In Memoriam: Dr. Ryuzo “Yana” Yanagimachi

Hidenori Akutsu

Center Regenerative Medicine, National Center for Child Health and Development, Japan

We deeply mourn the passing of the distinguished scientist, Dr. Ryuzo Yanagimachi, a luminary in the realm of reproductive biology. Dr. Yanagimachi's pioneering work has profoundly influenced a multitude of researchers. He departed on September 27, 2023, leaving behind a legacy at the age of 95. Among his myriad accomplishments, he is celebrated for his innovative advancements in mammalian fertilization and seminal techniques like ICSI (Intracytoplasmic Sperm Injection). These methodologies have been adopted by infertility clinics across the globe. His seminal work on "in vitro" fertilization of hamster eggs set the trajectory for his lifelong dedication to research.

Dr. Yanagimachi's spectrum of achievements is vast, and he remained a relentless beacon of inspiration for researchers, medical practitioners, and the emerging generation. Throughout his distinguished career, he consistently championed the cause of budding scientists, mentoring them and serving as a wellspring of inspiration.

Reflecting on Dr. Yanagimachi's monumental contributions, it becomes evident that he has etched an indelible legacy in reproductive biology. Beyond his scientific breakthroughs, he stood as a paragon of mentorship and inspiration. His unwavering dedication to the discipline was paralleled only by his fervor to cultivate the forthcoming generation of scientists. Colleagues privileged to collaborate with him frequently lauded his humility, benevolence, and steadfast support. Dr. Yanagimachi was more than a scientist; he was a beacon of hope and a stalwart pillar for the broader scientific fraternity. His enduring legacy transcends his scientific discoveries, resonating in the myriad lives he enriched and galvanized throughout his eminent career.

Biography

Hidenori Akutsu, M.D., Ph.D. is a director of the Center for Regenerative Medicine at the National Center for Child Health and Development (NCCHD) in Tokyo, Japan. He has experienced human ES cells (hESCs) derivation work since 2004. As a member of the hESCs derivation team at the NCCHD, they have successfully generated eight hESC lines in Japan. One of the ESC lines was successfully used in the world-first liver cells from hESCs in transplant as a first-in-baby clinical trial.
He is also engaging in bioethical governance in Japan and is a member of Expert Panel on Bioethics, Council for Science and Technology Innovation of Japan and also a Secretary of the Committee on Genome Editing Technology in Medical Sciences and Clinical Applications of the Science Council of Japan. He is also a member of the International Commission of on the Clinical Use of Germline Genome Editing. Akutsu received his M.D. from Hirosaki University and completed his clinical training in obstetrics gynecology at Fukushima Medical University. He completed his Ph.D. at Fukushima Medical University School of Medicine.

Truth Telling in Reproductive Medicine

Robert J Norman

Robinson Research Institute, The University of Adelaide, Australia

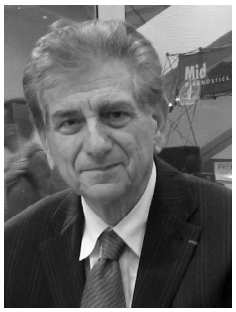
Reproductive medicine is a unique branch of health care in that we usually deal with healthy younger patients who are frustrated and distressed by a failure to achieve their ambitions in terms of achieving a family. They face a bewildering array of choices in terms of options to investigate and treat their condition and the outcome is not guaranteed. In addition, the clinical interactions are often expensive and open-ended in terms of financial obligations. This can often cause frustration, anger and emotional distress. Added to that are the peculiar ethical, moral and religious concerns of society and individuals.

In the early days of reproductive medicine, our attitudes were often patriarchal, and communication clouded by scientific and clinical uncertainty. Several high-profile instances of poor behaviour from clinical leaders resulted and that led to suspicion from some quarters of the community. These days patients are seen as consumers who demand delivery of an expensive service to their requirements and with full informed consent. We are often seen as reproductive “waiters" delivering items from a reproductive menu, often added to by the patients we see.

Our challenge is to remain professionals amidst a discipline that has succumbed to marketing pressures from commercialisation. We have demands for full information from some patients while others do not seek full knowledge. There are many varied implications for treatment and advice dependent on personality, ethnic and family background and identity group. We have often departed as a profession from our professional training and lapsed into becoming marketeers for our business. In this talk I plead for us to rediscover our skills as health professionals in an industry that has occasionally deviated from medical dedication and calling.

Biography

Robert Norman is an Emeritus Professor of Reproductive and Periconceptual Medicine at the University of Adelaide and was the Founding Director of the Robinson Research Institute, which is one of the largest and most prestigious research organisations covering health from before birth to adulthood. He is a subspecialist in reproductive medicine of the Royal Australia New Zealand College of Obstetrics and Gynaecology, a Fellow of the Australian Academy of Health and Medical Sciences and has received the top awards in his field from Europe, the USA and Asia. He was the medical director of two fertility groups, Repromed and FertilitySA. He graduated from the medical school in Harare, Zimbabwe and has worked in Durban, South Africa and London.



IVF & Prof. Robert G. Edwards

Victor Gomel

University of British Columbia, Canada

Biography

Dr. Gomel holds the rank of **Professor Emeritus** in the Department of Obstetrics and Gynecology, University of British Columbia. He served as Chairperson of his Department for fifteen years, during which the Department was greatly expanded and attained international recognition.

He is internationally known for his **pioneering work in both gynecologic microsurgery and operative laparoscopy**. With his team, their IVF program was the first to achieve success, resulting in the birth (on December 25, 1983) of **the first IVF baby in Canada.**
Dr. Gomel authored a long list of scientific articles published in prestigious international journals, numerous book chapters and several books. A new updated edition of his book ***"Reconstructive and Reproductive Surgery in Gynecology"*** was published in 2019.

He has received *honorary memberships* and *awards of excellence* from numerous international scientific societies and universities, including his own Faculty of Medicine, in recognition of his pioneering work in reproductive medicine and gynecologic surgery.

Professor Gomel was also the recipient, of the prestigious distinction of ***Chevalier*** of the order of ***Légion d'Honneur***, awarded by ***Jacques Chirac, President of France*** in 2003. In 2008, he was elected ***"Fellow"*** to the ***World Academy of Art and Science***, and in 2009 he received the degree of ***Doctor of Science, Honoris causa***, from the *Simon Fraser University*. He has been awarded ***"Honorary Membership"*** by the *European Society of Human Reproduction & Embryology* (ESHRE) in 2012 and the AAGL in 2015. In 2013 he was awarded the prize ***"Jacques Salat-Baroux"*** in reproduction from the *"National Academy of Medicine of France."* He has since been elected as foreign member to the same academy. He was awarded the rank of ***Professor Honoris causa*** by the *National Medical Research Center for Obstetrics*, *Gynecology and Perinatology of the Russian Federation*, and in 2018 he received the medal of ***the Order of Valor*** *from the Government of Cameroon*.

Reconstitution of Gametogenesis Using Pluripotent Stem Cells

Katsuhiko Hayashi

Department of Genome Biology, Graduate School of Medicine, Osaka University, Japan

The reconstitution *in vitro* of oogenesis using pluripotent stem cells, which eventually produces functional oocytes, has long been sought in reproductive biology and developmental biology, since it would contribute to not only a better understanding of mechanisms underlying totipotency, but also an alternative source of gametes for reproduction. So far, we developed culture systems that induce primordial germ cells, oocytes and female gonadal somatic cells from mouse pluripotent stem cells, such as embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs). By using these systems, it becomes possible to produce functional eggs from ESCs/iPSCs entirely in culture without a need of embryonic cells. These culture systems are extremely useful, as genetic function in not only germ cells but also surrounding somatic ells can be easily and swiftly evaluated in culture. In ISIVF 2023, I will update recent advances in reconstitution of gametogenesis and gonadogenesis using pluripotent stem cells.

Biography

2021-Present	Professor, Graduate School of Medicine, Osaka University.
2014-2021	Professor, Graduate School of Medical Sciences, Kyushu University.
2009-2014	Associate professor, Graduate School of Medicine, Kyoto University.
2005-2009	Post-doctoral fellow, the Gurdon institute, University of Cambridge.
2002-2005	Staff researcher, Osaka Medical Center.
1996-2002	Assistant professor, Tokyo University of Science.

Current Advancements in Regenerative Medicine

Kwang-Yul Cha

CHA Stem Cell Institute, CHA University, CHA Health Systems, Korea

Since the establishment of human embryonic stem cells (ESCs) in 1998, ESCs are the gold standard for pluripotent stem cells (PSCs) and have been used in research on differentiation into various cells such as retina pigment epithelium (RPE), neurons, pancreatic cells, and cardiomyocytes. Lately, stem cell R&D field is aggressively developing in two directions, basic research as well as translational clinical application, simultaneously. By adding the advanced new technology to the PSCs would become a powerful tool for finding new possibilities in overcoming aging process, new type of stem cells, new methods for curing disease, and new paths for evolving the regenerative medicine.

The PSCs could also be generated by reprogramming somatic cells using induced pluripotent stem cell (iPSC) and somatic cell nuclear transfer (SCNT) technologies developed in 2007 and 2013, respectively, and research using these cells expanded to include disease models and drug screening. Although attempts are being made to generate iPSCs similar to ESCs, increased epigenetic memories and aberrations still emerge and more comparative thorough studies are required. Particularly, in the embryonic field, ESCs are the main source of cells due to their blastocyst origin. In fact, ESC-derived oocytes in mouse and synthetic embryo models in mouse and human have been generated.

Recently, research on anti-aging has been conducted in various fields such as transfusion of young blood, cell reprogramming, and the use of existing drugs. Premature ovarian insufficiency (POI) is a disease in which the ovaries stop functioning prematurely and the clinical trials in POI using stem cells from various sources, such as cord blood stem cells, bone marrow, or adipose-derived stem cells, have been conducted continuously since 2011, and additionally using platelet-rich plasma (PRP) recently.

For the details in every issue, I would like to share the progress about recent advanced regenerative medicine.

Biography

Dr. Kwang-Yul Cha is the chair of CHA Global Institute for Bioscience and founder of CHA Biomedical Group, a global healthcare enterprise in Korea which owns and operates 90 medical centers and clinics and 15 bio-companies in 7 countries. As a physician-scientist, he achieved World's first IVF babies-delivery via in-vitro maturation of the immature oocytes (IVM), human oocyte/embryo cryopreservation by vitrification, and establishment of cloned stem cell lines using adult somatic cells. World's first IVM baby in human was featured in many famous reproductive medicine books including NOVAK. His achievements including the establishment of the first Egg-Baking were featured in TIMES magazine three times. He also published many medical reviews and over 200 peer-reviewed journal articles. He is also one of the founders of Asia's first and most notably recognized academic society –Pacific Society for Reproductive Medicine.

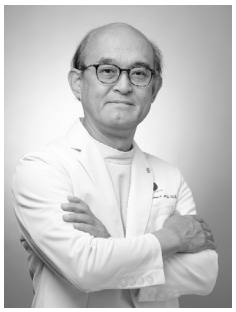
Regenerative Medicine in Infertility Treatment: Revolutionizing Reproductive Medicine

Kamthorn Pruksananonda

Chulalongkorn University, Thailand

Introduction
Traditional treatment options for infertility have limitations, necessitating the exploration of innovative approaches. Regenerative medicine, with its remarkable potential to restore and replace damaged tissues and organs, is emerging as a groundbreaking field in reproductive healthcare. By harnessing the power of stem cells, tissue engineering, and other regenerative techniques, this rapidly advancing discipline is revolutionizing the landscape of infertility treatment.
Material & Methods
Regenerative medicine encompasses a range of techniques aimed at regenerating, repairing, or replacing damaged tissues and organs. At its core lies the utilization of stem cells, which possess the unique ability to self-renew and differentiate into various cell types. These cells can be derived from different sources, including embryonic stem cells, adult stem cells, and induced pluripotent stem cells (iPSCs). In addition to stem cells, tissue engineering techniques and biomaterials are employed to create functional tissues or organs, providing a comprehensive approach to regenerative medicine, such as:
Male Infertility
Regenerative medicine offers promising solutions by targeting the restoration of sperm production using stem cells. Researchers have successfully derived sperm-like cells from pluripotent stem cells in laboratory settings, opening doors for future clinical applications. Regenerative techniques could potentially reverse the effects of testicular damage caused by cancer treatments or genetic abnormalities.
Female Infertility
Ovarian regeneration through stem cell-based approaches offers hope for restoring ovarian function and hormone production. Studies have demonstrated successful generation of functional oocytes and restoration of fertility in animal models, paving the way for future human applications. Furthermore, regenerative techniques may enable the regeneration of the uterine lining, providing solutions for women with uterine factor infertility or recurrent implantation failure.
Assisted Reproductive Technologies (ART)
Regenerative medicine complements and enhances existing ART procedures. It can improve the success rates of embryo implantation by optimizing the uterine environment through tissue regeneration and improving the quality of gametes through stem cell interventions. These advancements have the potential to significantly enhance the outcomes of ART procedures.
Results
While regenerative medicine in infertility treatment holds immense promise, several challenges lie ahead. Further research is required to optimize the safety and efficacy of regenerative techniques and to establish long-term outcomes. Clinical trials and collaboration among scientists, clinicians, and regulatory bodies are crucial to advance this field. Additionally, accessibility and affordability of regenerative treatments need to be addressed to ensure equitable distribution of these innovative therapies.
Conclusion
Regenerative medicine is ushering in a new era in infertility treatment, revolutionizing reproductive medicine. Stem cells, tissue engineering, and regenerative techniques offer novel solutions to address the complexities of male and female infertility. By harnessing the potential of regenerative medicine, we can envision a future where infertility is treated with greater success rates, improved patient experiences, and enhanced emotional well-being. Continued research, ethical considerations, and collaboration are key to realizing the full potential of regenerative medicine in revolutionizing reproductive healthcare and bringing hope to millions of individuals and couples worldwide.

Biography
Dr. Kamthorn Pruksananonda is a distinguished Professor of ObGyn at Chulalongkorn University in Bangkok. He has held prominent roles, including the Chairman of the Reproductive Medicine at the Royal Thai College of ObGyn. Currently, he serves on the Advisory Board for Reproductive Health Policy at the Ministry of Public Health and the National Committee for Reproductive Medicine in Thailand.
At the University, he leads the IVF Unit, Reproductive Medicine Division, and Embryonic Stem Cells Research Center. His research focuses on epigenetics in human reproduction, assisted reproductive technology.
He has been recognized with several prestigious awards, including the Rockefeller Foundation Fellowship, AOFOG's Young Gynaecologist Award, and National Research Award 2021 from the National Research Council.



Mitochondria Strategy in Reproduction - Cell Engineering and Holistic Approach

Yoshiharu Morimoto

President, ISIVF, Japan

Introduction

The most troublesome cases in the front line of reproductive medicine are patients who repeat IVF trials due to poor oocyte quality. Clinicians consider taking some approaches to solve the issue. They may change the ovarian stimulation protocols. They have options to select natural cycles, mild stimulation cycles, or other types of hyperstimulation methods. They may choose the GnRH agonist, antagonist method, or PPOS. Otherwise, they change culture medium or conditions. However, those efforts mostly fail and repeat more failures. Herein we propose other options: cell engineering and holistic methods that may enhance mitochondrial competence.

Material and Methods

We have tried two strategies such as cell engineering and holistic approach.

As the former, we have conducted mitochondrial transfer. We transferred autologous mitochondria extracted from oogonial stem cells to mature oocytes with sperm at intracytoplasmic sperm injection in 52 patients with recurrent failures (average 5.3 times). We assessed embryo quality using the following three methods: good-quality embryo rates, transferable embryo rates, and a novel embryo-scoring system (embryo quality score; EQS) in 33 patients who meet the preset inclusion criteria for analysis. The mitochondrial transfer using oogonial stem cells was an effective measure for patients with recurrent pregnancy failures, however, it needed laparoscopy and cost. Therefore, we conduct experimental research to improve this method using mice. We are trying to change the source of mitochondria from oogonial stem cells to adipose stem cells.

As the latter, we provide patients with several holistic procedures to improve the oocyte/ embryo quality. To reduce the mental stress that is a problem in infertility patients, we provide psychological counseling, autogenic training, and hypnotherapy by reproductive psychologists. Also, patients take oxidative stress measurement and counseling by the nutritionist. Appropriate supplements are instructed to match their purposes. As adjuvant therapies, patients can take acupuncture, low-level laser therapy, aromatherapy and foot massage.

Results

By the autologous mitochondrial transfer into mature oocytes, the good-quality embryo rates, transferable embryo rates, and EQS significantly increased, resulting in 13 babies born in normal conditions. Autologous mitochondrial transfer harvested from adipose stem cells in mice significantly improved embryo quality and ATP production. The new type of mitochondria transfer to oocytes would be an effective option for patients with recurrent pregnancy failure. The holistic approach showed effective results in patients to enhance the quality of embryos.

Conclusions

Mitochondrial transfer into human oocytes is an effective clinical option to enhance embryo quality in recurrent in vitro fertilization- failure cases. An alternative source of mitochondria from adipose tissues may be a preferable option considering the patient's burden. As adjuvant therapies, a holistic approach should be proactively induced.

Biography

Yoshiharu Morimoto M.D., Ph.D. is an internationally recognized clinician, researcher, educator and pioneer in the field of reproductive medicine and biology. He is the CEO of IVF Japan Group consisted of 3 clinics: HORAC Grand Front Osaka Clinic, IVF Osaka Clinic, and IVF Namba Clinic. He started to offer and spread a new idea of integrated medical method to the world and his cutting-edge technology "AUGMENT (Autologous Germline Mitochondrial Energy Transfer)" has been introduced for intractable patients. These active scientific works have enabled him to treat more than 2 million patients so far with a high pregnancy success rate.

Endoplasmic Reticulum Stress: a Key Regulator of the Follicular Microenvironment in the Ovary

Miyuki Harada

The University of Tokyo, Japan

Endoplasmic reticulum stress (ER stress) is defined as a condition in which unfolded or misfolded proteins accumulate in the ER because of an imbalance in the demand for protein folding and the protein-folding capacity of the ER. ER stress results in the activation of several signal transduction cascades, collectively termed the unfolded protein response (UPR), which affect and regulate various cellular functions. In principle, the UPR exists to restore homeostasis and keep the cell alive. However, if the ER stress cannot be resolved, the UPR induces programmed cell death.
Recent studies have revealed diverse roles of ER stress in physiological and pathological conditions in the ovary, as a local factor of follicular microenvironment. In this talk, I'll share with you our finding elucidating the role of ER stress in pathophysiology of polycystic ovary syndrome (PCOS). We demonstrated for the first time that ER stress pathways are activated in the granulosa cells of both a mouse model of PCOS and in humans (Sci Rep. 2017). We also found that local hyperandrogenism in the follicular microenvironment of PCOS is an activator of ER stress in human granulosa cells (Endocrinology. 2019). Activated ER stress contributes to the pathophysiology of PCOS, including interstitial fibrosis, follicular growth attest and ovulatory dysfunction, through multiple functional alterations in granulosa cells (Reviewed in Ref. 1 to 3). Furthermore, I'll discuss with you the clinical and translational implications of these findings, with the most recent findings from our laboratory.

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Biography

Miyuki Harada, M.D., Ph.D., is an Associate Professor of the Department of Obstetrics and Gynecology, Graduate School of Medicine, at the University of Tokyo. She is a board-certified specialist in Obstetrics/Gynecology, Reproductive Science, Women's Health, and Laparoscopic Surgery. Dr. Harada received her degrees, M.D. and Ph.D., from the University of Tokyo. Her postdoctoral training included a fellowship at Prof. KMJ Menon Lab in ObGyn/Biochemistry, Medical School, at University of Michigan in Ann Arbor, USA. Her research goal is to overcome ovarian dysfunction caused by various environmental and/or chronological insults and to provide preconception care targeting ovarian function. Her basic science research has focused on follicular microenvironment regulating ovarian pathophysiology including PCOS, chemotoxicity, and ovarian aging. Recently, she has also been interested in gut microbiome in these pathologies. She has published 154 articles, including 12 reviews, as of Aug 2023.

Improving Mitochondria in the Ovarian Stroma, Granulosa Cells and Gametes to Restore Embryo Development and Fertility

Rebecca Robker

The University of Adelaide, Australia

Aging and obesity cause female subfertility, and as age of childbearing and obesity rates increase globally, it is essential to understand the molecular defects underpinning these changes. We have completed a series of studies investigating whether mitochondrial dysfunction is an underlying cause of ovarian decline in response to obesity and aging, which cell types are most impacted and whether mitochondrial defects can be reversed to improve female fertility.

Using mouse models, we identified that fibrosis within the ovarian stromal compartment is initiated by mitochondrial dysfunction leading to diminished bioenergetics, oxidative damage, inflammation and collagen deposition. Further, anti-fibrosis drugs reduce oxidative damage, eliminate fibrotic collagen and restore ovulation in reproductively old and obese mice. This is the first evidence that ovarian fibrosis is reversible and indicates that drugs targeting mitochondrial metabolism may be a viable therapeutic strategy for women with metabolic disorders or advancing age to maintain ovarian function and extend fertility.

Secondly, we mapped energy metabolism dynamics (mitochondrial respiration, glycolysis, fatty acid oxidation and ATP production) in mouse granulosa cells and cumulus-oocyte complexes (COCs), across a detailed timecourse in the lead up to ovulation, and examined the effects of obesity and age. The metabolic dynamics of human granulosa cells from infertility patients with normal or abnormal ovarian function were also analyzed. Overall, we found dynamic increases in multiple energy metabolism pathways in response to the LH-surge in key ovarian follicle cells. Mitochondrial respiration and glycolysis were impaired with obesity and aging, in granulosa cells of both mice and women, providing new insights into the cellular mechanisms of subfertility, and demonstrating specific metabolic perturbations that are associated with poor oocyte quality.

Lastly, we investigated a new therapeutic to better support the critical early stages of embryo development. Treatment of male or female gametes in vitro with the small molecule BGP-15, a known inhibitor of mitochondrial stress, improved gamete quality and embryo developmental potential in mice and humans. Aging or obesity impaired both oocyte mitochondrial function and pre-implantation embryo development after IVF. Critically, however, treating these oocytes with BGP-15 during maturation, fertilization and/or embryo culture normalized oocyte maturation and embryo development. BGP-15 treatment of non-human primate and human embryos demonstrated normal development and, in human oocytes, BGP-15 decreased chromosomal misalignment. In male mice, aging-induced decreases in sperm quality and poor embryo development were improved by treating spermatozoa with BGP-15 prior to IVF. In men, BGP-15 treated spermatozoa exhibited increased motility and reduced DNA damage. Thus BGP-15 can repair damage to both male and female gametes that is caused by oxidative stress, age or obesity.

Overall, these studies investigating mitochondrial defects in the ovary shed new light on the normal metabolic processes and how they are impacted by aging and obesity, and provide promising new candidate therapies for assisted reproduction therapy.

Biography

Prof. Rebecca Robker is a biomedical scientist whose vision is to improve health of women and children by discovering how the ovary generates oocytes and then releases them for fertilisation and the creation of a new individual. Her work is also uncovering cellular mechanisms by which different maternal physiological signals, such as obesity and age, affect ovarian function, and early embryo development. Her lab team is based within the University of Adelaide's Robinson Research Institute, where she is a Leader of the Early Origins of Health Theme, which is identifying biological mechanisms by which events in early life, including at conception, influence lifetime health.

Effects of Time-restricted Feeding on Fertility Competence in Female Mice

Shu Hashimoto

Reproductive Science, Graduate School of Medicine, Osaka Metropolitan University, Japan

Introduction
Our current lifestyle has led us to eating at inappropriate times or irregular hours and erratic patterns of eating, increasing the risk of chronic diseases, including cancer, cardiovascular diseases, infertility, and other related chronic conditions.

Material & Methods
Here, we examined the effects of feeding regimen (ad libitum vs. time-restricted food access) and type of food (normal chow (NC: 12% fat) vs. moderately high calorie diet (mHCD: 31% fat)) on oocyte quantity and quality of female mice.

Results
Mice fed mHCD had higher number of oocytes than mice fed NC. On the other hand, when mice were fed NC under time-restricted access to food (NT), the blastulation rate per normally-fertilized ova was significantly decreased compared to others. The reactive oxygen species (ROS) level in oocytes increased in time-restricted food access and NC group. Transcriptome analysis of whole ovarian tissues from these mice showed a change in the cholesterol metabolism among the 4 groups. Time-restricted food access decreased serum LDL cholesterol level. Moreover, the number of atretic follicles increased in NT mice compared to ad libitum food access mice.

Conclusions
The data of the present study shows that mHCD feeding increases the number of antral follicles and ovulated oocytes and that time-restricted feeding of NC impairs the development of oocytes after fertilization, probably due to the changes in serum cholesterol levels and an increase in the ROS content in oocytes.

Biography

Dr. Hashimoto obtained his PhD in Reproductive Physiology at Kyoto University in 2001.
He developed assisted reproduction technology in cattle at Snow Brand Milk Products and in human at IVF Namba Clinic. Currently, he is the professor of Osaka Metropolitan University Graduate School of Medicine. He received the JSAR innovative technology Award in 2008, the Japanese Society of Mammalian Ova Research outstanding presentation Award in 2009, 2014 and 2020, the memorial award of World Congress on In Vitro Fertilization in 2015, and the ASRM Star Award in 2016-2019.

Lifestyle, Reproduction, and Health: Unveiling Pathways for Enhanced Maternal and Offspring Well-being

Svend Lindenberg

Copenhagen Fertility Center, Denmark

Objective
This comprehensive abstract amalgamates findings from the studies on lifestyle, reproduction, and focus on the impact of GLP-1 analogues, to elucidate the holistic benefits for maternal health prior to pregnancy, pregnancy likelihood, pregnancy risk mitigation, and long-term offspring health.

Maternal Health Prior to Pregnancy
A pivotal prelude to successful reproduction lies in optimizing maternal health. Hyperandrogenism, a defining characteristic of polycystic ovary syndrome (PCOS), is linked to pregnancy complications. Elevations in body mass index (BMI) further exacerbate maternal health risks. The strategic management of hyperandrogenism and BMI emerges as a compelling imperative for maternal health enhancement prior to pregnancy. As hyperandrogenism only is an example of the more complicated factors such as insulin resistance and inflammations this will also be discussed.

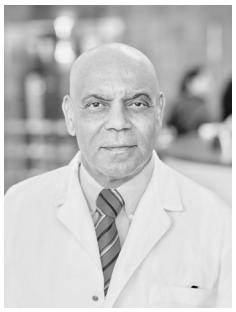
Pregnancy Likelihood Enhancement
Beyond pre-pregnancy health optimization, BMI's intricate interplay with reproductive outcomes in PCOS women unveils an essential facet. Studies reveal that higher baseline BMI is associated with reduced pregnancy likelihood. However, the integration of GLP-1 analogues, renowned for their safety in managing type 2 diabetes and obesity, introduces a novel paradigm. Harnessing their therapeutic potential could revolutionize fertility treatment strategies, potentially improving pregnancy chances together with other anti-inflammatory and insulin receptor modulators.

Pregnancy Risk Mitigation
As the journey transitions to pregnancy, the nexus between hyperandrogenism, obesity, and maternal risks gains prominence. Studies revelations resonate with earlier evidence, highlighting the adverse influence of hyperandrogenism on pregnancy complications. Additionally, studies underscore that higher baseline BMI amplifies the risk spectrum. While hyperandrogenism remains a challenge, the prospect of leveraging GLP-1 analogues / and other agents as a fertility treatment warrants further exploration, albeit with caution.

Long-Term Offspring Health
Beyond immediate maternal concerns, the far-reaching implications of maternal health on offspring cannot be overstated. Maternal hyperandrogenism and high BMI interweave into the fabric of offspring health, casting long-term shadows. This encompasses not only the risk of PCOS in the next generation but also broader metabolic and cardiovascular health trajectories. The identification of never developed drugs as a potential avenue for enhancing maternal reproductive outcomes potentially extends their influence to shaping the long-term health of the offspring.

Conclusion
This abstract weaves threads across maternal health, pregnancy chances, risk management, and offspring well-being. It navigates hyperandrogenism, obesity, and PCOS challenges, unveiling GLP-1 analogues' innovation. Science's convergence offers novel interventions, empowering women's reproductive journeys, fostering better maternal health, improved pregnancy outcomes, and lasting well-being for generations.

Biography
Professor Svend Lindenberg has contributed to the field of reproduction, notably as a part of the team behind Denmark's first successful IVF birth in 1983. With a series of publications in reputable international scientific journals and a history of delivering informative lectures, he also held the position of Chairman of the Medical Faculty at Copenhagen University. Currently, he serves as the Medical and General Director at the Copenhagen Fertility Center and is honored to be a member of the Eugin Group.



Professional and Environmental Exposures to EDCs: Impact in Gametes and IVF Reproductive Outcomes

Moncef Benkhalifa[1,2,3], Debbie Montjean[2], Hafida Corsi-Cauet[3], Marwa Lahimer[1,3]

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Over the past 30 years, the literature reported that fertility decline can be associated with the occupational and the environmental exposures to EDCs factors. The Human body is directly or indirectly exposed to a variety of toxins having the potential to disrupt endocrine homeostasis. The negative effects of EDCs on fertility potential declining have been investigated and demonstrated in clinical experiments and epidemiological studies. It's accepted that there are numerous environmental and occupational factors that can affect one's fertility and fecundity capacity during the peri/post conception period. The most of EDCs interfere with, or mimic steroid hormone action; predominantly affecting estrogen, androgen, and thyroid hormone signaling pathways. A disruption in the normal homeostatic control of these steroid hormones can have a great impact on specific molecular processes altering single or multiple biological functions and molecular process.

Some EDCs can interact with the male and female reproductive systems, leading to endocrine disruption in the testis and ovaries. Although EDCs have various mechanisms of action, they exert their effects mainly via binding transcription factor receptors. During peak reproductive age, EDCs may alter the expression and activity of enzymes required for the synthesis and catabolism of testicular and ovarian sex steroids. Moreover, these chemicals can affect the expression of hormone receptors and their ability to bind endogenous ligands. For example, in males, the literature has reported a negative correlation between disrupted spermatogenesis and lifestyle factors, such as, alcohol consumption, cigarette smoking, drug use, and obesity caused by a high-energy diet.

In females, the negative impact of EDCs on infertility diseases has been predominantly studied in animals. Many disorders have been described, such as low ovarian weight, impaired folliculogenesis, high aneuploidy rates, and the acceleration of follicular atresia. Indeed, women exposed to some endocrine-disrupting pesticides (such as atrazine, lindane) have an elevated risk of long menstrual cycles, anovulation, premature ovarian insufficiency, and the presence of endometriosis pathophysiologies.

In our experience, in an IVF clinic in the Picardie region of France, we have observed that exposure to various pesticides, with an endocrine-disrupting action, are associated with poor oocyte quality (maturation and competency), embryonic defects, and poor IVF outcomes. Additionally, some pesticide compounds are linked to specific causes of female infertility, such as premature ovarian insufficiency, polycystic ovarian syndrome, and endometriosis. It was reported that EDCs can reduce embryo implantation rates, increase the chance of miscarriage, and increase the incidence of placental and post-natal abnormalities. EDCs can affect endometrium receptivity, leading to implantation failure, by modifying keys elements of the immune response relevant to pregnancy and immune tolerance. This can have a detrimental effect on placentation, fetal development, and can be a contributing risk factor in recurrent miscarriage, preeclampsia, and preterm birth.

During pregnancy, exposure to EDCs during critical periods of fetal development can alter DNA methylation patterns, leading to inappropriate developmental gene expression and elevated disease risk. Moreover, EDCs can influence gene expression without modifying DNA sequences. It is commonly accepted that the transgenerational inheritance of parentally acquired traits is conveyed by epigenetic alterations also known as "epimutations".

In conclusion, the negative impact of exposure to various endocrine-disrupting chemicals is becoming a worldwide public health issue. Indeed, the community should be informed about the fertility decline, low ongoing pregnancy rates, and elevated risk of miscarriage associated with exposure to high doses of pesticides for example. However, it is important to keep in mind that humans are exposed to EDCs mixtures composed of hundreds of chemicals every day and not a single chemical in isolation.

Future prospective studies should consider assessing the impact of EDCs exposure histologically and immune-histologically of reproductive organs. Finally, raising awareness about EDCs exposure in the population, especially the youngest, should be implemented to enhance the increase of life expectancy and slow the decline of fertility.

Biography

Dr. Moncef Benkhalifa is qualified from the School of Medicine of Clermont Ferrand Auvergne University France, with the habilitation to direct research programs from the School of Medicine of Amiens, Jules Verne University France and mainly involved in ART, genetics and molecular diagnostics development and practices. He was for many years the scientific & technical director of Unilabs France and a member of the operation excellence team for ART & Genetics development. He is Founder of ATL R&D in France for training and education and Cofounder of Fertilys International, Fertility and Diagnostics Centres in Canada.

Since 2017 he is full professor at the School of Medicine of Picardy University Jules Verne, directing the reproductive biology & genetics laboratory and Co-ordinating the Assisted Reproductive Technology (ART) Services of the University Hospital.

New Horizons in the Treatment of Endometriosis

Yutaka Osuga

The University of Tokyo, Japan

Previously, diagnosis and surgical removal of the lesion by laparoscopy was thought to be a golden rule of the treatment of endometriosis. It was also expected that the best surgeon could give “a cure once and for all” to patients. However, as we’ve been getting more and more knowledge on endometriosis, we noticed that that was not the case. Now, we recognize endometriosis as a chronic disease, which requires a long-term management from the early stage. In the long-term management, medical treatment takes a central role. Representative drugs used for endometriosis and adenomyosis are oral contraceptives*, dienogest, GnRH agonist, GnRH antagonist, and LNG-IUS. Each drug has its advantages and disadvantages. Therefore, it is important to consider the characteristics of the drugs, the disease status, and the desire of a patient in selecting a drug. In general, oral contraceptives, dienogest, and LNG-IUS are selected as a first line therapy while GnRH agonist and GnRH antagonist as a second line. Recently, we found that dienogest 1mg/ day has a unique advantage that the dose is as equivalent as 2mg/ day while it keeps the serum estradiol levels despite 2mg/ day decreases the serum estradiol levels. More recently, GnRH agonist add-back treatment has been introduced for endometriosis treatment. In the treatment of infertility associated endometriosis, subsiding subclinical inflammation would benefit the patient. To this end, long-term pretreatment with GnRH analogues or COCs has been recommended before ICF/ICSI while freeze-all strategy using PPOS and thawed embryo transfer is also favorable. Understanding the features of different drugs and treatment strategies for endometriosis would contribute to a personalized treatment and better outcomes.

*: In Japan, estrogen + progestin combination tablets for the treatment of dysmenorrhea/endometriosis are distinguished from oral contraceptives and are called LEP (low dose estrogen-progestin combination tablet).

Biography

- Professor and Chair, Obstetrics and Gynecology, Graduate School of Medicine, the University of Tokyo
- Deputy director, the University of Tokyo Hospital
- Vice Chairperson of the Executive Board, Chairperson of International Relations Committee, Japan Society of Obstetrics and Gynecology
- President, Japan Society for Reproductive Medicine
- President, Japan Society of Fertilization and Implantation

Prof. Osuga received his MD in 1985 and PhD in 1995 from the Faculty of Medicine of the University of Tokyo, Japan. He completed his OB/GYN residency training at the University of Tokyo. He trained as a postdoctoral fellow in the field of ovarian physiology in Stanford University from 1995 to 1997. He is board certified by Japan Society of Obstetrics and Gynecology, Japan Society of Gynecologic and Obstetric Endoscopy and Minimally Invasive Therapy, Japan Society for Reproductive Medicine, and Japanese Society of Anti-Aging Medicine.

Prof. Osuga provides clinical services in gynecology and reproductive medicine with special expertise in laparoscopic surgery and assisted reproductive technology. His main research targets cover a wide variety of physiology and pathology of reproduction including endometriosis, implantation, folliculogenesis, and reproductive aging. He has authored over 500 research papers published in eminent peer-reviewed journals and has written and edited many textbooks. He serves as an executive board member of several medical groups and associations and an editor of several international journals. He is frequently sought out to provide his expertise at international medical conferences and academic institutions.

Reproductive Health Issues in Endometriosis

Akira Iwase

Obstetrics and Gynecology, Gunma University Graduate School of Medicine, Japan

Endometriosis is a disease in which endometrium-like tissues develop on the ovaries and other organ/tissues where endometrium does not normally reside, causing a variety of symptoms. Although the pathophysiology of the disease has not been fully elucidated, it is thought to be caused by the ectopic growth of endometrial tissue in menstrual blood that flows back into the abdominal cavity through the fallopian tubes during menstruation. The number of menstrual periods a woman experiences in her lifetime is increasing due to decreased frequency of pregnancy and childbirth and avoidance of breastfeeding, which may be associated with an increase in the number of women with endometriosis.

Endometriosis often causes infertility due to the local inflammation, deterioration of the pelvic environment, adhesion formation and so on. Data indicate that approximately 1/3 of patients with endometriosis exhibit infertility. In cases of endometriosis-related infertility where spontaneous conception is expected, surgical treatment for endometriotic ovarian cysts is effective, but the reduced ovarian reserve caused by surgery is problematic. Needless to say, surgical indications and appropriate surgical techniques are important. In recent years, the perinatal risk of pregnancies complicated by endometriosis has come under close scrutiny. Increased placental malposition is commonly reported, but the details of how the risk is increased with endometriosis are not clear.

It has been well known that ovarian carcinoma is often associated with endometriotic ovarian cysts. Various authors have estimated its frequency to be about 0.7-0.8%. There are several reports of carcinogenesis of uncommon and rare site endometriosis such as the intestinal tract or surgical wounds.

It is becoming increasingly recognized that endometriosis is a disease that affects women throughout their lives, from puberty to beyond reproductive age. It is a disease that should be treated by specialists, including early introduction of pharmacotherapy, appropriate surgical and fertility interventions, and follow-up care with complications in mind.

Biography

1995	M.D., Nagoya University School of Medicine
2001	Ph.D., Nagoya University Graduate School of Medicine
2001-2003	Postdoctoral Fellow, Weill Medical College of Cornell University
2003-2018	Professor (at the time of resignation), Center for Maternal-Neonatal Care, Nagoya University Hospital
2018-	Professor and Chair, Department of Obstetrics and Gynecology, Gunma University Graduate School of Medicine

Endometriosis and ART

Young Min Choi[1,2]

[1]Grace Hospital, [2]Seoul National University College of Medicine, Korea

Approximately 25–40% of infertile women have endometriosis. Endometriosis is one of the underlying etiology of infertility requiring the use of assisted reproductive technology (ART), found in 6%-8% of women undergoing ART cycles. Even though women with endometriomas had a reduced number of oocytes retrieved when compared to women without, no other differences in reproductive outcomes were identified,
In infertile women with endometriosis, the decision to either perform surgery or choose ART (IVF/ICSI) should be guided by the presence or absence of pain symptoms, patient age and preferences, history of previous surgery, presence of other infertility factors, and ovarian reserve.
Both GnRH antagonist and agonist protocols can be offered based on patients' and physicians' preferences as no difference in pregnancy or live birth rate has been demonstrated.
Initial studies suggested that extended administration of GnRH agonist prior to ART treatment improve live birth rate in infertile women with endometriosis. However, it is not recommended, at present, as the benefit is uncertain.
The combination of depo-leuprolide acetate monthly for 60 days combined with daily letrozole was associated with better clinical outcomes at IVF in women with endometriomas than depo-leuprolide acetate treatment alone.
There is insufficient evidence to recommend prolonged administration of the COC/progestogens as a pre-treatment to ART to increase live birth rate.
Deferred embryo transfer in women with endometriosis was associated with significantly higher live birth rates in some studies, but more prospective studies are necessary.
Women with endometriosis can be reassured regarding the safety of ART since the recurrence rates are not increased compared to those women not undergoing ART.
In conclusion, ART has proven efficacy in infertile women with endometriosis.

Biography

Prof. Choi obtained his medical degree from the Seoul National University College of Medicine in 1980. He completed his internship and obstetric and gynaecology residency and fellowship at the Seoul National University Hospital.
He became the faculty staff in 1989 and Professor in 2000 in the Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology at Seoul National University College of Medicine.
Dr. Choi majors in reproductive endocrinology and infertility. His research interests are focused on assisted reproductive technology, endometriosis, polycystic ovary syndrome, and human embryonic stem cell. He has published 177 articles in SCI journals.
He was the President of the Korean Society for Reproductive Medicine, and the President of the Korean Society for Assisted Reproduction, and the President of the Korean Society of Medical Genetics. He is now the Director of Fertility Center at Grace Hospital, Goyang, Korea.

Unveiling the Paradox of Silent Endometritis: A Novel Diagnostic Approach Merging Hysteroscopy and 3D-PD

Shinnosuke Komiya

HORAC Grand Front Osaka Clinic / Kansai Medical University, Japan

Background
Chronic endometritis poses a complex challenge in infertility treatment, partly attributed to the absence of standardized diagnostic criteria. This study addresses a unique subset of cases that exhibit conflicting diagnostic results and aims to validate a multifaceted diagnostic approach that combines hysteroscopy with 3D Power Doppler using virtual organ computer-aided analysis (VOCAL) software.

Methods
We retrospectively analysed patients who experienced recurrent assisted reproductive technology failures between January 2018 and December 2022. All participants underwent hysteroscopic evaluations and endometrial biopsies. Microbial analyses were employed to investigate endometrial bacterial flora, while immunohistochemical staining for CD138 was used to detect plasma cells. Additionally, the role of VOCAL in appraising local endometrial blood flow was assessed.

Results
Our study identified two distinct categories of cases. The first included cases with entirely normal hysteroscopic findings but showed abnormalities in bacterial flora or plasma cell expression. The second category comprised cases with abnormal hysteroscopic findings yet exhibited normal bacterial flora and lacked plasma cell expression. VOCAL assessments showed increased local endometrial blood flow in these conflicting cases.

Conclusion
The findings indicate that a multifaceted diagnostic strategy may improve diagnostic precision, particularly for cases manifesting conflicting results—referred to herein as "Silent Endometritis." This integrated methodology provides a novel avenue for a more nuanced understanding and diagnosis of these perplexing clinical scenarios.

Biography

I earned an MD from the National Defense Medical College and am a Graduate Researcher at Kansai Medical University. I served as a resident physician and medical corps captain early in my career, acquiring a diverse healthcare perspective. Transitioning into reproductive medicine, I gained experience at IVF Osaka Clinic and HORAC Grand Front Osaka Clinic. During my graduate studies, I specialized in researching vaginal and endometrial microbiomes using NGS techniques. A frequent contributor to peer-reviewed journals, I've presented my research at international conferences. My work aims to bridge gaps in understanding women's reproductive health through microbiological research.

Impact of Chronic Endometritis on Reproduction

Fuminori Kimura

Nara Medical University, Japan

Recovery of endometrial receptivity is thought to bring a new treatment strategy to many patients with implantation failure. We focused on chronic endometritis (CE) as the cause of implantation failure. In the present study, the effects of CE on implantation and pregnancy outcomes, the effects of CE on endometrial function, and the effects of progesterone as treatment for CE were examined.
It was found that the pregnancy rate and live birth rate were significantly lower in CE patients, and the miscarriage rate was significantly higher in CE patients in a prospective study. When patients were diagnosed with CE, even though in vitro fertilization was carried out for 1 year, not only were the pregnancy rate and live birth rate significantly lower, but the miscarriage rate and preterm birth rate were high after conception.
In in vitro study, we revealed the secretions of TNFα, IL1β, and IL6 per cell were significantly higher in CE. The rate of Th1 was greater and it of Th2 was significantly lower in CE, and those of Tregs and Th17 was not different. Both PRL and IGFBP1, decidualizing markers, showed significant decreases in secretion with CE, and conversely, the number of cells was significantly higher in the CE group.
Based on the results of bench studies, we hypothesized that an altered administration route and increased dosage of progestogen may improve clinical outcomes. The clinical outcomes of patients who underwent single frozen-thawed blastocyst transfer were examined for each hormone replacement therapy. It was found that using a progesterone vaginal suppository in combination with an oral progestin for hormone replacement improved the pregnancy rate and live birth rate in CE patients when compared with using an oral progestin alone.
CE can cause implantation failure and affect pregnancy outcomes. CE altered the subpopulation of immune cells in the endometrium and caused decidualization disorders. Although the pregnancy rate was improved when luteal support was devised, there was a high preterm birth rate. It has been suggested that the treatment of CE by the administration of antibiotics may improve uterine receptivity, and further verification including investigating pregnancy outcomes is necessary.

Biography

EDUCATIN
2002 Ph.D. Department of Obstetrics and Gynecology,
Shiga University of Medical Science, Otsu, Japan
1993 M.D. Department of Obstetrics and Gynecology,
Shiga University of Medical Science, Otsu, Japan

PROFESSIONAL TRAINING AND EMPLOYMENT
2022- Professor, Department of Obstetrics and Gynecology
Nara Medical University, Kashihara, Japan
2015- Associate Professor, Department of Obstetrics and Gynecology,
Shiga University of Medical Science, Otsu, Japan
2010 Assistant Professor, Department of Obstetrics and Gynecology,
Shiga University of Medical Science, Otsu, Japan
2008 University of Massachusetts Amherst
Department of Biology Senior Research associate
2007 University of Massachusetts Amherst
Pioneer Valley Life Sciences Institute Postdoctoral fellow

Can NAD Supplementation Improve Oocyte Quality?

William Leigh Ledger

Discipline of Women's Health, University of New South Wales, Australia

Introduction
there is a clear need to improve the ability of Assisted Reproductive Technology to assist older female patients to achieve a healthy pregnancy. Older women under-perform in IVF due to both low oocyte number and poor oocyte quality. NAD (Nicotinamide adenine dinucleotide) is a coenzyme central to metabolism. NAD and the primary NAD+ synthesizing enzyme nicotinamide phosphoribosyltransferase (NAMPT) are key regulators of aging and longevity in mammals (Imai et al 2009) and may be involved in regulation of sirtuins that are essential to the function of the meiotic spindle. Errors of chromosome segregation at anaphase lead to embryonic aneuploidy, a major cause of poor embryo quality and age related subfertility.

Material & Methods
In 2020, our laboratory published results of a study in which aged mice were supplemented with low or high doses of nicotinamide mononucleotide (NMN), an NAD+ metabolic precursor. Low doses led to improvement in oocyte quality with restoration of fertility, an effect which can also be achieved by transgenic overexpression of the NAD+-dependent deacylase SIRT2.

Results
Low doses of NMN in drinking water led to improvement in oocyte quality with restoration of fertility, an effect which can also be achieved by transgenic overexpression of the NAD+-dependent deacylase SIRT2. These finding have now been translated to a study in humans using nicotinamide riboside, another NAD+ metabolic precursor given to IVF patients of advanced reproductive age. The results of the RCT will not be available until early 2024.

Conclusions
NAD precursors may (or may not) be helpful in improving embryonic ploidy for older women undergoing IVF treatment. Many couples now defer pregnancy due to complex socio-economic reasons, and the age at which women present for IVF now frequently exceeds 40 years. Hence there is a need for more efficient approaches to this group of patients.

Biography

Professor William Ledger is Head of Discipline of Obstetrics and Gynaecology of the Faculty of Medicine at the University of New South Wales, Director of Reproductive Medicine and Senior Staff Specialist at the Royal Hospital for Women and a fertility specialist at City Fertility in Sydney. He founded the Fertility and Research Centre in Sydney as a centre for translational research in reproductive biology and reproductive medicine. The FRC provides a Statewide service in oncofertility and is currently running three randomised trials, two observational studies and an early stage translational project to improve techniques for in vitro maturation of human oocytes.

Adjuvant Treatments for Poor Responders: Does Something Really Work?

Omar Sefrioui

Women's Clinic and African Fertility Center, Morocco

Despite recent striking advances in assisted reproductive technology (ART), poor ovarian response (POR) diagnosis and treatment is still considered challenging. Poor responders constitute a heterogeneous cohort with the common denominator of under-responding to controlled ovarian stimulation. Inevitably, respective success rates are significantly compromised. As POR pathophysiology entails the elusive factor of compromised ovarian function, both diagnosis and management fuel an ongoing heated debate depicted in the literature. From the criteria employed for diagnosis to the plethora of strategies and adjuvant therapies proposed, the conundrum of POR still puzzles the practitioner. What is more, novel treatment approaches from stem cell therapy and platelet-rich plasma intra-ovarian infusion to mitochondrial replacement therapy have emerged, albeit not claiming clinical routine status yet. The complex and time sensitive nature of this subgroup of infertile patients indicates the demand for a consensus on a horizontally accepted definition, diagnosis and subsequent effective treating strategy. This critical review analyzes the standing criteria employed in order to diagnose and aptly categorize POR patients, while it proceeds to critically evaluate current and novel strategies regarding their management. Discrepancies in diagnosis and respective implications are discussed, while the existing diversity in management options highlights the need for individualized management.

Biography

Professor in obstetric and gynecology and reproductive medicine and surgery since 2001
General Manager of Women's Clinic 5african fertility center) in Casablanca Morocco
Received several awards from Europe for the fertility clinic in London and Vienna
Chairman and founder of the Moroccan society of reproductive medicine and fetal medicine
Chairman Of The Mediterranean society of reproductive medicine(MSRM) since 2022
Chairman of the world IVF congress in Marrakech 2024
ASRM AND ESHRE MEMBER
Organized several international and national meetings in the field of gynecologic surgery and ART
Published more than 50 papers in the field of gynecology , reproductive surgery and ART

Advantages of Progestin Primed Ovarian Stimulation(PPOS) -New Controlled Ovarian Stimulation Method-

Masahide Shiotani

Hanabusa Women's Clinic, Japan

Introduction
The history of the development of ART can be viewed as the history of the development of ovarian stimulation, which in the early days of ART was a battle against the premature LH surge. The timing of egg retrieval was 36 hours after the initiation of the LH surge, while monitoring the LH surge. Thus, there were often cases of emergency egg retrieval during the night. This was the first generation. In 1984, a controlled ovarian stimulation method that suppressed the LH surge in combination with a GnRH agonist was reported, and since then, this method has spread rapidly. This is the second generation. However, this method required HCG for maturation triggering, which raised concerns about inducing a high degree of OHSS. The third generation of using GnRH antagonists has emerged. This method does not require desensitization of the pituitary gland, thus allowing the use of GnRH analogues as maturation triggers. However, GnRH antagonists are relatively expensive and sometimes fail to suppress the LH surge and thus ovulation. PPOS which suppresses the LH surge with progestin, is the fourth generation of controlled ovarian stimulation

Background of the Development of PPOS
In 2002, it was reported that LH surge was suppressed in sheep by progestin administration. The disadvantage of the PPOS method is that it requires all embryos freezing, and fresh embryo transfer cannot be performed. However, in recent years, the number of treatment cycles that are based on all-freezing has been increasing, including OHSS prevention, PGT, autologous egg preservation, and egg donation. Hence, the number of treatment cycles using the PPOS is increasing.

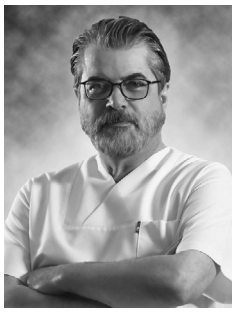
The PPOS Method in Practice
When implementing the PPOS method, there are two points to consider: what progestin to use and how much to use, and the timing of progestin initiation. Medroxyprogesterone, Dydrogesterone, Clormadinone Acetate, and Dinogest have been reported as progestins to be used. Most reports indicate that progestin should be administered at the same time as FSH/HMG initiation, but there are also reports of flexible PPOS in which progestin should be administered after the leading follicle is over 16 mm. The type and dose of progestin should be selected with attention to the patient's ovarian function. Basically, higher doses of progestin should be considered in cases of ovarian dysfunction. Usually, GnRH agonists are effective as maturation triggers for PPOS. Since PCOS patients tend to have high LH levels, PPOS may be useful in keeping LH levels low during ovarian stimulation, thereby improving clinical outcomes and reducing the risk of developing OHSS.

Biography

Medical corporation Hanabusa women's clinic (Board chairman)

Educational Background
Shimane University, School of Medicine Graduation Date (1985)

Doctoral License Information
Certified physician of Japan Society of Obstetrics and Gynecology
Certified physician of Japan Society of Genetics
Specialist doctors in reproductive medicine of Japan Society for Reproductive Medicine
Certified physician of Japanese Society of Clinical Cytology



Preliminary Study of Intraovarian Injection of Autologous Platelet-rich Plasma (PRP) in Women with Clomiphene Citrate Resistant Polycystic Ovary Syndrome with a History of Recurrent IVF Failure

Timur Gürgan

Bahçeşehir University / Gürgan Clinic, Turkey

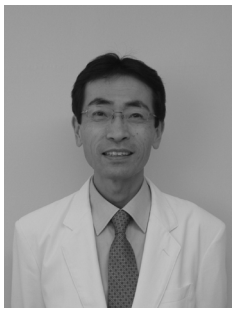
Recurrent implantation failure (RIF) is a common issue faced by couples undergoing assisted reproductive technology (ART). RIF is defined as the failure of an embryo to implant in the endometrium after multiple attempts. There are various causes of RIF, including anatomical issues hematological problems ‘ genetic, and immunological factors. Testing for chromosomal abnormalities in oocytes and sperm DNA damage can also help to identify the cause of RIF and guide treatment options.

Various tests and approaches are used to evaluate RIF, including assessing uterine receptivity, thrombophilia examination, immunological tests, and chromosomal examination. Treatments for RIF include personalized embryo transfer, intralipid, and adjuvant treatments. However, it is essential to note that while these treatments have shown promise in some cases, the definition of RIF is still not clear and needs to be clarified to standardize scientific studies and treatment options.

In this lecture the avaible scientific data on recent novel treatment options which can help the couples to achieve pregnancy diagnosed as RIF will be discussed. The presentation will also cover preliminary data of the impact of PRP treatment on the women with clomiphene citrate resistant PCOS.

Biography

Prof. Timur Gürgan is a renowned figure in the field of obstetrics and gynecology. He is a founder of the gynecological endoscopy, IVF center, andrology, and menopause divisions of the Ob/Gyn Department. He has served in various capacities, including Chairman of the Department of Ob/Gyn at Hacettepe University, and founding president of the Society of Reproductive Medicine in Turkey. He has also served on the boards of various international societies and is the author or co-author of more than 100 journal articles and several international books. He is currently a professor and chairman in the Department of OB&Gyn, Faculty of Medicine, Bahçeşehir University, Istanbul, and the scientific director of the GÜRGAN CLINIC Women's Health, infertility, and IVF in Ankara.



How Recurrent Implantation Failure (RIF) should be Defined and Managed?

Hiroaki Shibahara

Hyogo Medical University, Japan

As a treatment for infertile couples, a condition in which pregnancy does not occur even after repeated ART is performed is called "repeated ART failure". Among them, although good embryos can be developed, pregnancy cannot be established even if the implantation is repeated is called "recurrent implantation failure (RIF)". The causes of RIF are assumed to be problems on the part of the fertilized egg, problems in the environment in the uterus, and abnormalities in immune tolerance to accept fertilized eggs.
The definition of RIF has changed over time. In the early 2000s, it was defined as a case who could not obtain a clinical pregnancy where a total of 10 or more embryos were transferred. In 2014, Coughlan et al. proposed that RIF is diagnosed when a woman under the age of 40 does not become pregnant after transferring four or more good embryos and three or more times, and this definition has been widely adopted. Since then, the diagnosis of aneuploidy in embryos by PGT-A has become established, and recently it has been recommended to define RIF in consideration of the number of euploid embryos are transferred.
As for the management for RIF, only 3 investigations are recommended by ESHRE in 2023, including re-assessment of lifestyle factors, re-assessment of endometrial thickness, and assessment of antiphospholipid antibodies and antiphospholipid antibody syndrome in case of risk factors. Other investigations such as karyotyping for both partners, 3D US/hysteroscopy, endometrial function testing, chronic endometritis testing, assessment of thyroid function, and progesterone levels are positioned that can be considered. However, all other well-known testing methods have been concluded to be not recommended because they are empirical and lacking in sufficient scientific basis. Therefore, they state that further studies of empirical interventions in patients with RIF of unknown cause are unlikely to be helpful and may be considered a waste of research resources.
So far, there are few reports of the interventions for the scientifically clear causes of RIF. For efficient and successful ART treatment in RIF patients, further research in high-quality studies verifies their usefulness and safety.

Biography

Hiroaki Shibahara, M.D., Ph.D. is a Professor and Chairman, Department of Obstetrics and Gynecology at School of Medicine, Hyogo Medical University, Nishinomiya, Japan. He is also the Division Director of the Reproduction Center at Hyogo Medicine University Hospital. In his research he examines topics related to the reproductive immunology, among them, especially gamete immunology. In 2022, he published a text entitled “Gamete Immunology” by Springer. With that text, he was responsible for writing 15 chapters and in total 208 pages on anti-sperm antibody.
Regarding as a researcher, he has been working in the laboratory of Professor Shinzo Isojima and Professor Koji Koyama at Hyogo College of Medicine from 1984. He has also been working in the laboratories of Professor Nancy J. Alexander at Eastern Virginia Medical School, USA, in 1990, and Professor John C. Herr at University of Virginia, USA, between 1996 and 1997.
Dr. Shibahara promoted to be a Professor, Department of Obstetrics and Gynecology at Jichi Medical School in Tochigi, Japan, between 2007 and 2012. He was then appointed to his current position as a Professor and Chairman at Hyogo Medical University in 2013.
Dr. Shibahara has been the Editor-in-Associate Chief of the Reproductive Medicine and Biology since 2003. He has also been the Chief Editor of the Journal of Reproductive Immunology since 2020.
Dr. Shibahara was the President of the Japan Society for Immunology of Reproduction from 2017 to 2020. He is still active in important positions in several academic societies.

AMH and Ovarian Aging: Between Quantity or Quality of Oocytes

Budi Wiweko

Department of Obstetrics and Gynaecology, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo General Hospital, Indonesia

Anti Mullerian Hormone (AMH) is a reproductive hormone that is produced by granulosa cells, reflecting the number of growing follicles in the ovary. Currently, available evidence strongly supports the correlation between serum AMH and the number of follicles as proof of ovarian reserve in every woman. Serum AMH is an effective biomarker to predict the number of oocytes that can be retrieved for assisted reproduction technologies (ART). Also, as women increase in age, serum AMH levels will decline steadily until menopause with a rapid decline in AMH levels observed in women aged 45 to 50 years old. This opens up the possibility that serum AMH can be used to detect menopause-related diseases.

However, no strong correlation was found between serum AMH level and the quality of oocytes. Hence, serum AMH concentration can not be directly used to assess the remaining oocyte quality in the ovary. Younger women who have a similar concentration of serum AMH to older women tend to demonstrate better oocyte quality. This is due to AMH playing an important role in ovarian follicle growth regulation.

Aside from its association with the decline in AMH level, increasing age has also been demonstrated to be correlated with the decrease in mitochondrial DNA (mtDNA) copy number. Mitochondrial damage leads to reactive oxygen species (ROS) production which disrupts the respiratory chain of mitochondria and further creates DNA damage. Supplementation of antioxidants in women with occult premature ovarian insufficiency resulted in improvements of respiratory chain of mitochondria along with an increase in AMH level. Therefore, this highlighted that the decline in AMH level could potentially reflect the decrease in mtDNA copy number.

In conclusion, chronological age is able to be considered as one of the essential factors that affect the quality of oocytes, instead of other factors such as PCOS, endometriosis, and others.

Biography

Prof. Budi Wiweko is an expert in obstetrics and gynecology, particularly in IVF. He founded Indonesian Reproductive Medicine Research and Training Center (INA-REPROMED), the Vice Director of the Indonesian Medical Education and Research Institute (IMERI), president-elect of the Indonesian Society of Obstetrics and Gynecology, Chairman of Indonesian Ministry of Health's Health Technology Assessment Committee, member of Indonesian National Academy of Sciences, founder and general secretary of Asian Society for Fertility Preservation (ASFP), and former president of Asia Pacific Initiative on Reproduction (ASPIRE). He published 178 original articles indexed in Scopus, Pub-Med, and H-Index. He did numerous researches especially in AMH, individualized controlled ovarian stimulation (iCOS), ovarian tissue vitrification and embryo metabolomics. He is an AMH expert in Asian region since he developed AMH nomogram and AMH based iCOS formula, which is important for daily practice on infertility.

Safety of Routine Clinical Use of IVM from Our Long-term Experience

Aisaku Fukuda[1], Yoshiharu Morimoto[2]

[1]IVF Osaka Clinic, [2]HORAC Grand Front Osaka Clinic, Japan

In vitro maturation (IVM) was initially performed by Dr. Robert Edwards on his development to successful clinical application of in vitro fertilization (IVF). Recovery of immature oocyte followed by IVM was thought to be a potentially effective treatment for infertility. Therefore, IVM is a prototype of IVF and has advantages as well as disadvantages as an ART. Despite its long history, IVM was recently in 2021 recognized as nonexperimental ART by the American Society for Reproductive Medicine at last, and its clinical usage remains small when compared with controlled ovarian stimulation IVF. Weak point of IVM is lack of standard protocol and safety of outcoming neonate due to relatively small numbers of children. However, advantage of IVM is no ovarian hyperstimulation syndrome (OHSS) at all in any protocol. However, with the development of IVF in modern clinical practice, OHSS rate has significantly reduced because of GnRH antagonist protocol, progesterone primed ovarian stimulation (PPOS), use of GnRH-agonist trigger and the adaption of freeze-all transfer strategy. We have performed 1310 cycles of IVM oocyte retrievals with 832 embryo transfer since 2000 and achieved clinical pregnancy rate of ~22% per transfer and 151 babies born so far. Although IVM clinical pregnancy rate per retrieval is lower than that of IVF, IVM has a clear tangible benefit to the patient in terms of notably reduced gonadotropin stimulation and cycle monitoring, expedited treatment time, reduced expense, and elimination of OHSS risk.

As to the babies conceived from IVM, average gestational age at birth was 38.5 weeks with average weight of 2976g. Congenital malformation rate was 1.98% that was identical to natural pregnancy babies statistics in Japan. Moreover, 127 babies (60 male and 66 female) were followed by age of 3 years old. Physical development was not significantly different from standard curve of Japanese children from natural pregnancy. Details of our clinical experience of IVM for 23 years is demonstrated in the presentation. Although IVM is a still frontier of ART and has many obstacles, IVM is important technology not only for infertility, but also for future ART such as onco-fertility, nuclear transfer and so on.

Biography

Dr. Fukuda is graduated from Kansai Medical University with MD. in 1978 and finished residency at Kyoto University Hospital. He finished Kyoto University Graduate School with PhD. in 1989. He moved to East Tennessee State University in 1990 and worked as an assistant professor tenured for 9 years. He directed an ART team as HCLD (ABB) and conducted research and education of medical student and undergraduate.. He returned to Japan in 1998 to join IVF Japan group and has been working at IVF Osaka Clinic. He received awards from AFS (present ASRM) in 1992 and ISIVF memorial award from Japan Society for Fertilization and Implantation in 2000 by his IVM study. He is a major contributor of the first successful IVM pregnancy in Japan. He also started outpatient routine practice of Falloposcopic tuboplasty. He is a board-certified OB/GYN specialist and also REI subspecialist. He is only one HCLD holder in Japan.

Development of IVM and Applications to Infertility and Cancer Patients

Robert B. Gilchrist

Fertility & Research Centre, Discipline of Women's Health, School of Clinical Medicine, University of New South Wales Sydney, Australia

Oocyte in vitro maturation (IVM) makes use of oocytes from patients that have received minimal or no gonadotrophin stimulation. Whilst this brings many advantages to patients, this typically means oocytes are collected from small – medium sized (4- 12 mm) antral follicles. These oocytes are under-developed, and yet removal of these from the follicle and culture in vitro leads to spontaneous oocyte meiotic maturation, without the benefit of the physiological signals that naturally induce oocyte maturation at ovulation. Using animals models, over the past decade seminal advances have been made in our understanding of the fundamental mechanisms regulating oocyte maturation in vivo. Most IVM systems, as practised clinically today, typically do not recapitulate these key cellular processes, possibly accounting for the lower efficiency of IVM compared to IVF. A key objective of modern approaches to IVM is to restore in vitro, as far as possible, the natural processes that occur during oocyte maturation in vivo. One strategy to achieve this in IVM is to: 1) prevent spontaneous meiotic resumption at oocyte collection using phosphodiesterase inhibitors, then 2) artificially maintain or elevate cumulus-oocyte complex (COC) cAMP levels, and finally to 3) induce oocyte meiotic resumption using EGF-like peptides. This typically requires the use of biphasic or 2-step IVM systems. One such biphasic IVM system is called capacitation-IVM (CAPA-IVM), as the oocyte is "capacitated" for development in vitro. CAPA-IVM uses the follicle's natural oocyte meiotic inhibitor, c-type natriuretic peptide (CNP), in the pre-IVM phase, and amphiregulin as the oocyte meiotic inducer in the second IVM phase. Such biphasic-IVM systems typically lead to subsequent improvements in embryo yield compared to standard IVM, and indeed this is the case for CAPA-IVM. Several pilot RCTs and a large RCT of CAPA-IVM vs conventional IVF have been completed, and CAPA-IVM is now practiced in a few centres globally, including in our own centre in Sydney. The development and clinical application of modern IVM systems, built on decades of animal scientific research, is a bench-to-bedside success story of translational research. IVM is now classified as a routine (non-experimental), safe, minimally invasive procedure for the treatment of infertility in specific patient groups and for fertility preservation in female cancer patients.

Biography

Professor Robert Gilchrist is a research scientist and a NHMRC Investigator Fellow. He is Research Lead of the Discipline of Women's Heath UNSW, and Head of the Oocyte Biology Research Unit, and is a Fellow of the Society for Reproductive Biology. He is or has been a Scientific Advisory Board member and/or consultant to; City Fertility CHA Global, IVF Australia, CooperSurgical, Repromed, Fertility SA, Cook Medical, and the NZ Ministry of Health.

Professor Gilchrist is a reproductive biologist whose research encompasses basic and applied aspects of ovarian folliculogenesis, oocyte maturation and preimplantation embryo development. He conducts discovery research on oocyte-somatic cell interactions as a determinant of subsequent embryonic development. He has made important scientific contributions demonstrating that oocyte paracrine signalling determines cumulus cell differentiation and function. Dr Gilchrist also studies new biomarkers of oocyte quality. In addition, he leads a translation research program with the objectives of improving oocyte in vitro maturation (IVM) procedures for treatment of infertility and fertility preservation in women/girls with cancer. One of his IVM procedures is now in clinical practice.

Improvement in the Clinical Application of IVM

Johan E.J. Smitz

Free University Brussels, Belgium

The current methods for IVM using commercialised IVM media recommend significant ovarian stimulation (e.g., hCG, FSH) prior to oocyte retrieval. While this technique has benefits (i.e., allows for a maturation of oocytes in vivo, allows follicles to more easily release immature oocytes for IVM), the use of gonadotrophins increases the risk of OHSS in high responder patients and the cost of treatment. Use of a non-hCG-triggered IVM system minimizes the risk of OHSS and avoids the collection of a mixture of mature and immature oocytes. However, a non-hCG-triggered system leads to poor clinical pregnancy rates when fresh embryos are transferred (De Vos et al.,2011) while if vitrification of embryos was performed, with warming of the embryo prior to embryo transfer clinical results improve (Ortega-Hrepich et al.,2013; Vuong et al.,2021). A "vitrify-all" embryo strategy and a transfer during in a natural or artificial cycle with luteal phase support improved results (Vuong et al.,2021).
Adjustments in the clinical IVM procedures and in the IVM culture are needed to improve the amount of mature oocytes as well as of the number of good quality embryos to enhance the efficacy of IVM. A pre-maturation capacitation (CAPA) culture step preceding IVM culture, recognized as "CAPA-IVM", first actively arrests nuclear oocyte maturation (at prophase 1 of meiosis) with C-type Natriuretic Peptide (Kawamura et al 2011; Franciosi et al 2013). In this first incubation (22-26hr) in complex rich medium with FSH, E2 and Insulin oocyte's cytoplasmic maturation and developmental competence in vitro is accomplished (Romero et al.,2015; Sanchez et al 2017). The final maturation medium brings the physiological supplements (FSH and Amphiregulin) that stimulate the nuclear maturation (to metaphase II oocyte) during a 30hr maturation. (Inoue et al., 2009 ; Richani et al., 2013; Richani et al., 2014A, 2014B; Peluffo et al., 2012), and improved clinical outcome (Akin et al., 2021).
Following in vitro, non-clinical and clinical studies, CAPA-IVM was progressively incorporated into clinical use (Vuong et al., 2020a, 2020b, 2022). CAPA-IVM underwent clinical research providing evidence of its effectiveness and safety (Saenz-de-Juano et al.,2019). Three controlled clinical studies (Sanchez et al.,2017; Sanchez et al 2019; Vuong 2020b) supported the efficacy of CAPA-IVM technology versus IVM using the same "basal" maturation medium (MediCult IVM Medium vial 2). The 3 clinical studies repetitively showed a significantly higher oocyte maturation rate in the CAPA-IVM groups compared to the MediCult IVM System, which led to higher clinical pregnancy rates after CAPA-IVM. Live birth rates as high as 44-60% were registered in those three RCT's. From published RCTs using CAPA-IVM a total of 131 live births were reported. The safety profile of neonates born after CAPA-IVM does not differ from those observed with controlled ovarian stimulation for ART. Published reports contribute to the safety package with CAPA-IVM. A 2-year development follow-up of infants born after CAPA-IVM indicates no differences in psychomotor development from infants born after controlled ovarian stimulation for ART (Vuong et al, 2022).
With its recent acceptance as a valuable technology in ART (Practice Committee of ASRM, 2021), infertile couples might prefer CAPA-IVM for its less-invasive nature, its briefness and potential reduced cost.

Biography
Emeritus Prof Johan Smitz MD PhD is based at the Faculty of Medicine and Pharmacy at the Free University Brussels (VUB), Belgium. He graduated as M.D. in 1980 and obtained his specialty in Clinical Pathology/ Biochemistry/ Radio-Isotopes in 1986. He sub-specialised in Reproductive Medicine and got his PhD in 1993. From 1986 onwards he has been the head of the Endocrine Laboratory of the University Hospital. He became Professor of Endocrine Physiology and Reproductive Medicine in 1997 at VUB and founded the Follicle Biology Research Laboratory (FOBI). His main research activities are directed towards the implementation of basic techniques related to oocyte biology from the research laboratory into the clinical activities. He developed 1- ovarian follicle culture systems, 2- non-invasive tests on cumulus cells for oocyte quality and 3- pre-IVM techniques. Prof Johan Smitz is co-founder of two spin-off biotech companies 'Fertiga' and 'Lavima Fertility' from the Free University Brussels (VUB). They bring innovative technologies to the ART laboratory.

Current Status and Issues Related to Oncofertility in Japan

Nao Suzuki

St. Marianna University, Japan

Oncofertility is "An interdisciplinary medical specialty that bridges biomedical and social sciences to examine issues related to the reproductive choices, intentions, and goals of individual patients in light of their diagnosis, treatment, and survival status. In clinical practice, it aims to bring physical, emotional, and social enrichment to cancer patients of reproductive age and beyond by providing biomedical and social science support for patients and their families to have and rethink the meaning of parenthood (Japanese Society for Fertility Preserrvation).
In April 2021, financial support for fertility preservation therapy for pediatric and AYA generation cancer patients and others by the national and local governments began as part of the research project. Since the target patients of cancer and reproductive medicine are cancer patients, not infertility patients in general, the objective of this research promotion project is to generate evidence in this area by accumulating outcomes (cancer side and reproductive side) of fertility preservation treatment. In addition, when providing decision support to patients and their families in cancer and reproductive medicine, it is important to ask whether or not they wish to preserve fertility, but it is also important to establish a decision support system that provides reliable information at the right time so that patients can choose not to choose fertility preservation. While prioritizing cancer treatment above all else, there is an urgent need to develop human resources among healthcare professionals in charge of Oncofertility in order to provide decision-making support to cancer patients and their families, who face uncertainty and fear in the future. In particular, there are many issues that need to be resolved, such as how informed and in-home consent should be provided to pediatric cancer patients, the establishment of a long-term storage system for fertility preservation specimens that can be used for more than 10 years, and technological innovation in fertility preservation therapy for male cancer patients before the start of semen penetration. This presentation, entitled "Current status and issues related to Oncofertility in Japan," will introduce some of Japan's unique initiatives.

Biography

Dr. Nao Suzuki is a Professor and Chair of the Department of Obstetrics and Gynecology at St. Marianna University School of Medicine, Kanagawa, Japan since 2011. He completed his medical training at the School of Medicine, Keio University (Tokyo, Japan) in 1990, and obtained his Ph.D. in Obstetrics and Gynecology, Graduate School of Medicine, Keio University in 2000. His specialties are Gynecologic Oncology, Palliative Medicine, and Reproductive Medicine (fertility preservation for the CAYA cancer patients: Oncofertility). He established the Japan Society for Fertility Preservation (JSFP) in 2012 and the Asian Society for Fertility Preservation (ASFP) in 16 countries in Asia in 2016. He is the president of the International Society for Fertility Preservation (ISFP) from 2023.1 till 2024.12. The gynecologic oncologist, who is the patient's primary caregiver, should perform fertility-sparing surgery with a complete understanding not only of ART and FP but also of preconception care and social issues. Therefore, as a board member of the Asian Society of Gynecologic Oncology (ASGO), he organized the Special Task Force, Fertility Preservation in Gynecologic Oncology, which is an ASGO group of nearly 40 young gynecologic oncologists from 10 Asian countries who will identify country-specific guidelines on 5 topics (cervical cancer, uterine cancer, ovarian cancer, ovarian borderline malignancies, and social issues) and share country-specific differences and cultural competencies. His wish is to improve CAYA cancer survivorship not only in Asia but also in the world so that patients can fight cancer with hope.

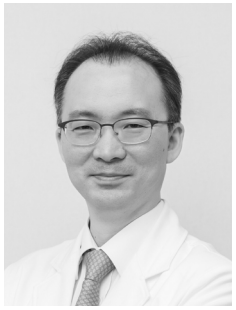
Options to Restore Fertility with Prepubertal Testicular Tissue

Christine Wyns

Cliniques Universitaires Saint-Luc, Catholic University of Louvain, Belgium

Introduction
Chemo- and radiotherapy administered for both benign and malignant conditions often induce gonadal damage leading care providers to develop fertility preservation measures. For prepubertal boys who do not yet produce spermatozoa cryostorage of immature testicular tissue (ITT), containing spermatogonial stem cells (SSCs), with the perspective of in vitro or in vivo development into mature sperm is so far the only option to give these young patients a hope for future parenthood. The procedure of testicular tissue sampling and freezing has been developed since the early 2000s and is now ethically accepted. So far over 3000 boys have their ITT stored worldwide, although this number is most likely underestimated. Some of these boys have now reached the reproductive age and await strategies to restore their fertility with their banked tissue. Follow-up data of boys who participated to such fertility preservation programs are reassuring so far.
Materials and methods
The presentation is a narrative overview of the in vivo and in vitro fertility restoration approaches with cryostored ITT and achievements in humans and non-human primates.
Results
Several techniques such as transplantation of ITT pieces or selected and propagated SSCs, in vitro maturation of SSCs as isolated cells or within their own niche, and creation of an artificial testis are all under investigation. Fertility restoration with cryopreserved human SSCs has not yet been achieved but based on encouraging achievements in animals, some of the strategies are likely to become applicable in clinical practice in the future. The most important breakthrough was the report in 2019 on the birth of a baby monkey using sperm developed in ITT autografts. With regard to in vitro maturation of ITT from primates, including humans, haploid germ cells (round and elongated spermatids) were obtained although full characterization and function of these cells has not been demonstrated yet. Perspectives and challenges towards clinical translation for the various approaches will be discussed.
Conclusion
Human ITT cryobanking is still at the experimental stage as fertility restoration options are still under investigation in contrast to progress made in non-human primates where a livebirth was already reported after use of cryopreserved ITT in vivo. Based on this achievement, it is likely that in a near future, autografting of human frozen-thawed ITT could be proposed in very selected cases within an ethically- approved clinical pilot trial. However, in vitro maturation has led to offspring only in rodents and remains by far the most challenging technique.

Biography
Christine Wyns has a Doctor in Medicine degree, graduate in Gynecology, Health and Biomedical Sciences (Catholic University of Louvain) and applied Andrology (University of Limoges).
Director of the Reproductive Tissue and Cell Bank. current head of IVF and andrology and former Head of the Department of Gynecology and Andrology (for 10 years) at Cliniques Universitaires Saint Luc, Brussels, Belgium.
Professor at the Catholic University of Louvain.
Head of the research lab in Andrology with special focus on fertility preservation for prepubertal boys.
Past Chair of the European IVF monitoring committee-ESHRE, current member of the steering committee.
Member of the Board of the EU affairs committee-ESHRE.
Board of directors of the ISIVF and coordinator of the SIG on fertility preservation.
Associate editor for Human Reproduction Update
Over 100 articles in medical journals and medical books.
Regular communications at major international conferences



Oocyte Cryopreservation for Fertility Preservation in Women with Endometriosis

Jung Ryeol Lee

Seoul National University Bundang Hospital, Korea

Endometriosis, a prevalent gynecological condition, is increasingly associated with declining ovarian reserve, raising significant fertility concerns for many women. In this presentation, the multifaceted relationship between endometriosis and decreased ovarian reserve will be explored. Emerging evidence suggests that endometriosis itself may contribute to a reduced ovarian reserve, leading to fertility complications. While medical treatments aiming to prevent this decline are available, their effectiveness is yet to be conclusively proven. Moreover, it's recognized that surgical interventions for endometriosis can exacerbate the reduction in ovarian reserve.
Given these challenges, the crucial role of oocyte cryopreservation as a viable fertility preservation strategy for women with endometriosis, especially those anticipating surgery, will be emphasized. The necessity of oocyte cryopreservation prior to surgical intervention will be underscored, with a focus on the importance of timely decision-making in fertility management. Additionally, the significance of multiple ovarian stimulations and oocyte collections in ensuring an adequate number of oocytes are harvested before surgical procedures will be discussed. The aim of this lecture is to equip healthcare professionals with a comprehensive understanding of the proactive measures that should be taken to preserve the fertility of women diagnosed with endometriosis.

Biography

Professor Jung Ryeol Lee graduated from the Seoul National University College of Medicine, where he also earned his Ph.D. Following this, he completed his residency and fellowship at Seoul National University Hospital and Seoul National University Bundang Hospital. He is currently a professor at Seoul National University College of Medicine and Seoul National University Bundang Hospital and serves as the chairman of his department.

Professor Lee has conducted extensive research and published numerous articles in the areas of fertility preservation, minimally invasive surgery, and assisted reproductive technologies. He is recognized as a leading figure among Korean clinicians and researchers. He is also a leading surgeon in the field of minimally invasive surgery, including single-port laparoscopic and robot-assisted surgery.

Why We Need to Teach Reproductive Health Education

Joyce Harper

Reproductive Science and Society Group, Institute for Women's Health, University College London, UK

Reproductive health includes puberty, the menstrual cycle, fertility, infertility, pregnancy, and menopause. Historically these topics are rarely covered in school education in any detail. For those countries that deliver sex education, it usually concentrates on how not to get pregnant and how not to get a sexually transmitted infection.
We have formed the International Reproductive Health Education Collaboration (IRHEC), a multidisciplinary group of experts working in reproductive health education and research (www.eshre.eu/IRHEC). Our mission is 'To increase fertility awareness using the life course approach, in order to improve reproductive health and facilitate decision-making in family planning among adolescents, people of reproductive age, primary healthcare, education professionals, and policymakers through development, evaluation and dissemination of inclusive educational resources.'
Reproductive health education is not just for women; it is for all, including the LGBTQ+ community. Some of this information is important even for those who do not want children. Menstrual cycle education should include information on ovulation and periods, what is a normal menstrual cycle, and what can go wrong, including endometriosis and polycystic ovarian syndrome (PCOS). Our study in UK schools show that the vast majority of students have not learnt about these issues, but 1 in 10 women will get endometriosis or PCOS.
Understanding the fertile window is important for all who menstruate but especially for those trying to conceive. It is also important to know that female fertility declines with age, especially after age 35. We are seeing a delay in the age of the birth of the first child globally, being over age 30 in many countries. We are also seeing a decrease in the total fertility rate (the average number of children a woman will have). This has reached 1.3 in several European countries. Our studies have shown that the majority of people who want children, want between 2 and 3 children. This would indicate that the majority of people are not having their desired family size.
Infertility affects a growing number of people, and it is key that people know the limitations of fertility treatment, costs, etc. Our studies have found that most people stop fertility treatment due to emotional reasons.
Preconception health, for both men and women, is key to fertility, a healthy pregnancy and the health of our future children. Many people do not realise how common miscarriage is.
We have carried out extensive research on the menopause and many women are entering this key stage in their lives with no knowledge. Understanding what the menopause is, the symptoms, and treatments are key for all women.
Reproductive health education for all is necessary, starting in schools and continuing throughout life.

Biography
Joyce Harper is an award winning educator, author, podcaster, academic, and scientist. She is Professor of Reproductive Science at University College London in the Institute for Women's Health where she is Head of the Reproductive Science and Society Group.
She has worked in the fields of fertility, genetics and reproductive science since 1987, written over 240 scientific papers and published three books.
She is leading the development of a National Menopause Education and Support Programme with support from key organizations.
She is co-founder of the UK Fertility Education Initiative (www.fertilityed.uk) and founder of the International Reproductive Health Education Collaboration (www.eshre.eu/IRHEC). She is working with schools in the UK and globally to help deliver reproductive health education.
Her latest book, Your Fertile Years, What you need to know to make informed choices, was published in 2021.
Her podcast is called Why Didn't Anyone Tell Me This? Available on all podcast channels.
Further information – www.joyceharper.com
Follow on Twitter, Instagram, Tiktok and Linkedin - @ProfJoyceHarper

How Preconception Care is Ring Bell for the ART?

Kuniaki Ota

Department of Obstetrics and Gynecology, Tokyo Rosai Hospital, Japan

The prevention of the onset of various diseases and improvement of pathological conditions have been recently reported by adhering to nutritional intake based on the Mediterranean diet and the traditional Japanese diet. In the field of obstetrics and gynecology, it has been reported that appropriate nutritional intervention as preconception care can prevent perinatal complications and modulate gene expression in the next generation.
In this context, we have been analyzing nutrition and fertility function as preconception care. Our work was cited in the 2017 edition of the guidelines for the treatment of infertility published by ESHRE, and the involvement of vitamin D in the treatment of infertility was noted for the first time. However, we could not deny the existence of discrepancies between vitamin D and reproductive medicine in actual clinical practice. We therefore searched for a coupling factor that would complement this discrepancy and focused on one-carbon metabolism, which is centered on a metabolic pathway in which folate and methionine are conjugated. Our findings revealed that the involvement of vitamin D in folate metabolism differs depending on the genetic polymorphism of methylenetetrahydrofolate reductase (MTHFR), which is involved in folate metabolism, and that the homocysteine-mediated metabolic pathway is related to reproductive function. Recently, we reported that folic acid supplementation improves the miscarriage rate in women and reduces oxidative stress of semen in men through a one-carbon metabolism-mediated mechanism. However, there are still many clinical questions that cannot be resolved by vitamin D alone or folic acid alone, and they continue to plague us.
We as medical professionals have little opportunity to learn about the essence of nutrition during our medical and healthcare studies, and while we understand the necessity of nutrition, we struggle to apply it practically in the field. However, numerous big journals in other fields have reported that nutrition leads to prevention and improvement of diseases, and those of us who specialize in reproductive medicine should not lag behind this trend. In this time, my topics will be educational in nature, reviewing the effects of nutritional interventions in reproductive medicine as reported to date, discussing what has emerged from our research and the potential benefits of nutritional interventions yet to be seen, and outlining future perspectives.

Biography

2021.11-present	Director, Department of Obstetrics and Gynecology, Tokyo Rosai Hospital
2020.11-2022.3	Assistant Professor in Fukushima Medical University, Fukushima Medical Center for Children and Women
2020.11-2021.10	Associate Professor in Toho University, School of Medicine, Department of Obstetrics and Gynecology
2018.1-2020.10	Assistant Professor in Fukushima Medical University, Fukushima Medical Center for Children and Women
2015.4-2017.12	Vice director in Nasu Red Cross Hospital, Tochigi
2013.9-2015.3	Fellow in Keio University, Department of Obstetrics and Gynecology, Tokyo
2011.7- 2013.9	Postdoctoral Fellow in Rosalind Franklin University of Medicine and Science Department of Microbiology and Immunology Clinical Fellow in Chicago Medical School at Rosalind Franklin University of Medicine and Science, Reproductive Medicine , Department of Obstetrics and Gynecology, Illinois USA
2009.7-2011.7	Research Fellow in Mayo Clinic Endocrine Research Unit, Minnesota USA
2009.6-2009.7	Research Trainee in Mayo Clinic Endocrine Research Unit, Minnesota USA
2008.8-2009.5	Senior resident in Toho University, Omori Medical Center, Tokyo
2007.9-2008.7	Medical Staff in obstetrics / gynecology, Ageo Central General Hospital, Saitama
2007.4-2007.8	Senior resident in Toho University, Omori Medical Center, Tokyo
2005.4-2007.3	Graduate Researcher (studying within the country), Graduate School of Medicine, Keio University, Department of Obstetrics / Gynecology, division of reproductive endocrinology, Tokyo
2002.4-2004.3	Resident in Internal Medicine, Toho University, Omori Hospital, Tokyo

Management of Gynecological Diseases as "Preconception Care"

Kaori Koga

Department of Reproductive Medicine, Chiba University Graduate School of Medicine, Japan

With the recent increase in the age of first childbearing, gynecological diseases are increasingly being discovered in women who are not yet planning to have a baby but wish to retain hope for the future, and the management of these diseases is often challenging. Furthermore, the treatment of these diseases itself may have a negative impact on fertility and the course of pregnancy, and the type of treatment and its timing has a significant impact on the maintenance and improvement of the fertility of patients affected by these diseases. This presentation will discuss the management of typical gynecological diseases in reproductive age from the aspect of "preconception care".

1) Endometriosis
According to recent international trends, surgery should be avoided for women who do not yet wish to become pregnant, and long-term medical therapy should be continued. On the other hand, there are also concerns about the impact of endometriosis on ovarian function and on the subsequent perinatal period if pregnancy does occur. Epidemiological data and basic findings from our mouse model will be presented in this lecture.
(2) Uterine fibroids
It is often difficult to evaluate and compare the risks of surgery prior to conception with those of infertility treatment and pregnancy without surgery. We would like to introduce methods of performing surgery prior to egg retrieval and after embryo freezing, as well as cases that are difficult to handle, such as diffuse uterine leiomyomatosis.
3) Adenomyosis
Pregnancies complicated with adenomyosis can lead to various complications such as pregnancy-induced hypertension as well as miscarriage and premature delivery. On the other hand, debulking surgery for adenomyosis carries the risk of uterine rupture during pregnancy. We would like to discuss this issue based on clinical data and findings from basic research.
(4) Endometrial cancer
Fertility preservation therapy using MPA is used for early-stage endometrial cancer. On the other hand, many patients are obese or have irregular menstrual periods, which often make subsequent infertility treatment and perinatal management difficult. We would like to propose the need for seamless care from treatment to pregnancy and after delivery, including an introduction of the Preconception Care Clinic at the Department of Obstetrics and Gynecology, the Chiba University Hospital.

Biography

Kaori Koga is the Professor and Chair of the Department of Reproductive Medicine, Graduate School of Medicine, Chiba University, Japan. She received her M.D. degree from Chiba University in 1996, and her Ph.D. degree from the University of Tokyo in 2003. She then worked as a post-doctoral fellow in the Uterine Biology Group (Lois Salamonsen's laboratory) at the Prince Henry's Institute, Australia, and in the Reproductive Immunology Unit (Gil Mor's laboratory) at Yale University. Her expertise is in the management of endometriosis, including MIS and ART. She is a board member of the World Endometriosis Society and the Society of Endometriosis and Uterine Disorders, and a member of the European Society of Human Reproduction and Embryology, the American Society for Reproductive Immunology and the International Society for Immunology of Reproduction.