

Ontwikkelingen en regelgeving rond het invriezen van eicellen

Femke Mol, Mariette Goddijn, Fulco van der Veen,
Annemiek de Melker, Sjoerd Repping,
Centrum voor Voortplantingsgeneekunde
Vrouwenkliniek AMC
(f.mol@amc.nl)



UNIVERSITEIT
VAN AMSTERDAM



Introduction

- What can we freeze?
- How do we freeze?
- Why do we freeze?
- Is it safe?
- What is the state of affairs in the Netherlands/AMC?
- How does society react?
- Oocyte freezing: Quo vadis?

What can we freeze?

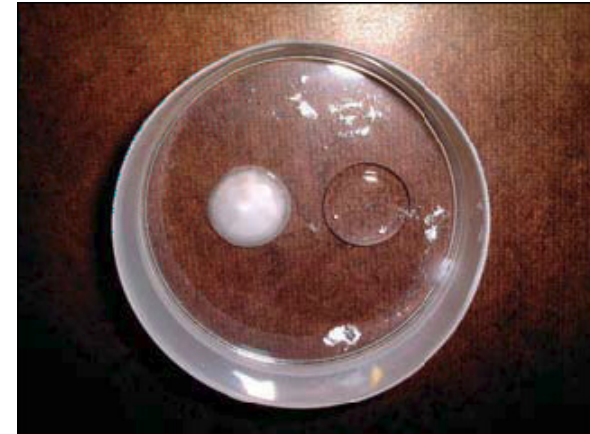
- Semen
- Embryos
- Oocytes
- Testicular tissue (adult, spermatozoa)
- Ovarian cortex
- Testicular tissue (prepubertal, spermatogonial stem cells)

What can we freeze?

- Semen
 - First human pregnancy 1953
- Embryos
 - First human pregnancy 1983
- Oocytes
 - First human pregnancy 1986
- Testicular tissue (adult, spermatozoa)
 - First human pregnancy 1993
- Ovarian cortex
 - First human pregnancy 2004
- Testicular tissue (prepubertal, spermatogonial stem cells)
 - No pregnancies yet

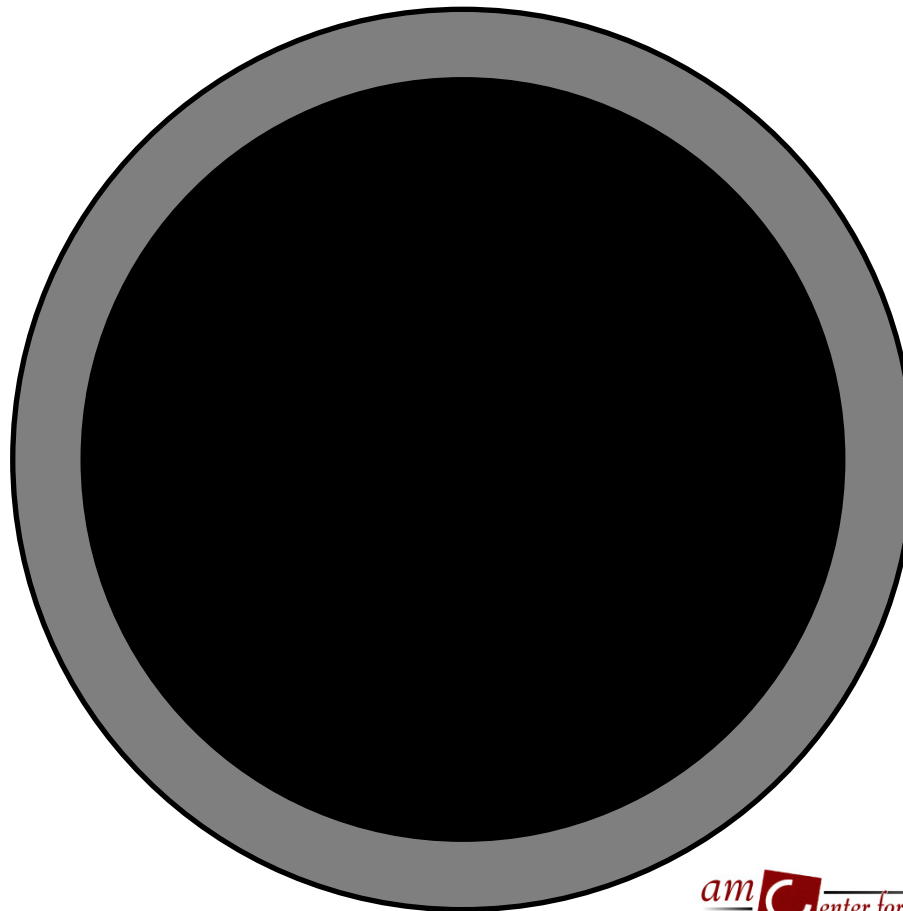
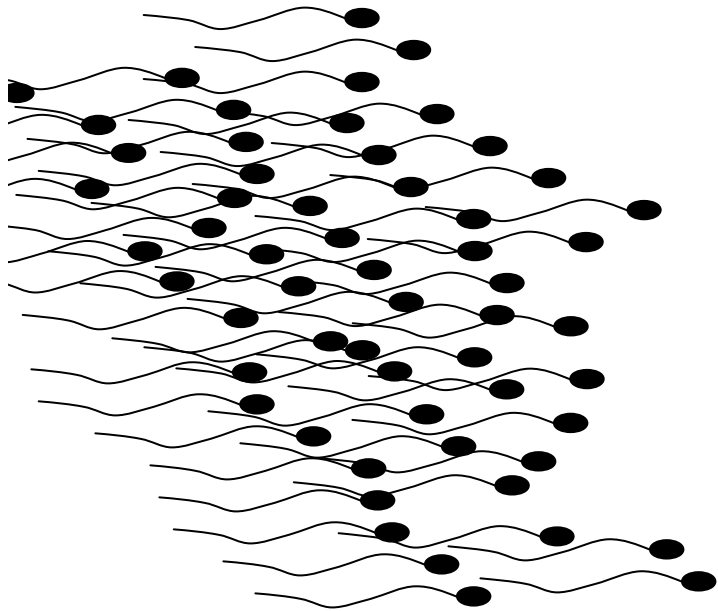
How do we freeze?

- Two methods
 - Slow cooling
 - Vitrification
- Vitrification
 - To make into a glassy substance without structure by lowering the temperature
 - How?
 - High concentrations cryoprotectants
 - High speed of cooling (ultra-fast freezing, >20.000 °C/min)
 - Small volumes
 - Direct contact with liquid nitrogen (-196 °C)

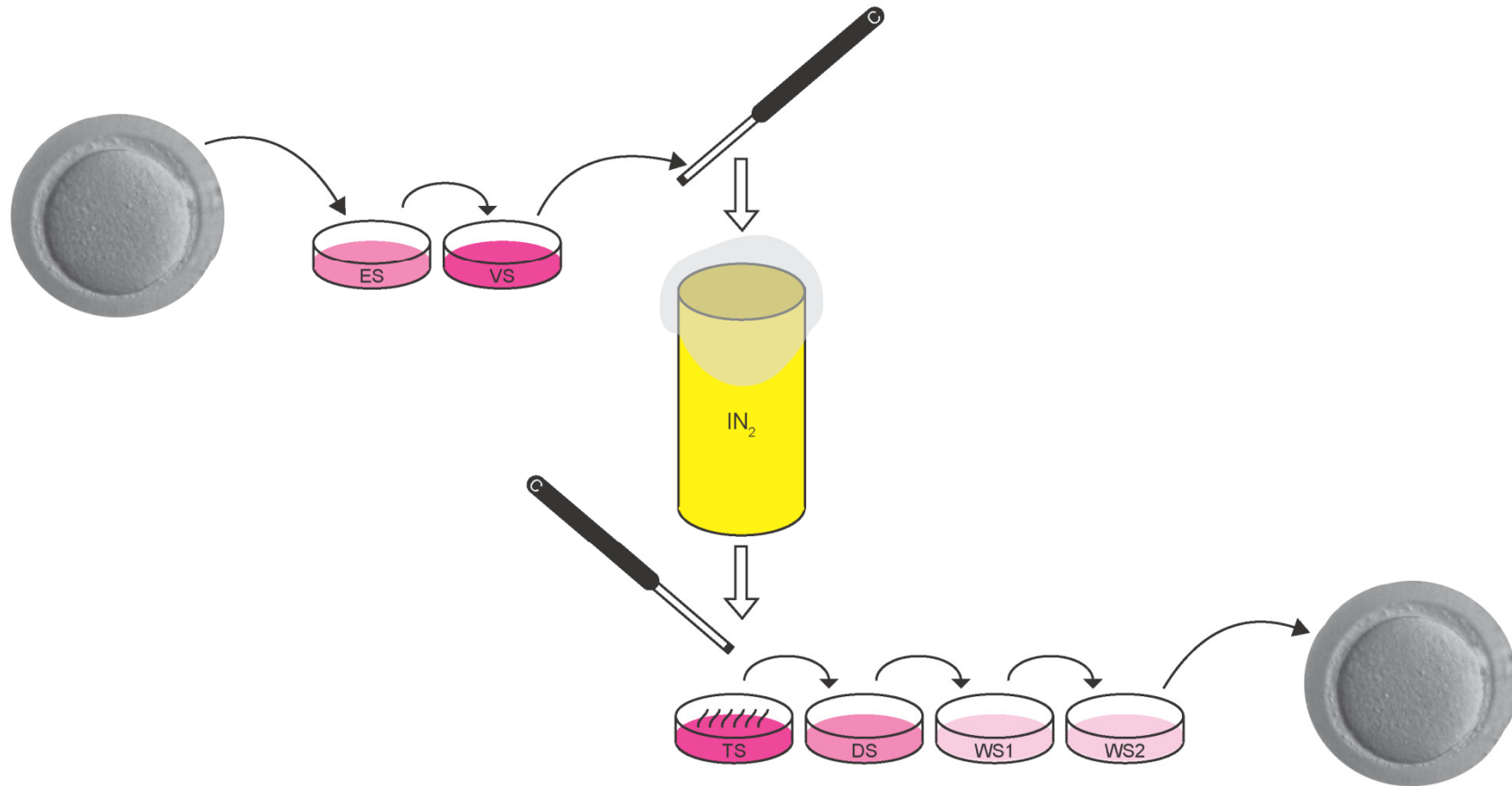


How do we freeze?

- Results for slow freezing of oocytes disappointing
- Why?
 - Cell size
 - Cell number



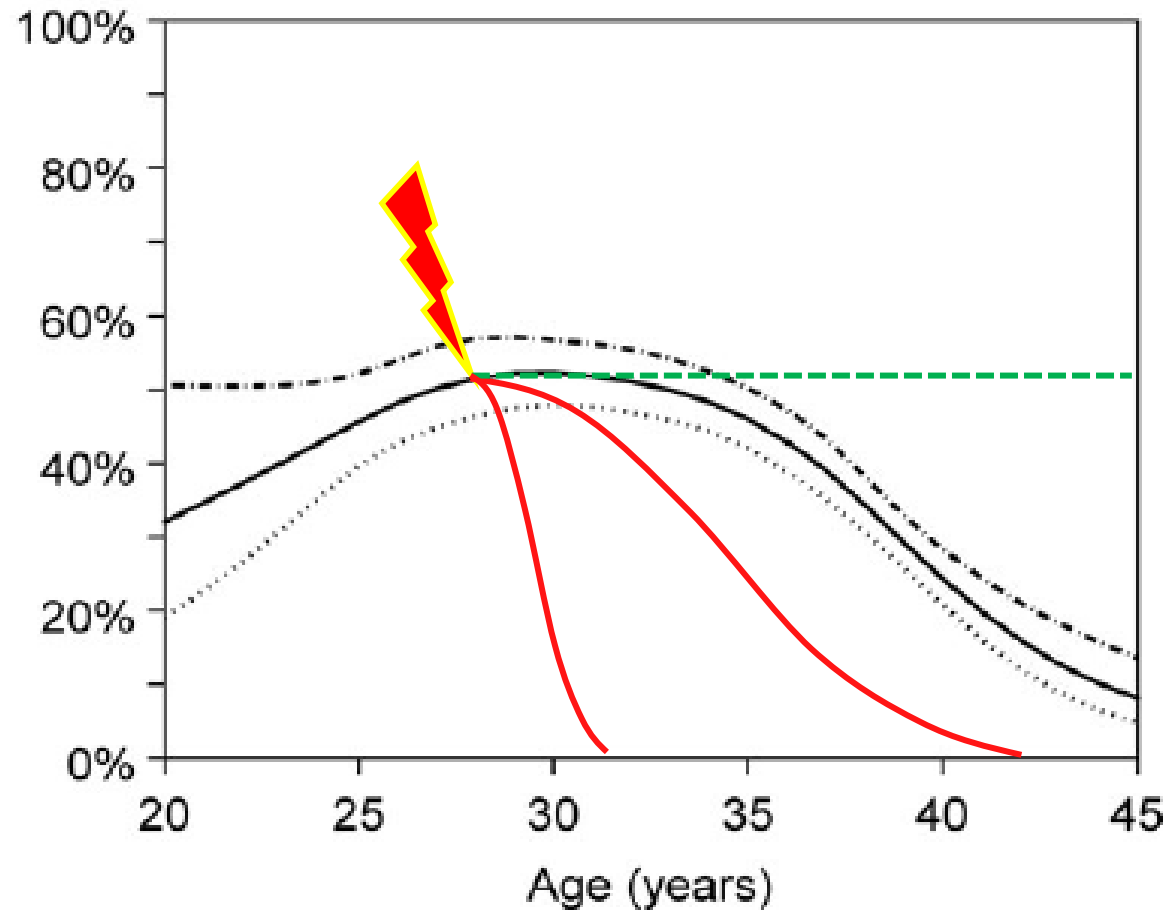
How do we freeze?



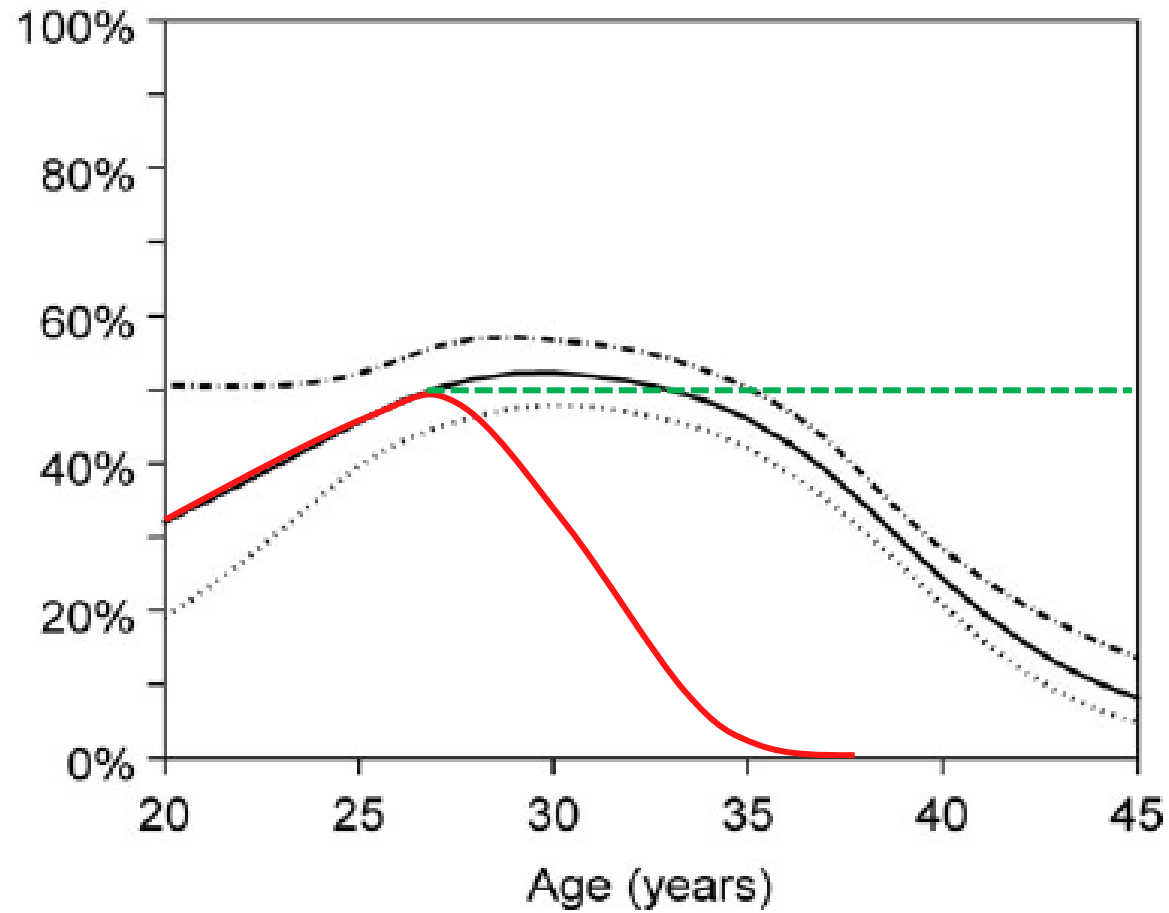
Why do we freeze?

- Emergency situation in IVF/ICSI
 - No semen, no spermatozoa, bacterial infection of semen
- Religious belief
- Imminent ovarian failure
 - Gonadotoxic treatment
 - Chemotherapy, radiotherapy, MTX / bone marrow transplant
 - Time / age
 - Premature (POF, Turner syndrome)
 - “Normal”
 - Average maternal age in NL 29.4 years
 - Average age IVF patients AMC 35.7 years
 - 20% >40 years

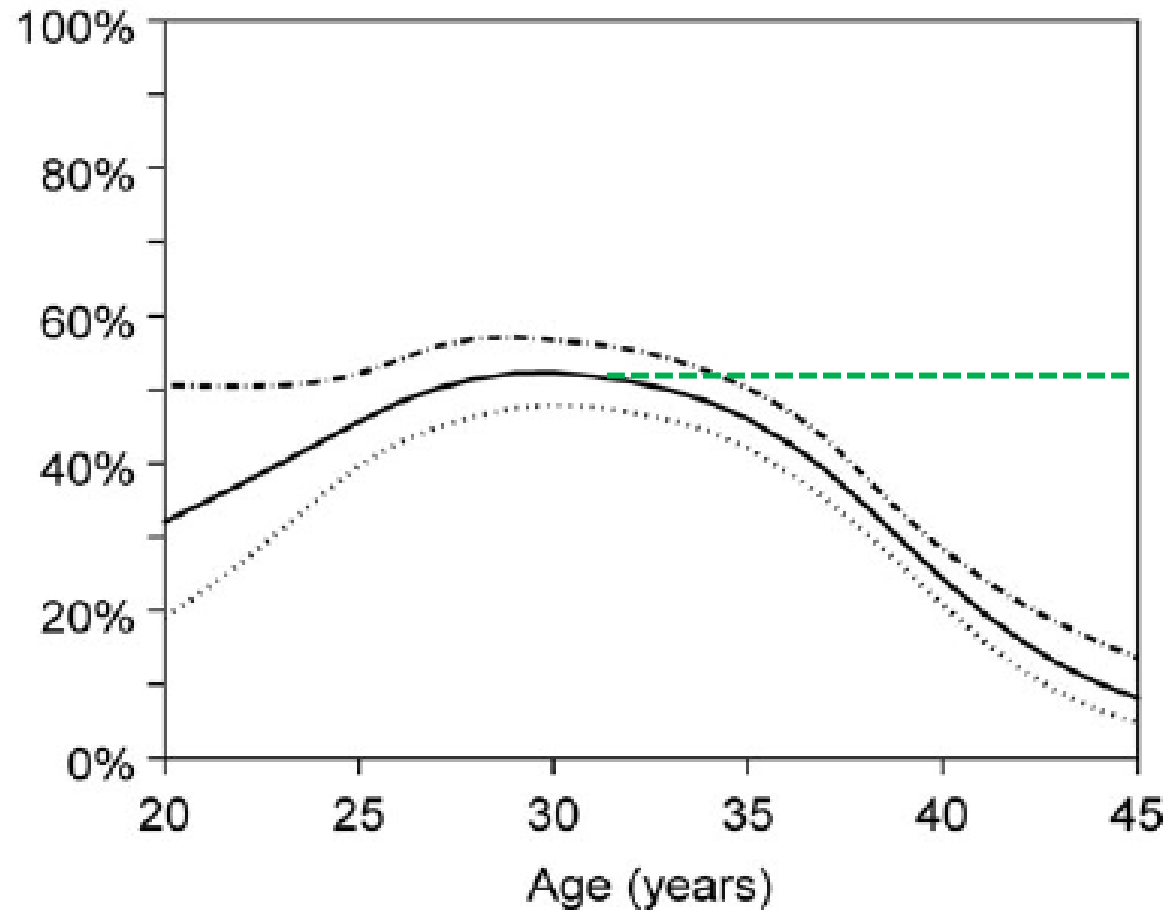
Gonadotoxic treatment



Time / age



Time / age



Safety: preclinical

- First mouse birth 1977
- Also there low success rates
 - Slow cooling
 - Species differences
- Effects of freezing
 - Zona hardening
 - Overcome by ICSI
 - Damage to spindle apparatus
 - Restored 2-3 hrs after thawing
 - Altered transcriptome and proteome
 - All cell manipulation affects this
 - Vitrification has less effect than slow freezing

Safety: preclinical

- Health of offspring
 - Chromosomally normal
 - No reported health effects
 - Not rigorously studied
 - Once it is done in humans
 - Too late
 - Of less significance
 - » Humans are better model systems for humans than mice are
 - Also not for IVF, ICSI, etc.

Safety: clinical

- ASRM SART 2008
 - 9350 vitrified oocytes
 - 88% survived
 - 81,4% fertilised
 - 619 pregnancies out of 1589 ETs (39%)
 - 360 live births (23%)
- Comparison fresh / frozen
 - Donor oocytes (fresh versus 1 hr vitrification)
 - No difference in fertilisation
 - No difference in embryo development

Safety: clinical

- 924 babies born after oocyte freezing
 - 392 after vitrification
 - 12 congenital anomalies (1.5%)
 - 4 minor
 - 8 major
 - equal to population risk

State of affairs in NL

- Standpunt NVOG / KLEM (2008)
 - *De commissie adviseert dan ook om vitrificatie van eicellen en embryo's in Nederland toe te staan. Hierbij dient een gedegen follow up van kinderen die geboren worden na vitrificatie plaats te vinden.*
- Controlled clinical introduction

How does society react?



Oocyte vitrification—Women’s emancipation set in stone

published online April 14, 2008.

Roy Homburg, F.R.C.O.G.^{a,b}
Fulco van der Veen, M.D.^c
Sherman J. Silber, M.D.^d

nrc handelsblad

Een slimme meid vriest haar eicellen in
Zo vergroot zij de kans dat ze op latere leeftijd nog steeds kinderen kan krijgen

Opinie | Donderdag 14-05-2009 | Sectie: Overig | Pagina: 07 | Wybo Dondorp; Guido de Wert

Na een carrièrestart zijn vrouwen soms te oud om kinderen te krijgen. Laat vrouwen hun eicellen tijdig invriezen en weer gebruiken als zij iets ouder zijn, aldus Wybo Dondorp en Guido de Wert ...



NR. 78, 14 JULI 2008, JAARGANG 76, 62. WWW.VRIJ.NL



KIND UIT DE KOELKAST
Het AMC vriest eicellen in

How does society react?



NRC



'Kamer botst over invriezen eicellen'

NOS/NOVA



How does society react?



CCMO application

- Requested by minister of state (Bussemaker)
- Introduction of oocyte freezing in the context of a clinical study
 - Coordinator: dr. Mariette Goddijn
 - Outcome: Safety & Efficacy
 - Health of children born
 - Congenital abnormalities
 - Normal rate 4% / maximum increase of 5%
 - » 190 children
 - Social context

CCMO application

- Inclusion criteria
 - Women up to 40 years of age who are at risk of ovarian failure due to iatrogenic gonadotoxic treatment
 - Women up to 40 years of age who are at risk of premature ovarian failure and women between the ages of 30 and 40 years who are at risk of ovarian failure due to increasing age
 - Women up to 42 years of age undergoing an IVF/ICSI cycle during which no spermatozoa can be obtained at the time of follicle aspiration.
- Centers recruiting
 - AMC, VuMC, MUMC, UMCG, Erasmus MC, UMCU, UMCN, LUMC, Isala, Voorburg, MCKinderwens

NVOG / KLEM addendum



Vitrificatie voorwaardelijk toestaan

Vitrificatie van eicellen is een belangrijke nieuwe ontwikkeling die de mogelijkheden voor hulp bij voortplanting kan verbeteren en vergroten. Er zijn geen goede argumenten om het uitnemen, vitrificeren en opslaan van eicellen (fase 1) bij voorbaat af te wijzen, ook als er geen sprake is van strikt medische redenen. Wel moet de behandeling nog beschouwd worden als experimenteel; een systematische follow-up van de kinderen is een voorwaarde voor het gebruik van gevitriceerde eicellen (fase 2).

NVOG / KLEM addendum



State of affairs in the AMC

- Patients treated
 - Started in 2006
 - 2006 – 2009 Only in case of absence of sperm
 - Since 2009 In case of medical emergency (cancer)
 - From 2011... In case of advanced age
 - Numbers
 - 2006 – 10/2009 20 patients
 - 10/2009 – today 37 patients

State of affairs in the AMC

Freeze cycles

Indication	Patients (n)
No sperm cells	27
Infection in semen	2
Oncology	28

Vitrification cycles	number
Cycles	54
Oocytes	
retrieved	587
vitrified (MFII)	450 (77%)

Thaw cycles

Thaw cycles	12
oocytes thawed	85
oocytes found	83
oocytes survived	59
oocytes fertilised	41
embryos transferred	24
embryos implanted	3*
Cycles with ET	12
Pregnancy	3*
Ongoing pregnancy	2*
Live birth	2*
Singleton pregnancy	2*
Multiple pregnancy	0

- Follow up children
 - at birth, 3 months and one year normal development

Egg freezing: quo vadis?



CALL TODAY: (800) 841-7179 OR [EMAIL US](#)

WHY FREEZE EGGS

THE EXTEND SERVICE

FROM THE EXPERTS

ABOUT US

[HOME](#)

[REQUEST INFORMATION](#)

Egg Freezing



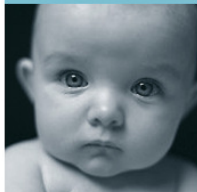
Egg Freezing Center

Options for Life

[Contact Us](#)

[Home](#) [About Us](#) [Egg Freezing Overview](#) [Patient Center](#) [Financials](#) [In The News](#)

Egg Freezing Center



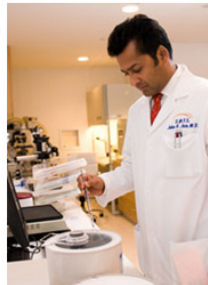
We are committed to providing reproductive choices by combining innovative technology, accountability and quality personal care.

Our Physician

John K. Jain, MD, FACOG

Dr. John Jain is a board-certified reproductive endocrinologist and a pioneer in the field of reproductive medicine. He is federally funded by the National Institutes of Health and was appointed to the National Ethics Committee of the American College of Obstetricians by President Vivian Dickerson. In 2006, the Pacific Coast Reproductive Society awarded him their top research prize.

Dr. Jain has twenty-five years of academic experience including a decade as a decorated professor of Obstetrics and Gynecology at the USC Keck School of Medicine. During his tenure at USC, he spearheaded egg freezing research and subsequently created the university's egg freezing program. He now brings that expertise to the Egg Freezing Center.



Cost

The cost of egg freezing is approximately \$12,750. This fee includes all testing, monitoring and the first year of storage. Each additional year is billed at a rate of \$600. There is also a cost for the medications which is paid directly to the pharmacy. The egg thaw, fertilization and embryo transfer procedure total approximately \$5,500. Exact costs will be set and guaranteed at the time of the initial egg freezing cycle. Discounts for additional cycles and payment plans are available.



[Forward to a Friend](#)

[Test Your Fertility Knowledge](#)

[Learn the Facts](#)

[LaterBaby Community](#)

[About Us](#)



[Egg Freezing > Egg Freezing Services](#)

Egg Freezing Services

As more women are waiting longer to have children, egg freezing is becoming more relevant and in demand as many women are facing the real challenge of having successful, healthy pregnancies later in life. While we have made great strides in other areas, our fertility is still limited by basic biology – the "biological clock" generally stops ticking in our late 30's or early 40's. Our opportunities are endless, but our egg supply and egg quality are not, that is why more women are seeking egg freezing services.

amC *center for reproductive medicine*

Egg freezing: quo vadis?

- Proper introduction in the Netherlands
 - Proper patient information
 - No commercial basis
- Other developments
 - Alternative for vitrification of embryos
 - Current partner \neq future partner
 - Alternative for freezing of ovarian tissue
 - CONS
 - Egg freezing takes time
 - PROS
 - No laparoscopy needed
 - No risk of reintroduction of malignant cells

“Een Ei voor later”

- Rode Hoed: **Woensdag 3 november, aanvang 20.00 uur**

Debat over de worsteling van vrouwen met de aftikkende biologische klok naar aanleiding van de NCRV documentaire ‘Ei voor later’.