

Kunstmatige baarmoeder

Droom of 'binnenkort' werkelijkheid?

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Amalia Children's Hospital
Radboudumc

Ontwikkelingen in de neonatale zorg



Belangrijkste mijlpalen

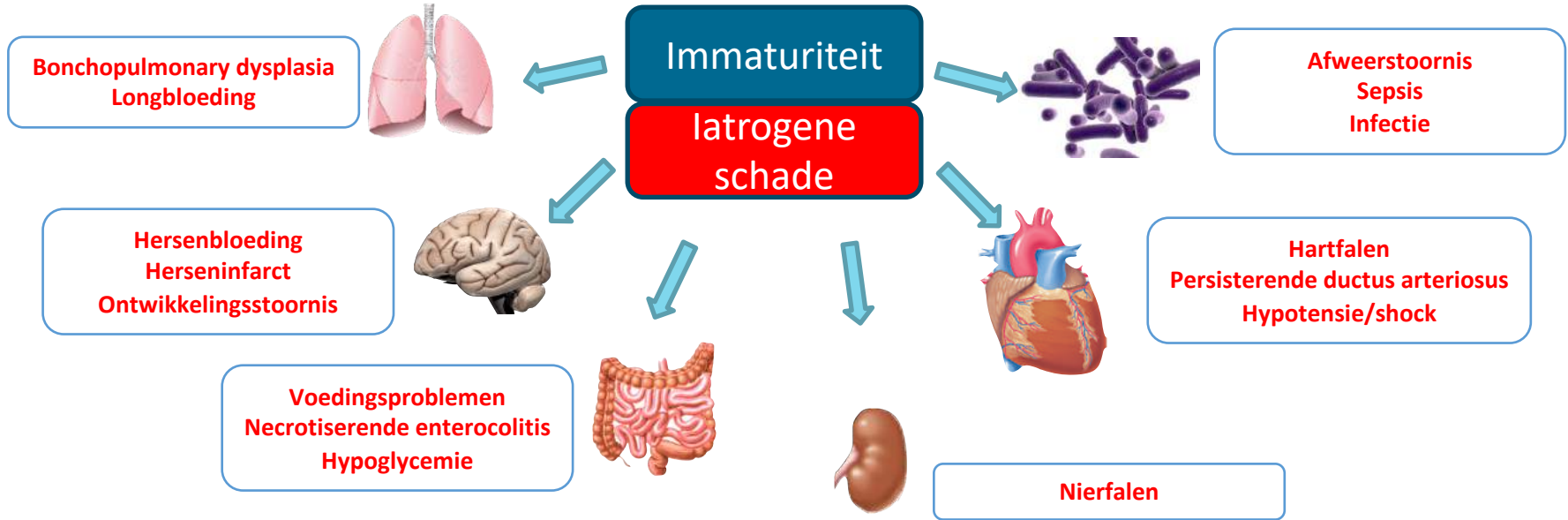
- Antenataal corticosteroiden
- Exogene surfactanttoediening
- Beademingsstrategieën, zoals hoogfrequente ventilatie, 'gentle ventilation', volume-gestuurde beademing, non-invasieve ondersteuning van de ademhaling
- Selectieve pulmonale vaatverwijding (NO-inhalatie)

Ontwikkelingen in de neonatale zorg

- Grens van levensvatbaarheid verschuift naar 22-23 weken zwangerschapsduur
- Overleving van extreem prematuur geboren baby's is verbeterd
- Echter, geen afname van complicaties van vroeggeboorte, zoals bijvoorbeeld bronchopulmonale dysplasie



Consequenties van vroeggeboorte



Consequenties van vroeggeboorte

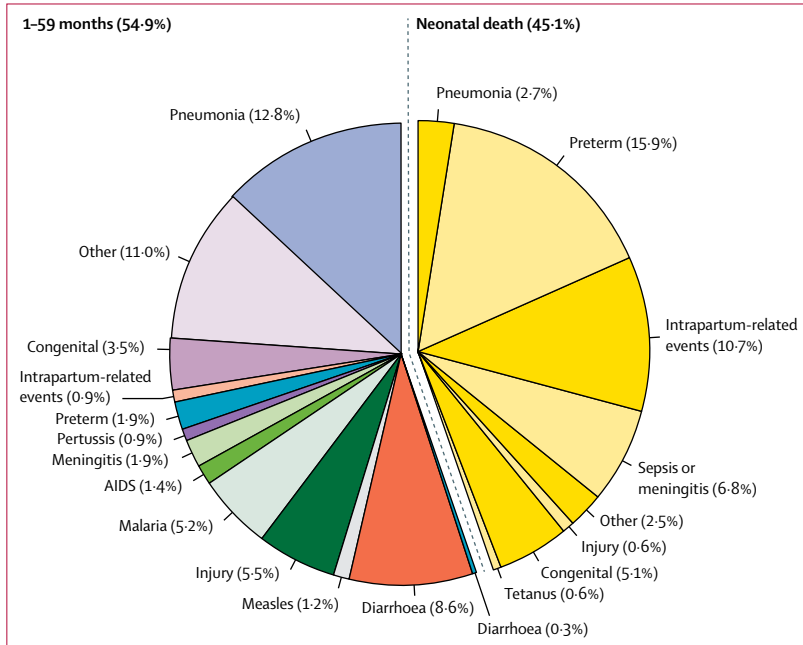
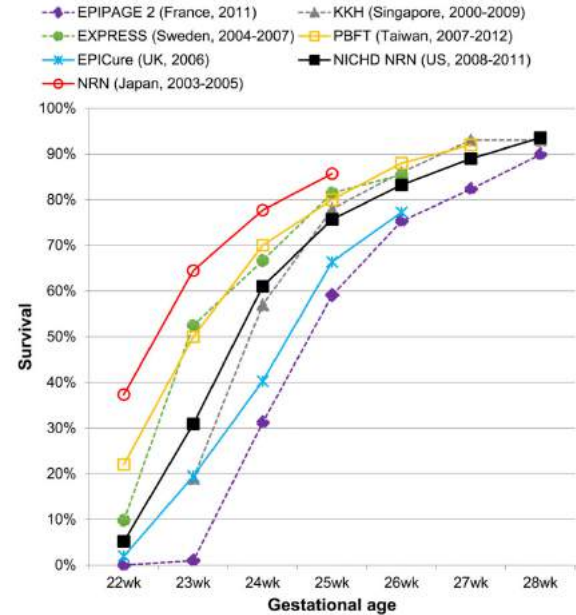


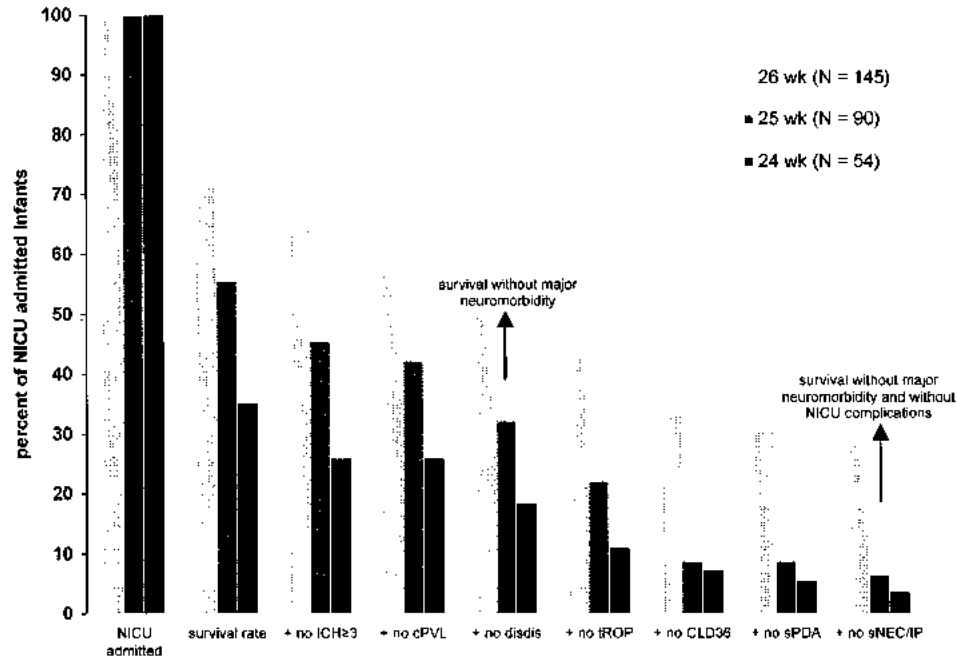
Figure 1: Global causes of under-5 deaths in 2015

Liu L, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. *The Lancet*. 2016;388(10063):3027–35.



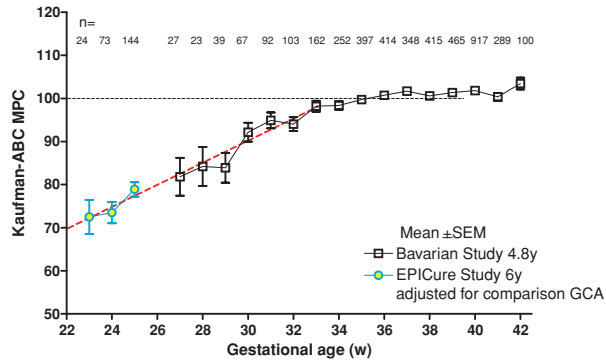
Patel RM. Short- and Long-Term Outcomes for Extremely Preterm Infants. *Am J Perinatol*. 2016;33(3):318–28.

Consequenties van vroeggeboorte



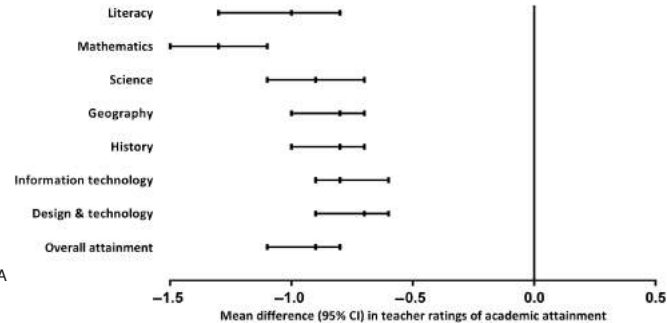
Consequenties van vroeggeboorte

IQ



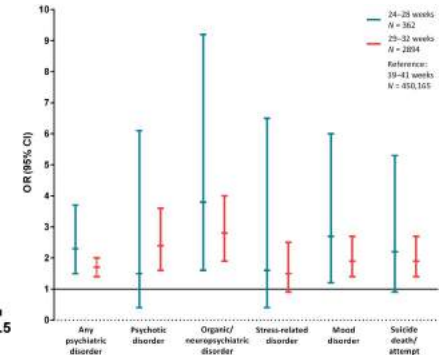
Lagercrantz H. The hard problem. Acta Paediatr. 2008;97(2):142-3.

Schoolprestaties



Johnson S, Marlow N. Early and long-term outcome of infants born extremely preterm. Arch Dis Child. 2017;102(1):97-102.

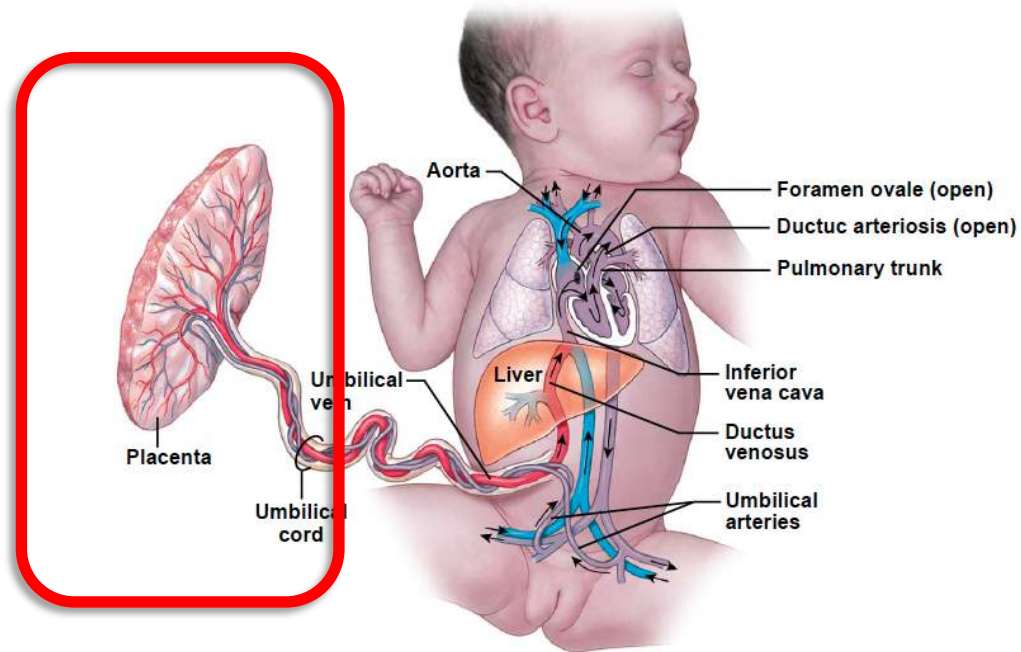
Psychiatrische problematiek



Consequenties van vroeggeboorte

- De gestoorde ontwikkeling van de longen bij BPD lijkt met name te berusten op een te vroege overgang van vloeistof-gevulde longen naar gas-gevulde longen
- Zoektocht naar een meer fysiologische ondersteuning van een extreem prematuur met als doel
 - voortzetting van de foetale groei en ontwikkeling,
 - zonder de iatrogene schade door postnatale intensive care interventies,
 - leidend tot een verbetering in overleving èn kwaliteit van leven voor kritisch zieke prematuren

Artificial placenta



- Reeds 50 jaar onderwerp van onderzoek
- Nog maar weinig succesvol

Artificial placenta/womb

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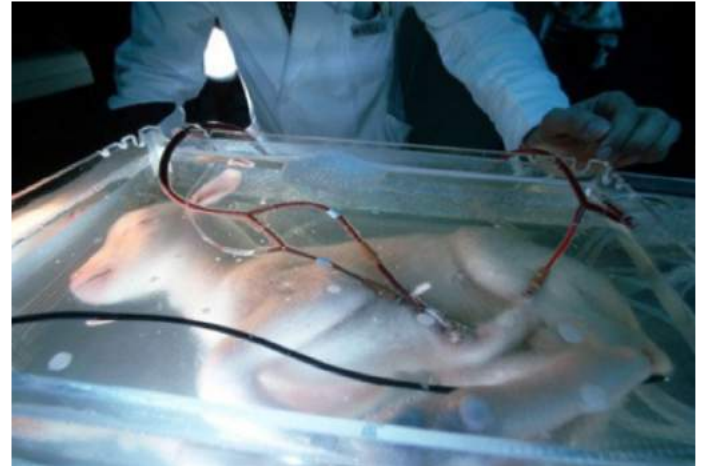
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Japanese pioneers raise kid in rubber womb

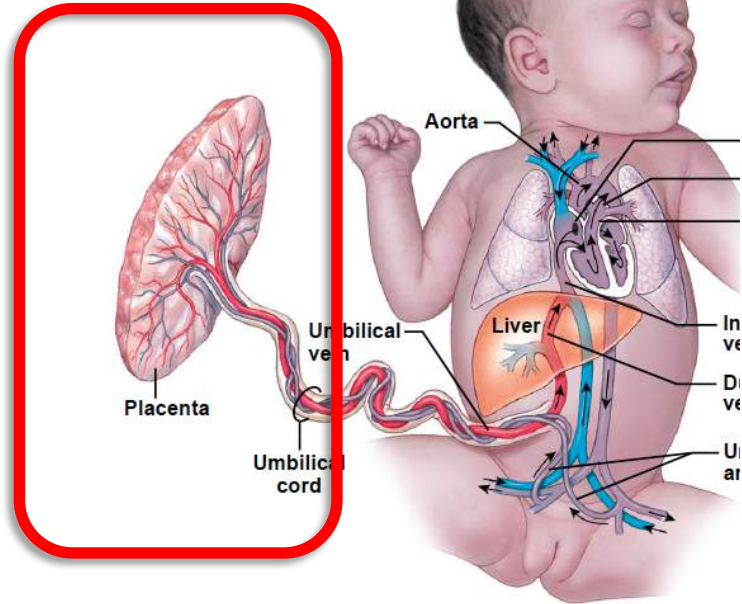


25 April 1992

By
PETER HADFIELD
in
TOKYO



Artificial placenta

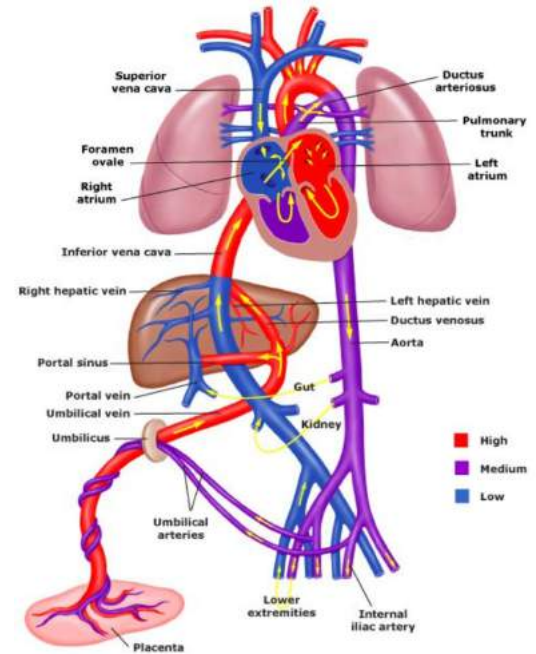


Problemen:

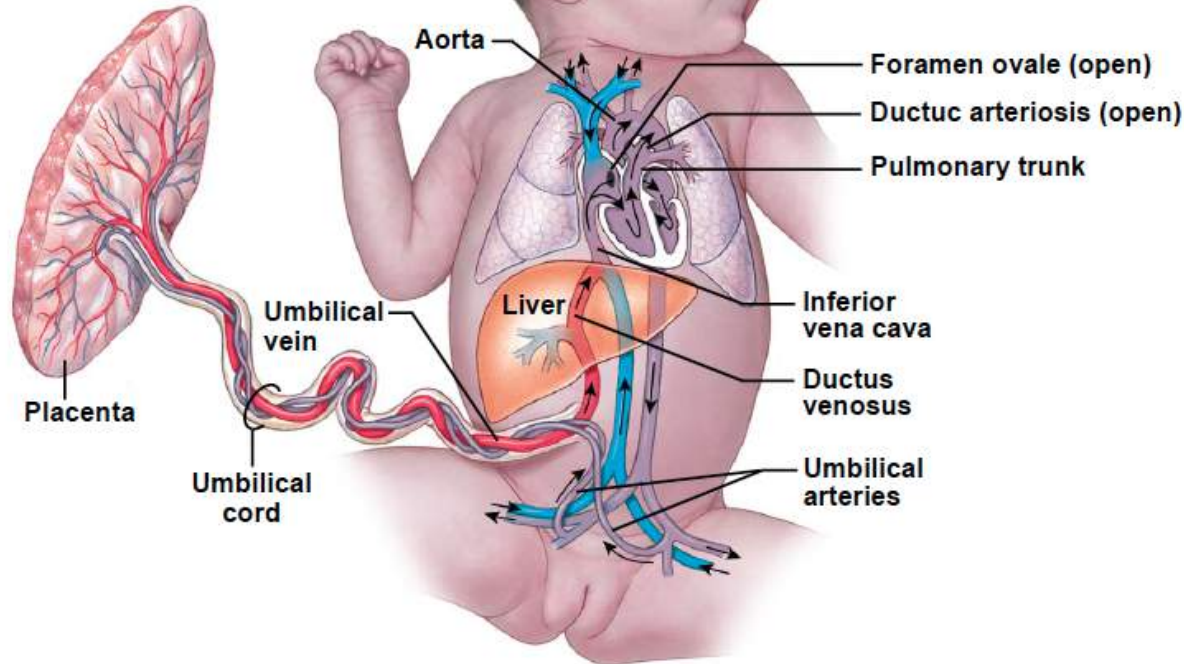
1. Progressief cardiocirculatoir falen door veranderingen in zowel preload als afterload van het hart (weerstand oxygenator, gebruik van pomp met extracorporeel circuit)
2. Gebruik van open “couveuses” met risico op contaminatie en sepsis
3. Vaatspasmen bij het verkrijgen van vasculaire toegang

Ideale kunstmatige placenta

De ideale kunstmatige placenta komt overeen met het 'natuurlijke' foeto-placentaire systeem, waarbij de perfusie bepaald wordt door de foetale cardiac output



Foetale circulatie



EXTEND - EXTrauterine Environment for Neonatal Development

ARTICLE

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OPEN

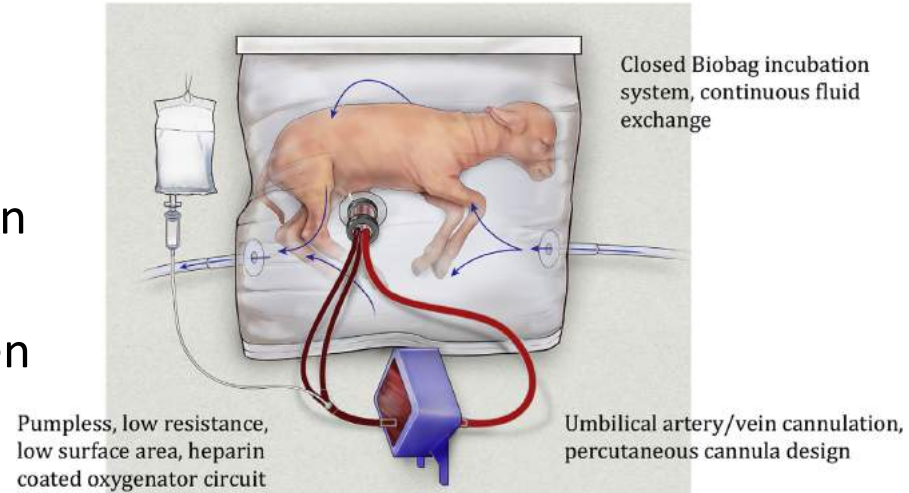
An extra-uterine system to physiologically support the extreme premature lamb

Emily A. Partridge^{1,*}, Marcus G. Davey^{1,*}, Matthew A. Hornick¹, Patrick E. McGovern¹, Ali Y. Mejaddam¹, Jesse D. Vrecenak¹, Carmen Mesas-Burgos¹, Aliza Olive¹, Robert C. Caskey¹, Theodore R. Weiland¹, Jiancheng Han¹, Alexander J. Schupper¹, James T. Connelly¹, Kevin C. Dysart², Jack Rychik³, Holly L. Hedrick¹, William H. Peranteau¹ & Alan W. Flake¹

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Drie essentiële componenten

- Arterioveneus circuit met lage weerstand zonder pomp
- Gesloten steriele vloeistof omgeving ('Biobag') met continue verversing van het kunstmatige vruchtwater
- Specifieke techniek voor het verkrijgen van toegang tot de navelstrengvaten



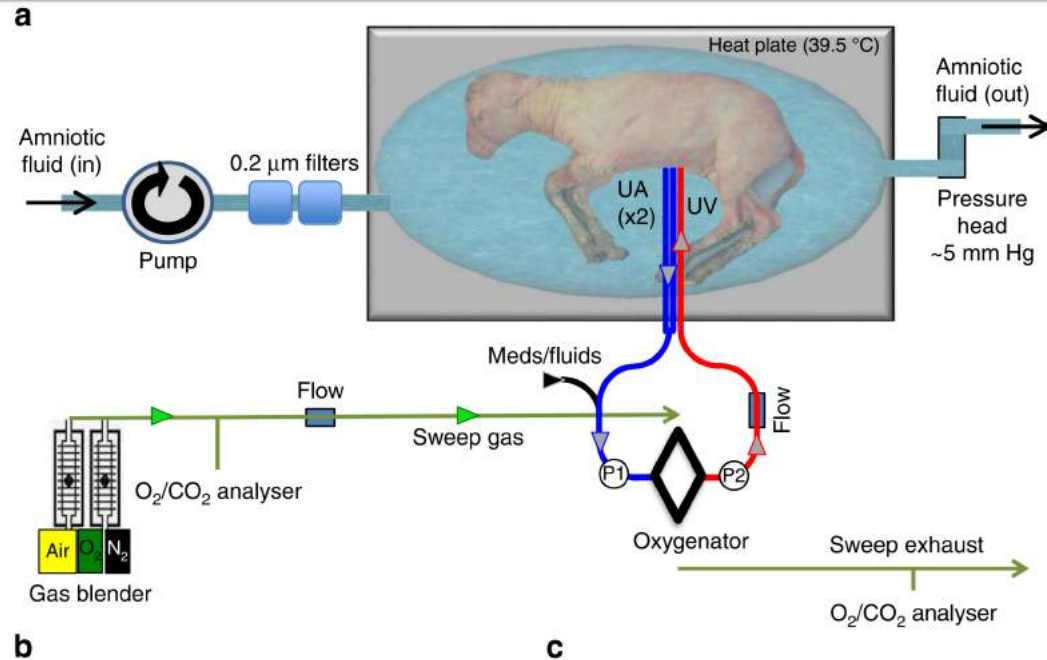
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CHILDREN'S HOSPITAL OF PHILADELPHIA
Alan W. Flake, left, Emily A. Partridge, and Marcus G. Davey led the artificial womb research at Children's Hospital of Philadelphia.

First succesful report
of the use of an 'artificial
womb' in a series of 8
lambs

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EXTEND - EXTrauterine Environment for Neonatal Development



Partridge EA, Davey MG, Hornick MA, McGovern PE, Mejaddam AY, Vrecenak JD, et al. An extra-uterine system to physiologically support the extreme premature lamb. Nat Commun. 2017;8:15112.

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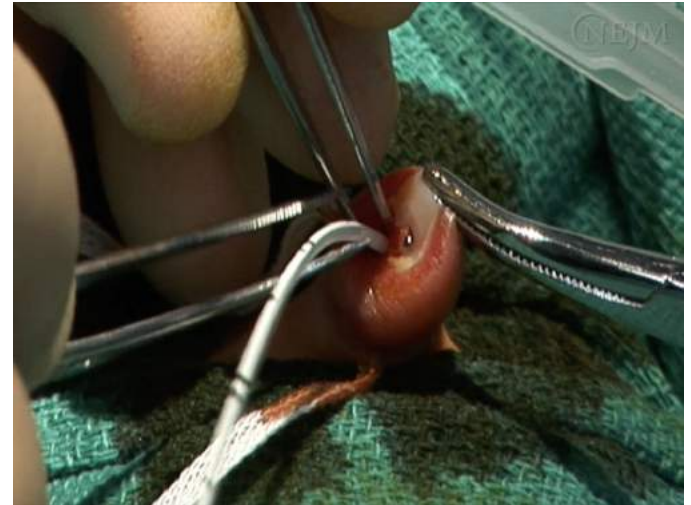
LICU

Lamb Intensive Care Unit



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- Canulatieprocedure kan binnen 2 minuten (!) tussen instrumentatie en start bloed flow door extracorporeel circuit
- Gemodificeerde EXIT-procedure noodzakelijk, waarbij de navelstreng(vaten) kunnen worden benaderd voor canulatie

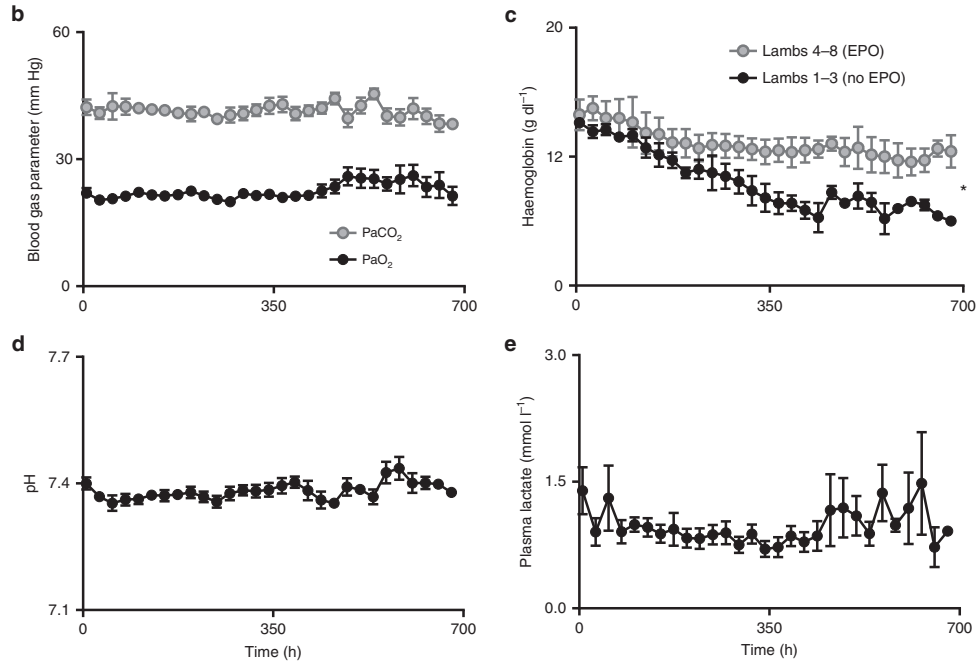


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- Stabiele bloedflow door extracorporele circuit overeenkomstig met normale foetale transplacentaire bloedflow (150-200 mL/kg/min)
- Fysiologisch zuurstoftransport en -aanbod
- Dagelijks erythropoïetine (EPO) toediening

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UA/UV lambs

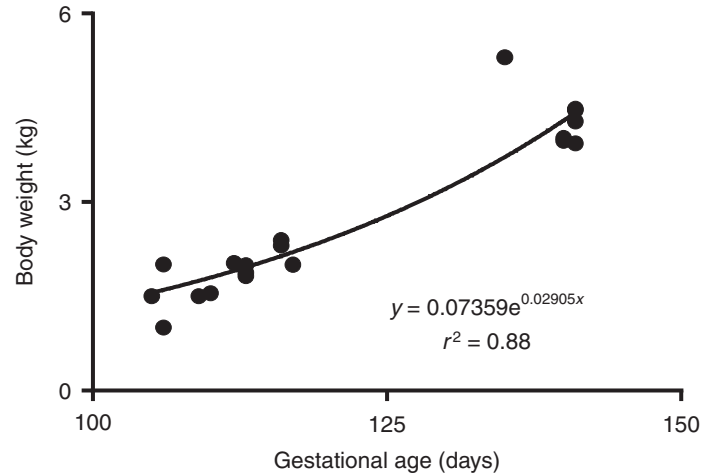


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- Normale groei en voortzetting orgaanrijping in plaats van 'arrest'

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Growth in UA/UV lambs



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b 5 dagen support



c 28 dagen support



EXTEND - EXTrauterine Environment for Neonatal Development

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- Lammeren (GA 105-120 dagen) konden stabiel worden ondersteund gedurende 20-28 dagen
- Dagelijks echocardiografisch onderzoek: cardiac output in de fysiologische range, nagenoeg normale foetale transductale en interatriale shunt flow

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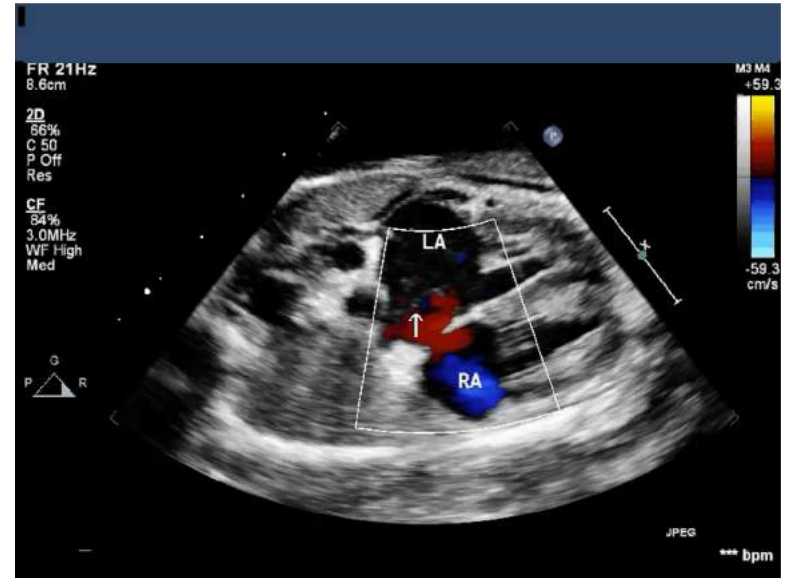


Transductale RtL-shunt

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Antegrade flow ductus venosus



Interatriale RtL-shunt

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- Parenterale voeding via het extracorporele circuit (voornamelijk koolhydraten en eiwitten met slecht weinig vetten)
- Preventie van hyperglycaemie en hoog ureum (osmotische diurese en/of hyperosmolaliteit)
- Observatie van foetale ademhalingsbewegingen; correlatie met PaCO₂ in systemische circulatie
- Openen van de ogen, steeds actiever worden, slikbewegingen
- Toename in gewicht; groei van wolvlacht

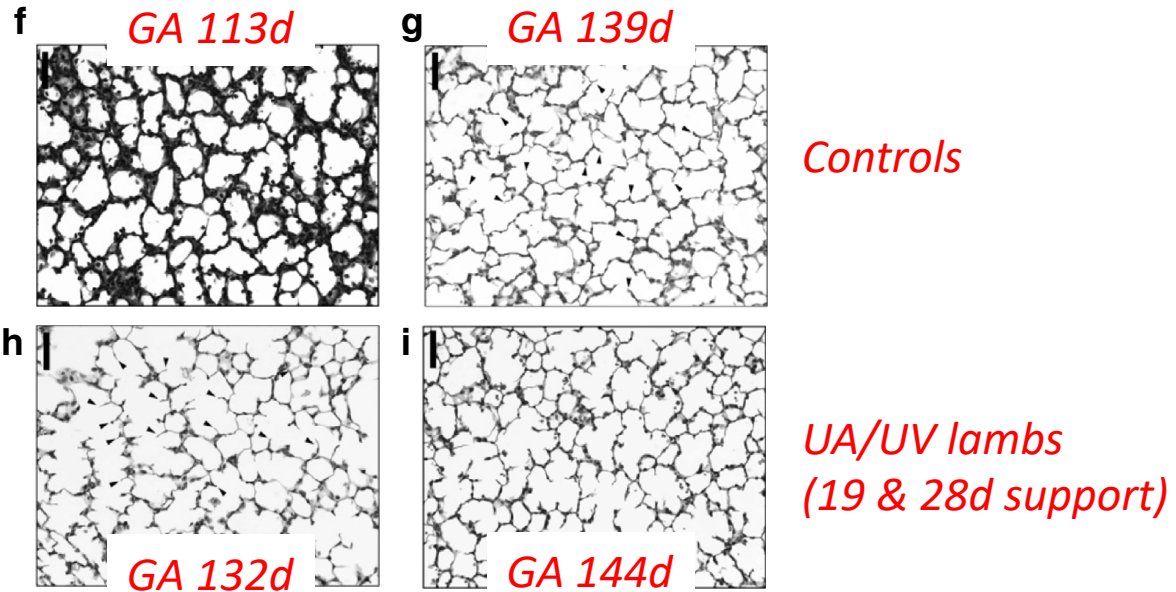
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Partridge EA, Davey MG, Hornick MA, Flake AW. An EXTrauterine environment for neonatal development: EXTENDING fetal physiology beyond the womb. Semin Fetal Neonatal Med. 2017;22(6):404-9.

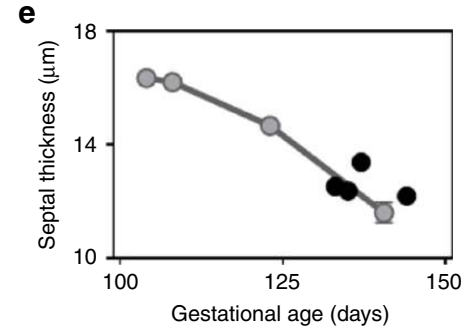
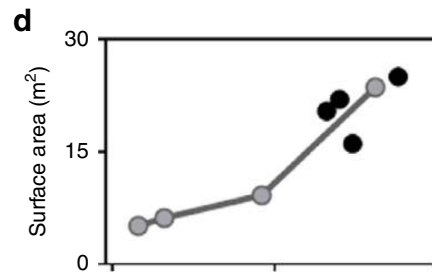
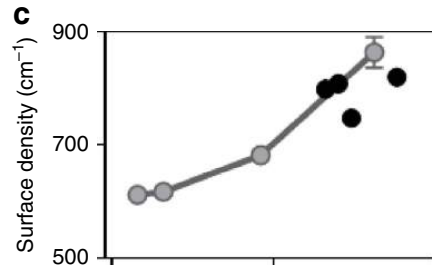
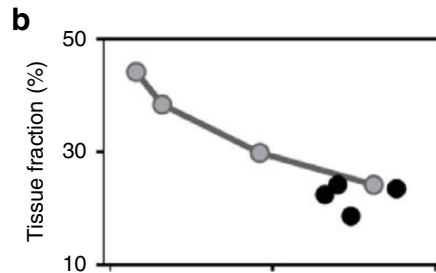
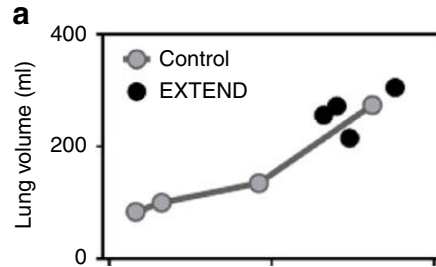
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Objectieve verbetering van de longrijpheid



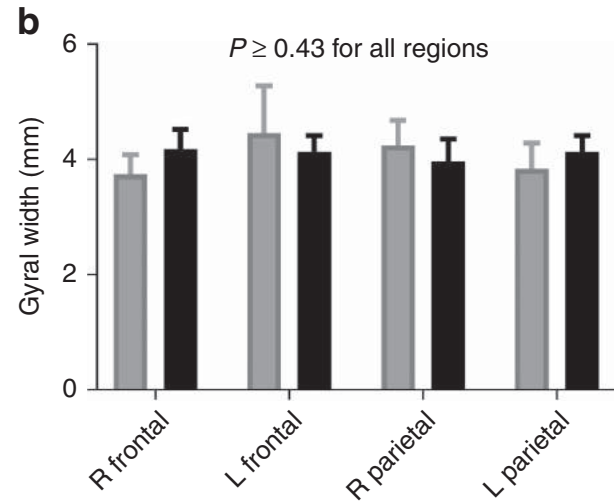
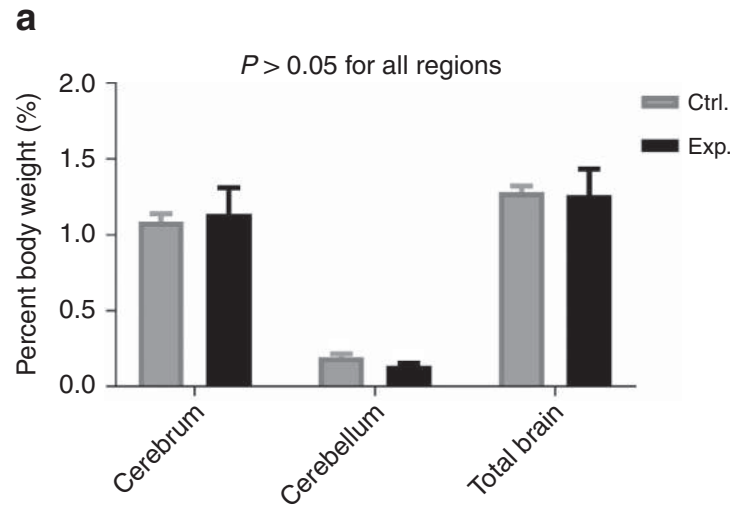
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Objectieve verbetering van de longfunctie



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Normale opbouw, gewicht van de hersenen zonder aanwijzingen voor bloedingen of infarcteringen



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Fresh hope for preemies: Scientists successfully use artificial womb to save premature lambs for the second time in history

- Researchers in Australia kept lambs in artificial wombs for one week
- The device was tested on fetal lambs equivalent to a 23-week-old baby fetus
- The goal is for the womb to eventually help premature babies develop their organs during the critical period of 23 to 28 weeks
- Clinical trials on babies won't start for another five years, researchers say

By [DANIELLE ZOELLNER FOR DAILYMAIL.COM](#)

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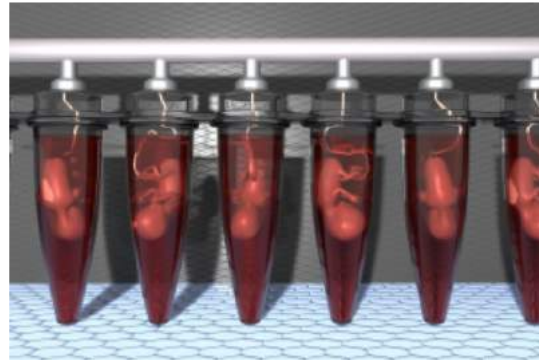
Artificial wombs

New artificial womb technology could keep babies born prematurely alive and healthy

Science is providing us with such useful advances, the ability to save babies born before they are viable by holding them in an artificial womb gives hope to so many women who can not hold the fetus to full term.



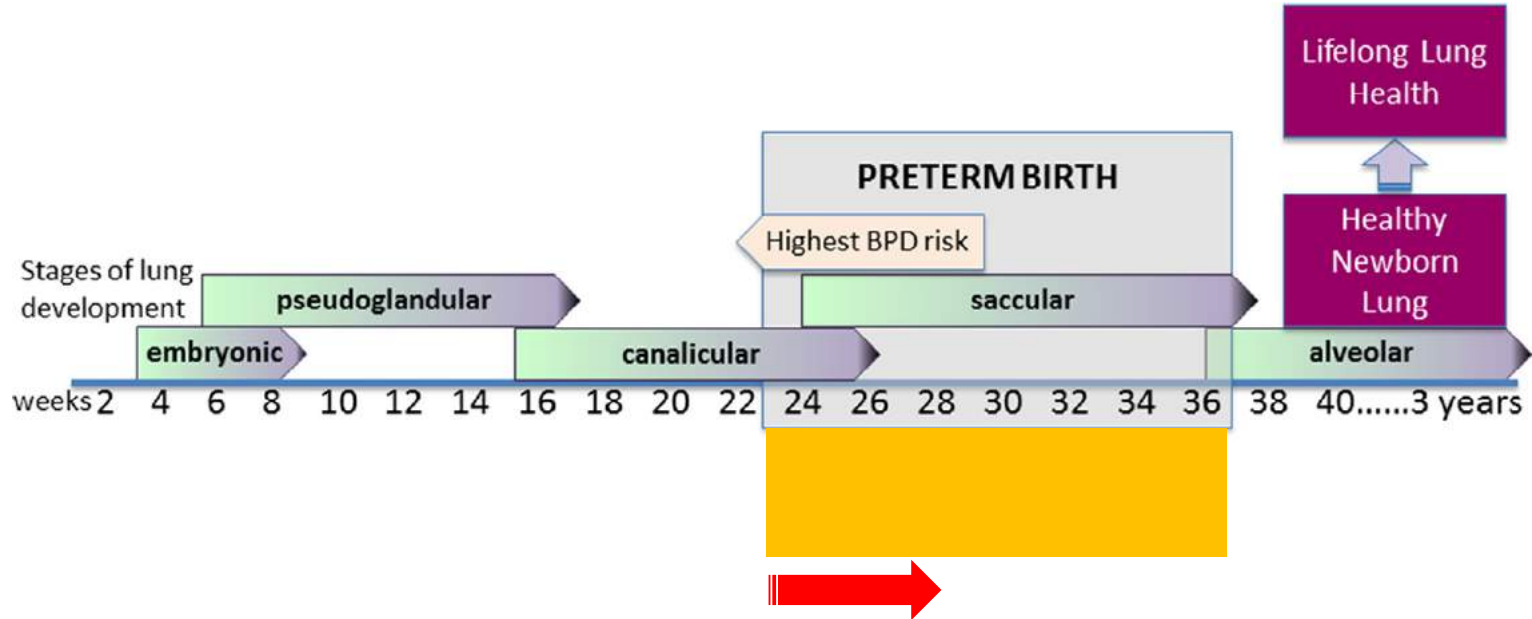
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Ethische vraagstukken



EXTEND - **EXT**rauterine **E**nvironment for **N**eonatal **D**evelopment



EXTEND - EXTrauterine Environment for Neonatal Development

Aanvullende vragen

- Invloed op hechting en binding moeder/ouders
- Juridische aspecten
- Afweging risico's versus voordelen
- Grens van levensvatbaarheid

Alan Flake, a foetal surgeon at the Children's Hospital of Philadelphia (CHOP) and lead author, said the proposed system could act as an urgently needed bridge between the mother's womb and the outside world for babies born at between 23 to 28 weeks gestation.

"If we can support growth and organ maturation for only a few weeks, we can dramatically improve outcomes for extremely premature babies," he said.

The team is in discussions with the US Food and Drug Administration (FDA) and predicts that babies could be incubated in the system within three years in the first clinical trial.

Artificial womb



- UMC's
- TU's
- Overheidsinstanties
- Bedrijven

Dank voor aandacht!

