# International Human Research Academy

# EMBRYO CHAT

## "COMMUNICATION"

JANUARY 2025
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## Topic of Discussion

# "Factors that influence the decision-making process for insemination methods – ICSI / IVF"

**CHAT DISCUSSIONS COMPILED BY**


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# SUMMARY OF SURVEY RESULTS

**By Team Ihera**

## *Factors that influence the decision-making process for insemination methods – ICSI / IVF*

### *Introduction:*

### IVF (InVitro Fertilization) and ICSI (Intracytoplasmic Sperm Injection):

IVF and ICSI are advanced techniques that fall under assisted reproductive technologies (ART) that are utilised to address infertility issues. IVF is widely used to treat infertility caused by female factor, tubal factor, and unexplained infertility [1]. ICSI is a technique designed to introduce a single spermatozoon into the oocyte mechanically and has successfully improved fertilisation rates in the presence of low sperm parameters [2]. The development of ICSI was driven by the need to resolve severe male factor infertility, where bypassing natural Fertilization was essential [3]. Comparative studies have highlighted no significant differences in fertilisation, embryo development, pregnancy, or live birth rates when ICSI was unnecessarily favoured, leading to ongoing debates between clinical practice and evidence [4].

### What are the indications for IVF and ICSI based on guidelines & thorough research insights:

| Indications for IVF [5] | Indications for ICSI[6] | NON ICSI Indications[6] |
|---|---|---|
| ➢ Tubal Factor | ➢ Severe Male Factor Infertility | ➢ Non-Male Factor Infertility |
| ➢ Endometriosis | ➢ Prior Failed Fertilization with IVF | ➢ Poor-Quality Oocytes |
| ➢ Ovulatory Dysfunction | ➢ Pre-Implantation Genetic Testing (PGT) | ➢ Advanced Maternal Age |
| ➢ Unexplained Infertility | ➢ In Vitro Maturation (IVM) Oocytes | ➢ Low Oocyte Yield |
| ➢ Fertility Preservation | ➢ Cryopreserved Oocytes | |

### Why ICSI should be reserved for indicated cases ?

- Numerous studies have shown that for non-male factor infertility ICSI does not improve outcomes
- ICSI is invasive
- Added Cost in many programs and for insurance
- Many Patients would prefer conventional insemination more ‘natural’
- Misdirected guidance that ICSI improves fertilization rates
- Concerns that ICSI has been associated with increased incidences of chromosomal abnormalities, imprinting disorders, autism, intellectual disability and birth defects although these risks may be related to other underlying patient specific factors
- Every practice should evaluate how best to apply ICSI

## Short Vs long co incubation during IVF :

Short co-incubation in IVF involves a limited sperm-oocyte contact period of3- 4 hours. This method has gained traction due to its advantages, such as reduced exposure to reactive oxygen species (ROS), produced by the sperm cells and cumulus cells, which can negatively affect oocyte quality and Low embryo fragmentation rates and Significant increase in pregnancy rates [4].

Long co-incubation usually lasts for 16 to 18 hours, providing an extended period for natural fertilization to occur between sperm and cumulus-intact oocyte. Research suggests that long incubation may lead to improved fertilization rates. However, prolonged exposure to sperm and cumulus oocyte complex may increase ROS levels, leading to heavy oxidative stress which can negatively impact embryonic development. Despite its traditional preference, modern trends favour shorter co-incubation to reduce cellular stress and optimize embryo outcomes [4].

Embryologists expressed mixed preferences regarding incubation protocols. While some favoured short incubation (3-6 hours) after noticing significant positive results, others preferred long incubation (16-18 hours) as their standard practice.

## Role of Trimming/cutting of Cumulus cells prior to IVF :

Cumulus cells surround the oocyte and play a crucial role in fertilization. They produce chemo attractions to attract sperms and also play a role in oocyte maturation process. Although the mechanisms of their function with oocyte and spermatozoa remain unclear, a possibility of them mechanically trapping and guiding hyper activated spermatozoa toward the oocyte, subsequently filtering out of abnormal sperm has been discussed. They also create a micro-environment conducive to sperm capacitation and penetration, and may prevent unfavourable changes in the oocyte, either at the zona pellucida or cytoplasmic level [8].

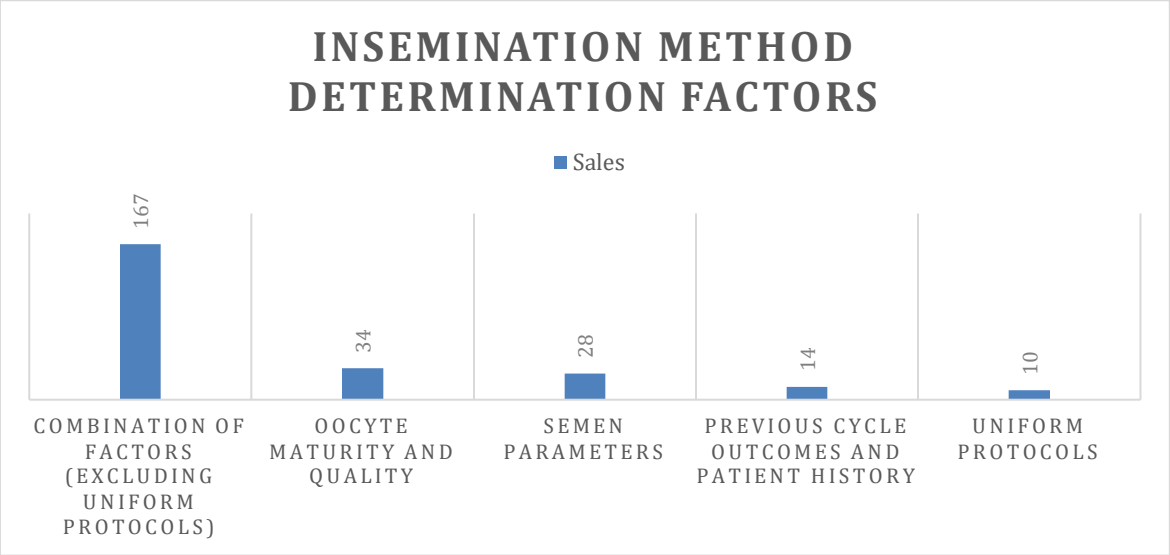
While research concludes that IVF results heavily relay on oocyte quality & maturity rather than Cumulus quality &Cumulus cutting practices [9] . The opinions of embryologists during the discussion varied from elaborating its function in IVM & sperm recognition during IVF to emphasising on its down side such as increased medium turbidity, ROS production by blood clots / tissues attached to the cumulus cells making Trimming / Cumulus cutting a mandatory practice but with caution.

# POLL RESULTS

*Summary – By Team iHERA*

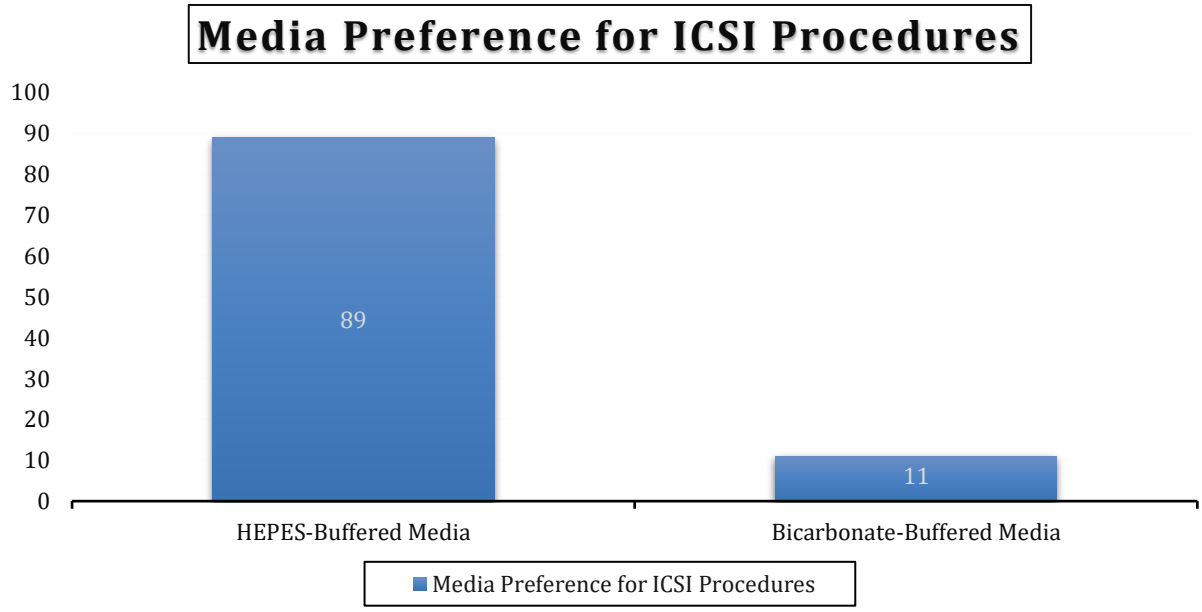
## ***Poll 1*: Insemination Method Determination Factors**

This poll participated by 253 embryologists aimed to explore the key factors that guide in choosing between IVF and ICSI for insemination, emphasizing patient-specific considerations.




## ***Poll 2*: Media Preference for ICSI Procedures**

This poll was conducted during the embryo chat with 100 participating Embryologists, this poll investigated their' media preferences during ICSI, assessing the choice between HEPES-buffered and bicarbonate-buffered media.



# SUMMARY OF CHAT DISCUSSION

**By Shaik Sabiha Sulthana**

This discussion delved into the critical factors influencing the decision-making process between conventional IVF and ICSI. Embryologists shared their diverse practices, experiences, and evidence-based approaches, addressing key questions and emphasizing the complexity of tailoring protocols to achieve optimal patient outcomes.

## Perspectives on Performing Conventional IVF

Conventional IVF is typically considered after thoroughly evaluating all essential parameters. The selection process is notably more intricate compared to ICSI, as it requires careful consideration of multiple factors to ensure the best possible outcomes. It is generally recommended for cases without male factor infertility and is typically avoided in situations with prior fertilization failures using ICSI.

## Discussions on the factors that hinder the decision-making process.

- ICSI is often used in fear of total fertilization failure& abnormal fertilisation (3PN), despite normal semen parameters,
- Worries on high DFI influencing embryo quality drives some embryologists toward ICSI
- A lack of confidence in IVF leads many to opt for ICSI in normozoospermia cases.
- The practice of IVF vs. ICSI varies significantly based on lab setup and clinician preferences.

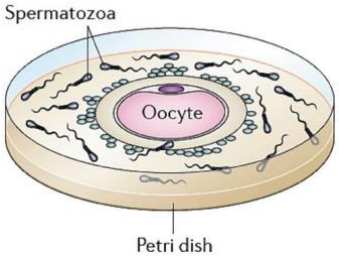
## Perspectives challenging these concerns:

Most embryologists agree that conventional IVF should be the first choice when semen parameters are normal, and there is no prior history of fertilization failure. The decision to use ICSI should be guided by a thorough evaluation of previous cycle outcomes and the patient's medical history, rather than being the default option. While the DNA Fragmentation Index (DFI) can offer valuable insights, embryologists recommend it as a complementary diagnostic tool rather than a definitive criterion for selecting fertilization methods. Consequently, a detailed semen analysis combined with patient-specific protocols should drive the selection of the fertilization method, ensuring personalized, evidence-based treatment.

## WHAT IS THE PREFERRED PROTOCOL WHILE PERFORMING CONVENTIONAL IVF

### Media Preparation & sperm – oocyte ratio:

- 4-well or 5-well dishes are optimally preferred. At the same time a few embryologists prefer droplets or Centre wells over 4-well dishes, concerning around unequal distribution of temperature.
- A drop size of 200 microns is used for 4 oocytes, or 10-12 oocytes are placed in a central well dish with a sperm Concentration of 1-2 million/mL.
- A sperm concentration required for a single oocyte during IVF is 10,000 and some prefer between 70000 to 100000.



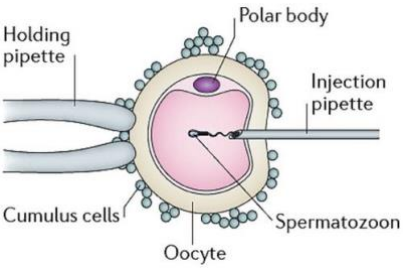




**Fig 1 & 2 Showing IVF & ICSI Illustratively [7]**

### OPINIONS ON PERFORMING ICSI:

Embryologists convey that preferring ICSI over IVF sometimes depends upon the clinician choice, a tertiary care centre where most of the patients have previous failed cycles. Preferring ICSI at small centres , where there's no need of hiring a full time Embryologist also adds to the choice .

### Preferred Media during ICSI:

- A poll revealed support for the use of HEPES or MOPS media, but some embryologists also advocated for bicarbonate media.
- Using HEPES during screening and switching to bicarbonate media for ICSI has been mentioned to cause ionic changes hampering fertilisation rates & embryo development.
- However, bicarbonate media requires optimal timing, and ICSI to be performed as quick as possible as its pH fluctuations are rapid.
- ICSI with bicarbonate media must be performed quickly and under controlled conditions, such as in a closed chamber with 37°C temperature and 5-6% $CO_2$ infusion.

### What If There Are Only 1-2 Oocytes - ICSI or IVF?

Embryologists remain divided on the method of fertilization for cases with fewer oocytes (<4). Some prefer IVF, while others opt for ICSI due to fear of poor fertilization. While others highlighted ICSI or IVF can equally be a better choice, depending on factors such as:

- Female profile
- Couple's age
- Treatment cycle history
- Risk of previous fertilization failures

## Opinions on rescue ICSI:

- Rescue ICSI remains as a debated practice. Some avoid it, believing failed fertilization indicates compromised oocyte or sperm quality, which may not yield good embryos.

## Opinions on freezing embryos of sibling Oocytes where half were inseminated via ICSI and other via IVF

Mixing IVF and ICSI embryos is generally not recommended due to procedural differences and the invasive nature of ICSI. Some embryologists suggested freezing embryos separately in different straws and labeling them based on the method used.

## DISCUSSIONS ON CUMULS CELLS & THE PRACTICE OF CUMULS CUTTING

### Why the cumulus should not be cut?

- Facilitate oocyte maturation, meiotic resumption, and embryo development.
- They Provide chemo attractant for sperm and cushion the oocyte.
- As it Act as a critical intermediary between the oocyte and follicular environment, mimicking natural conditions.
- Many Embryologists prefer keeping cumulus cells intact as they play a significant role in cytoplasmic maturation during Incubation.
- Studies have indicated a lag between cytoplasmic and nuclear maturation in IVF. Hence not cutting the Cumulus is crucial.

### Opinions of trimming the cumulus instead of cutting it :

- Benefits of trimming include easier oocyte visualization after incubation, prevention of cell clumping, and Reduced medium turbidity.
- While some Embryologists convey that bloody tissue or RBCs attached to the cumulus should be removed, to prevent the formation of a mesh-like structure, which can hinder sperm movement and result in Fertilization failure.
- Some embryologists encourage trimming or teasing cumulus cells, as reducing the cumulus load helps Sperm reach the oocyte faster
- Trimming is most beneficial when fewer sperm are used for insemination.
- Partial trimming can also be performed to remove unwanted tissues or RBCs .
- Others prefer trimming even for ICSI cases to minimize hyaluronidase use and reduce enzyme exposure.

### Why is patient counselling essential in IVF?

- Counselling helps patients understand risks, outcomes, and financial implications.
- It ensures informed decisions, especially in cases with limited embryos or financial constraints.
- Proper counselling supports better patient cooperation and realistic expectations.

## What is the role of an embryologist in IVF decision-making?

- An embryologist should think scientifically and consider all clinical and laboratory factors.
- Their role involves pre treatment diagnostics and contributing to patient-tailored approaches, rather than just following standard protocols

## DISCUSSIONS ON CULTURE MEDIA AND PLOIDY STATUS:

## OPINIONS ON MEDIA – SINGLE STEP vs SEQUENTIAL MEDIA

The discussion revealed a neutral stance between the two media types, with an emphasis on protocol influencing the results rather than the media itself. While some embryologists expressed a preference for IVF media over other options. Specific points include:

### Single-Step Media:

- Widely preferred by many embryologists.
- Some participants highlighted improved results with single-step media compared to sequential media.
- The higher glucose levels in single-step media were noted as beneficial.

### Sequential Media:

- Initially used by some embryologists, but no significant changes in results were observed when transitioning to single-step media.

### Day 3 Media Change and Its Significance

- Embryologists emphasized the importance of changing the media on Day 3, regardless of the type of media used, to achieve significantly better results.
- Changing the media on Day 3 helps maintain the pH and osmolarity of the media.
- Without this change, osmolarity can rise to 300-310 mOsmol by Day 5, affecting embryo growth.
- A Day 3 media change increases the blast utilization rate, particularly improving the yield of A- and B-grade blastocysts.
- Even in time-lapse incubators, changing the media on Day 3 has been shown to improve outcomes.

## CAN CULTURE MEDIA INFLUENCE PLOIDY STATUS IN EMBRYOS?

- The discussion emphasized that culture media itself has minimal impact on embryo ploidy status.
- Factors such as culture system stress and mitotic errors within the IVF lab are more likely contributors.
- The pH of the culture media may also influence ploidy rates.
- Aneuploidy is largely influenced by patient age, particularly in women aged 37 years and older.
- Strong evidence supporting these findings in India is limited due to the lack of published data

# Conclusion

Embryologists highlighted the need for individualized ART protocols tailored to patient history and clinical indications. While conventional IVF is preferred in normozoospermic cases, fears of fertilization failure and other factors often lead to ICSI overuse. Short incubation was favored to reduce oxidative stress, while long incubation allowed natural fertilization. Bicarbonate-buffered media, despite requiring precise handling, was recommended over HEPES-buffered media for ICSI. Day 3 media changes and intact cumulus cells were emphasized for optimizing blastocyst yield and oocyte maturation. The discussion underscored the critical balance between technical precision and patient-specific approaches to achieve optimal outcomes in ART.

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