# Women in Transplantation: History of Reproductive Medicine IVF Ovarian Tissue Reimplantation UTx

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5<sup>th</sup> Congress of the ISUTx Antalya, Turkey October 2-3, 2025

## Disclosures

## **FINANCIAL DISCLOSURES (during last 12 months)**

I am on the Advisory Board for Igyxos Biotherapeutics

I am on the organizing committee for IBSA Narture 2026

I receive honoraria from:

- Wolkers Kluwer
- Springer Verlag
- Elsevier
- Cambridge University Press

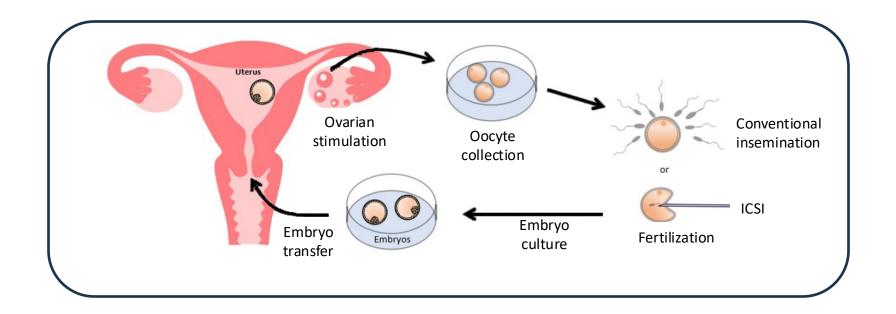
## Introduction

- History often highlights male pioneers
- Women have been (and continue to be!) central as scientists, clinicians and patients in so many fields, including:
  - ✓ In vitro fertilization (IVF)
  - ✓ Ovarian tissue reimplantation (OTR) and
  - ✓ Uterus transplantation (UTx)
- Aims:
  - ✓ To recognize key women and their contributions across IVF, OTR, and UTx
  - ✓ To inspire women to play key roles in their chosen field

## Cornerstones to clinical translation

- Research with animal models
  - To understand the physiology
  - To clarify the challenges
  - To provide enough evidence for potential efficacy
- To undertake proof-of-principle research to demonstrate potential clinical translation
- To be courageous enough to undertake the basic work to move towards clinical translation ......
- And then to perform the clinical translation

## The Road Towards Clinical IVF



## It was a long and difficult road .....

# 12 years, 280 oocyte retrieval attempts and 102 embryo transfers before the first success

### The very low efficiency was due to:

- Suboptimal culture conditions
- Challenges in harvesting the oocytes
- At best, only ~ 2 oocytes were retrieved (mean of 0.7 oocytes/retrieval)



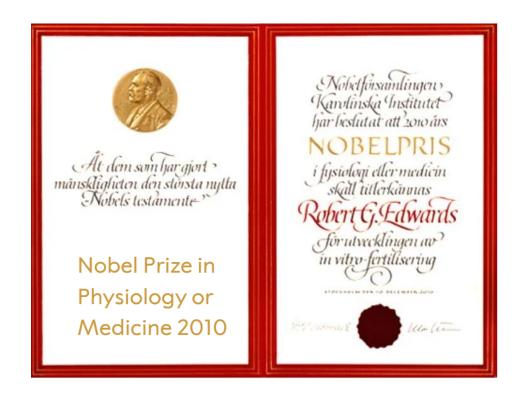


## The first clinical IVF success



Patrick C. Steptoe, MD 1913 - 1988

Robert G. Edwards, PhD 1924 - 2013



But there were many who preceded this success.....

## The Key Foundational Work

Achievement	Investigator(s)
Embryo transfer experiments in animals	Heape, 1891; Pincus & Enzmann, 1934; Chang, 1959
Embryo culture studies with in vivo and in vitro fertilized oocytes and transfer to surrogate animals	McLaren & Biggers, 1958; Whittingham, 1968
Advances in culture media to support preimplantation development in mice	Whitten, 1956; Brinster, 1963
Claim of in vitro fertilization of human oocytes	Rock & Menkin, 1944
Maturation of human oocytes in vitro	Edwards, 1965
Unequivocal demonstration of fertilization of human oocytes in vitro	Edwards, 1969
Laparoscopic recovery of human oocytes after gonadotropin priming	Steptoe & Edwards, 1970

## The Key Foundational Work

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Laparoscopic recovery of human oocytes after gonadotropin priming	Steptoe & Edwards, 1970

## Miriam Menkin: The first to successfully fertilize a human oocyte in vitro

## Miriam Menkin 1901-1992



- It took her 6 years of failure with 800 oocytes and 138 inseminated before her success ... in 1944
- Her success proved that clinical IVF might be feasible
- She was not admitted to medical school (Harvard) because she was a woman!

#### In Vitro Fertilization and Cleavage of Human Ovarian Eggs

John Rock, Miriam F. Menkin

Science, New Series, Volume 100, Issue 2588 (Aug. 4, 1944), 105-107.

## Dame Anne McLaren: A key trail-blazer towards clinical IVF!

## Dame Anne McLaren DBE, FRS, FRCOG

1927 –2007



- Foundational mouse embryo work for clinical IVF (with Professor John D. Biggers)
- The first female officer in the 330-year history of the Royal Society, London
- A member of the Warnock Committee who wrote the HFEA guidelines on IVF in 1990
- An inspiration to women in science breaking barriers and achieving numerous scientific honors

The Road to IVF: Dame Anne McLaren — Google Arts & Culture

## The first clinical IVF team was not just Steptoe and Edwards!

## The Steptoe-Edwards-Purdy Team



Patrick C. Steptoe, MD 1913 - 1988

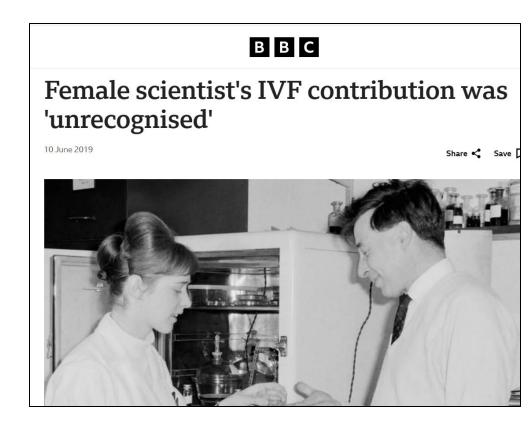
Robert G. Edwards, PhD 1924 - 2013

Jean M. Purdy, RN 1945 - 1985

## The first clinical IVF team was not just Steptoe and Edwards!

## The Steptoe-Edwards-Purdy Team

- Jean Purdy was a nurse who became the world's first "clinical" embryologist
- She kept the lab and clinical records meticulously and was essential to the team's success
- She worked with Bob for 20 years and remained a critical member of the team through all their failures before their first success.
- Yet, her role went unrecognized for decades



## The unfortunate history of plaques commemorating the IVF pioneers



A lapse of over 40 years





Royal Oldham Hospital: Overlooked IVF pioneer nurses honoured

## Other key women in the Steptoe-Edwards-Purdy success

Sister Muriel Harris 1923 - 2007



Operating theatre superintendent for 1st IVF team

**Lillian Howell 1921 - 2014** 



A wealthy Californian heiress, who provided considerable financial support for the work from 1968 - 1978

Ruth Fowler Edwards 1921 - 2014



Bob's remarkable wife, eminent scientist, geneticist and mother of five children

## Other key women in the Steptoe-Edwards-Purdy success

## Steptoe's nurses and midwives



## They were essential to IVF's early acceptance

- Provided care and reassurance amid social stigma
- Enabled patient trust in early IVF
- Contributed significantly to acceptance of IVF

## And all the women who were Patrick Steptoe's patients

- 282 women had consultations
- 280 underwent hormone stimulation and laparoscopy for their oocyte retrieval
- 7% underwent more than four retrievals
- Only 2 of these 282, the mothers of their first 2 IVF babies, are known:
   Leslie Brown and Grace McDonald



## Finally, Louise Brown: The first IVF baby (born July 25,1978)

- Her birth was a global turning point in reproductive medicine
- It changed public perceptions of assisted reproduction
- She is a symbol of hope for infertile couples worldwide
- She is currently an ambassador for Bourn Hall and for helping infertile couples in India





#### Netflix

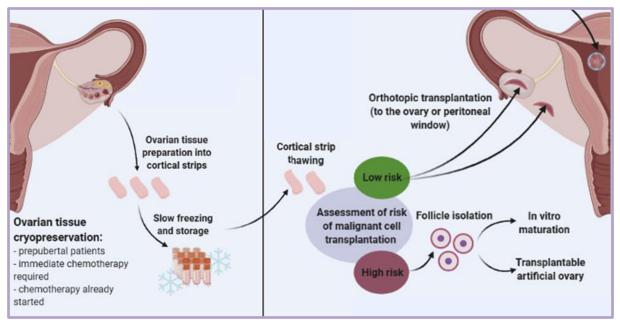
https://www.netflix.com > joy-release-date-cast-news

#### Joy Tells the Moving Story Behind the World's First 'Test ...

Nov 22, 2024 — Joy tells the remarkable true story behind the birth of Louise Joy Brown in 1978, the world's first "test-tube baby," and the tireless 10-year journey to make ...

Watch JOY - The Birth of IVF | Netflix Official Site

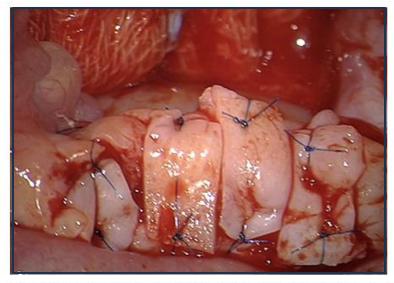
# The Road Towards Ovarian Tissue Reimplantation



Adapted from Dolmans et al. Fertil Steril 2021;115:1102–15

## Why are we discussing OTR – and the role of women in its development?

- Each year, an estimated 0.9 million prepubertal girls and young women require aggressive cancer treatment, which is gonadotoxic
- Survival is greater than 90% in most cases
- Live birth rate of ~30% post OTR¹
- What roles from basic science to clinical translation have women played in the landmark developments in this groundbreaking field?



Donnez J et al 2013; Fertil Steril 99:1503-13

## Dr. Ruth Deanesly: A woman scientist far ahead of her time!

#### Basic science research to clinical translation

# PROCEEDINGS OF THE ROYAL SOCIETY B

**BIOLOGICAL SCIENCES** 

1957

**Article** 

# Egg survival in immature rat ovaries grafted after freezing and thawing

R Deanesly

Published: 03 December 1957

https://doi.org/10.1098/rspb.1957.0060

#### **Abstract**

Immature rat ovaries grafted subcutaneously after freezing and thawing show a heavy loss of eggs. A number of variations in the freezing technique have been tried but have not led to any substantial increase in egg survival. Similarly treated ovaries may show a wide variation as grafts. Methods for estimating and comparing the effects of different freezing techniques on the eggs have been worked out.

## Dr. Debra Gook: A pioneer in cryopreservation of follicles & ovarian tissue



#### **Debra Gook**

Human Reproduction vol.14 no.8 pp.2061-2068, 1999

1999

Effect of cooling rate and dehydration regimen on the histological appearance of human ovarian cortex following cryopreservation in 1,2-propanediol

Debra A.Gook<sup>1,3,4</sup>, D.H.Edgar<sup>1,2</sup> and C.Stern<sup>1,2</sup>



2000



Molecular and Cellular Endocrinology 169 (2000) 99-103

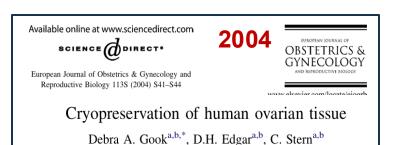
The effects of cryopreservation regimens on the morphology of human ovarian tissue

Debra A. Gook a,b,\*, D.H. Edgar a,c, C. Stern a,c

Human Reproduction Vol.16, No.3 pp. 417-422, 2001

Development of antral follicles in human cryopreserved ovarian tissue following xenografting 2001

Debra A.Gook<sup>1,3</sup>, B.A.McCully<sup>2</sup>, D.H.Edgar<sup>1,2</sup> and J.C.McBain<sup>1,2</sup>



## Dr. Christiani Amorim: A pioneer in cryopreservation of follicles & ovarian tissue



#### **Christiani Amorim**

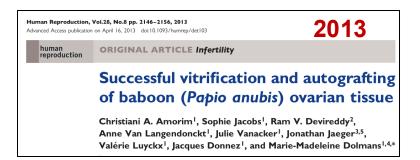


Vitrification of human ovarian tissue: effect of different solutions and procedures 2011

Christiani Andrade Amorim, V.M.D., Ph.D., Anu David, M.Sc., Anne Van Langendonckt, Ph.D., Marie-Madeleine Dolmans, M.D., Ph.D., and Jacques Donnez, M.D., Ph.D.

Department of Gynecology, Institut de Recherche Expérimentale et Clinique, Université Catholique de Louvain, Brussels, Belgium

Fertil Steril 2011;95(3):1094-7



J Assist Reprod Genet (2011) 28:1157–1165 **2011**DOI 10.1007/s10815-011-9672-z

#### FERTILITY PRESERVATION

Impact of freezing and thawing of human ovarian tissue on follicular growth after long-term xenotransplantation

Christiani A. Amorim · Anu David · Marie-Madeleine Dolmans · Alessandra Camboni · Jacques Donnez · Anne Van Langendonckt



2025

Human Reproduction, 2025, 40(3), 410-419

https://doi.org/10.1093/humrep/deae291 Advance Access Publication Date: January 2, 2025 Mini-Review

Developments in reproductive biology and medicine

Human ovarian tissue xenotransplantation: advancements, challenges, and future perspectives

Paweena Thuwanut<sup>1</sup>, Ellen C. R. Leonel<sup>2</sup>, Thalles Fernando Rocha Ruiz<sup>3,4</sup>, Porntip Sirayapiwat<sup>1</sup>, Stine Gry Kristensen (6), and Christiani A. Amorim (6)<sup>4,\*</sup>

## Dr. Kirsten Schmidt: A ground-breaker toward the clinical translation of OTR

#### **Kirsten Schmidt (Macklon)**





## Article February 2004

Orthotopic autotransplantation of cryopreserved ovarian tissue to a woman cured of cancer – follicular growth, steroid production and oocyte retrieval



Dr Kirsten L Tryde Schmidt graduated as a medical doctor from the University of Copenhagen in 1992. After some years of clinical work at various departments of obstetrics and gynaecology, she enrolled in a PhD programme on cryopreservation of human ovarian tissue at the University Hospital of Copenhagen, Rigshospitalet, Denmark. Her research also includes culture of ovarian tissue. After obtaining her PhD she hopes to continue her clinical work with special attention to the field of infertility treatment.

Kirsten L Tryde Schmidt<sup>1,2,4</sup>, Claus Yding Andersen<sup>2</sup>, Jørgen Starup<sup>3</sup>, Anne Loft<sup>1</sup>, Anne Grete Byskov<sup>2</sup>, Anders Nyboe Andersen<sup>1</sup>

The first documentation that cryopreserved transplanted ovarian tissue was functional for more than 1 cycle and produced a mature oocyte

## Dr. Marie-Madeleine Dolmans: A key pioneer in OTR

#### **Marie-Madeleine Dolmans**



## Livebirth after orthotopic transplantation of cryopreserved ovarian tissue September 2004



J Donnez, M M Dolmans, D Demylle, P Jadoul, C Pirard, J Squifflet, B Martinez-Madrid, A Van Langendonckt

Published online September 24, 2004

Donnez J, Dolmans MM, Demylle D, Jadoul P, Pirard C, Squifflet J, Martinez-Madrid B, Van Langendonckt A. Livebirth after orthotopic transplantation of cryopreserved ovarian tissue. The lancet. 2004 Oct 16;364(9443):1405-10.

## Dr. Marie-Madeleine Dolmans: A key pioneer in OTR



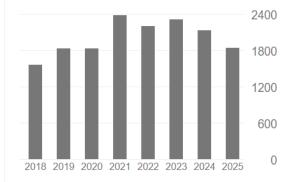
#### **MM Dolmans**

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<u>Université catholique de Louvain, Brussels,</u> Belgium Verified email at uclouvain.be - <u>Homepage</u> infertility fertility preservation fibroids endometriosis

TITLE	CITED BY	YEAR
Livebirth after orthotopic transplantation of cryopreserved ovarian tissue J Donnez, MM Dolmans, D Demylle, P Jadoul, C Pirard, J Squifflet, The lancet 364 (9443), 1405-1410	2229	2004
Uterine fibroid management: from the present to the future J Donnez, MM Dolmans Human reproduction update 22 (6), 665-686	1023	2016
Fertility preservation in women J Donnez, MM Dolmans New England Journal of Medicine 377 (17), 1657-1665	925	2017
Restoration of ovarian activity and pregnancy after transplantation of cryopreserved ovarian tissue: a review of 60 cases of reimplantation  J Donnez, MM Dolmans, A Pellicer, C Diaz-Garcia, MS Serrano,  Fertility and sterility 99 (6), 1503-1513	703	2013
Ovarian tissue cryopreservation and transplantation: a review J Donnez, B Martinez-Madrid, P Jadoul, A Van Langendonckt, D Demylle, Human reproduction update 12 (5), 519-535	600	2006

#### Citations 25,267 H-index 81



Public access	VIEW ALL
25 articles	109 articles
not available	available
Based on funding mandates	

## Dr. Teresa K. Woodruff: A champion for oncofertility!!!



#### Teresa K. Woodruff

#### Oncofertility: a grand collaboration between reproductive medicine and oncology

TK Woodruff - Reproduction, 2015 - rep.bioscientifica.com

There has never been a greater need for scientists trained in reproductive science. Most developed countries are witnessing unprecedented rates of recourse to assisted conception ...

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#### The Oncofertility Consortium—addressing fertility in young people with cancer

TK Woodruff - Nature reviews Clinical oncology, 2010 - nature.com

... Late on a Friday afternoon, the Oncofertility Consortium national helpline (Fertline) received a call from a pediatric **oncologist** with an urgent request. His patient was a girl of high-school ...

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#### The emergence of a new interdiscipline: oncofertility

TK Woodruff - Oncofertility fertility preservation for cancer survivors, 2007 - Springer

... girls diagnosed with cancer, means most medical **oncologists** do not discuss potential threats

to ... Woodruff was part of a panel including a patient advocate (Lindsay Nohr-Beck, Founder ...

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#### Incorporating fertility preservation into the care of young **oncology** patients

AJ Redig, R Brannigan, SJ Stryker, TK Woodruff... - Cancer, 2011 - Wiley Online Library

... care offered to younger **oncology** patients to include discussions ... **oncologists**, radiation **oncologists**, and medical **oncologists** ... **oncology** practice to enhance the lives of cancer survivors. ...

# The Road Towards Clinical Uterus Transplantation

## The first successful live birth following UTx (2014)

## Achieved by the fabulous team led by Professor Mats Brannstrom!!

## Livebirth after uterus transplantation



Mats Brännström, Liza Johannesson, Hans Bokström, Niclas Kvarnström, Johan Mölne, Pernilla Dahm-Kähler, Anders Enskog, Milan Milenkovic, Jana Ekberg, Cesar Diaz-Garcia, Markus Gäbel, Ash Hanafy, Henrik Hagberg, Michael Olausson, Lars Nilsson

#### Summary

Background Uterus transplantation is the first available treatment for absolute uterine infertility, which is caused by absence of the uterus or the presence of a non-functional uterus. Eleven human uterus transplantation attempts have been done worldwide but no livebirth has yet been reported.

Lancet 2015; 385: 607-16
Published Online
October 5, 2014
http://dx.doi.org/10.1016/

## However, the first UTx was actually performed by a woman in 2000



**Dr. Wafa Fageeh**, a professor at Abdulaziz University, performed the first UTx in Apri 2000 at King Fahad Hospital and Research Center in Jeddah, Saudi Arabia but the graft had to be removed after 99 days due to a vascular occlusion

### **April 2000**



International Journal of
GYNECOLOGY
& OBSTETRICS

International Journal of Gynecology & Obstetrics 76 (2002) 245-251

www.elsevier.com/locate/ijgo

#### Case report

#### Transplantation of the human uterus

W. Fageeh\*, H. Raffa, H. Jabbad, A. Marzouki

Multiorgan Transplant Unit, King Fahad Hospital and Research Center, Jeddah, Saudi Arabia

Received 30 October 2000; received in revised form 30 October 2001; accepted 10 November 2001

#### Abstract

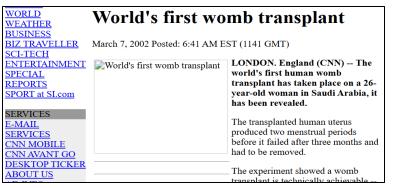
Human uterine transplantation was performed on 6 April 2000 on a 26-year-old female who lost her uterus 6 years earlier due to post-partum hemorrhage. The donor, a 46-year-old patient with multiloculated ovarian cysts, underwent a hysterectomy modified to preserve tissue and vascular integrity. The donor uterus was connected in the

## The press was appropriately excited!









However, there were controversies surrounding the animal experimentation performed by this team, the lack of ethical approvals obtained and the reasons for graft failure. A lapse of 13 years followed ...

# Clinical pregnancy after uterus transplantation

Munire Erman Akar, M.D.,<sup>a</sup> Omer Ozkan, M.D.,<sup>b</sup> Batu Aydinuraz, M.D.,<sup>c</sup> Kerem Dirican, Ph.D.,<sup>c</sup> Mehmet Cincik, M.D.,<sup>d</sup> Inanc Mendilcioglu, M.D.,<sup>a</sup> Mehmet Simsek, M.D.,<sup>a</sup> Filiz Gunseren, M.D.,<sup>e</sup> Huseyin Kocak, M.D.,<sup>f</sup> Akif Ciftcioglu, M.D.,<sup>g</sup> Omer Gecici, M.D.,<sup>h</sup> and Ozlenen Ozkan, M.D.,<sup>b</sup>

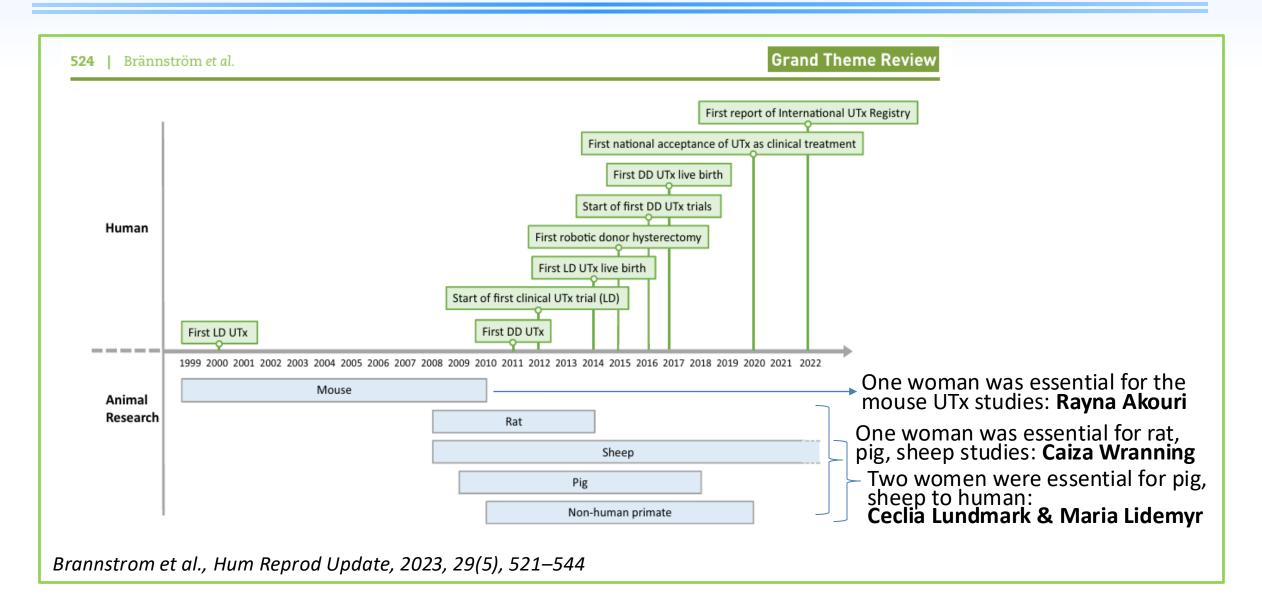
2 of the 12 authors were women

# Preliminary results of the first human uterus transplantation from a multiorgan donor

Omer Ozkan, M.D.,<sup>a</sup> Munire Erman Akar, M.D.,<sup>b</sup> <u>Ozlenen Ozkan, M.D.</u>,<sup>a</sup> Okan Erdogan, M.D.,<sup>c</sup> <u>Necmiye Hadimioglu, M.D.</u>,<sup>d</sup> Murat Yilmaz, M.D.,<sup>d</sup> <u>Filiz Gunseren, M.D.</u>,<sup>e</sup> Mehmet Cincik, M.D.,<sup>f</sup> <u>Elif Pestereli, M.D.</u>,<sup>g</sup> Huseyin Kocak, M.D.,<sup>h</sup> Derya Mutlu, M.D.,<sup>l</sup> <u>Ayhan Dinckan, M.D.</u>,<sup>d</sup> Omer Gecici, M.D.,<sup>j</sup> <u>Gamze Bektas, M.D.</u>,<sup>b</sup> and Gultekin Suleymanlar, M.D.

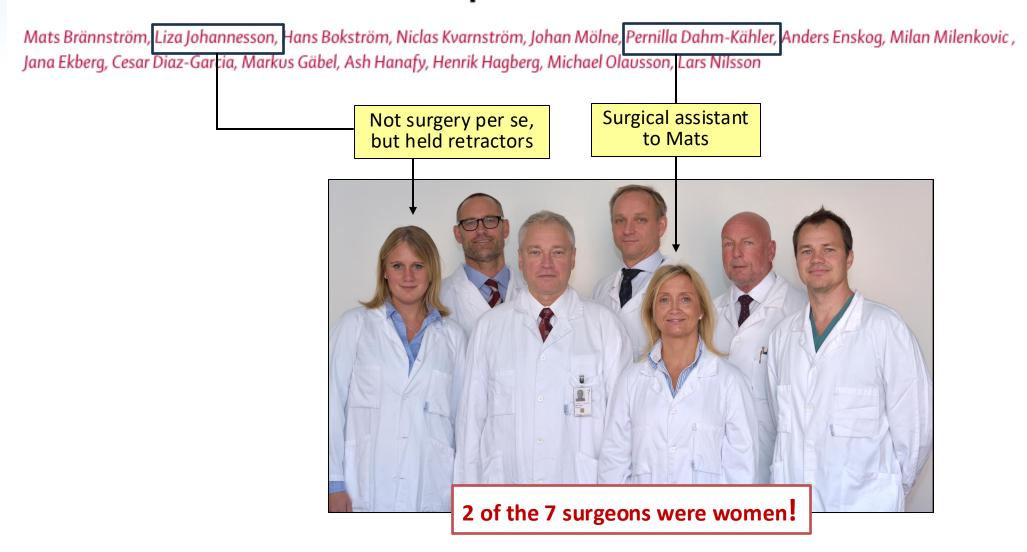
6 of the 15 authors were women

## Meanwhile critical foundational research with animal models was underway



## Livebirth after uterus transplantation





## Several of the OR nurses and surgical support staff were women!



## Now look where we are today .... at least 10 key women in UTx!!



Rayna Akouri



**Past President** Sara Brucker

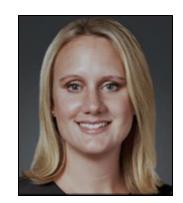




Marie Carbonnel Permilla Dahm Kähler



Rebecca Dean



Liza Johannassen



Ozlenen Ozkan



**President Paige Porrett** 



**Katharina Rall** 



**Padmapriya Vivek** 

## Reflections and legacies

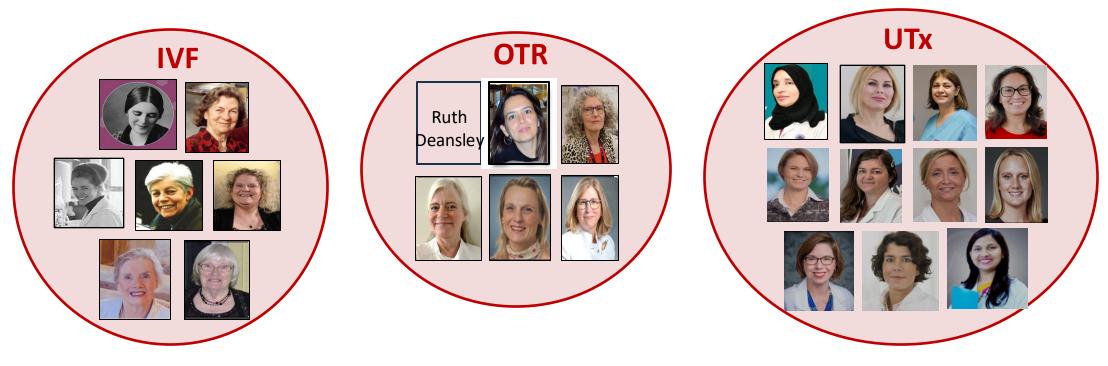
- Women's contributions were, and still are, essential in these remarkable fields but were often previously overlooked
- We must always appreciate the vital role of support staff





## Reflections and legacies

• In all 3 of the fields we've discussed, women's roles have spanned laboratory, clinical care, and patient advocacy. Their legacy continues to inspire.



And we must not forget all the women patients who had the courage to participate in the pioneering work, often not for themselves, but to give hope to other women with similar medical problems