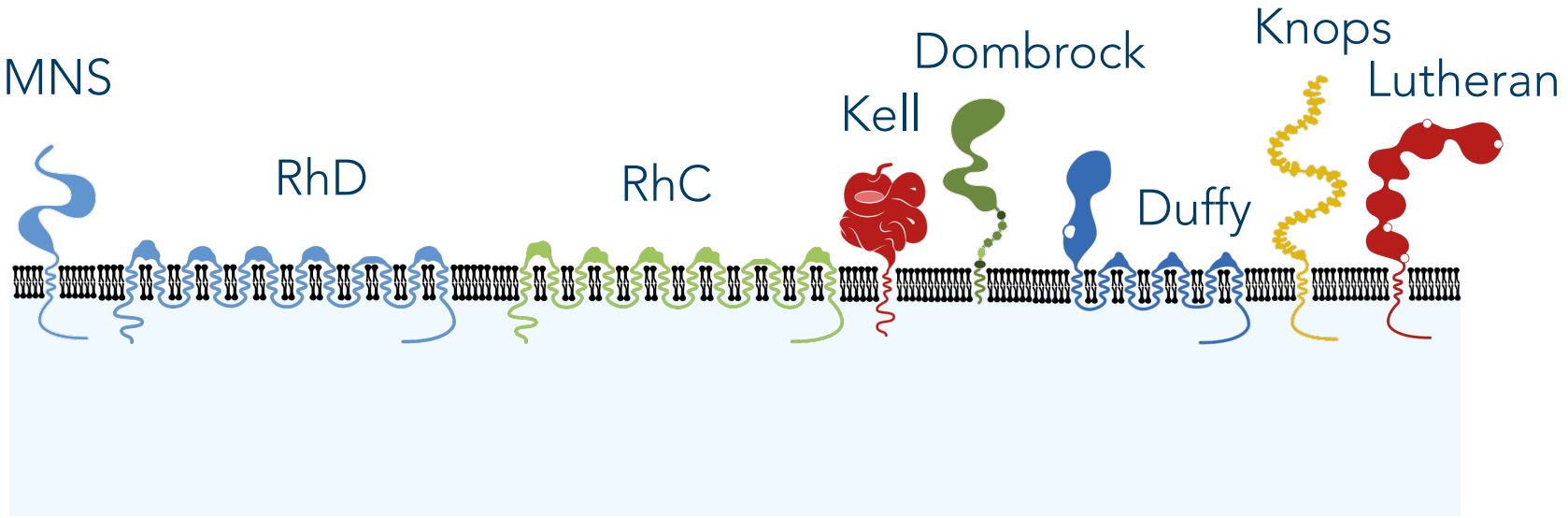
Bloedbroeders!!

Waar gaan we het over hebben?



Introductie

Veel verschillende typen antigenen



Typen antistoffen

REGULAIRE ERYTROCYTEN ANTISTOFFEN (REA)

- Anti-A, anti-B, anti-AB

IRREGULAIRE ERYTROCYTEN ANTISTOFFEN (IEA)

- Anti-D, -c, -C, -K, -k, -Fya, -Fyb, -S, -s, M

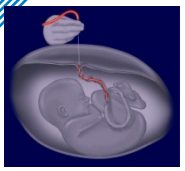
Oorzaken alloimmunisatie

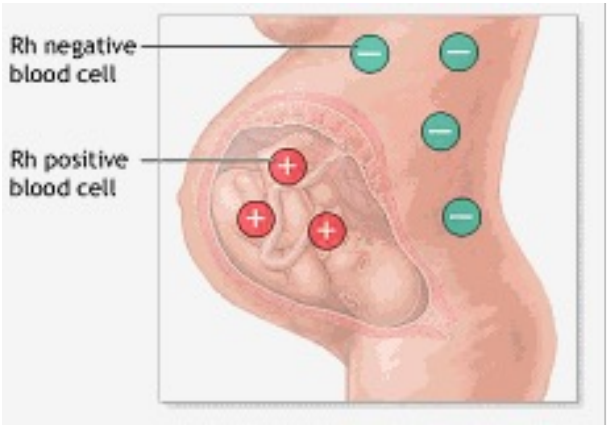
zwangere heeft in het verleden een **BLOEDTRANSFUSIE** gehad

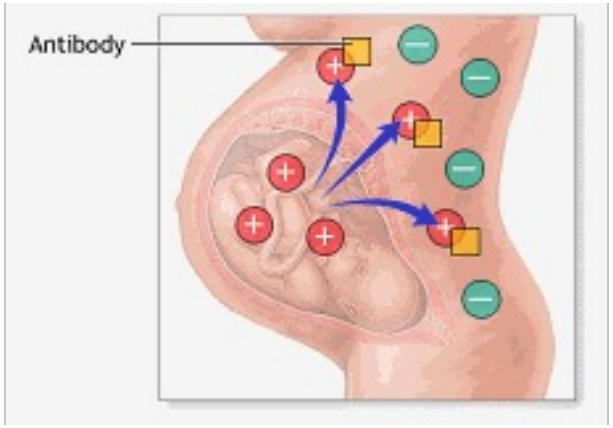
FOETO-MATERNALE TRANSFUSIE tijdens zwangerschap of partus

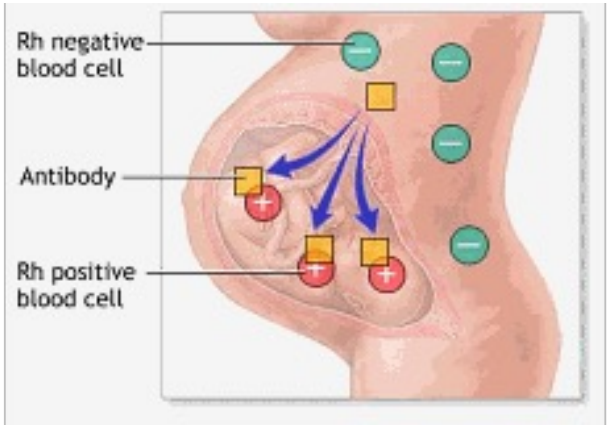
NATUURLIJK VOORKOMENDE IEA geen duidelijk moment

Alloimmunisatie en zwangerschap









Foetomaternale transfusie

EERSTE TRIMESTER

3%

TWEEDE TRIMESTER

12%

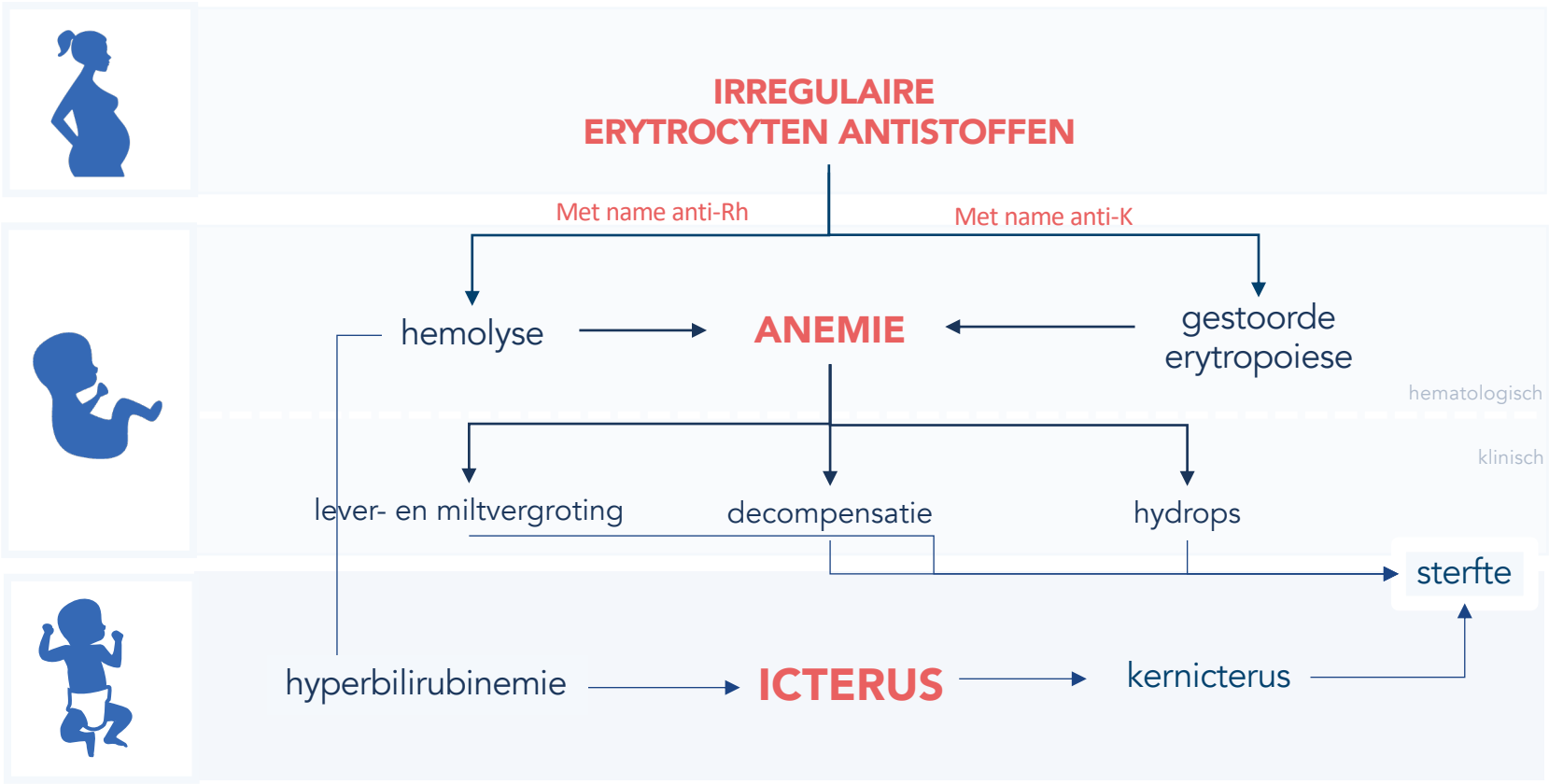
DERDE TRIMESTER

45%

POSTPARTUM

64%

Alloimmunisatie en hemolytische ziekte



Definitie

GEEN HZFP

Geen foetale/neonatale anemie of hyperbilirubinemie

MILDE HZFP

Hyperbilirubinemie waarvoor **fototherapie** nodig is

ERNSTIGE HZFP

Foetale anemie waarvoor **intra-uteriene erytrocytentransfusie**

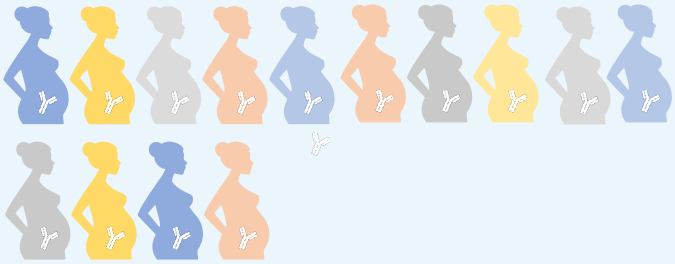
Neonatale anemie waarvoor **erytocytentransfusie**

Neonatale hyperbilirubinemie **partiele wisseltransfusie**

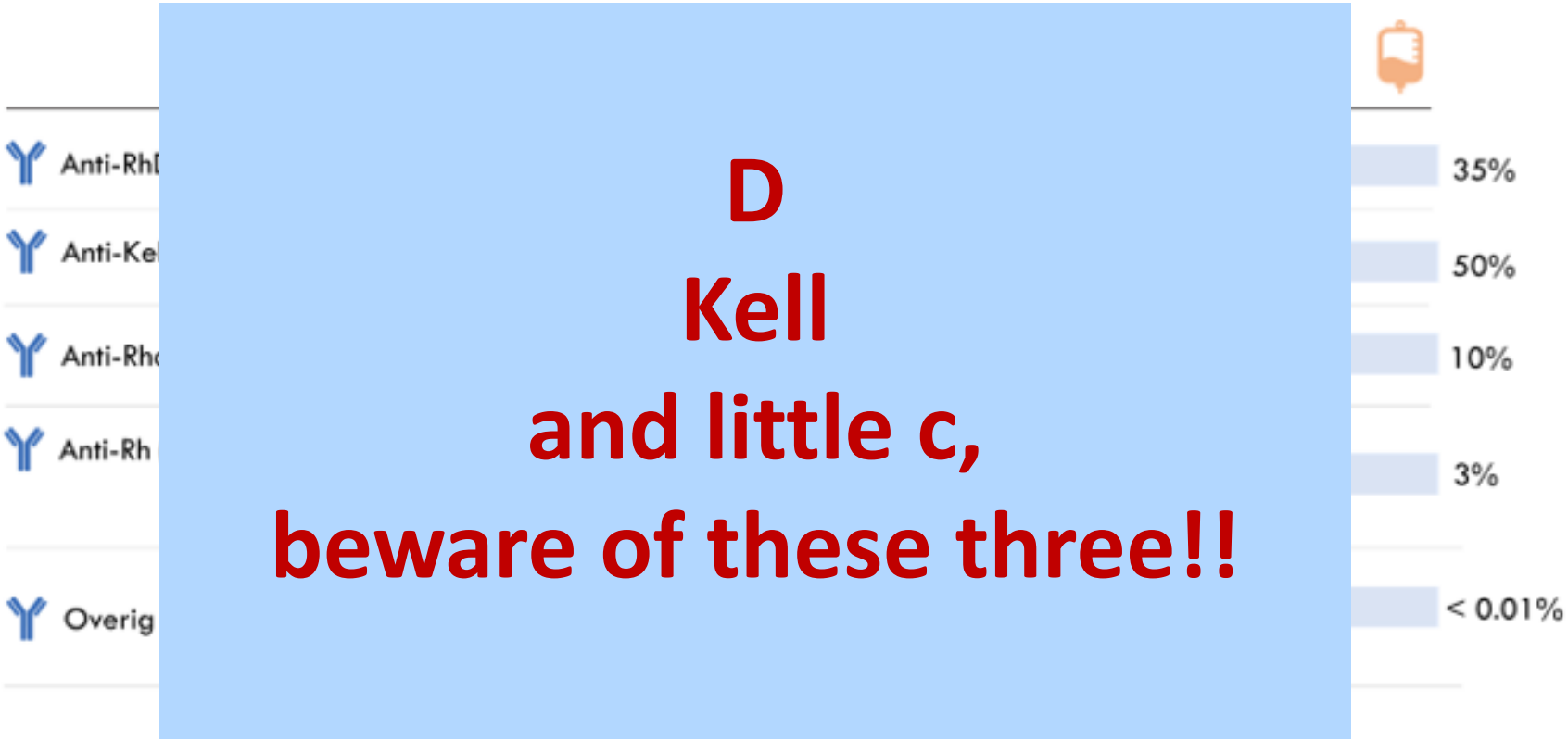
Ernstige HZFP – hoeveel per jaar?

RhD antistoffen | ~60 ZWANGEREN

Andere antistoffen | 14 ZWANGEREN

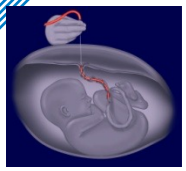


Type IEA en beloop



D
Kell
and little c,
beware of these three!!

Alloimmunisatie en hemolytische ziekte



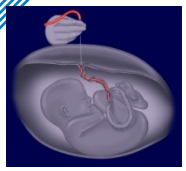
Alleen IgG passeert placenta, IgM nooit!

RhD is het meest immunogene erytrocyten-antigeen

Natuurlijke antistoffen A en B zijn alléén geassocieerd met neonatale hemolyse

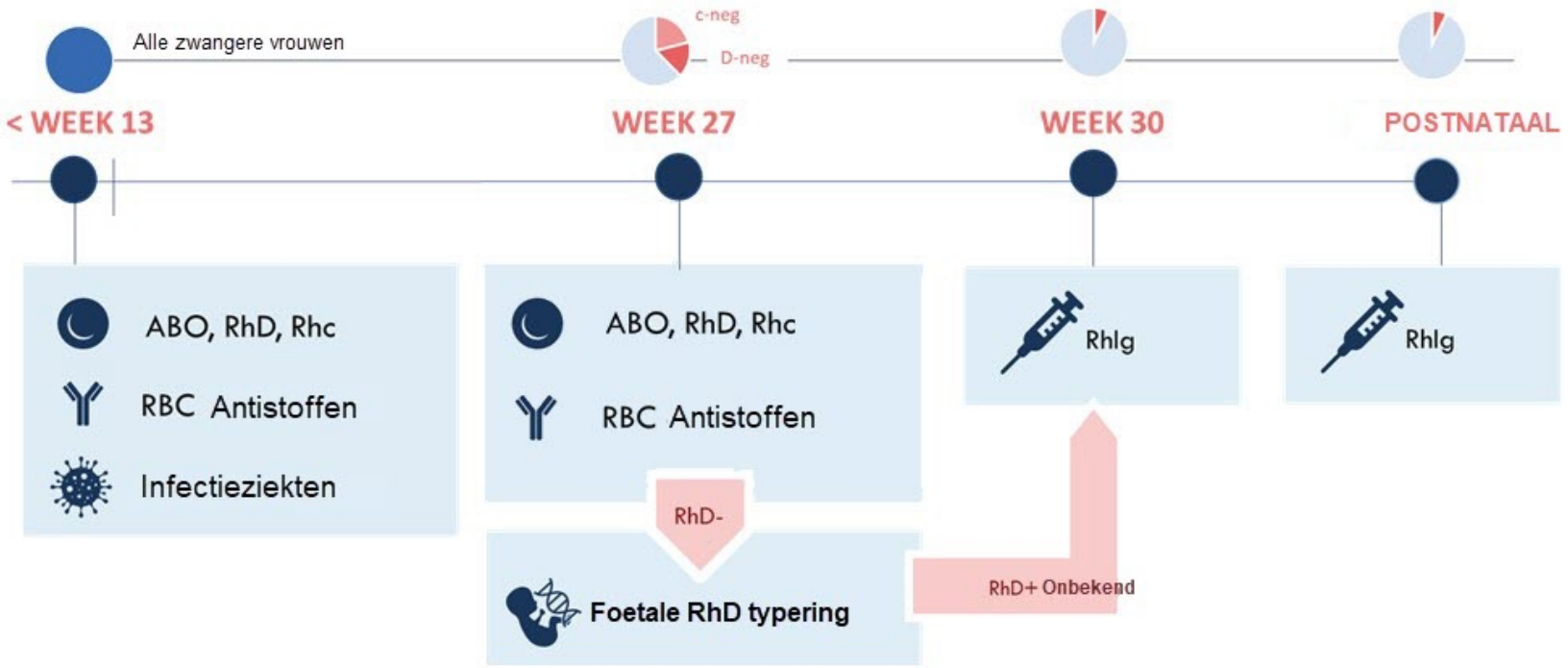
AB0 incompatibiliteit beschermt tegen RhD-immunisatie
(moeder 0 met A en B antistoffen, foetus A, B of AB)

Waar gaan we het over hebben?

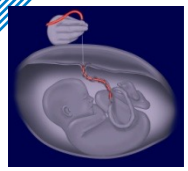


Screening en preventie

Preventieprogramma



Preventie bloedgroepimmunisatie



Anti-D immunoglobuline (IgG) *post*nataal (1969)

Anti-D *ante*nataal bij risico FMT

Anti-D *ante*nataal 30 wk (1998)

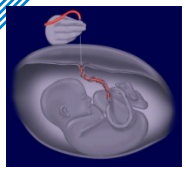
RhD immunisatiekans door anti-D gedaald

14,7% → 1,5% → 0,2%

Circa 40% van de RhD neg zwangeren heeft een RhD neg foetus
Anti-D niet nodig!

Compatibele bloedtransfusie (cEK) vrouwen < 45 jaar

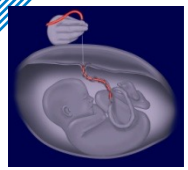
Feiten betreffende Anti-D



- polyclonaal anti-D is humaan product (risico's)
- hypothese werking: anti-D op RhD+ cellen, aan Fc-receptor van macrofagen, antigeenpresentatie en immuunrespons blijven uit.
- antenatale profylaxe preventieve werking 10 weken

- SCHAARSTE

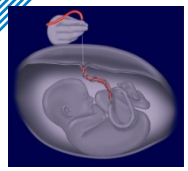
anti-D toediening: wanneer?



Risicofactoren foetomaternale transfusie en sensibilisatiemoment	*Dosis anti-D*
	375 IE
Vlokkentest of amniocentese < 26 weken	
Instrumenteel >7 weken	**375 IE**
Medicamenteus of spontaan (>7 en <10 weken overweeg…) >10 weken	**375 IE**
Extra-uteriene graviditeit	**375 IE**
Evacuatie mola hydatiforma	**375 IE**
Partus immaturus, abortus provocatus, zwangerschapsbeëindiging > 20 weken	**1000 IE**
Vlokkentest of amniocentese > 26 weken, cordocentese	**1000 IE**
Routine 30e week zwangerschap	**1000 IE**
Uitwendige versie (poging)	**1000 IE**
Bloedverlies 2e / 3e trimester	**1000 IE**
Postpartum bij RhD-positief kind (dosis ↑? na sc, MPV, expressie, meerling)	**1000 IE**
Stomp buiktrauma in de graviditeit (Kleihauer)	**1000 IE**
Intra-uteriene vruchtdood (Kleihauer)	**1000 IE**
Foetomaternale transfusie	**Dosis berekenen**
Transfusie (of transplantatie) met materiaal van RhD-positieve donor	**Dosis berekenen**

bij tweelingen dubbele dosis toedienen bij 2 maal foetus rhesus D positief (www.rivm.nl/pns/downloads)

Preventie bij grote foetomaternale transfusie

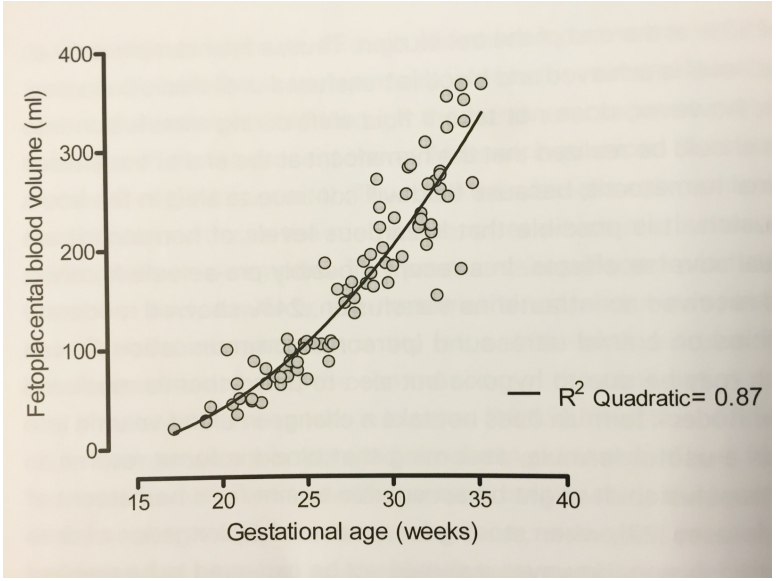


Volume berekenen:

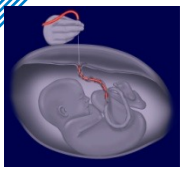
- Kleihauer test: ml
- Flowcytometrie: ‰, 5‰ = 20 ml

1000 IU anti-D neutraliseert

- 20 ml vol bloed
- 10 ml PC



Preventie bij grote foetomaternale transfusie

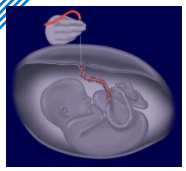


Indien geen test voorhanden: dubbele dosis

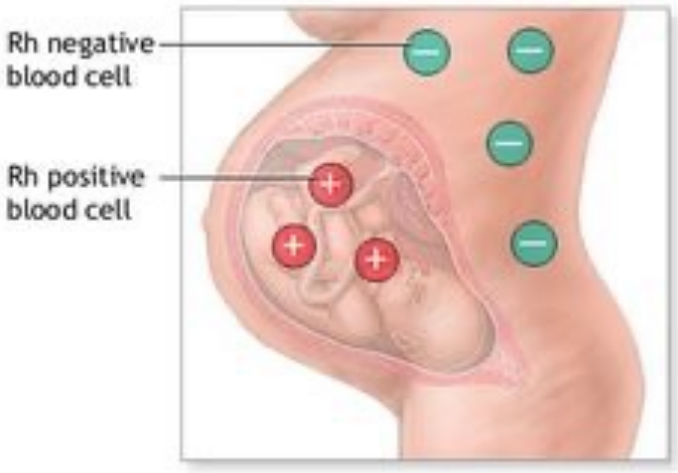
IV toediening anti-D is mogelijk bij grote dosis
(òf 6000 IE IM elke 12 uur)

Anti-D gift bij voorkeur binnen 48 uur post partum
effectief tot 13 dagen

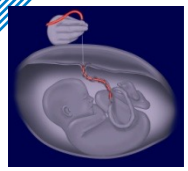
Waar gaan we het over hebben?



Identificatie risicozwangerschap



Casus D



G4 P2

blanco VG

O negatief

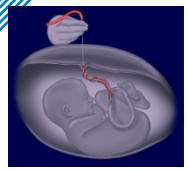
2 kinderen

2x anti-D gehad

sp. ab. 8 wk

antistoffen D en C 1e trimester

Maternale bloedgroepimmunisatie



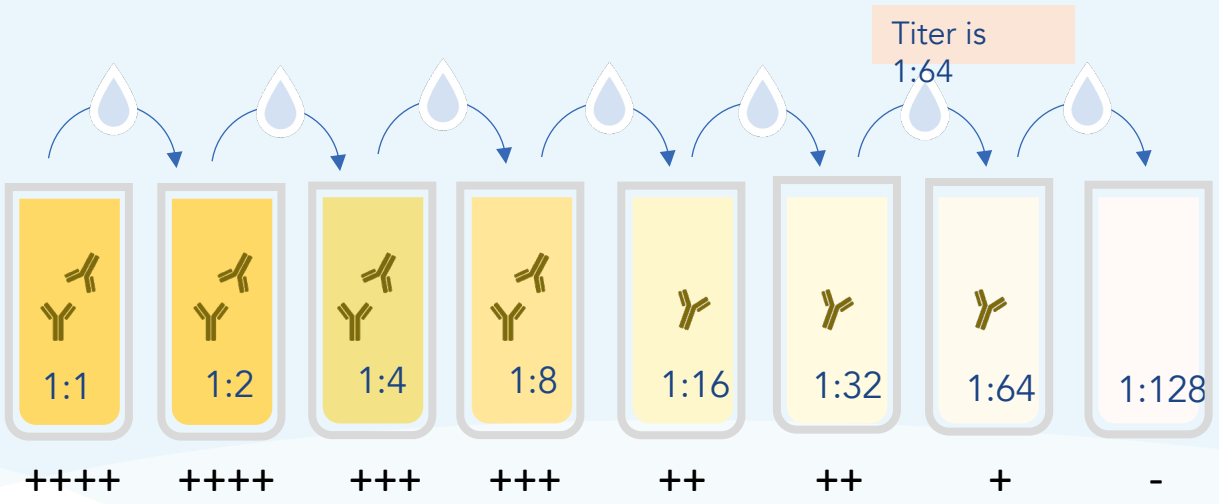
Eerste screening positief: wat nu?

- Klinische relevantie maternale antistoffen (IgG en type)
- Partner typeren en indien positief: zygotie typeren
- Partner heterozygoot D (C negatief)
- Foetus typeren
  - ✓ PCR op foetaal DNA in maternaal plasma
- Foetus positief: antistof titers en ADCC vervolgen

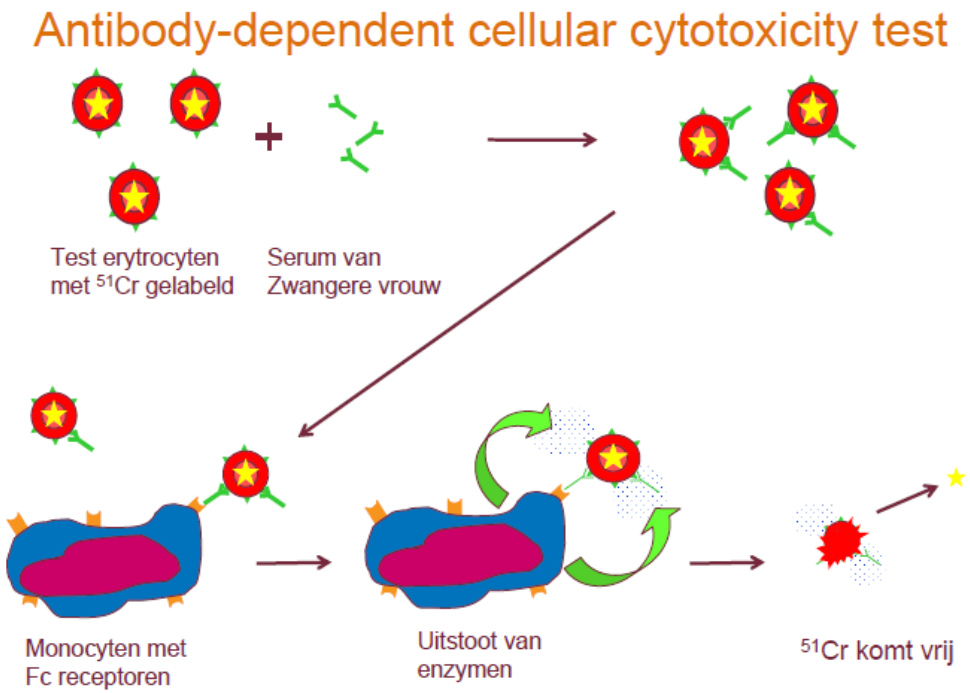
Titerbepaling

De verdunning waarbij de antistof nog aantoonbaar is in het serum van de moeder

Maat om concentratie aan te geven.



ADCC test



Gevalideerd voor Rhesus(D):

0-30% geen tot geringe hemolyse

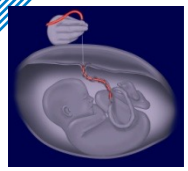
30-50% geringe tot matige hemolyse

50-80% matige tot ernstige hemolyse

>80% (zeer) ernstige hemolyse

Urbaniak 1981; Ouwehand (CLB/Sanquin) 1984; Oepkes 2001

Vervolg casus D

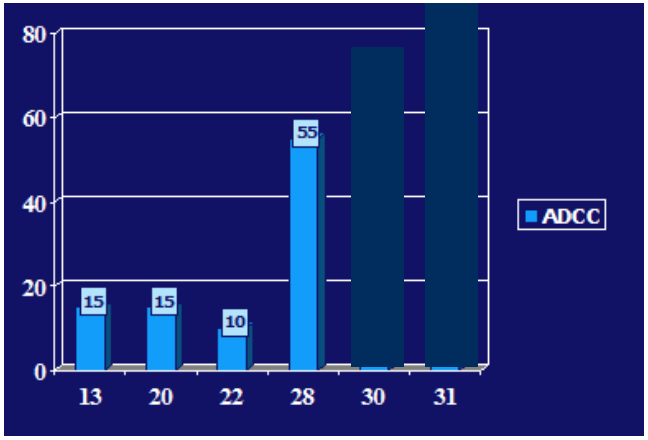


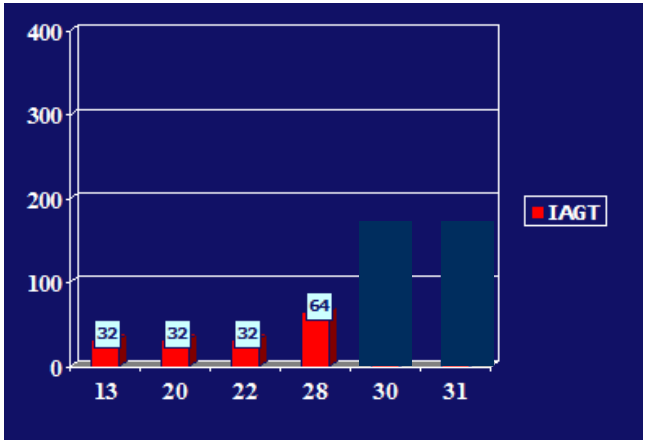
Volgens advies van Sanquin: ADCC en titers vervolgd

AD 28 weken

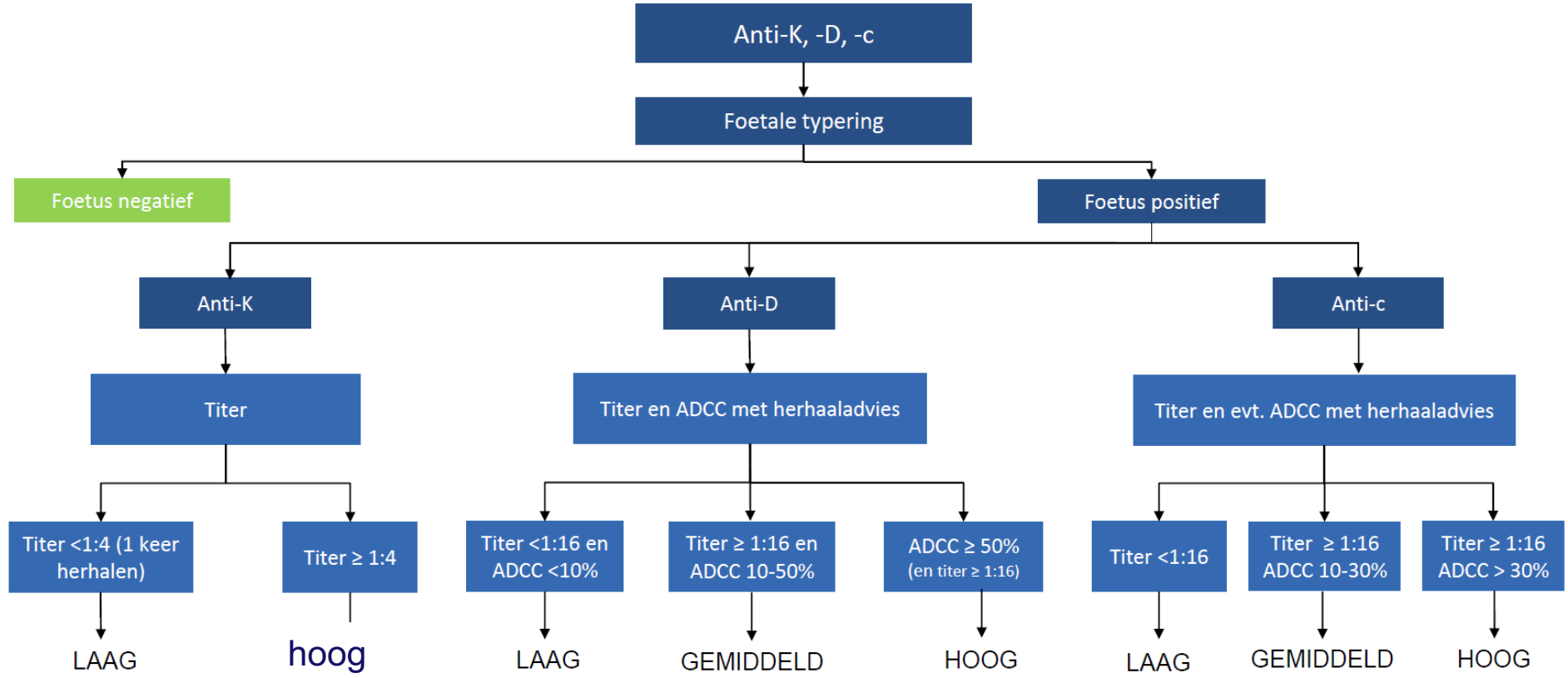
- ADCC 55%
- titer 1:64

Wat nu??





Kell, D, c immunisatie

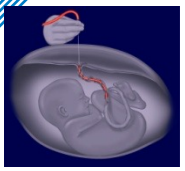


LAAG RISICO op ernstige anemie
Monitoring: 2e lijn, mogelijk shared care 1e lijn
Partus: in elk ziekenhuis mogelijk
Timing: AD 37-38 weken
Direct post partum: kans op WT laag, consult kinderarts.

GEMIDDELD RISICO op ernstige anemie
Monitoring: 2e lijn, z.n. 3e lijn gespecialiseerde monitoring#
Partus: ziekenhuis WT mogelijk
Timing: AD begin 37 weken
Direct post partum: kans op WT medium, opname neonatologie.

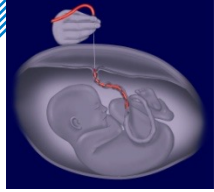
HOOG RISICO op ernstige anemie
Monitoring: LUMC, wekelijks gespecialiseerde monitoring#
Partus: LUMC of ziekenhuis WT mogelijk
Timing: AD begin 37 weken
Direct post partum: Anti-D: kans op WT hoog; Opname Neonatologie. Anti-K: kans op WT laag, consult kinderarts.

Waar gaan we het over hebben?



Diagnostiek

Diagnostiek foetale anemie: overwegingen



- alloimmuun anemie ontstaat geleidelijk
- foetus kan anemie door hemolyse lang compenseren
- cardiomegalie, hepato- en splenomegalie
- voorkom hydrops door tijdige diagnose!!!

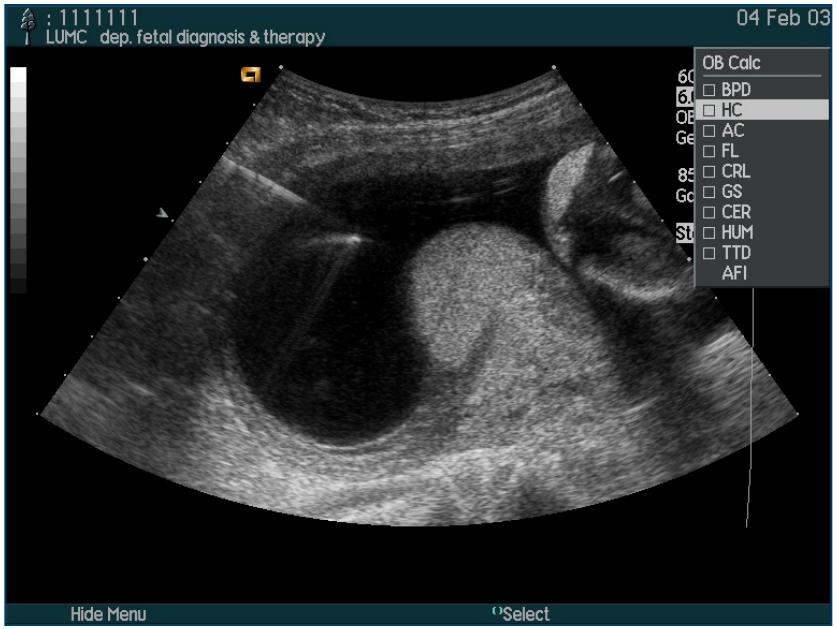
NB Kell anemie ontstaat vaak al < 20 weken!

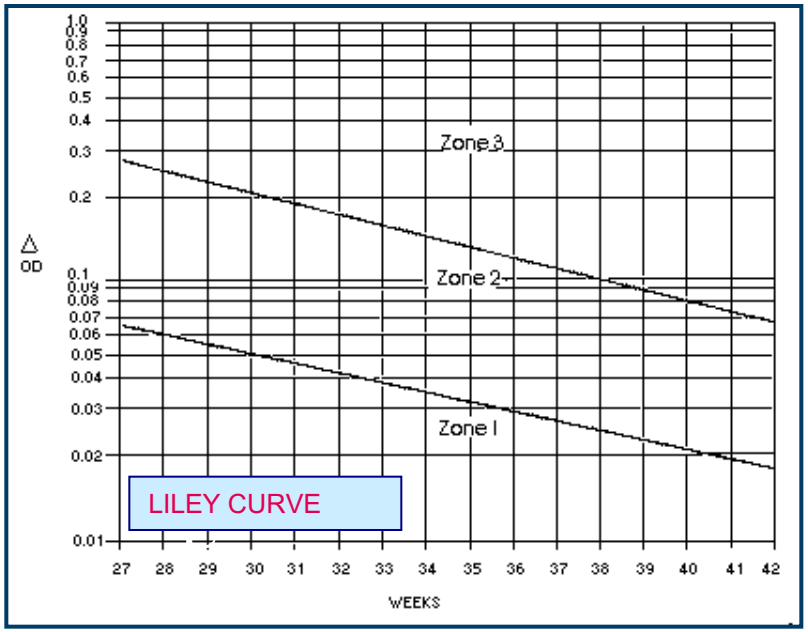
Lindenburg & van Kamp 2006

Diagnostiek van foetale anemie 1

BILIRUBINE-EXTINCTIE IN VRUCHTWATER

(Bevis 1952, Liley 1961)

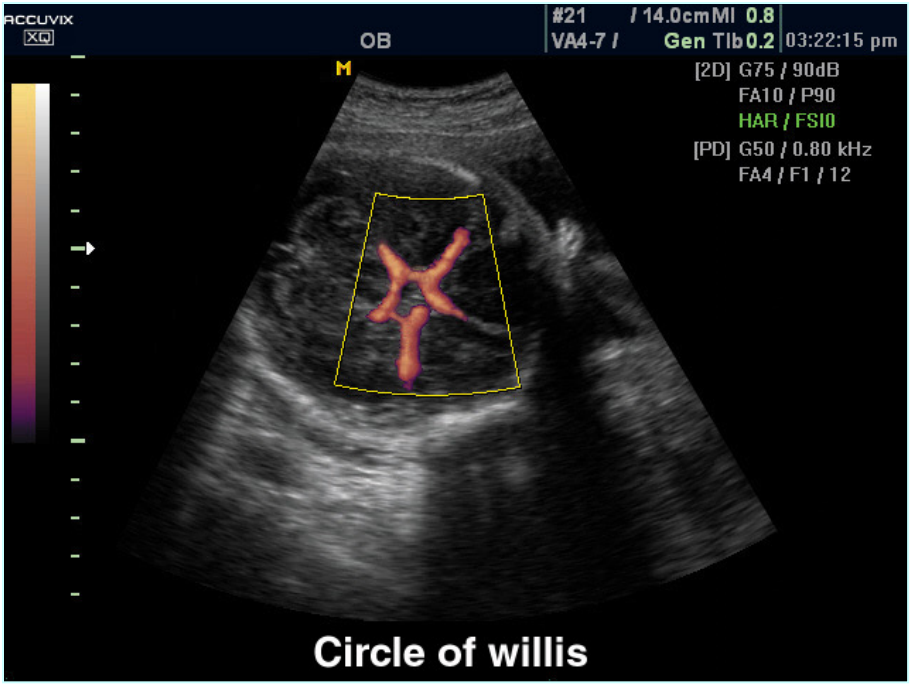




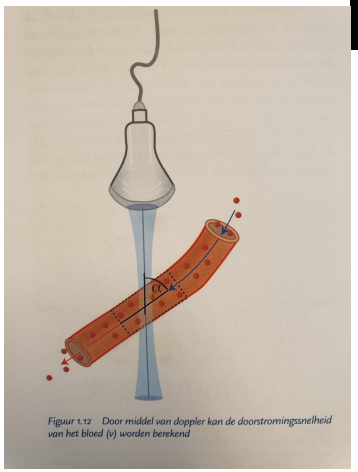
Nadelen:

- invasief onderzoek met kans op complicaties 0,3%
- meet alleen de hemolyse en niet de extra aanmaak
- niet bruikbaar bij Kell

Diagnostiek van foetale anemie 2



Echografische kenmerken anemie



Peak systolicvelocity (PSV) in a. cerebri media (ACM)

- Hoek < 20°
- Geen foetale bewegingen
- Weinig druk

Echografische kenmerken anemie: PSV-MCA

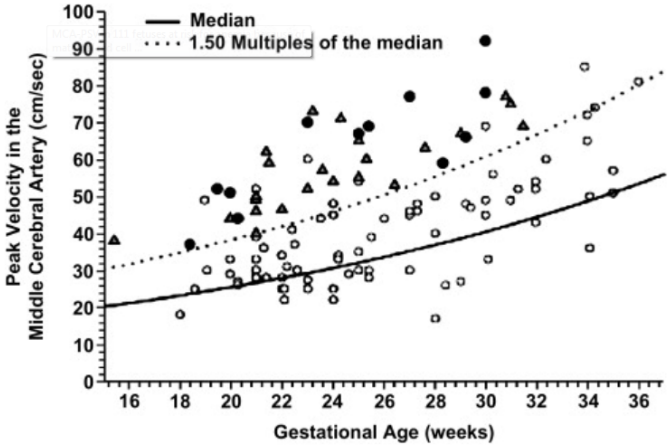


Fig. 2.
MCA-PSV in 111 fetuses at risk for anemia because of maternal red cell alloimmunization. Open circles indicate fetuses with either no anemia or mild anemia (>0.65 MoM hemoglobin concentration). Triangles indicate fetuses with moderate or severe anemia (<0.65 MoM hemoglobin concentration). The solid circles indicate the fetuses with hydrops. The solid curve indicates the median MCA-PSV, and the dotted curve indicates 1.5 MoM.

Mari G et al, N Eng J Med 2000

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Doppler Ultrasonography versus Amniocentesis to Predict Fetal Anemia

Dick Oepkes, M.D., P. Gareth Seaward, M.B., B.Ch.,
Frank P.H.A. Vandenbussche, M.D., Rory Windrim, M.B., John Kingdom, M.D.,
Joseph Beyene, Ph.D., Humphrey H.H. Kanhai, M.D., Arne Ohlsson, M.D.,
and Greg Ryan, M.B., for the DIAMOND Study Group*

Conclusion: Doppler measurement of the peak velocity of systolic blood flow in the middle cerebral artery can safely replace invasive testing in the management of Rh-alloimmunized pregnancies.

Oepkes et al., N Eng J Med 2006

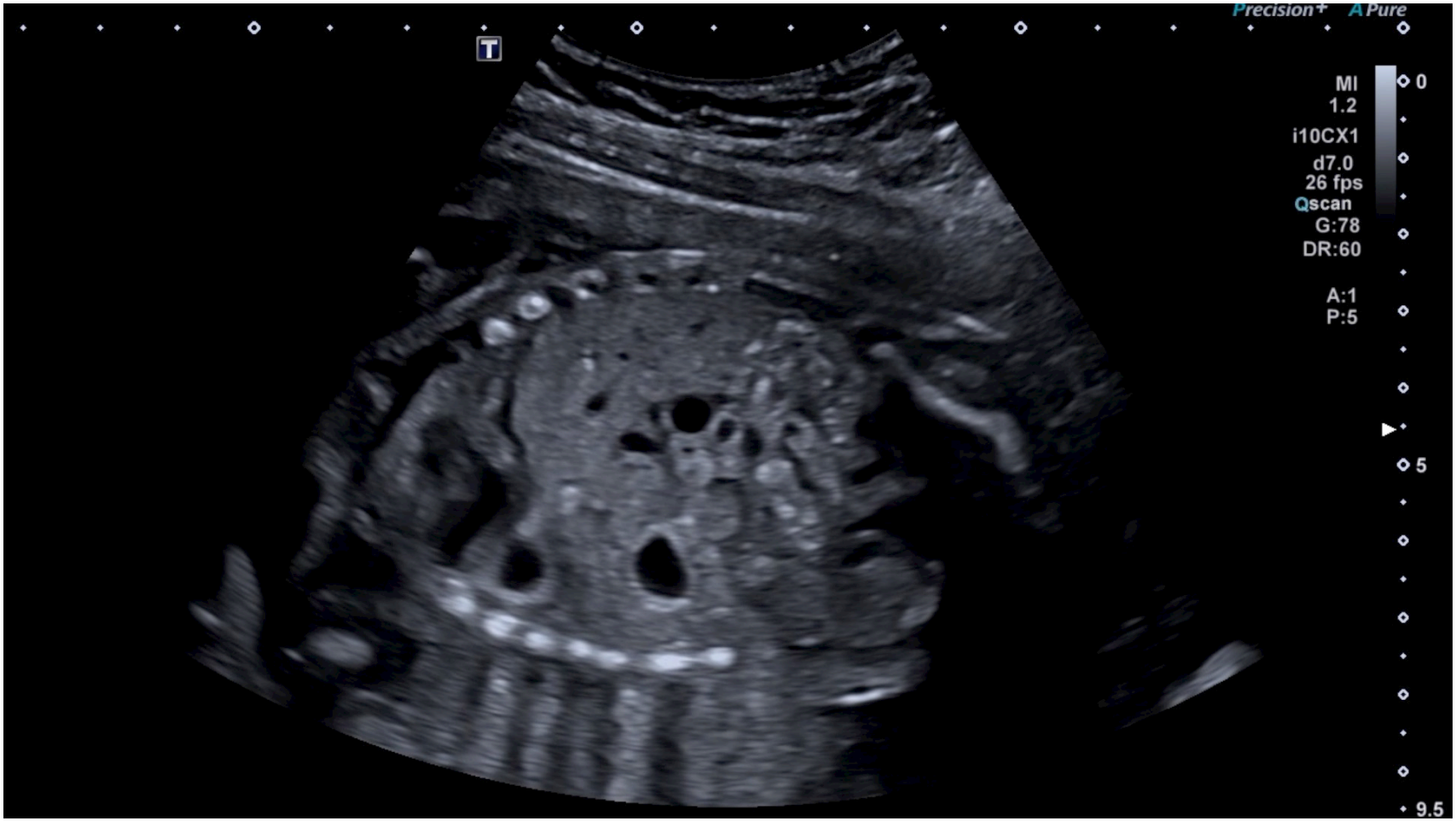
Echografische kenmerken anemie: cardiomegalie

normale CT-ratio

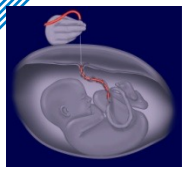
toegenomen CT-ratio

Sikkel et al 2006: sensitiviteit 47%, specificiteit 90%

Echografische kenmerken anemie: natte darmen



Classificatie ernst van foetale hydrops



Hydrops mild

- rand ascites
- eventueel pericardvocht

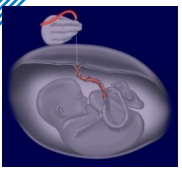
Hydrops ernstig

- massale ascites (organen ‘free-floating’)
- pericardvocht
- en/of huidoedeem of pleuravocht

Hydrops: pericardvocht

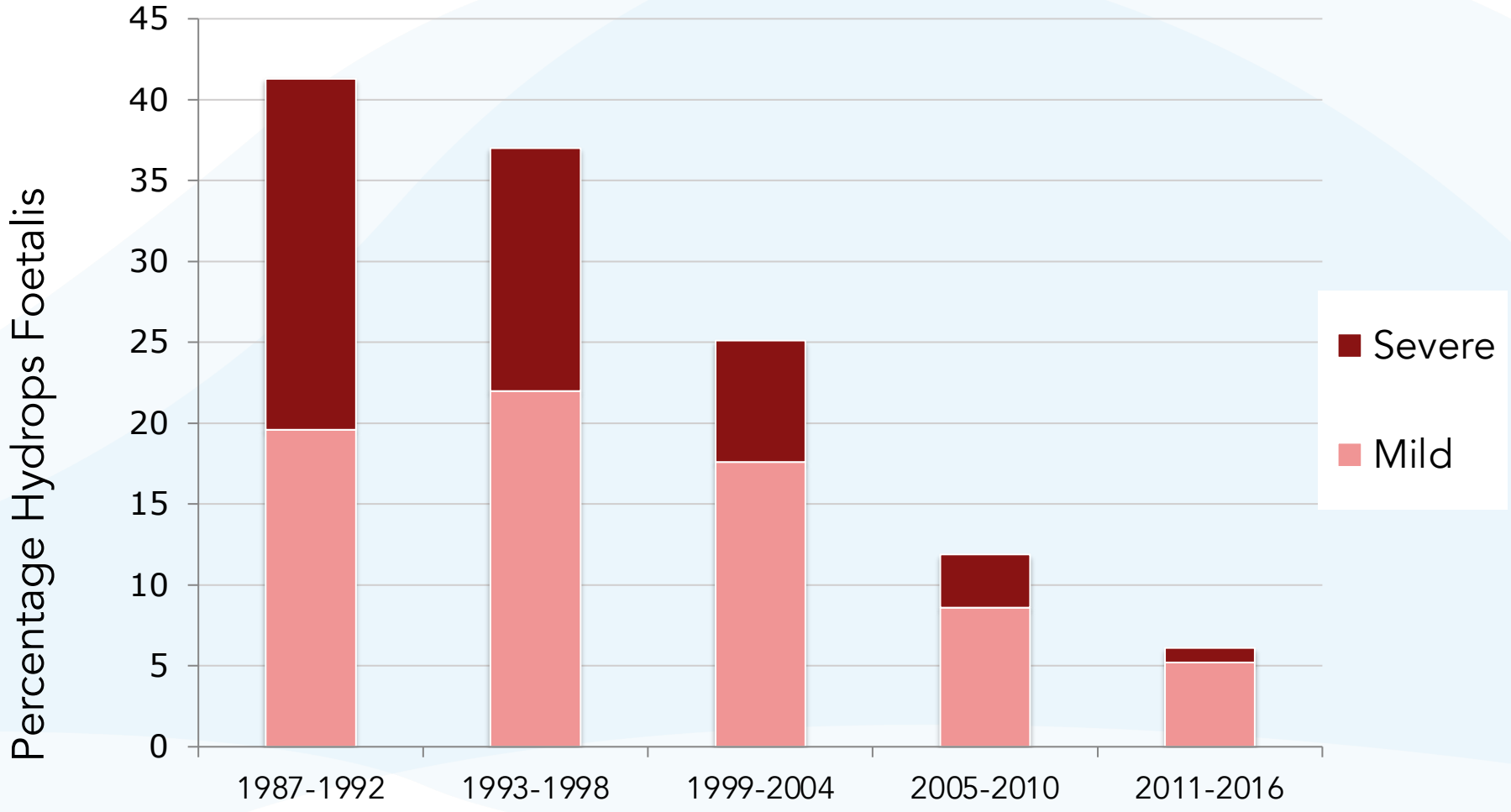
Hydrops: ascites mild

Hydrops: ascites ernstig



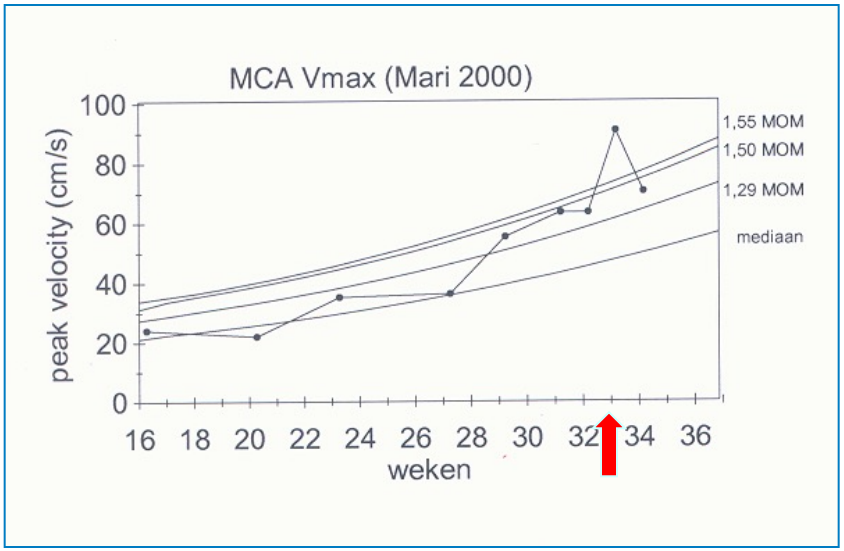
Hydrops: huidoedeem

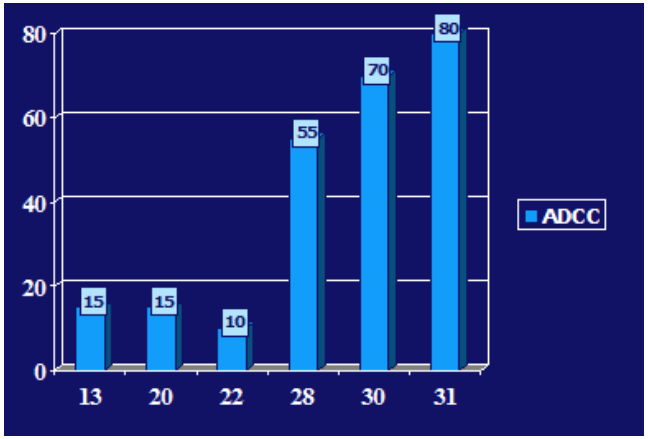
Hydrops door de jaren

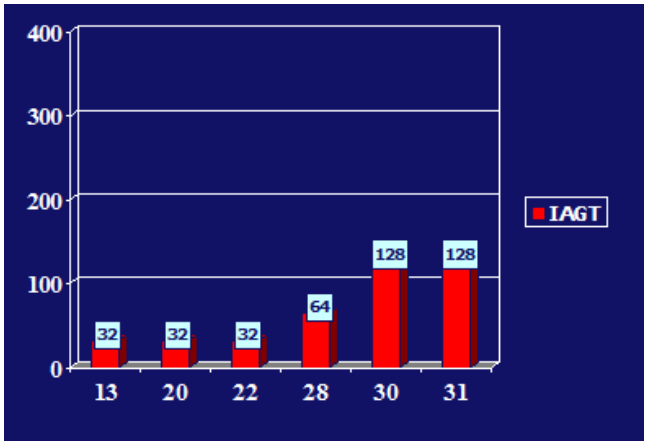


Zwiers C, et al., *Prenat Diagn.* 2018

Vervolg Casus

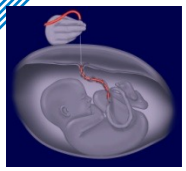






IUT 1 33 wk Hb 4,6 → 8,2 mmol/l

Casus Kell



G3P2M1

OVG:

A terme partus

IUVD bij 20 weken, Kell immunisatie, ADCC 50% en titer 1:256

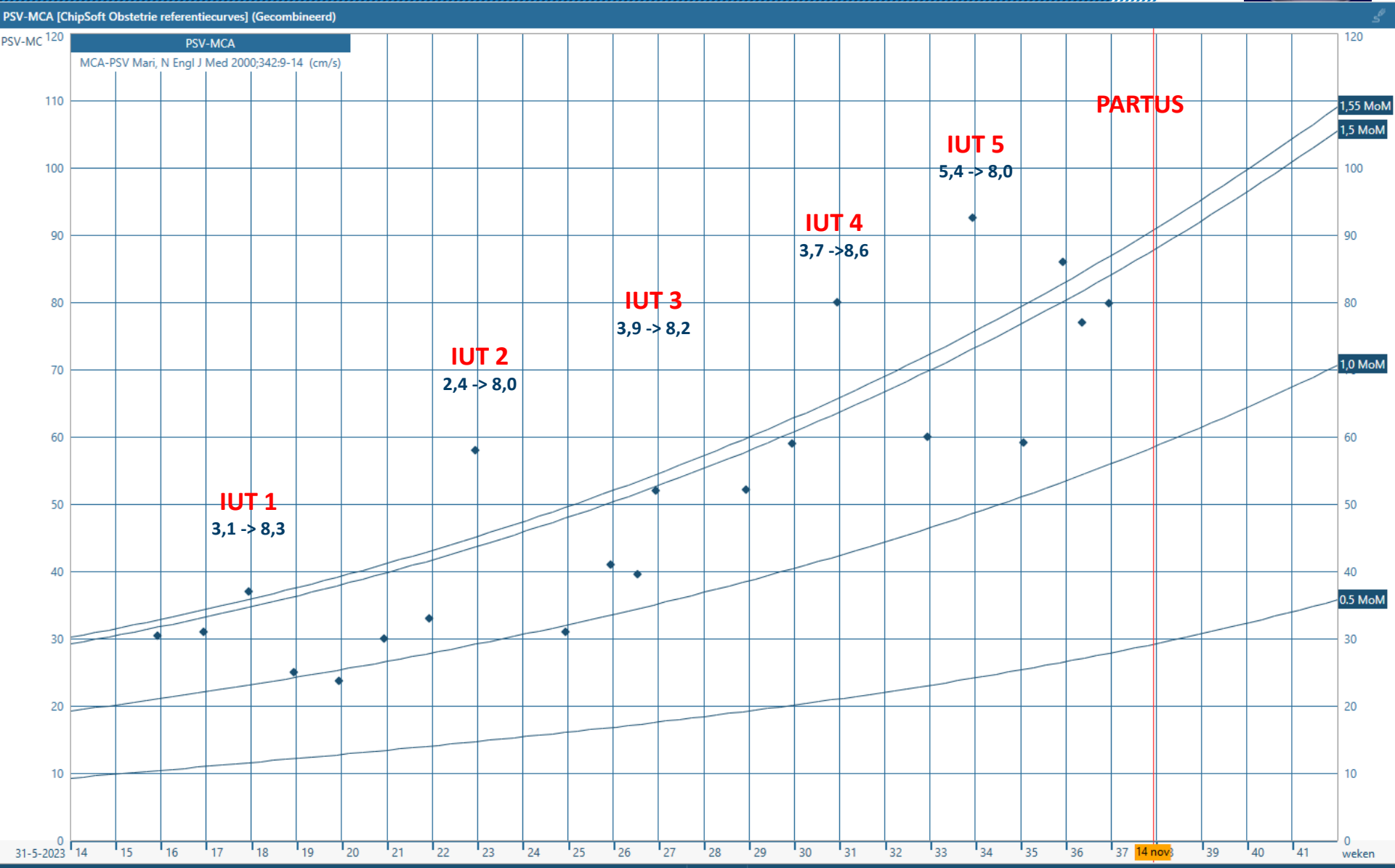
Huidige graviditeit:

Partner heterozygoot Kell

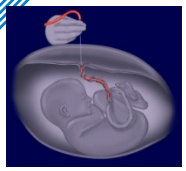
Foetus Kell-positief

ADCC 35% en titer 1:1000

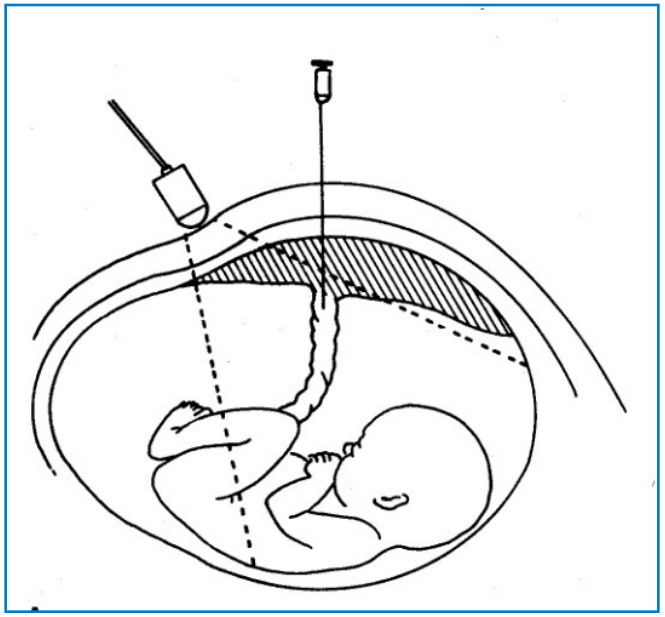
Casus Kell


PSV-MCA [ChipSoft Obstetrie referentiecurves] (Gecombineerd)
PSV-MC
PSV-MCA
MCA-PSV Mari, N Engl J Med 2000;342:9-14 (cm/s)
PARTUS
IUT 1
3,1 -> 8,3
IUT 2
2,4 -> 8,0
IUT 3
3,9 -> 8,2
IUT 4
3,7 ->8,6
IUT 5
5,4 -> 8,0
1,55 MoM
1,5 MoM
1,0 MoM
0.5 MoM
31-5-2023
14 nov
weken

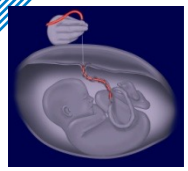
Waar gaan we het over hebben?



Intra-uteriene behandeling



Invasieve behandeling foetale anemie

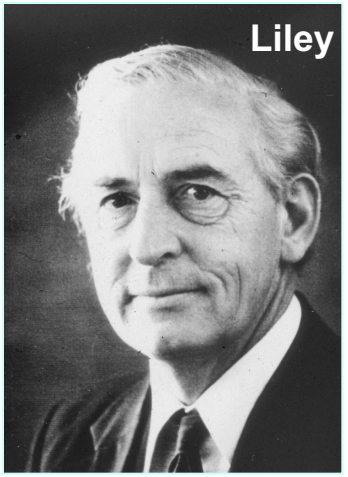


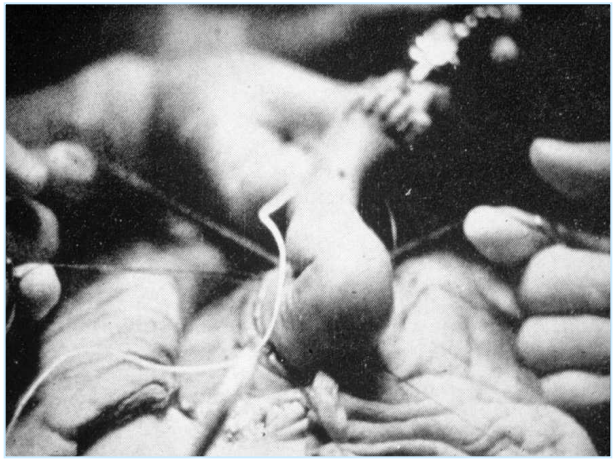
Foetale transfusie (IUT)

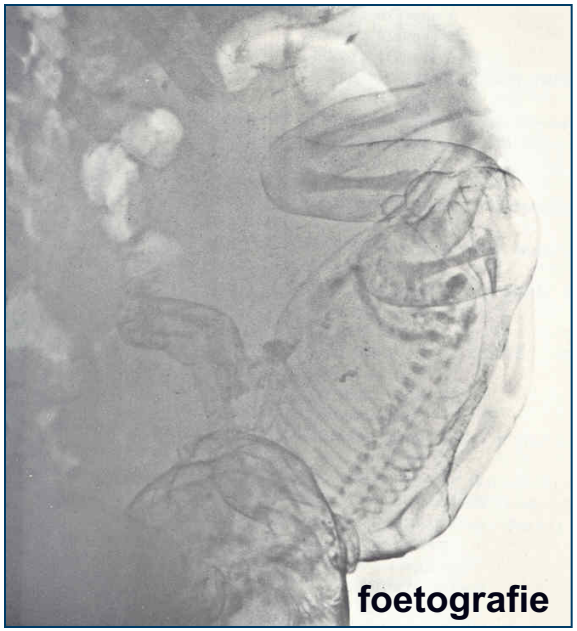
intra-peritoneaal (Liley 1963)

open foetale therapie (Freda 1964)

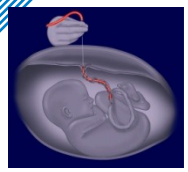
percutaan intravasculair (Daffos 1983)







LUMC: landelijk expertisecentrum

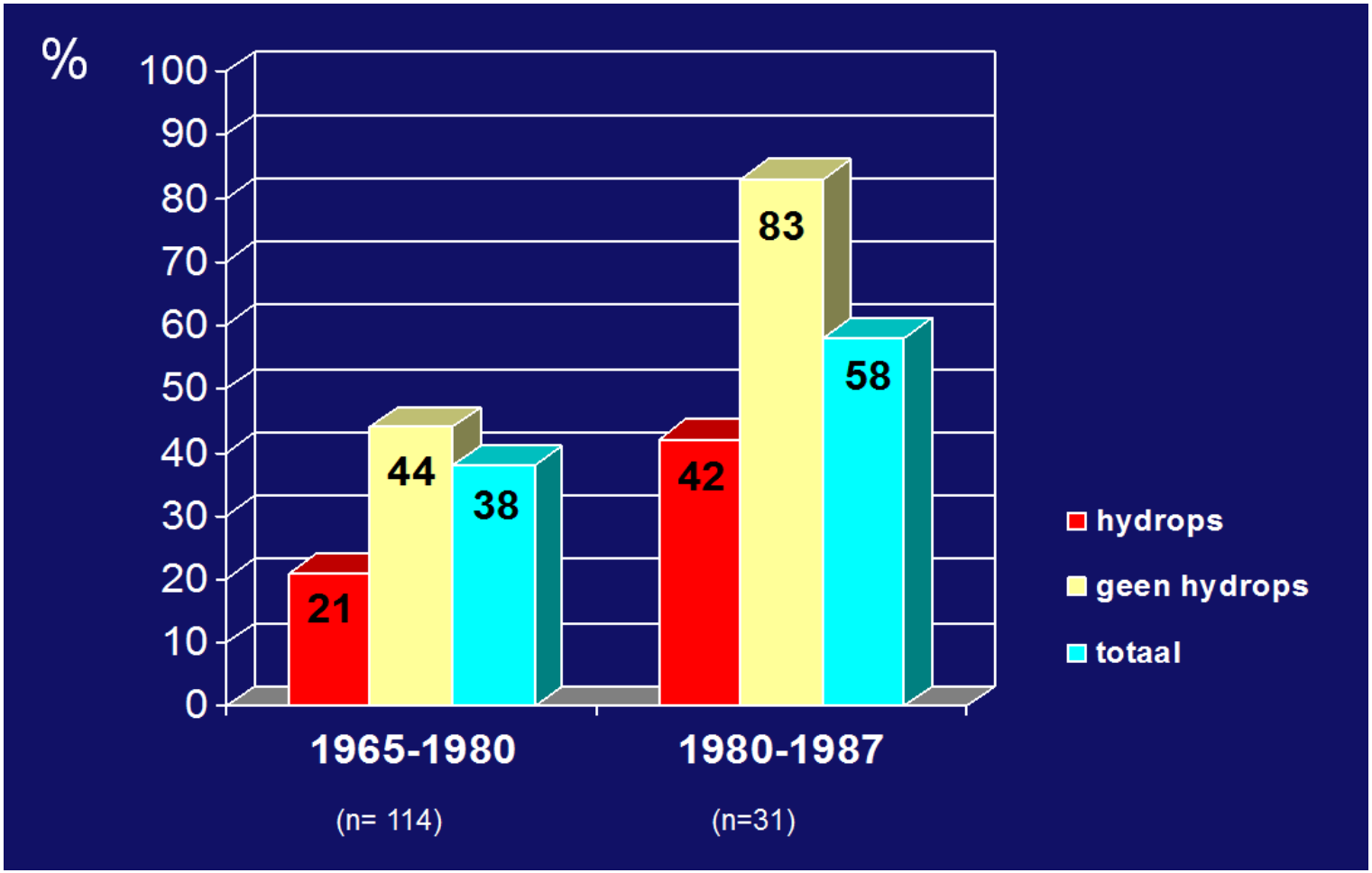


1965 intraperitoneale transfusies

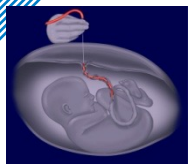
centralisatie behandeling in LUMC

1987 intravasculaire transfusies

Overleving IPT: Leiden 1965-1987



Behandeling foetale anemie anno 2023



Intra-uteriene transfusie (IUT)

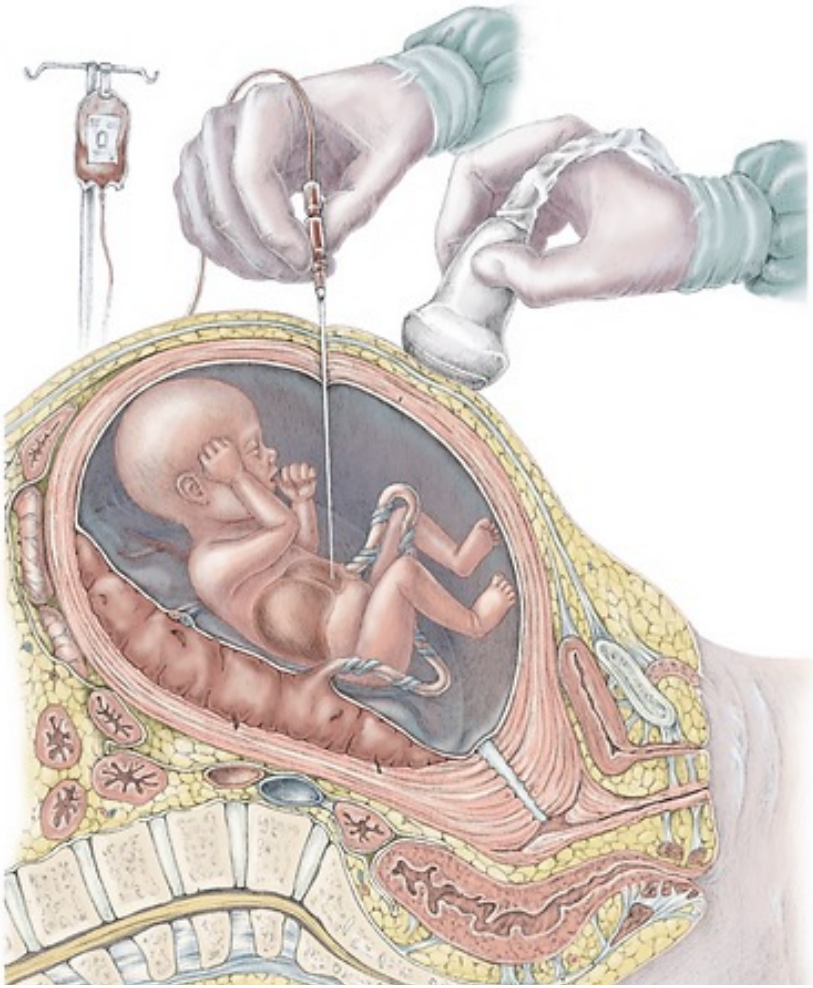
<u>Technieken:</u>

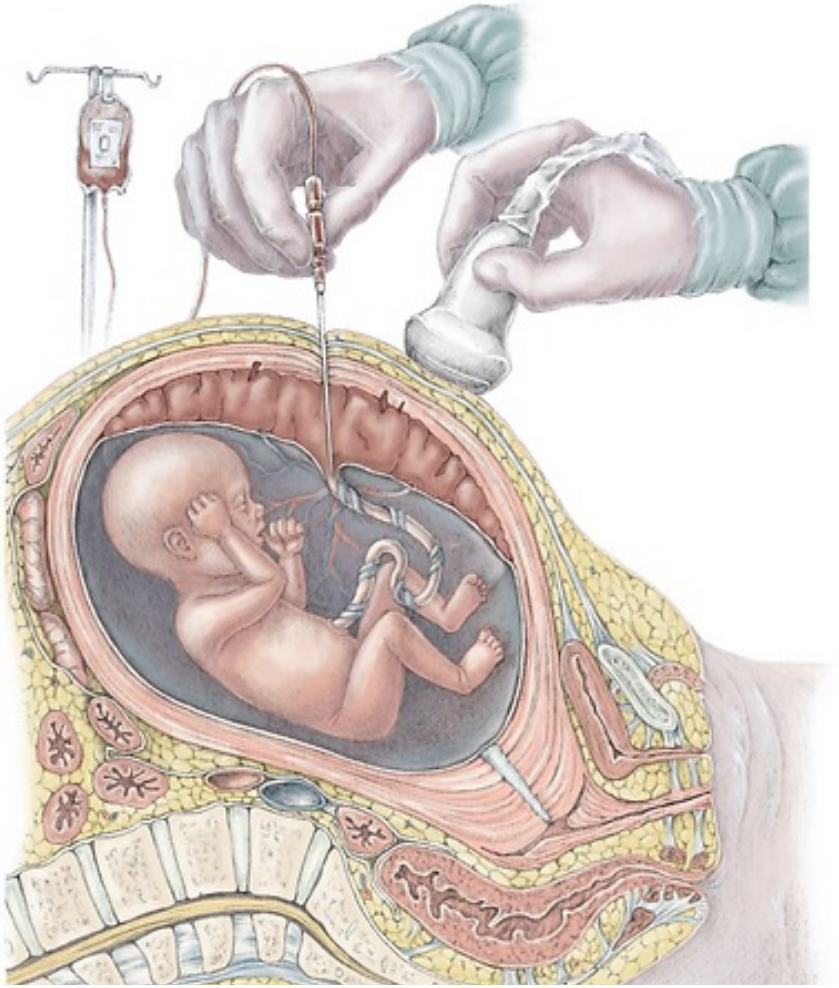
Intravasculair

Intraperitoneaal

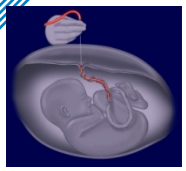
Gecombineerd

Benaderingsroute IUT





Procedure intravasculaire bloedtransfusie



dagopname

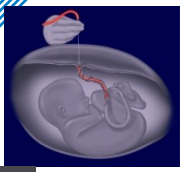
premedicatie: Indomethacine

steriele omstandigheden

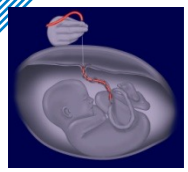
lokale verdoving

0,9 (0,7) mm naald (7-15 cm)

Procedure intravasculaire bloedtransfusie



Procedure intravasculaire bloedtransfusie



aanprikken v. umbilicalis in NS of lever

afname bloedmonster

foetale paralyse (spierverslapper)

Transfusiebloed

O RhD neg

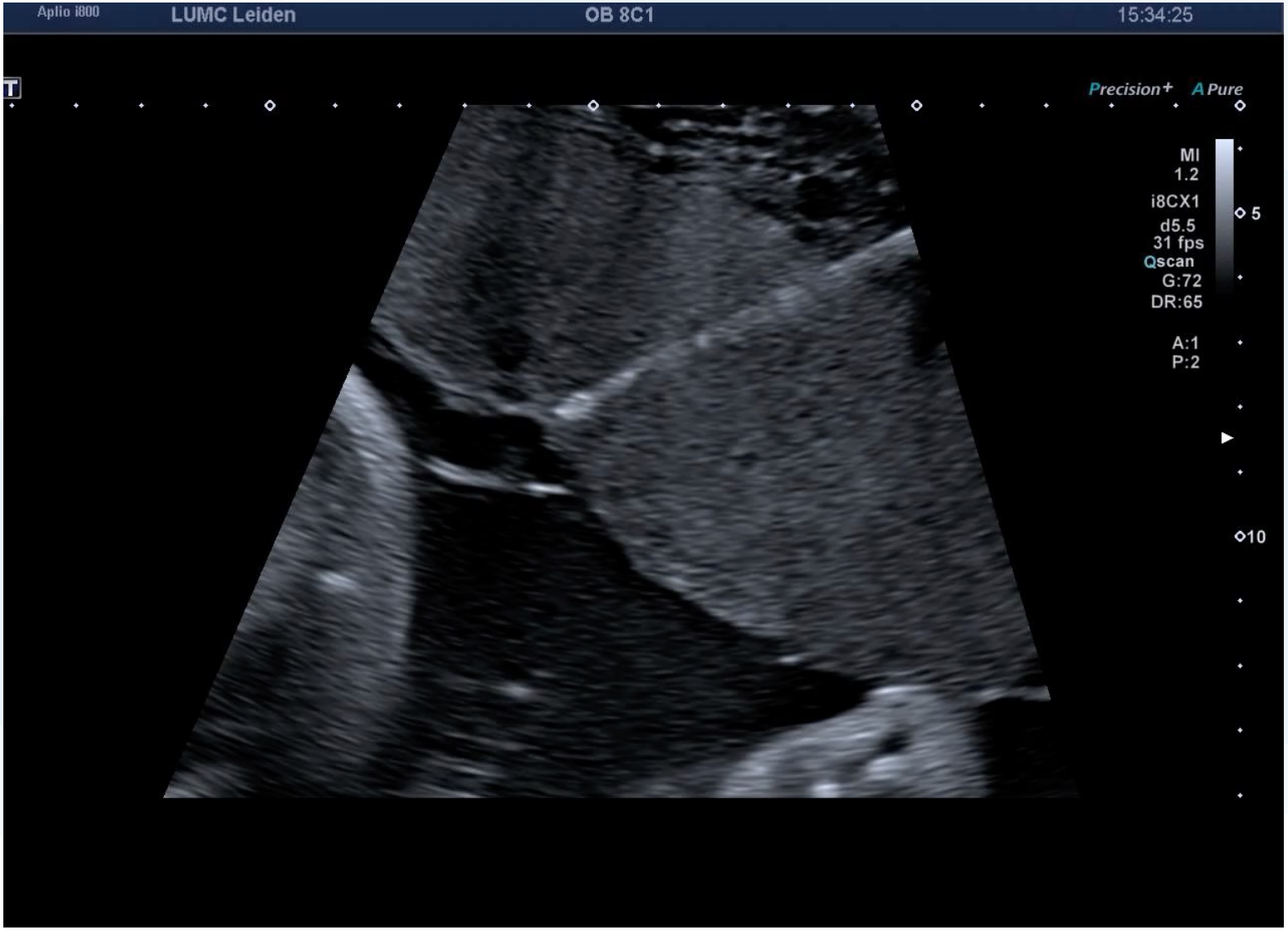
kruisproef moeder negatief

Ht circa 85

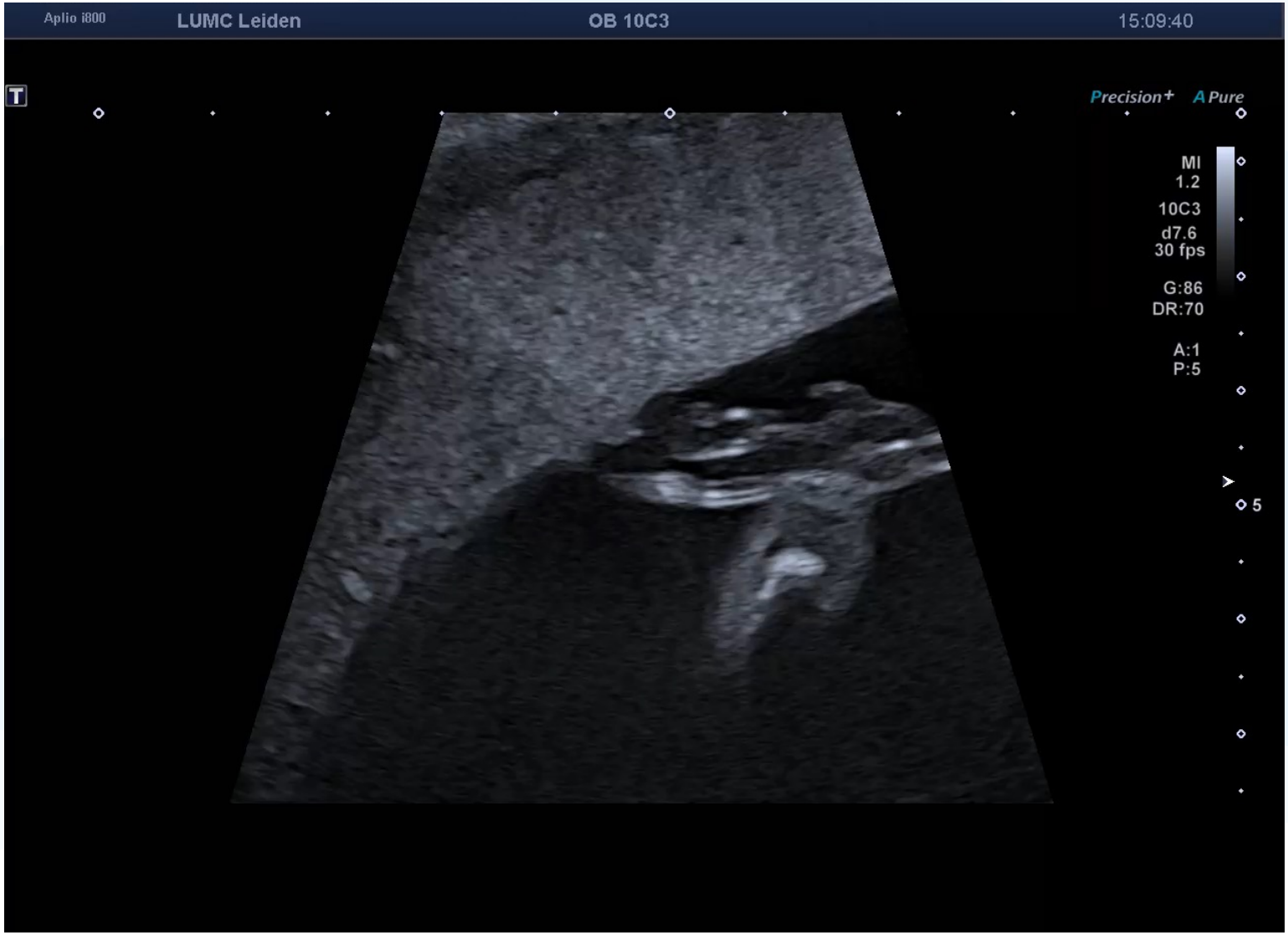
CMV en PARVO negatief

bestraald

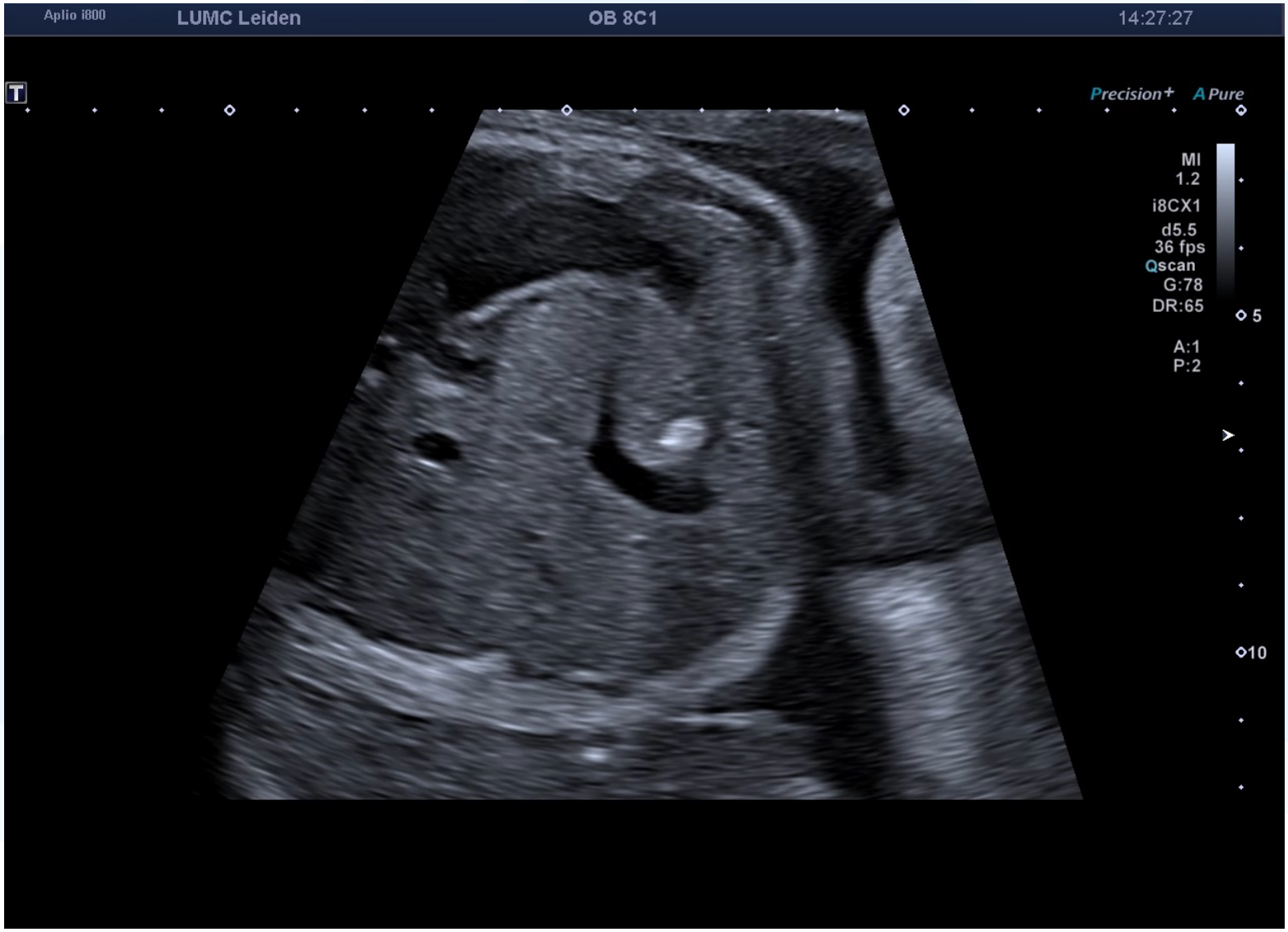
IUT in de wortel



IUT in de wortel

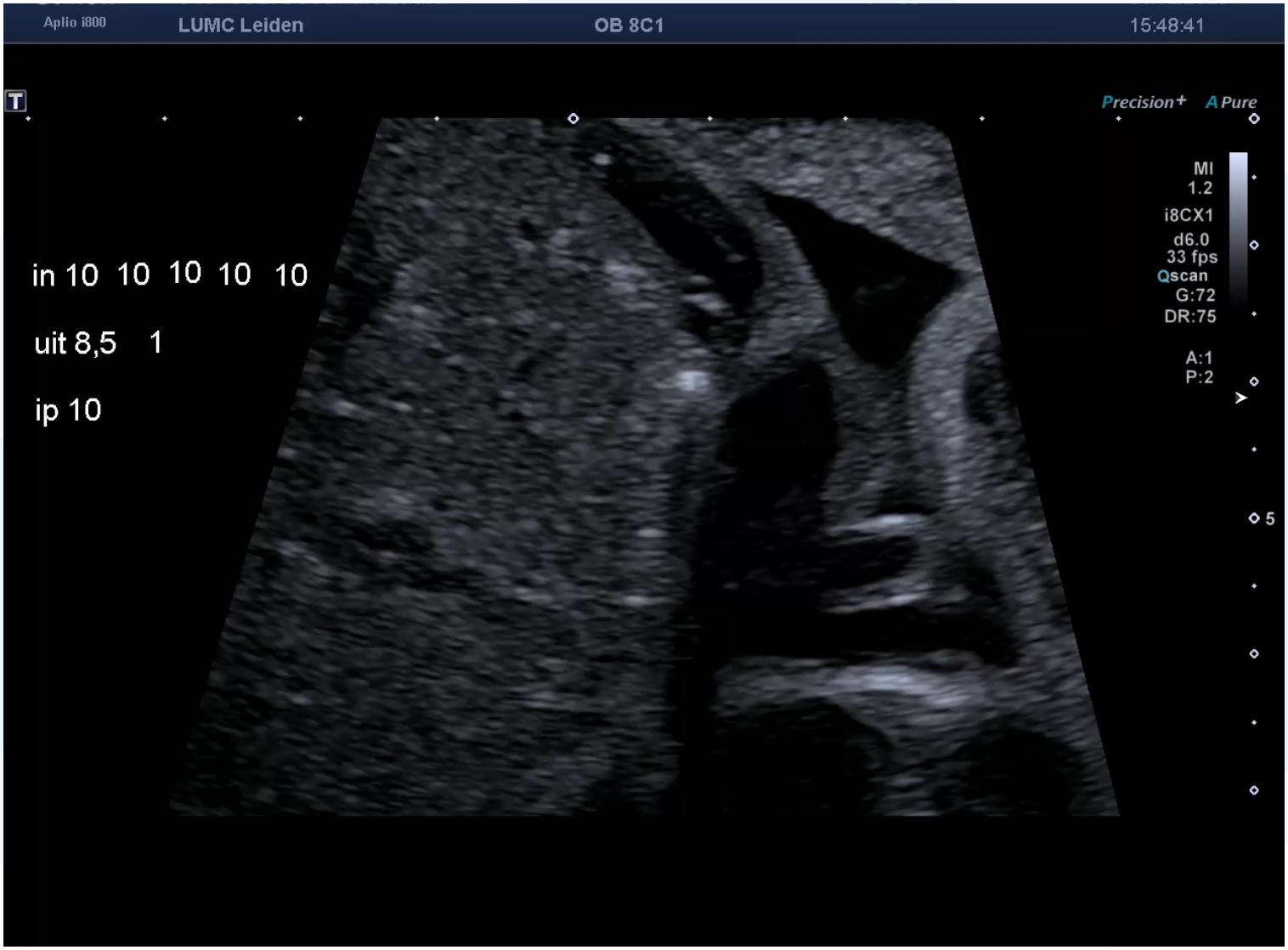


IUT in de levervene

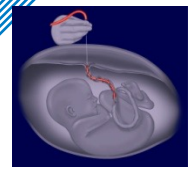


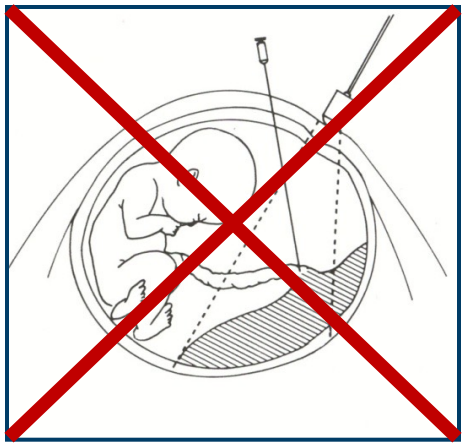
IUT in de levervene

IUT – intraperitoneaal



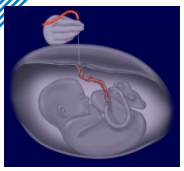
Intravasculaire transfusie: losse lus

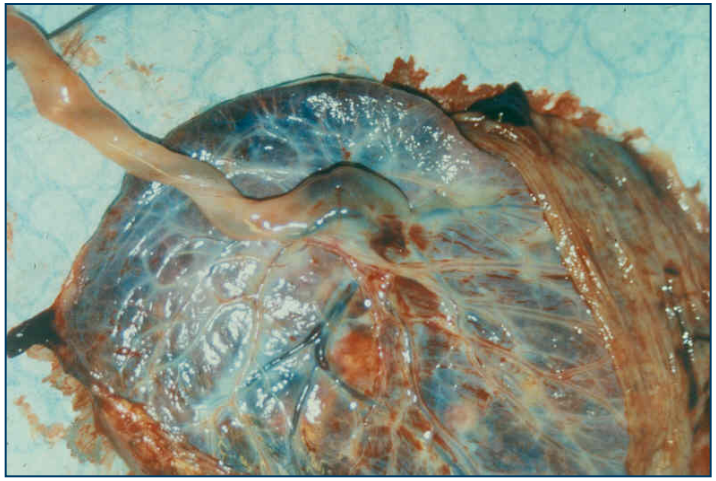




kindsbewegingen

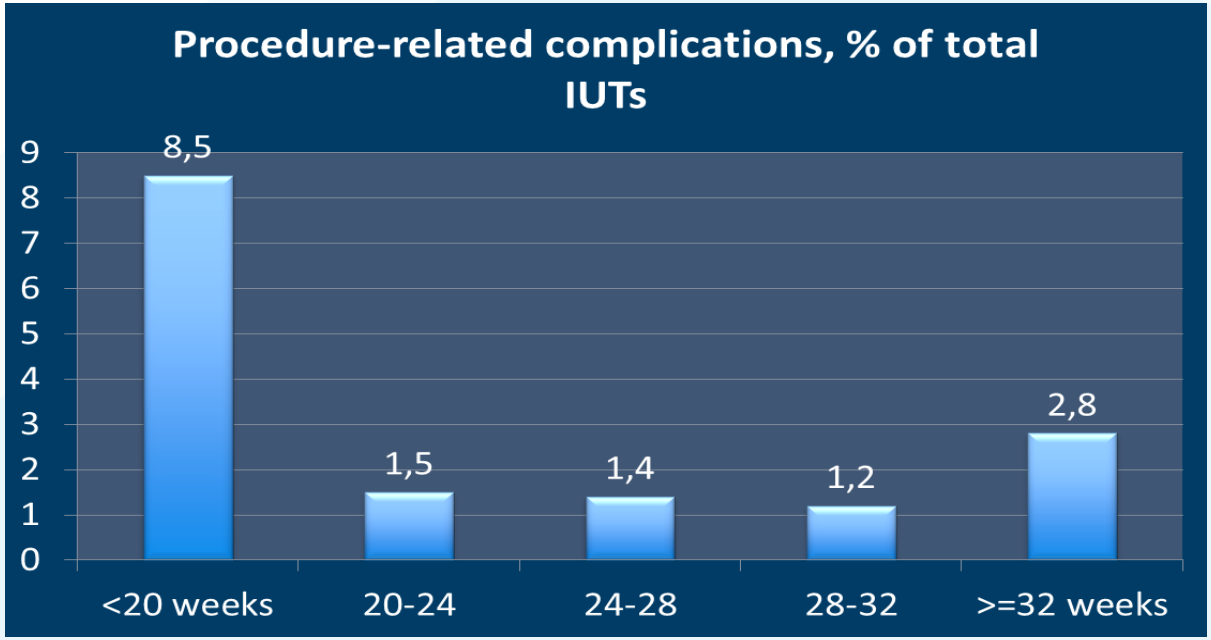
Complicaties intravasculaire bloedtransfusie





- gebroken vliezen
- infectie
- foetale nood
- spoedsectio
- sterfte

Risico IUT



Overleving > 95% (tenzij ernstige hydrops)
< 20 (-22) weken sterfte 4x zo hoog

Zwiers et al. Ultrasound Obstet Gynecol 2017; **50**: 180–186. Zwiers et al EXPERT REVIEW OF HEMATOLOGY, 2017 VOL. 10, NO. 4, 337–344

Intraveneus Immunoglobulines

Hypothetical prevention of anemia through reducing transplacental transfer of maternal antibodies

Postponing Early intrauterine Transfusion with Intravenous immunoglobulin Treatment; the PETIT study on severe hemolytic disease of the fetus and newborn

Presented as interim analysis only at the 16th World Congress in Fetal Medicine, the Fetal Medicine Foundation, Ljubljana, Slovenia, June 25–29, 2017.

Carolien Zwiers MD [a], Johanna G. van der Bom MD, PhD [d, f], Inge L. van Kamp MD, PhD [a], Nan van Geloven PhD [b], Enrico Lopriore MD, PhD [c], John Smoleniec MD, PhD [g], Roland Devlieger MD, PhD [h], Pauline E. Sim BSc [i], Marie Anne Ledingham MD, PhD [i], Eleonor Tiblad MD, PhD [j], Kenneth J. Moise Jr. MD, PhD [k], Karl-Philip Gloning MD, PhD [l], Mark D. Kilby MD, PhD [m], Timothy G. Overton MD [n], Ditte S. Jørgensen MD [o], Katrine V. Schou MD [o], Bettina Paek MD [p], Martin Walker MD [p] ... Masja de Haas MD, PhD [e, f, r]

IVIG: Unadjusted 15 days delay in onset

Hydrops: 4% in IVIG treated, 24% in non-IVIG treated

Conclusion

Intravenous immunoglobulin treatment in mothers pregnant with a fetus at risk for hemolytic disease **seems to have a potential clinically relevant, beneficial effect** on the course and severity of the disease. Confirmation in a multicenter randomized trial is needed.

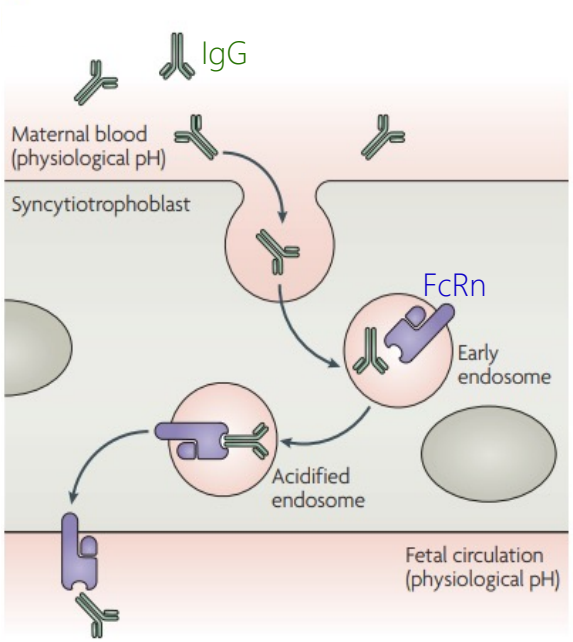
Toekomstperspectief

Early-onset ernstige HZFP (IUT ≤ 24 weeks): **groot probleem!!**

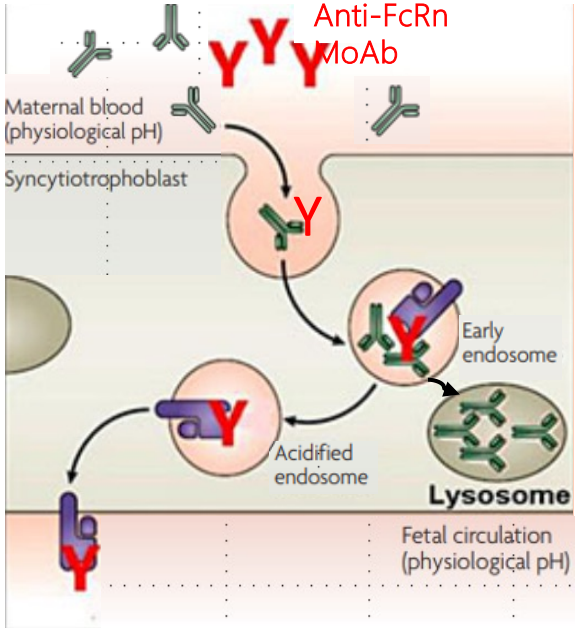
1. Herhalingsrisico >90% in een volgende antigeen-postieve zwangerschap
2. IUT ≤ 22 weken (vooral ≤ 20 weeks) hoog complicatie risico
3. Frequente IUT's in de orde van 5-6 of meer

New therapeutic options to treat HDFN
Nipocalimab

FcRn inhibitors to block IgG transport to fetus



Maternal IgG is transported to fetus



Maternal IgG is degraded in lysosome

Phase 2 study with FcRn inhibitor Nipocalimab

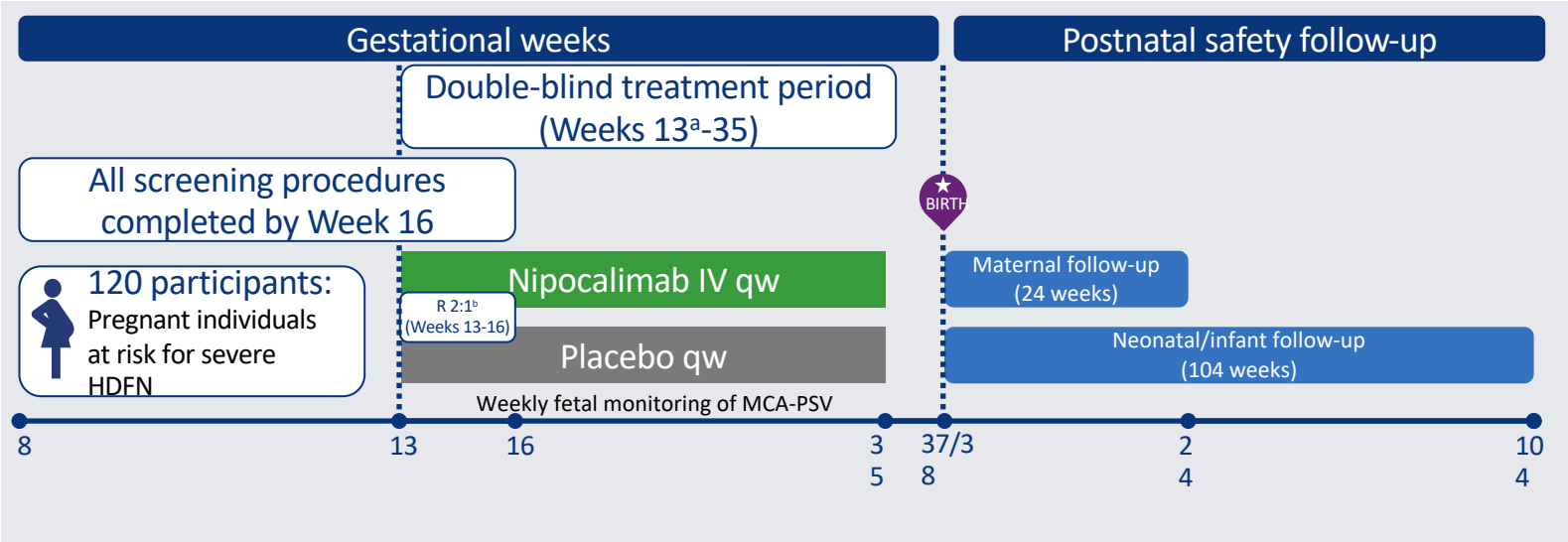
Moise K et al. Phase 2 UNITY study, FMF congress June 2023, Valencia

13 women with **high risk early onset** HDFN (= previous fetal loss or hydrops or IUT < week 24)

	Previous pregancy (n=13)	**anti-FcRn treated Pregnancy (n=13)**
Live birth	**5 (38%)**	**12 (92%) ***
GA at birth	**median 23^{+6} (18^{+3}-36^{+6}) weeks**	**median 36^{+5} (29^{+2}-37^{+3}) weeks**
IUT	**11 (85%)**	**6 (46%)**
GA at first IUT	**median 20^{+4} (17^{+1}-23^{+5}) weeks**	**median 28^{+3} (24^{+1}-31^{+5}) weeks**
number of IUT	**median 3 (1-11)**	**median 3 (1-5)**

*one fetal demise following complications of an IUT at 22 5/7 wks GA

AZALEA – phase 3 study



Start studie in NL verwacht medio 2024

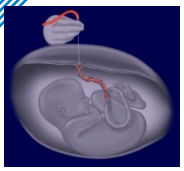
Bij IUT in VG vroeg contact LUMC

Verweij et al, IFMSS 2023

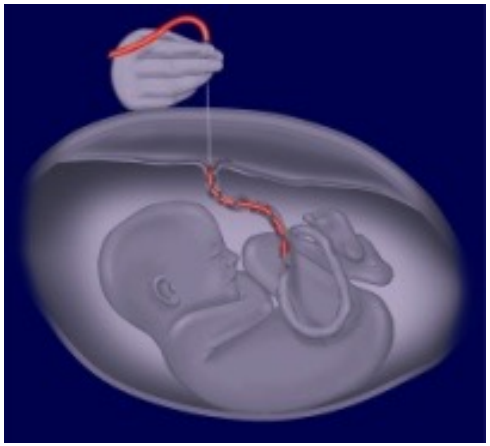
[a]Treatment can start any day from Week 13 to 16.

[b]Randomization Day 1 (first dose of study intervention) can occur from GA Weeks 13 to 16.

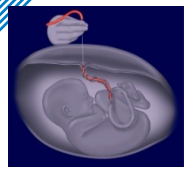
GA, gestational age; HDFN, hemolytic disease of the fetus and newborn; IUT, intrauterine transfusion; IV, intravenous; MCA-PSV, middle cerebral artery peak systolic velocity; qw, weekly; R, randomization.



Conclusies



Conclusies



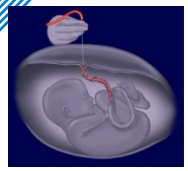
Identificatie risicozwangerschap

- aard immunisatie, klinische relevantie
- typering en zygotie partner
- typering foetus
- ADCC en titers vervolgen conform advies Sanguin
- leidraad is NVOG richtlijn erytrocyten-immunisatie

Monitoren hoog risicozwangerschap

-wekelijks echoscopie met Doppler
- cave Kell
- controles zo mogelijk om en om met LUMC
- partus na IUT vindt plaats in LUMC

Conclusies



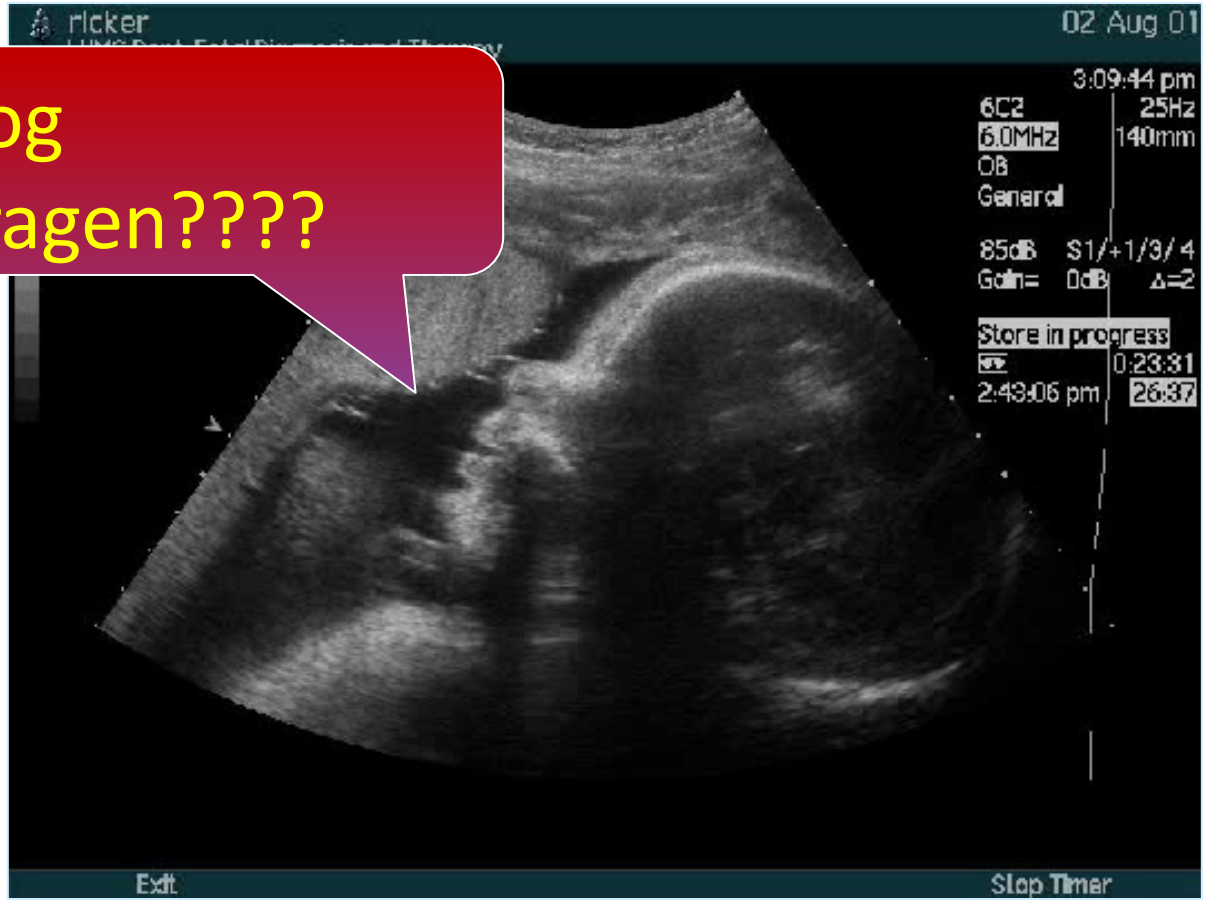
Foetale anemie is behandelbaar

Laagdrempelig overleg en spoedverwijzing is ALTIJD mogelijk!!!

Foetaal behandelteam LUMC
Antenataal 071 – 5298866 (overdag)/5299417(dienst)
Postnataal 071 – 5299588

met dank aan Sanquin

Kom naar Leiden… indien nodig



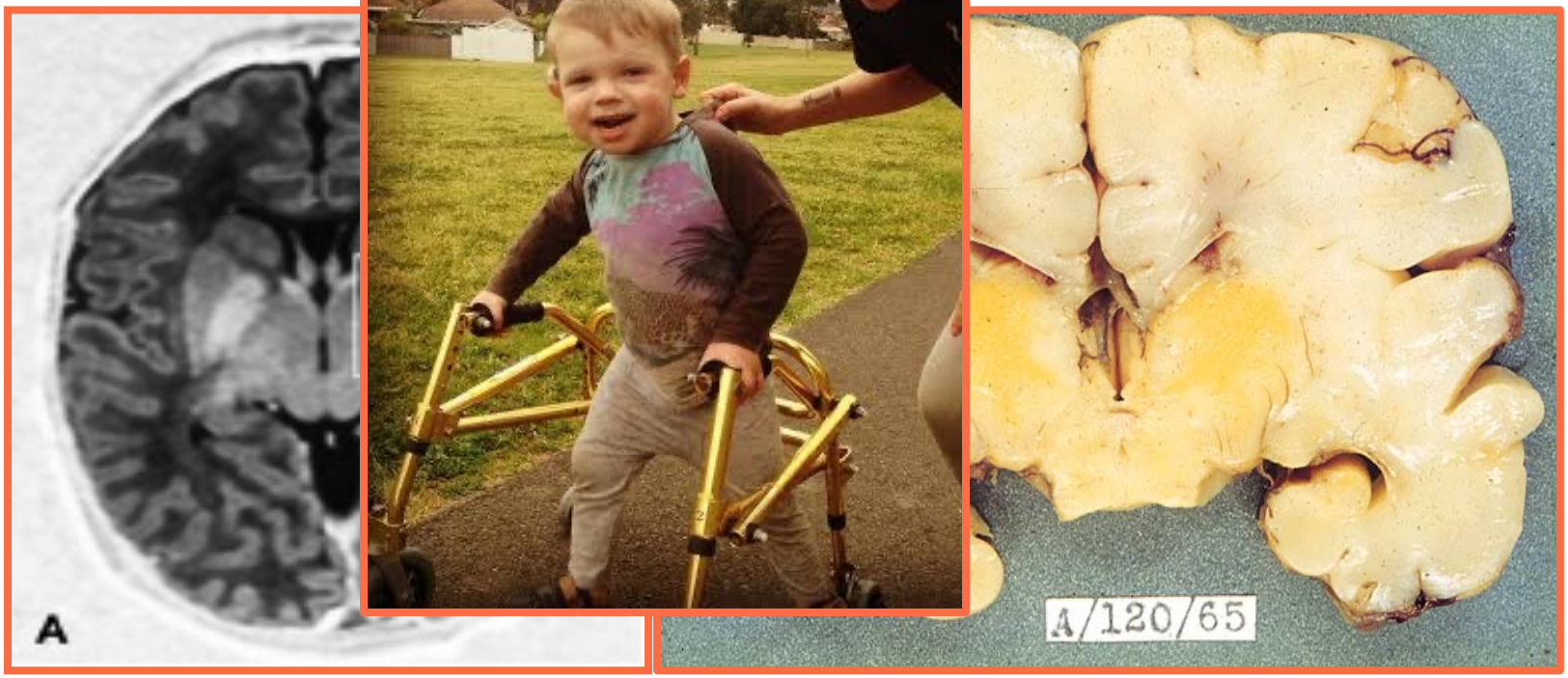
Postnatal management and outcome Hemolytic Disease of the Fetus and Newborn

Enrico Lopriore, neonatologist, *chief of NICU, Leiden University Medical Center, The Netherlands*

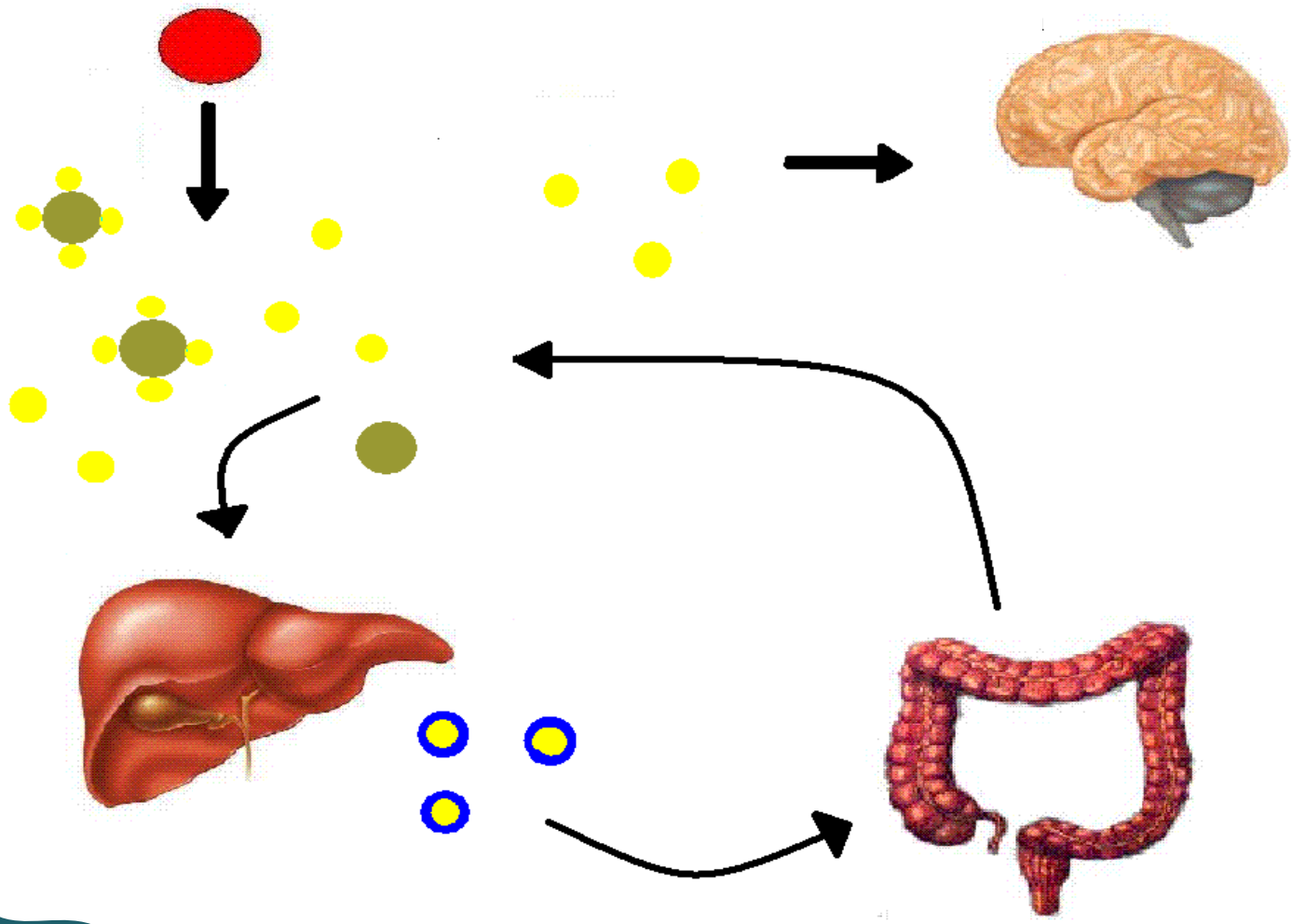
Sanquin

Leiden University Medical Center

Prevent kernicterus!



Bilirubin encephalopathy



Management

Early phase (1st wk)

Intensive phototherapy

Exchange transfusions

IVIG?

Late phase (up to 3m)

Top-up transfusions

EPO?

Intensive phototherapy (PT)

Early phase (1st wk)

Lowers bilirubin through photo-oxidation/isomerisation

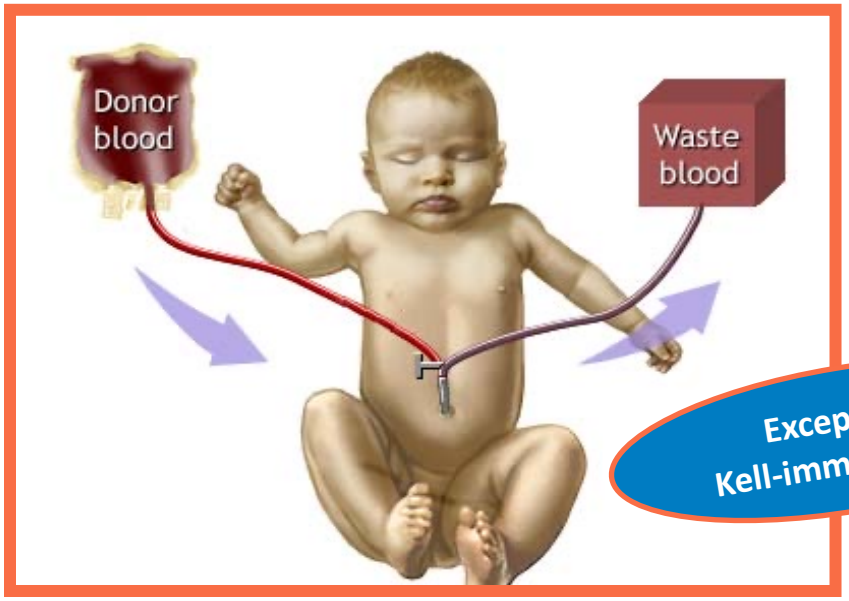
Most effective: blue light (450nm)

- Start directly after birth
- Intensive PT: 3 to 4 lamps
- No dipers!
- Bili check every 3h
- No breastfeeding in first 2-3d
- *Avoid umbilical lines if possible*

Exchange transfusion (ET)

Early phase (1st wk)

- Complex procedure
- Invasive and long (2-3h)
- 160ml/kg



Exception: Kell-immunization

Mortality: 0.3%
Morbidity: 6-24%

Sepsis, NEC, catheter-related complications, thrombocytopenia, hypocalciemia

Neonatal morbidity after exchange transfusion for red cell alloimmune hemolytic disease.
Smits-Wintjens et al. **Neonatology.** 2013;103(2):141-7.

Late phase

Anemia & top-up transfusions

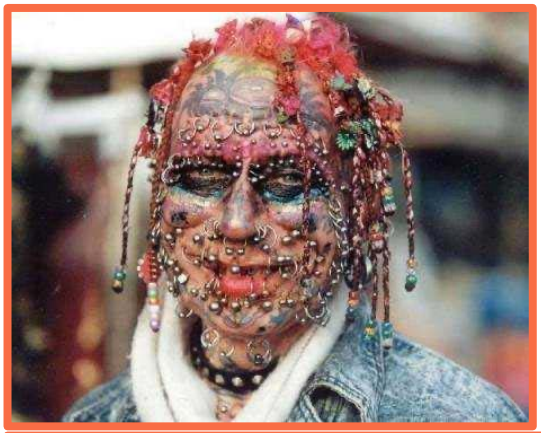
Late phase (up to 3m)

- Hb + reticulocyte count:1x/wk
- 60-85% at-least 1 top-up transfusion
- ± 5% 6 top-up transfusions

Persisting hemolysis

Hyporegenerative anemia

- **NO IRON!**
- **NO BONEMARROW ASPIRATION!**



EPO-4-Rhesus trial

Darbepoetin alfa to reduce transfusion episodes in infants with haemolytic disease of the fetus and newborn who are treated with intrauterine transfusions in the Netherlands: an open-label, single-centre, phase 2, randomised, controlled trial

Isabelle M C Ree, Masja de Haas, Nan van Geloven, Sandra E Juul, Derek de Winter, E J T Verweij, Dick Oepkes, Johanna G van der Bom, Enrico Lopriore

Lancet Haematol 2023; 10: e976–84

Comment page e943

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of Neonatology,

Summary

Background Up to 88% of infants with haemolytic disease of the fetus and newborn who are treated with intrauterine transfusions require erythrocyte transfusions after birth. We aimed to investigate the effect of darbepoetin alfa on the prevention of postnatal anaemia in infants with haemolytic disease of the fetus and newborn.

Methods We conducted an open-label, single-centre, phase 2 randomised controlled trial to evaluate the effect of darbepoetin alfa on the number of erythrocyte transfusions in infants with haemolytic disease of the fetus and

Results

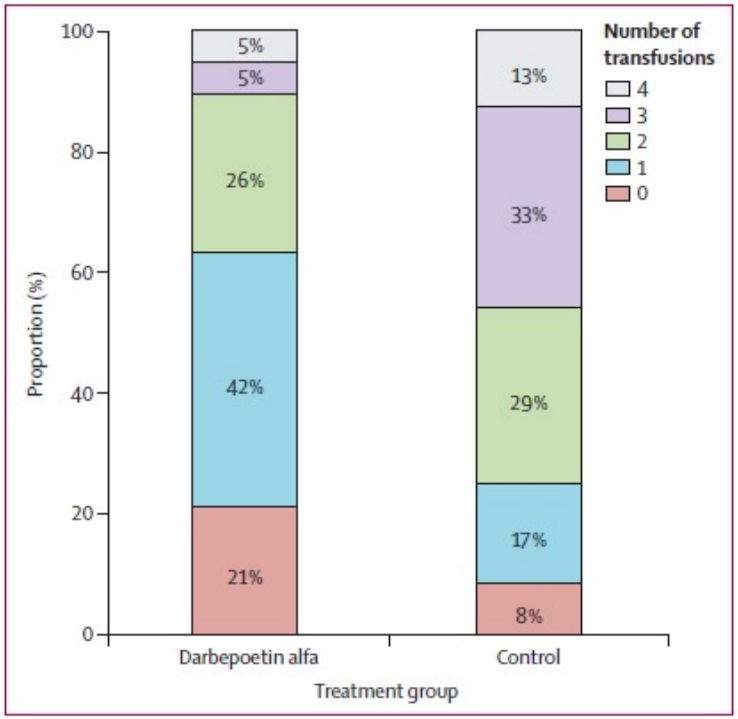
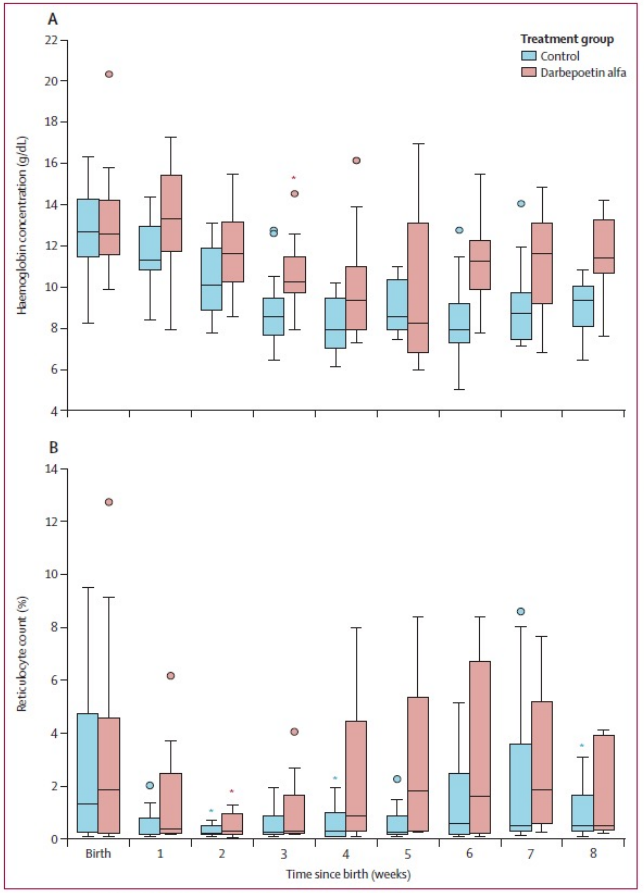
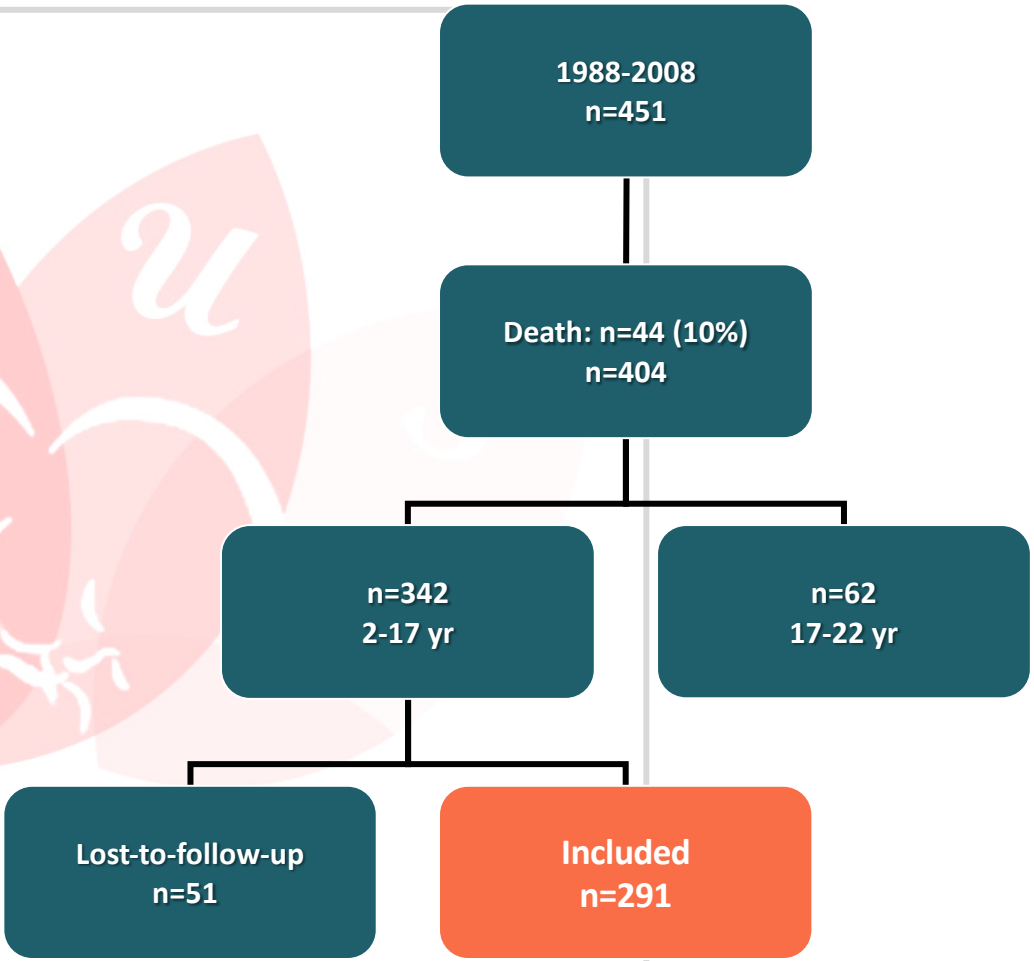


Figure 2: Stacked bar chart of total transfusions after birth



Long-term neurodevelopmental outcome

LOng-Term outcome after IUT Study

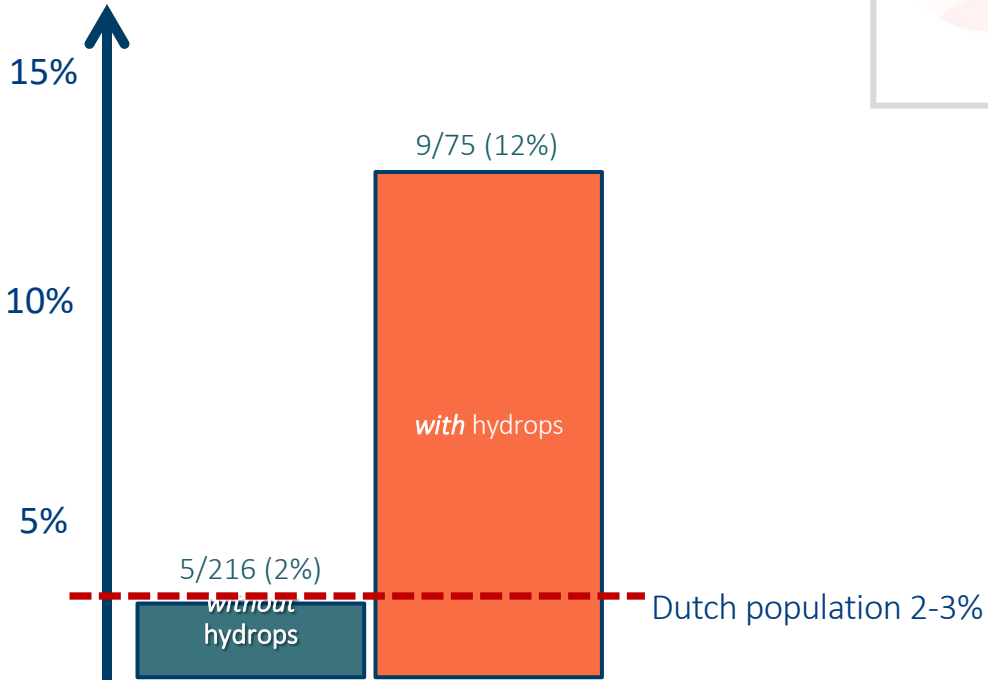


LOng-Term outcome after IUT Study

	n = 291
Cerebral palsy (CP) - *% (n)*	2.3% (6)
Severe developmental delay - *% (n)*	3.2% (9)
Bilateral deafness - % *(n)*	1.0% (3)
Neurodevelopmetal impairment - % *(n)*	**4.8% (14)**

Long-term neurodevelopmental outcome after intrauterine transfusion for hemolytic disease of the fetus/newborn: the LOTUS study.
Lindenburg et al. **Am J Obstet Gynecol**. 2012;206(2):141.e1-8.

Risk factors NDI



Conclusions

Early phase

1. Optimize intensive PT
2. ET if needed, but be cautious!
3. No routine IVIg
4. Optimal gestational age at birth?

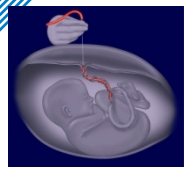
Late phase

5. Hb + retic count 1x/wk
6. Top-up transfusions
7. Consider EPO

Long-term outcome

8. Outcome is good, except in hydrops
9. Do all you can to prevent kernicterus!

www.foetaletherapie.nl



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