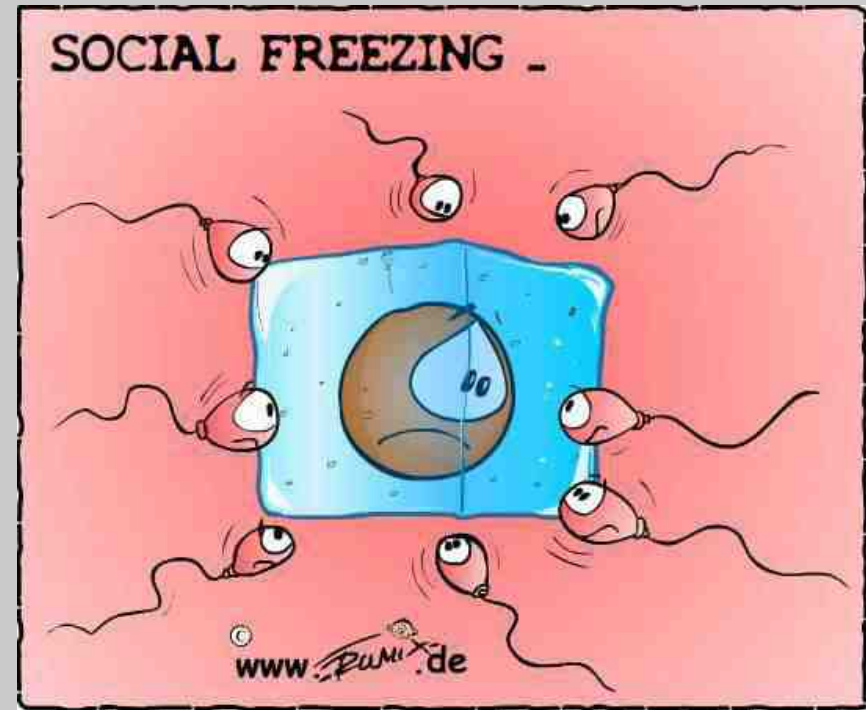
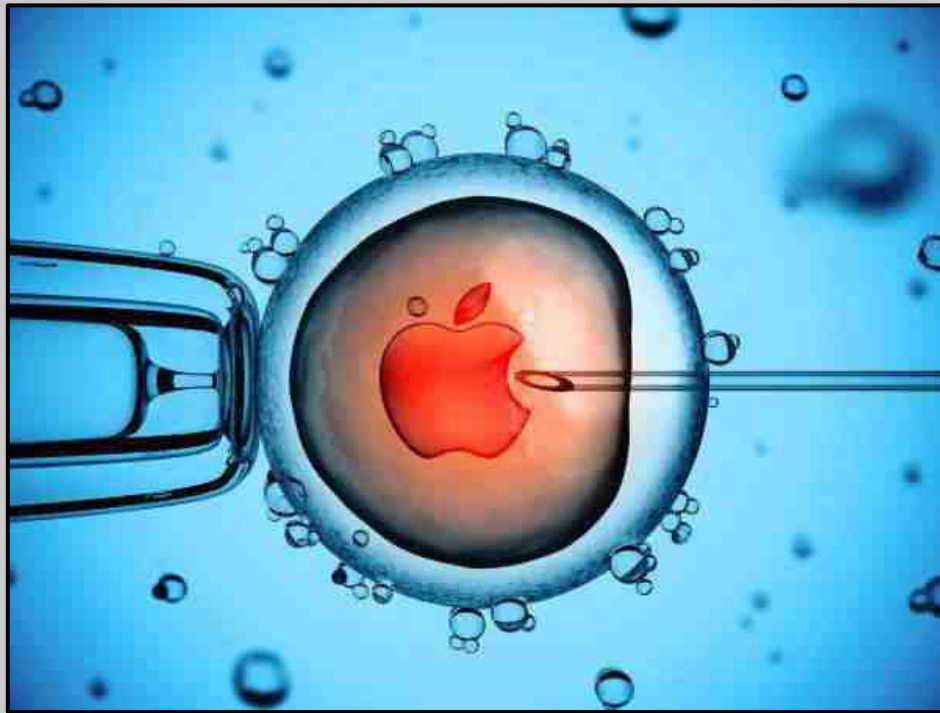


# Oocyte cryopreservation for social reasons: Where are we now?

Professor Claus Yding Andersen, MSc, DMSc



Laboratory of Reproductive Biology, University Hospital Copenhagen,  
University of Copenhagen, Copenhagen, Denmark, E-mail: [yding@rh.dk](mailto:yding@rh.dk)

# Take home message

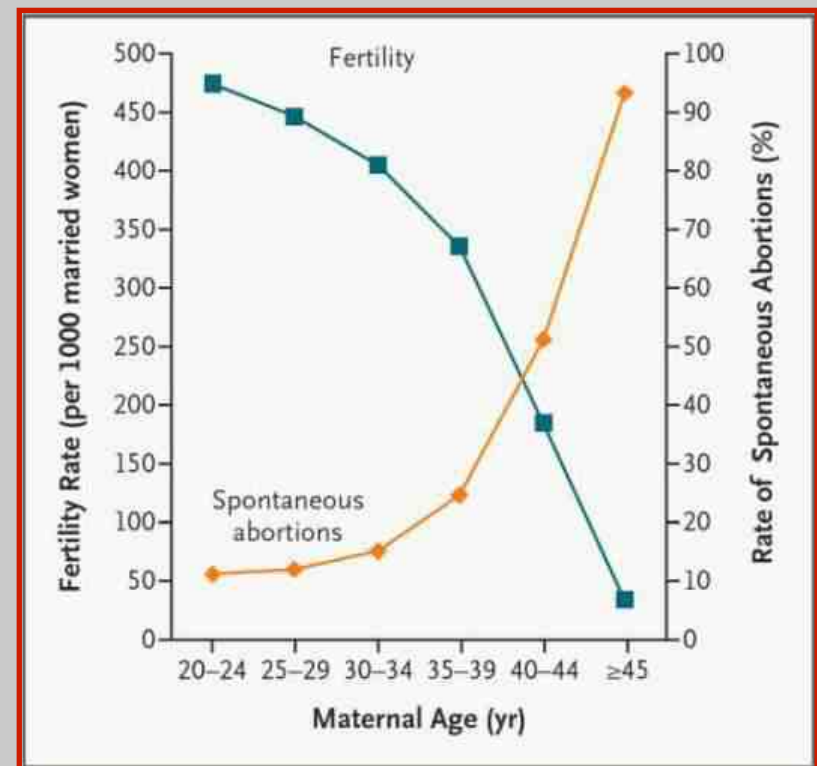
- ❖ Freezing of mature oocytes for non-medical indications is a huge media created issue
- ❖ As a profession we have available methods to cryostore oocytes, but what do we offer to patients
- ❖ Especially reproductive aged women may only to a limited extent benefit from the procedure
- ❖ Cryopreservation of ovarian tissue is suggested as an alternative – a better chance to utilise and justify the intervention

# Non-medical egg freezing: medical advance and social need?

## Fertility declines and birth defects increase with age

- ❖ Female fertility declines with age – Many women delay childbearing
- ❖ Focus on education and carrier – Awareness of biological facts are limited
- ❖ Methods for fertility preservation are available – are methods causing demand or does a real problem exist?
- ❖ Are we as a profession tackling this issue in a professional way?

| Maternal Age at Delivery (yr) | Risk of Down's syndrome abnormality | Risk of Any Chromosomal Abnormality |
|-------------------------------|-------------------------------------|-------------------------------------|
| 20                            | 1/667                               | 1/526                               |
| 25                            | 1/1200                              | 1/476                               |
| 30                            | 1/952                               | 1/385                               |
| 35                            | 1/378                               | 1/192                               |
| 40                            | 1/106                               | 1/66                                |
| 45                            | 1/30                                | 1/21                                |



# Where are we now?



**Social freezing – Elective egg freezing – Non-medical egg freezing –  
Banking for anticipated gamete exhaustion – Prevention of age related  
fertility loss – Stopping the biological clock**



# Where are we now?



## Business

### Tech giants to freeze eggs for their female employees

© 15 October 2014 | Business



Apple and Facebook are offering to help women put off pregnancy until later in their careers

Women working for Facebook and Apple are being offered an additional perk: they can have their eggs frozen.

## **The great equalizer for women**

**The attraction of egg freezing was precisely its promise to synchronise their biological clocks with other timelines in their life course.**

*Waldby C. Cult Health Sex. 2015;17:470*

**By freezing their eggs women may believe they have “bought a little biological time” and the costs and small risks associated with the procedure may well be worth taking for that sense of empowerment.**

**However, at the present level of efficacy of oocyte freezing, it is vital that women, especially if they are over 35, are made aware that their frozen eggs do not represent an insurance policy against age-related infertility**

*Loockwood G & Johnson HM, RBMOnline, 2015;31:126*

# Going above the individual level: Many societies desperately needs children



The screenshot shows the homepage of The Japan Times website. The main headline is "Urayasu to be Japan's first municipality to subsidize freezing women's eggs". The article is dated February 24, 2015, and is categorized under "NATIONAL / SCIENCE & HEALTH". The text of the article states that Urayasu, Chiba Prefecture, is set to become the first municipality in the country to effectively subsidize women who have their eggs frozen for use to get pregnant in later years. The city said Monday it will provide Juntendo University's Urayasu Hospital with ¥90 million over the next three years to promote research on technologies to freeze and store eggs. Thanks to the subsidies, out-of-pocket expenses for female residents of the city who use the procedures will be limited to around 30 percent of the total, Urayasu officials said. The city included ¥30 million in such subsidies in a draft supplementary budget for the fiscal year ending in March. A quote from Koyo Yoshida, director of Urayasu Hospital, is also included: "This project is worth undertaking as it could lead to a clinical study of whether (such subsidies) really contribute to curbing the declining birthrate."

On the right side of the page, there is a promotional banner for "The Japan Times × お誕生日新聞" (The Japan Times × Birthday Newspaper) with the text "ジャパントイムズを大切な人へ 特別な日に贈る" (Gift The Japan Times to a loved one on a special day). Below this, there is a section titled "THE JAPAN TIMES ST THE JAPAN TIMES ON SUNDAY" and a link to "Japanese Language Schools" with a description: "Special feature on Japanese language schools that are successful at helping students enter employment or university and graduate school."

To augment the number of children born this municipality donated  
a total of around 700.000 Euro for freezing oocytes

# Where are we now?

The screenshot shows the website of the Progress Educational Trust. The header includes the logo, the name 'Progress Educational Trust', and the tagline 'informing debate on assisted conception and genetics'. There is a search bar and a link to subscribe to the BioNews newsletter. A left-hand navigation menu lists various sections: Home, About us, Events, Publications, Policy, Projects, Education, Friends of PET, Donate to PET, Work with PET, Annual reports, Contact us, and Search. The main content area is titled 'EVENTS' and features a specific event: 'Beating the Biological Clock: Should You Freeze Your Eggs?'. The event is organized by the Progress Educational Trust in partnership with the Anne McLaren Memorial Trust Fund. It is an evening event on 21 October 2013 at the JZ Young Lecture Theatre, Ground Floor, Anatomy Building, Bloomsbury Campus, University College London. The event is free to attend but requires advance booking. The text discusses the growing demand for egg freezing, the current UK law, and the ethical considerations surrounding the practice. It mentions that some clinics charge high fees for cryopreservation, which is criticized as being exploitative. It also notes that some companies offer egg freezing as a perk to employees. The event aims to explore these issues and the role of the state in regulating the practice. The website also features a sidebar on the right with a call to action for the 'WE NEED YOUR VIEWS BioNews Reader Survey 2015' and a link to the 'amazon.co.uk' store.

- ❖ What are the pregnancy success rates using frozen eggs, and what risks are involved?
- ❖ How many eggs would a woman need to freeze, to have a reasonable chance of pregnancy?
- ❖ Is it misleading to sell egg cryopreservation as an insurance policy?
- ❖ Can women achieve more control and gain greater reproductive autonomy by freezing their eggs?
- ❖ Where can patients go for reliable information about this subject?



# COST OF FREEZING EGGS

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**\$500/YEAR FOR STORAGE**



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EGG FREEZING  
AFFORDABLE**

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NOT SURE? LEARN MORE

HOW IT WORKS

SUCCESS MATTERS

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Provide us with some basic information by completing our [form](#) or calling us at

 **Finding a Trusted Doctor**

Egg Freezing and the process of vitrification is relatively new & complex. EggBanxx is the industry's first national network of highly skilled & specially

 **Consult & Finance**

Book your consultation today and pay up to 15% less by using a fertility clinic in our network. We

GOOGLE AND FACEBOOK  
ARE COVERING THE COST OF ELECTIVE  
EGG-FREEZING FOR THEIR  
EMPLOYEES!

THE ONLY THING  
OUR EMPLOYER IS  
WILLING TO FREEZE  
IS OUR WAGES!

BREAK  
ROOM

FRIDGE  
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DARKE  
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DAILY TRIBUNE  
GOSPELARTISTS.COM  
2014

ORIGINAL ARTICLE

## Ovarian stimulation for oocyte cryopreservation for prevention of age-related fertility loss: one in five is a low responder

Avi Tsafrir<sup>1</sup>, Ronit Haimov-Kochman<sup>2</sup>, Ehud J. Margalioth<sup>1</sup>, Talia Eldar-Geva<sup>1</sup>, Michael Gal<sup>1</sup>, Yuval Bdolah<sup>2</sup>, Tal Imbar<sup>2</sup>, Arye Hurwitz<sup>2</sup>, Avraham Ben-Chetrit<sup>1</sup>, and Doron Goldberg<sup>1</sup>

<sup>1</sup>Shaare-Zedek, IVF Unit, Department of Obstetrics and Gynecology, Affiliated with the Hebrew University School of Medicine, Jerusalem, Israel and <sup>2</sup>IVF Unit, Department of Obstetrics and Gynecology, Hadassah Hebrew University Medical Center, Mt Scopus, Jerusalem, Israel

- ❖ 105 women underwent 151 stimulation cycles
- ❖ Mean age 37.7 years (no known infertility)
- ❖ FSH mean dose per day 371 IU  $\pm$ 110 (225 – 600 IU)
- ❖ Mean number of MII oocytes cryopreserved 9.7  $\pm$ 7.5 (0-43)
- ❖ 21% of started cycles were cancelled or resulted in 0-3 MII oocytes

**Perform this procedure at a younger age than preferably 35**

# Number of oocytes required to have a child

- ❖ It is usually estimated that 15 – 20 oocytes are required to become pregnant – increasing with age
- ❖ Which fits to data from the ESHRE database:  
Live birth rate = 6.4% <35 year old  
Falls to 2.7% for the total database
- ❖ Results from IVI Spain indicate that results may be improved considerably (perhaps one in ten oocytes)  
fresh oocytes = vitrified warmed oocytes in oocyte donors only (IVI)





www.sciencedirect.com  
www.rbmonline.com



ARTICLE

## Oocyte cryopreservation for social reasons: demographic profile and disposal intentions of UK users



Kylie Baldwin <sup>a,\*</sup>, Lorraine Culley <sup>a</sup>, Nicky Hudson <sup>a</sup>, Helene Mitchell <sup>a</sup>,  
Stuart Lavery <sup>b</sup>

- ❖ 23 UK women undergoing “social freezing”
- ❖ Mean age 36.7 years (25% below 35 years)
- ❖ Well educated with 88% stating that they would donate surplus oocytes should they not need them.

# What effort is needed to achieve success

**Table 3** Number of cycles of oocyte cryopreservation attempted.

| Mean number of cycles | Number of cycles of oocyte cryopreservation attempted |     |     |       |      |
|-----------------------|---|-----|-----|-------|------|
|                       |   | One | Two | Three | Four |
| 1.65                  | <i>n</i>  | 13  | 6   | 3     | 1    |
|                       | (%)   | 57  | 26  | 13    | 4    |

**Table 4** Number of eggs frozen by participants.

| <i>Number of eggs cryopreserved</i> | <i>Number of participants</i> |
|-------------------------------------|-------------------------------|
| 0                                   | 1                             |
| 1-5                                 | 3                             |
| 6-10                                | 6                             |
| 11-16                               | 8                             |
| 17-21                               | 2                             |
| 22-26                               | 1                             |
| 27+                                 | 2                             |

## **Two severe problems with today's policy for non-medical egg freezing**

- ❖ Women are too old when they decide to store oocytes  
– more than 35 years**

One in five patients requesting SF is low responder

Often require several stimulation cycles

- ❖ Most women do not come back to collect the oocytes**

Utilisation rate of the stored oocytes is below 10%

**Is this the right approach?**

# Why not freeze ovarian tissue?

- ❖ In contrast to social freezing of mature oocytes – ovarian tissue will also restore endocrine function
- ❖ Ovarian tissue may serve both purposes – secure fertility or if not required for fertility for postponing menopause
- ❖ Ovarian tissue often restore natural fertility
- ❖ Develop *in vitro* competent oocytes for fertility purpose
- ❖ Ovarian tissue may be used to derive oogonial stem cells for mitochondrial isolation and transfer to oocytes
- ❖ *In vitro* follicle activation







ELSEVIER

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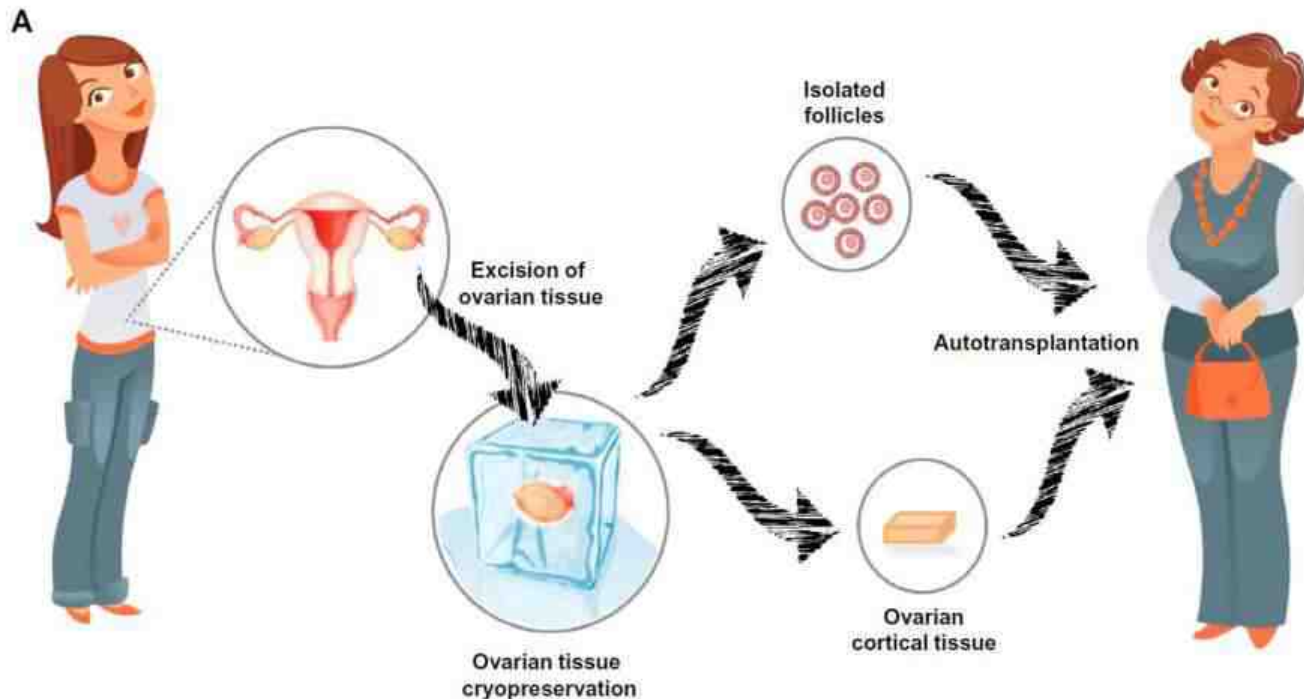


COMMENTARY

## Novel use of the ovarian follicular pool to postpone menopause and delay osteoporosis



Claus Yding Andersen <sup>\*</sup>, Stine Gry Kristensen



## Outcomes of transplantations of cryopreserved ovarian tissue to 41 women in Denmark

A.K. Jensen<sup>1,\*</sup>, S.G. Kristensen<sup>1</sup>, K.T. Macklon<sup>2</sup>, J.V. Jeppesen<sup>1</sup>, J. Fedder<sup>3</sup>, E. Ernst<sup>4</sup>, and C.Y. Andersen<sup>1</sup>

- ❖ Currently one in three have had children
- ❖ The tissue is still being active in most women
- ❖ Half of the children are conceived naturally
- ❖ Most have not exhausted their storage of tissue

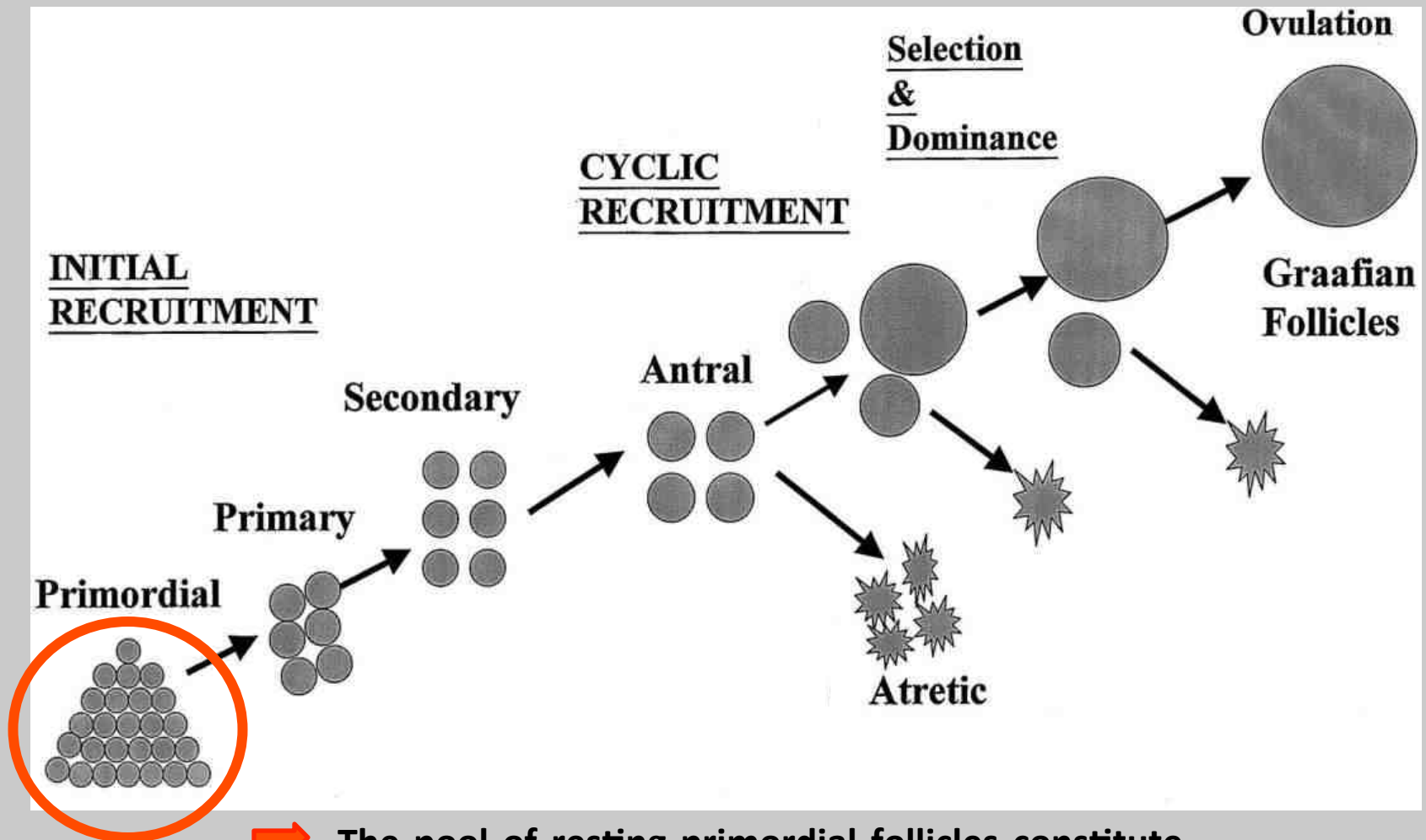
**The ovary is an endocrine organ – not only oocyte producer**



Potentially both objectives – fertility preservation and postponing menopause – could be accomplished



## A new approach – targeting the resting pool of follicles



➡ The pool of resting primordial follicles constitute 90% of the ovarian follicular reserve



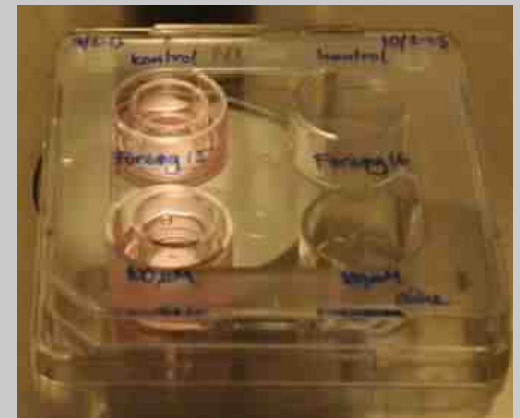


# Activation of follicle growth in vitro

Ovarian cortical



In vitro activation  
of the follicles



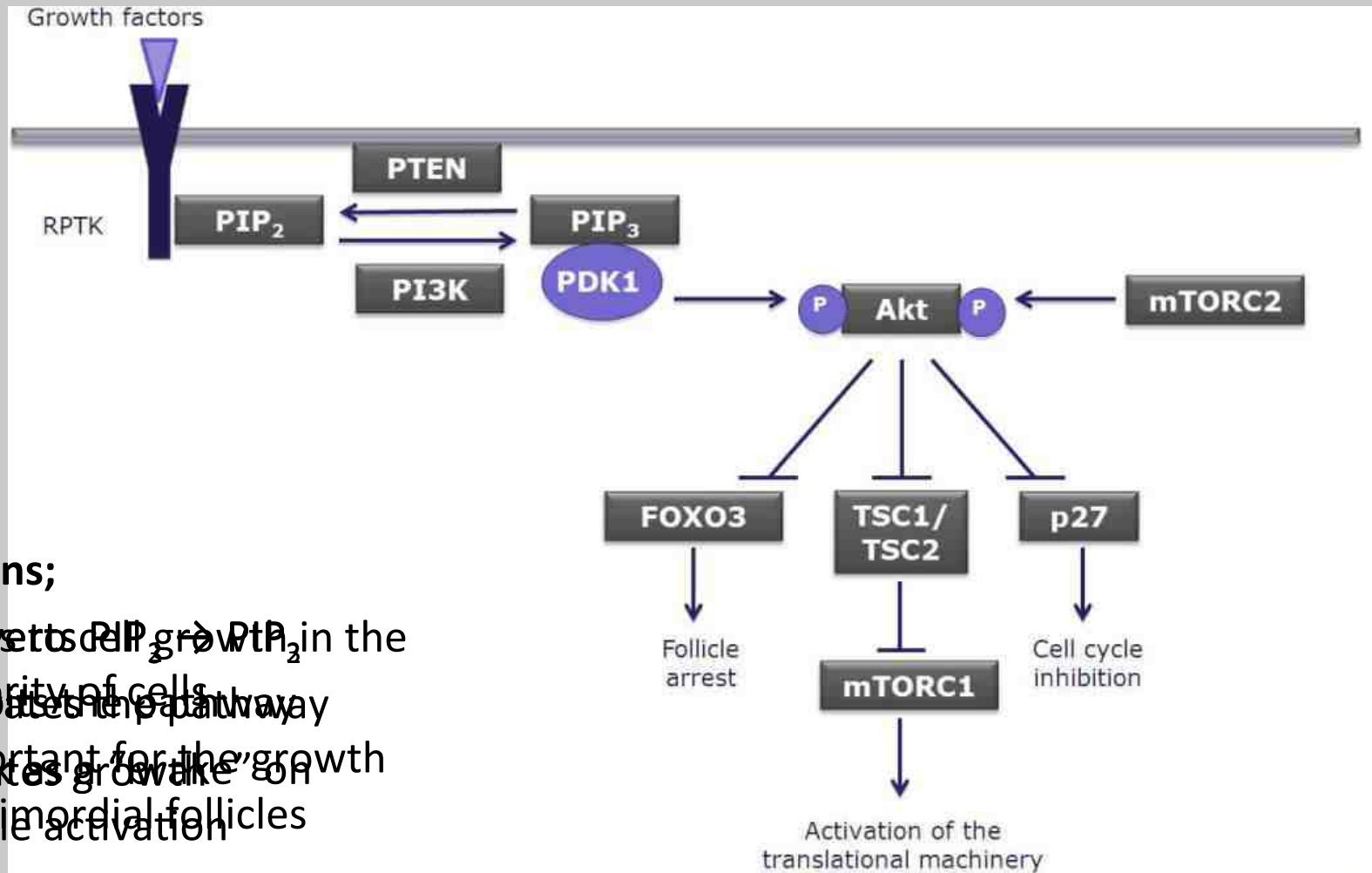
Autotransplantation

IVF





# The PI3K/Akt signaling pathway

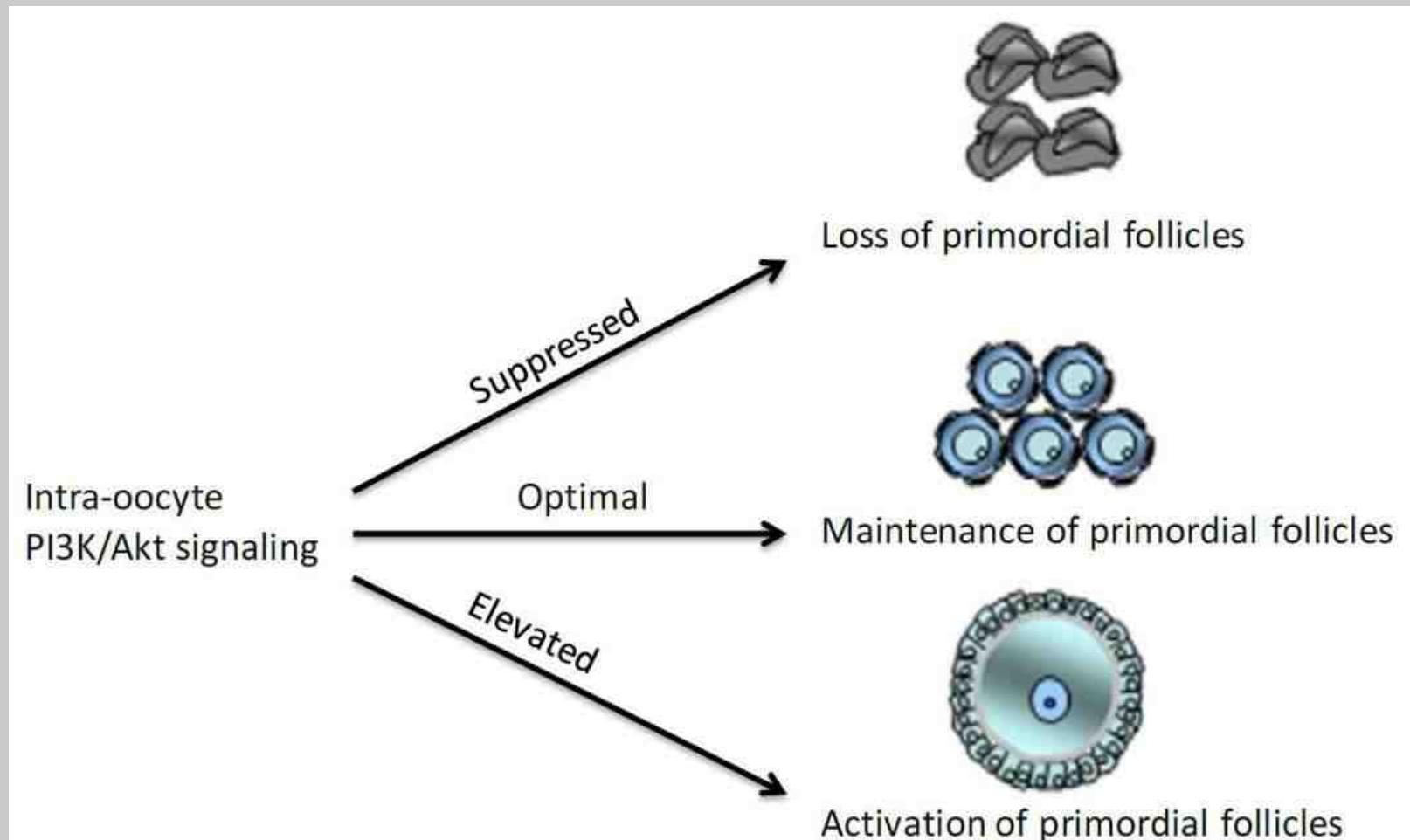


## Functions;

- Converts  $PIP_2$  to  $PIP_3$  in the majority of cells
- Activates the pathway
- Important for the growth of primordial follicles
- Follicle activation



# Basal level of PI3K signaling leads to survival of the follicles

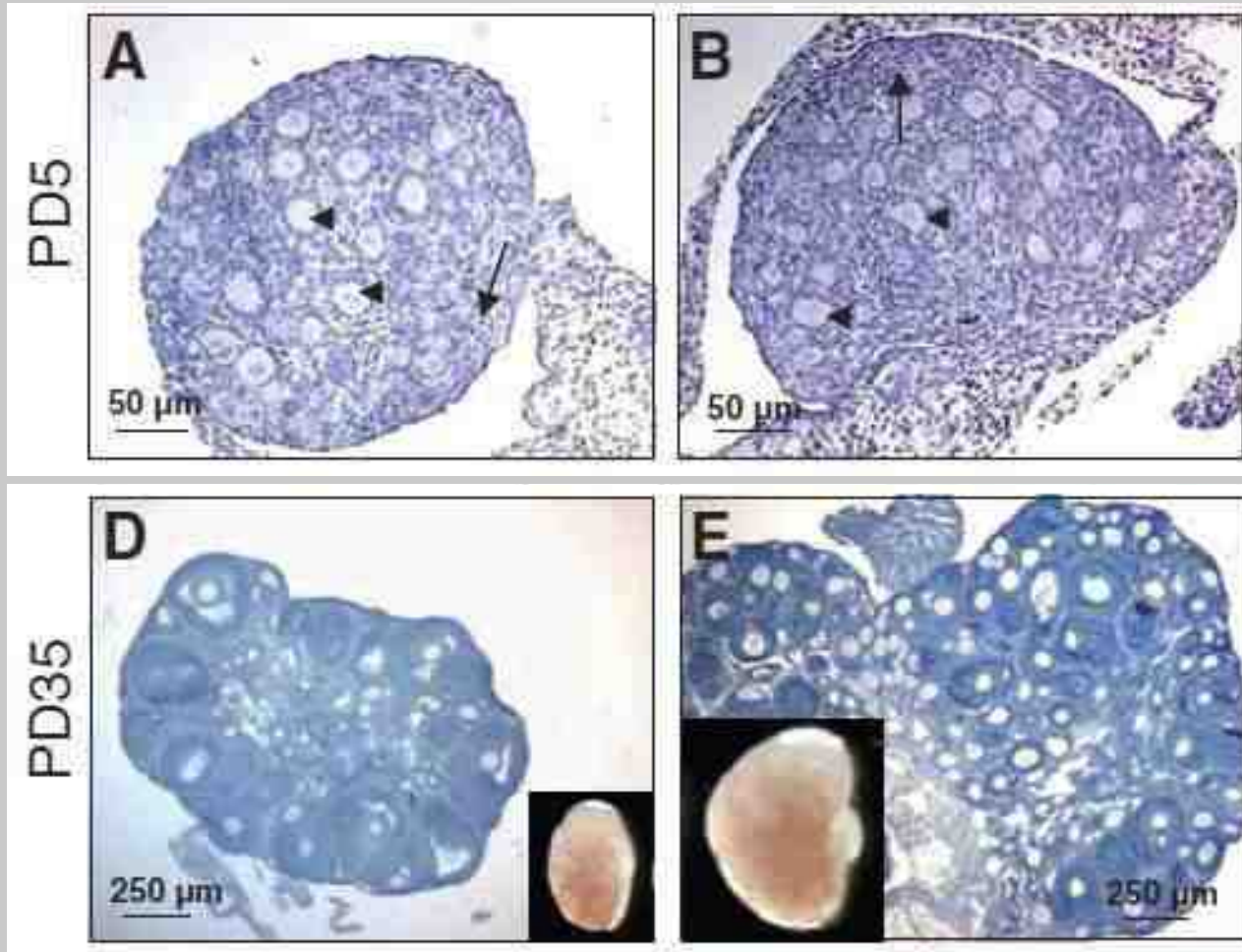




# PTEN knock-out mice have global activation of primordial follicles

Control

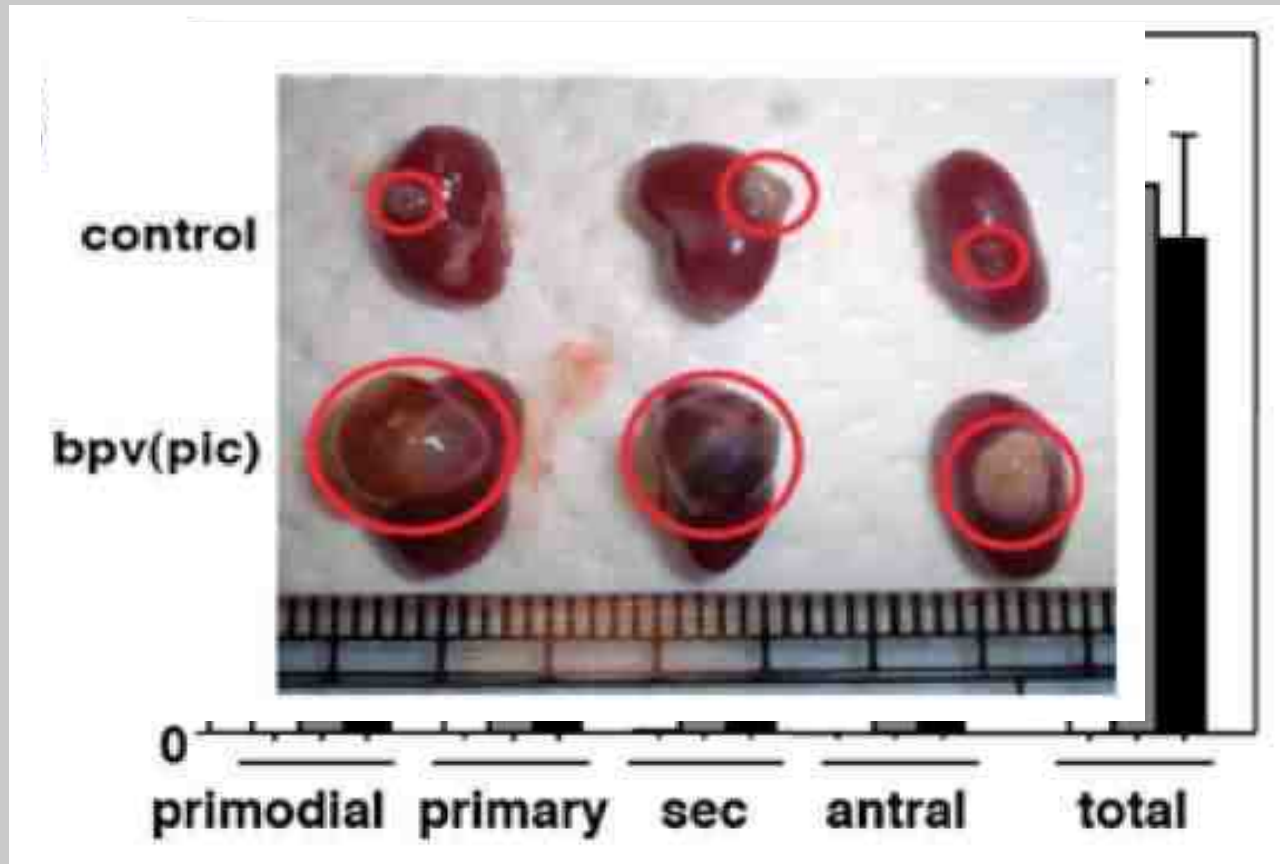
PTEN knock-out







## Activation of human primordial follicles using 100 $\mu$ M PTEN inhibitor for 24 hours



Li et al., 2010

30 September 2013 Last updated at 19:36 GMT



## Early menopause: Baby born after ovaries 'reawakened'

By James Gallagher

Health and science reporter, BBC News

**A baby has been born through a new technique to "reawaken" the ovaries of women who had a very early menopause.**

Doctors in the US and Japan developed the technique to remove the ovaries, activate them in the laboratory and re-implant fragments of ovarian tissue.

The technique, **reported in Proceedings of the National Academy of Sciences**, has resulted in one baby being born, with another expected.

The findings were described as early, but a "potential game-changer".

The 27 women involved in the study became infertile around the age of 30 due to "primary ovarian insufficiency". The condition affects one in 100 women who essentially run out of eggs too young, leading to an early menopause.

Women have a fixed number of eggs at birth and those with the condition tend to use them up too quickly or are born with far fewer eggs in the first place.



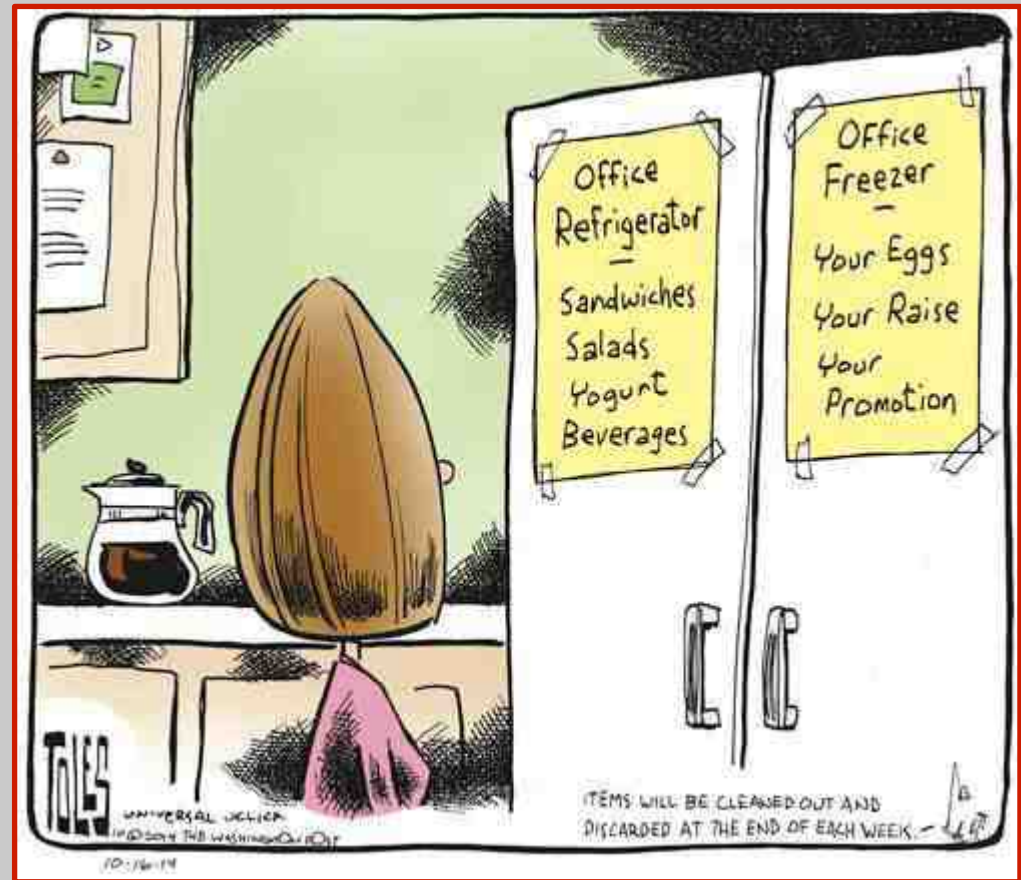
KAZUHIRO KAWAMURA

Dr Kazuhiro Kawamura of the St Marianna University medical school holding the newborn

### Related Stories

IVF guidelines raise age limit to 42  
Super-fertility

# No matter what – there is no reason not to enjoy the cartoons!





## Conclusion

- ❖ The media hype around non-medical egg freezing has forced fertility clinics to provide a treatment that may not be completely within the lines of what we normally would suggest
- ❖ Especially reproductive aged women (i.e. above 35 years) may

need to put a considerable effort into collecting oocytes without knowing whether they are useful

- ❖ Less than 10% appear to return to collect the stored oocytes
- ❖ Maybe ovarian tissue cryopreservation will become an option in the future also fulfilling steroid producing capacity