



# INNOVATIONS & CONTROVERSIES IN ART

### IFS SECRETARIAT

+91 11 40018184  
+91 9899308083  
+91 9667742015  
indianfertilitysocietydelhi@gmail.com  
www.indianfertilitysociety.org  
302, 3rd Floor, Kailash Building,  
26, Kasturba Gandhi Marg,  
C.P. New Delhi - 110001

f indianfertilitysociety

instagram indianfertilitysociety

twitter ifsdelhi

### INDEX

President Message	3
Secretary Message	4
From the Editor's Desk	5
Asking the Experts:	6-9
- Selecting the best embryo - <i>Dr Kuldeep Jain</i>	6
- COS - How to get the best outcome? - <i>Dr Sonia Malik</i>	7
- Embryo Transfer - The best Technique - <i>Prof Sudha Prasad</i>	8
- Selecting the best sperm - <i>Dr K D Nayar</i>	9
Invited Articles :	10-19
- Freeze All - Should it be the Norm? - <i>Dr Syed Sajjad Hussian</i>	10
- PGS in poor responders - Should it be advocated? - <i>Dr Mamta Dighe</i>	11
- Sperm DNA fragmentation - Incorporating It In Infertility Practice - <i>Dr Harinder kaur Oberoi, Dr Meenu Bhanot</i>	12
- Stem cells - Is their role in reproductive medicine a reality? - <i>Dr Sweta Gupta</i>	13
- Blast for all- Should that be the norm? - <i>Dr. Archana Kumari</i>	14
- Non-invasive PGS - Is it Accurate - <i>Dr Divyashree PS</i>	14
- Dual Trigger- Is it beneficial - <i>Anupama Bahadur, Dr Rajlaxmi Mundhra</i>	15
- Social egg freezing- Should it be propagated as the future reproductive technique? - <i>Dr Shilpi Sud</i>	16
- IUI in single tube blocked: Is it justified? - <i>Dr Roya Rozati, Dr Sweta Agarwal</i>	17
- Single versus double Intrauterine Insemination - <i>Dr Paapa Dasari</i>	18
- Endometrial Receptivity Array (ERA) & its Clinical Implications - <i>Dr. Sangita Sharma</i>	19
IFS Social Contribution	21
Training & Education - A Priority with IFS	23
IFS Representing India at Global Level	24
Chapter Activities 2019	26-35

## GOVERNING COUNCIL



**Dr Gouri Devi**  
President  
9810023111  
gouri48@ridgeivf.com



**Dr Sohani Verma**  
Immediate Past President  
9810116623  
drsohaniverma@gmail.com



**Dr Sudha Prasad**  
President Elect  
9968604341  
drsprasad@yahoo.com



**Dr KD Nayar**  
Sr. Vice President  
9810398765  
kdnayar@usa.net



**Dr Gita Radhakrishnan**  
Vice President  
9891178410  
gita.radhakrishnan@gmail.com



**Dr Pankaj Talwar**  
Secretary General  
9810790063  
pankaj\_1310@yahoo.co.in



**Dr Rashmi Sharma**  
Jt. Secretary  
9810252619  
drrashmisharma73@gmail.com



**Dr Neena Malhotra**  
Treasurer  
9891557707  
malhotraneena@yahoo.com



**Dr Ritu Khanna**  
Jt. Treasurer  
9415226900  
ritukhannayogesh@yahoo.co.in



**Dr Surveen Ghuman**  
Editor  
9810475476  
surveen12@gmail.com



**Dr Shweta Mittal**  
Jt. Editor  
9910303056  
mshwets@hotmail.com



**Dr Leena Wadhwa**  
Web Editor  
9910933447, 9818145296  
drleena\_123@yahoo.co.in

### EXECUTIVE ADVISORS

#### Dr. Umesh Jindal

M: 9876130501, 0172-2703222

E: drunjindal@gmail.com

#### Dr. S.N. Basu

M: 9810119072 E: ssndbasu@gmail.com

#### Dr Sandeep Talwar

M: 9810306455

E: sonutalwar2001@yahoo.co.in

### CO-OPTED MEMBERS

#### Dr. Alka Kriplani

M: 9810828717 E: kriplaniaalka@gmail.com

#### Dr. Urvashi Jha

M: 9811029310 / 9350550669

E: urvashijha@yahoo.com

#### Dr. R.K. Sharma

M: 9810442301

E: dr\_sharma1957@yahoo.co.in

#### Dr. Jayant Mehta

E: jayantmehta@gmail.com

#### Dr. Rama Raju

M: 9849110004

E: krishnaivf@gmail.com

### CHAPTER SECRETARIES

#### Dr. Renu Makkar (UP)

M: 9415002674

E: renumakkar@yahoo.com

#### Dr. (Mrs) Harinder Kaur Oberoi (Punjab)

M: 9888030729

E: drhkoberoi@yahoo.in

#### Dr. Neeru Thakral (Haryana)

M: 9810569387

E: drneeruthakral@gmail.com

#### Dr. Sangeeta Sinha (Chattisgarh)

M: 9752595605

E: sangeetasinha1988@yahoo.co.in

#### Dr. Dr Mamta Dighe (Maharashtra)

M: 9881125250

E: mamta\_dighe@yahoo.co.in

#### Dr. Sangita Sharma (Rajasthan)

M: 9549500137

E: sangi237@yahoo.com

#### Dr. Swati Verma (Greater Chandigarh)

M: 9646004459

E: swati7562@yahoo.com

#### Dr. Shilpi Sud (Vidharba)

M: 9923737304

E: sun\_shilpi@yahoo.co.in

## TEAM IFS



**Dr M Kochhar**  
Patron  
9810018277 / 24352514  
drmkochhar@yahoo.com



**Dr M Telang**  
Founder President  
9811030476/25822454  
drmangalatelang@gmail.com



**Dr Abha Majumdar**  
Past President  
9810315807  
abhmajumdar@hotmail.com



**Dr Nalini Mahajan**  
Past President  
9810087666  
dr.nalinimahajan@gmail.com



**Dr Kuldeep Jain**  
Past President  
9810018951, 22443069  
jainravi6@rediffmail.com



**Dr Sonia Malik**  
Past President  
9810122337  
sm\_doc@southendivf.com

### EXECUTIVE MEMBERS



**Dr Ritu Jain**  
9873183030 / 9999600410  
vmcurgaon@gmail.com



**Dr Renu Mishra**  
9811147217  
drrenumisra@gmail.com



**Dr Rupali Bassi Goyal**  
9818331760  
rupalibassi@hotmail.com



**Dr Sweta Gupta**  
8130140007  
swetagupta06@yahoo.com



**Dr Tanya Buckshee**  
9910003731  
tanyabrohatgi@gmail.com



**Dr Nymphaea Walecha**  
9873855738  
nymphaea2006@yahoo.co.in



**Dr Vandana Bhatia**  
9891967417  
vandanabhatia1971@yahoo.com



**Dr Gaurav Majumdar**  
9810794610  
gaurav1979@hotmail.com

### Dr. Uma Shrivastava (Nepal)

M: 977-9851074477, E: dr.ushrivastava@gmail.com

### Dr Jayesh S.Amin ( Gujarat)

M: 9824302671

E: dramin@wingshospitals.com

### Dr. Papa Dasari (Puducherry)

M: 9442566883

E: dasaripapa@gmail.com

### Dr. JK Goel (UP West)

M: 9458702304 E: drjkgol309@gmail.com

### Dr. Anupama Bahadur (Uttarakhand)

M: 9810326959

E: anupama.bahadur@gmail.com

### Dr. Roya Rozati (Telangana)

E: drroyarozati@gmail.com

### Dr. Archana Kumari (Jharkhand)

E: dr\_karchana@yahoo.co.in

### Dr. Syed Sajjad Hussain (Kashmir)

M: 9419000077 E: medageive@gmail.com

### Dr. Divyashree P.S (Karnataka)

M: 9663351451 E: dr.divashree@gmail.com

### Dr. Firuza Parikh (Mumbai)

M: 9812694923 E: frparikh@gmail.com

### Dr. Usha Prasad (Andra Pradesh)

M: +91 91777 44546

### Dr. Monica Singh (MP)

M: 9200002833

E: bttbcentre@gmail.com

### Dr. Surender Kumar (Jammu)

M: 09419188392

E: drsurender59@gmail.com

### Dr. Anita Singh (Bihar)

M: 9334111925

E: anitasinghob@gmail.com

### Dr. Alok Sharma (Himachal)

M: 9418477725

E: md.alok@gmail.com

### Dr. Suparna Banerjee (West Bengal)

M: 8697475255

E: suparnaban2@gmail.com

### Dr K.U.Kunjumoiden (Kerala)

T: 9895983376

E: drkmoideen@gmail.com

### Dr. P.M. Gopinath (Tamil Nadu)

M: 04426163884, 9840888878

E: dgopinath@yahoo.com

### Dr. Mujibur Rehman (North East)

M: 9435070660,

E: mrahman567@gmail.com

## MESSAGE FROM THE PRESIDENT'S DESK

**DR GOURI DEVI**  
President - IFS



Dear Friends

This issue of IFS conversation covers various interesting topics like endometrial receptivity assay, freeze all, non invasive PGT and PGT for low ovarian reserve, dual trigger for oocyte maturation ,social egg freezing and role of stem cells in fertility etc.

IFS conversation is not only a showcase of recent academic activities but also covers various academic topics encompassing fertility treatments and diagnostics with all the practical tips, which will be beneficial for practising fertility specialists.

I also extend my invitation for our forth coming annual congress Fertilvision 2019 to be held between 6-8th December 2019.No congress is complete without whole hearted participation and contribution. We have tried our best to have a plethora of eminent speakers from all across the globe. The conference topics are well chosen keeping in mind the advances in the field to improve fertility treatment outcomes. We hope each one of us goes back richer in knowledge at the end of this academic bonanza.

With Best wishes

Dr M. Gouri Devi

*Dr. Gouri Devi*

## IFS SPECIAL INTEREST GROUP (SIG 2018 - 2020)

SIG ADVISORY BOARD		4. EMBRYOLOGY	9. HOLISTIC MEDICINE (YOGA, ACUPUNCTURE)
DR NALINI MAHAJAN DR S.N.BASU DR ALKA KRIPLANI DR JAYANT MEHTA		Convenor : Dr Sarabpreet Singh Co Convenor : Mr. Gaurav Kant	Convenor : Dr Rajvi Mehta Co Convenor : Dr Shalini Gainder
1. PCO GROUP	5. ULTRASOUND	6. ENDOSCOPY	10. COUNSELLING & PATIENT SUPPORT
Convenor : Dr Bharati Dhorepatil Co Convenor : Dr Rashmi Sharma	Convenor : Dr Ashok Khurana Co Convenor : Dr Ritu Khanna	Convenor : Dr Nutan Jain Co Convenor : Dr Malvika Mishra	Convenor : Dr Poonam Nayar Co Convenor : Dr Puneet R.Arora
2. REPRODUCTIVE ENDOCRINOLOGY	7. FERTILITY PRESERVATION	8. ENDOMETRIOSIS AWARENESS GROUP	11. POOR OVARIAN RESPONSE
Convenor : Dr Sangeeta Sinha Co Convenor : Dr Shweta Mittal	Convenor : Dr Jayesh Amin Co Convenor : Dr Papa Dasari	Convenor : Dr K.U.Kunjimoideen Co Convenor : Dr Nymphaea Walecha	Convenor : Dr Geeta Khanna Co Convenor : Dr Rupali Bassi Goyal
3. MALE INFERTILITY	12. RESEARCH & METHODOLOGY	13. APPLIED GENETICS	
Convenor : Dr P.M.Gopinath Co Convenor : Dr Pranay Ghosh	Convenor : Dr Sandeep Talwar Co Convenor : Dr Vandana Bhatia	Convenor : Dr Ratna Puri Co Convenor : Dr Manisha Bajpai	

## MESSAGE FROM THE SECRETARY'S DESK

**DR (PROF) PANKAJ TALWAR**  
Secretary General - IFS



Dear Friends,

IFS conversation is an interesting platform to receive all the updates on IFS activities. It gives me immense pleasure to announce release of our latest update covering various topics like endometrial receptivity assay, freeze all, non invasive PGT, dual trigger for oocyte maturation and role of stem cells in fertility etc.

We have reached the end of the year and are eagerly awaiting our annual congress Fertilvision 2019 which will be held between 6<sup>th</sup> - 8<sup>th</sup> December 2019 at Leela Ambience, Gurugram. We extend our invitation and would be thrilled to host everyone. It will be an academic feast covering ten pre-congress workshops and followed by two day main congress. There is a galaxy of international and national speakers and you can get enlightened by their vast knowledge. The congress would also entail various post-congress cultural entertainment programs.

We hope you are updated and enriched with IFS activities through this issue of IFS conversation. We would encourage our readers to further give their academic contributions to forthcoming IFS conversation editions.

Dr (Prof) Pankaj Talwar

### WHY TO JOIN IFS

IFS is a Multi-disciplinary Society that values the input and participation of professionals in the scope of Reproductive Medicine.



#### IFS MEMBERSHIP Benefits At A Glance

**Pan India Society**

Collaboration with ESHRE & IFFS

2546 Members & 26 Chapters

National Conference Fertilvision every year with reduced registration fees

Special Interest Group (13) for IFS Members to showcase their talent

Research Wing of IFS has its own ethical committee for Research Project approval

Publication Wing - Fertility Science & Research Journal

IFS Fellowship Program in Clinical ART & Embryology in collaboration with Amity University

ESHRE Certified Embryologist Examination in India, conducted by IFS every year

IFS Outreach activities all over India

IFS Master Courses

Free access to IFS E-Pathshala contents and Official Journal

IFS E-Pathshala - IFS Conversation, Nexus, ARTtext, Fertility News, CATALYST



### Offline Registration Form

Download the form and send to the secretariat with recent pic and cheque/draft

\* Please make Cheque / Draft in favour of "INDIAN FERTILITY SOCIETY" payable at New Delhi.  
\* Please attaché two recent passport size photographs.

Who can apply for IFS Membership : All Professionals with postgraduate qualification such as Obstetricians & Gynaecologists, Clinical embryologists, andrologists, ultrasonologists, counsellors, geneticists and other involved in the care of infertility patients.

**IFS Secretariat**  
Flat No. 302, 3rd Floor,  
Kallash Building,  
26, Kasturba Gandhi Marg,  
C.P. New Delhi - 110001

+91 9667742015  
+91 9899200803  
91-1140018184

indianfertilitysocietydelhi@gmail.com  
info@indianfertilitysociety.org  
indianfertilitysocietyifs  
ifsdelhi  
indianfertilitysociety

### INDIAN FERTILITY SOCIETY

#### Online Registration Process

- STEP 1**

**Open IFS website**  
(www.indianfertilitysociety.org)


- STEP 2**

**Click on Online membership registration button**


- STEP 3**

**Fill all the details**


- STEP 4**

**Please note your Registration no. Then click on pay now button**


- STEP 5**

**Select your preferred payment method**


- STEP 6**

**Fill the card details and click on pay now button**


- STEP 7**

**After successful payment you will get a confirmation email on your register email id**
- STEP 8**

**Within 48 hour you will get the Membership no. and Member login detail on your register email id**

**Note:**

- ★ For Any Help or Query Regarding Payment Please email On support@host4asia.com
- ★ If you do not get the membership details within 48 hours, please email us at support@host4asia.com with your Registration no

**Contact**  
Ms. Poonam  
Office Sec. IFS  
+91 989 930 8083

Flat No. 302, 3rd Floor, Kallash Building,  
26, Kasturba Gandhi Marg, C.P. New Delhi - 110001  
+91 9899200803, 91-1140018184

indianfertilitysocietydelhi@gmail.com, info@indianfertilitysociety.org

# MESSAGE FROM THE EDITOR'S DESK



**DR SURVEEN GHUMMAN**  
Editor - IFS



**DR SHWETA GUPTA**  
Jt. Editor - IFS

Dear Members,

Greeting from team IFS!

This issue of IFS Vision brings us “Innovations and Controversies in ART”. It discusses new innovations with their controversies like ERA, non invasive PGS, Stem cells, Dual trigger, and Social egg freezing. The issue also debates controversies on PGS in low ovarian reserve, Blast for all, Double vs single IUI , IUI in unilateral tubal blockage, Freezing all embryos with transfer in next cycle and DNA fragmentation test and its impact on decision making. We have hoped to address some important controversies and evidence for and against it.

This issue coincides with our annual conference - Fertilisation. The annual academic event of our society which gets together global and national leaders in the field of ART. We are looking forward to more debates, discussions, evidence and experienced based sharing of data on this single platform and we hope to see you as part of this academic bonanza

IFS being a society rich in academics, it has held numerous CME, focused meetings, workshops, round table meets country wide in 2019. The fellowship program in ART and embryology are running successfully. The journal published by IFS - Fertility Science and Research is biannual and we invite contribution from members.

In 2019 IFS has expanded to 27 chapters distributed all over the country with over 2700 members. The theme - “Reaching the Outreach” has been truly fulfilled with members increasing in every corner of the country. Here, we would like to specially acknowledge our chapter secretary at Kashmir, Dr Sayed Sajjad Hussain for his special efforts to comply with our request for an article in this issue, with limited internet connectivity. IFS stands united at all fronts!

We wish you a merry Christmas and a happy 2020!

**Dr Surveen Ghumman**

**Dr Shweta Mittal Gupta**

## INDIAN FERTILITY SOCIETY INITIATIVES

## ASKING THE EXPERTS

### Selecting The Best Embryo



**Dr Kuldeep Jain**

Past President, IFS

Chairperson, International exchange committee, IFS  
Editor, Fertility Science and Research  
Director, KJIVF and laparoscopy centre Delhi  
Program Director, Asian - KJIVE, Faridabad

In my view, an embryo which results in a healthy live pregnancy can be termed a good embryo. This is logical but not applicable to clinical scenario. So, every lab needs to develop their own criteria to select the best embryos for transfer. There are many methods which can help in selecting the best embryo but selection of embryos based on morphology is still the core of daily laboratory practice. Various methods which have been used and suggested are morphological assessment and time lapse technology. Other technologies which are not practiced widely are

- Pyruvate, Lactate, Glucose or AA levels in embryo culture media
- Assessment of oxygen consumption by embryo
- Genomic and proteomic profiling
- Assessment of embryonic metabolome

A multivariable prediction model to rank embryos according to their implantation potential has been suggested. This model is based on sequential morphological assessment to predict implantation potential of the embryo. Five factors included in the final prediction model are early cleavage, number of blastomeres on days 2 and 3, morphological score and presence of morula on day 3.

Our routine selection is still based on Cleavage rates and Morphology. Faster cleavage is better Morphological appearance: Based on the consensus, following is the ideal timing of observation of fertilized oocytes and embryos, and expected stage of development at each time point

Type of observation Timing	(hours post insemination)	Expected Stage
Fertilization check	17±1	Pronuclear stage
Syngamy check	23±1	
Early cleavage check	26±1 post-ICSI; 28±1 h post-IVF	2-cell stage
Day 2 embryo assessment	44±1	4-cell stage
Day 3 embryo assessment	68±1	8-cell stage
Day 4 embryo assessment	92±2	Morula
Day 5 embryo assessment	116±2	Blastocyst

Following are important indicators of best quality embryos.

- Cell number should be appropriate to the age of the embryo (in hours post-insemination)
- Both slow and fast embryos have reduced implantation potential and are abnormal
- The degree of fragmentation of an embryo is strongly correlated with chromosomal mosaicism

and embryos that display fragmentation are less likely to implant

- Polarization of NPB in both pronuclei is a reliable marker of implantation; However, Pronuclear morphology assessment improves embryo selection only when it is combined with embryo morphology evaluation on day 3
- Blastocyst culture is not a means for improving embryo quality; It is simply a tool for selecting the best embryo

#### Limitations:

- Subjectivity
- Time pressure
- Inability to accurately estimate the reproductive potential of embryo.

- Assessment Problems
- Fragmentation
- Blastomere size
- Multi-nucleation

#### Selecting the best embryo morphology by sequential embryo assessment

- 18- 19 Hr- Post insemination
- 25- 26 Hr- Post insemination
- 42- 44 Hr- Post insemination
- 66-68 Hr- Post insemination
- 106-108 Hr- Post insemination

#### What is Ideal ? – Sequential embryo scoring system

- + Zygote – 2pn score
- + Early Cleavage – 24h PI
- + Day 2 embryo score
- + Day 3 embryo score
- + Blastocyst score

- Minimal time in suboptimal environment
- The New and exciting powerful tool - sequential embryo assessment.
- Gives information about development parameters that differs between implanting and more implanting potential.

Multi nucleation defined as presence of more than one nucleus in a blastomere(including micronuclei) and is associated with reduced implantation potential, increased risk of chromosomal abnormality and miscarriage

Assessment should be performed on day 2 at 44 + 1 hpi  
Grading is binary: present or absent

#### A: grade 4

- + fully compacted with all blastomeres compacting
- + cell boundaries not clear; some nuclei can be identified

#### B: grade 3

- + more than three-quarters of blastomeres compacting
- + spherical shape with a smooth profile

#### C: grade 2

- + irregular morphology with a deep indentation

#### D: grade 1

- + less than 50% of the blastomeres compacting
- + fragments/non-compacted blastomeres identifiable

**TABLE 1:** Consensus scoring system for day 4 embryos

Grade	Rating	Description
1	Good	<ul style="list-style-type: none"> <li>• Entered into a fourth round of cleavage.</li> <li>• Evidence of compaction that involves virtually all the embryo volume.</li> </ul>
2	Fair	<ul style="list-style-type: none"> <li>• Entered into a fourth round of cleavage.</li> <li>• Compaction involves the majority of the volume of the embryo</li> </ul>
3	Poor	<ul style="list-style-type: none"> <li>• Disproportionate compaction involving less than half of the embryo, with two or three cells remaining as discrete blastomeres</li> </ul>

#### How useful is embryoscope in routine clinical practice?

Embryoscope is one of the most technologically advanced and innovative devices. It integrates a multi-gas incubator, a microscope with an integrated camera

shooting continuous image and an advanced software for the acquisition and subsequent analysis of all data relating to the development of embryos. It operates in a completely safe and non-invasive manner. Time lapse video analysis provides precise division kinetics of cultured embryos which correlates with blastocyst formation and quality. It is very useful in training new embryologists embryoscope however the utility of the embryoscope in clinical practice still remains to be proven. It is extremely expensive - and is very unlikely to provide cost-effective use in clinical practice today. There is a need of a software based on a multivariate analysis of information from images recorded by all the centers that use the Embryoscope to create a predictive algorithm, which will provide the embryologist with further and useful indications to choose the embryo to implant.

Following is the time line for checkpoint using embryoscope morphokinetics based on algorithm developed.

#### Embryo Dynamics – Embryo Scope

Mesegueretal. 201 Stage	Check-point (hpICSI)
PN Fading	22 - 25
1st Cleavage (2 Cells)	24.6 – 28.2
2nd Cleavage (3 Cells)	35.6 – 40.5
3rd Cleavage (4 Cells)	36.0 – 41.6
Cleavage Dynamics (2 to 3 Cells)	<12 h
Cleavage Dynamics (3 to 4 cells)	<0.67 h
Five Cells	49.6 – 56.7

#### Non-invasive Quantification of Utilization & Metabolome

Techniques such as metabolomics / PGS may help in selecting best embryo and moving towards SET but there routine use requires to be substantiated by RCT'S. Additional methods for embryo selection, such as selection based on chromosomal status (preimplantation genetic screening) and metabolomic profiles of culture media, have been introduced, but upon proper evaluation these methods have been shown to be unable to increase pregnancy rates

#### Genetic markers

- PGS
- polar body analysis

#### Morphokinetics

- time-lapse

#### Biochemical markers

- amino acid profiling
- Infra-red spectroscopy
- PAF

#### Respiration

- oxygen consumption
- pyruvate/glucose turnover

#### Advantage

- Without damaging the embryo
- Quickly
- Consistently and accurately

#### Three approaches

- Analysis of carbohydrate utilization
- Turnover of Amino acids
- Analysis of Embryo metabolism
- Promising but have limitation, cumbersome and need standardization

#### So what is ideal method?

#### Combined approach

- Currently used embryo assessment strategies are largely based on embryo morphology and cleavage rates. Their precision is a limiting factor.
- Sequential morphological assessment, may be with time lapse at designated time combined with glucose uptake and estimation of other metabolic products
- Sequential assessment is important in selecting process and data from time lapse and may prove beneficial in improving selection
- Need for an objective, fast, accurate and affordable test

# ASKING THE EXPERTS

## COS – How To Get The Best Outcome?



**Dr Sonia Malik**

**DGO, MD, FICOG, FIAMS  
Past President-IFS  
Director & HOD, Southend Fertility & IVF  
Vasant Vihar, New Delhi**

ART has witnessed a sea of change over the three decades of its existence. This has primarily happened because of a better understanding of the physiology of reproduction and the advances in diagnostic aids like ultrasound and hormonal assays. Despite all this, 100% success still eludes us.

So, while we talk of the best embryo and the best sperm or the best lab, can we define the “best patient”? The parameters that would define the best patient have not been explored. Many attempts have been made to categorise the women who come to us for treatment. WHO divided women with Ovulatory dysfunction into 3 groups in 1976. Ever since then, ovarian stimulation for IVF has been carried out using the Baird’s theory after categorizing the patient into one of the three groups.

Over time we realized that there were many sub types within these groups and that every woman required individualized treatment. Hence came the concept of “iCOS” – individualized controlled ovarian stimulation. With it also came the realization that each woman responds differently to the same drug/ protocol. And thus, women were further reclassified into

- Hyper responders
- Normo responders
- Poor responders

Each group has their own idiosyncrasies and challenges. Stimulation needs to be tailored according to the type of patient.

### Hyper responders

These are patients who have the following:

- Young age
- AFC > 20,
- AMH > 3.5 pg/ml

COS is a challenge because of premature LH Surge and the strong association and risk of OHSS. The best protocol is gonadotrophins with an Antagonist followed by an agonist trigger and freeze all for the embryos formed. FET is done in a subsequent cycle. This “segmentation of IVF” was proposed by Paul Devroy and holds true for majority of cases. It nearly eliminates the risk of OHSS and also doubles the pregnancy rates. This is the standard protocol in all our centres. All our patients are pre treated with OCP’s or/ and metformin in order to stabilize the hormones and then stimulation is begun. In certain severe cases, GnRH agonist maybe required to down regulate the cycle. In such cases, the stop protocol is preferred wherein the agonist is stopped at the onset of period and a normal antagonist protocol is begun. This gives us the flexibility to use the agonist trigger once again. Our target is to limit the number of oocytes to not more than 20 in case of a severe PCOS or else just 14 -15. This gives us a pregnancy rate of 67% on carrying out a frozen embryo transfer.

### Normo responders

Normo responders are defined as patients who fulfill the following criteria:

- AFC of 5 -18
- AMH of 1.2 – 3.5ng/ml

These patients could actually be considered as the “best patient” that we are looking for. They respond well to any drug or protocol and give the best pregnancy rate. However, a small subgroup may be seen showing an unexpected hyper or hypo response to drugs. Hence one needs to be cautious even while stimulating this group. The starting dose of gonadotropins is 225 iu in both agonist or antagonist protocol. Our aim is to give the patient one fresh and one frozen embryo transfer and this can be achieved with this dose.

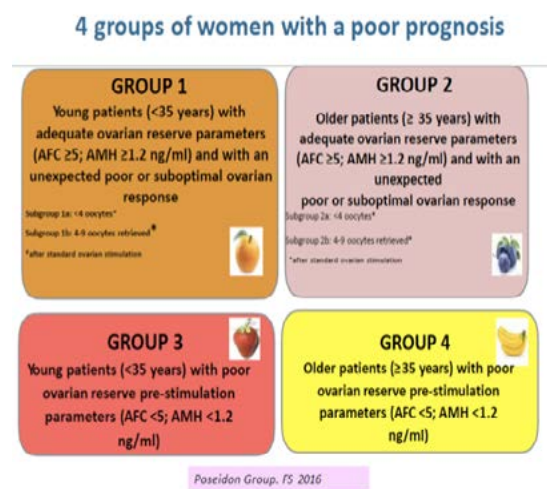
### Poor responders

Nearly 24 -25% of our patients fall in this category and can be of any age group ranging from 25 yrs to 40yrs. Generally have the following criteria:

- AFC < 5
- AMH < 1.2ng/ml.

Recently poor responders have been stratified into the following four categories (POSIEDON) and each one has to be dealt with depending on the category that she falls in. (Fig. 1)

**Fig 1: POSIEDON categorization of Poor Responder**



**Posiedon stratification for poor response.**

**Table 1**

	POSIEDON (N=218)
Group 1	93 (42.6%)
Group 2	59(27%)
Group 3	19(8.7%)
Group 4	45 (20.6%)

In a recently concluded study carried out at our centre, we found the incidence of various groups in a total of 200 patients. The largest group was 1 which is alarming. (Table 1) It was interesting to note that most of the patients were those with an unexpected poor response whether they were young or old.

### Group 1

These young normo gonadotropic women with normal ovarian reserve parameters, may be having an increased sensitivity to FSH hence will benefit by

- Increasing the starting dose of rFSH
- Adding 150 UI rLH to the rFSH.

### Group 2

These older women above age 35 years, maybe showing a normal ovarian reserve but do not respond to normal stimulation. This is due to a fall in androgen production by theca cells as a result of age. This group will do well by

pretreating with DHEAS or testosterone gel. Stimulation requires innovation so that the number of blastocysts produced are more in number. Hence, we may:

- Add 150 UI r.LH to 300 UI r.FSH from the beginning of stimulation
- Duo-stimulation: FPS +LPS to increase in the number of oocytes and therefore, euploid blastocysts

### Group 3 & 4

This group comprises of women where the ovarian reserve is low and again, may have women younger than 35 yrs or more than 35yrs. Not much can be done for them except carrying out multiple cycles for oocyte and embryo collection. This is called Accuvit - an acronym for accumulation and vitrification. This maybe helpful in the younger patient but in the older patient, because of the high incidence of aneuploidies, even this intervention may not give us a healthy live baby. The best option for such patients then is to go in for donor oocytes.

### Conclusion

There have been major developments in the field of ovarian stimulation and despite a fair amount of fine tuning, we still are unable to accurately predict response and outcome in all our patients. Controlled ovarian stimulation still continues to be challenge in all the patients but more so in both hyper or hypo responders. It is important to strike a balance in order to give good results. Many times one maybe swayed by the hopelessness of the condition of the patient, tempted to do away with COS and directly offer third party options to the patient. We must however always remember that the lady who has come to us, desires to have her own child. Moreover, science has evolved only when people have taken bold and unconventional steps. We should therefore not give up easily and try at least once to give the woman her own genetic child rather than taking a short cut.

## ASKING THE EXPERTS

### Embryo Transfer – The Best Technique



**Prof. Sudha Prasad**

**President Elect - IFS  
Director, Matritava Advanced IVF &  
Training Centre, Vasant Vihar, Delhi**

Embryo transfer is the placement of an embryo into the uterus.

A viable embryo, a receptive endometrium and an optimal embryo transfer technique are the prerequisite for the successful IVF procedures. Although embryo transfer is considered to be an easy procedure by most of the clinicians, but it is a very crucial stage which requires the skill. Hence a meticulous training and standard protocols for the procedure are desirable. If a standard embryo transfer protocol is followed the results will certainly increase.

Several variables play a role in the success of a transfer, including catheter type, atraumatic technique, and the use of ultrasound guidance. Because of the adverse effects of controlled ovarian hyperstimulation on the endometrium, frozen embryo transfers have demonstrated improved pregnancy rates.

Improvements in embryo culture, improved culture media have helped to grow viable blastocyst-stage embryos in vitro. The advent of successful methods of vitrification of blastocysts has facilitated storage of these embryos for later transfer without compromising viability. In addition, the evolving methods for embryo selection, which are noninvasive, seem to hold great promise for the future.

Variables which can affect ET success include the performance of a trial/mock transfer, and contamination of the catheter tip with blood, mucus, or endometrial tissue. The success rate are also affects if the embryos are retained or expelled. Important variable is to choose type of catheter, the volume and type of transfer media. It is very important to do cervical culture because the presence of bacteria in the cervix or on the catheter tip will directly hamper the implantation.

Placement of embryos is a skill and should be done as gently as possible to avoid any uterine contraction. Thus, avoiding difficult ET is important to optimize clinical outcomes, and ultrasound guided transfer definitely seems to be a key adjunct toward this goal. To avoid or minimize uterine contractility and to reduce the expulsion rates of embryos progesterone is to be started from the day of oocytes retrieval or in cases of frozen transfer, as a good triple line vascular endometrium is achieved.

There are several catheters available in the market which may be soft or stiff, pre-curved or straight. Soft and pre-curved catheters follow the contour of uterine cavity easily but may be difficult to introduce in tight cervical os, where as stiff one may be more traumatic which may lower the pregnancy rates. Hence, mock/trial transfer which mimics the actual transfer must be done few weeks before the ET irrespective of ultrasound guided transfers.

Flushing of cervix with culture media and removal of thick mucus plug is an important step before transfer.

In a retrospective comparison, Tomás et al.<sup>1</sup> evaluated 4,807 ETs with regard to the degree of difficulty. Easy or intermediate transfers resulted in a 1.7-fold higher pregnancy rate than difficult transfers ( $P < .0001$ ; 95% confidence interval 1.3–2.2). Contamination with blood and mucus indicates difficult transfer and are associated with an increased risk for poor ET outcome.

The timing surrounding ET is also an interesting variable involved in success. After retrospective assessment of timings, Matorras et al.<sup>2</sup> demonstrated that the interval between catheter loading and the transfer of the embryos into the uterine cavity affected IVF outcomes. When this delay was greater than 120 seconds, there was a decrease in pregnancy rates from 31.6% to 19.1% and a decrease in implantation rate from 15.9% to 9.4%. This may be related to how long the embryos are “outside the incubator.” The delay in injection might be a surrogate marker as well for the difficulty of ET. Therefore, minimizing the time between loading and transfer would seem to be important point to achieve better pregnancy rate.

To avoid the risk of multiple pregnancy it is advisable to do elective single embryo transfer (SET)<sup>3</sup> Not more than two embryos are to be transferred in case SET is not done.

Another concern is amount of media taken in transfer catheter. Minimal the media (12 to 20 microliters), better the pregnancy rate. The position of the air bubble transferred at the time of ET and its relation to pregnancy rate is also important. More recently, it was demonstrated that pregnancy and implantation rates in relation with air bubble flashes located <15 mm from the fundus were significantly higher than those with embryo flashes located >15 mm from the fundus<sup>4</sup>.

After transferring embryos, the catheter should be slowly withdrawn, maintaining pressure on the syringe plunger to avoid disrupting placement of the embryos/catheter contents.

After ET, bed rest has been a controversial subject, with some recommending extended bed rest and some virtually no bed rest. It has been suggested that it should be individualized for patients’ preferences and anxiety, anything more than a short period of bed rest is without proven benefit.

#### References

1. Tomás, C., Tikkinen, K., Tuomivaara, L., Tapanainen, J.S., and Martikainen, H. The degree of difficulty of embryo transfer is an independent factor for predicting pregnancy. *Hum Reprod.* 2002; 17: 2632–2635
2. Matorras, R., Mendoza, R., Exposito, A., and Rodriguez-Escudero, F.J. Influence of the time interval between embryo catheter loading and discharging on the success of IVF. *Hum Reprod.* 2004; 19: 2027–2030
3. J Gerris. Single embryo transfer versus multiple embryo transfer. *Reprod Biomed Online.* 2009;18 Suppl 2:63-70
4. Saravelos, S.H., Wong, A.W., Chan, C.P., Kong, G.W., Cheung, L.P., Chung, C.H. et al. Assessment of the embryo flash position and migration with 3D ultrasound within 60 min of embryo transfer. *Hum Reprod.* 2016; 31: 591–596



**Fig 1a.**  
Rocket catheter



**Fig 1b.**  
Labotect catheter



**Fig 1c.**  
Sydney cook catheter



## ASKING THE EXPERTS

### Selecting The Best Sperm



**Dr. Kanad Dev Nayar**

MD, DGO, Dip Obst. (Ireland), FICOG  
Senior Vice President - IFS  
SR Consultant & HOD  
Mata Chanan Devi Hospital  
Director, Akanksha IVF Centre, Delhi

The sperm is one of the most specialised cells of the human body. Eukaryotic DNA present in the mammalian sperm is sixfold more highly condensed than the DNA in somatic chromosomes. Selecting the best spermatozoa and elimination of damaged spermatozoa are important for successful ART outcomes in infertility clinics.

Most sperm selection protocols in use today fall in one of the following categories: sperm migration, filtration, density gradient centrifugation (DGC) or a combination of these methods. In semen samples with normal parameters, wash & swim up technique is used to isolate motile sperms. In patients with oligozoospermia, teratozoospermia or asthenozoospermia, density gradient centrifugation is the method of choice. The recovery of motile spermatozoa is higher in DGC than swim up technique. However these methods cannot differentiate between morphologically normal and abnormal sperms or sperms with fragmented DNA. Centrifugation also generates ROS which damages the spermatozoa. Hence, a number of advanced techniques have been designed in the recent years to select the best sperm. During the decision-making process, to select a sperm separation protocol it is important to consider both the type of infertility and the particular assisted reproductive approach to be used to treat it. For instance, high sperm numbers with vigorous motility are required for successful intrauterine insemination. On the other hand, few motile sperm cells, in the order of thousands, are required for conventional IVF, and even fewer to perform ICSI.

Application of advanced procedures for sperm selection have improved assisted reproductive technology (ART) outcomes. Some of these have been discussed below:

#### 1. Selection of non-apoptotic spermatozoa - Magnetic activated cell sorting (MACS)

This allows the separation of apoptotic sperms from non-apoptotic ones. MACS technology uses conjugated supermagnetic microbeads to separate non-apoptotic spermatozoa from those with deteriorated plasma membranes and externalized phosphatidylserine. MACS beads are biodegradable and do not alter the structure, function or activity of spermatozoa. Hence, it does not need any separate step for separation of the microbeads.

**Principle:** Externalisation of phosphatidyl serine is an early process in apoptosis. Depending on the concentration of calcium ions, phosphatidyl serine has a high affinity for Annexin V. Annexin V cannot cross the plasma membrane, so the binding of Annexin V to spermatozoa signifies disturbed sperm membrane integrity. Based on Annexin V binding and magnetic separation, 2 fractions are obtained: Annexin negative (unlabeled intact membrane; non-apoptotic) and Annexin positive (labeled altered membrane; apoptotic). Though MACS is highly effective in removing apoptotic sperm cells, it is not able to eliminate leukocytes, immature germ cells, seminal plasma and other

contaminants from the semen sample. This is why MACS separation is normally performed in conjunction with Density gradient centrifugation.

#### 1. Selection of motile spermatozoa - Microfluidics

Microfluidics is the science and technology of accurate manipulation of small amounts of fluids, which is typically done in microchannels with dimensions of a few hundred micrometers. The principle of sperm selection by this method is laminar flow by gravity-driven pumps in the microchannels. Microfluidic sperm sorter selects sperm cells that had >80% improvement in DNA integrity relative to the heterogeneous population present in the raw semen, and the selection was performed in <20 minutes. This method bypasses centrifugation and thus lessens the amount of DNA damage in the resultant sample.

#### 2. Selection based on live sperm morphology

##### a. Intracytoplasmic morphologically selected sperm injection, IMSI

Sperm evaluation at 400 magnification for ICSI is unable to provide enough resolution for an accurate sperm morphological assessment. Real-time sperm evaluation is known as motile sperm organelle morphology examination (MSOME). MSOME sperm evaluation is performed under an inverted light microscope equipped with high-power differential interference contrast optics (Nomarski/DIC; magnification x150) enhanced by digital imaging (magnification, x44) to achieve a total magnification of over 6000. At this magnification, it is possible to define the morphological normalcy of five sperm organelles (acrosome, post-acrosomal lamina, neck, tail and nucleus). Among these organelles, evaluation of sperm nucleus (shape and chromatin content) by MSOME appears to be the most important feature conditioning ICSI outcome. Intracytoplasmic morphologically selected sperm injection (IMSI) is a modification of ICSI, in which the injected spermatozoon is selected by the technician at high magnification using MSOME normalcy criteria.

##### b. Polarising microscopy

Another optical system used to select live sperm for ICSI is based on birefringence generated by the incidence of polarized light on longitudinally oriented protein filaments on the post-acrosomal region of the sperm. The proportion of birefringent sperm in a sample is correlated positively with sperm concentration, motility and viability. In addition, using this optical system, it is possible to differentiate acrosome-reacted from acrosome-intact sperm before microinjection.

#### 3. Selection based on sperm membrane maturity - Hyaluronic acid sperm binding (PICSI)

The presence of HA binding sites on the sperm outer membrane is regarded as a sign of sperm maturity, and constitutes the basic principle for this assay. Hyaluronic acid, HA is immobilized on a solid surface (polystyrene culture dish) and the washed sperm sample is allowed to interact with the HA coated surface for 15 min. An individual sperm attached to the dish is picked up with the ICSI pipette and used for oocyte injection. The device called PICSI (physiological intracytoplasmic sperm injection), uses a conventional polystyrene culture dish enhanced with microdots of hyaluronan where the sperm suspension is added. Sperm maturity has been associated with certain desirable sperm traits such as: improved viability and motility, intact acrosomes, lower caspase-3 activation and lower frequency of chromosomal aneuploidies.

#### 4. Sperm surface charge for sperm selection

There are two different approaches to select sperm based on the differential net electric charge on the sperm plasma membrane: electrophoretic system and zeta potential method.

##### a. Electrophoretic system

The electrophoresis-based technology uses an electric field to separate sperm cells based on size and electronegative charge. It is

composed of four chambers: two outer chambers and two inner chambers (incubation and collection). The outer chambers (filled with buffer) house the platinum-coated titanium mesh electrodes. A membrane separates the outer chambers from the inner chambers allowing for the movement of small molecules, water and ions between them. The inner chambers comprise the inoculation compartment and the collection compartment separated by a polycarbonate separation membrane whose pore size excludes leukocytes and precursor germ cells that normally contaminate semen samples. The semen specimen is loaded into the incubation chamber and allowed to equilibrate for 5 min before applying a current of 75 mA and variable voltage (18-21 V). The selected sperm subpopulation is recovered from the collection chamber after 5 min of application of the electric field.

##### b. Zeta potential method

Sperm cells can be selected based on their negative zeta electrokinetic potential which is the overall charge a spermatozoon acquires in a specific medium. A mature sperm cell has a negative zeta potential of -16 to -20 mV (differential potential between the sperm membrane and its surroundings). The zeta potential method is very simple to perform and does not require special equipment and is therefore inexpensive. Washed sperm in serum-free medium is introduced in a conical tube which has been positively charged by rubbing or rotating the tube on a latex glove. Electronegatively charged sperm (mature) attach to the walls of the tube by electrostatic force and the non-adherent sperm fraction along with other contaminants are removed by inverting the tube. Selected adherent sperm cells are recovered by rinsing the tube with serum-supplemented medium. This method scores over the conventional DGC in terms of percentage of morphologically normal sperm, hyperactivation, DNA integrity and maturity, but not motility.

#### 5. Emerging Techniques

##### a. Raman spectroscopy

Raman spectroscopy is a spectroscopic technique that examines the inelastic scattering of photons (a change in frequency of photons) caused by molecular bonds. The photons originated from a laser source are absorbed by the sample and then reemitted with a frequency different to that in the original source what is called Raman effect. In biological specimens, photon shifting provides information about conformation, composition and intermolecular interaction in macromolecules (e.g. DNA-protein).

##### b. Confocal light absorption and scattering microscopy (CLASS)

It is an optical system that combines confocal microscopy, a well-established high magnification microscopic technique, with light-scattering spectroscopy. This combination allows for observation of submicrometer structures in viable cells attaining the spatial resolution of electron microscopy.

#### Conclusion

In light of the known influence of the fertilizing spermatozoon on early and late embryonic development, selection of the best sperm from heterogeneous sperm samples is important for ART outcome. Accurate identification of healthy spermatozoa is of special importance during ICSI, in which a sperm cell is injected into the mature oocyte bypassing all natural barriers. There is great concern about the risk of using sperms with chromosomal abnormalities and/or damaged DNA which can lead to inadvertent transmission of genetic diseases to the offspring. Hence improvement in sperm selection techniques is extremely important. Despite encouraging preliminary results obtained with advanced sperm selection techniques, more research is warranted to address safety issues before widespread application of these methods.

## INVITED ARTICLES

### Freeze All – Should it be the Norm?



**Dr. Syed Sajjad Hussian**

Secretary IFS Kashmir Chapter  
Director, MED AGE Infertility Centre  
Srinagar, Kashmir

Many clinicians have started freezing all embryos and transferring at another cycle. There are many advantages but it is still not established whether the advantages are for all sects of patients

#### Advantages of freezing embryos

1. Better Endometrial Receptivity
2. Safety with Elimination of OHSS
3. Better Embryo-Endometrial Interaction
4. Better Pregnancy Outcome
5. Lesser Birth Defects
6. Lesser Ectopic Pregnancy
7. PGS/PGD

How does Superovulation affect endometrial receptivity?<sup>1</sup>

- Superovulation affects the depth of the surface epithelium, the number and length of microvilli, and the mitotic activity in the surface epithelium and stromal cells
- Superovulation lowers the expression of specific integrins associated with the window of implantation
- Superovulation brings Premature appearance of endometrial nuclear channels systems, subnuclear vacuoles, pinopodes, and secretory changes
- Superovulation affects the timing of window of implantation More so in younger patients with high E2
- Endometrial advancement of >3 days is detrimental for Implantation

With Superovulation, A significant difference in gene expression which are known to be important in estrogen-mediated uterine growth and implantation and STC1, which has been shown to be important in angiogenesis is seen A difference in gene expression of >150 genes regulating angiogenesis and early implantation is seen with superovulation which is consistent with a 2–4 day acceleration in maturation and associated shift in the window of receptivity.<sup>2</sup>

Table: 1<sup>3</sup>

TABLE 1

Gene expression profiles of simulated and nonstimulated human endometrium during the window of embryo implantation.

Study	No. of samples	Fold change considered to be significant	Number of genes	
			Up	Down
Mirkin et al. (45)	13	≥ 1.2	5–6 <sup>a</sup>	1–6 <sup>a</sup>
Horcajadas et al. (46)	19	≥ 3	281	277
Simon et al. (47)	28	≥ 2	22–88 <sup>a</sup>	24–100 <sup>a</sup>
Horcajadas et al. (48)	49	–	69	73
Liu et al. (49)	13	≥ 2	5–244 <sup>a</sup>	2–159 <sup>a</sup>
Haouzi et al. (50)	84	≥ 2	321–657 <sup>a</sup>	0–4 <sup>a</sup>

<sup>a</sup> Ranges represent variation seen between different stimulation protocols.

Weinerman. Frozen vs. fresh ET: translational rationale. Fertil Steril 2014.

- Superovulation alters the immune environment of the endometrium
- A lower concentrations of NK cells is seen in the endometrium compared to non-superovulated controls
- As implantation occurs, NK cells via IL-15, which turn into decidual NK cells which secrete multiple factors important for implantation and angiogenesis like VEGF and cytokines and growth factors like leukemia inhibiting factor (LIF)

#### Safety with Prevention of OHSS without compromising results

- COS in high responders who receive a “trigger” of hCG can land up in OHSS
- Frozen embryo transfer reduces early-onset OHSS and to eliminate late OHSS risk with the use of a GnRH agonist “trigger” for final oocyte maturation,
- The use of agonist trigger has been associated with abrupt termination of the luteal phase, complete and irreversible luteolysis, and reduced live birth
- In PCOS, FET resulted in a higher frequency of live birth (49.3% vs. 42.0%), a lower frequency of pregnancy loss (22.0% vs. 32.7%), and a lower incidence of OHSS (1.3% vs. 7.1%)<sup>4</sup>
- Methods to improve Luteal phase after GnRHa Trigger like Dual Trigger or low dose HCG in LPS or E+P does not eliminate OHSS risk and ART outcomes were significantly low<sup>5</sup>

#### Superovulation affects Embryo-Endometrial Interaction

- Superovulation is an independent factor adversely affecting placentation and fetal growth probably via impaired trophoblast differentiation
- Superovulation affects methylation of the developing oocyte, and de-methylation of the developing embryo, especially paternally imprinted genes which may have effects on placentation and fetal growth<sup>6</sup>

#### Pregnancy outcome is better with Frozen vs. Fresh

Risks linked to fresh transfer after Superovulation:<sup>7</sup>

- » Pre-eclampsia
- » Low birth weight (LBW)
- » Small for gestational age (SGA)
- » Preterm
- » Antepartum hemorrhage,
- » Placental abruption
- » Perinatal death

- Eleven studies : Singleton pregnancies after the transfer of frozen thawed embryos were associated with better perinatal outcomes compared with those after fresh IVF embryos.
- The relative risks (RR) and 95% confidence intervals (CI) APH (RR = 0.67, 95% CI 0.55–0.81) PT (RR = 0.84, 95% CI 0.78–0.90) SGA (RR = 0.45, 95% CI 0.30–0.66) LBW (RR = 0.69, 95% CI 0.62–0.76) Pr. MORTALITY (RR = 0.68, 95% CI 0.48–0.96) were lower in women who received frozen embryos<sup>7</sup>
- American registry showed increased risk of LBW in fresh probably due to uterine exposure to COS<sup>8</sup>
- Japanese registry showed in 48,158 deliveries a reduced incidence of SGA, LBW, and prematurity in FET.<sup>9</sup>

#### Birth Defects Frozen vs. Fresh

- » The increase in blastogenesis defects appears greater for fresh embryo transfer (more than 3-fold)
- » Cryopreservation process acting as a ‘selection gate’ for more viable embryos
- » Excessive ovarian hormonal exposures puts adverse effects on the very early pregnancy

#### Ectopic Pregnancy

- Probably becoz of supraphysiologic hormone levels resulting in altered uterine contractions or the effect of elevated progesterone on cilia
- FET has a reduced risk of ectopic pregnancy (both visualized ectopic pregnancies and pregnancies

of unknown location) when compared with fresh transfer<sup>10</sup> ( Table 2)

Table: 2<sup>11</sup>

Comparison of Fresh vs.FET with respect to maternal and Fetal Risks	
<b>Reduced Risks in FET</b>	<b>Risks without a clear difference</b>
<ul style="list-style-type: none"> <li>• OHSS</li> <li>• LBW(&lt;2500G)</li> <li>• PreTerm(&lt;37 wks)</li> <li>• PreTerm LBW</li> <li>• SGA</li> <li>• Placenta Previa</li> <li>• Abruptio</li> <li>• APH</li> <li>• Perinatal Mortality</li> </ul>	<ul style="list-style-type: none"> <li>• Implantation Failure</li> <li>• Ectopic</li> <li>• PreEclampsia</li> <li>• Very PreTerm(&lt;32 wks)</li> <li>• Very LBW(&lt;1500 g)</li> <li>• NICU Admissions</li> <li>• Congenital Abnormalities</li> </ul>

The advantages of freezing all embryos is established for OHSS and thin endometrium. To establish it for all patients further studies are needed.

#### References

1. Sendag F1, Akdogan A, Ozbilgin K, Giray G, Oztekin K Effect of ovarian stimulation with human menopausal gonadotropin and recombinant follicle stimulating hormone on the expression of integrins alpha3, beta1 in the rat endometrium during the implantation period. Eur J Obstet Gynecol Reprod Biol. 2010 May;150(1):57-60.
2. Horcajadas JA1, Minguez P, Dopazo J, Esteban FJ, Dominguez F, Giudice LC, Pellicer A, Simón C Controlled ovarian stimulation induces a functional genomic delay of the endometrium with potential clinical implications. J Clin Endocrinol Metab. 2008 Nov;93(11):4500-10.
3. Weinerman R1, Mainigi M2 Why we should transfer frozen instead of fresh embryos: the translational rationale. Fertil Steril. 2014 Jul;102(1):10-10.
4. Chen ZJ et al Fresh versus Frozen Embryos for Infertility in the Polycystic Ovarian Syndrome N Engl J Med 2016; 375:523-533
5. Humaidan P GnRH agonist for triggering of final oocyte maturation: time for a change of practice? Hum Reprod Update. 2011 Jul-Aug;17(4):510-24
6. Haworth KE1, Farrell WE, Emes RD, Ismail KM, Carroll WD, Hubball E, Rooney A, Yates AM, Mein C, Fryer AA Methylation of the FGFR2 gene is associated with high birth weight centile in humans. Epigenomics. 2014;6(5):477-91
7. Maheshwari A1, Pandey S, Shetty A, Hamilton M, Bhattacharya S.Obstetric and perinatal outcomes in singleton pregnancies resulting from the transfer of frozen thawed versus fresh embryos generated through in vitro fertilization treatment: a systematic review and meta-analysis. Fertil Steril. 2012 Aug;98(2):368-77. e1-9.
8. Kalra SK1, Ratcliffe SJ, Barnhart KT, Coutifaris C. Extended embryo culture and an increased risk of preterm delivery. Obstet Gynecol. 2012 Jul;120(1):69-75.
9. Ishihara O1, Araki R2, Kuwahara A3, Itakura A4, Saito H5, Adamson GD6Impact of frozen-thawed single-blastocyst transfer on maternal and neonatal outcome: an analysis of 277,042 single-embryo transfer cycles from 2008 to 2010 in Japan. Fertil Steril. 2014 Jan;101(1):128-33.
10. Shapiro BS1, Daneshmand ST, De Leon L, Garner FC, Aguirre M, Hudson C Frozen-thawed embryo transfer is associated with a significantly reduced incidence of ectopic pregnancy. Fertil Steril. 2012 Dec;98(6):1490-4.
11. Shapiro BS1, Daneshmand ST, Garner FC2, Aguirre M3, Hudson C3 Clinical rationale for cryopreservation of entire embryo cohorts in lieu of fresh transfer. Fertil Steril. 2014 Jul;102(1):3-9.

## PGS in poor responders – Should it be advocated?



**Dr Mamta Dighe**

**Secretary- Western Maharashtra Chapter - IFS  
Director- Xenith Advanced Fertility Centre, Pune**

The European Society of Human Reproduction and Embryology (ESHRE) published the Bologna criteria in 2011 in order to standardize the definition of poor ovarian response (POR) in a simple and reproducible manner<sup>1</sup>

At least two of the following three criteria had to be present to establish the definition:

1. Advanced maternal age (>40 years) or any other risk factor for POR.
2. A previous POR ( $\leq 3$  oocytes with a conventional stimulation protocol).
3. An abnormal ovarian reserve test [i.e. antral follicle count (AFC) less than 5–7 follicles or anti-Müllerian hormone (AMH) below 0.5–1.1 ng/ml.

Though the POSEIDON criteria,<sup>2</sup> now helps us categorize women depending on an expected poor response based on the above criteria and the unexpected poor response in the presence of normal ovarian reserve parameters, for the scope of this article we would be considering women who would fulfill the Bologna criteria and are expected to have a poor response.

Preimplantation genetic testing for aneuploidy (PGT-A) has been demonstrated to improve implantation and pregnancy rates and decrease miscarriage rates over standard morphology-based embryo selection. However, there are limited data on its efficacy in patients with diminished ovarian reserve or a poor response to stimulation who may have fewer embryos to select amongst.

Despite consensus guidelines defining what constitutes DOR, there is still great debate regarding whether the low pregnancy rates observed in poor responders are simply a reflection of the quantitative challenge of starting with fewer oocytes, or if there is also a diminution in oocyte quality and an increase in aneuploidy.<sup>3,4</sup> This is an important question in the context of PGT-A, because a young poor responder may have a different prognosis than an older poor responder.

Application of PGT-A in all the poor responders runs the risk of no embryos being available for transfer, if the initial numbers are too low, and also if none of those few tested are reported to be euploid. However, a poor responder may still benefit from this by avoiding futile transfers with aneuploid embryos<sup>5</sup> and expeditiously moving into either another stimulation cycle or egg or embryo donation. Thus, time to pregnancy may be a better metric with miscarriage rate being a useful secondary measure. However, one has to consider the potential downside of the possibility of a false aneuploid result.

### Arguments in favour of PGS

Early findings demonstrate that PGT-A reduces the miscarriage rate and decreases the time to delivery in poor responders. PGS significantly decreased time to live birth by an average of three months in patients with diminished ovarian reserve. Further, PGS appears to have a decreased risk for ongoing aneuploid gestations.<sup>6</sup>

In one study looking at all responders 40 years or older at the time of oocyte retrieval, the CPR was 62.4%, OPR was 60.0%, and clinical miscarriage rate was 15.3%. This compares to a miscarriage rate of 12.9% in women younger than 40 years ( $p=0.68$ ), and also gives similar CPR and OPR (7) In a study by Rubio et al,<sup>8</sup> involving women between the ages of 38-41 years, the authors reported that although more patients in the PGT-A arm had no transfer performed because of no euploid embryos being available, the PGT-A arm had a higher delivery rate per randomized patient (36 versus 21.9%). This improvement was because of a significantly higher pregnancy rate per transfer (52.9 versus 24.2%,  $P < 0.001$ ) and a significant reduction in miscarriage (2.7 versus 39%,  $P < 0.001$ ) in the PGT-A arm. As a result, despite more cycles being cancelled prior to embryo transfer, the time to ongoing pregnancy was significantly shorter in the PGT-A arm (7.7 versus 14.9 weeks).

The SOLAIRE study utilized AMH less than 1.1 or antral follicle count of less than 8 as inclusion criteria. This study also performed all embryo biopsies at the blastocyst stage unlike the Rubio study<sup>6</sup> The preliminary data demonstrated a 90-day reduction in the achievement of ongoing pregnancy in the PGT-A arm. There was also a trend toward reduction in clinical pregnancy losses

Thus preliminary data conclude that, the true benefit of PGT-A in these patients is the avoidance of futile transfers and associated loss of time and emotional burden of miscarriage and ongoing aneuploid pregnancies

### Arguments against PGS

Despite many studies examining the clinical performance of patients with DOR or POR, there is still a lack of consensus regarding whether the poor IVF outcomes observed in these patients are solely the product of the inability to produce a sufficient number of oocytes to withstand the normal attrition seen at each stage of the ART process, or whether there is an additional qualitative penalty.<sup>9</sup> In other words, does an oocyte derived from a poor responder also demonstrate reduced developmental potential or an increase in aneuploidy when compared to age-matched controls with better ovarian responsive-ness? It has been difficult to assess this since most studies about poor responders have not been adequately controlled for the confounding impact of age. It is important to see if these patients also exhibit evidence of an accelerated reduction in oocyte quality to understand the true impact of applying PGT-A to this group.

Without knowledge of how often an embryo diagnosed as aneuploid produces an ongoing gestation, it is difficult to make an informed decision regarding whether the benefits of PGT-A (avoidance of futile transfer, miscarriages, and associated lost time) are worth the risk of a false diagnosis of aneuploidy

Studies have also demonstrated that different subpopulations of patients with low response exhibit different clinical characteristics and hence need to be looked at as separate subgroups.

The additional diagnostic categories of mosaicism and segmental imbalance and whether and which mosaic embryos can be transferred in the absence of euploid embryos in this group of patients with very few embryos, further complicate this issue and prospective, blinded data regarding the reproductive potential of such embryos is sorely needed.<sup>10</sup>

Poor responder patients may have very few embryos going to the blastocyst stage and adding a PGT-A to these may carry a risk of no transfer or the risk of wrong diagnosis of aneuploidy preventing a transfer. It is to be borne in mind that biopsy at blastocyst stage means fewer available embryos for transfer, particularly so among women of advanced age who may actually benefit more from this procedure than good prognosis ones. Also, procedural damage to the embryos, however rare, could be a significant loss for this category of patient.

### Conclusion

Defining the role of PGT-A in ART for poor responders is slowly emerging. Early results suggest that utilizing aneuploidy screening improves efficiency in these patients by avoiding the time lost to futile transfers and associated miscarriages and ongoing aneuploid gestations. However, a complete assessment of the efficacy in this population will require a better understanding and more information is needed on characterizing the physiology of ovarian aging across multiple phenotypes of diminished ovarian reserve and establishing the predictive value of aneuploid results across multiple PGT-A platforms. However, initial data suggests benefit of PGT-A in poor responders.

### References

1. Ferraretti AP1, La Marca A, Fauser BC, Tarlatzis B, Nargund G, Gianaroli L; ESHRE working group on Poor Ovarian Response Definition ESHRE consensus on the definition of 'poor response' to ovarian stimulation for in vitro fertilization: the Bologna criteria. *Hum Reprod.* 2011 Jul;26(7):1616-24
2. Alviggi, Carlo et al., A new more detailed stratification of low responders to ovarian stimulation: from a poor ovarian response to a low prognosis concept, *Fertility and Sterility*, Volume 105, Issue 6, 1452 – 1453
3. Tarasconi B, Tadros T, Ayoubi JM, et al. Serum antimüllerian hormone levels are independently related to miscarriage rates in in vitro fertilization-embryo transfer. *Fertil Steril* 2017; 108:518–524.
4. Riggs R, Kimble T, Oehninger S, et al. Anti-Müllerian hormone serum levels predict response to controlled ovarian hyperstimulation by not embryo quality or pregnancy outcome in oocyte donation. *Fertil Steril* 2011; 95:410–412.
5. Meldrum DR, Su HI, Katz-Jaffe MG, Schoolcraft WB. Preimplantation genetic screening 2.0: an evolving and promising technique. *Fertil Steril* 2016; 106:64–65.
6. Fransaik JM, Hong KH, Werner MD et al. Preimplantation genetic screening (PGS) in low responders shortens time to pregnancy: a randomized controlled trial. *Fertil Steril* 2017; 108:e60-e61
7. Kaye LA, Antero MC, Bartolucci AF et al. Pregnancy rates after euploid embryo transfer for poor responders in IVF *Fertil Steril* 2017; 107, Issue 3, Suppl: 34
8. Rubio C, Bellver J, Rodrigo L, et al. In vitro fertilization with preimplantation genetic diagnosis for aneuploidies in advanced maternal age: a randomized, controlled study. *Fertil Steril* 2017; 107:1122–1129
9. Practice Committee of the American Society for Reproductive Medicine. Testing and interpreting measures of ovarian reserve: a committee opinion. *Fertil Steril* 2012; 98:1407–1415.
10. Brezina PR, Anchan R, Kearns WG. Preimplantation genetic testing for aneuploidy: what technology should you use and what are the differences. *J Assist Reprod Genet* 2016; 33:823–832.

## Sperm DNA Fragmentation - Incorporating It In Infertility Practice



**Dr Harinder kaur Oberoi**

MBBS, DGO, ART from Cambridge (U K)  
Secretary, Punjab Chapter IFS  
Consultant Gynecologist & ART Specialist



**Dr Meenu Bhanot**

MSC Biotechnology,  
Master In Biotechnology  
from Valencia institute of infertility Spain.  
Embryologist

Infertility is described as inability to establish pregnancy within 12 consecutive months of unprotected intercourse in couples of reproductive age. Among infertile couples around 20% contribute to male factor alone.<sup>1</sup>

Conventional semen analysis till date has been considered as a cornerstone laboratory examination during evaluation of male infertility. When performed under strict guidelines and quality control this test can give information regarding male fertility potential. Also, one can find out radical forms of sperm dysfunctions like azoospermia or globulozoospermia which has negative consequences on conception. An estimated 15% of men with normal basic semen analysis profiles have been associated with infertility.<sup>2</sup> Various factors which cause male infertility includes varicocele, oxidative stress, genetic abnormalities, systemic diseases, infections, altered lifestyle and exposure to xenobiotics.<sup>3</sup> All these factors can influence Sperm DNA fragmentation which acts as potential mediator for establishing an infertility status in men. Many recent studies demonstrated that spermatozoal DNA integrity is a prerequisite for normal fertilization and transformation of paternal genetic information to the offspring.<sup>4</sup> Also, reproductive timeline in men is one of the factors affecting sperm parameters.

In general semen volume, pH, sperm concentration, motility, vitality and morphology are determined according to WHO 2010 guidelines. But, it cannot accurately differentiate fertile from infertile men. Nearly 15% of infertile men have normal sperm parameters according to WHO 2010. This clearly indicates the presence of other subcellular and nuclear factors that have a major contributions towards male infertility that is not identified by conventional semen analysis.

Nuclear component of spermatozoa, especially DNA integrity, is essential for normal fertilization, implantation, pregnancy and fetal development.<sup>5</sup> Within the last decade, infertility researchers have turned

their attention to sperm molecular architecture for good reason—mammalian fertilization and subsequent embryo development depend in part on the inherent integrity of sperm DNA.<sup>6</sup>

Sperm cell is different from other somatic cell at the expense of Cytoplasm and hence cell mass. Reduced cell mass means impaired production of enzymes required for genetic repair. Chromatin in somatic cells is a relatively loose structure but in sperm cell it is very tightly packed, Compacted, haploid genome which must adopt to a volume 40 times less than a somatic cell.

The extremely tight complexes formed by the interaction of spermatozoal DNA with proteins generate highly stable and transcriptionally inert chromatin. The replacement of the largest part of histones (85%) by transition proteins (TPs) and subsequently by protamines takes place during spermiogenesis and epididymal transit.<sup>7</sup>

Etiology of DNA Fragmentation- it is multifactorial but this is best explained on the basis of three mechanisms;<sup>8,9</sup>

1. Abnormal Chromatin/Remodeling.
2. Oxidative Stress.
3. Abortive Apoptosis.

### Causes for Sperm DNA Fragmentation

#### Intrinsic Factors

- Remodelling and packaging problems.
- Stage specific transient DNA Strand Breakage are introduced during Spermatogenesis. DNA breaks are needed for transient relief of torsional stress, favouring the Histones replacement with protamines during the final maturation from round to elongated spermatozoa. These physiological, temporary breaks if not repaired leads to Sperm DNA fragmentation or genetic mutation in ejaculate.
- Protamine deficiency or complete absence of it in some leads to defective packaging.
- Damage by ROS-excessive reactive oxygen species (ROS) production and/or decreased seminal antioxidants.
- Apoptotic events during sperm maturation within the epididymis.

#### Extrinsic Factors

- Chemotherapy.
- Cigarette smoking.
- Genital tract infection.
- Testicular Hypothermia.
- Varicoceles.
- Advanced age.
- Febrile illness.

#### Types of DNA Fragmentation

- Single Stranded Breaks (SSB)-due to unrepaired DNA nicks and ROS.
- Double Stranded Breaks (DSB)- due to abortive apoptosis, gross alteration in chromosomal structure. This leads to more serious and deleterious effect development of progeny.

#### Effect on Reproductive outcome

Oocytes and early embryos have shown to repair DNA damage. Also fertilization is independent of DNA damage. Post fertilization development is affected by improper repair by oocyte. This leads to implantation failure, early miscarriages, and diseases in offspring.

Currently, there seems to be insufficient evidence to support the routine use of SDF in male factor evaluation. Nevertheless the importance of DNA fragmentation in spermatozoa has been acknowledged in the latest American Urological Association (AUA) and European Association of Urology (EAU) guidelines on male infertility(10). Although a precise understanding of the specific utility of such tests in different clinical scenarios is still lacking, studies defining specific indications for DNA testing are now emerging.<sup>11,12</sup>

#### Diagnostic Tests

There are two types of assays that have been developed

to measure SDF: Those that can directly measure the extent of DNA fragmentation through the use of probes and dyes and those that measure the susceptibility of DNA to denaturation, which occurs more commonly in fragmented DNA.

Below are the various diagnostic tests.

**AO test:** Metachromatic shift in fluorescence of AO when bound to single strand (ss) DNA. It works on principle of fluorescent microscopy. It is a rapid, simple and inexpensive but there are inter-laboratory variations and lack of reproducibility.

**AB staining:** There is Increased affinity of AB dye to loose chromatin of sperm nucleus. It works on the principle of optical microscopy. It is rapid, simple and inexpensive but there is an inter-laboratory variations and lack of reproducibility.

**CMA3 staining:** CMA3 competitively binds to DNA indirectly visualizing protamine deficient DNA. It works on the principle of fluorescent microscopy. It yields reliable results as it is strongly correlated with other assays. There is an inter-observer variability.

**TB staining:** There is increased affinity of TB to sperm DNA phosphate residues. It works on the principle of optical microscopy. It is rapid, simple and inexpensive but there is inter-observer variability

**TUNEL:** It quantifies the enzymatic incorporation of dUTP into DNA breaks. It can be done using both optical microscopy and fluorescent microscopy. It uses optical microscopy, fluorescent microscopy and flow cytometry. It is very sensitive, reliable with minimal inter-observer variability. This can be performed on few sperm. Although it requires standardization between laboratories.

**SCSA:** Measures the susceptibility of sperm DNA to denaturation. It is a cytometric version of AO test. It works on the principle of flow cytometry. It gives the reliable estimate of the percentage of DNA damaged sperm. But requires the presence of expensive instrumentation (flow cytometer).

**SCD or Halo test:** This test assesses dispersion of DNA fragments after denaturation. It works on the principle of optical or fluorescent microscopy. It is a very simple test, but there is inter-observer variability

**SCGE or comet assay:** This is electrophoretic assessment of DNA fragments of lysed DNA. It works on principle of fluorescent microscopy. This can be done in very low sperm count. It is sensitive and reproducible, but requires an experienced observer. There is inter-observer variability.

#### Clinical Utility

Most studies define upper normal level of percentage of cells with DNA fragmentation. Unit of measurement is DNA Fragmentation Index (DFI). Percentage of spermatozoa with fragmented DNA less than 15% is good fertility potential, 15-25% is average and more than 25% is poor fertility potential.

#### Advantages and Disadvantages

These assays do not differentiate between clinically significant or insignificant DNA damage. Some DNA nicks occur as a normal process during winding or unwinding of DNA and these analysis do not differentiate between physiological and pathological nicking. Assays do not evaluate genes that may be affected by the fragmentation, as fragmentation in area containing certain genes may be more detrimental than area in relatively inactive region of genome. All assays depend on the concept that more nicking, and more fragmentation is pathologic.

#### What should be the practice?

- Successful human reproduction depends on inherent integrity of Sperm DNA.
- There appears to be a threshold of sperm DNA damage beyond which embryo development and subsequent pregnancy outcomes are impaired.
- Spermatozoa of infertile men possess substantially more DNA damage as compared to fertile men. Our

understanding of the etiology of sperm damage is still rudimentary.

- During any ART procedure sperm handling should be done to avoid DNA damages.
- Life style modifications should be done to avoid such circumstance.
- More research is required to understand the concept and its implication to improve reproductive outcome.

## Stem cells – Is their role in reproductive medicine a reality?



**Dr Sweta Gupta**

**MBBS, MD(Obs & Gynae, Delhi)  
MRCOG (London, UK), DFSRH (UK)  
MSc (Reproduction & Development, Bristol, UK)  
Fellowship in Reproductive medicine & ART  
(London, UK)  
Executive member-IFS  
Clinical Director & Sr Consultant  
(Reproductive Med. & IVF )  
Medicover Fertility, Delhi.**

Infertility affects about 10% of couples of reproductive age globally. Stem cells are considered as new therapeutic agents for infertility treatment. Stem cells are undifferentiated cells that are present in the embryonic, fetal and adult stages of life and give rise to differentiated cells that make up the tissues and organs. Recently there have been progress in potential of stem cells into oocyte production and ovarian regeneration in female infertility. Similarly, derivation of male germ cell from pluripotent undifferentiated stem cells.<sup>1</sup>

Pluripotent stem cells are able to differentiate into cells that arise from the three germ layers—ectoderm, endoderm and mesoderm—from which all the tissues and organs develop. Commonly, stem cells are derived from the following two main sources: early embryos [embryonic stem cells (ESCs)] and adult tissue (adult stem cells).<sup>1</sup> ESCs are pluripotent stem cells derived from the inner cell mass of the blastocyst. The essential characteristics of ESCs include derivation from the preimplantation embryo, prolonged proliferation in their pluripotent state and stable developmental potential to form the derivatives of all three embryonic germ layers. Stem cells can also be derived from the extraembryonic tissues (amnion, chorion, placenta and umbilical cord). The advantage of stem cells derived from extraembryonic tissues is the efficient isolation from tissues normally discarded at birth avoiding ethical concerns that plague the isolation of human ESCs.<sup>2</sup> Mesenchymal stem cells (MSCs) are one of the most common adults, multipotent stem cells. They can be derived from a variety of tissues including the bone marrow, adipose tissue, bone, Wharton's jelly, umbilical cord blood and peripheral blood.

Male infertility accounts for approximately half of all cases of infertility. ESCs can differentiate into male germ-like cells in vitro, but they are genetically unrelated to the patients, and the sources of human hESCs are limited. The ectopic expression of transcription factors leads to the reprogramming of somatic cells to induced pluripotent stem cells (iPSCs), which resemble ESCs in morphology, pluripotency marker expression and differentiation ability. hiPSCs can be generated from patients' somatic cells but may not faithfully recapitulate the characteristics of hESCs at both genetic and epigenetic levels. Hayashi et al.<sup>3</sup> made the remarkable finding that primordial germ cell-like cells PGCLCs could be obtained from mouse ESCs and mouse iPSCs. The PGCLCs could be differentiated into spermatozoa in vivo resulting in the birth of healthy offspring via ICSI. In spite of the progress in mice, the differentiation of hiPSCs to male germ cells still presents a significant challenge. Unlike miPSCs in naive state, hiPSCs exhibit a primed pluripotency with less potential for the germ cell fate. Therefore, the success rate of germ cell derivation from hiPSCs is much lower than that from miPSCs. hiPSCs may not lead to clinical approaches addressing infertility resulting from defects in gametogenesis. Currently, human studies cannot be validated by transplantation or the production of offspring. At present, stem cells

in male infertility is not leading to realistic treatment approach but has provided us new area of research.

For female infertility, stem cell-based strategies for ovarian regeneration and oocyte production have been proposed as future clinical therapies. White et al<sup>4</sup> identified a rare population of mitotically active germ cells in human ovaries that can be purified and cultured in vitro to spontaneously form oocytes. Herraiz et al<sup>5</sup> introduced the beneficial effects of autologous stem cell ovarian transplant (ASCOT) on ovarian reserve and IVF outcomes for poor reserve. Herraiz et al<sup>6</sup> studied 17 poor responder young women, bone marrow derived stem cells (BMDSC) were delivered directly to one ovary for each patient to optimize the recruitment of existing dormant follicles to improve IVF outcomes. The study consisted of BMDSC mobilization to peripheral blood by granulocyte colony stimulating factor treatment and subsequent collection by aphaeresis. Cells were delivered into the ovarian artery by intra-arterial catheter. The contralateral ovary in each patient served as a control. Patients then proceeded with controlled ovarian hyperstimulation for IVF with preimplantation genetic screening. Results after ASCOT were promising for poor responders, ASCOT resulted in a significant improvement in AFC two weeks after treatment. They defined success as an increase in AFC  $\geq 3$  follicles and/or two consecutive increases in AMH levels and with these criteria ovarian function improved in 81.3% of women. These positive effects were associated with the presence of fibroblast growth factor-2 and thrombospondin in the aphaeresis sample. Among the 15 patients, five pregnancies were achieved: 2 after embryo transfer and 3 by natural conception. In allogeneic stem cell transplant (SCT), the recovery of ovarian function ranges from 14 to 24%, and the interval from SCT to first spontaneous menstruation ranges from 21 to 87 months. Recovery rates as high as 84% have been reported among patients with favourable predictors.

Stem cells has also been considered for the regeneration of human endometrium disorder like Asherman syndrome and thin endometrium. Azizi e al<sup>7</sup> evidenced that the transplantation of different stem cells with a diverse source in the endometrial zone had effects on endometrium such as decrease of fibrotic area, an elevated number of glands, stimulated angiogenesis, the enhanced thickness of the endometrium, better formed tissue construction, protected gestation, and improved pregnancy rate. Though role of stem cells looks promising, but it has still not become standard treatment, it requires further larger trials to recommend it as safe effective option.

Current assisted reproductive technology has become more successful but unable to help couples who lack functional gametes, unless donor gametes are used. Most couples wish to have their own genetically related child. With the rapid development of stem cell technology, the possibility to derive artificial gametes from human pluripotent stem cells may provide new therapeutic strategies for infertile couples. Presently, evidence is limited, whether healthy offspring can be produced from the gametes derived from pluripotent stem cells remains unclear.

## References

1. Volarevic V, Bojic S, Nurkovic J, Volarevic A, Ljubic B, Arsenijevic N et al. Stem cells as new agents for the treatment of infertility: Current and future perspectives and challenges. *Biomed Res Int* 2014;2014:507234.
2. Volarevic V, Ljubic B, Stojkovic P, Lukic A, Arsenijevic N, Stojkovic M. Human stem cell research and regenerative medicine-present and future. *Br Med Bull* 2011;99:155-68.
3. Hayashi K, Ohta H, Kurimoto K, Aramaki S, Saitou M. Reconstitution of the mouse germ cell specification pathway in culture by pluripotent stem cells. *Cell* 2011;146:519-32
4. White YA, Woods DC, Takai Y, Ishihara O, Seki H, Tilly JL. Oocyte formation by mitotically active germ cells purified from ovaries of reproductive-age women. *Nat Med* 2012;18:413-21.
5. Herraiz, S., Romeu, M., Buigues, A., Martínez, S., Díaz-García, C., Gómez-Seguí, I. et al. Autologous stem cell ovarian transplantation to increase reproductive potential in poor responder patients. *Fertil Steril*. 2018; 110: 173–182.e1
6. Herraiz, S., Buigues, B., Díaz-García, C., Romeu, M., Martínez, S., Gómez-Seguí, I. et al. Fertility rescue and ovarian follicle growth promotion by bone marrow stem cells. *Fertil Steril*. 2018; 109: 908–918
7. Azizi R, Aghebati-Maleki L, Nouri M, Marofi F, Negargar S, Yousefi M. Stem cell therapy in Asherman syndrome and thin endometrium: Stem cell- based therapy. *Biomed Pharmacother*. 2018 Jun;102:333-343. doi: 10.1016/j.biopha.2018.03.091. Epub 2018 Mar 22. Review. PubMed PMID: 29571018.

## References

1. Saleh RA, Agarwal A, et al increased sperm nuclear damage in normozoospermic infertile men fertile steril 2005;(2)313-8.
2. Agarwal A, Allamaneni SS; Sperm DNA Damage Assessment a test whose time has come. *Fertil Steril* 200517(3);255-60,
3. Cho CL Novel insights into the pathophysiology of varicocele and its association with reactive oxygen species and sperm DNA fragmentation *Asian Journal of Andrology* 2016 18, 186-93.
4. Benchaib M, Lornage J, Mazoyer C et al Sperm DNA fragmentation as a prognostic indicator of assisted reproductive Technology outcome. *Fertil Steril* 2007;87(1)93-100.
5. Collins JA, Barnhart KT, Schegel PN. Do Sperm Integrity test predicts pregnancy with In Vitro Fertilization *Fertil Steril* 2008;89,(8) 23-31.
6. DP Evenson LK, Jost D, Marshall Utility of the sperm chromatin structure assay as a diagnostic and prognostic tool in the human fertility clinic. *Hum Reprod* 1999;14:1039-49.
7. Collins JA, Barnhart KT, Schlegel PN, authors. Do sperm DNA integrity tests predict pregnancy with in vitro fertilization? *Fertil Steril*. 2008;89(4):823–31.
8. J Gosálvez C, López-Fernández JL, Fernández Unpacking the mysteries of sperm DNA fragmentation: Ten frequently asked questions. *Journal of Reproductive Biotechnology and Fertility* 2015;4:1-16.
9. D Sakkas O, Moffatt GC, Manicardi Nature of DNA damage in ejaculated human spermatozoa and the possible involvement of apoptosis. *Biol Reprod* 2002;66:1061-7.
10. MB Shamsi R, Kumar Dada. Evaluation of nuclear DNA damage in human spermatozoa in men opting for assisted reproduction. *Indian J Med Res* 2008;127:115-23. 18403788.
11. Gosálvez C, López-Fernández JL, Fernández Unpacking the mysteries of sperm DNA fragmentation: Ten frequently asked questions. *Journal of Reproductive Biotechnology and Fertility* 2015;4:1-16.
12. Arow J, Sigman M, Kolettis PN, et al. The optimal evaluation of the infertile male: best practice statement reviewed and validity confirmed 2011. Available online: <https://www.auanet.org/education/guidelines/male-infertility-d.cfm>
13. Jungwirth A, Diemer T, Dohle GR, et al. Guidelines on male infertility. Available online: <https://uroweb.org/guideline/male-infertility>.

## Blast for all - Should it be the norm?



**Dr. Archana Kumari**

**Founder Secretary  
IFS Jharkhand Chapter  
Associate Professor  
Dept. of OBGYN, RIMS, Ranchi**

A blastocyst transfer involves transfer of embryo at later stage of development at blastocyst stage. It is usually done on 5th day after follicular aspiration. The stages of development are: pronuclear stage on day 1 (fertilized egg), 2-4 cell stage on day 2, 8 cell stage on day 3, the morular stage on 4th day, and the blastocyst stage on 5th day. Recent advances in cell culture media have led to shift in IVF practice from early stage cleavage embryo transfer to blastocyst stage transfer with many advantages.

### Advantages of blastocyst transfer

- 1. More Physiological:** Synchronization of embryo transfer with the stage of endometrium as in natural conception is more physiological. During natural pregnancy, it takes around 5 days after fertilization for the embryo to reach the uterine cavity.
- 2. Selection of best quality embryo.** This is based on the fact that best embryo will self select themselves and poor quality ones will fail to reach the blastocyst stage.
- 3. Improved pregnancy & implantation rates:** Several studies suggest higher implantation rate of blastocyst stage as compared to early cleavage stage transfer on day 3. Recent Cochrane review of 12 RCT that reported live birth rate per couple favoring blastocysts culture (Day 2 to 3: 31% Day 5 to 6 : 38.8%). This means that for clinics that use early cleavage stage cycles, the rate of live births would increase from 32% to 42% if clinics used blastocyst transfer.<sup>1</sup>
- 4. Decreased risk of multiple pregnancy:** The high implantation rates of blastocyst transfer accompanied by the methods used for selecting the best embryo for transfer makes it possible to achieve a respectable ongoing pregnancy rate after the transfer of a single embryo with no dizygotic twinning.<sup>2</sup>
- 5. Pre-implantation Genetic Diagnosis (PGD):** Blastocyst culture facilitates PGD of biopsied blastomeres as well as trophoctoderm. Following the biopsy of the cleavage stage embryo on day 3 post insemination, continued culture up to day 5 gives time for genetic analysis as well as assessment. Culture of embryos till trophoctoderm makes it possible to biopsy the trophoctoderm for PGD. Trophoctoderm biopsy has the advantage over cleavage stage in that more than 2 cells can be removed improving the accuracy of analysis.<sup>[3]</sup> Furthermore, biopsy of the trophoctoderm reduces the incidence of mosaicism which is nearly just about 10% as compared with nearly 43% with cleavage stage embryos.<sup>4</sup> Nevertheless, technically, biopsy of trophoctoderm is more difficult than the cleavage embryo.
- 6. Derivation of Human Embryonic Stem (hES) cell:** One of the most vital applications of blastocyst culture is the derivation of hES cell lines from the ICM of the blastocyst.

### Limitations of blastocyst transfer

- 1. Poor Rate of Blastocyst Development in Vitro and Cancellation of Transfer:** One of the major limitation of blastocyst transfer is that not all cleavage stage embryos develop into blastocyst. Some patients may not have any blastocysts available for transfer on day 5 despite having cleavage stage embryo on day 3 leading to cancellation of transfer. The question that would then remain unanswered is that would that woman have conceived with a day 3 transfer?
- 2. Monozygotic Twinning:** Da costa et al. (2001) reported that 3% of the pregnancies following blastocyst transfer were complicated by monozygotic twinning as compared with 0.7% after 4-8. cell stage embryo transfer<sup>5</sup> while 0.42% of natural pregnancies result in monozygotic twinning (Bulmer et al, 1970). In a recent retrospective analysis of 14,956 clinical pregnancies from single blastocyst transfer indicated a 1% monozygotic twinning with an odds ratio of 2.0 irrespective of zona drilling. ICSI or type of stimulation used.<sup>6</sup>
- 3. Failure of Blastocyst Development and No Embryos Available for Transfer:** Large offspring Syndrome: In vitro culture of embryos for 5-7 days in vitro has been associated with large offspring syndrome in certain animal species. This has been attributed to the suboptimal embryo culture conditions. This syndrome manifests as abnormal growth and development at fetal, neonatal and later stages of life.<sup>7</sup> It has been shown that extended culture of embryos to the blastocyst stage can compromise many aspects of development including metabolism, differentiation, gene expression, imprinting and subsequent fetal development after embryo transfer in several mammalian species.

Blastocyst culture, although a little time consuming with its inherent limitations, is an important step ahead in the field of ARTs. However, before it can be routinely applied in an ART laboratory, it is essential that the laboratory first has the requisite infrastructure, maintenance and skills. Although, the pregnancy rate per blastocyst transfer is higher than pregnancy rates following cleavage stage transfer but if one were to look at the cumulative pregnancy rate per cycle started or per patient, then the result are not that dramatic. Because, the number of embryos that grow to blastocyst and are available for transfer or cryopreservation are much lesser.

One should use extended culture to blastocyst only when there are multiple cleavage stage embryos available for transfer so that those that do not develop to the blastocyst get deselected. As of now, its routine blast transfer for all does not seem justified. Further studies are still required to have an optimal understanding of the metabolism of embryos and nutritional requirements. In the luminal secretions, the embryo is exposed to a variety of growth factors and cytokines while these are not routinely added to culture media. Growth factors are known to have pleiotropic effects on embryo development including blastocyst formation and hatching and it needs to be seen whether the addition of these would further improve the development of blastocysts in vitro. Development of culture media closer to physiological environment might lead to blast for all.

### References

1. Glujovsky D, Blake D, Farquhar C et al. Cleavage stage versus blastocyst stage embryo transfer in assisted reproductive technology. Cochrane Database Syst Rev. 2012(7) : CD002118
2. Gerris JMR. Single embryo transfer and IVF/ICSI outcome: a balanced appraisal. Hum Reprod Update 2005; 11:105-21
3. Kuo HC, Ogive CM, Handyside AH. Chromosomal mosaicism in cleavage stage human embryos and the accuracy of single-cell genetic analysis. J Assist Reprod Genet. 1998;15:276-80
4. Evikov S, Verlinsky Y. Mosaicism in the inner cell mass of human blastocysts. Hum Reprod. 1998;13: 3151-5
5. Da Costa ALE, Abdelmassih S, de Olivaria FG, et al. Monozygotic twins and transfer at the blastocyst stage after ICSI. Hum Reprod. 2001;16:333-6
6. Kawachia S, Bodri D, Shimada N, et al. Blastocyst Transfer is associated with elevated incidence of monozygotic twinning after single embryo transfer. Fertil Steril 2011;95:2140-2
7. McEvoy TG, Sinclair KD, Young LE, et al. Large Offspring syndrome and other consequences of ruminant embryo culture in vitro: relevance to blastocyst culture in human ART. Hum Fertil (Camb) 2000;3:238-46

## Non-invasive PGS – Is it Accurate?



**Dr. Divyashree P S**

**MS, DNB (OBG), FNB (Reprod Med) PGDMLE  
Secretary, IFS Karnataka Chapter  
Clinical Director Milann Jayanagar**

**Dr. Shravya Thalapureddy**

Forty years since the first IVF baby, the development of an accurate method to assess embryo competency, thereby allowing the transfer of a single embryo and leading to improved live birth rates, remains one of the main challenges. Around 20–80% of human embryos are estimated to be chromosomally aneuploid<sup>1</sup>. In the recent years, advent of trophoctoderm biopsy and preimplantation genetic testing (PGT), supported by rapid advances in molecular based screening technologies have provided significant improvement in embryo selection by comprehensive chromosome screening. Clinical applications of PGT may be imperative, but it is not without shortcomings. Two challenges remain – one, technical aspects like specialized equipment, trained operators, suitability of embryos and concern regarding possible damage to embryo from the biopsy. Another major concern is regarding the embryo mosaicism<sup>2</sup>. Taken together, interest in non-invasive alternatives seems very timely and reasonable.

The field of prenatal aneuploidy testing was revolutionized by the isolation of cell-free DNA of fetal origin in the peripheral blood of pregnant women (Lo et al., 1997). More recently, human embryos were demonstrated to release DNA fragments by diffusion into their environment – inwards into the blastocoel and outwards through zona pellucida into the culture media (Assou et al., 2014)<sup>3</sup>. These cell-free DNA are short fragments of double-stranded molecules released following physiological cell apoptosis and pathological necrosis<sup>4</sup>. Identification and amplification of these molecules in combination with improved genetic sequencing technology were key elements in the breakthrough concept of non-invasive pre-implantation genetic testing (NI-PGT).

### Blastocoel Fluid (BF) Analysis

Palini et al. reported for the first time the identification of cell-free DNA by real-time PCR in 90% of expanded blastocysts prior to vitrification<sup>5</sup>. The researchers demonstrated amplification rate of 95% for the testis-specific protein Y-linked 1 (TSPY1) multicopy gene on the Y chromosome, for the identification of male embryos. But a study by Tobler et al in 2015, showed high amplification failure and diagnostic non-concordance rates, thereby calling for more technical improvements<sup>6</sup>. But the research by other investigators was more supportive, especially underlining the role BF cell-free DNA analysis in screening monogenic disorders.

### Limitations and future research

Technical reliability of the procedure and appropriate sample volume required for successful DNA isolation and amplification have not yet been defined. Blastocentesis or BF aspiration is not a non-invasive method but is rather a less invasive method than PGT for obtaining embryo-derived DNA. But, in view of the practice of collapsing artificially expanded blastocysts before vitrification

gaining popularity to improve ART success rates, BF analysis is being studied extensively<sup>7</sup>. However, it is not known whether depletion of the BF would alter the cell-to-cell communication within the developing embryo and how it would impact the embryo competency and its interaction with the environment.

#### Spent Blastocyst culture Media (SBM) analysis

Cell-free DNA from blastocysts culture media can be isolated, amplified and analysed by 24 chromosomes comprehensive screening NGS. This represents a potential source of DNA for non-invasive detection of chromosome abnormalities. Assou et al. in a proof-of-concept study using quantitative PCR (qPCR), confirmed the presence of cf DNA in the media of Day-5/6 embryos, measuring up to 27 ng/ml DNA per sample. They were successful in amplifying the multicopy gene TSPY1 on the Y chromosome enabling identification of embryos based on gender<sup>3</sup>. These findings heralded the way for a newer and non-invasive approach to the pre-implantation diagnosis of sex-linked diseases. Soon after, numerous reports from different research groups followed. Multiple studies have compared cf DNA from SBM with the standard PGT-A from trophoectoderm biopsies. Amplification rates of cell-free DNA from spent culture media in various studies ranged between 80 – 100%, however, concordance rates have been variable. This may be attributed to discrepancies in methodologies applied in – Embryo culture – drop volume, time in culture, single vs sequential culture; Blastocyst manipulation – assisted hatching, vitrification and associated blastocentesis; DNA analysis – different amplification and detection methods and finally different criteria being used to define concordance rates. A recent study in 2019 by Rubio et al, using an optimised protocol, accounting for the above-mentioned discrepancies, found high concordance rates (78.7 – 84%) between TE biopsies and SBM analysis. The investigators also found threefold greater implantation rates for euploid TE/ euploid SBM embryos than for euploid TE/aneuploid SBM embryos (52.9% vs. 16.7%). And no clinical miscarriages were reported in euploid TE/ euploid SBM embryos group<sup>8</sup>.

#### Limitations and future research

##### Sample collection

It is still unclear whether the choice of a sequential or single culture medium system potentially influences the yield of cell-free DNA. Feichtinger et al. (2017) proposed culturing embryos in a single continuous medium system until blastocyst formation in order to improve the cumulative yield of cell-free DNA<sup>9</sup>. However, higher testing accuracy was demonstrated by Lane et al. (2017) when the culture medium has been in contact with embryos from Day 4 to 5 compared to Day 3 to 5<sup>10</sup>. This observation may be explained by the increase in the embryonic-to-maternal DNA ratio, which occurs with the exponential rise in the embryonic cell number at blastulation. In a study by Rubio et al. (2019), higher concordance rates were noted for day 6/7 samples compared to day 5 samples<sup>8</sup>. Further studies are required to identify ideal sampling times in relation to the stage of embryo development that are associated with better DNA detection, amplification and concordance rates.

##### Controls and contamination<sup>11</sup>

Control samples were obtained from embryo free culture droplets, but human DNA is often noted in embryo free droplets of protein supplemented culture media. Further, DNA from residual cumulus cells could lead to maternal DNA contamination leading to decreased sensitivity and false negatives. Some studies have shown sex discordance between SBM and TE biopsies – male SBM identification from TE diagnosed female embryo – this could be attributed to external DNA contamination from plasticware, media or manipulation during IVF. Also, presence of residual polar bodies can lead to discrepancies in sex or complementary aneuploidies.

##### Origin of cell-free DNA and significance:

The biological significance of fragmented cell-free DNA is yet unknown. Some studies have suggested a role

in cell-to-cell communication within the developing embryo and its surroundings (Hammond et al., 2017)<sup>12</sup>. Some researchers believe them to be generated from apoptosis during normal embryo development or should mosaic embryos shed their excluded cells into the blastocoel cavity/ culture media during development as part of a natural repair mechanism then this could then result in a potential mismatch between the ploidy profile of the cell-free DNA and its corresponding embryo. Research remains inconclusive regarding the origin of cf DNA – is it from ICM / TE? Questions also remain if the obtained DNA material is truly indicative of the genetic constitution of the embryo as a whole.

Over the past few years, with the rapid emergence of efficient molecular platforms for genetic testing, utilisation of PGT has been increasing in ART. Trophoectoderm biopsies are a definite representative of meiotic errors but for mitotic errors and mosaicism, embryonic cell-free DNA might open new avenues for insight and understanding. While liquid biopsy (Cf DNA) seems like an attractive option especially considering that it avoids invasiveness, potential embryo harm, minimises lab and personnel expenses and extends feasibility and accessibility to wider population, several challenges must be addressed before accepting NI-PGT as a reliable method of pre-implantation genetic testing. Hurdles include questions regarding the completeness of representation of the embryonic genome by cell-free DNA present in the BF and spent culture media. Further techniques are required to minimise external DNA contamination and optimise DNA isolation and amplification methods. Molecular testing and analytical platforms for cell-free DNA also need rigorous validation before clinical applications. Well-designed studies are required to improve this technology for potential translation into standard genetic testing and better pregnancy outcomes.

#### References

1. Franiak JM, Forman EJ, Hong KH, Werner MD, Upham KM, Treff NR, et al. Aneuploidy across individual chromosomes at the embryonic level in trophoectoderm biopsies: changes with patient age and chromosome structure. *J Assist Reprod Genet* 2014; 31:1501–9.
2. Vera-Rodriguez M, Rubio C. Assessing the true incidence of mosaicism in preimplantation embryos. *Fertil Steril* 2017; 107:1107–12.
3. Assou S, Ait-Ahmed O, El Messaoudi S, Thierry AR, Hamamah S. Non-invasive pre-implantation genetic diagnosis of X-linked disorders. *Med Hypotheses*. 2014 Oct;83(4):506–8.
4. Hardy K, Handyside AH, Winston RM. The human blastocyst: cell number, death and allocation during late preimplantation development in vitro. *Development*, 1989, vol. 107 (pg. 597–604)
5. Palini S, Galluzzi L, De Stefani S, Bianchi M, Wells D, Magnani M, Bulletti C. Genomic DNA in human blastocoel fluid. *Reprod Biomed Online*. 2013 Jun;26(6):603–10.
6. Tobler K, Zhao Y, Ross R, Benner A, Xu X, Du L, Broman K, Thrift K, Brezina P, Kearns W. Blastocoel fluid from differentiated blastocysts harbors embryonic genomic material capable of a whole-genome deoxyribonucleic acid amplification and comprehensive chromosome microarray analysis. *Fertil Steril* 2015; 104:418–425.
7. Kovačić B, Taborin M, Vlaisavljević V. Artificial blastocoel collapse of human blastocysts before vitrification and its effect on re-expansion after warming – a prospective observational study using time-lapse microscopy. *Reprod Biomed Online*. 2018 Feb;36(2):121–129.
8. Rubio C, Rienzi L, Navarro-Sánchez L, Cimadomo D, García-Pascual CM, Albricci L, Soscia D, Valbuena D, Capalbo A, Ubaldi F, Simón C. Embryonic cell-free DNA versus trophoectoderm biopsy for aneuploidy testing: concordance rate and clinical implications. *Fertil Steril*. 2019 Sep;112(3):510–519.
9. Feichtinger M, Vaccari E, Carli L, Wallner E, Mädel U, Figl K, Palini S, Feichtinger W. Non-invasive preimplantation genetic screening using array comparative genomic hybridization on spent culture media: a proof-of-concept pilot study. *Reprod Biomed Online*. 2017 Jun;34(6):583–589.
10. Lane M, Zander-Fox D, Hamilton H, Jasper MJ, Hodgson BL, Fraser M, Bell F. Ability to detect aneuploidy from cell free DNA collected from media is dependent on the stage of development of the embryo. *Fertil Steril* 2017;3: e61
11. Vera-Rodriguez M, Diez-Juan A, Jimenez-Almazan J, Martinez S, Navarro R, Peinado V, Mercader A, Meseguer M, Blesa D, Moreno I, Valbuena D, Rubio C, Simon C. Origin and composition of cell-free DNA in spent medium from human embryo culture during preimplantation development. *Hum Reprod*. 2018 Apr 1;33(4):745–756.
12. Hammond ER, McGillivray BC, Wicker SM, Peek JC, Shelling AN, Stone P, Chamley LW, Cree LM. Characterizing nuclear and mitochondrial DNA in spent embryo culture media: genetic contamination identified. *Fertil Steril* 2017;1:220–228.e5

## Dual Trigger- Is it beneficial?



**Dr. Anupama Bahadur**

Secretary, IFS Uttarakhand Chapter  
Additional Professor  
AIIM, Rishikesh Uttarakhand



**Dr Rajlaxmi Mundhra**

Assistant Professor  
Department of Obstetrics & Gynaecology  
All India Institute of Medical Sciences, Rishikesh  
Uttarakhand, India

Poor Responder to ovarian stimulation remains one of the most challenging aspects in the field of infertility management. Stimulating ovulation using exogenous human chorionic gonadotrophin remains the standard trigger in women undergoing ovulation induction but there remains a risk of ovarian hyperstimulation syndrome and premature luteinizing hormone surge with its use.

#### Physiology behind the use of HCG and GnRH

During the follicular phase of the menstrual cycle, there is pulsatile release of Gonadotrophin hormone (GnRH) which then results in release of Follicular stimulating hormone (FSH) and luteinising hormone (LH) in pulsatile pattern thereby regulating the follicular growth. Rapidly rising oestradiol from the dominant follicle along with a small rise of progesterone leads to gonadotrophin surge during midcycle. Increased LH surge ultimately results in ovulation. LH exposure results in resumption of meiosis with maturation of the oocyte from the immature “metaphase I” phase to the mature “metaphase II” phase of development. A critical step in current IVF protocol is a well-planned LH exposure thereby enabling the efficacious retrieval of mature oocytes.

Human chorionic gonadotrophin being structurally similar to LH and with a longer half life has been the most widely used trigger to stimulate ovulation as well as for pick-up of mature oocytes from stimulated ovaries in cases of in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) cycles. Nakano et al. showed that LH surge could be induced using a bolus of GnRH agonist (GnRHa) when given intravenously<sup>1</sup>. The endogenous surge of LH and FSH via use of GnRHa closely resembles the natural midcycle surge. This midcycle FSH surge is important due to the fact that it up regulates LH receptor site formations in granulosa cells. FSH also promotes resumption of oocyte meiosis, expansion of cumulus cells - critical steps in the oocyte maturation process. Hence, one of the anticipated benefits of GnRH-a trigger is retrieval of increased number of mature oocytes. Another added advantage of GnRH trigger is that it reduces the risk of ovarian hyperstimulation syndrome. Researchers have shown a higher abortion rate with reduced implantation, ongoing pregnancy and live birth rates in GnRH-agonist trigger as compared to standard luteal phase support and hCG trigger. Difficulty with GnRH agonist trigger when used alone is that it reduces early corpora lutea thereby

requiring luteal phase support. Several methods have been proposed to eliminate this risk of luteal insufficiency with GnRH a trigger. One such method is Dual trigger.

#### Dual trigger

It involves combining GnRH $\alpha$  with a low dose of hCG to trigger oocyte maturation. It has been seen that use of hCG simultaneously with GnRH $\alpha$  trigger negates its luteolytic effects. It was first used by Shapiro et al. in GnRH antagonist cycles for the purpose of Ovarian Hyperstimulation syndrome (OHSS) prevention.<sup>2</sup> Various studies have been conducted in the past comparing the efficacy of hCG with GnRH $\alpha$  as ovulation trigger for IVF with varying results. Griffin et al conducted a retrospective cohort study to compare live birth rates with dual trigger versus GnRH $\alpha$  alone and found that dual-trigger group had a significantly higher live birth rate (52.9% vs. 30.9%), implantation rate (41.9% vs. 22.1%), and clinical pregnancy rate (58.8% vs. 36.8%) as compared with the GnRH $\alpha$  trigger group.<sup>3</sup> Haas et al. suggested that co-administration of GnRH-agonist and hCG for final oocyte maturation, 40 and 34 hours prior to ovum pick up, respectively (double trigger) yields significantly higher number of oocytes retrieved as compared to their previous hCG only trigger group in patients with low/poor oocyte yield.<sup>4</sup>

In another retrospective cohort study conducted by Zhou et al, women with normal ovarian reserve were grouped by whether oocyte maturation was triggered with GnRH agonist plus 5000-10 000 IU of hCG (dual trigger) or hCG alone. Though the live birth rate did not differ significantly between the two groups ( $P=0.083$ ), the mean number of two-pronuclear embryos ( $P=0.004$ ), the mean number of embryos available ( $P=0.001$ ), and the mean number of high-quality embryos ( $P=0.011$ ) was higher in the dual trigger group.<sup>5</sup>

Ding N et al conducted a meta-analysis involving 4 RCT with 527 patients, to investigate the efficacy of the dual trigger in comparison with hCG alone. The results of this meta-analysis showed that the dual trigger group had a significantly higher pregnancy rate (relative risk [RR], 1.55; 95% confidence interval [CI], 1.17-2.06) as compared to the hCG-only trigger group but no significant differences were noted in the number of retrieved oocytes, number of mature oocytes retrieved number of fertilized oocytes, number of good-quality embryos, or implantation rate between the two groups.<sup>6</sup> In a retrospective cohort analysis using 427 GnRH antagonistic cycles, Lin and colleagues investigated the role of dual trigger in improving live birth rates in women with diminished ovarian reserve. The control group ( $n=130$ ) received standard dose of 6500 IU of recombinant hCG for trigger, and the study group ( $n=297$ ) had 0.2 mg of triptorelin along with 6500 IU of recombinant hCG for trigger. They found significant improvement in mature oocytes, implantation rate, clinical pregnancy rate and live birth rate in their dual trigger group.<sup>7</sup>

In summary, though dual trigger seems to be a promising trigger for oocyte maturation yielding the number of retrieved oocytes and improving reproductive outcomes, further randomised controlled trials need to be undertaken to prove its efficacy.

#### References

1. Nakano R, Mizuno T, Kotsuji F, Katayama K, Wshio M, Tojo S. "Triggering" of ovulation after infusion of synthetic luteinizing hormone releasing factor (LRF) Acta Obstet Gynecol Scand. 1973;52:269-72.
2. Shapiro BS, Daneshmand ST, Garner FC, Aguirre M, Thomas S. Gonadotropin-releasing hormone agonist combined with a reduced dose of human chorionic gonadotropin for final oocyte maturation in fresh autologous cycles of in vitro fertilization. Fertil Steril 2008; 90: 231-3.
3. Griffin D, Benadiva C, Kummer N, Budinetz T et al. Dual trigger of oocyte maturation with gonadotropin-releasing hormone agonist and low-dose human chorionic gonadotropin to optimize live birth rates in high responders. Fertil Steril. 2012 Jun;97(6):1316-20.
4. Haas J, Zilberberg E, Dar S, Kedem A, Machtinger R, Orvieto R. Co-administration of GnRH-agonist and hCG for final oocyte maturation (double trigger) in patients with low number of oocytes retrieved per number of preovulatory follicles--a preliminary report. J Ovarian Res. 2014;2(7):77.
5. Zhou X, Guo P, Chen X, Ye D, Liu Y, Chen S. Comparison of dual trigger with combination GnRH agonist and hCG versus hCG alone trigger of oocyte maturation for normal ovarian responders. Int J Gynaecol Obstet. 2018 Jun;141(3):327-331.
6. Ding N, Liu X, Jian Q, Liang Z, Wang F. Dual trigger of final oocyte maturation with a combination of GnRH agonist and hCG versus a hCG alone trigger in GnRH antagonist cycle for in vitro fertilization: A Systematic Review and Meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2017 Nov;218:92-98.
7. Lin MH, Wu FS, Hwu YM, Lee RK, Li RS, Li SH. Dual trigger with gonadotropin releasing hormone agonist and human chorionic gonadotropin significantly improves live birth rate for women with diminished ovarian reserve. Reprod Biol Endocrinol. 2019 Jan 4;17(1):7

## Social egg freezing- Should it be propagated as the future reproductive technique?



Dr Shilpi Sud

Secretary, Vidharbha Chapter-IFS  
Consultant Gynaecologist, IVF Specialist  
Laparoscopic surgeon  
Safal Hospital & Diva Fertility Centre, Nagpur

Initiated by the success of contraception in the 1960s and accelerated by the subsequent rise in female employment and tertiary academic opportunity, the age of first-time mothers continues to rise. While this has enhanced female reproductive autonomy, advanced reproductive age coincides with a decrease in oocyte quantity and quality, which manifests clinically with reduced fecundity and an exponential age-related increased risk of miscarriage. It is therefore unsurprising that the trend of postponing childbearing has coincided with increased rates of involuntary childlessness.

The development of oocyte vitrification techniques has significantly improved oocyte survival (81–89% versus 46–67%) and clinical pregnancy rates (38–64% versus 13–29%), when compared with traditional freeze/thaw techniques. This improvement is exemplified by recent data demonstrating there is now no difference in pregnancy, miscarriage or live birth rates between autologous fresh and cryopreserved oocyte cycles. This has created the opportunity for women to freeze their eggs electively prior to the inevitable physiological decline, nullifying further age-related oocyte deterioration and allowing the preservation of their reproductive potential.

Although delaying childbearing to physiological extremes for social reasons is a reproductive gamble, some women have no alternative, e.g, single women approaching the end of their reproductive years. While follow-up data currently remain scarce, the most comprehensive study included 1382 women who underwent social egg freezing (SEF), 120 (8.7%) of whom returned to use their eggs after a mean duration of 2.2 years. The oocyte survival rate was 85%, with subsequent clinical and ongoing pregnancy rates of 39 and 27%, respectively. Despite the short follow up, the fact that 45 of the 95 women who were single at the time of cryopreservation had a partner when they returned, truly epitomises the potential of SEF. Although the best chance of successful live birth is following oocyte cryopreservation prior to the age of 34, the most cost-effective time is before 38 years, where it has been shown to reduce the costs of obtaining a live birth. We therefore argue that single women approaching their late thirties, who desire biologically related children in the future, should consider SEF. Not only does it extend the window of opportunity to find a partner but it also retains the possibility of using a sperm donor as a last resort.

Oocyte freezing consists of two separate steps that are clearly distinct in time: first, ovarian stimulation, oocyte retrieval, cryopreservation and storage. At the time of the first step, women who request social freezing are healthy persons who ask for a procedure that results in stored oocytes that may or may not be used, depending on the further course of their lives. From a medical point of view, we have to consider the balance between the risks of the procedures (ovarian hyper stimulation, oocyte pick up and pregnancy) and the benefits, for the mother and the child. In bioethical terms the balance between the respect of the woman autonomy (including the reproductive autonomy) and the beneficence both for the mother and the child.

Extensive fertility and preconception counseling are essential, including the risk of age-related obstetrical complications and the possibility of future unsuccessful treatment. It is also important that good clinical practice for IVF treatment continues to be adopted to ensure

women achieve pregnancy in their natural reproductive years, to avoid potential negative social aspects and economic implications of raising children near retirement age. This is further safeguarded by HFEA regulations that only allow the storage of eggs for up to 10 years.

But there are points against SEF. First, the majority of women are taking measures to preserve their fertility too late, as a 'last ditch' effort, instead of a planned and informed choice in their early to mid-thirties.

Second, the majority of published studies on egg freezing efficacy are from experienced centres with large egg freezing numbers, and these data cannot necessarily be extrapolated to smaller clinics that have only recently started oocyte vitrification.

Third, egg freezing is indirectly encouraging women to have children at an advanced maternal age, which carries with it significantly increased risk of medical complications in pregnancy. This is especially relevant to women freezing their eggs when they are already in their late thirties.

Finally, social egg freezing is not government funded. Because of lower success rates per egg, women in their late thirties would need approximately 30 eggs to have a good chance of achieving pregnancy. They would therefore require on average three cycles of stimulation and the cost for the same. This does not include the annual storage fee or the cost of the fertility treatment she would need in the future to use her frozen eggs.

Success rates for egg freezing have improved significantly in recent years so offer an opportunity for women to freeze their eggs for social reasons if they're not ready to have children yet. However, it must be stressed that egg freezing does not guarantee a baby in the future.

"While women should be supported in their choices, they must be informed about the relatively low success rates, high costs and side effects associated with egg freezing and IVF treatment. If a woman does decide to freeze her eggs for social reasons, she should have counselling with a reproductive specialist and choose a clinic that has plenty of experience. The clinic should provide a realistic idea of potential success related to her age. Evidence suggests that the best time to freeze eggs is in a woman's early twenties and certainly under the age of 37 years old. It is extremely important to provide accurate and balanced information about fertility and how it changes with increasing age. Relationships and sex education, particularly for young people, must include information to enable women and their partners to make informed decisions about when to start a family to ensure the healthiest outcomes.

Today, Israel is one of the first countries in which egg freezing for non-medical reasons has been regulated and authorised for public support, with the justification of "permitting egg freezing to prevent both disease- and age-related fertility decline ... so women are then free to exercise their reproductive autonomy and decide for themselves whether or not the technology is beneficial to them". This choice is based on conviction that social egg freezing is grounded in liberal ideology promoting the individual autonomy exercised through informed consent, supporting that a relational approach to autonomy may be a more suitable model for considering women's choices about egg freezing, also for non-medical purposes

In conclusion, doctors should continue to perform egg freezing for those single women in their late thirties for whom the high costs and low success are acceptable. However, the future focus should be on providing accurate information by educating women from an early age. This would allow women to plan their reproductive behaviour more realistically, present to fertility clinics at a younger age, thus reducing the chance of involuntary childlessness.

#### Reference

1. Crawford et al. Cryopreserved oocyte versus fresh oocyte assisted reproductive technology cycles Fertil Steril 2017;107:110–8.
2. Smith et al. Fertil Steril Prospective randomized comparison of human oocyte cryopreservation with slow-rate freezing or vitrification. 2010; 94:2088–95.
3. Schiewe MC, Nugent N, Zozula S, Stachecki JJ, Anderson RE. Donor oocyte cryopreservation: A randomized clinical trial comparing microsecure vitrification (mS VTF) to choline-enriched Cj3 slow-freezing (SF). Fertil Steril 2010;94(4, Supplement):S117-8.
4. Cobo A, Garcia-Velasco JA, Coello A, Domingo J, Pellicer A, Remohi J. Oocyte vitrification as an efficient option for elective fertility preservation. Fertil Steril. 2016 Mar;105(3):755-764.e8.
5. Devine K, Mumford SL, Goldman KN, Hodes-Wertz B, Druckenmiller S, Propst AM, Noyes N. Baby budgeting: oocyte cryopreservation in women delaying reproduction can reduce cost per live birth. Fertil Steril. 2015; 103: 1446–1453.
6. Hvidman HW, Petersen KB, Larsen EC, et al. Individual fertility assessment and pro-fertility counselling: should this be offered to women and men of reproductive age? Hum Reprod 2015; 30:9-15.
7. Shkedi-Rafid S, Hashilioni-Dolev Y. Egg freezing for nonmedical uses: the lack of a relational approach to autonomy in the new Israeli policy and in academic discussion. J Med Ethics 2012; 38:154-7



## IUI with unilateral tubal block- Is it justified?



**Dr Roya Rozati**

Secretary, Telangana Chapter - IFS  
Fertility Specialist, MHRT Hospital  
Hyderabad



**Dr Sweta Agarwal**

EB member, IFS Telangana  
Fertility Specialist  
Southern Gem Hospital, Hyderabad

- Controlled ovarian hyperstimulation (COH) and intrauterine insemination (IUI) through one patent tube and an attempt to achieve pregnancy
- In-vitro fertilization (IVF) to bypass the problem

In some cases, when an HSG, shows a proximal tubal block, there is actually no blockage. It is just a false reading in which the tube is actually open on subsequent testing. Most often tubal spasm, temporary mucous plugging and underfilling of the tube may cause a false-positive by HSG. The false-positive rate for proximal tubal obstruction may be as high as 15% in some studies. (4) Whenever HSG shows a proximal occlusion, most often confirmation by repeat HSG or laparoscopic chromopertubation should be considered. In one study, a second HSG showed a bilateral tubal patency in 60% of patients who were diagnosed with proximal tubal obstruction.<sup>5</sup>

### IUI with One Blocked Tube

When one fallopian tube is blocked, IUI can still give a good chance of conception, but the location of the blockage itself on the tube (proximal or distal) is likely to determine the chances of success. Patients with a proximal-only blockage do better than those with a distal-only block, and both have lesser chances of conception compared to patients who undergo IVF.

In a study published by Lin et al in 2012, where 133 patients with unilateral tubal occlusion underwent stimulated IUI and control group of 570 patients of unexplained infertility. The pregnancy rate was better in patients with proximal occlusion (25.0%) than in those with distal occlusion (13.9%) or unexplained infertility (16.5%). Therefore, stimulated IUI can be suggested as the initial treatment option in women with unilateral proximal tubal occlusion. They suggested that stimulated IUI can be offered as the first-line option in women with unilateral distal tubal occlusion because the pregnancy rate was similar to those with unexplained infertility.<sup>6</sup>

Farhi et al (2007) reported that the cumulative pregnancy rate in women with unilateral mid or distal tubal occlusion (19%) was lower than in those with unilateral proximal tubal occlusion (38.2%) and was significantly lower than in those with unexplained infertility (42.6%). Thus, in this study the authors concluded that in patients with unilateral proximal tubal occlusion stimulated IUI can be suggested as the initial treatment option but in patients with unilateral distal tubal occlusion on HSG should be referred for laparoscopic assessment or IVF.<sup>7</sup>

Yi et al (2012) study compared 17.3% pregnancy rate for the unilateral tubal occlusion group and 16.5% for the unexplained infertility group. The pregnancy rate was higher in patients with proximal occlusion (25.0%) compared with distal occlusion (13.9%) or unexplained infertility, but not statistically significant.<sup>8</sup> Thirty-seven infertile women (52 cycles) with unilateral tubal occlusion diagnosed by HSG and without other causes of infertility against one-hundred fourteen patients with unexplained infertility who served as a control group (182 cycles). There was about

Therefore, some studies have suggested that stimulated IUI can be the first-line option in women with unilateral proximal tubal occlusion whereas patients with unilateral distal tubal occlusion on HSG, should be referred for laparoscopic assessment or IVF. Other studies have proposed that stimulated IUI should be recommended as the first-line option in women with unilateral proximal or distal tubal occlusion.

In younger women with mild distal tubal occlusive disease, laparoscopic surgery can be considered as an alternative to IVF. In cases where disease is severe or pregnancy does not occur during the first postoperative year, IVF should be considered. For older women with any significant degree of distal tubal disease, IVF should be considered as first and best option because cycle fecundability after distal tubal surgery is low (1% to 2%), time is limited, and IVF is both more efficient and more effective.<sup>9</sup>

The risk of ectopic pregnancy in patients with one blocked tube who undergo IUI is slightly high compared to patients with bilateral patent tubes. This is because most conditions that affect the tubes, like endometriosis or pelvic inflammatory disease, tend to impact both tubes. A tube that is open, but has issues, is more likely to have difficulty passing the embryo into the uterus, so the embryo can become embedded in the tube resulting in an ectopic pregnancy. The patients should be counseled about this risk.

### Conclusion

- Unilateral proximal tubal occlusion, stimulated IUI can be offered as the first line option
- Whenever HSG shows a proximal occlusion, most often confirmation by repeat HSG or laparoscopic chromopertubation should be considered as it is just a false reading in which the tube is actually open on subsequent testing.
- The success of IUI in women with only one patent fallopian tube is comparable to those with both patent tubes.
- Pregnancy rates seems to be more affected by the woman's age and male factor infertility if present.
- For women with mid-distal tubal occlusion, stimulated IUI might not be a good choice because of a lower success rate, and either surgical intervention or IVF might be preferred
- These patients undergoing IUI should be counseled about a small but increased risk of ectopic pregnancy

### References

1. Miller JH, Weinberg RK, Canino NL, Klein NA, Soules MR. The pattern of infertility diagnoses in women of advanced reproductive age. *Am J Obstet Gynecol.* 1999; 181:952-957
2. Veenemans LM, van der Linden PJ. The value of Chlamydia trachomatis antibody testing in predicting tubal factor infertility. *Hum Reprod.* 2002; 17:695-698.
3. Balasch J. Investigation of the infertile couple: investigation of the infertile couple in the era of assisted reproductive technology: a time for reappraisal. *Hum Reprod.* 2000; 15:2251-2257
4. Burney RO. Infertility. In: Berek JS, Novak E, editors. *Berek & Novak's gynecology.* 14th ed. Philadelphia: Lippincott Williams & Wilkins; 2007. pp. 1185-1275.
5. Dessole S, Meloni GB, Capobianco G, Manzoni MA, Ambrosini G, Canalis GC. A second hysterosalpingography reduces the use of selective technique for treatment of a proximal tubal obstruction. *Fertil Steril.* 2000; 73:1037-1039.
6. Ming-Huei Lin, Yuh-Ming Hwu. Treatment of infertile women with unilateral tubal occlusion by intrauterine insemination and ovarian stimulation. *Taiwanese Journal of Obstetrics Gynecology* Volume 52, Issue 3, September 2013, Pages 360-364
7. Farhi J, Ben-Haroush A, Lande Y, Fisch B. Role of treatment with ovarian stimulation and intrauterine insemination in women with unilateral tubal occlusion diagnosed by hysterosalpingography. *Fertil Steril.* 2007; 88:396-400.
8. Gwang Yi, Byung Chul Jee, Chang Suk Suh and Seok Hyun Kim Stimulated intrauterine insemination in women with unilateral tubal occlusion. *Clin Exp Reprod Med* 2012;39(2):68-72

Tubal dysfunction with or without associated peritoneal pathology accounts for about 35% of all infertility and accounts for more than 50% of female infertility. It has become one of the most common causes of infertility and its incidence is increasing, mainly because of increasing incidence of sexually transmitted infection and resultant pelvic inflammatory disease.<sup>1,2</sup>

Risk factors for tubal disease<sup>2,3</sup>

Prior pelvic infection	Prior ectopic pregnancy
Intrauterine device use	Septic abortion
Appendiceal disease	Tubal surgery
Diethylstilbestrol exposure	

Hysterosalpingography (HSG) or laparoscopy are the two most common procedures used for evaluation of tubal patency. HSG is often the first line approach to check for tubal patency. Treatment of women presenting with infertility with bilateral patent or obstructed tubes detected on HSG is clear and direct. However, there is no standard management for patients with unilateral occlusion.

Proximal tubal occlusion prevents the sperm from reaching the ampullary portion of tube where fertilization happens. Whereas, distal tubal occlusions affect the ovum capture from the ovary. Proximal tubal occlusion is all or none phenomenon, whereas distal tubal occlusion exhibits a spectrum ranging from mild (fimbrial agglutination) to moderate (varying degree of fimbrial phimosis) to severe (complete obstruction).

The possible option for patients with unilateral tubal occlusion are:

- Repeat HSG
- Laparoscopy and hysteroscopy for evaluation and possible correction of tubal block
- Selective salpingography and fluoroscopic tubal catheterisation

## Single versus double Intrauterine Insemination



**Dr Papa Dasari**

Secretary-IFS Puducherry Chapter  
Senior Prof Dept of OBGY, JIPMER, Puducherry

Intrauterine insemination in modern era is a refined technique that originated from artificial insemination of semen in to the vagina by John hunter in 1770 (for managing childlessness of a couple whose husband had hypospadiasis) and later in to the uterine cavity by J Marion Sims in 1866 for a women with prolonged infertility with vaginal narrowing. Currently the indications have broadened that include most commonly unexplained infertility, mild male factor infertility, minimal or mild endometriosis, cervical factor and azospermia requiring donor semen. The procedure is undertaken with washed or frozen semen of husband or donar for women during natural cycle or with ovulation induction depending on the clinical situation after consent of the couple.

The aim is to make sperms available for fertilisation around the time of ovulation so as to improve success of achieving pregnancy. There are many factors that are responsible for success like total motile sperm count, vitality, semen collection and storage, semen preparation techniques, ovulation, tubal factors , uterine and endometrial factors. The key to success is the contact and cross talk of the sperm within 12 hours of ovulation as ovum lives only for 12 hours. Keeping this concept in mind to enhance the chances of conception intrauterine insemination is being undertaken twice around the time of ovulation. There are some studies which reported increase rate of success with double IUI and others did not show any such increase in success rate. As we need to practice a procedure only when benefits outweigh the risks or costs it is essential to examine or know the evidence whether one needs advice or undertake the procedure.

### Indications for Intrauterine Insemination in the era of IVF and ICSI

IUI is the first line of treatment for mild factor male infertility and unexplained infertility. The success of IUI is better than timed intercourse with ovulation induction. But it can be done for couples when the female partner age is less than 40 years without any tubal factor. If no conception after 4 cycles of IUI , IVF/ICSI to be offered.<sup>1</sup>

### Success of IUI

Success is optimum with normal semen parameters and is about 10-20% per cycle. The success increases up to 3 to 6 cycles and not beyond that. The success decreases when TMSC (total motile sperm count) is less than 10 million, sperm survival less than 70% and normal spermatozoa are less than 5%. Because of the low success rates IVF/ICSI is considered to be more cost effective but the results of randomized controlled trials using live birth rates revealed that IUI is the initial treatment for unexplained infertility when complications, efficacy and patient compliance was taken in to account.<sup>2</sup>

### Timing of IUI

IUI is performed usually by 34±2 hours after HCG trigger when the dominant follicle is ≥ 18 mm expecting ovulation to occur. Ovulation is not always confirmed by USG or LH kits in a clinical set up. Hence to achieve the objective of the presence of sperms around the time of ovulation a double IUI has been undertaken usually after 24 to 48 hours and or after confirming ovulation. A study undertaken on 1146 stimulated cycles concluded that a single IUI timed post -ovulation gives higher pregnancy rates in non male factor infertility and double IUI gives better pregnancy for male factor infertility.<sup>3</sup>

### Success rates more with Double IUI

Matilsky and colleagues in 1998 reported the probability of 2 times the cumulative pregnancy rate with double IUI over 15 cycles with frozen-thawed donor semen.<sup>4</sup> Liu W and colleagues in 2006 undertaken double IUI initially at 18 to 24 hours after hCG trigger and second insemination 36 to 48 hours later among 1270. Pregnancy rates were 19.87% when compared to 11.06% with single IUI undertaken 34 hours after trigger.<sup>5</sup> Randall and Gant in 2008 reported statistically significantly high success rates with double IUI when compared to single IUI 19.5% vs 12.9% in women with Ovarian dysfunction and 17.5% vs 7.9% in couples with mild male factor.<sup>6</sup> A Cochrane systematic review on single versus double IUI in stimulated cycles for subfertile couples published in 2003 which included 5 trials concluded that double IUI was beneficial as it resulted in increased clinical pregnancy rates.<sup>7</sup>

### Success not significantly higher with Double IUI

A randomised controlled trial from Iran published in 2016 concluded that there was no statistically increased pregnancy rate in double IUI group compared to single IUI though the pregnancy rate was marginally high (Single Vs Double:11.7% Vs13.4%).<sup>8</sup> A prospective randomised controlled study in 2017 undertaken in 197 subjects found a success rate of 13.86% with single IUI and 18.75% with double IUI and the difference is not statistically significant.<sup>9</sup>

A meta analysis which included 6 trials found no significant difference in clinical Pregnancy rates per cycle between single versus double IUI in women with unexplained infertility.<sup>10</sup>

Choudhary and colleagues in 2018 published a study in a small sample size of 100 subjects and concluded that though there was no statistically significantly higher pregnancy rates overall with double IUI, in women who received gonadotropins for ovulation induction double IUI resulted in higher pregnancy rates.<sup>11</sup>

### Key Messages

- » IUI is the first line of therapy for couple below 40 years of age.
- » The success rates are typically 10-20%
- » Success rates may be increased with double IUI in certain clinical situations like mild male factor infertility or unexplained infertility
- » Overall single IUI is as effective as double IUI when properly timed. Single IUI timed post-ovulation for non-male factor infertility and double IUI performed pre-ovulation for male factor result in better pregnancy rates. However each case has to be individualized and IUI should be done close to the time of ovulation or very soon after ovulation.

### References:

1. Katzorke T1, Kolodziej FB. Significance of insemination in the era of IVF and ICSI. *Urologe A*. 2010 Jul;49(7):842-6. doi: 10.1007/s00120-009-2219-6
2. Allahbadia GN. Intrauterine Insemination: Fundamentals Revisited. *J Obstet Gynaecol India*. 2017 Dec;67(6):385-392. doi: 10.1007/s13224-017-1060-x. Epub 2017 Oct 25.
3. Ghanem ME, Bakre NI, Emam MA, Al Boghdady LA, Helal AS, Elmetwally AG, Hassan M, Albahlol IA, Elzayat MM. The effects of timing of intrauterine insemination in relation to ovulation and the number of inseminations on cycle pregnancy rate in common infertility etiologies. *Hum Reprod*. 2011

Mar;26(3):576-83. doi: 10.1093/humrep/deq362. Epub 2010 Dec 21

4. Matilsky M, Geslevich Y, Ben-Ami M, Ben-Shlomo I, Weiner-Megnagi T, Shalev E. Two-day IUI treatment cycles are more successful than one-day IUI cycles when using frozen-thawed donor sperm. *Androl*. 1998 Sep-Oct;19(5):603-7.
5. Liu W , Gong F, Luo K and Lu G. Comparing the pregnancy rates of one versus two intrauterine inseminations (IUIs) in male factor and idiopathic infertility. *J Assist Reprod Genet*. 2006 Feb; 23(2): 75-79..
6. Randall GW1, Gantt PA. Double vs. single intrauterine insemination per cycle: use in gonadotropin cycles and in diagnostic categories of ovulatory dysfunction and male factor infertility *J Reprod Med*. 2008 Mar;53(3):196-202.
7. Cantineau AEP, Heineman MJ, Cohlen BJ. Single versus double intrauterine insemination (IUI) in stimulated cycles for subfertile couples. *Cochrane Database of Systematic Reviews* 2003, Issue 1. Art. No.: CD003854. DOI: 10.1002/14651858.CD003854.
8. Zahiri Sorouri Z, Rashid Shomali R, Pourmarzi D. Single versus double intrauterine insemination in controlled ovarian hyperstimulation cycles: A randomized trial. *Arch Iran Med*. 2016; 19(7): 465 – 469.
9. Pathak B.. Comparision of single versus double intrauterine insemination. *Int J Reprod contracept Obstet Gynecol*. 2017;6(12):5277-5281.
10. Polyzos NP1, Tzioras S, Mauri D, Tatsioni A. Double versus single intrauterine insemination for unexplained infertility: a meta-analysis of randomized trials *Fertil Steril*. 2010 Sep;94(4):1261-6. doi: 10.1016/j.fertnstert.2009.06.052. Epub 2009 Aug 8.
11. Choudhary V, Choudhary M, Shekhawat U. Single versus double intrauterine insemination—in artificial insemination donor stimulated cycles—impact on the clinical pregnancy rate: A randomized trial. *Fertil Sci Res [serial online]* 2017 [cited 2019;4:106-11.

## Endometrial Receptivity Array (ERA) & its Clinical Implications



**Dr. Sangita Sharma**

MD(OBGY), DNB, MNAMS, FNB (Reprod.Med.)  
DGES (Germany)  
Secretary- IFS Rajasthan Chapter  
Centre Head - Jaipur Fertility Centre, Jaipur

This article highlights the need for methods to objectively diagnose endometrial receptivity as a factor contributing to infertility in female patients. The correct identification of the appropriate window of implantation in a given patient, by using endometrial receptivity biomarkers, can help to prevent reproductive failure resulting from misplaced timing of the endometrial window of implantation (WOI). Although to date no single, clinically relevant morphologic, molecular, or histologic marker capable of indicating endometrial receptivity status has been identified, global transcriptomic analysis of human endometria performed in the last decade has given us insights into a genomic signature that is capable of identifying endometrial receptivity. As a consequence, a genomic tool named the Endometrial Receptivity Array (ERA), based on a customized microarray, was developed, and along with it a specially trained bioinformatic prediction computer algorithm was created to identify WOI timing in the endometrium. This tool has proven more accurate and consistent than histologic (Noyes) dating at identifying the personalized WOI day, thus leading to the new clinical concept of personalized

Embryo transfer (pET) on the optimum day of endometrial receptivity, identified individually case by case.

### Window of Implantation

The embryo is unable to adhere to the endometrium through most of the menstrual cycle in humans, except during a short, self-limited period, in which the endometrial tissue acquires a functional and transient status that permits blastocyst adhesion<sup>1</sup> and is therefore receptive. This specific period, which is regulated by a combination of ovarian steroid hormones and genetic factors, is known as the window of implantation (WOI) and lasts 5 to 6 days after an exogenous or endogenous P impregnation.

### Markers of Endometrial Receptivity

Unfortunately, no single specific endometrial receptivity biomarker has been identified, meaning that objective diagnosis of endometrial receptivity remains neglected in the patient infertility workup. Despite the historical relevance of traditional Histologic endometrial dating: Histologic endometrial dating criteria defined by Noyes,<sup>2,3</sup> its accuracy, reproducibility, and clinical utility has been repeatedly questioned in randomized<sup>4, 5</sup> and prospective studies,<sup>6-12</sup> and thus it is no longer used to guide clinical practice owing to its real and perceived limitations. It has been suggested that pinopodes, ectoplasmic projections on the surface of endometrial epithelial cells,<sup>13, 14</sup> may be a good morphologic marker for diagnosing endometrial receptivity status. However, it has been reported that pinopodes are still present in the postreceptive period and therefore cannot be used as a reliable morphologic receptivity marker.<sup>15</sup>

**Biochemical markers:** Biochemical markers like

integrins,<sup>16</sup> mucin 1 (MUC1),<sup>17</sup> calcitonin,<sup>18</sup> leukemia inhibitory factor (LIF),<sup>19</sup> cyclo-oxygenase 2,<sup>20</sup> and homeobox A10 (HOXA10)<sup>21</sup> have been studied, but none of them has been translated into clinical practice as an endometrial biomarker.<sup>22</sup>

**Microarray technologies:** Microarray technologies now allow more reliable, quantifiable gene expression monitoring,<sup>23</sup> and these technologies have been used to investigate the transcriptomics of human endometria in the different phases of the menstrual cycle, including within the receptivity phase.<sup>24, 25</sup> Importantly, these studies demonstrated that differential gene expression patterns exist in different phases, thus allowing the molecular status of the endometrium to be classified according to its transcriptomic signature regardless of its histologic appearance.

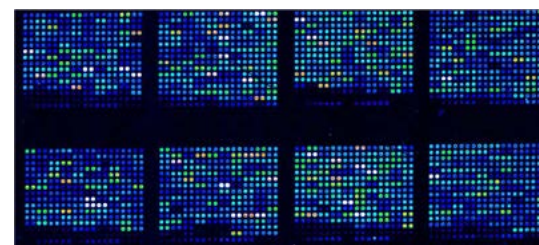
### Transcriptomics Of The Human Endometrium

The transcriptome reflects the genes that are actively expressed at any given time within a specific cell population or tissue.

### Endometrial Receptivity Array

The Endometrial Receptivity Array (ERA) is a customized array based on the transcriptomic signature of human endometrial receptivity, specifically when human endometrium is receptive to blastocyst adhesion (26). It has been designed to identify endometrial receptivity by comparing the genetic profile of a test sample with those of LH+7 controls in a natural cycle, or on day 5 of P administration (P+5) after E2 priming in a hormonal replacement therapy (HRT) cycle. It consists of a customized array, containing 238 genes that are differentially expressed between these profiles, which is coupled to a computational predictor that can diagnose the personalized endometrial WOI of a given patient regardless of their endometrial histology.<sup>26</sup> To select the genes for inclusion in the ERA platform, this group analyzed the expression profile of endometrial samples obtained on day LH+7 in a natural cycle compared with the prereceptive phase (LH+1, +3, +5).<sup>27</sup> Using stringent criteria of a 3.0-fold change increase and false discovery rate of <0.5, 238 genes were selected that were incorporated into a customized Agilent gene expression microarray using the 569 probes already existing on the array. The ERA expression values for the training set were used to train the bioinformatic predictor to classify an endometrial sample as "receptive" or "nonreceptive." (Fig 1)

**Fig 1: Customized microarray (238 genes)**



Bioinformatic analysis of data obtained by the customized microarray

Classification and prediction from gene expression (as receptive or nonreceptive)

Once the array and the predictor were designed, a cohort of samples obtained in the prereceptive (LH+3, +5), receptive (LH+7), and proliferative phases (days 8–12 of the menstrual cycle) were used to validate this transcriptomic signature. Specificity and sensitivity figures of 0.8857 and 0.99758, respectively was obtained.<sup>26</sup>

The reproducibility of the ERA was tested by analyzing a second biopsy obtained from the same patient, on the same day of the menstrual cycle, 2 to 3 years after the first one. Paired-sample gene expression analysis showed the reproducibility of the tool and demonstrated that the transcriptomic profile of the mid-secretory phase endometrium did not substantially change between cycles for over relatively long periods of the women's reproductive life. Concordance for ERA endometrial

receptivity dating against the LH peak showed a value of 0.922 (0.815-1.000), and the reproducibility of the ERA test was 100% consistent (28) (table 1)

**Table 1: Consistency of ERA**

ERA test analyzed in the same patient, same day, 3-years apart

Code	Date First Biopsy	Date Second Biopsy	Months between	First Biopsy Results	Second Biopsy Results
CON1	09/2009	02/2012	29	Receptive	Receptive (0.908)
CON2	09/2009	03/2012	30	Receptive	Receptive (0.908)
CON3	05/2009	04/2012	35	Receptive	Receptive (0.908)
CON4	05/2009	05/2012	36	Proliferative	Non Receptive (0.864)
CON5	01/2009	05/2012	40	Proliferative	Non Receptive (0.864)
CON6	07/2009	05/2012	35	Receptive	Receptive (0.908)

Ref: Díaz-Gimeno, et al. Fertil Steril 2013

Hence, for the first time, a molecular tool based on the expression of a cluster of endometrial biomarker genes can be clinically used in reproductive medicine to assess the endometrial receptivity factor with proven accuracy and consistency.

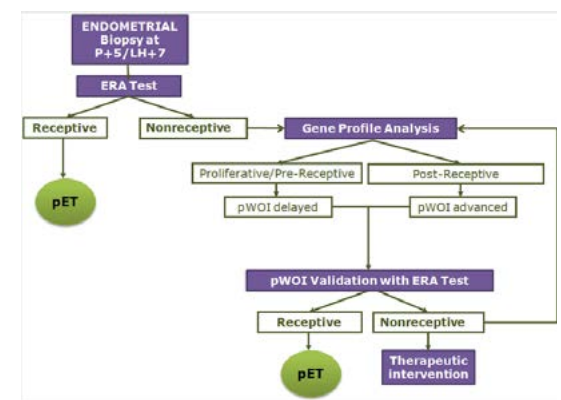
### Clinical Applications

The diagnostic and clinical value of the ERA test has been tested in a prospective, interventional, multicenter, clinical trial<sup>28</sup> in which patients with recurrent implantation failures (RIFs) and controls underwent endometrial receptivity diagnosis using an endometrial biopsy obtained either on

- day LH+7 in a natural cycle or on
- day P+5 in an HRT cycle.

Patients with at least three previous failed ovum donation cycles, and IVF patients aged <40 years, with at least three failed IVF cycles, made up this group. The ERA test identified 73.7% of the samples as receptive and 26.3% of them as nonreceptive. Patients with a receptive ERA diagnosis achieved a 62.8% pregnancy rate and a 37.9% implantation rate, when transferred the day after the receptive ERA diagnosis, which was similar to controls for whom the embryos were transferred in a subsequent cycle.

At the clinical level, the most important contribution of the ERA test is the objective diagnosis of the window of implantation, thus leading to the creation of the concept of personalized ET (pET) (Fig. 2).



**Fig 2: Clinical algorithm for pET.**

Ref: Ruiz-Alonso. Personalized ET in patients with RIF. Fertil Steril 2013<sup>28</sup>

Personalised medicine is a well-accepted concept in reproductive medicine. However, the medical community has always considered that all infertile patients must be equally treated in terms of the day of ET, which is guided by the embryo development stage and supported by the administration of P/hCG in the luteal phase. Given that personalized endometrial receptivity diagnosis is now possible, it is considered of utmost importance that a personalized approach to improving clinical success from the endometrial perspective be used.

This test is recommended for patients RIF with apparently normal uterus and with normal endometrial thickness (>6mm), in which no problems are apparent.

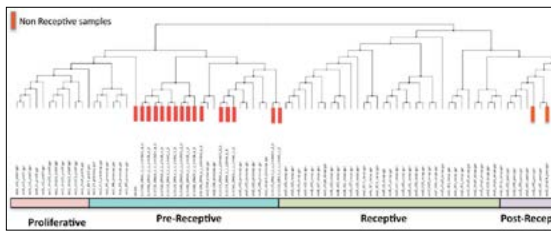
A displaced implantation window is detected in approximately 20% of these patients.

#### Further plan of action based on ERA report

The ERA test informs us whether the endometrial biopsy obtained during the expected WOI is really in a receptive state or whether it is nonreceptive at the time of testing. In the first case, ET must be performed in a subsequent natural or HRT cycle on the designated day. In case the result is nonreceptive, it can then be classified by our predictor as pre- or postreceptive (Fig 3), and a second ERA test following this guideline can be performed to validate a personalised WOI resulting from displacement caused by some intrinsic genomic alteration inherent in the patient, an observation which has been made in one in four RIF patients (29). This new concept has been functionally proven by applying pET, following ERA results indicating a displaced WOI, in RIF patients with a previously non-receptive endometrium, either on days LH+9 or P+7; their implantation rate and pregnancy rate rose to similar levels as those in normally receptive control patients.<sup>29</sup>

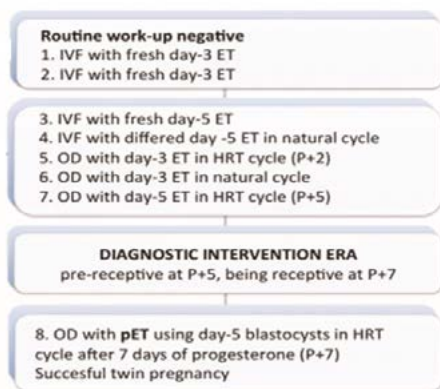
#### Fig 3:

The importance of pET can be understood by a case presented by Ruiz Alonso et al in 2014, where 7 embryo transfers failed including all possibilities viz self day 3 transfer, self day 5 transfer, IVF with donor oocyte in a natural cycle, IVF with donor oocyte in a HRT



day 3 and day 5), including both fresh and frozen transfers. On performing ERA, the WOI was found to be displaced, and the women conceived with pET by transferring day 5 blastocysts (with donor oocytes) in HRT cycle after 7 days of progesterone supplementation (P+7). So it is evident what a difference two days can make. ( Fig 4).<sup>30</sup>

#### Fig 4. Successful Treatment after pET



Ruiz-Alonso, et al. 2014

#### Wider implications of ERA in future

Although this molecular tool currently focuses on RIF patients, research is underway to test the ERA in patients with endometriosis and hydrosalpinx. However, a prospective, randomized study on the effectiveness of the ERA test in the infertility workup, to guide pET in patients receiving assisted reproductive technology treatments, is the need of the hour. Whether these technological improvements will translate into clinical diagnostic advances, remains to be seen. Moreover, this molecular tool could be useful not only for clinical diagnosis but also for research based on the analysis of variations in receptive expression profiles due to different treatments or conditions.

Summarized from - Garrido Gomez et al, Fertil Steril\_2013 ;99:1078–85. 2013 by American Society for Reproductive Medicine

#### References

1. Psychoyos A. Uterine receptivity for nidation. *Ann N Y Acad Sci* 1986;476: 36–42.
2. Noyes RW, Hertig AT, Rock J. Dating the endometrial biopsy. *Fertil Steril* 1950;1:3–25.
3. Noyes RW, Hertig AT, Rock J. Dating the endometrial biopsy. *Am J Obstet Gynecol* 1975;122:262–3.
4. Coutifaris C, Myers ER, Guzick DS, Diamond MP, Carson SA, Legro RS, et al. Histological dating of timed endometrial biopsy tissue not related to fertility status. *Fertil Steril* 2004;82:1264–72.
5. Murray MJ, Meyer WR, Zaino RJ, Lessey BA, Novotny DB, Ireland K, et al. A critical analysis of the accuracy, reproducibility, and clinical utility of histologic endometrial dating in fertile women. *Fertil Steril* 2004;81:1333–43.
6. Balasch J, Vanrell JA, Creus M, Marquez M, Gonzalez-Merlo J. The endometrial biopsy for diagnosis of luteal phase deficiency. *Fertil Steril* 1985;44:699–701.
7. Balasch J, Fabregues F, Creus M, Vanrell JA. The usefulness of endometrial biopsy for luteal phase evaluation in infertility. *Hum Reprod* 1992;7:973–7.
8. Scott RT, Snyder RR, Strickland DM, Tyburski CC, Bagnall JA, Reed KR, et al. The effect of interobserver variation in dating endometrial histology on the diagnosis of luteal phase defects. *Fertil Steril* 1988;50:888–92.
9. Scott RT, Snyder RR, Bagnall JW, Reed KD, Adair CF, Hensley SD. Evaluation of the impact of intraobserver variability on endometrial dating and the diagnosis of luteal phase defects. *Fertil Steril* 1993;60:652–7.
10. Gibson M, Badger GJ, Byrn F, Lee KR, Korson R, Trainer TD. Error in histologic dating of secretory endometrium: variance component analysis. *Fertil Steril* 1991;56:242–7.
11. American Society for Reproductive Medicine. A Practice Committee report: optimal evaluation of the infertile female. Birmingham, AL: ASRM; 2000. 1–6.
12. Landis JR, Koch GC. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159–74.
13. Nikas G. Cell-surface morphological events relevant to human implantation. *Hum Reprod* 1999;14:37–44.
14. Lessey BA. Assessment of endometrial receptivity. *Fertil Steril* 2011;96: 522–9.
15. Quinn CE, Casper RF. Pinopodes: a questionable role in endometrial receptivity. *Hum Reprod Update* 2009;15:229–36.
16. Lessey BA, Damjanovich L, Coutifaris C, Castelbaum A, Albelda SM, Buck CA. Integrin adhesion molecules in the human endometrium. Correlation with the normal and abnormal menstrual cycle. *J Clin Invest* 1992;90:188–95.
17. Meseguer M, Pellicer A, Simon C. MUC1 and endometrial receptivity. *Mol Hum Reprod* 1998;4:1089–98.
18. Kumar S, Zhu LJ, Polihronis M, Cameron S, Baird DT, Scholtz F, et al. Progesterone induces calcitonin gene expression in human endometrium within the putative window of implantation. *J Clin Endocrinol Metab* 1998;83: 4443–50.
19. Stewart CL, Kaspar P, Brunet LJ, Bhatt H, Gadi I. Blastocyst implantation depends on maternal expression of leukaemia inhibitory factor. *Nature* 1992; 359:76–9.
20. Davis BJ, Lennard DE, Lee CA, Tiano HF, Morham SG, Wetsel WC, Langanbach R. Anovulation in cyclooxygenase-2-deficient mice is restored by prostaglandin E2 and interleukin-1beta. *Endocrinology* 1999;140:2685–95.
21. Taylor H, Igarashi P, Olive D, Arici A. Sex steroids

mediate Hoxa11 expression in the human peri-implantation endometrium. *J Clin Endocrinol Metab* 1999;84:1129–35.

22. Aghajanova L, Simon C, Horcajadas J. Are favorite molecules of endometrial receptivity still in favour? *Exp Rev Obstet Gynecol* 2008;3:487–501.
23. Schena M, Shalon D, Davis RW, Brown PO. Quantitative monitoring of gene expression patterns with a complementary DNA microarray. *Science* 1995; 270:467–70.
24. Horcajadas JA, Pellicer A, Simon C. Wide genomic analysis of human endometrial receptivity: new times, new opportunities. *Hum Reprod Update* 2007;13:77–86.
25. Ruiz-Alonso M, Blesa D, Simon S. The genomics of the human endometrium. *Biochim Biophys Acta* 2012;1822:1931–42.
26. Diaz-Gimeno P, Horcajadas JA, Martinez-Conejero JA, Esteban FJ, Alama P, Pellicer A, et al. A genomic diagnostic tool for human endometrial receptivity based on the transcriptomic signature. *Fertil Steril* 2011;95:50–60.
27. Horcajadas JA, Sharkey AM, Catalano RD, Sherwin JR, Domínguez F, Burgos LA, et al. Effect of an intrauterine device on the gene expression profile of the endometrium. *J Clin Endocrinol Metab* 2006;91:3199–207.
28. Díaz-Gimeno P, Ruiz-Alonso M, Blesa D, Bosch N, Martínez-Conejero JA, Alam\_a P, et al. The accuracy and reproducibility of the endometrial receptivity array is superior to histology as a diagnostic method for endometrial receptivity. *Fertil Steril* 2013;99:508–17.
29. Simon C. The endometrial receptivity array (ERA) as diagnosis and personalized embryo transfer (pET) as treatment for patients with repeated implantation failure (RIF). Available at: <http://clinicaltrials.gov/ct2/show/NCT01668693>.
30. Ruiz Alonso et al. What a difference two days make: “personalized” embryo transfer (pET) paradigm: A case report and pilot study. *Hum Reprod* (2014) 29 (6): 1244–1247.
31. Garrido Gomez et al, Fertil Steril\_ 2013;99:1078–85. 2013 by American Society for Reproductive Medicine.

# IFS – Contributing To The Society And Touching Livs

## Kerala

### Tribal Fertility Healthcare project

- 116 TRIBAL VILLAGES IN KERALA with an average population of 17,000-21,500 women of reproductive age group in extreme poverty.

#### Aims:

- Women’s healthcare screening
- Supply of healthy food
- Reproductive care - Obstetric care
- Fertility support

Project approved by Govt of Kerala and partially funded; Will be operational with the help of Reproductive Health committee of KFOG.

### Flood - 2 relief activities

- Northern Kerala affected
- 1800 plus families totally dislocated
- 46 families could not be traced following landslide in western ghats
- 20 member team from IFS Kerala Chapter joined with IMA and local health admin and visited many camps and supplied medicines, food materials and dress items worth total 7 lakhs rupees
- Follow up activities are on place



## Uttarakhand

Infertility Camp under aegis of IFS held in Muzaffarnagar



## Chattisgarh

Dr Manoj Chelani Founder Secretary is doing free check up once a month Dr Yeronica Yule jt. Secretary is doing free checkups



## Rajasthan

Infertility Awareness & Free Consultation Camp & Talk on 16<sup>th</sup> May, 2019 at Jhunjhunu Attended by 21 Patients



## UP West

Regular out station IVF Camps organised by Deptt of Obs & Gynae, SRMSIMS

19.02.2019	Pilibhit
26.03.2019	Badaun
27.03.2019	Sambhal
08.05.2019	Badaun
04.05.2019	Pilibhit
19.06.2019	Ujhani
10.07.2019	Bisoli
23.07.2019	Rudrapur
And many more to come...	

## Fertility Science and Research Journal – An IFS Publication...

Fertility Science and Research, a publication of Indian Fertility Society, is a peer-review journal with triannual print on demand compilation of issues published. The journal's full text is available online at <http://www.fertilityscienceresearch.org>. The journal allows free access (Open Access) to its contents and permits authors to self-archive final accepted version of the articles on any OAI-compliant institutional / subject-based repository. The journal does not charge for submission, processing or publication of manuscripts and even for color reproduction of photographs.

We are circulating an approximate of 2500 copies. Initially frequency of publication was biannual. Now it has been made triannual.

**The Current Issue .....** The current issue deals with interesting and pertinent issues faced by the current day ART specialists. Stem-cell therapy, although still in its nascent stage, has come out with certain options in the management of male as well as female infertility. The subsequent articles deal with the extremely important and burning issue of ovarian reserve and its testing and a study of poor responders and comparison of their managements in the diagnosis as well as the management of infertile couples. Another retrospective analysis of the antagonist cycles to assess the ovarian reserve parameters gives an overall view of the clinical parameters assessing the success of in vitro fertilization (IVF) cycles. An interesting analysis correlates the interleukin concentrations in the follicular fluid states it to be a reliable predictive marker of successful IVF/ outcome. Comparison of fresh versus frozen embryo transfer in IVF cycles highlights the utility of frozen embryo transfer cycles in polycystic Ovarian syndrome (PCOS) and hyperstimulated patients, with comparable efficacy. An article clearly specifies the use of single versus double IUI in ovulation induction cycles. This issue has been nicely brought out the importance of mental and psychological health of patients undergoing treatment of infertility.

### EDITOR-IN-CHIEF

Dr. Kuldeep Jain, Delhi

### EXECUTIVE EDITOR

Dr. Bharati Dhorepatil, Pune

### ASSOCIATE EDITORS

Col. Pankaj Talwar VSM, Delhi

Dr. Gita Radhakrishnan, Delhi

Dr. Abha Maheshwari, UK

### ASSISTANT EDITORS

Dr. Surveen Ghumman (Delhi)

Dr. Neena Malhotra (Delhi)

Dr. Umesh Jindal (Chandigarh)

Dr. Shweta Gupta (Delhi)

Dr. Rupali Bassi Goyal (New Delhi)

Articles can be submitted online  
<http://www.fertilityscienceresearch.org>



## IFS PATHSALA - Certified Master Courses

In its endeavor to spread knowledge in the field of fertility, IFS organized two editions of IFS Pathsala -Certified Master Courses in year 2018-2019.

Master courses were uniquely designed with very precise and specific modules covering concepts and latest advancements alongside state of ART laboratory techniques and procedures. Due to excellentcourse content, Experienced faculty, and effective management, master courses was well received and in fact organizers have to increase minimum limit of participants per session.

Master courses also put lot of effort to bring in very heterogenous mix of participants with experience and established practitioners along with young enthusiasts so that participants can tap in to each other experience along with the knowledge shared by faculty. It also had clinicians and embryologists synchronizing among each other.

Master courses in its holistic approach covered “Triad” of Concepts, Hands on laboratory techniques and Standard operating procedures. Experienced faculty with national reputeshared their experiences in the field of ovulation induction, reproductive endocrinology and applied genetics. Master courses also witnessed hands on laboratory procedures like semen analysis, IUI setup, comprehensive advanced andrology techniques, cryopreservation of semen, oocytes, embryos and Concepts of embryo culture , media and labware. Master courses also detailed QA/QC (Quality Assurance and Quality Control) measures along with ICMR guidelines for ART Centre.

IFS Pathsala with its first edition laid foundation for future of training in field of fertility with extremely encouraging and satisfying feedback, many enquiries are already flowing in for next and bigger version of IFS Pathsala.



## IFS E-PATHSALA IFS - Reaching Every Corner of the Nation



**DR GOURI DEVI**  
President, IFS



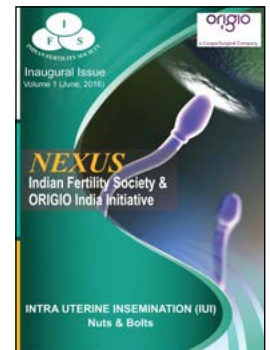
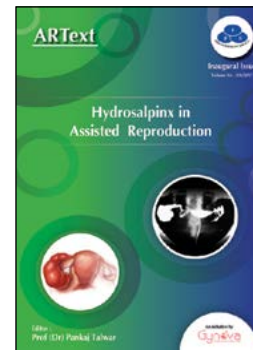
**DR PANKAJ TALWAR**  
Secretary General, IFS

**ART TEXT :** this has been brought out on various topics like hydrosalpinx , Poor ovarian reserve, adenomyosis and thin endometrium. This was an initiative by Prof Pankaj Talwar who is the chief editor .

**NEXUS:** An embryology update brought out by Indian fertility society on topics like Semenanalysis, Intrauterine insemination, Semen freezing, sperm function test, media, vitrification, oocyte retrieval and embryo Transfer . This was an initiative by Prof Pankaj Talwar who is the chief editor. New editions onco navi



**DR PANKAJ TALWAR**  
Chief Editor



**FERTILITY NEWS**



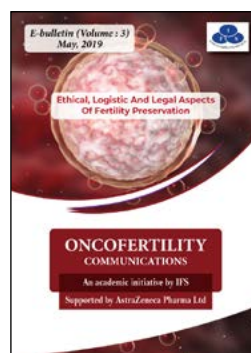
**Compiled by  
DR SWETA GUPTA**



**CATALYST**



**Compiled by  
DR MOHAN KAMATH**



**ONCOFERTILITY**



**Compiled by  
DR PUNEET RANA ARORA**



**SONONAVIGATOR**



**Compiled by  
DR GUNJAN BHATNAGAR**

## TRAINING AND EDUCATION – A PRIORITY WITH IFS

**IFS Conducts along with Amity University a one year Diploma in Clinical ART and Diploma in Clinical Embryology 2019**  
**18 candidates of Diploma in Clinical ART and 5 of Diploma in Clinical Embryology passed out successfully**



### Congratulations to all the candidates successfully passing the Examination DCR & DCE 2018-2019

DCR			
NAME	CENTER	NAME	CENTER
Ms Shrotri Tejashri Murlidhar	SGRH	Ms Niti Vijay	Ridge IVF
Ms Nikita Jindal	SGRH	Ms Deepmala	KJIVF
Ms Renu Lamba	Southend	Ms Jyoti Gupta	KJIVF
Ms Aneesha Minocha	Southend	Ms Indrani Ghosh	Guwahati
Ms Divya Lakshmi A	Jindal	Ms Rachita Chawla	Kochi, Kerala
Ms Princy Mittal	Akanksha IVF	Ms Simmi Arora	Jodhpur
Ms Ruchi Chhabra	Pune	Ms Manvi Tyagi	Ahmedabad
Ms Zeepee Godha	Akanksha IVF	Ms Shilpa Singhal	Primus
Ms Soumya Dash	Mother & Child		

DCE	
NAME	CENTER
Ms Charu Goel	Jindal
Ms Nupur Ahuja	Primus
Mr Shivam Malhotra	SGRH
Ms Andleeb Rubab Shuaib	Southend IVF
Ms Swati Mishra	Akanksha IVF



### An IFS - ESHRE Initiative

**IFS Embryology Certification & Preparatory Course for ESHRE on 4<sup>th</sup> & 5<sup>th</sup> Dec 2019 at IHC Delhi With**  
**Dr kuldeep Jain, Prof Arne Sunde, Norway,**  
**Dr Jayant Mehta, UK and Dr Gouri Devi**  
**Candidates taking preassessment exams, exhaustive teaching and evaluation for 72 hours. Total 30 Candidates with 10 Delegates from Thailand**



**DR GOURI DEVI**  
President, IFS



**DR KULDEEP JAIN**  
Course Chairperson



**DR JAYANT MEHTA**  
Course Director



**DR PANKAJ TALWAR**  
Secretary General, IFS



**DR ARNE SUNDE**  
Course Director

# IFS - Representing India At Global Level



**ESHRE 2019**

**Gouri Devi**

**Dr Gouri Devi (President IFS) At ESHRE 2019 – IFS/ISAR Session**



**Dr Gouri Devi, Dr KD Nayar and Dr Neena Malhotra at the IFS ISAR session in ESHRE 2019, Vienna**



**Dr KD Nayar ( Vice President, IFS) Oral presentation at ESHRE Vienna 2019**

Faculty/Oral Presentation at European Society for Human Reproduction & Embryology (ESHRE), Date and Time: 26th June 2019, 14.30 hours.  
 O- 280 Topic: **“Evaluation of the hormone Dehydro-epiandrosterone sulphate (DHEAS) as a potentially compelling ‘oocyte-related factor’ in mammalian oocyte activation : A paradigm shift?”**

**Dr Uma Srivastava**  
(Nepal Chapter)

Poster presentation in World Conference on PCOS in Abu Dhabi

**Dr Randir Singh and Dr Monica Singh**  
from Bhopal (MP Chapter, IFS) - 3 Posters presented at ESHRE 2019

O- 003 Topic: **“Mapping the follicular fluid bio-molecular profile: Dynamic interactions set the algorithm for oocyte maturation, embryo development and successful outcomes in IVF cycles”**

**Dr Bindu N. Chimote**  
(Nagpur, Vidharbha Chapter IFS)

Presented an Oral Presentation at ESHRE

**Dr. Natachandra M. Chimote**  
(Nagpur, Vidharbha Chapter IFS)

Faculty/Oral Presentation at European Society for Human Reproduction and Embryology (ESHRE),  
Date and Time: 24th June 2019, 10.00 am

**IS THE 'DRESTRO-ANDROGENIC' HORMONE DEHYDRO-EPIANDROSTERONE SULPHATE (DHEAS) THE INTRACRINE REGULATOR OF IMPLANTATION AND EARLY PREGNANCY?: A PROSPECTIVE STUDY IN WOMEN UNDERGOING IVF**

Poster No. 206  
**Dr. Bindu N. Chimote, Dr. Natachandra M. Chimote**  
Vunashdhara Fertility Centre, Nagpur-India

Dr Monica Varma from Punjab Chapter IFS presented a poster at ESHRE 2019 **“Higher risk of preeclampsia in singleton pregnancies from donor versus autologous oocytes, with similar endometrial preparation, in a healthy, young cohort: a prospective study”** She had also suggested seven points for the ESHRE 2019 Guidelines for Good Practice Recommendations for Ultrasound in ART: Oocyte Pick- up and all 7 were accepted in the final guidelines. Her name is in the Reviewers List of these guidelines.



**Congratulations! Dr Bindu and Dr Natachandra Chimote on receiving Peoples Choice Best Video Poster Award**

**Congratulation! Dr Monica Varma for being part of Reviewers List in ESHRE GUIDELINES 2019 Good Practice Recommendations for Ultrasound in ART**



**The Joint session of IFS / ISAR was conducted at IFFS world congress  
Held in Shanghai from 11<sup>th</sup> - 13<sup>th</sup> April, 2019**

**3 panels on improving ART outcome - clinical and embryology perspective and Recurrent implantation failure were held which were highly appreciated and well attended IFS represented by Dr Kuldeep Jain, Dr Gouri, Dr KD Nayar, Dr Shweta Mittal, Dr Kunjumoiddin, Dr Mohan Kamath, Dr Gaurav Majumdar, Dr Saumya**



**Congratulations! Dr Kuldeep Jain for being selected on the IFFS Scientific Board for 3 years**

**Akanksha IVF Centre team lead by DR. K.D. Nayar**

**Oral Presentations : International**

1. Oral presentation : Role of recombinant Luteinizing hormone as adjuvants to antagonist protocol in poor responders - *Kanad Dev Nayar, Minal Singh, Monica Gupta, Gaurav Kant, Divya Nayar, Shweta Gupta*
2. Trigger Day Progesterone level ã: A guide towards Fresh or frozen transfer and clinical outcome - *Shweta Gupta, K D Nayar*

**Oral presentation / poster presentation (National)**

Impact of day 5 vs day 6 blastocyst on pregnancy outcome of frozen thawed donor recipient cycle. *Shweta Mittal Gupta, Gaurav Majumdar.* 15th May 2019. Sir ganga Ram Hospital research day

**26<sup>th</sup> Annual Scientific Meeting of Middle Eastern Fertility Society (MEFS) 31<sup>st</sup> Oct -2<sup>nd</sup> Nov. at Cairo, Egypt**

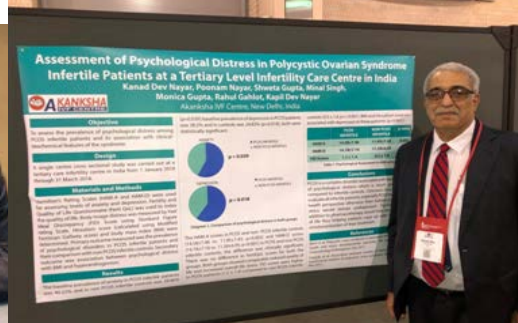
**Dr Gouri, President IFS with Dr. Michel Abdallah, Exc. Director of MEFS and Dr Johnny Aavaad, The Scientific Chair**

**Dr Gouri President IFS with Botros Rizk, President MEF at the Annual Meet**

**American Society for Reproductive Medicine (ASRM) Annual Meeting 2019 Philadelphia**

**Dr Kuldeep Jain and Dr KD Nayar representing IFS at ASRM**

**Moderated the Oral Abstract Session OR03-10 on Professional Development along with Rachel Whyntt**



**Dr KD Nayar Poster Presented**

# CHAPTER ACTIVITIES 2019

## TELANGANA



**Chapter Secretary  
Dr. Roya Rozati**

Vision Statement : "Vision for IFS Telangana chapter is to encourage research, broadcast educational information, and promote the advanced clinical care of patients in all aspects of reproductive medicine, Assisted Reproduction Technology (ART) and embryology related research in stem cells and cloning."

**Executive Committee**

- Chief Patron : Prof PP Reddy
- Secretary : Dr. Roya Rozati
- Joint Secretary : Dr.Meera Raj Gopal
- Treasurer : Dr.Krishna Leela .B
- Executive Council Members : Dr. Padmaja, Dr. Charulata Chatterjee, Dr. Srilatha Gorthi, Dr. Ch Swapna, Dr. Survachala Vardan Chekuri, Dr. Srinivas Warangale

**Activity 1**

**CME - The Setting up of an ART LAB/ Clinic on 24th March 2019 at Hotel Marriott Tankbund.**

Inauguration of the CME was done by the dignitaries Secretary Dr. RoyaRozati, Dr. Renu Mishra- Executive member of IFS, Prof PP Reddy The chief patron & Joint Secretary Dr. MeeraRajgopal. The CME program was divided into three sessions, Shift from Gynecology to ART, Ethical Challenges & Daily Challenges, Shift from Gynecology to ART. An informative talk was given on Setting up of an IUI facility by Dr. Renu Mishra the Executive Member IFS. Another talk was given on how to Set up of an IVF lab- Dr. SuvarchalaVardhanChekuri, QA QC at an ART Centre was given by Dr. CharulataChatterjee. Ethical Challenges. Another informative talk was given on ICMR guidelines Part b-Dr.RoyaRozati, Part A-SwetaAgarwal Desirable and Mandatory at an ART Lab was given by Dr.ChandanaLakkireddy. The session was concluded by Vote of Thanks By Dr. Krishna Leela B Meeting was well covered by Press.

The academic activity was well organized & appreciated by all delegate

It was an interactive CME, well attended and appreciated. About 60 delegates attended it, both clinicians and Embryologists



**Activity 2**

**Environment and Reproduction in ART On 7th April 2019 at Hotel Marriott Tankbund**

Inauguration by Dr. RoyaRozati , Dr. RS Sharma Executive member Secretary ICMR, Dr. Sweta Gupta and other IFS members & Prof P.P.Reddy represented as Patron of the IFS Telangana Chapter.

Mesmerizing talk on Environment Toxicants and Female Reproduction by Dr. RoyaRozati, Secretary IFS Telangana with an interactive session with queries addressed by the audience. The entire hall was spell bound by an enlightening talk on Interesting cases (Testicular Dysgenesis syndrome malformation, miscarriages etc, by Dr. Sweta Gupta. A talk was presented given on options and advances in air purification technologies by -Mr DilipPatil . A talk on optimizing the culture environment in the IVF lab was given by Dr. CharulataChatterjee. On 7th April CME was conducted on Environment and Reproduction in ART which focuses on the importance of Environmental chemicals exposure in men and women were associated with reduced fertility and a higher risk of adverse outcomes, whereas some dietary factors improved the probability of successful reproductive outcomes. Dr RS Sharma our chief guest of ICMR delivered a talk on biomagnetic and hazardous effects of mobiles on our reproductive health which now has scientific evidence. Vote of Thanks was given by Dr. RoyaRozati.

Around 60 gynecologists mostly from Telangana had participated in the CME.



**Activity 3**

**CME at Hotel Park Hyatt, on 11th August 2019 in Banjara Hills, Hyderabad.**

It was represented by Prof P.P.Reddy represented as Patron of the IFS Telangana Chapter. The program was jointly inaugurated by IFS Telangana Chapter Secretary Dr. RoyaRozati & Joint Secretary Dr. Meera Rajgopal and other dignitaries. Inauguration and Welcome Speech was delivered Prof P.P. Reddy. Lectures on Newer Trends in ART was given by Dr. Meera Rajgopal and Endometriosis-A Challenge was given by Dr. Krishnaleela.B. Poor Ovarian Reserve - IVF Protocol was given by Dr. Srilatha Gorthi Panel

Discussion : Trouble Shooting in IVF moderated by Dr. Charulata Chatterjee Dr. Sweta Agarwal.

Around 50 gynecologists mostly from Telangana had participated in the CME .



## TAMIL NADU



**Chapter Secretary  
Dr. PM Gopinath**

Vision Statement : Moving and marching towards the academic and clinical excellence under the umbrella of IFS.

**Executive Committee**

- Secretary : Dr P M Gopinath
- Joint Secretary : Dr. RajapriyaAyyappan
- Treasurer : Dr.RamaniCheniappan
- Joint Treasurer : Dr. PriyaKannan
- Patrons : Dr. Mirudhubashini, Dr. Geetha Haripriya
- Executive members Dr. Buyaneswari, Dr. A Charmila, Dr. Uma Maheswari, Dr. Krithika Devi, Dr. Rajeswari, Dr. Manu Lakshmi, Dr. Gayathre

**Activity 1**

**Recent advances in ART - 17/3/19 Trident Hotel Chennai**



**Activity 5**

**NADI women infertility camp Madhavaram MARCH 8,2019 Womens Day**



**Activity 9**

**IFS -GENETICS 17/5/19 CME**



**Activity 2**

**IFS Regular RTM-22nd Feb at Hotel Ramada, Egmore Interesting or difficult case discussions Critical Appraisal of an Article**



**Activity 6**

**Peripheral Manali Camp 5/19**



**Activity 10**

**Genetics CME- LILAC insights**



**Activity 7**

**Muthamilnagar camp June2019**



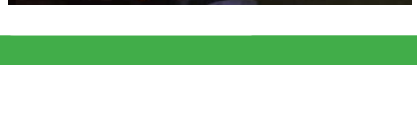
**Activity 11**

**IFS -IMA CME 23/6/19**



**Activity 3**

**RTM - 21st June - Interesting or difficult case discussions. Critical Appraisal of an article**



**Activity 8**

**DON BOSCO School- PCOS awareness talk 6/2019**

**Activity 12**

**Male infertility SIG CME 2/6/19**



**Activity 13**

**Dr Gopinath SIG Activity-SIMS**



**Activity 4**

**FEB 23-2019 Infertility Camp**

# PUDUCHERRY



**Chapter Secretary  
Dr. Papa Dasari**

Vision Statement : The vision is to create awareness of fertility and related issues among the general public

### Executive Committee

Chapter Secretary - Dr. Papa Dasari  
Chapter Jt. Secretary - Dr. Jisha R.  
Chapter Treasurer - Dr. Chitra T.

**IFS Puducherry Chapter organized Annual CME at Annamalai International, Puducherry on Male Infertility on 7.4.2019**

#### Lectures delivered on

1. DNA Fragmentation Index & Its implication delivered by Dr.Siddarth, Porur, Chennai
2. Effectivity of Oral Formulation on sperm DNA Fragmentation Pilot Study by Dr.SayaliKandare, Mumbai.
3. Management of Vericocele in Infertile men – Current Consensus by Dr.Ashok Kumar, Chennai.
4. Medical Management in Male Infertility by Dr.Raghavendra, K Urologist & Andrologist, Hyderabad.
5. Management of Anejaculation by Dr.Kubera, Puducherry.
6. The programme was well attended by the Post Graduates and the practioners of Puducherry and TamilNadu.



# GREATER CHANDIGARH



**Chapter Secretary  
Dr. Swati Verma**

Vision Statement : "To deliver evidence based academic content in the national annual conference Fertilvision 2020 in Chandigarh, in collaboration with Haryana, Himachal and Punjab Chapters. To encourage young members to improve communication and participation. Motto is to impart quality education to our fellows and achieve excellence in the field of teaching, learning and research"

### Executive Committee

Patron - Dr Umesh Jindal  
Secretary - Dr Swati Verma  
Joint secretary - Dr lavleen Sodhi  
Treasurer - Dr Sanjeev Maheshwari  
Advisors - Dr Umesh Jindal,  
Dr Dhaliwal, Dr Yash Bala,  
Dr Shalini Gainjender  
Executive Members -  
Dr Lovleen Sodhi, Dr Nirmal Bhasin,  
Dr Shanujit Sodhi, Dr Harpreet Sidhu,  
Dr Sheetal Jindal, Dr Bharti Joshi

**ACTIVITY 1**  
SIFCON 2019: 21 April 2019 at Chandigarh

Organizing chairperson - Dr Lovleen Sodhi  
Organizing co-chairperson - Dr Shalini Gainer

More than 200 Delegates

Dr Abha Majumdar, Dr Pankaj Talwar, Dr Vineet Malhotra and other local faculty discussed various issues related to cryopreservation and updated current trends in male infertility management.



#### Press coverage of the event



#### Debates

- Septum removal before ART
- D3 Transfer v/s blastocyst transfer



**ACTIVITY 2**  
16th ART Update 25-27th May 2019

#### Preconference workshops

- Endo -suturing
  - Hystero- trainer
  - IVF lab set up
- More than 50 participants in each
- Poster presentation session to encourage the young talent
  - Case discussion



#### ACTIVITY 3

Genetics Conference "How to apply genetics in ART practice: Basics to Advance" 7th Oct 2018

Attended by more than 100 delegates. Dr Ratnapuri, Dr Michal Richardson and Dr Manisha Vajpayee interacted with the delegates and highlighted about Aneuploidy screening, role of ART in genetic predisposition and case selection of PGD.



# VIDHARBHA



**Chapter Secretary  
Dr. Shilpi Sud**

Vision Statement : To sort out controversies in infertility management and come to consensus with clear understanding of subject Aim is to create awareness regarding evidence based management of infertility To reach every corner of Vidarbha

### Executive Committee

Secretary - Dr. Shilpi Sud  
Joint Secretary - Nishad Chimote  
Treasurer - Dr. NeelamPuniyani  
Past Secretary - Dr. Rohini Dravid  
Past Joint Secretary - Dr. Anjali Bhandarkar

**ACTIVITY 1**  
CME on Cancer and Fertility on 10th March 2019 at TuliImperial, Nagpur

Dr Anand Pathak, renowned Oncologist spoke on "Fertlity concerns in cancer patients" and highlighted the fact that not just the disease itself but the treatment modalities like chemotherapy, radiotherapy used for the cancer treatment may lead to sexual dysfunction, gonadal -toxicity and impaired reproductive function in male and females. Dr. Sadhana Patwardhan, IVF specialist spoke on Clinical Aspect on infertility. Dr. Pankaj Talwar, National Secretary IFS delivered lecture on techniques on fertility preservation. Dr. Amol Dongre spoke on "Challenges in fertility management & need of proper counselling. Dr Pankaj moderated panel on Facts and dilemmas of fertility preservation. Panelist were Dr Darshana Pawar, Dr. Tanushree Jain, Dr. Naresh Jadhav, Dr. Anita Salpekar, Dr. Bindu Chimote.



#### Coordination of Gynaecologists, Oncologists needed for Onco-Fertility Preservation



**ACTIVITY 2**  
Annual Conference of IFS Vidarbha Chapter Fertilquest 2019

One day annual conference held 15th September 2019 at Hotel Centre point Nagpur. ART Expert from all over India shared their knowledge. IFS President Dr. Gouri Devi delivered lecture on Newer Approach For Poor Responders. First Late Dr.MeenaChimote Oration was delivered by IVF Specialist Dr. MamtaDeendayal on "Managing Congenital Genital Tract Abnormalities, My Experience Of 36 Years". Dr. Kuldeep Jain Past President spoke on Double Stimulation, Double Trigger, Double Transfer: Double Trouble? Dr. K.D. Nayar spoke on Explaining Unexplained Infertility. Conference was appreciated by faculty and delegates.



#### Executive Members -

Dr Amogh Chimote, Dr Bindu Mehta Chimote, Dr Chaitanya Shembekar,  
Dr Darshana Powar, Dr Kanchan Sortey, Dr Riju Chimote, Dr Sushma Deshmukh

# KERALA



**Chapter Secretary  
Dr. KU Kunjimoideen**

**Vision Statement :** "Our Mission: Our mission is to educate the reproductive healthcare personnel to promote research and to encourage the superior ethical healthcare for patients seeking fertility treatments  
**Our Vision:** All women to have access to quality fertility health care."

### Executive Committee

**Chapter Secretary-**Dr KU Kunjimoideen  
**Jt Secretary –** Dr M Venugopal  
**Treasurer –** Dr G Parasuram  
**Executive members -**  
Dr KK Gopinath, Dr Fessy Louis,  
Dr Raju Nair, Dr Sheela Balakrishnan,  
Dr Sunil G Nayar, Dr Sankalp Singh,  
Dr Ramgopal Pillai

**ACTIVITY 1**  
CME on Infertility management and Fetal Anomaly Scans

IMA Perinthalmanna- Gynaecologists, Obstetricians, Urologists attended. 62 delegates



**ACTIVITY 3**  
CME on Male infertility Management at Kondotty, Kerala Organized in association with IMA and Urology Club

**ACTIVITY 4**  
CME on what's new in Infertility Management Organised in association with Calicut OG Society & IMA73 Gynaecs attended Half day CME Program



**Participation in IFFS China**

**ACTIVITY 5**  
Projects 360 degree Andrology

- In association with 1300 member KFOG
  - For orientation of all gynaecs and urologists
  - For uniform training of all registered and unregistered laboratory technicians
  - Uniform pattern and quality of Semen analysis reporting
  - Started the project with first meeting at Calicut in April 2019
  - Two more meetings conducted at Thrissur and Kannur
  - One training program for lab technicians conducted at Kochi
  - Submitted the project to Government of Kerala for state funding
- Program at Thrissur – June 2019



**ACTIVITY 2**  
CME on Endometriosis and Fibroids In association with OG Club Mannarkkad34 Gynaecs participated



**ACTIVITY 6**  
Tribal Fertility Healthcare project

- 116 TRIBAL VILLAGES IN KERALA with an average population of 17,000-21,500 women of reproductive age group in extreme poverty
  - Aims:
    - Women's healthcare screening
    - Supply of healthy food
    - Reproductive care – Obstetric care
    - Fertility support
- Project approved by Govt of Kerala and partially funded; Will be operational with the help of Reproductive Health committee of KFOG



**ACTIVITY 7**  
Public Health Activities Flood - 2 Relief Activities

- Northern Kerala affected
- 1800 plus families totally dislocated
- 46 families could not be traced following landslide in western ghats
- 20 member team from IFS Kerala Chapter joined with IMA and local health admin and visited many camps and supplied medicines, food materials and dress items worth total 7 lakhs rupees
- Follow up activities are on place



**ACTIVITY 8**  
Training programme for IVF Nurses



**ACTIVITY 9**  
World Womens Day



**ACTIVITY 12**  
International Girl Child Day

A Seminar was conducted on reproductive health and importance of healthy food habits, hygiene and exercise for higher secondary school girls of Tharakan's High School, Angadipuram in connection with observance of International Girl Child Day. Dr. Kuchu S. Mani inaugurated the seminar. The seminar was conducted by IFS Kerala chapter, POGS and Malabar District Police. A sensitization about sexual atrocities and training on self defence were given by District Police Superintendent team. More than 300 students participated in the seminar.



**ACTIVITY 11**  
Menstrual Hygiene Awareness Class

IFS Kerala Chapter in association with OG Society organised an awareness class on menstrual hygiene and menstrual disorders at Sai Snehatheeram tribal hostel, PERINTHALMANNA on 8th October 2019. Dr Kochu S Mani delivered the lecture on the importance of menstrual hygiene and its impact on future reproduction. About hundreds of students were attended the class.



**ACTIVITY 13**  
World Menopause Day

World Menopause Observance day was inaugurated by IFS Kerala Chapter Secretary, Dr. Kunjimoideen at ARMC Aegis Hospital, Perinthalmanna. In observation of World Menopause Day, a free medical camp on women's health and wellbeing was conducted by IFS Kerala

Chapter in association with ARMC AEGIS hospital, Perinthalmanna. The seminar was organised on the subject 'Reproduction after 40' and highlighted the proposed surrogacy bill etc. The medical camp was envisioned to raise awareness on the impact of menopause in women above 45 years of age. Bone Mineral density test, Ultrasound scanning and medicines are offered to the attendees free of cost.



IFS Kerala chapter has organised a CME on 'Care of ART pregnancy' on 17th November at Perinthalmanna in association with local OG Society. Profd Muralidhar Pai from KMC Manipal, delivered the lecture. There was a panel discussion on 'Case scenarios in ART Pregnancy' moderated by Dr Seneeshkumar and Dr Mumthaz. 88 delegates participated

**ACTIVITY 14**  
CME on Care of ART Pregnancy



# HARYANA



Chapter Secretary  
Dr. Neeru Thakral

Vision Statement : "Our main focus is on increasing Awareness about infertility and IFS ideology among Gynecologist as well as General population in Haryana."

### Executive Committee

- Secretary - Dr. Neeru Thakral
- Jt. Secretary- Dr. Shalu Gupta
- Treasurer- Dr. Priya Varshney
- Executive Members - Dr. Meenakshi Chauhan, Dr. Seema Mittal, Dr. Astha Chakravorty, Dr. Veenu Sangwan, Dr. Meenakshi Dua, Dr. Sonu Balara, Dr. Reema Goel



### ACTIVITY 1 Infertility Camps

For awareness among general public, we had organized infertility camps in rural areas. We have chosen two villages (Patoudi & faruknagar) in Haryana for this purpose.



### ACTIVITY 2 ME Organised on 10<sup>th</sup> Feb 2019 at REWARI

- conducted on 10th February at Golden Huts Resorts, Rewari.
- This fertility update well attended by more than 60 delegates. Update started with comprehensive talk by Dr. Sohani Verma on "Recurrent abortions". Quite Interactive Panel on Endometriosis & infertility moderated by Dr. Shweta Mittal & Dr. Neeru Thakral.
- Dr. Umesh Jindal from Chandigarh gave Fantastic talk on "Endometrial Receptivity". Lastly panel on Male infertility by Dr. Pankaj Talwar. He left no stone unturned in Demystifying Male infertility.

- Meeting was well covered by Press coverage like - Amar Ujala, DanikBhasker, DanikJagran. The academic activity was well organized & appreciated by all delegates.



### बांझपन के कारण और निवारण पर का चर्चा



from Spain to make it rich and satisfying experience for the delegates. It was an honour to have all stalwarts under one roof imparting the pearls of knowledge and wisdom and sharing recent updates & best clinical practices.

- Conference started with mesmerising panel discussion on "Azoospermia - What next" by Dr Pankaj Talwar and Dr Priya Varshney. It gave clear guidelines, how to proceed in these males and what all need to be done. Our international expert Dr Jose Miravat from Spain - unravelled the role of endometrium in successful implantation.
- Wonderful panel discussions were conducted on "Ovulation induction- Different Case Scenario" by Dr. Neeru Thakral and Dr Shalu Gupta. The discussion started from basic level to IUI then IVF cases so that every gynaecologist and beginners could understand do's and don'ts of ovulation induction. Final Key points were highlighted by our expert advisor Dr Sonia Malik.
- This was followed by plenary session with guest lecture by Dr Hrishikesh Pai on Testing and Editing of embryo followed by Key Note Address by Dr Alka Kriplanian Adenomyosis & infertility. Entire hall was spell bound by Presidential Oration by Dr Gouri Devi on Vision - Future of ART.
- Post lunch video session by Dr Kuldeep Jain and Dr Dinesh Kansal gave insight on Fertility Enhancing surgeries. It was followed by debate on need of the day by Dr Neena Malhotra from AIIMS and Dr Vikas Swarnkar from Jaipur on,

whether freeze all for all should be done or not. Dr umesh Jindal gave insight by her talk on unexplained infertility its management.

- Dr Sudha Prasad highlighted on Managing ART pregnancies and obstetrical complications. Dr Kuldeep Singh simplified the role of ultrasound in infertility. Lastely the ROLE PLAY and Expert Dr Abha Majumdar summarised about managing patients with recurrent implantation failure and medicolegal issues.
- IUI hands - On workshop was attend by almost 50 delegates and OPU & ET workshop ( Hands - on simulator) by 32 delegates. Dr. Shweta Mittal, Dr. Surveen Gumman, Dr Rashmi Sharma, Dr Ila Gupta, Dr Neeru Thakral guided delegates by giving tips on various steps. CME was awarded by SICOG credit point & 4 Haryana Medical Council credit Hours.
- Academic feast was appreciated by one and all.



### ACTIVITY 3 IFS Haryana Chapter Annual Conference 19<sup>th</sup> May 2019

- IFS Haryana Chapter First Annual Conference Superbly arranged on 19th May at Hotel Leela Ambiance. Conference was well attended by 360 infertility specialists & Gynaecologists from all over Haryana & Delhi NCR. Two hands on workshops (IUI and Ovum pick-up / Embryo transfer) along with free paper session.
- Conference was inaugurated by Dr. Satish Aggarwal ( DGHS Haryana ) & Guest of Honour Dr Smiti Nanda (HOD PGI Medical College Rohtak ) and CMO Dr B.K. Rajora.
- Academic session is backbone of any conference and our conference was academic bonanza with participation of almost all national faculty along with international speaker Mr. Jose miravat



### गुड़गांव : लीला एम्बियन्स में बांझपन पर कार्यशाला



### ACTIVITY 4 Round Table Meet Campus



### ACTIVITY 5&6 Two Camps at Patoudi & Farrukhnagar



## NORTH EAST



Chapter Secretary  
**Dr. Mujibur Rahman**

Vision Statement : "Taking Infertility treatment to every nook and corner of Northeast.....Making sure the benefits of recent advances in Reproductive medicine reach every one."

### Executive Committee

Secretary - Dr Mujibur Rahman  
Jt. Secretary - Dr Arpitasharma  
Treasurer - Dr. Diganta Chetia  
Executive Members -  
Dr. Diganta Deka, Dr. J.B. Bhattacharjee  
Dr. M. Belho, Dr. Clarindya,  
Dr. Pankaj Barua, Dr. F.R. Choudhury,  
Dr. Salim Ahmed

### ACTIVITY 1

The 1st CME was conducted in Hotel Lily in Guwahati

**Organising Secretary Dr. M.Rahman**  
The topic was Fertility preservation. The local cancer hospitals were involved in the CME with the Director B.Barooah cancer institute was made the chief guest. Around 50 delegates participated in the CME..There was active discussion with some case presentations. The Q&A session was very interesting with a lot of delegates coming up with lot of questions. There were speakers from Delhi and our General secretary Dr.Pankaj Talwar was the guest of honour.



### ACTIVITY 2

IUI Workshop was held on 22<sup>nd</sup> June in Dimapur, Nagaland

45 delegates participated in the hands on workshop. Dr M.Belho was the organising chairperson...speakers in the workshop included Dr Gouri Devi Dr Umesh Jindal, Dr Rupali Bassi, Dr M. Rahman.



On 27<sup>th</sup> of August an awareness programme on Reproductive health was conducted in Beltola college. DrM.Rahman addressed the girl students. Around 350 girls attended the programme. There was a Q&A session after the talk

### ACTIVITY 3

Another IUI Workshop was held on 23<sup>rd</sup> June in Kohima

20 delegates participated and there was a good discussion between the faculty and the delegates.



### ACTIVITY 4

Awareness Programme on Reproductive Health 27<sup>th</sup> August



## GUJRAT



Chapter Secretary  
**Dr. Jayesh Amin**

Vision Statement : "To Increase the No of IFS Members from Gujarat and Provide Qualitative Academics and Learning programme to the Fraternity."

### Executive Committee

Secretary - Dr Jayesh Amin  
Jt. Secretary - Dr Nimesh Shelat  
Treasurer - Dr. Paresh Makawana  
Jt. Treasurer - Dr. Hitendra Somani  
Executive Members -  
Dr Sanjay Desai, Dr. Minesh Prajapati, Dr. Divyang Kadakiya, Dr. Bharat Thakkar, Dr. Bhavin Prajapati, Dr. Jaya Goyal, Dr. Shailendra Rathod, Dr. Nila Mehta, Dr. Ravindra Khorat, Dr. Amit Kalyani, Dr. Paresh Patel

### CME on Medical Advances in Infertility

8<sup>th</sup> Sep 2019 at Hotel Starotell, Ahmedabad - Meyer-IFS Initiative



## MADHYA PRADESH



Chapter Secretary  
**Dr. Monica Singh**

Vision Statement : "To start an initiative to tackle infertility in couples by offering evidence based medicine at an affordable cost"

### Executive Committee

Chapter secretary – Dr Monica Singh  
Jt Secretary - Dr Anju Verma  
Treasurer- Dr Asha Jindal  
Executive Members -  
Dr Viraj Jaiswal, Dr Abha Jain,  
Dr Archana Srivastava,  
Dr Manju Rathi, Dr Sunita Pandey,  
Dr Yatinder Verma, Dr Gajender Tomar

### ACTIVITY 1

JAN 2019: Flag hosting-cultural programme, Free Camps – Sehore, Raisen



### ACTIVITY 2

MARCH: CME with BOGS : Endometriosis



### ACTIVITY 3

MAY: CME –with BOGS ; Male Factor



### ACTIVITY 4

JUNE : Work-Shop- IUI With BOGS



ACTIVITY 5  
JULY:Free Camp  
Ashok Nagar

### ACTIVITY 6

Aug: Green Planet-Plantation Drive / Flag Hosting- Independence Day



### ACTIVITY 7

Organ Donation Day Motivation ( 11/08/19)



### ACTIVITY 8

Every Month on 09<sup>th</sup> PMSMA:IFS-IMA- Members Participate



PUNJAB



**Chapter Secretary**  
**Dr. Harinder Kaur Oberoi**

**Vision Statement :** "Core value IFS -Punjab Chapter believe that everyone you meet daily knows something that you don't, hence regular meetings and interaction spreads knowledge and make you wiser than you were on the previous day. The other priority of our organization would be to mass aware the public about the fertility fears, myths and facts through our regular community activities.

**Moto - Regular workshops, CMEs and meetings are arranged so that knowledge is shared and spread."**

**Executive Committee**

**Secretary - Dr Harinder Kaur Oberoi**

**Jt Secretary - Dr Sukriti Bansal**

**Treasurer - Dr Sarabjeet Singh**

**Executive Members**

- Dr Sarabjit
- Dr Jaslin
- Dr Sukriti
- Dr Monika verma
- Dr jasmine dahiya
- Dr Anupama Chopra
- DrRitu nanda

**ACTIVITY 1**  
IUI work shop on 28<sup>th</sup> April 2019 at Jalandhar

Under the expert guidance of our esteemed leadership of IFS general secretary and president Dr Gauri Devi madam, IFS Punjab chapter conducted Annual conference on Fertility Concepts at Jalandhar and IUI work shop on 28th April 2019. For the conference and IUI work shop honorable Punjab Medical Council granted us 8 credit hours. Worthy Speakers from Delhi Dr Pankaj Talwar highlighted on 'ultrasound in infertility "Dr Neena Malhotra gave deliberation On optimization outcome in poor responders " Dr Sonia Malik through light on "ovulation induction in obese Pcos and Nonpcos ". DrUmesh Jindal very well discussed "Trouble shoots in OPU and embryo transfer". DrAloksharma from Shimla threw light on Endometriosis updates "DrArunArora from Jammu highlighted on pearls of wisdom in treating infertility with out ivf". mDrHarinderKaurOberoi discussed latest tips on ' Repeated implantation failure " "Solving mystery of thin endometrium " was dealt by DrRimmy from Chandigarh. Many points on" practical dilemmas in infertility management " were discussed by experts panelists. One more panel on Tips and Tricks in achieving faster success rate in infertility management " discussed in detail. Efforts of IFS Punjab chapter appreciated and applauded by faculties and all the delegates. They learnt many newer advances in management of ART.

**ACTIVITY 2**  
CME - 16<sup>th</sup> of June 2019 at Ranjit Avenue Amritsar

IFS Punjab chapter organized a CME in collaboration with sun pharma on 16th of June 2019 at Ranjit Avenue Amritsar from 11am to 3pm. List of organizing committees Dr Harinder Kaur Oberoi, Dr Sarabjeet, Dr Archana Berry, Dr Jyotsna. Name of speakers Dr C Nagori, Dr Sonal Panchal from Ahmedabad, Dr Jyotsna and Dr Sarabjeet Singh Worthy speaker Dr C Nagori highlighted on "Role of progesterone in luteal phase defect" Dr Sonal Panchal discussed on " Sonoendocrinology" Dr Sarabjeet delivered lecture on diagnosis of PCOS Dr. Jyotsna Gupta highlighted on chromosomal defect by sonograph. All topics were very interesting and informative. All lectures appreciated and applauded by faculties and all the delegates of Amritsar.

**ACTIVITY 3**  
Conference on Infertility Updates & ART Workshop 22<sup>nd</sup> September 2019 at Harpal Tiwana Hall at Patiala

IFS Punjab chapter in association with POGS organized a conference on infertility updates and art workshop on 22<sup>nd</sup> September 2019 at Harpal Tiwana hall at Patiala. Organizing Committee - chairperson : Dr Harinder kaur Oberoi and Dr Sarita Agrawal Organizing Secretary: Dr Monica Verma & Dr Ranjana Joint Organizing Secretary: Dr Sarabjit, Dr Shalini and Dr Sarabpreet Singh Workshop Coordinator : Dr Deepa Goel, Dr Sukriti and Dr Jaslin Guest Speakers: Dr K D Nayar, Dr Surveen Ghuman, Dr Umesh Jindal, Dr Shweta Mittal, Dr Sarabpreet Singh, Dr Lakhbir Dhaliwal, Dr Sarla Malhotra, Dr Manjit Mohi, Dr Shalini Gaidher, Dr Lovleen Sodhi. 215 delegates and 35 faculty members attended the conference, 80 attended the Hysteroscopy work and 25 attended the OPU and ET workshop. This was wonderful gathering from all over North. Topics and discussion were excellent with good interactions. Punjab medical council granted 4 CME hours. There was a good panel discussion which was appreciated by audiences and faculty members Topics- free papers, unexplained infertility, panels on fibroids and male infertility, PGD In aneuploidy, ovulation induction , first trimester treatments of IVF pregnancy, pregnancy in art and workshop on Hysteroscopy, OPU and embryo transfer, vitrification and cryobiology workshop were discussed in detail. Panels and Hysteroscopy workshop Appreciated by delegates Whole conference was enjoyed and applauded by all the faculty and delegates.



**ACTIVITY 4**  
CME on 1<sup>st</sup> Navrata day at Jalandhar Hotel Ramada encore conducted on 29<sup>th</sup> Sept 2019

Shivani meeting with IFS Punjab chapter conducted a CME on 1st Navrata day at Jalandhar, Hotel Ramada encore, conducted on 29<sup>th</sup> September 2019 from 9 to 2pm. 40 delegates participated including Embryologist Attendance good with good discussion and exchange of views. Very good informative and interactive topics



**ACTIVITY 5 & 6**  
2 Camps Organized

S.no.	Date	Venue	Patients Seen
2.	Oct 2018	Sultanpur Lodhi	106
3.	March 2019	Basti Sheikh Jalandhar	50



**Dr Monica Verma from Punjab Chapter IFS presented a poster at ESHRE 2019**

Higher risk of preeclampsia in singleton pregnancies from donor versus autologous oocytes, with similar endometrial preparation, in a healthy, young cohort: a prospective study" She had also suggested seven points for the ESHRE 2019 Guidelines for Good Practice Recommendations for Ultrasound in ART: Oocyte Pick-up and all 7 were accepted in the final guidelines. Her name is in the Reviewers List of these guidelines



# RAJASTHAN



**Dr. Sangita Sharma**  
Chapter Secretary

**Vision statement :** "Strengthening the chapter by increasing the number of members. Aim of increasing awareness on infertility issues Updating on recent evidence based approaches . Benefiting the society by planning awareness programmes (eg PCOS in schools/colleges) and free OPDs (eg in rural areas) Strengthening Embryology part in the state."

**Executive Committee**

**Patron :** Dr. M. L. Swaankar  
**Advisors :** Dr. Neela Baheti, Dr. Sanjay Makwana, Dr. Namita Kotia  
**Secretary -** Dr. Sangita Sharma  
**Joint Secretary -** Dr. Nidhi Kabra  
**Treasurer -** Dr. Hemant Chakarwarty  
**Executive Members -** Dr. Usha Shekhawat, Dr. Narendra Gupta, Dr. Anita Sharma, Dr. Sunita Yogi, Dr. Sapna Basandani, Dr. Harpreet Bajwa, Mr. Rahul K Sen

**ACTIVITY 1**  
CME on "Updates on Embryology"  
(30<sup>th</sup> March, 2019 at Jaipur)

Attended by 40 Clinicians & Embryologists.  
First Talk : Trouble Shooting in IVF lab : Different Case Scenarios by Dr Sangita Sharma.  
Second Talk : Evidence on Newer Technologies in IVF Lab by Dr. Rahul K Sen, Senior Embryologist, Jodhpur



Haji Milan & A Focused CME on "Updates on Embryology"  
Date & Place - 30<sup>th</sup> March, 2019; Jaipur  
Attendance - 40 clinicians & Embryologists.  
First Talk : "Trouble Shooting in IVF Lab : Different Case Scenarios", by Dr Sangita Sharma.  
Second talk : "Evidence on Newer Technologies in IVF Lab" delivered by Dr Rahul K Sen, Senior Embryologist, Jodhpur.

**ACTIVITY 2**  
RTM of IFS Rajasthan Chapter

Agenda : Discussion on PCPNDT issues and different forms (After FOGSI lost the case regarding PCPNDT issues in Supreme Court)  
\* 8.04.2019, Jaipur \* Attended by 14 members of IFS.

**ACTIVITY 3**  
RTM - Recent Updates in Management of PCOS  
(16 May 2019 at Jhunjhunu)



Attended by 20 Doctors from Jhunjhunu, Pilani, & Chairawa

**ACTIVITY 4**  
Infertility Awareness & Free Consultation Camp & Talk ( 16<sup>th</sup> May 2019 at Jhunjhunu)



Attended by 21 Patients

**ACTIVITY 5**  
CME on Updates on Ovulation Induction  
(26<sup>th</sup> May 2019 at Jaipur)



CME on "Updates on Ovulation Induction" (Jaipur) ; 26<sup>th</sup> May 2019  
Attendance - 100  
Guest Faculty :  
Dr. K. D. Nayar (Role of Recombinant LH in Ovarian Stimulation) and Dr. Neeru Thakral (Unexplained Infertility: Etiology or IVE) and one panel discussion on Different situations in ovulation induction moderated by Dr Neeru Thakral.  
Local Faculty :  
Dr Sangita Sharma (Investigations and Evaluations before Ovulation Induction) and Dr Namita Kotia (Individualised Controlled Ovarian Stimulation icon)

**ACTIVITY 6**  
CME on Updates on Ovulation Induction  
(26<sup>th</sup> May 2019 at Jaipur)



CME : 26.05.2019 (Jaipur)  
Topic : Male Infertility and DNA Fragmentation Index  
First talk : Overview on Male Infertility : from guidelines to clinical practice', (Dr Sujatika Mangal from Jaipur ).  
The Guest Speaker : Dr Sayali Kandelari (Mumbai), Her talk was : First Clinical Study of India on the effect of Medical Therapy on Sperm DNA Fragmentation and Improved Clinical Pregnancy Rates'. (Recently presented in ESHRE 2019)  
It was attended by about 30 Gynaecologists and Embryologists

# WEST BENGAL



**Dr Suparna Banerjee**  
Chapter Secretary

**Vision Statement :** "To increase awareness of infertility problems and early referral of those couple to specialised fertility clinic. Increase IFS members in west Bengal"

**Executive Committee**

**Secretary :** Dr Suparna Banerjee  
**Jt Secretary:** Dr Piya Ray  
**Treasurer:** Dr Kausiki Ray  
**Executive members :** Dr Rohit Gutgutia, Dr Debashree Ganguly, Dr Madhumita Roychowdhury, Dr Sudip Basu, Dr Madhab Das, Dr Aindri Sanyal, Dr Sunita Sharma

**ACTIVITY 1**  
TVS Workshop - March 2019

- Attended by 10 PG students, 2 junior gynae practitioners, one senior gynaecologist.
- Encouraged juniors to become life members and informed the training courses organised by IFS.

**ACTIVITY 2**  
Round Table Meet - April 2019

- Core committee members
- Plan for regional conference
- Plan for public awareness programme
- Plan for regular update programme and journal club

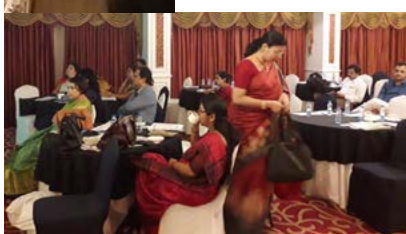
**ACTIVITY 3**  
Regional Conference- July 2019

Chief guest was Dr BN Chakraborty, we felicitated him. Our guest speaker was Dr Vineet Malhotra . Our whole team was present with all the fertility specialist from Kolkata were present along with many eminent Gynaecologists of Kolkata were present. IUI workshop was a hit among our junior colleagues.



**ACTIVITY 4**

Meyer IFS Initiative 29th September Inauguration and lamp lighting was done along with Rabindra Sangeet The meeting was blessed by Geeta Ganguly a very senior Colleague of Prof BN Chakraborty Speakers were renowned Gynaecologists of Kolkata  
Dr Kaushiki Ray Dr Indrani Lodh Dr S. Chatterji Dr SM Rehman Dr Mamta Dighe from Pune



# UP (EAST)

**Executive Committee**

**Chief Patron -** Dr Chandrawati  
**Secretary -** Dr Renu Makker  
**Jt. Secretary -** Dr Surheeta Kareem  
**Treasurer -** Dr Manju Shukla  
**Executive Council :**  
Dr Malvika Mishra, Dr Geeta Khanna  
Dr Sunita Chandra, Dr Amita Pandey  
Dr Yogesh Khanna, Dr G C Makker



**Dr. Renu Makkar**  
Chapter Secretary

**Vision Statement :** "To engage and involve gynecologists of UP in understanding importance of infertility management and management of ART pregnancies To develop simple protocol system for investigation, diagnosis and management of infertile couples in a structured manner in order to save time and energy, reduce time to pregnancy and financial burden."





# UP (WEST)



**Dr. JK Goel**  
Chapter Secretary

**Vision Statement :** "To create awareness among the general masses. Bridging up the gap between general public and professionals. Promote a forum for the exchange of ideas and information.

To update the knowledge and skill of health professionals through continued medical education, by organizing workshops, conferences and CME's on regular basis. To promote and grant recognition to research in the field of ART. To make IFS Chapter visible to common mass of the state."

**Executive Committee**

- Secretary- Dr J K Goel
- Joint Secretary - Dr Neera Agrawal
- Treasurer - Dr Ruchica Goel
- Executive Council :
- Dr Lata Agrawal, Dr Nutan Jain
- Dr Poonam Goyal, Dr Anshu Jindal
- Dr Shashi Bala Arya, Dr Jyoti Bhaskar
- Dr Shashi Singh

**ACTIVITY 1**  
Infertility Summit 2019- 24<sup>th</sup> February 2019

Attended by around 120 delegates from different parts of Uttar Pradesh and Uttarkhand.



**ACTIVITY 2**  
Setting up an ART Lab- 21<sup>st</sup> April 2019



**ACTIVITY 3**  
Fertimed 2019

A CME cum Workshop on "FertiMed" 2019 with the theme 'optimizing infertility management' was organized by Department of Obstetrics and Gynecology, Teerthanker Medical College, Moradabad on 20th October 2019 under the aegis of IFS Western UP Chapter.

This prestigious event was inaugurated by Dr. Neena Mohan, senior most President, Moradabad Obstetrics and Gynaecological Society. It was graced by renowned Obstetrician & Gynecologist from Aligarh, Meerut, Bareilly, Noida, Haldwani and Moradabad. Huge spectrum of topics were discussed like follicular monitoring, present status of IUI, setting up IUI lab, luteal phase support in IUI, optimizing its results, and when to stop IUI and think of IVF, ICSI, endometriosis & infertility, ovarian rejuvenation so that all can be benefitted starting from general practitioners, post graduates, practicing gynecologists and faculty in various medical colleges.

Dr. J.K.Goel enlightened the audience about the medicolegal & ethical aspects of ART. The event had panel discussions on Ovulation Induction Protocols and Male Subfertility. A hands on workshop on IUI-tips and tricks was conducted by Dr. Kanthi Bansal, Dr. Mukesh Bansal and team, renowned IVF specialist from Ahmedabad.

The response was very heartening and overwhelming. Around 110 delegates from various places of Uttar Pradesh and Uttarakhand attended the CME. Feedback from delegates was very positive and complimentary on both professional and administrative arrangements



**Outreach Activities :** Regular out station IVF Camps organised by Deptt of Obs&Gynae, SRMSIMS (2019)

- 22/1/2019- Rudrapur
- 19/2/2019- Pilibhit
- 26/3/2019- Badaun
- 27/3/2019- Sambhal
- 8/5/2019- Badaun
- 4/5/2019- Pilibhit
- 19/6/2019- Ujhani
- 10/7/2019- Bisoli
- 23/7/2019- Rudrapur
- And many more to come...

**Research Projects**

- Role of Real Time PCR to diagnose Genital Tuberculosis in infertile women- concluded that the role of Real Time PCR is not very certain in diagnosis of Genital Tuberculosis in infertile women.
- Ultrasonography and Doppler study to predict uterine receptivity in infertile patients undergoing embryo transfer- on going project.
- Study of sperm morphology and motility using Strict criteria as a prognostic factor in Intrauterine Insemination- on going project.

# CHATTISGARH



**Dr. Sangeeta Sinha**  
Chapter Secretary

**Vision statement :** "Aim is to disseminate Basic and Advanced Knowledge, Stimulate Research and Encourage Best Clinical Practice in field of infertility and reproductive medicine. Training the doctors at periphery, general practitioners and junior doctors. Public awareness programmer to be done. Increase membership"

**Executive Committee**

- Patron - Dr. (Prof) Abha Singh
- Secretary - Dr. Sangeeta Sinha
- Joint Secretary - Dr. Veronica Yuel
- Treasurer - Dr. Prakriti Verma
- Executive Members
- Dr. Vijaya Wakodkar, Dr. Palak Gawri
- Dr. Neeraj Pahlajani, Dr. Sushma Verma
- Dr. Anuradha Tiberewal,
- Dr. Jyoti Jaiswal, Dr. Nalini Madharaia

**ACTIVITY 1**  
Reaching The Outreach

Adopting two villages will be the doing free check up of infertile patient on monthly basis



**ACTIVITY 2**  
Social Contribution

Dr Manoj Chelani our Founder Secretary is doing free check up once a month. Dr Veronica Yule our Joint Secretary is doing free checkups



**ACTIVITY 3**

Awareness programme for general practitioner-**Knowledge sharing activity** is done every month in collaboration with The Srijjan Bhilai Test Tube Baby Center



**ACTIVITY 4 : PCOS Awareness Programme**

PCOS awareness programme under the aegis of IFS C.G chapter at THE Srijjan Bhilai Test Tube Baby Center on 15<sup>th</sup> April 2019

*The Srijjan Bhilai*  
FREE SEMINAR  
ON  
PCOS AWARENESS  
(POLYCYSTIC OVARY SYNDROME)

Everything you need to know about PCOS and Diet weight Management brought to you by The Srijjan Bhilai Test Tube Baby Center.

Topics to be covered on Seminar by our Experts:

- Symptoms of PCOS
- Tips to lose weight while PCOS
- Exercise to do on PCOS
- Diet Plan for PCOS

DATE: 15<sup>th</sup> APRIL 2019    TIMING: 11:00 AM TO 02:00 PM

**ACTIVITY 5**  
Training

Adopting two villages will be the doing free check up of infertile patient on monthly basis



# UTTARAKHAND

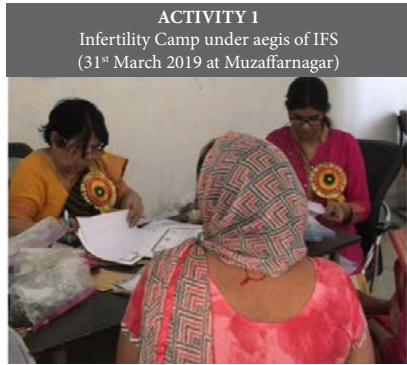


**Dr Anupama Bahadur**  
Chapter Secretary

**Vision Statement :** "Conduct CMEs: to train doctors & paramedical staff. Conduct Conferences: to update knowledge of recent advances in infertility Organize Awareness Camps for patients in remote regions of Uttarakhand to start investigations early"

**Executive Committee**

**Patron -** Prof Jaya Chaturvedi  
**Advisor -** DrSavitriUniyal  
**Secretary -** DrAnupama Bahadur  
**Joint Secretary- Dr** Latika Chawla  
**Treasurer- Dr** Ritu Prasad  
**Executive Members :**  
Dr Sumita Prabhakar,  
Dr Vinita Gupta, Dr ArchanaTandon,  
Dr Arti Marwah Luthra, Dr Usha Joshi,  
Dr Vandana Grover, DrAditiGutpa



Dr Pankaj Talwar Secretary General IFS, Dr Sumana Gurunath, Bengaluru, Dr S.M Rahman, Kolkatta, Dr Aditi Gupta, Haridwar, Dr Arti Marwah Luthra, Dehradun, Dr Chitra Joshi, HOD Doon Medical College, DrRitu Prasad Senior Consultant IVF, Rishikesh, Dr Archana Tandon Associate Professor SGRR Dehradun

Poster presentation by Junior Residents from AIIMS Rishikesh, SGRR Dehradun & Himalayan Hospital well appreciated by Judges



**ACTIVITY 3**  
Annual CME at Seyfert Sarovar  
6th October, 2019 in Dehradun (Uttarakhand)

Annual CME at Seyfert Sarovar Premiere on 6th October, 2019 in Dehradun, Uttarakhand on "Optimization of Ovarian Stimulation". It was jointly inaugurated by the National Coordinator of IFS, Dr. Leena Wadhwa, Dr. Shweta Mittal, Dr. Neeti Tiwari and Dr. Anupama Bahadur

# KASHMIR

**Dr Sayed Sajjid Hussain**  
Chapter Secretary



**Vision Statement :** "Our Vision is to support and facilitate the process of conception through Assisted Reproductive Technologies (ART) for couples facing infertility

and to promote interest in research findings in human reproduction and embryology to the concerned doctors.

**Mission:** The mission of IFS Kashmir Chapter is to make the ART (Assisted Reproductive Technology) affordable & accessible to every infertile couple of J&K State at their door steps with quality expertise to achieve positive outcome."

**Executive Committee**

**Patron -** Prof (Dr) ShahnazTeng  
**Advisor -** Prof (Dr) Aabida Ahmed  
**Spokesperson- Dr.** Samiya Mufti  
**Executive Body**  
**Jt. Secretary -** Dr. Ambreen Qureshi  
**Treasurer -** Dr. Gulshan Ara  
**Executive Council -**  
Dr. Samiya Mufti, Dr. Masooda Shah,  
Dr. Zohra Bano, Dr. Kripal Kour,  
Dr. IramShafi, Dr. Sajada Tak,  
Dr. Zeenat u Nisa



# NEPAL



**Dr Rashmi Shirish**  
Chapter Secretary

**Vision Statement :** "We hope to do public awareness camps , Andrology and ultrasound workshops and more CME this year..we are proud to be a part of academically rich IFS.."

**Executive Committee**

**Patron -** Dr Rita Bakshi  
**Advisor -** Dr Uma Srivastav  
**Secretary -** Dr Rashmi Shirish  
**Jt Secretary -** Dr Mira Thapa  
**Treasurer -** Dr Swasti  
**Executive members -**  
Dr Girdhari , Dr Pradeep Srivastav  
Dr Rajesh Adhikari, Dr Da lucky  
Dr Nutan, Dr Chetana, Dr Nikita  
Dr Sangeeta Chakravarty

Annual CME at Pokhara on 29th March 2019

IFS Nepal Chapter hosted their Annual CME at Pokhara on 29th March 2019. IFS were represented by the treasures Dr. Neena Malhotra prof. AIIMS &Dr. Rita Bakshi - Patron of the IFS Chapter Nepal.

Pokhara has around 50 gynecologists and we are glad to inform our turned out was around 50 with a few doctors from Kathmandu, Butwal and Biratnagar also. In fact according to Pokhara doctors it was a rare day with nearly all doctors except a few on Call/ Duty not attending.

1. Dr. Uma Srivastava - History of IVF in Nepal
2. Dr. Kanchan Prasad - Asst. Prof. TMMC Moradabad spoke on Genital Tuberculosis.
3. Dr. Rita Bakshi - Patron IFS Nepal Chapter spoken unexplained infertility.
4. Dr. Neena Malhotra - Prof. AIIMS Ovulation Induction followed by
5. Dr. Asma - Fibroids & Endometriosis in infertility

IUI workshops were attended by the entire 50 gynecologist and practical demonstration of Sperm Washing & IUI procedure was done. 8 out of 50 people became IFS members there itself and also paid up.



PANEL on Male Infertility Moderators  
Dr. Rita Bakshi, Dr. Kanchan Prasad



# JHARKHAND



**Dr. Archana Kumari**  
Chapter Secretary

**Vision Statement :** "To make the state of art infertility treatment services to people of Jharkhand so that they don't need to move to Metro cities, thus preserving their valuable time and money. Also, to create awareness about fertility services outreaching every district of Jharkhand."

**Executive Committee**

- Patron – Dr Karuna Jha  
Secretary - Dr. Archana Kumari  
Joint Secretary - Dr. Sunita Jha  
Treasurer - Dr Rupashree Purshottam  
Executive Members -  
Dr. Anubha Vidyarthi,  
Dr. Nirmalasingh, Dr. Puja Rani,  
Dr. Jyoti Gupta, Dr. Kaushik Das,  
Dr. Rupashkehar, Dr. Sashibala

**ACTIVITY 1 : IUI Workshop**  
12.08.2019/Hotel Capitol Hill, Ranchi

**Guest Speaker :** Dr (Col) Pankaj Talwar, Delhi, Dr Suparna Banerjee, Kolkata  
The pleasant cloudy weather in the holy month of Sawan on 12th August, 2019, Monday, witnessed the 1st annual conference of IFS Jharkhand Chapter, exactly one year after the formation of Jharkhand Chapter on 11th August 2018. The conference started with welcome address by Patron Jharkhand chapter, Dr. Karuna Jha and traditional lamp lighting by the dignitaries. It was followed by Secretary general IFS Dr Pankaj Talwar report where he presented the mission and vision of IFS, the outreach programme, the academic calendar of IFS for 2019-2020, various courses conducted by IFS and about FERTIVISION -2019. Half day live workshop on intrauterine insemination was conducted by infertility stalwart Dr Pankaj Talwar. Live demonstrations of semen analysis and various semen preparation methods was very informative as well as interactive. A detailed discussion on semen analysis (WHO 2010) and male factor infertility by Dr. Pankaj Talwar kept the audience mesmerized. Dr. Suparna Banerjee, secretary IFS Bengal chapter, discussed evidence based practices in IUI and tricks to improve the success rate in IUI. Both the sessions were very interactive and held the utmost attention of the audience. A case based panel discussion on secondary subfertility was moderated by Dr. Archana Kumari,

Dr. Sunita Jha being the co-moderator. Panelists were infertility specialists of Ranchi-Dr. SashiBala Singh, Dr, Nirmala Singh, Dr. Rupashree Puroshotam, Dr. Sakshi Singh. Expert inputs were made by Dr. Karuna Jha and Dr. Pankaj Talwar. The programme ended with vote of thanks proposed by Dr. Archana Kumari, Secretary Jharkhand Chapter.  
Around 70 delegates attended the workshop which included the postgraduates students from Rajendra Institute of Medical Sciences, Ranchi

**Learning Point:**

1. Clinical understanding of Semen analysis (WHO-2010), male factor infertility.
2. Methods of semen preparation for IUI
3. Evidence based practice in IUI.

**Comment from audience:**

"A very interesting and captivating workshop which gave everyone a chance to understand the very basis of IUI and semen analysis".....Dr. Suman Sinha  
"A new insight to old topic" .....Dr. Soumya Sinha  
Very helpful for newcomers in the field of infertility especially who wish to start IUI setup.... Dr. Reena Godara

**Comment from faculty :**

A very enthusiastic audience and in such large number with active participation in all sessions, gives the reason to promote many such basic workshops in future and give Jharkhand more importance in academic activities of IFS in future... Dr. Pankaj Talwar



# WEST MAHARASHTRA



**Dr. Mamta Dighe**  
Chapter Secretary

**Vision Statement :** Making quality Reproductive Medicine and IVF training available to Gynaecologists, along with training Postgraduates and creating awareness regarding increasing burden of infertility .

**Executive Committee**

- Secretary- Dr. Mamta Dighe  
Jt Secretary- Dr Nikita Naredi  
Treasurer- Dr Shebaaz Daruwala  
Executive Members :  
Dr Bharati Dhorepatil, Dr Nitin Lad  
Dr Kishore Pandit, Dr Jyotsana Daule,  
Dr Anjali Patil, Dr Bushra Khan

**ACTIVITY 1**  
Annual Conference of Western Maharashtra Chapter of IFS, 13<sup>th</sup> and 14<sup>th</sup> July 2019 at Hotel Hyatt, Pune

Attended by over 350 delegates 100 eminent faculty from all over the Nation 2 orations, Ssmile IVF Oration by Dr. Jatin Shah and Xenith IVF Oration by Dr. Firuz Parikh  
**4 targeted workshops-**  

- Ovulation Induction and COH
- IUI and IVF Lab setup
- Male Infertility and IUI
- Recurrent Implantation Failure

 Panel discussions were held on various topics such as USG in Infertility, Endometriosis, Management of PCOS, etc, which had a very interactive discussion. The Chief Guest was Prof Rekha Diwekar, Prof of Chemistry and well known Nutritionist. She spoke on Diet and Fertility and the impact food can have on increasing infertility. The program was highly appreciated and the faculty was extremely well chosen and were authorities in their field. It was a crisp, completely academic focused conference with precise take home points for the delegates.

**ACTIVITY 2**  
IFS WMC organized Masterclass on Infertility for the Post graduate students

The intention was to expose the postgraduate students to practical infertility practice.  
Four modules were created,  

- Female Infertility,
- Male Infertility,
- Controlled Ovarian Stimulation and IUI
- IVF and Recent advances.

 Lectures and in depth discussions on all aspects right from Pathophysiology to work up and management were discussed.  
The highlight of the sessions, were the Panel Discussions, which had the postgraduates participate as panelists and a senior faculty presided as the Expert. The students enjoyed the active participation and got the opportunity, to participate and experience as panelists.  
ACTIVITY 3 Practical session on Laboratory aspects of Semen Analysis and Semen Preparation taken at IVF Centre, Armed Forces Medical College.  
Over 40 participants attended and all practical tips and methods were taught to them.  
CMEs are planned in January and February in Pune and nearby cities like Ahmednagar and Nashik.



# ANDRA PRADESH

**inauguration of 27<sup>th</sup> chapter of IFS Andra Pradesh Chapter on 22<sup>nd</sup> Sept 2019 at Hotel Fortune Murali Park at Vijayavada.** Chief guest Dr Gouri Devi and guest of honor Dr Roya Rozati were present. The secretary Dr Usha Prasad, joint secretary Dr P Jayanthi and treasurer L Shalaja organized the CME



**Dr. Usha Prasad**  
Chapter Secretary

**Vision Statement**  
To make state of art infertility treatments accessible to the poor and unreached

**Executive Committee**

- Secretary- Dr Usha Prasad  
Jt Secretary- Dr Potharaju Nalluri  
Treasurer- Dr Sailaja Nalluri  
Executive Council : Dr Ganti Ratna,  
Dr P Himabindu, Dr J.Sowjanya Kumari,  
Dr Paidi Durga Kumari, Dr Rekha,  
Dr Deepthi Shalini, Dr Ravella Sowjanya



# KARNATAKA



**Dr Divyashree PS**  
Chapter Secretary

**Executive Committee**

- Secretary – Dr Divyashree P S  
Jt Secretary – Dr Vyshnavi A Rao  
Treasurer – Dr Chandrika Kulkarni  
Executive Members  
Dr Mangala Devi, Dr Jyothi Patil  
Dr Chaitra Naik, Dr Rekha Rajendra  
Dr Yogita Rao, Dr Mir Jaffar,  
Mr Hemanth Kumar

**ACTIVITY 1**

- CME on Luteal phase support on 24/03/2019
  - Original research presented : 2
1. The prognostic value of endometrial receptivity array in women with RIF – Dr Divyashree P S
  2. Triple stimulation vs conventional stimulation for embryo pooling : to optimise IVF outcome in poor responders- Dr Shrayya T. External faculty : Dr Raju Nair from Kerala. Total number of faculty: 11. Total number of delegates: 43

**ACTIVITY 2 :**

- CME on Setting up ART Lab/Clinic on 19/05/2019  
Original research presented : 2
1. PGS - 2 studies, the learning so far- Dr Gautham T Pranesh
  2. Does PGT-A impact live birth rate and reduces time to pregnancy in RPL - Dr Ashwini Karjol
- External faculty : Dr Nympha Walecha. Total number of faculty: 10  
Total number of delegates: 64

**ACTIVITY 3 \***

- CME on Implantation on 28/07/2019 \* Original research presented : 2
1. Obstetric complications and neonatal outcomes in donor egg IVF vs self egg IVF vs Natural conception – Dr Rinki Tiwari
  2. Comparison of clinical outcome of IVF cycles with or without PGT – A, A

prospective case control study- Dr Sumi Maria

- External faculty : Dr Ruma Satwik, Delhi • Total number of faculty: 10 • Total number of delegates: 77

**ACTIVITY 4**

- CME on Practical tips to Ovarian stimulation on 29/09/2019 • Sponsored by Cipla Pharmaceuticals • Original research presented : 2 • External faculty : Dr Sachin Kulkarni, Kolhapur • Total number of faculty: 11 • Total number of delegates: 70



The ultimate cover ...  
in times of  
Reproductive needs

With

# Vitacover<sup>TM</sup> Gold

Treat infertility & other Gynaecology Complication

## In male infertility

**CoQ10** Available as **Trans CoQ10** form

- Improves sperm count, functional sperm concentration, motility & morphology

Indian J Urol 2001;18:57-61

**Methylcobalamin** administration increases

- Sperm concentration 38.4%
- Sperm count 53.8%
- Sperm motility 50.0%

Methylcobalamin enhances the testicular functions, resulting in a increased output of motile sperm.

Ref.: Isoyama R, KAWAI S, Shimizu Y et al. Clinical Experience with Methylcobalamin for male infertility. Hinyokika kiyo 1984;30:581-586



CoQ10	100 mg
Lycopene 6%	10000 mcg
Methylcobalamine	500 mcg
Vit C	100 mg
Niacinamide	50 mg
Vit B1	10 mg
Vit B2	10 mg
Vitb 6	3 mg
Calcium Pantothoate	12.5 mg
Folic Acid	1 mg
Vit A	5000 I.U
Vit D3	500 I.U
Vit E	25 I.U
Zinc Oxide	15 mg
Cupric Oxide	2.5 mg
Sodium Selenate	60 mcg
Mangnese Chloride	1.4 mg
Chromium Chloride	65 mcg



**Infertile couple**

**Male Infertility**

**Prostate Cancer**

**Pre-eclampsia & IUGR**

**Uterine Fibroid Tumours**

**Habitual & Spontaneous Abortion**

Tackles complicated conditions .... naturally