21st Annual National Conference of the Indian Fertility Society

FERTIVISION 2025

Theme:
Green ART - Global Sustainability Initiative

INDIAN FERTILITY SOCIETY

12th to 14th DECEMBER

The Leela Ambience Hotel & Residences, Gurugram, Delhi NCR

Dr Prof (Col) Pankaj Talwar, VSM
President IFS
Organizing Chair

Dr (Prof) Shweta Mittal Gupta
Secretary General IFS
Organizing Secretary

Dr (Prof) Neena Malhotra
President Elect, IFS
Scientific Committee Chair

Souvenir

Souvenir

www.fertivision2025.com

INDEX

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महानिदेशक (संगठन एवं कार्मिक) ए एफ एम एस

Lt Gen Bhupesh K Goyal, AVSM, VSM
Director General (Org & Pers) AFMS

ASCON : 33089
Tele : 011-24199806
Fax : 011-24199741
Mobile : 9831423985
Email : bkgnona@gmail.com

कार्यालय महानिदेशक
सशस्त्र सेना चिकित्सा सेवा
रक्षा मंत्रालय
रक्षा कार्यालय परिसर
'ए' ब्लॉक चौथी मंजिल, रूम नं० 416
अफ्रीका एवेन्यू, नई दिल्ली-110023

Office of Director General
Armed Forces Medical Services
Ministry of Defence
Defence Offices Complex
'A' Block, 4th Floor, Room No. 416
Africa Avenue, New Delhi-110023

MESSAGE

1. Preventing postpartum haemorrage (PPH), a leading cause of maternal mortality, is one of the most crucial pillars of safe motherhood. Timely anticipation, unwavering vigilance and proactive care can avert this obstetric emergency and protect a mother's life. When clinicians maintain alertness, systems ensure adequate resources, and policies reinforce evidence-based practices, a coordinated and effective defence can be created against PPH.

2. To strengthen outcomes, standardized protocols for diagnosis, prevention, and management must be uniformly implemented across all levels of healthcare serving as a roadmap for all involved in maternal health. Outlining of these evidence-based steps in the form of well-structured guidelines for assessment, prevention, and intervention for PPH is an admirable step taken by the Department of Obstetrics and Gynaecology, Army Hospital (R&R), Delhi Cantt. The team deserves sincere appreciation for addressing such a pertinent and lifesaving topic with dedication, expertise, and foresight.

3. In the sacred moment when a new life enters the world, no mother should face the shadow of a preventable mishap. As an institution we pledge to protect, to respond, and to stand united for every mother's wellbeing.

'Jai Hind'

(Bhupesh K Goyal)
Lt Gen
DG (Org & Pers) AFMS

Station: New Delhi

Dated: 01 Dec 2025

Message from Guest of Honor

Dr. Mandeep Sachdeva
HMC Registrar
GOH

Dr. Mandeep Sachdeva

HMC Registrar

Date: 04/12/2025; Panchkula, Haryana

To the Esteemed Delegates, Colleagues, and Friends of FERTIVISION 2025,

Greetings!

It is with great pleasure and enthusiasm that I extend my heartiest congratulations to the Indian Fertility Society (IFS) for organizing FERTIVISION 2025, which is the 21st Annual Conference of the Indian Fertility Society. The conference is set to be held from December 12th to 14th at The Leela Ambience Hotel & Residences, Gurugram.

The theme for this year's conference, "Green ART – Global Sustainability Initiative", is highly relevant and forward-thinking. In line with this theme, the focus of the conference will be on evidence-based practices and the latest advancements in the field. The academic program promises comprehensive updates in Reproductive Medicine—covering everything from foundational principles to emerging innovations—with topics including Artificial Intelligence in ART and Non-invasive Pre-implantation Genetic Screening.

FERTIVISION 2025 offers a great platform for academic exchange, and it provides a huge platform for the young doctors to learn and exchange their views. Attendees will benefit from access to a stellar lineup of renowned national and international speakers who will share their cutting-edge research and clinical expertise. Furthermore, the event will feature oral presentations, E-posters, and opportunities to win awards in multiple categories. Moreover HMC credit hours will help in renewal of registration

This Souvenir serves as a valuable record of this significant event, capturing the spirit of science, camaraderie, and the vibrant culture and hospitality of Delhi. We look forward to your enthusiastic participation.

With best regards,

Sincerely,

MS

Dr. Mandeep Sachdeva

HMC Registrar FERTIVISION 2025

Message from the IFS President Pen

Dr (Col) Pankaj Talwar, VSM MD PhD
President, Indian Fertility Society 2024-26
Organizing Chair, FERTIVISION 2025

Dear Esteemed Participants,

On behalf of the organizing team of IFS 2025, I am honoured to welcome you all to this academic event the **21th Annual Conference of Indian Fertility Society, Fertivision** from **12th, 13th & 14th December 2025** at the **Leela Ambience Hotel and Residences, Gurugram. Haryana, India.** The theme of this conference is " Theme - Green ART Global sustainability initiative". The scientific programme has been put together in accordance with this. We have aimed to bring together various stakeholders with dedicated sessions and workshops carefully crafted to deliberate on their fields of impact and interest. There are 17 pre- conference workshops on 12th December focussing on skill and knowledge enhancement. These include Optimizing Practice for Level 1 Art Clinician, Optimizing Practice for Level 2 Art Clinician, OPU & ET: Techniques, Challenges & Best Practices, Gamete & Embryo Cryo Preservation: Practical Approach, Role Of Andrology In ART: From Diagnosis To Conception, Endoscopy: A Key To ART Success (Video Workshop), Mastering USG In ART : From Basics To Advanced, Advanced ICSI: Optimising For IVF Success, Regenerative Therapies In IVF, Immunogenetics In RIF And RPL: Strategies For Better Outcome, Art Of Counselling In ART: Navigating Fertility Challenge, Essential Skills For ART Nurses: A Practical Approach, Fertility Preservation In ART: Case Based Approach, Genetics And PGT: Case Based Approach & Embryo Biopsy Workshop, AI In Manuscript Writing, Effective Lab Management: Ten Commandments, Law In ART: Best Practices & Compliance. Hope you all will enjoy this scientific feast.

In this Fertivision 2025 Souvenir, we have a galaxy of national and international experts to deliberate on various related subjects during this conference. There are more than 12 renowned International faculty present physically for interaction, dedicated sessions with other societies like International Federation of Fertility Societies (|FFS), British. Fertility Society (BFS), Indian Society of Assisted Reproduction (ISAR).

Annual awards will be distributed under various categories based on scientific and academic excellence. This much-awaited mega event shall provide an opportunity to our faculty, delegates from various streams and fellows to interact, share their experiences and go back enriched and motivated to work towards providing quality care. Keeping up with the theme **Green ART Global sustainability initiative**, this conference has been specially focused on the green IVF , a global initiative encouraging sustainable and environmental friendly measures in the arena of assisted reproduction .Hope that all participants leave with good take home messages

Best regards,

Dr (Col) Pankaj Talwar, VSM MD PhD
President, Indian Fertility Society 2024-26
Organizing Chair, FERTIVISION 2025

Message from the IFS President Elect

Dr (Prof) Neena Malhotra
MD, DNB, FRCOG, FAMS, FICOG),
Head Department of Obstetrics and Gynecology, AIIMS, New Delhi
President Elect , Indian Fertility Society
Scientific Committee Chair, FERTIVISION 2025

Dear Esteemed Participants,

It gives me immense pleasure to write a message for the **21st Annual Conference of the Indian Fertility society (IFS)**, at Delhi. Two decades of hard work, camaraderie, and a vison to reach great heights, a society with humble 50 members to begin with is now an illustrious society of over 6000 members. The journey has been stupendous with amazing goals achieved and the society being recognized at National and International platforms as an organization dedicated to training, learning and disseminating knowledge in Reproductive Medicine.

IFS has made great strides in achieving a status with academic and teaching training as its core ethos and continues to deliver this through its meetings all year round. But the annual conference is when the society surpasses all to create an event that goes as a memorable landmark year after year. We have done 20 conferences in the past, each excelling over the previous, and so is this one at Ahmedabad. The theme **"Green ART-Global Sustainability Initiative "** is aptly chosen to update knowledge considering the rapid and evolving technology that is working towards improving outcomes in ART. The scientific programme has been curated by the committee keeping the dynamism related to the sub-specialty of Reproductive Medicine. The pre-congress workshops and the main conference shall rightfully give the delegates insights into the recent developments through deliberations by renowned faculty. The galaxy of International and National faculty has been peer selected to share their vast enriching experience such that we not just learn but unlearn to benefit patient care and outcomes in ART

The city of Gurgaon in Delhi NCR, is an opportune venue as it is the cusp of Indian culture and technology, often called the Millenium city. The gourmet delight at the hotel Leela Ambience attracts tourists across the country. The Indian hospitality and warmth will be felt all through your stay and the organizing team has left no efforts to make this event that will be remembered by all for a life-time.

I am truly humbled to be a part of this prestigious organization that has given me opportunity over years to be mentored by seniors who have fueled my growth both at academic and personal level. As a President Elect, I take the privilege to welcome you all to this mega event of the year which is historic milestone as we move forward in our journey of delivering excellence in academics and research.

With Best wishes

Neena Malhotra

Dr (Prof) Neena Malhotra
MD, DNB, FRCOG, FAMS, FICOG),
Head Department of Obstetrics and Gynecology, AIIMS, New Delhi
President Elect , Indian Fertility Society
Scientific Committee Chair, FERTIVISION 2025

Message from the IFS Secretary General

Dr (Prof) Shweta Mittal Gupta
Secretary General, Indian Fertility Society 2024-26
Organising Secretary, Fertivision 2025

Dear Esteemed Participants,

On behalf of the Organizing Committee, it is with immense pleasure that I extend a warm welcome to all esteemed faculty members and delegates attending the **21st Annual Conference of the Indian Fertility Society (IFS) – Fertivision 2025**, scheduled to be held from **12th–14th December 2025 in Gurugram.**

The theme for this year, **"Green ART- Global Sustainability initiative"**, has been thoughtfully chosen to highlight the urgent need for environmentally responsible and resource-efficient practices in Assisted Reproductive Technology (ART). This theme reflects not only the evolving landscape of reproductive medicine but also our collective responsibility toward a sustainable future.

We are proud to share that the conference will feature 17 dedicated workshops, designed to provide in-depth learning and practical exposure to participants. This will be followed by two days of the main conference, comprising enriching sessions, panel discussions, and keynote lectures by some of the most distinguished national and international experts in reproductive medicine. Their presence and insights will undoubtedly elevate the academic and scientific standards of this event.

This congress places special emphasis on nurturing the next generation of ART specialists—the innovators who will lead India into a new era of reproductive medicine. Their enthusiasm, ideas, and dedication will be instrumental in transforming the future of fertility care, nationally and globally.

The inauguration ceremony will also mark the release of a Souvenir, a memorable keepsake of this landmark event. We are also delighted to announce the launch of several important books in reproductive medicine, along with a special publication dedicated to self-empowerment that will serve as valuable guides for professionals in the field.

Over the next three days, together we will explore new ideas, share expertise, and build partnerships that will redefine the future of fertility treatment and reproductive well-being.

It is our privilege to host you at this milestone event, and we hope it will leave you with enriching experiences, lasting connections, and cherished memories.

Warm regards,

Dr Shweta Mittal Gupta
Secretary General, Indian Fertility Society 2024-26
Organising secretary,
Fertivision 2025

IFS President Oration

Dr (Col) Pankaj Talwar, VSM MD PhD
President, Indian Fertility Society 2024-26
Organizing Chair, FERTIVISION 2025

“She Heals All, But Who Heals Her? A Gynaecologist's Silent Journey"

Today, I write this note to celebrate a very special group of individuals—women gynaecologists of India. They are the quiet pillars of our healthcare system, the compassionate healers of our society, and the invisible architects of nation building. In every part of this country—from bustling metros to remote rural corners—women gynaecologists work tirelessly to safeguard the health, dignity, and future of millions of women, mothers, and families.

The contribution of a gynaecologist goes far beyond clinical practice. We are custodians of life at its most delicate stages. We guide young girls through the storms of adolescence, support women through the joys and perils of pregnancy, and stand beside families during their most vulnerable moments. We hold the responsibility of ensuring safe motherhood, healthy childbirth, and long-lasting reproductive health—issues that directly shape the nation’s demographic strength, social stability, and economic progress. When we empower a woman with good health, we empower an entire generation.

Yet behind this noble service lies a deep personal story—one of extraordinary perseverance. Most women gynaecologists in India work close to 70–80 hours a week, often stretching themselves beyond physical and emotional limits. We juggle the never-ending demands of emergency calls, night duties, surgeries, and clinics while simultaneously fulfilling the roles of mothers, wives, daughters, and caregivers at home. It is a dual responsibility that requires immense strength, discipline, and sacrifice—yet we carry it with grace and unwavering dedication.

Despite this, our contributions remain largely unrecognized. The world sees the outcomes—the saved mother, the healthy newborn, the relieved family—but rarely the person behind the achievement. Rarely the sleepless nights. Rarely the missed family moments. Rarely the emotional weight we silently carry. But today, let us acknowledge this truth: women gynaecologists are among the greatest unsung heroes of our nation.

We are not just medical professionals; we are nation builders. Every safe delivery is a step towards reducing maternal mortality. Every counselled adolescent girl is a step towards a healthier society. Every empowered woman creates ripple effects that strengthen families, communities, and the country’s future. Our service to women’s health is not just a profession—it is a patriotic duty.

India’s progress depends on the health and empowerment of its women, and women gynaecologists stand at the frontline of this mission. With compassion as our tool, knowledge as our strength, and resilience as our armour, we have shaped countless lives quietly and selflessly.

We all must pay a rich tribute to every woman gynaecologist who has ever rushed to the hospital leaving her sleeping children behind, who has ever worked through exhaustion because a mother needed her, who has ever put her own needs aside to serve humanity. You are the pride of our profession. You are the heartbeat of our healthcare system. You are the true heroes of India.

May your dedication continue to inspire, uplift, and strengthen our nation.

President Elect Oration

Dr (Prof) Neena Malhotra
MD, DNB, FRCOG, FAMS, FICOG),
Head Department of Obstetrics and Gynecology, AIIMS, New Delhi
President Elect , Indian Fertility Society
Scientific Committee Chair, FERTIVISION 2025

"Challenges and Opportunities for ART in the 21st Century"

Ever since the birth of Louise Brown, over 10 million babies have been born from Assisted Reproductive Techniques world over. Currently, IVF accounts for approximately 2–5% of all births globally. Research and advancement in technology, have improved our understanding of the process of ART, resulting in better availability and accessibility of ART services. However, the dramatic advances in technology have not translated to similar improvements in live birth rates. The pregnancy rates per fresh are at best 40% among good prognosis patients at 20-34 years, declining to just 25% in women at 38-39 years. The challenges to improve ART success have been growing over the last
The growing challenges to ART in the current decade include:

• **Growing demand and disparity in availability of IVF –** There is a stark disparity with dismal availability and accessibility in countries where demand is highest. The availability of ART services in India is 79 as against 2747 per million inhabitants in Belgium. The affordability is another major issue in developing countries as India. While over 60% have affordability for ART in USA where couples are capable of spending out of pocket it lesser than 10% in countries including Australia and even Israel where ART is partially and fully funded respectively.

• **Changing Patient profile-** The profile of patients undergoing in vitro fertilization (IVF) has shifted, primarily characterized by an increase in the average maternal age, and a rise in women with poor ovarian reserve despite young age. The evolving rise in women with diminished reserves at any age may probably be the outcome of epigenetic changes given the role of Endocrine disruptors that may be responsible.

• **Evolving Technologies that have not met our expectations to improve LBR –**The availability of high technology from embryoscope to PGT-A, have improved laboratory comfort for the scientist but has it translated to higher live births is a matter of debate.

• **Expectations of couples-** as couples approach parenting second to their careers, reaching for ART services at advanced ages have spiralled in the last decade across the globe including India. While advanced maternal age is known to lower pregnancy rates, are we confident to say results are not compromised with older men. Yet expecting optimal outcomes from ART is a big challenge to clinicians, embryologists alike

• **Ethics and Law.** With the new ART bill in place, challenges for both service providers and clients continue to daunt. While India may no longer be a surrogacy haven, oocyte donation remains limited with centres designated. This brings on added costing to couples, considering the added burden to centres as well.
In terms of law, we still do not have a robust registry and are still not sure on the number of cycles or live birth that India contributes globally.

OPPURTUNITIES FOR ART

Despite the challenges, there is optimism as far as ART in India. While new technology is available, there is wider acceptance both on the part of clinician and patients. Improvising technology and tailoring to our patients profile for ovarian stimulation to NIPGT are all possible. With artificial intelligence creating new hopes we are likely to use it precisely for better outcomes. Robotic labs created live birth, are given reasons to use technology when human resources are limited and questionable.
Overall while challenges continue there are reasons to triumph with advances in technology and AI, but certainly leaving us still with many unanswered questions.

Oration

Dr Elizabeth S. Ginsburg, US
ASRM President
Professor of Obstetrics, Gynecology and Reproductive Biology
Harvard Medical School

“Is AMH only a Predictor of egg Number or Does it also predict Quality?"

AMH predicts oocyte quantity not quality

Prospective studies have not found a low AMH to predict women who develop infertility, as it does not differ from those who conceive naturally. AMH has also not been found to differ in women who conceive with oral ovulation induction IUI and those who do not conceive. AMH is an excellent predictor of response to gonadotropins, and women with low AMH levels develop fewer follicles than women with normal or high AMH levels. It does not predict pregnancy rate, but a high AMH is associated with a higher risk of multiple birth in these patients. In women undergoing IVF, embryo cell division, blastocyst development, and euploidy rates are consistent with oocyte age, and not AMH levels. All these data support that AMH is a predictor of oocyte number but not quality.

Oration

Dr Nikolaos P. Polyzos
Spain

Artificial Intelligence : The digital renaissance in Reproductive Medicine

Artificial intelligence (AI) is rapidly advancing the field of reproductive medicine, impacting both laboratory and clinical practice. In IVF labs, AI technologies automate and refine critical steps such as sperm analysis, oocyte classification, and embryo selection. Machine learning models assist in determining sperm morphology, motility, and DNA integrity, facilitating more accurate selection for fertilization and improved blastocyst formation. AI-based embryo assessment using time-lapse and static imaging demonstrates promising predictive power for successful IVF outcomes and chromosomal normality (euploidy), with performance rivaling or exceeding human embryologists in several studies.

Clinically, AI enhances ultrasound reliability, automates follicular assessment, and supports the individualized selection of ovarian stimulation protocols by integrating patient demographic, hormonal, and genetic data. These models optimize dosing, save resources, and enable more precise timing for ovulation triggers and oocyte retrieval, which translates into improved clinical workflow and outcomes.

Furthermore, AI offers tools for comprehensive IVF clinic management, including scheduling, workload prediction, and planning natural cycle frozen embryo transfers. While AI brings significant improvements in efficiency, consistency, and decision-making, current evidence supports its role as an augmentative tool rather than a replacement for fertility specialists. The future of reproductive medicine is expected to see human expertise synergistically partnered with AI-driven innovation, leading to more personalized patient care and better outcomes.

13th Embryology Certification & ESHRE Preparatory Course

IFS Conducts 13th Embryology Certification & ESHRE Preparatory Course
Five-Day Flagship Program Sees Enthusiastic Participation from 67 Delegates

The Indian Fertility Society (IFS) successfully conducted its 13th Embryology Certification and Embryology Preparatory Course for ESHRE Exams on 2nd, 9th, 16th, 23rd and 30th November 2025, held from 3:00 PM to 7:30 PM with academic support from CooperSurgical. Widely regarded as one of the most prestigious embryology training programs in India, this year's edition saw 67 delegates participate, reflecting strong national interest in structured embryology training aligned with international standards.A total of 67 delegates participated in this edition—reflecting a strong interest among embryologists and ART professionals in formal certification and ESHRE-aligned preparation.

The course was led by a distinguished faculty panel, including Course Chairperson Dr. Kuldeep Jain, IFS President Dr. (Prof) Pankaj Talwar, IFS General Secretary Dr. (Prof) Shweta Mittal Gupta, and Course Directors Dr. Jayant Mehta and Dr. Arne Sunde

The program was enriched by an eminent and diverse course faculty, which included:
Dr. Bodhana Dhole, Dr. Rajvi Mehta, Prof. Rima Dada, Dr. Deepak Modi, Dr. (Prof) Pankaj Talwar, Dr. Rupali Bassi, Dr. Shweta Mittal, Dr. Neena Malhotra, Dr. Gaurav Majumdar, Dr. Surveen Ghumman, Dr. Venugopal, Prof. Dr. Kuldeep Jain, Dr. Oriol Oliana, Dr. Ethiraj Balaji Prasath, Dr. Steven Fleming, Dr. Martine Nijs, Dr. Arne Sunde and Dr. Jayant Mehta.

Delegates benefited from high-quality lectures, case discussions, lab-oriented insights and practical preparation for the ESHRE Clinical Embryology Exam. A major highlight was the Mock ESHRE-style Exam, providing participants with realistic assessment experience. All attendees received the IFS Course Attendance Certificate, while those fulfilling exam requirements qualify for the IFS Embryology Certification, an important step for career advancement in ART.

The program covered a wide range of embryology themes—from basic laboratory principles and gamete handling to troubleshooting embryology workflow, new technologies, embryonic development assessment and international quality benchmarks. With faculty representation from both India and overseas, participants gained an excellent blend of global perspectives and practical, India-specific guidance.

The strong turnout of 67 delegates reaffirmed the relevance of this flagship IFS program and its contribution to strengthening embryology competency across the country.

21 September 2025 | JIO World Convention Centre, Mumbai
Theme: New Ovarian Stimulation Protocols – Are They Better?

The ESHRE Campus program held in collaboration with IFS (Indian Fertility Society) and ISAR (Indian Society for Assisted Reproduction) successfully concluded on 21st September 2025, drawing an impressive 250 delegates from across the country. The half-day academic event took place at the prestigious JIO World Convention Centre, Mumbai, and focused on the rapidly evolving landscape of ovarian stimulation strategies in ART.

Key Highlights

The scientific theme, "New Ovarian Stimulation Protocols: Are They Better?", drew strong interest from clinicians, embryologists, and ART specialists.

The meeting featured leading ESHRE faculty including Carlos Calhaz-Jorge, Karen Sermon, Christophe Blockeel, and Anis Feki, who shared insights on global best practices and future directions.

Indian faculty, led by Organising Chairpersons Dr. Kuldeep Jain, and Dr. Nandita Palshetkar , col Pankaj talwar and Dr Ameet patki and Organising Secretaries Dr. Sunita Tandulwadkar and Dr. Shweta Mittal, delivered high-value lectures with practical clinical perspectives.

Scientific Sessions at a Glance

The program covered a broad range of timely topics, including:

Adjuvants in ovulation induction
GnRH agonist use in the antagonist era
PPOS in ART cycles
Managing PCOS-related ovulation challenges
Poor responders and stimulation optimisation
Luteal phase support: individualisation and evidence
FET and fresh cycle regimen considerations

International speakers Erkan Kalafat (Turkey), Annalisa Racca (Italy), and Caroline Roelens enriched the discussions with global viewpoints.
Panel discussions, moderated by senior faculty such as Dr. Asha Baxi and Dr. Surveen Ghumman, brought forward practical case-based learning with contributions from leading ART experts.
Participation & Engagement

The enthusiastic turnout of m9re than 250 delegates highlighted the strong momentum within the reproductive medicine community and the continued commitment to evidence-based practice. The programme offered a vibrant platform for academic exchange, networking, and collaborative learning.

Take-Home Message

The 2025 ESHRE–IFS - ISAR Campus event reinforced the need for continuous updating of ovarian stimulation approaches. With new protocols emerging and patient needs becoming increasingly diverse, the interactions and deliberations at this meeting will undoubtedly support improved clinical decision-making across ART centres.

Tubal Surgery a Sustainable Option to treat Infertility

A.Watrelot
Hôpital NATECIA-LYON
FRANCE

Tubal factor infertility remains a significant global health issue, accounting for approximately one-third of female infertility cases. While in vitro fertilization (IVF) has become the dominant treatment strategy over the past decades, there is renewed interest in tubal surgery as a sustainable, effective, and patient-centered alternative for selected individuals. We explore the contemporary role of tubal surgery in infertility management, examining its clinical effectiveness, long-term value, and relevance in diverse healthcare settings.

Advances in minimally invasive techniques, like laparoscopy, have substantially improved the outcomes of tubal reconstructive procedures. For women with focal adhesions,sterilization reversal, or distal tubal occlusion surgical intervention can restore natural fertility with pregnancy rates that, in appropriate candidates, rival or exceed cumulative IVF success rates. Importantly, tubal surgery allows repeated cycles of natural conception without additional interventions, thereby reducing the physical, emotional, and financial burden often associated with assisted reproductive technologies.

Sustainability has become an increasingly important dimension of medical decision-making, encompassing economic accessibility, environmental responsibility, and long-term patient autonomy. Compared with IVF—which requires repeated cycles, intensive laboratory resources, and significant energy consumption—tubal surgery offers a one-time, resource-sparing solution. This advantage is particularly relevant in low- and middle-income countries, where access to IVF is limited and affordability remains a major barrier. By restoring natural fertility, tubal surgery also aligns with patient preferences for less medicalized conception and reduces dependency on technologically intensive treatments.

Despite these benefits, tubal surgery is underutilized, partly due to declining surgical expertise and misconceptions regarding its success rates and risks, particularly ectopic pregnancy. However, recent data demonstrate that, when performed by experienced surgeons and in properly selected patients, complication rates remain low and reproductive outcomes are compelling.

In conclusion, tubal surgery represents a viable and sustainable option for the treatment of infertility. It offers meaningful advantages in terms of cost-effectiveness, patient autonomy, and ecological impact, while providing competitive reproductive outcomes. Reconsidering its role within contemporary fertility care can expand treatment choices and promote more equitable and sustainable reproductive healthcare worldwide.

Dr Akshaya Kumar Mahapatro
M.D (O&G),Postdoctoral Fellowship in Reproductive Medicine.
Medical Director , Shreya IVF Centre Pvt Ltd.
Bhubaneswar ,Odisha.

Rejuvenate meaning - To make something more effective, modern and successful by using new ideas and methods.

Ovarian Rejuvenation- A procedure intended to re-awake egg maturation and development within the ovary by activating dormant follicles. It is a

process by which the production of eggs is artificially stimulated, giving women the chance to produce more eggs than they would do naturally, therefore giving them the chance to conceive using their own genetic material. Ovarian rejuvenation aims at inducing differentiation of ovarian stem cells to oocytes, transitioning primordial follicles to primary follicles and delaying apoptosis of existing follicles.

It is indicated in infertile women having low ovarian reserve and low AMH levels, women with premature ovarian failure, Primary ovarian Insufficiency, loss of ovarian function due to chemotherapy.

These experimental protocols involve: (i) Platelet-rich plasma (PRP), (ii) Exosome therapy, (iii) In vitro activation (IVA), (iv) Stem cells therapy, (iv) microRNAs, (v) Mitochondrial targeting therapies and vi) Ovarian rejuvenation with human placenta hydrolyzate.

1. Platelet-rich Plasma ---(PRP) is an autologous blood derivative, containing greater concentration of platelets and has a 5- to 10

fold higher concentration of growth factors (GFs) (>800 types) than peripheral blood. PRP helps in induction of cell migration, chemotaxis, angiogenesis, keeping balance between oxidative stress. Growth factors contained in PRP helps in the recruitment of uncommitted OSCs to differentiate into de novo oocytes (de novo oogenesis) , the activation of dormant primordial follicles (Pfs) and support of each step of folliculogenesis from Pf to pre-ovulatory follicle, and the decrease in apoptosis (atresia) of existing follicles. In all studies the route of intraovarian PRP administration is via USG guided trans vaginal 17G-18G needle, performed under minimal sedation . In mostof the studies, PRP is delivered intramedullary, at multiple sites, except two studies, in which it is also diffused in the subcortical layers .

2. Exosomes(exos) therapy--Exosomes (exos) are extracellular vesicles released, principally from mesenchymal stem cells (MSCs), ranging in size from 30 nm to 150 nm. The main mechanism of ovarian rejuvenation induced by exos therapy is exerted at the level of granulosa cells, the quality of which is implicated in POI, there is increased proliferation in parallel with decreased apoptosis, being associated with upregulation of phosphoinositide 3 kinase– protein kinase B (PI3K/Akt) and B-cell lymphoma 2 (Bcl2) , alongside with down regulation of SMAD and Bcl-2 associated X protein (Bax) signalling pathways. Exos are considered as potentially safer than stem cells (SCs) due to lack of tumorigenicity, low immunogenicity and no ethical concerns.

3.In vitro activation— Primodial follicle activation occours mainly due to three signal pathways PTEN–PI3K–Akt/transcription factor fork head box

O-3 (FOXO3), the mammalian target of Rapamycin complex 1 (mTORC1) and Hippo pathways. The most important observation, based on these

studies is that mature oocytes were retrieved only by patients whose histological examination of the removed ovary revealed primordial follicles.

4. Stem cell therapy---Stem cell therapies have been employed using mainly human pluripotent stem cells (hPSCs) or MSCs Stem cell therapy.it can either be autologous (using the patient's own SCs) or allogenic (SCs provided by a healthy donor) . According to the reported results, MSCs induce menses resumption at 2.9%-44%, increased level of E2, decreased level of FSH and LH , increased ovarian volume and ovarian blood low.

Nevertheless, SC therapy does not appear to improve AMH and AFC. The principal mechanism of SC-mediated ovarian rejuvenation is improvement of ovarian microenvironment, exerted by secretion of growth factors, transcription factors and enzymes such as heme oxygenase 1. Potential risk of SC therapy includes tumorigenicity and immune rejection and also high cost therapy.

5. Micro-RNAs--Micro-RNAs are short, 18–24 nucleotides long, non-coding RNAs, which regulate cell proliferation, differentiation and

apoptosis . Their pathogenetic role in POI has been increasingly recognized over the last years, being involved in steroidogenesis, granulosa cell proliferation/apoptosis, autophagy and follicular development by regulating specific pathways, such as the PI3K/Akt/mTOR, TGFβ, mitogen-activated protein kinase (MAPK) and Hippo pathways.

6. Mitochondrial targeting therapies---Mitochondrial dysfunction is mainly associated with ovarian aging . In addition, patients with idiopathic POI have significantly less mitochondrial DNA content , to bear more mitochondrial mutations, especially in the respiratory chain, and to have higher reactive oxygen species level and lower adenine triphosphate level . Studies with nutrients targeting mitochondrial function, such as Q10, Resveratrol and Melatonin reveal that the latter might be effective in delaying ovarian aging, via increasing antioxidant capacity, maintaining telomerase activity and activating Sirtuin 1. photobiomodulation therapy (PBMT) with low-level laser light therapy (LLLT) is known to exert its rejuvenative effects via targeting the chromophore cytochrome C oxidase in mitochondrial membrane .

7.Ovarian rejuvenation with human placenta hydrolyzate—Human placenta hydrolyzate contains growth factors, hormones, trace elements, vitamins. Administration of human placenta hydrolyzate directly to the ovaries can also activate folliculogenesis and oogenesis.

Conclusion—

POI is a condition of heterogenous aetiology affecting 3.7% of female population worldwide. Ovarian rejuvenation is currently an adjuvant therapy, high-level evidence is not yet available. However, for women with POI and POR, any opportunity to improve the chances of obtaining their own oocytes is valuable. Among the above experimental methods of ovarian rejuvenation, intraovarian PRP administration seems to be better technique, less invasive, and more efficacious, especially considering spontaneous conception (7.4%–10%). In contrast to SC based therapies which are expensive, PRP and IVA protocols are low-cost approaches. Biological therapies such as Ovarian rejuvenation shows promising results but are still in their initial experimental stage. Among the existing clinically applied techniques such as PRP, IVA, SC transplantation therapies, the short-term follow-up of the conducted studies does not allow us to draw conclusions either about the duration of ovarian rejuvenation by each method or about safety of the techniques.

Key words- POI(Premature ovarian insufficiency), OSCs(ovarian stem cells), PRP(plate rich plasma)

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Unveiling Hidden Patterns in IVF Laboratory Data: A PCA-Guided Cluster Validation Approach

Abstract

Dr Sergei Sergeev
Sergei Sergeev. Lasha Nadirashvili, Veniamin Kazarinov
Georgia German Reproductive Center, Tbilisi

Background and Objectives

In vitro fertilization (IVF) laboratories generate complex, multidimensional datasets encompassing patient demographics, ovarian stimulation parameters, embryological outcomes, and laboratory key performance indicators (KPIs). Traditional quality control approaches rely on univariate metrics that fail to capture the multifactorial nature of IVF success. We developed a comprehensive unsupervised machine learning framework integrating dimensionality reduction with cluster validation to identify natural groupings within IVF laboratory data, enabling case-mix-adjusted performance benchmarking.

Methods

We analyzed 571 fresh IVF cycles from a single center, incorporating 18 continuous variables: patient age, cycle attempt number, ovarian response metrics (follicle count, oocytes retrieved), embryological outcomes (fertilization, cleavage, blastocyst formation rates), and neural network-predicted pregnancy probabilities. Four dimensionality reduction techniques were systematically compared: Principal Component Analysis (PCA), t-distributed Stochastic Neighbor Embedding (t-SNE), Uniform Manifold Approximation and Projection (UMAP), and Isomap. Cluster quality was assessed using silhouette coefficient, Calinski-Harabasz index, Davies-Bouldin index, and elbow method. K-means, hierarchical agglomerative, and DBSCAN clustering algorithms were compared. External validation was performed on 847 cycles from two independent centers.

Results

PCA explained 57.88% of total variance (PC1: 42.84%, PC2: 15.04%), while t-SNE demonstrated superior local structure preservation (trustworthiness=0.969, pseudo-explained variance=0.684). Despite statistical validation metrics favoring k=2 (silhouette=0.235), we selected k=3 based on clinical interpretability and biological plausibility, achieving silhouette=0.186 while maintaining highly significant separation across 17 of 18 measured parameters ($p<0.01$, Kruskal-Wallis tests).

Three distinct IVF phenotypes emerged: Cluster 0 (Standard Responders, 32%) - mean age 32.4 years, 16.7 oocytes, 10.6 blastocysts, 54% predicted pregnancy rate; Cluster 1 (Poor Responders, 34%) - mean age 20.3 years, 9.5 oocytes, 4.9 blastocysts, 33% predicted pregnancy rate; Cluster 2 (High Responders, 34%) - mean age 31.6 years, 28.2 oocytes, 17.3 blastocysts, 63% predicted pregnancy rate. K-means outperformed hierarchical clustering (silhouette=0.119) and DBSCAN (75.3% classified as noise).

External validation across independent centers yielded consistent results: t-SNE remained optimal (trustworthiness=0.930), k-means achieved silhouette=0.190 (k=3), confirming generalizability. Physicians showed no significant differences in actual pregnancy rates ($\chi^2=3.86$, $p=0.278$) but significant differences in neural network-predicted probabilities ($\chi^2=28.48$, $p<0.001$), demonstrating case-mix heterogeneity that crude pregnancy rate comparisons fail to capture.

Conclusions

Unsupervised machine learning successfully identified three clinically meaningful IVF protocol categories with robust external validation. The framework enables fair, case-mix-adjusted embryologist performance evaluation, overcoming limitations of crude success rate comparisons. Integration with neural network prediction models provides a comprehensive quality control system accounting for protocol heterogeneity in assisted reproduction.

Rachel Chin
MBBS, MD (Obstetrics and Gynaecology)
Department of Reproductive Medicine and Research

Sperm preparation prior to assisted reproduction aims to eliminate seminal plasma while at the same time to concentrate good quality motile sperm with high DNA integrity. The two main conventional methods are swim-up and density gradient centrifugation. Swim-up method is based on sperm motility. Density gradient centrifugation separates sperm based on its density after one round of centrifugation step with two di erent density of silane-coated silica particles, follow by at least one more centrifugation step as washing step using sperm preparation media. Though both methods have demonstrated a significant lower sperm DNA fragmentation index in its post processed sample as compared to raw semen sample, the concern of repeated centrifugation steps, inconsistency in the yield, time consuming, high risk in SOP drift and sample mismatch due to multiple handling steps have prompted IVF laboratories to explore alternative sperm preparation methods. New sperm preparation methods such as electrostatic sperm separation, magnetic activated cell sorting or electrophoretic sperm preparation have been developed. Most of these methods require a new set of equipment which can be a financial challenge to IVF laboratory. Above all, the lack of compelling clinical evidence is the key factor why these methods fail to gain popular use for sperm preparation. The development of sperm separation device, ZyMōtÔ that uses a chip to isolate most motile sperm with good morphology and low DNA fragmentation has revolutionized sperm preparation for assisted reproduction technologies. The device uses a permeable polycarbonate membrane with 8µm pores, allowing motile sperm to swim through the pore and to be harvested for use. Various clinical studies have shown a significant better sperm motility with lower sperm DNA fragmentation index for ZyMōtÔ sperm separation device harvested sperm than swim-up, density gradient centrifugation or even magnetic-activated cell sorting. Banti M, et al. 2024 shared their data where significantly higher euploid rate registered from ZyMōtÔ sperm separation device arm versus density gradient centrifugation arm. Apart from the clinical evidence, the added value of ZyMōtÔ sperm separation device on streamlining sperm preparation process, and improving lab e iciency on time, cost and risk mitigation on error would make it a new horizon in sperm preparation for assisted reproduction.

Sperm DNA Fragmentation: A Contemporary Approach to Management

Robert E. Brannigan, MD
President, ASRM
Janice Binstein Professor and Vice Chair of Clinical Urology
Head, Division of Male Reproductive Surgery & Men's Health
Department of Urology
Northwestern University, Feinberg School of Medicine
Chicago, Illinois

Sperm DNA fragmentation can have adverse effects on male reproduction across the spectrum, adversely impacting success rates with efforts for natural conception, IUI, and IVF/ICSI. In this session, we will discuss both intrinsic factors (inflammation, infection, obesity, and varicocele, etc.) and extrinsic factors (tobacco use, certain medications, etc.) that can cause elevated sperm DNA fragmentation levels. In addition to discussing behavioral and lifestyle approaches that can mitigate elevated sperm DNA fragmentation levels, we will explore three newer approaches to mitigate the adverse effects of sperm DNA fragmentation. The approaches include short ejaculation abstinence intervals (< 24 hours), use of commercially available sperm processing system, and finally use of testicular sperm for IVF/ICSI. While all three approaches have promising results based on the current literature, prospective "head-to-head" comparisons are needed to determine which approach provides the greatest clinical efficacy.

Optimizing ovarian stimulation in a known poor responder

Dr. Shweta Mittal Gupta
Co-Director, Centre of IVF & Human Reproduction
Sir Ganga Ram Hospital, New Delhi

Despite the remarkable progress in ART, management of Poor Ovarian Responders (POR) still remains a challenge. They do not respond to ovarian stimulation The prevalence of POR varies from 5.6% to 35.1% There is no clear superiority of one treatment versus another for POR to enhance reproductive outcome. The POSEIDON classification redefined the understanding of “poor ovarian responders” by distinguishing between low prognosis subgroups based on age, ovarian reserve markers, and previous ovarian response. Groups 3 and 4 specifically represent expected poor responders due to diminished ovarian reserve.Currently, the tailoring of Controlled Ovarian Stimulation (COS) is based on different daily doses and type of gonadotrophins, use of GnRH antagonists or agonists to inhibit the LH peak. & triggering final oocyte maturation with (hCG or GnRH agonist) and finally resorting to newer ovarian stimulation protocols. 1. Managing such patients include Ovarian using high-Dose of gonadotropins usually doses not exceeding 300–450 IU/day FSH or rFSH ± LH. Increasing >300 IU/day rarely improves oocyte yield. Additionally addition of LH activity by recombinant LH or HMG may benefit for Group 3 in improving follicular support & in Group 4 to improve androgen substrate & potentially oocyte competence. Using antagonist protocols is preferred for flexibility, lower OHSS risk, and suitability for DuoStim. It Allows rapid conversion to DuoStim if follicular recruitment is poor. Microdose flare / agonist Flare may be useful in Group 4 for maximizing endogenous FSH surge& may improve recruitment in severe poor responders. DuoStim (double Stimulation in Same Cycle) can be particularly beneficial for Group 4 and & for Group 3 with extremely low AFC. The rationale is two retrievals in one menstrual cycle, faster accumulation of oocytes, capitalizes on luteal-phase follicular waves. Trigger Strategies in these groups to be preferred as dual Trigger (GnRH agonist + low-dose hCG). It may improve maturation rates & oocyte yield. Lastly discussing use of adjuvant therapies like androgen supplementation, DHEA 25 mg TID for 6–12 weeks or transdermal testosterone priming may improves follicular sensitivity to FSH in group 4 patients. CoQ10 / Ubiquinol seem to enhance mitochondrial function especially beneficial for Group 4 (age-related decline).Using GH (Growth Hormone)is controversial but may help selected patients with repeated poor response . All patients are counselled for lifestyle & metabolic optimization with Vitamin D repletion if required, thyroid optimization & Weight management. PGT-A is recommended for Group 4 (age-related aneuploidy means more embryos needed).It reduces miscarriage & improves time-to-live-birth.

Embryo accumulation strategy is the key in managing known poor responders undergoing IVF.

Conclusion

Management of POSEIDON Groups 3 and 4 requires a personalized, multi-cycle, and physiology-driven approach. While biological limits exist, strategic stimulation, adjuvant therapies, and optimized lab practices can significantly enhance outcomes.

IVM IN FERTILITY PRESERVATION

E. Balaji Prasath, MSc, PhD
Head & Chief Embryologist
Thomson Fertility Singapore (Paragon)
Singapore.

In Vitro Maturation (IVM) has emerged as a promising adjunct and alternative to conventional controlled ovarian stimulation for fertility preservation, particularly for patients who cannot delay treatments for their diseases or who have a risk of hormone sensitive malignancies.

IVM involves retrieval of immature oocytes with mild stimulation or without any stimulation, mature them in the laboratory with supplementing hormones in culture and either fertilize or cryopreserve them. Developments have been made with culture techniques and vitrification of oocytes which significantly improved IVM outcomes.

This presentation discusses two recent developments in IVM, CAPA-IVM and IVM with ovarian supporting cells (OSC). The CAPA-IVM (Capacitation Assisted IVM) involves pre-IVM incubation with signaling agents followed by IVM. OSC-IVM involves co-culture of immature oocytes with ovarian supporting cells which function like granulosa cells.

This presentation demonstrates how IVM was used in two cancer cases for fertility preservation and achieving pregnancy and live birth. The first case had ovarian cancer and underwent oophorectomy with hysterectomy and the ovary was sent to the IVF lab. The visible follicles were punctured and ovarian tissue teased out to find immature oocytes. They were subjected to IVM with FSH and LH. ICSI was done with her husband's sperm on mature oocytes and resulting embryos were cryopreserved. She is awaiting surrogacy.

The same approach was carried out with a second case ovarian cancer patient who underwent oophorectomy only. She was disease free in her follow up and underwent frozen embryo transfer with two embryos. She achieved pregnancy and live birth of a healthy boy, which is first of its kind in the world.

IVM has a promising place in fertility preservation and recent developments enhance IVM with better outcomes

Role of Tubal Reconstruction in Modern ART

Dr. Arti Luthra MS
M.D Dr. ArOBGYN consultant
Gynec. Endoscopic surgeon & Fertility Specialist

• Tubal disease accounts for 25%– 35% of female factor infertility, with more than half of the cases due salpingitis .

• In addition, up to 20%–30% of women regret having a tubal ligation .

• Thus, there is a need to determine the optimal treatment methods for patients with tubal-factor infertility.

• This lecture will provide insight on surgical options for reparative tubal surgery and the factors that must be considered when deciding between surgical repair and in vitro fertilization (IVF).

Diagnosis of tubal Block –

• A history of ectopic pregnancy, pelvic inflammatory disease, endometriosis, or prior pelvic surgery raises the index of suspicion for tubal-factor infertility.

HSG -is the standard first-line test to evaluate tubal patency.

Hysteroscopic Canulation for management of Proximal Tubal Block-

Proximal tubal blockage accounts for 10%–25% of tubal disease .

It may be because of obstruction resulting from plugs of mucus and amorphous debris, spasm of the uterotubal ostium, or occlusion, which is a true anatomic blockage from fibrosis due to salpingitis isthmica nodosa, pelvic inflammatory disease, or endometriosis. Tubal patency rates are similar with both fluoroscopic and hysteroscopic techniques

SURGERY FOR DISTAL TUBAL DISEASE

• Patients with limited filmy adnexal adhesions, mildly dilated tubes (<3 cm) with thin and pliable walls, and a lush endosalpinx with the preservation of the mucosal folds have good prognosis

• Patients with extensive dense peritubal adhesions, largely dilated tubes with thick fibrotic walls, and/or sparse or absent luminal mucosa have poor prognosis.

• Laparoscopic salpingectomy is indicated in patients with hydrosalpinges of poor prognosis as they have a detrimental effect on IVF success rates.

SURGERY FOR STERILIZATION REVERSAL

- Laparoscopic tubal recanalization can give pregnancy rates upto 70 %.
- Patient age, partner semen quality, surgical technique that was used to perform the sterilization, expense, chance of success, and reproductive preferences are essential elements in decision-making

Summary

- HSG should be considered the standard first-line test to assess tubal patency, but it is limited by false-positive diagnoses of proximal tubal blockage.
- Tubal cannulation for proximal tubal obstruction in young women with no other significant infertility factors is recommended.
- Laparoscopic fimbrioplasty or neosalpingostomy is recommended for the treatment of mild hydrosalpinges in young women with no other significant infertility factors.
- Laparoscopic salpingectomy should be used for proximal tubal occlusion in cases of surgically irreparable hydrosalpinges to improve IVF pregnancy rates.
- Microsurgical anastomosis is the recommended technique for tubal ligation reversal.

Individualisation of Controlled Ovarian stimulation

Abstract

Dr. Nisha Bhatnagar
Medical Director Aveya Fertility centre (Rajouri Garden)
Medical director Infinite - Egg Freezing (Vasant Vihar)

Background: Traditional “one-size-fits-all” protocols in controlled ovarian stimulation (COS) do not account for the wide variability in ovarian reserve and response among women undergoing IVF. This often leads to suboptimal outcomes, avoidable complications, and increased patient burden.

Objective: To highlight the rationale, methodology, and clinical benefits of individualized controlled ovarian stimulation (iCOS) based on reliable ovarian reserve markers and predictive models.

Methods: Key elements of individualization were reviewed, including protocol selection (agonist vs antagonist), personalized gonadotropin dosing, choice of trigger, and the use of prediction tools integrating AMH, AFC, and age to anticipate poor or hyper-response.

Results: Evidence demonstrates that iCOS improves treatment efficiency and safety by optimizing ovarian response, increasing oocyte yield and embryo competence, and reducing rates of OHSS, cycle cancellation, and treatment dropout. The approach also enhances patient experience and long-term cost-effectiveness.

Conclusion: Individualized COS represents a significant advancement in IVF practice. By tailoring stimulation strategies to each woman’s biological profile, iCOS achieves better outcomes, minimizes risks, and aligns with modern, patient-centred reproductive care. Individualization is not hype—it is now essential for achieving safer, more effective, and more predictable IVF success.

Minimizing Obstetric Complications in ART-Conceived Pregnancies: A Comprehensive Review

Abstract

Brig Prasad R Lele
MS,DNB, MNAMS, PDCC (RM)
Brig Med HQ 16 Corps
Prof ObGyn 166 MH

Assisted reproductive technology (ART) has dramatically transformed the field of reproductive medicine, offering new hope to millions of individuals and couples facing infertility by enabling conception through advanced techniques such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). While ART has been responsible for the birth of more than nine million children globally since the late 20th century, accumulating evidence indicates that pregnancies conceived via ART are accompanied by a higher incidence of maternal, fetal, and perinatal complications compared to those conceived spontaneously. This narrative review aims to provide a comprehensive synthesis of current research, elucidating the multifactorial causes underlying the increased obstetric risks observed in ART pregnancies.

To achieve this, the review draws on a wide range of meta-analyses, cohort studies, and clinical guideline recommendations published between 2015 and 2024, with literature sourced from reputable databases such as PubMed and the Cochrane Library, as well as major professional societies including the American College of Obstetricians and Gynecologists (ACOG), the European Society of Human Reproduction and Embryology (ESHRE), the American Society for Reproductive Medicine (ASRM), and the Society of Obstetricians and Gynaecologists of Canada (SOGC). Careful emphasis is placed on large-scale studies and high-quality evidence that examine both the epidemiology and pathophysiological mechanisms driving obstetric complications in ART pregnancies, as well as interventions that may mitigate these risks.

The review identifies several contributing factors to the heightened risk profile of ART pregnancies. These include demographic trends such as advanced maternal age and delayed parenthood, a higher prevalence of underlying health conditions like polycystic ovary syndrome (PCOS), endometriosis, uterine anomalies, and metabolic disorders in ART patients, and the effects of ART-specific interventions such as controlled ovarian stimulation, supraphysiological hormonal environments, and embryo manipulation. Furthermore, the review discusses how these factors, combined with possible epigenetic changes induced by ART procedures, can adversely impact early implantation, placentation, and fetal development, thereby increasing the risk of early pregnancy loss, preterm birth, low birth weight, hypertensive disorders, gestational diabetes, placental abnormalities, and other perinatal complications.

Data synthesized in this review indicate that early pregnancy loss occurs at a significantly higher rate in ART pregnancies (25–35%) compared to spontaneous conceptions (approximately 10%), with contributing factors including embryonic genetic abnormalities, impaired implantation, luteal phase insufficiency, and altered endometrial receptivity. The review also highlights the increased risks of other major obstetric complications associated with ART, such as multiple gestations, preeclampsia, and cesarean delivery, and explores strategies for risk reduction, including individualized stimulation protocols and improved embryo selection techniques.

In conclusion, the review underscores the importance of understanding the unique risk landscape of ART pregnancies and calls for ongoing research and targeted clinical strategies to optimize outcomes. By integrating current evidence and expert guidance, this review aims to inform clinicians, researchers, and patients about the complex interplay of factors influencing ART-associated obstetric complications, while advocating for tailored risk assessment and management approaches to improve maternal and neonatal health.

Surgical repair of isthmocele-Placebo or Promise in reproductive Medicine

Abstract

Dr Reeta Mahay, MD , DNB
Professor, Deptt of Obstetrics & Gynaecology,
AIIMS, New Delhi

Isthmocele, also known as a cesarean scar defect (CSD) or niche, is an iatrogenic myometrial discontinuity at the site of a previous lower segment cesarean section. It represents an increasingly recognized clinical entity in gynecology and reproductive medicine due to rising cesarean delivery rates. Although many women remain asymptomatic, isthmocele can lead to a spectrum symptoms. Most characteristic presentation of CSD is post-menstrual spotting, caused by pooling of blood within the niche. Other symptoms include prolonged/irregular menstrual bleeding, dysmenorrhea, chronic pelvic pain, and occasionally dyspareunia. In more severe cases, patients may present with chronic vaginal discharge, scar tenderness, or complications such as scar abscess. Importantly, isthmocele has emerged as a significant contributor to secondary infertility.

The association between isthmocele and infertility is multifactorial. The niche often serves as a reservoir of menstrual blood and inflammatory fluid, creating an unfavorable intrauterine environment that impairs sperm motility, embryo transport, and endometrial receptivity. Persistent fluid accumulation can disrupt the implantation window, alter uterine peristalsis, and interfere with embryo apposition, particularly in ART cycles. Sometimes, it is incidentally diagnosed as a cause of fluid in cavity in women undergoing IVF. Furthermore, a severely thinned myometrium overlying the defect increases the risk of complications in future pregnancies, including cesarean scar ectopic pregnancy and uterine rupture, underscoring the importance of timely diagnosis and management.

Treatment selection for isthmocele is guided by symptom severity, fertility goals, niche dimensions, and residual myometrial thickness. Transvaginal ultrasound or saline infusion sonography serves as the primary diagnostic tool, with MRI reserved for complex cases. Women with mild symptoms or no fertility concerns may be managed conservatively through observation or hormonal therapy. Hysteroscopic repair is generally preferred when the residual myometrial thickness >3 mm. This minimally invasive technique involves resection of the fibrotic margins of niche to improve drainage and reduce menstrual retention, offering excellent results in patients with post-menstrual spotting or infertility associated with niche fluid.

Conversely, when residual myometrium is < 3 mm and patient is desirous of future fertility, laparoscopic repair is recommended to restore myometrial integrity and reduce obstetric risks. Surgical excision of defect followed by multi-layer myometrial suturing helps re-establish normal uterine anatomy and improves reproductive outcomes. For women with large defects, significant pain, or recurrent fluid accumulation despite conservative measures, combined laparoscopy–hysteroscopy may offer optimal correction.

Overall, accurate diagnosis and tailored treatment of isthmocele can significantly improve symptoms, enhance fertility outcomes, and reduce complications in subsequent pregnancies.

Does Morphology Add Predictive Value

Abstract

Dr Paresh M Makwana
M.V.Sc., MBAHCS
ASRM Certified Embryologist

The shift from morphology-based embryo selection to the use of Preimplantation Genetic Testing for Aneuploidy (PGT-A) has significantly refined embryo transfer strategies in In Vitro Fertilization (IVF). PGT-A, which screens for whole-chromosome aneuploidies, has become the definitive tool for identifying the chromosomal health of an embryo, leading to reduced miscarriage rates and improved implantation rates per transfer, particularly in patient cohorts with advanced maternal age or recurrent pregnancy loss. However, a critical question remains: Does traditional morphological assessment, including standard grading (Inner Cell Mass [ICM] and Trophectoderm [TE] quality) and developmental timing, retain prognostic value for live birth rates in the context of already-identified euploid embryos?

The primary role of PGT-A is to exclude embryos incompatible with life due to significant chromosomal abnormalities. By achieving this, it is hypothesized that the cohort of euploid embryos becomes largely homogeneous in terms of viability, thereby reducing the influence of conventional morphological parameters. Early studies and meta-analyses suggested that the predictive power of morphology is indeed diminished after a euploid result, proposing that a euploid embryo, regardless of its grade (within a reasonable transfer limit), has a high and comparable chance of leading to a live birth.

However, more recent, robust evidence suggests that morphology continues to provide independent and incremental predictive value. Studies focusing on single euploid frozen-thawed embryo transfers (sFET) have demonstrated that the specific grading of the blastocyst—particularly the Inner Cell Mass (ICM) grade, which represents the fetal lineage—remains a strong determinant of ongoing pregnancy and live birth. Embryos graded as 'Good' or 'Excellent' in morphology have shown significantly higher odds of success (e.g., a 2.8 to 4.6-fold increase) compared to 'Poor' quality embryos, even after confirming euploidy. This finding underscores that PGT-A and morphology assess two independent yet essential aspects of embryonic competence: PGT-A for genetic viability, and morphology for the intrinsic developmental potential and cellular integrity of the blastocyst.

Furthermore, blastocyst developmental timing and the grade of the Trophectoderm (TE), the cell layer sampled for PGT-A, also show nuanced contributions. While some studies find TE grade and expansion less significant than ICM grade in euploid transfers, others report an association between A-grade TE and higher live birth rates. This complexity suggests that while aneuploidy is the most common cause of implantation failure, morphological quality likely reflects other critical, non-genetic factors such as mitochondrial function, metabolic health, or competence of the ICM to establish a healthy pregnancy.

In conclusion, while PGT-A acts as a powerful pre-screening filter for chromosomal viability, morphology serves as a secondary discriminator for developmental competence. For clinical decision-making, particularly when multiple euploid embryos are available, morphological quality—especially the ICM grade—is not redundant but rather a crucial factor for prioritizing the embryo most likely to lead to a successful outcome. Future research should leverage advanced tools, such as time-lapse imaging and machine learning, to fully integrate morphological and morphokinetic data with PGT-A results to create a more comprehensive and accurate predictive model for embryo selection.

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OMICS-Driven Development of Novel Diagnostic Approaches in Endometriosis

Abstract

Dr Roya Rozati
M.D (AIIMS) FRCOG (London)
Former Organizing Secretary-ISSRF 2024,
IFS National Advisor,
Professor and HOD, Obst & Gynec, Shadan Institute of Medical Sciences
Medical & Research Director, MHRI, Hyderabad

Endometriosis is a multifactorial disease that affects about 10-15% of women of reproductive age globally. It's an estrogen-dependent chronic inflammatory disease that often associated with symptoms like chronic pelvic pain, dysmenorrhea, dyspareunia, dysuria and infertility. The symptoms can vary widely from person to person, and there aren't any reliable, noninvasive tests available yet. Diagnosis is often delayed or missed, which can further complicate patient outcomes and quality of life. The application of omics technologies has significant progress in comprehending the molecular mechanisms that underlie endometriosis and other intricate diseases. By combining genomics, transcriptomics, epigenomics, proteomics, metabolomics, and other high-throughput methods, researchers can thoroughly map gene-environment interactions, identify cellular pathways, and discover molecular signatures specific to the disease.

Genomic studies, using genome-wide association and next-generation sequencing, have identified spots in our DNA linked to disease susceptibility and common mutations like KRAS and ARID1A having pathogenetic heterogeneity and revealing genetic biomarkers for risk stratification. Research studies on Epigenomics and transcriptomics revealed DNA methylation patterns and changes in microRNA profiles play a key role in hormone-driven signaling and immune dysfunction, both of which are crucial for the development of lesions. proteomic analyses have uncovered some exciting biomarker panels from endometrial tissue, serum, and peritoneal fluid. These findings help us map out important pathways related to inflammation, blood vessel formation, and cell adhesion, which could be really useful for both diagnosing and predicting outcomes in patients.

Metabolomics and lipidomics techniques have revealed amino acids, fatty acids, and lipid metabolites that can differentiate between various stages and subtypes of endometriosis using minimal fluid or tissue samples. Additionally, microbiome profiling indicates that dysbiosis in the reproductive tract and gut not only plays a role in the disease's development but may also aid in noninvasive diagnosis when paired with molecular biomarkers.The application of artificial intelligence and machine learning algorithms enhances the synthesis of multi-omics data, aiding in pattern recognition, the development of classifier models, and the quicker validation of biomarkers across various cohorts.Together, these omics-based approaches indicate a major transition towards early, noninvasive, and subtype-specific diagnostics, laying the foundation for patient-centered disease management.Future initiatives should concentrate on multicenter validation, standardizing biomarker panels, and leveraging computational power to develop clinically relevant diagnostic tools for endometriosis.

Keywords:

Endometriosis, Omics, Genomics, Epigenomics, Proteomics, Metabolomics, Transcriptomics.

Dr. Rahul Sen
(Chief Consultant Embryologist)
NEELKANTH IVF (RAJASTHAN)

Abstract

The conventional preference for early blastulation (DAY-5 development) has influenced embryo selection strategies for decades. However, advancing scientific evidence and improved embryo-culture technologies challenge the assumption that delayed blastocyst formation reflects diminished developmental potential. This article critically evaluates the biological, clinical, and ethical implications of discarding or deprioritizing slow-growing embryos, emphasizing the need for evidence-based interpretation rather than speed-based bias. Drawing on morphokinetic studies, time-lapse analyses, and clinical outcome data, we argue that delayed blastulation may represent developmental precision rather than impaired competence. As reproductive medicine transitions toward personalized and data-driven embryology, embryo selection must shift from a timeline-centered paradigm to a comprehensive, competence-based approach.

Introduction

Embryo selection in IVF laboratories has traditionally favored the embryo reaching the blastocyst stage by DAY 5, with later-developing embryos often considered suboptimal. This long-standing bias equates rapid development with superior reproductive potential. Yet, the introduction of continuous time-lapse monitoring, enhanced sequential media, and artificial intelligence-based morphokinetic analysis is reshaping our understanding of embryo developmental trajectories.

The Myth of the Perfect Timeline

Traditional static grading systems have ingrained the belief that DAY-5 blastocysts are superior to DAY-6 counterparts. However, several studies challenge this linear framework. Euploid DAY-6 blastocysts have been shown to achieve comparable implantation and live birth rates to DAY-5 blastocysts in optimized FET cycles. The rate of blastulation is multifactorial. Developmental tempo is affected by:

- Oocyte competence and cytoplasmic maturity
- Sperm chromatin integrity
- Embryonic metabolic state
- Timing and efficiency of zygotic genome activation

A slight delay may represent physiological adaptation, self-repair, or cellular reorganization rather than developmental incompetence.

Slow Growth ≠ Poor Quality

Embryos requiring additional time may be performing essential corrective processes. Time-lapse observations reveal symmetric cleavage, minimal fragmentation, appropriate compaction, and stable blastocoel expansion even in delayed or slow growing blastocysts. Delayed blastulation may therefore reflect developmental precision. Mechanisms implicated include DNA repair pathways, spindle reorganization, metabolic recalibration, and mitochondrial redistribution—processes essential for embryonic competence. Viewing slow growth as inherently abnormal dismisses these biologically protective phenomena.

Time-Lapse Imaging

Conventional morphology assessment provides isolated snapshots, potentially missing key developmental events. Time-lapse incubators have revolutionized embryology by enabling continuous, non-invasive observation of cleavage patterns, cell-cycle intervals, compaction, blastulation kinetics, and abnormal events such as reverse cleavage or multinucleation. Morphokinetic models increasingly show that:

•Multiple developmental trajectories—not just the fastest—can lead to high-quality blastocysts.

•Slow-growing embryos may follow stable and biologically coherent patterns despite delayed timing.

•Time-lapse-derived annotations outperform static grading alone for implantation prediction.

AI-assisted platforms now incorporate kinetic signatures that do not necessarily penalize late blastulation, supporting a more holistic evaluation.

Consensus, Morphology, and Critical Evaluation

The Istanbul Consensus and subsequent guidelines emphasize that embryo grading is a decision-support tool—not a definitive measure of viability. Embryo assessment should integrate:

• Morphological quality

• Kinetic trends

• PGT-A results (when available)

• Laboratory conditions and culture environment

Relying solely on timing contradicts the principle of comprehensive evaluation. A high-quality Day-6 euploid embryo should not be deprioritized based on chronology alone.

Clinical Evidence

DAY-6 euploid blastocysts demonstrate similar outcomes to DAY-5 when transferred in controlled FET cycles. DAY-7 blastocysts, though slightly less efficient, yield ongoing pregnancies and healthy live births.

Laboratory Implications

Modern labs should consider routine culture to DAY 6 and selected culture to DAY 7, freezing morphologically competent blastocysts regardless of timing, and using morphokinetic markers instead of rigid timelines.

Conclusion

Discarding delayed blastocysts is outdated and reduces cumulative live birth rates. A competence-based, holistic evaluation is more scientifically valid and ethically aligned with patient-centered care.

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Ovarian Stimulation in Fertility Preservation Cycles

Dr VIRGILIO M. NOVERO, JR.
MD, Obstetrics & Gynecology,
Professor at University of the Philippines Manila
Philippines

The treatment protocols utilized during ovarian stimulation in standard IVF cycles will need to undergo a few changes to adjust to the requirements of patients undergoing fertility preservation. There are a variety of patients undergoing ovarian stimulation for fertility preservation. Most of these are cancer patients who will need to undergo cancer treatment via chemotherapy and/or radiotherapy soon after ovarian stimulation and oocyte retrieval to manage the progression of cancer. But there are also patients who undergo fertility preservation because of a progressive decline in ovarian reserve due to non-cancer reasons such as genetics (mosaic Turner), benign gynecologic disease (endometriosis), gender reassignment (LGBTQ+), and age (social egg freezing).

In the ovarian stimulation for fertility preservation of oncologic patients, the key considerations are to do random start stimulation to shorten the waiting time before the planned cancer therapy and letrozole co-administration in cases of hormone-dependent cancers. Random start ovarian stimulation allows commencement of COS in any part of the ovarian cycle (early or mid-follicular, peri-ovulatory or mid to late luteal) and results are relatively similar. In the latter, letrozole mitigates cancer progression by limiting testosterone conversion to estrogen. Because there will be no fresh transfer after COS, progesterone primed OS may also be utilized resulting in similar outcome compared to GnRH antagonist protocol yet with lower expenditure. Dual stimulation (Duostim) may also be done when time permits where a second ovarian stimulation is immediately started soon after oocyte retrieval of the first and where the output of oocytes retrieved is doubled. In non-cancer fertility preservation cycles as in endometriosis, key issue is to maximize oocyte yield so best measures include a slightly increase stimulation dose of FSH (50-75 iu higher) and the use of dual stimulation. In those with genetics issues as in mosaic Turner where there is accelerated decline of ovarian reserve, the biggest issue is the proper timing of the fertility preservation cycle.

Ovarian Rejuvenation Techniques : Hype or Hope?

Ovarian rejuvenation techniques are a set of regenerational medical techniques aimed at restoring or enhancing ovarian function, particularly in women with diminished ovarian reserve or premature ovarian insufficiency, by activating dormant follicles or improving ovarian response. It seems to have been triggered by an increased number of women with diminished ovarian reserve (DOR) and primary ovarian insufficiency) in the last decade because of a number of reasons. These include delay in marriage or in having children resulting in increased age of first pregnancy, desire to have biological children (with rejection of adoption/ oocyte donation), and increased cancer treatment survivors all of which contributing to the worldwide decline in fertility rates.

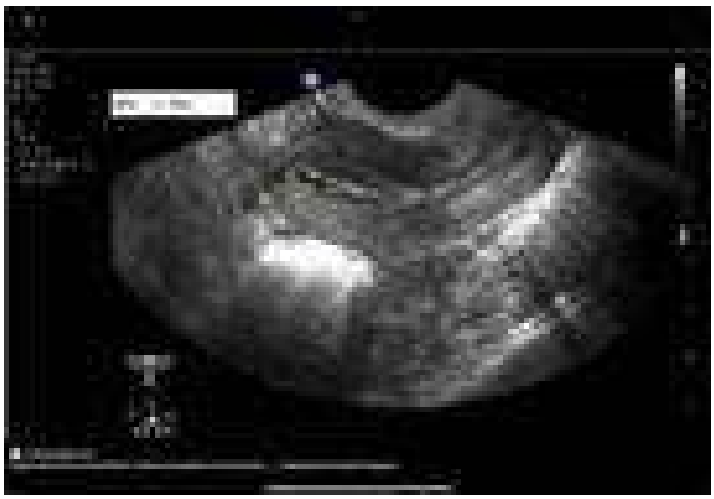
There many medical strategies that fit the above definition, but there are four methods that are the most popular because of the theoretical and practical possibilities of these techniques. These include In Vitro Activation of primordial follicles (IVA), Platelet Rich Plasma (PRP) therapy, Stem cell therapy, and Exosome/ Extracellular vesicle therapy. All these techniques are considered experimental ways to increase ovarian reserve and improve chances to achieve pregnancy. Although a strong attempt by research studies to document the efficacy of these methods have been shown within the past years especially with PRP therapy, the evidence is limited (in the case of the IVA and the last 2) or lacks randomized controlled trails (in the case of PRP therapy). Until enough robust research appears, these methods will be regarded as experimental and must be mentioned as such when hope is given in the clinics.

Recurrent Endometrial Cavity Fluid Effect & Management –

Abstract

Dr. Sangeeta Sinha
DGO,FICOG,FAMS,FARIS(Robotic),PGA(ART)UK
Senior Infertility Specialist,
Robotic and Laparoscopic Gynecologist
Treasurer IMA AMS Chhattisgarh
Secretary IMA Durg.

Recurrent endometrial cavity fluid is a significant clinical challenge in Assisted reproductive technology (ART), with a documented negative impact on implantation , clinical pregnancy, and live birth rate.



Endometrial cavity fluid refers to the accumulation of anechoic or hypoechoic fluid within the uterine cavity. ECF negatively affects reproductive outcome through :

- Impaired implantation – Fluid prevents embryo-endometrium apposition and impairs adhesion.
- Poor endometrial receptivity – Due to inadequate secretory transformation and a poor progesterone response.

ECF may be because of Tubal Factor—Hydrosalpinx , Chronic Endometritis (Endometrial inflammation) , Cervical Stenosis /Blockage, Adenomyosis /Uterine peristalsis abnormalities , Leutal phase deficiency or Progesterone resistance , or may be because of supraphysiological Estrogen level in ART cycle. The volume and

Persistence of ECF correlates strongly with reproductive outcome. Even small, persistent collections detected during the per-implantation period are associated with a lower implantation period, whereas transient /trace fluid often has less clinical impact.

ECF serves as a surrogate marker of poor endometrial synchronization, abnormal secretory transformation, and possibly impaired immune-endocrine balance.

DIAGNOSIS — Comprehensive diagnostic workup includes

- Transvaginal ultrasound (evaluate volume and persistence)
- Assessment of hydrosalpinx
- Hysteroscopy for cavity pathology or infection ,endometrial biopsy for chronic endometritis (CD 138)
- Evaluation of cervical canal patency
- Review the stimulation protocol for the high E2 cycle.

MANAGEMENT — Strategies are based on identifying the underlying cause as well as optimizing endometrial receptivity.

In case of **hydrosalpinx,** laparoscopy proximal tubal occulution or salpingectomy decreases the incidence and enhances the outcome.

Chronic **endometritis** / inflammation can be managed with doxycycline /antibiotics.

Cervical **stenosis** can be managed with dilation or stenting.

Adenomyosis can be managed with prolonged downregulation,dinogest LNG -IUD

During the transfer cycle, management options include —

Aspiration of ECF under ultrasound guidance, hysteroscopy drainage in recurrent cases.

Intrauterine PRP /G-CSF in refractory cases

Reduce estrogen level/mild stimulation to prevent supraphysiological estrogen levels.

Enhance leutal support.

Emerging Intervention

- Hysteroscopic drainage with canal stenting
- intrauterine antibiotic gel
- targeted immunomodulator

Conclusion

ECF is both a symptom and a mediator of impaired uterine receptivity.

A structured diagnostic approach and individualized management plan, and cautious timing of Embryo transfer significantly improve implantation and pregnancy outcome.

Impact of Day 5 versus Day 6 Transfer in Patients with Low Serum Progesterone Levels on the Day of Frozen Embryo Transfer: A Prospective Study

Dr. Seema Pandey
Obstetrics and Gynaecology

Objective:

This study aimed to evaluate and compare reproductive outcomes of Day 5 (D5) versus Day 6 (D6) frozen embryo transfers (FET) among patients with low serum progesterone levels on the day of transfer.

Materials and Methods:

This prospective study was conducted at the Fertility Clinic in India between April 2024 and September 2025. A total of 114 patients undergoing FET were included. Patients were categorized into two groups: D5 blastocyst transfer (n = 73) and D6 blastocyst transfer (n = 41). Serum progesterone (P4) levels were measured on Day 0 (start of progesterone), Day 5, and Day 6. Clinical outcomes and overall pregnancy results were compared between groups.

Results:

Total (n=114) frozen embryo transfer cycles were analysed, comprising (n=73) Day-5 and (n=41) Day-6 blastocyst transfers. Baseline hormonal parameters were comparable between the two groups. Mean age (32.54 vs 33.34), AMH (2.93 (ng/mLvs 2.69 ng/mL), TSH (2.73 µIU/mL vs 2.90 µIU/mL), PRL (18.23 ng/mL vs 19.16 ng/mL), P4 Day 0 (0.37 ng/mL vs 0.38 ng/mL), P4 D5 (26.38 ng/mL vs 26.57 ng/mL), and endometrial thickness (9.98 mm vs 10.33 mm) showed minimal differences between D5 and D6 transfers. Clinical pregnancy rate for D5 was 38(52%) and for D6 was 18(43.9%). while ongoing pregnancy rate (>20 weeks) was 30(41%) on D5 and was 16(39%)on D 6. Although the miscarriage rate showed a trend toward being lower in D-6 transfers (2.4% vs 9.5%). There was no statistically significant difference ($p > 0.05$ for all variables).

Conclusion:

Postponing embryo transfer by a day after giving one extra day of intramuscular progesterone does not yield better pregnancy outcomes. It also emphasises that the window of implantation is not different in people with low progesterone on day 5.

Keywords: Frozen embryo transfer; Progesterone; Endometrial receptivity; Day 5 transfer; Day 6 transfer

Academics, role and responsibilities of an embryologist in an Era of ART

Abstract

Dr Charudutt Joshi
Medical Director, Genes India ART Bank.
Lab Director, R.D.Gardi Medical college

The Assisted Reproductive Technology (Regulation) Act, 2021, has brought a defining transformation to the practice of clinical embryology in India. Once viewed as a laboratory-based technical discipline, embryology has now emerged as a recognized clinical science governed by legal, ethical, and academic standards. This presentation explores the evolution of embryology from its experimental origins to its current position as a regulated, evidence-based profession central to modern reproductive medicine.

It discusses the academic prerequisites, structured training pathways, and continuous competency requirements introduced under the ART Act, alongside the professional, ethical, and documentation responsibilities expected of every registered embryologist. Emphasis is placed on the embryologist's expanding role as a clinical scientist, quality custodian, and research collaborator within multidisciplinary ART teams.

The presentation further examines the practical challenges arising from compliance, cost implications, and balancing regulation with innovation, while also highlighting opportunities in areas such as reproductive genetics, AI-driven embryo assessment, and translational research. Ultimately, it reflects on the embryologist's evolving identity — from technician to ethical guardian — underscoring the need for integrity, accountability, and lifelong learning in shaping the future of reproductive science under a robust legal framework.

Dr Charudutt Joshi
Medical Director, Genes India ART Bank.
Lab Director, R.D.Gardi Medical college

Testicular Tissue Cryopreservation – From Bench to Bedside in Fertility Preservation

Dr Krishna Chaitanya Mantravadi
Scientific Head & Clinical Embryologist

Testicular tissue cryopreservation (TTC) represents a critical advancement in the field of male fertility preservation, addressing the distinct needs of both prepubertal and postpubertal males at risk of losing reproductive potential. For prepubertal boys, who have not yet initiated spermatogenesis and thus cannot provide ejaculate or sperm for banking, TTC offers the only option by preserving testicular tissue containing spermatogonial stem cells (SSCs). Worldwide, over 2000 prepubertal boys have undergone tissue cryostorage under research protocols, with promising translational data from animal models demonstrating restoration of spermatogenesis and live offspring following SSC transplantation. While human clinical application remains experimental, this approach offers hope for future fertility in childhood cancer survivors and other at-risk groups.

In postpubertal males, testicular sperm cryopreservation has become an established component of fertility preservation, especially for patients with azoospermia, testicular failure, or those undergoing gonadotoxic therapy. Modern laboratory protocols involve careful mechanical disaggregation of seminiferous tubules, optimized cryoprotectant use (typically glycerol or DMSO-based), and controlled-rate or vitrification-based freezing. Post-thaw recovery rates for motile sperm range from 30–50%, with fertilization and pregnancy outcomes after ICSI comparable to those achieved using fresh testicular sperm. Challenges remain, including variable sperm recovery rates, post-thaw DNA fragmentation, and the lack of universal vitrification standards for low-volume samples.

From a translational perspective, TTC exemplifies the evolution of oncofertility care—spanning from experimental SSC banking in prepubertal boys to clinically proven cryopreservation and utilization of testicular sperm in adult men. As techniques in organoid culture, in vitro spermatogenesis, and cryobiology advance, TTC stands poised to bridge the gap between experimental research and routine clinical application, safeguarding male fertility across all ages.

Dr. Poonam Nayar
Consultant Clinical Psychologist
Akanksha IVF Center ,New Delhi ,India

Is it necessary to have face to face counselling in an era where practically every transaction is becoming virtual? A comparison of online counselling Vs offline face to face counselling shows interesting differences across various parameters.

The tradeoff is between conveniences of online counselling with the depth of counselling. Language is only one part of how we communicate; the non-verbal gestures or expressions are dynamic, ongoing and continuously emitted without conscious awareness of the client. The brain continuously picks up micro-signals that relay what we're thinking and feeling to others even when the verbal communication stops. The "interbrain" is the brain's ability to detect subliminal signals and understand others' emotions, fostering direct brain-to-brain connections between the patient and the therapist for mutual awareness. In-person communication fosters interbrain synchrony through shared sensory experiences like gestures, eye contact, and even subtle cues like scent or touch. These elements create a rich, immediate connection that enhances empathy and understanding. The continuous exchange of signals from one person to the other occurs at a very high speed, enabling mutual adjustment and synchronization of awareness and understanding based on feedback loops. In contrast, video communication lacks these sensory dimensions, leading to diminished interbrain synchrony. Delays in audio and video, limited visual frames, and the absence of physical presence disrupt the natural flow of interaction. This can hinder the depth of connection or empathy, making virtual interactions feel less engaging and more cognitively demanding. Prolonged screen use can lead to "Zoom fatigue " with reduced physical activity and constant adaptation to screen-based interactions . The vast network lacks an interbrain connection between its human participants

Dual Stimulation in the Same Menstrual Cycle: A Time-Efficient Strategy to Maximize Oocyte Yield and Improve Outcomes especially in Poor Responders.

Abstract

Dr. Navina Singh
MRM (LONDON), DRM (GERMANY), FRM (INDIA),
DIPLOMA IN MEDICO-LEGAL,
M.S. (OBSTETRICS AND GYNAECOLOGY), M.B.B.S

Background

Dual stimulation (DuoStim), which involves controlled ovarian stimulation during both the follicular and luteal phases of a single menstrual cycle, has gained increasing attention for patients with diminished ovarian reserve, advanced age, previous poor ovarian response, and those requiring urgent fertility preservation. Modern insights into follicular dynamics show that recruitment occurs in multiple waves within one cycle, challenging the traditional view that stimulation is limited to the follicular phase. This physiological understanding forms the basis for employing DuoStim to maximize oocyte yield in a constrained reproductive window.

Objective

To present the scientific rationale and clinical benefits of DuoStim and propose a framework for a future study evaluating its effectiveness compared to conventional single-phase stimulation protocols.

Methods / Rationale

Evidence from prospective and retrospective studies demonstrates that luteal-phase stimulation is both feasible and effective, often yielding a comparable or greater number of mature oocytes than follicular-phase stimulation. Embryo quality, blastulation rate, and euploidy outcomes from luteal-derived oocytes have shown equivalence to follicular-derived cohorts. DuoStim enables rapid oocyte accumulation, minimizes cycle-to-cycle variability, and reduces patient dropout—advantages particularly relevant in poor responders and time-sensitive cases such as oncofertility.

Key Findings from Current Literature

- Luteal-phase stimulation produces competent oocytes with similar developmental potential.
- Total oocyte yield per menstrual cycle increases significantly with DuoStim.
- Time-to-treatment completion is shortened without compromising outcomes.
- Preliminary data support comparable euploidy rates across both stimulation waves.
- Patient-centric metrics (dropout, cancellation) appear more favourable with DuoStim.

Proposed Future Study

A prospective comparative study assessing:

1. Total oocyte and embryo yield in dual vs. single stimulation cycles.
2. Blastulation and euploidy rates across follicular and luteal cohorts.
3. Time-to-treatment completion.
4. Cycle cancellation and patient dropout rates.
5. Cost-effectiveness in poor responders.

Conclusion

Dual stimulation represents a biologically sound, time-efficient, and clinically valuable strategy for patients with diminished ovarian reserve or urgent fertility timelines. By maximizing oocyte yield within a single cycle, DuoStim offers meaningful advantages over conventional protocols. Well-designed prospective studies will further define patient selection, refine protocols, and solidify DuoStim's role as a mainstream approach in modern ART practice.

Antibiotic Treatment of Chronic Endometritis

Regimen	Drug(s)	Dose	Duration	Target Organisms	Comments
First-line empiric therapy	Doxycycline	100 mg orally twice daily	14 days	Mycoplasma, Ureaplasma, Chlamydia, others	Common empiric choice, well tolerated
	Metronidazole (optional add-on)	500 mg orally twice daily	7–14 days	Anaerobes	Added if anaerobic infection suspected
Broad-spectrum regimen	Doxycycline + Metronidazole + Ciprofloxacin or Levofloxacin	Doxy 100 mg BID + Metro 500 mg BID + Cipro 500 mg BID or Levo 500 mg OD	14 days	Gram-negative, anaerobes, atypicals	Used for severe or recurrent cases
Chlamydia-focused	Azithromycin	1 g orally once, then 500 mg daily × 2 days	3 days total	Chlamydia trachomatis	Alternative to doxycycline
Gonorrhea coverage (if suspected)	Ceftriaxone + Doxycycline	Ceftriaxone 500 mg IM once + Doxy 100 mg BID	7–14 days	Neisseria gonorrhoeae, Chlamydia	Follow CDC PID treatment
If resistant/refractory CE	Repeat broad-spectrum or culture-based antibiotics	Based on sensitivity	Variable	Persistent pathogens	Consider 16S rRNA or hysteroscopy-guided therapy
Post-treatment confirmation	—	—	After 2–4 weeks	—	CD138 IHC or repeat hysteroscopy to confirm resolution

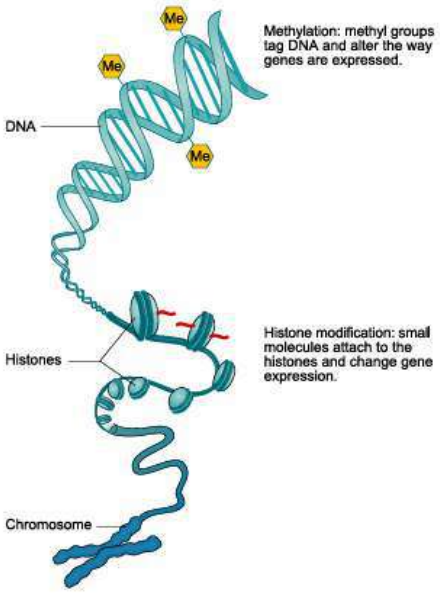
In summary, current evidences support a plausible causal role of CE in a subgroup of patients with infertility and RIF, while acknowledging that in other contexts CE may be a consequence or coincident marker of endometrial pathology. Resolving cause-versus-marker questions requires large, well-designed randomized trials that (1) use standardized, validated diagnostic criteria (including CD138 IHC), (2) confirm microbiological / histological cure after treatment, and (3) evaluate reproductive endpoints. Until such data are available, clinicians should individualize evaluation and management of CE in infertile patients, balancing the potential benefits of targeted therapy against diagnostic uncertainty.

DNA METHYLATION ALTERATIONS IN ART CONCEIVED CHILDREN: EVIDENCE & IMPLICATIONS

Dr. Arun Arora
MBBS.DSM.MD.FICOG
Former Head of Department,
Government Medical College, Udhampur

Background: DNA methylation and imprinting

Epigenetic modification controls gene activity without changes in the DNA sequence. The epigenome is a network of chemical compounds which tags on to the DNA; its role is to determine which genes are active in a particular cell. Hence, epigenetic modification is an important form of controlling gene activity without changes in the DNA sequence. Several mechanisms of epigenetic control exist, including DNA methylation, histone modification, non-coding RNA, remodelling of nucleosomes and organization of chromatin structure. DNA methylation is the best studied of these epigenetic mechanisms.



DNA methylation (methyl-group addition to cytosine residues mostly at CpG dinucleotides) is a key epigenetic mechanism regulating gene expression, chromatin structure, and genomic stability. During mammalian development, widespread demethylation and remethylation phases occur. The first phase of epigenetic reprogramming takes places during gametogenesis.

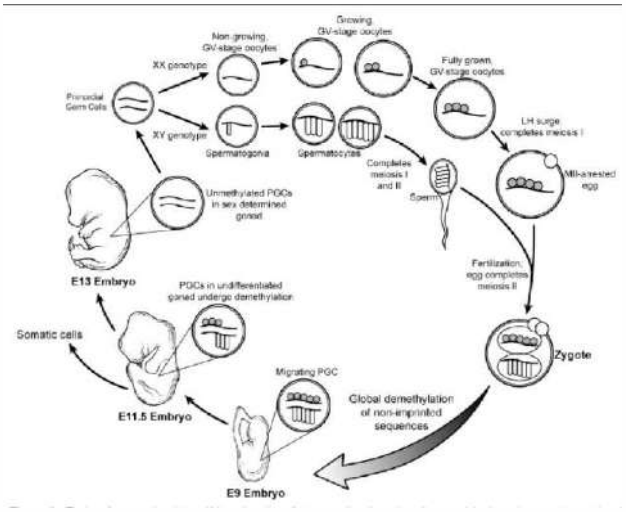
When the primordial germ cells have migrated to the genital ridge, their genome undergoes erasure of epigenetic marks. This enables subsequent epigenetic reprogramming and parent-of-origin controlled activity of specific genes. This reprogramming is gender-specific, as a proportion of genes are only active when inherited from the mother and are inactivated when inherited from the father and vice versa, a phenomenon called genetic imprinting. While methylation is completed in the mature spermatozoa, the same phenomenon in oocytes is nearly complete at the time of ovulation. After fertilization, the **second wave** of epigenetic reprogramming occurs with demethylation of the paternal and maternal genome, after which another phase of DNA methylation takes place. While the demethylation-methylation occurs in the entire genome of the early embryo, the imprinted genetic regions are protected and maintain their gender-specific methylation patterns created during gametogenesis. The remethylation is completed by implantation. Imprinted genes (genes expressed in a parent-of-origin specific manner) require correct establishment and maintenance of methylation marks at imprinting control regions (ICRs) in germ cells and early embryos. Aberrancies in epigenetic programming, such as hypermethylation or hypomethylation of DNA within a specific genetic region, can result in disturbances of gene activity and imprinting disorders (e.g., Beckwith Wiedemann syndrome, Angelman syndrome, Silver Russell syndrome) and potentially long-term health consequences. The epimutations causing diseases are maintained through cell division and can be inherited. Because ART manipulations coincide temporally with epigenetic reprogramming windows, concern has arisen that such procedures may influence methylation and imprinting stability.

Evidence for methylation alterations in ART-conceived offspring

Imprinting disorders and targeted loci

Several case series and registry-based analyses report an increased incidence of rare imprinting disorders in children conceived via ART. For example, early reports indicated that the risk of Beckwith-Wiedemann syndrome (BWS) among children born after IVF was markedly higher than the population baseline. Some reviews emphasise that these findings suggest ART may sometimes perturb methylation at key imprinted loci. Nonetheless, more recent population-based work indicates the absolute risk remains low and that parental fertility/infertility factors may contribute.

Regarding specific loci, meta-analysis has shown that methylation levels of the H19 CTCF3 region were significantly lower in ART offspring compared to spontaneously conceived controls. However, for other imprinted regions (e.g., H19 CTCF6, KCNQ1OT1, PEG3, SNRPN) consistent differences were not observed.



Genome-wide methylation and tissue-specific studies

More recently, high-throughput methylation profiling (arrays, sequencing) has revealed subtle but measurable differences in DNA methylation between ART and naturally conceived offspring, particularly in placental tissue and cord blood. For example, a global methylation study found that placentas from ART conceptions differed from controls in both hypomethylation and hypermethylation at specific CpG sites; of note, some “outlier” ART individuals had particularly extreme methylation values. A large systematic review found that although differences are modest, they exist:

approximately four thousand CpG sites differed in cord blood between ART/hypofertility and controls, with the majority showing <10% methylation differences. Another recent meta-analysis found that while differences exist, they are modest and their functional relevance remains unclear.

Animal and mechanistic evidence

Animal studies provide stronger mechanistic evidence: for instance, in mice, combinations of superovulation plus embryo culture increased the frequency of imprinted methylation errors at Snrpn, Kcnq1ot1 and H19 loci in blastocysts; interestingly advanced maternal age alone did not. These findings support that early embryonic manipulations as they resemble ART can perturb imprinting maintenance.

Mechanistic considerations: how might ART influence methylation

Several mechanisms are plausible:

1. Temporal alignment with reprogramming windows: ART steps (oocyte retrieval after stimulation, fertilisation, in-vitro embryo culture, transfer) overlap with critical windows of methylation erasure, de novo methylation and imprinting establishment/maintenance. Any perturbation here could leave persistent epigenetic marks.

2. Culture conditions and embryo environment: In vitro culture exposes embryos to artificial media, non-physiologic oxygen tension, potential oxidative stress, suboptimal methyl donor availability (methionine, folate cycle), and non-natural flushing and handling. Such stress may impair methylation maintenance or cause demethylation/hypomethylation especially of repetitive elements (e.g., LINE-1) or imprinted regions.

3. Parental infertility and gamete/epigenome status: It is plausible that underlying infertility, parental age, sperm/oocyte epigenetic defects or suboptimal gamete maturation contribute to methylation perturbations in offspring. Some studies show that donor oocyte conceptions also display methylation differences, suggesting procedure effects; but parental factors cannot be fully excluded.

4. Outlier effect and mosaicism: Rather than uniform shifts, several studies show that the effect may arise from a subset of ART conceptuses that exhibit “outlier” methylation patterns (extreme hyper- or hypomethylation) which may contribute disproportionately to the group-level signal.

Clinical and epidemiological implications

- Imprinting disorders: The increased incidence of rare imprinting disorders among ART-conceived children (e.g., BWS) mandates awareness and monitoring, though the absolute risk remains low. Genetic epigenetic counselling may consider ART history among risk factors.
- Perinatal outcomes: ART is associated with higher rates of preterm birth, low birth weight and placental abnormalities; epigenetic perturbations (especially in the placenta) provide a mechanistic pathway. For example, altered cord blood methylation was found to mediate part of the birth weight difference by mode of conception.

- Long-term health: Could subtle methylation differences translate into later disease susceptibility (e.g., metabolic, cardiovascular, neurodevelopmental)? At this stage evidence is limited and inconsistent. The modest effect sizes, heterogeneity of findings and limited long-term follow-up make it difficult to draw firm conclusions. A recent review states that while ART is associated with methylation differences, "functional relevance in adult tissues is unknown".
- Laboratory/clinical practice: The findings suggest that optimisation of ART laboratory conditions (culture media, oxygen tension, embryo handling, freezing/thawing protocols) might help minimise epigenetic perturbations. Clinics may consider incorporating epigenetic risk into quality control and counselling.

Conclusion

In sum, evidence to date supports the view that ART is associated with modest but measurable differences in DNA methylation — especially in placental and cord blood tissues — and that these differences are biologically plausible given the timing of ART relative to epigenetic reprogramming windows. A small increased incidence of imprinting disorders in ART-conceived children further underscores this possibility. At the same time, the effect sizes are small, findings are heterogeneous, and functional/clinical consequences remain largely speculative. Accordingly, while ART remains a safe and effective option for many couples, ongoing monitoring, improved mechanistic research and refinement of ART protocols are warranted to ensure that epigenetic risks if any are minimised.

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Dr. Vikram Jeet Singh
Zonal Head Embryology
Cloudnine Group of Hospitals,
Gurugram, Haryana.

The routine use of EmbryoGlue in assisted reproductive technology (ART) remains a topic of active debate. While EmbryoGlue is an embryo transfer medium enriched with hyaluronic acid (HA) and it has been promoted as a way to enhance implantation rates and pregnancy outcome. However, current scientific evidence does not strongly support its widespread use for all IVF patients. Instead, findings from multiple peer-reviewed studies suggest that its benefits are limited, inconsistent, and potentially confounded by patient-specific factors. Several randomized controlled trials (RCTs) and meta-analyses have reported that EmbryoGlue does not consistently improve clinical pregnancy or live birth rates. For example, a Cochrane review by Bontekoe et al. (2014) found that although HA-enriched media may offer a small improvement in clinical pregnancy rates, the evidence was of low to moderate quality, and live birth outcomes remained uncertain. More recently, a systematic review by Heymann et al. (2020) reiterated that the advantage of EmbryoGlue was minor and not clearly significant when controlling for variables such as embryo quality, endometrial receptivity, or laboratory culture conditions. A well-designed RCT by Fancsovits et al. (2019) concluded that EmbryoGlue did not significantly influence implantation or pregnancy outcomes in unselected IVF patients. This raises doubts about whether EmbryoGlue adds meaningful value beyond standard optimized embryo culture systems.

Additionally, EmbryoGlue may raise theoretical risks. High concentrations of HA may alter embryo–uterine interactions in ways that are not fully understood. Some researchers caution that artificially modifying the peri-implantation microenvironment could unintentionally affect long-term developmental processes, even though evidence is limited. In the absence of proven long-term safety benefits, routine use becomes harder to justify. Cost is another important factor. For many patients, EmbryoGlue adds a significant expense without guaranteed benefits, thereby increasing the financial burden of IVF. Ethical considerations argue that add-on treatments should not be routinely offered unless supported by strong evidence of efficacy and safety.

In conclusion, while EmbryoGlue may benefit select subgroups—such as patients with recurrent implantation failure—the current body of scientific evidence does not justify its routine use. Treatment decisions should remain individualized and grounded in robust, unbiased research.

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Neurodiverse Individuals – Emerging Evidence and Clinical Implications on Gynaecological Differences

Dr. Supriya Malik, Ph.D. (UK), C.Psychol. (UK), Dip. CBT (UK);

Developmental Psychologist, Founder-CEO eMbrace;
President, Indo-Canadian Autism Network

Neurodiversity—including autism spectrum conditions, ADHD, and other neurodevelopmental profiles—is increasingly recognised as relevant to gynaecological health due to distinct biological, hormonal, and metabolic patterns observed in these populations. Emerging research indicates that neurodivergent individuals may exhibit unique gynaecological profiles across adolescence and adulthood, with implications for diagnosis, treatment planning, and long-term reproductive outcomes.

Several studies highlight higher prevalence of menstrual irregularities, including early menarche, heavy menstrual bleeding, and dysmenorrhea among autistic and ADHD populations. Hormonal fluctuations appear to interact with neurodevelopmental pathways, contributing to more pronounced premenstrual symptoms, cyclical mood changes, and heightened risk of premenstrual dysphoric disorder. Additionally, individuals with ADHD show increased rates of menstrual-related exacerbation of attention, executive functioning, and sleep disturbances, suggesting a distinct neuroendocrine sensitivity.

Neurodivergent cohorts also demonstrate higher incidence of gynaecological conditions, notably polycystic ovarian syndrome (PCOS), endometriosis, and chronic pelvic pain syndromes. Associations between autism and PCOS have been linked to atypical androgen profiles, altered HPA axis activity, and metabolic differences such as insulin resistance. Endometriosis prevalence appears elevated in autistic adults, with hypotheses pointing to shared inflammatory and genetic pathways. All these will have a direct impact on reproductive health.

Reproductive outcomes also show variation. Increased rates of subfertility, anovulatory cycles, and hormonal dysregulation have been documented, particularly among individuals with ADHD and those with co-occurring metabolic syndromes. Pubertal development patterns may also differ, with some evidence of earlier or more rapid pubertal progression in autistic and ADHD populations.

This presentation synthesises current evidence on gynaecological differences in neurodiverse individuals, examines proposed physiological and hormonal mechanisms, and identifies priority areas for clinical management. By consolidating biological and epidemiological insights, the session aims to support more precise, data-driven approaches to gynaecological assessment and reproductive health management in neurodiverse populations.

Key Words: Autism, ADHD, Neurodiversity, Reproductive Health, PCOS

Chronic endometritis (CE) in infertility : Cause , coincidence or consequence ?

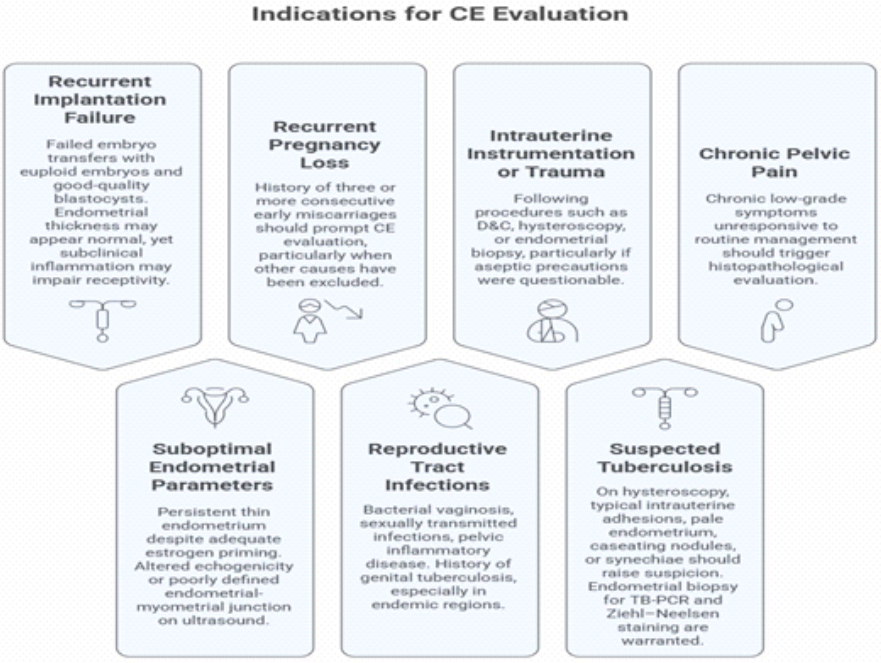
Abstract

Dr. Jayesh Amin
OBSTETRICS AND GYNAECOLOGY

Chronic endometritis (CE) is a frequently discussed and often contentious—entity in reproductive medicine, implicated in infertility, recurrent implantation failure (RIF) and recurrent pregnancy loss (RPL). Accumulating observational evidences suggest that CE, defined histologically by endometrial stromal plasma-cell infiltration (commonly detected by CD138 immunostaining), is more prevalent among infertile cohorts and those with RIF/RPL than in fertile controls, suggesting a strong association with impaired reproductive outcomes.

Biologically, CE plausibly disrupts endometrial receptivity due to persistent local inflammation, altered cytokine and immune-cell milieu, disruption of decidualization and aberrant expression of implantation-related genes. These mechanistic links support a causal pathway , leading to chronic endometrial inflammation which reduces implantation potential and increases early pregnancy loss. However, much of the mechanistic data come from small translational studies and animal models, which limits causal inference in humans.

Clinical data addressing whether CE is a reversible cause of infertility remain mixed. Several cohort studies and meta-analyses report improved clinical pregnancy and live birth rates after antibiotic therapy when CE is documented and successfully eradicated, implying that treatment of CE can restore fertility potential in at least a subset of patients.



Conversely, other systematic reviews and newer cohort analyses have failed to demonstrate consistent benefit of empirical antibiotic treatment on IVF outcomes, particularly when diagnostic criteria and post-treatment confirmation of cure are variable—raising the possibility that CE may sometimes be an epiphenomenon or marker of broader endometrial immune dysfunction rather than the primary driver for adverse ART outcomes.

Interpretation is further complicated by substantial heterogeneity in diagnostic approaches (hysteroscopy vs. histology vs. CD138 immunohistochemistry), inconsistent thresholds for diagnosis, and variable antibiotic regimens and follow-up testing, all of which undermine comparability across various studies. Notably, recent diagnostic accuracy work emphasizes that hysteroscopic signs sometimes may correlate poorly with CD138 confirmed CE, reinforcing the need for standardized diagnostic methods before causal claims can be robustly tested.

During the transfer cycle, management options include —

Aspiration of ECF under ultrasound guidance, hysteroscopy drainage in recurrent cases.

Intrauterine PRP /G-CSF in refractory cases

Reduce estrogen level/mild stimulation to prevent supraphysiological estrogen levels.

Enhance leutal support.

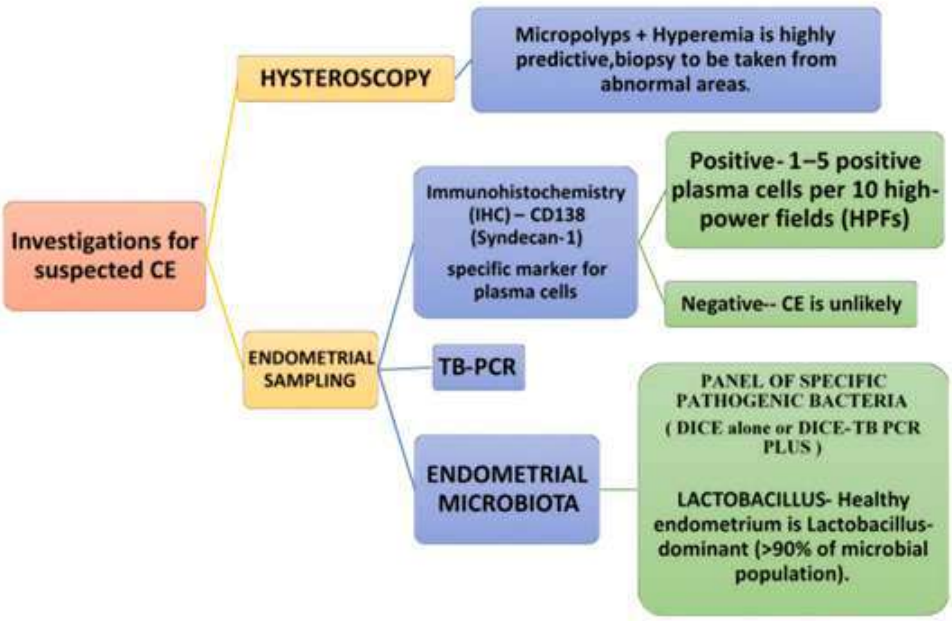
Emerging Intervention

- Hysteroscopic drainage with canal stenting
- intrauterine antibiotic gel
- targeted immunomodulator

Conclusion

ECF is both a symptom and a mediator of impaired uterine receptivity.

A structured diagnostic approach and individualized management plan, and cautious timing of Embryo transfer significantly improve implantation and pregnancy outcome.



16S rRNA Gene Sequencing

- Used for **detection of non -culturable pathogens** in endometrial tissue.
- Especially useful when conventional cultures are negative but CE is suspected.
- A panel may include **pathogens like Mycoplasma, Ureaplasma, Gardnerella, E. coli**, and **Chlamydia** .

Early egg freezing in Women with endometriosis: timings, indications and outcomes

Dr. Puneet Rana Arora
Sr. Consultant Minimal Ascess Surgery
Sir Ganga Ram Hospital
New delhi

The incidence of Endometriosis in reproductive age group is around 5 to 10%. The incidence of infertility in such group is noted in 30 to 50% .

Endometriosis can affect fertility not only by itself but also due to the surgical intervention needed for this condition.

The reason for fertility affection due to endometriosis as a disease itself could be many fold but one of its effect is on ovarian reserve. The effect on ovarian reserve may get worsened after surgery for endometriosis.

Due to age related decline in fertility along with effect of endometriosis on ovarian reserve -this condition may increase the chance of having decline in ovarian reserve earlier than expected.

Counselling for Fertility preservation hence plays a vital role in management of such women. If fertility preservation is offered at correct time before the ovarian reserve starts declining, the number of good quality oocytes retrieved and hence the live birth rate are much better than done at a point when the ovarian reserve has already dropped. The ideal option for preserving fertility at this age is Oocyte cryopreservation. Success of fertility preservation in endometriosis depends on age as in any other population. Endometriosis being a progressive condition makes it more important to discuss and preserve fertility as early as possible after diagnosis is made if women is not keen to have pregnancy soon.

Conference Secretariat

Indian Fertility Society
302, 3rd Floor, Kailash Building
26, Kasturba Gandhi Marg C.P.
New Delhi - 110001
Phone: +91 1140018184
Mobile: +91 9899308083

Conference Manager

Conferences International
B-220/2, 2nd Floor,
Opposite Kali Masjid, Savitri Nagar
New Delhi - 110017
Mobile: +91 9560493999
Email: secretariat@fertivision2025.com

www.fertivision2025.com

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