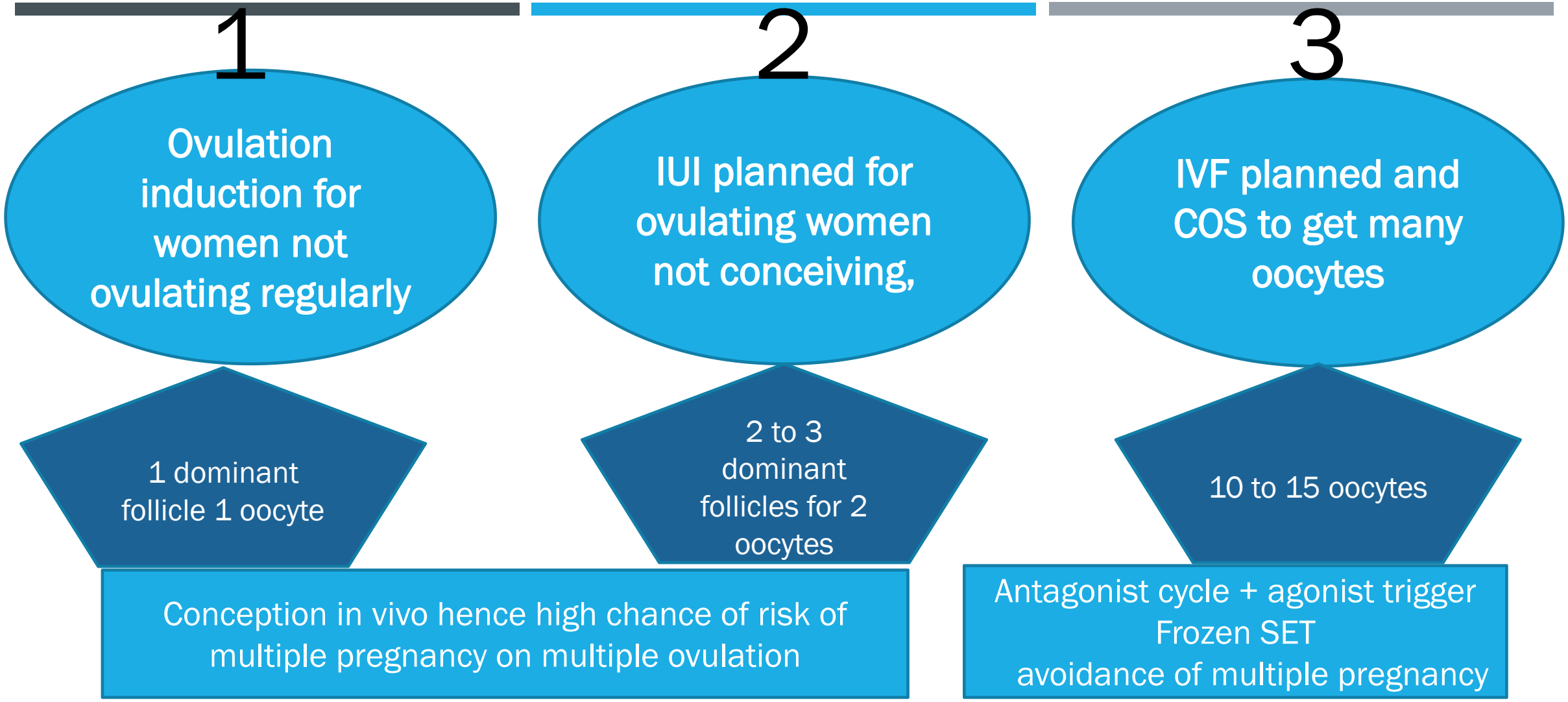

DR. ABHA MAJUMDAR
MBBS, MS, FICS
Director & Head of IVF Department
IVF Sir Ganga Ram Hospital
Expertise
Infertility, assisted reproductive techniques, reproductive endocrinology, endoscopic surgery for pelvic resurrection.
SGRH
IVF SIR GANGARAM HOSPITAL

HOW IS AN IVF STIMULATION DIFFERENT FROM IUI OVARIAN STIMULATION?

NO CONFUSIONS

WHEN DO WE NEED TO STIMULATE OVARIES WITH OVULATION INDUCING AGENTS

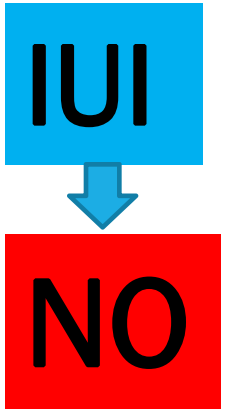


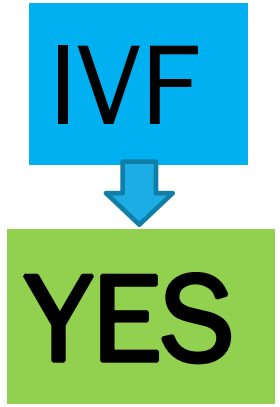
Aim is to have a singleton live birth

IUI and IVF both require ovarian stimulation

OVARIAN STIMULATION CAN LEAD TO OHSS & MULTIPLE PREGNANCY

Can these complications be prevented?





WHAT IS SUCCESSFUL TREATMENT

To have a single live pregnancy is successful treatment

Twins are failure of treatment

Triplets are disaster for the woman and family both

IVF

DO WE NEED STRONG OVARIAN STIMULATION IN IVF ?

Human Reproduction, Vol.31, No.10 pp. 2261–2267, 2016
Advanced Access publication on September 2, 2016 doi:10.1093/humrep/dew184

human reproduction

ORIGINAL ARTICLE *Infertility*

Live birth and perinatal outcomes following stimulated and unstimulated IVF: analysis of over two decades of a nationwide data

Sesh Kamal Sunkara[1,*], Antonio LaMarca[2], Nikolaos P. Polyzos[3], Paul T. Seed[4], and Yakoub Khalaf[5]

DATA FROM HUMAN FERTILISATION AND EMBRYOLOGY AUTHORITY (HFEA) 1991 TO 2011

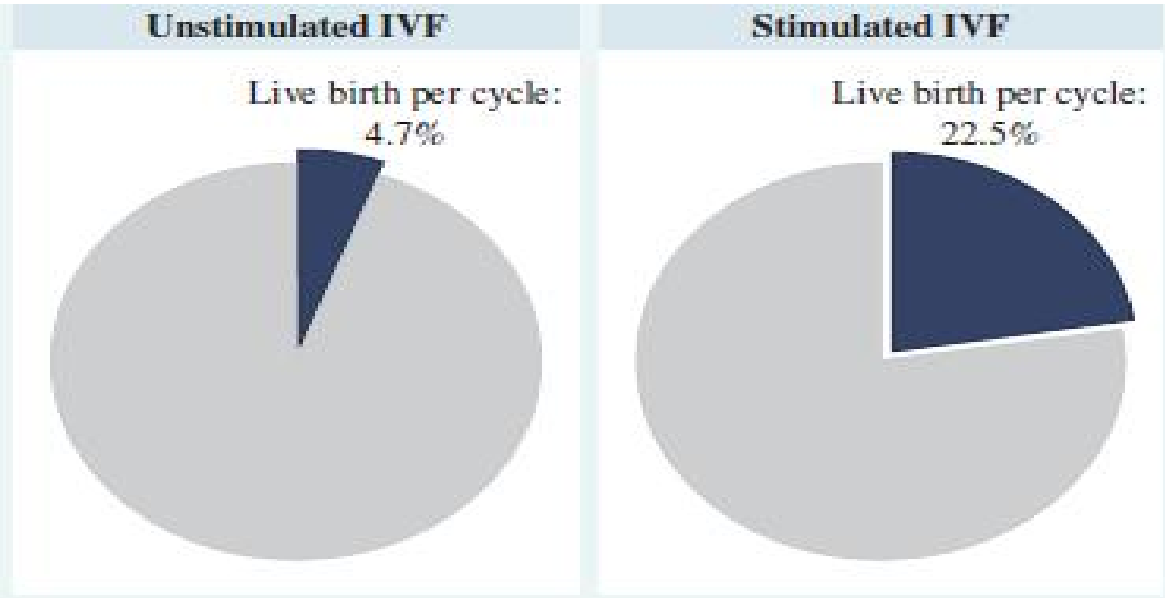
5,91,003 fresh IVF ± ICSI cycles

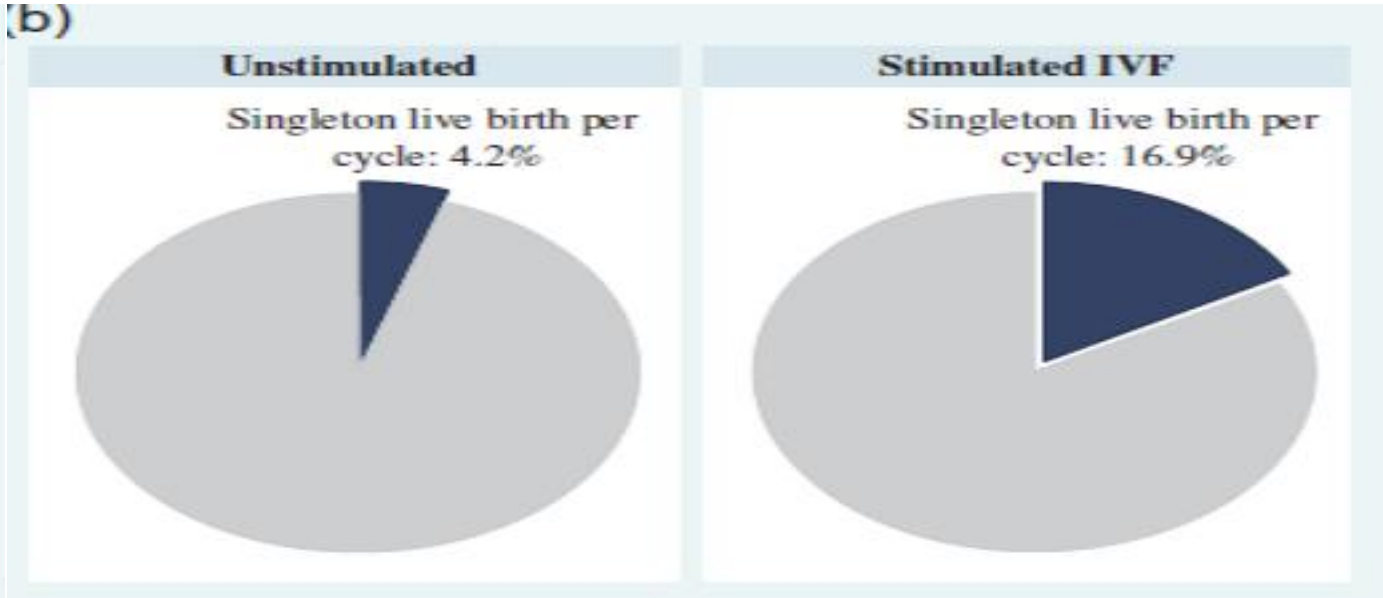
- **5,84,835 stimulated IVF cycles**
- **6,168 unstimulated IVF cycles**

Chances of no oocytes retrieved

- 44.2% - unstimulated cycles
- 7.1% - stimulated cycles

- To achieve live birth
  - 3.5 times more unstimulated IVF cycles required compared to stimulated IVF
- To achieve one singleton live birth
  - 2.9 times more unstimulated IVF cycles required compared to stimulated IVF.
- TTP shorter with stimulated IVF cycle





OHSS & MULTIPLE PREGNANCY FREE CLINIC

BY SEGMENTATION OF IVF TREATMENT

IVF SIR GANGARAM HOSPITAL

STEP 1

Antagonist protocol

-Patients friendly

- Fewer injection

- Shorter stimulation

- OHSS much lower

-Sam

STEP 2

GnRH agonist trigger

-LPD thus lower PR

-Aggressive luteal support if fresh ET

-Cryo-preserve and subsequent transfer best option

STEP 3

Cryopreserve embryos

eSET

Higher PR

NO OHSS

Ethical issues of CP

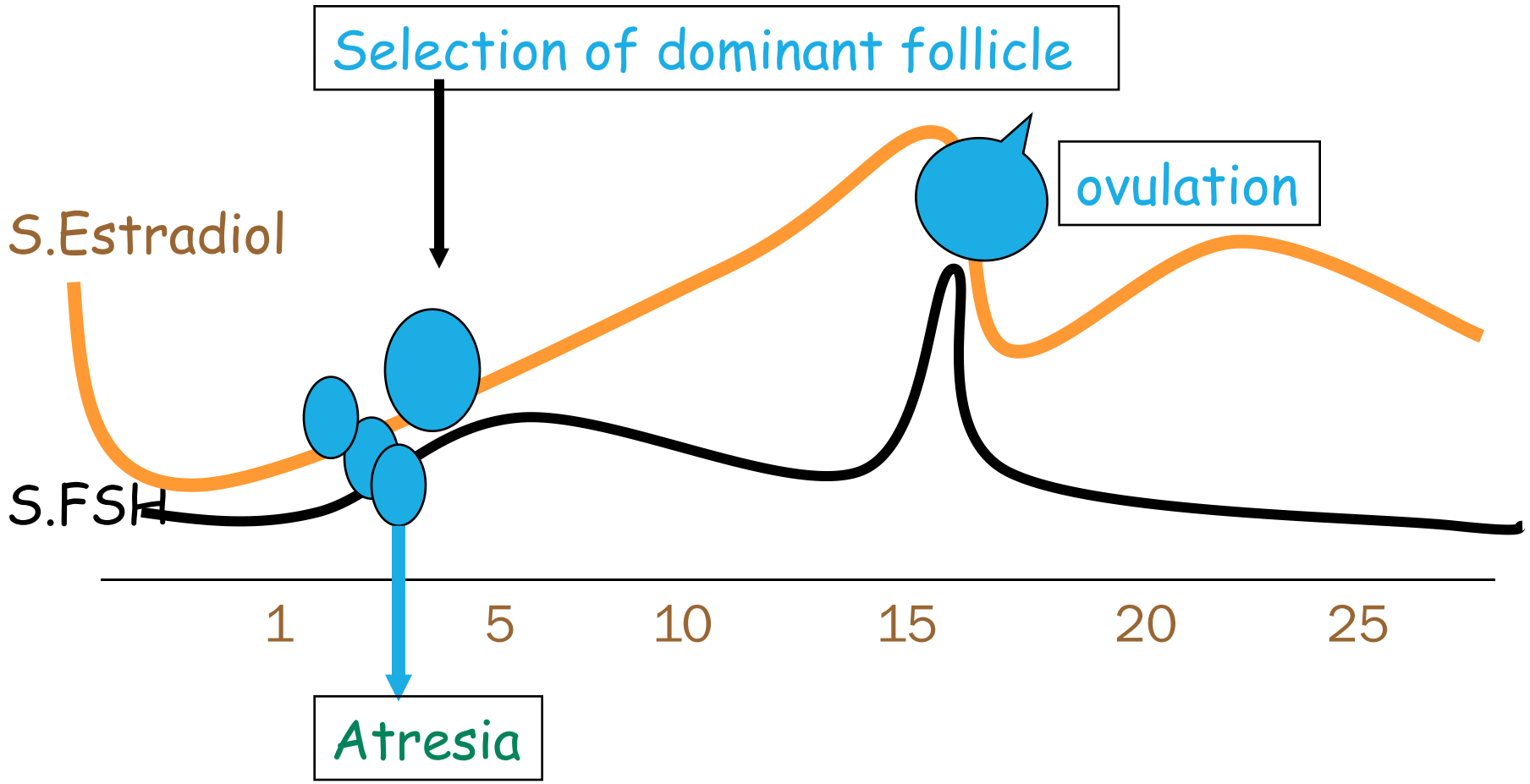
IUI

Ovarian Stimulation and IUI

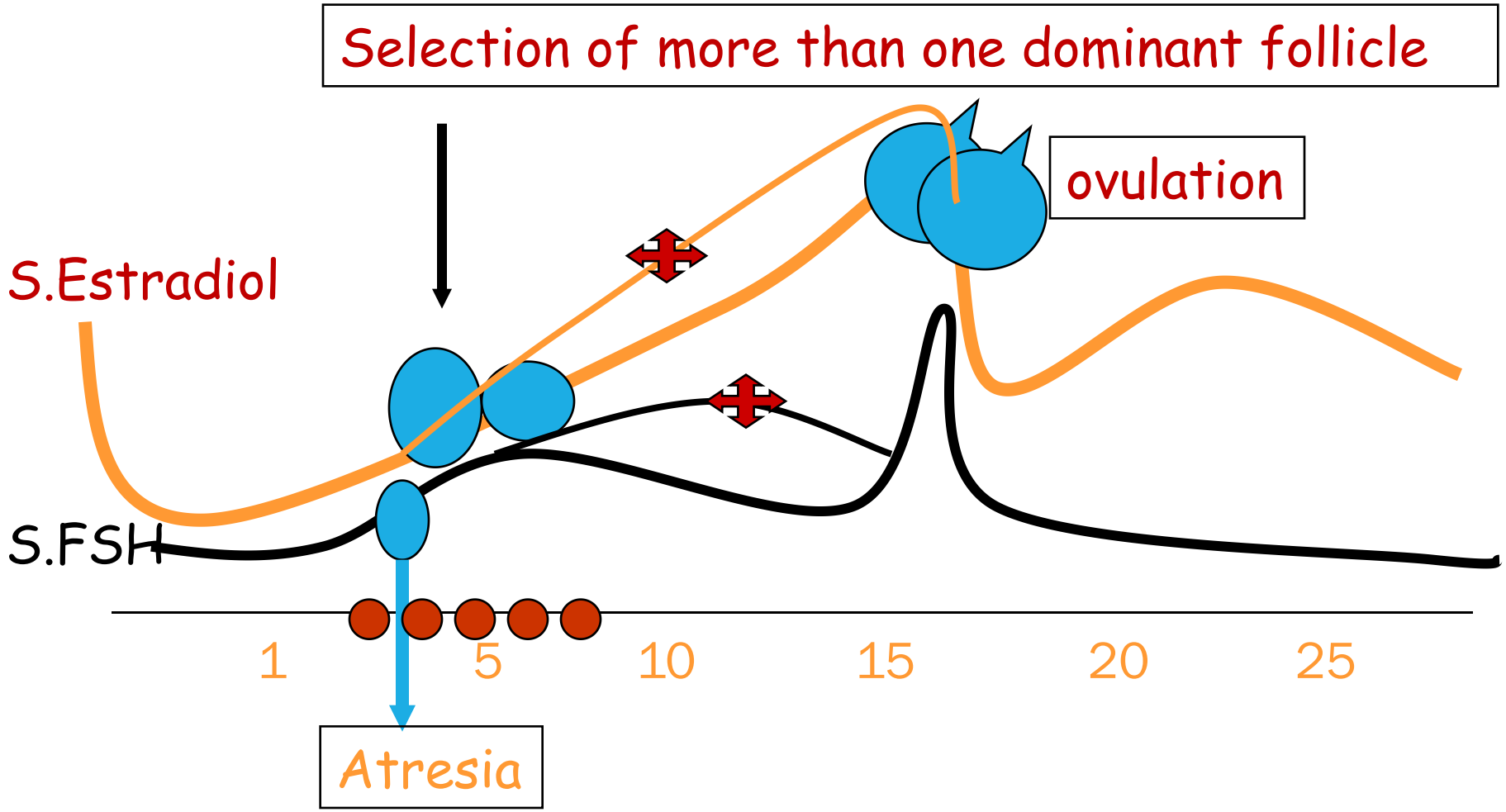
The rationale behind the use of Ovarian stimulation in IUI is :

- Increase in number of available oocytes for tubal pickup and site of fertilization
- Correction of subtle endocrinological or ovulatory dysfunction
- Higher concentration of energy laden sperms at site of fertilization

Events in a natural cycle



Events in a stimulated cycle cycle



Common drugs used for OI in IUI

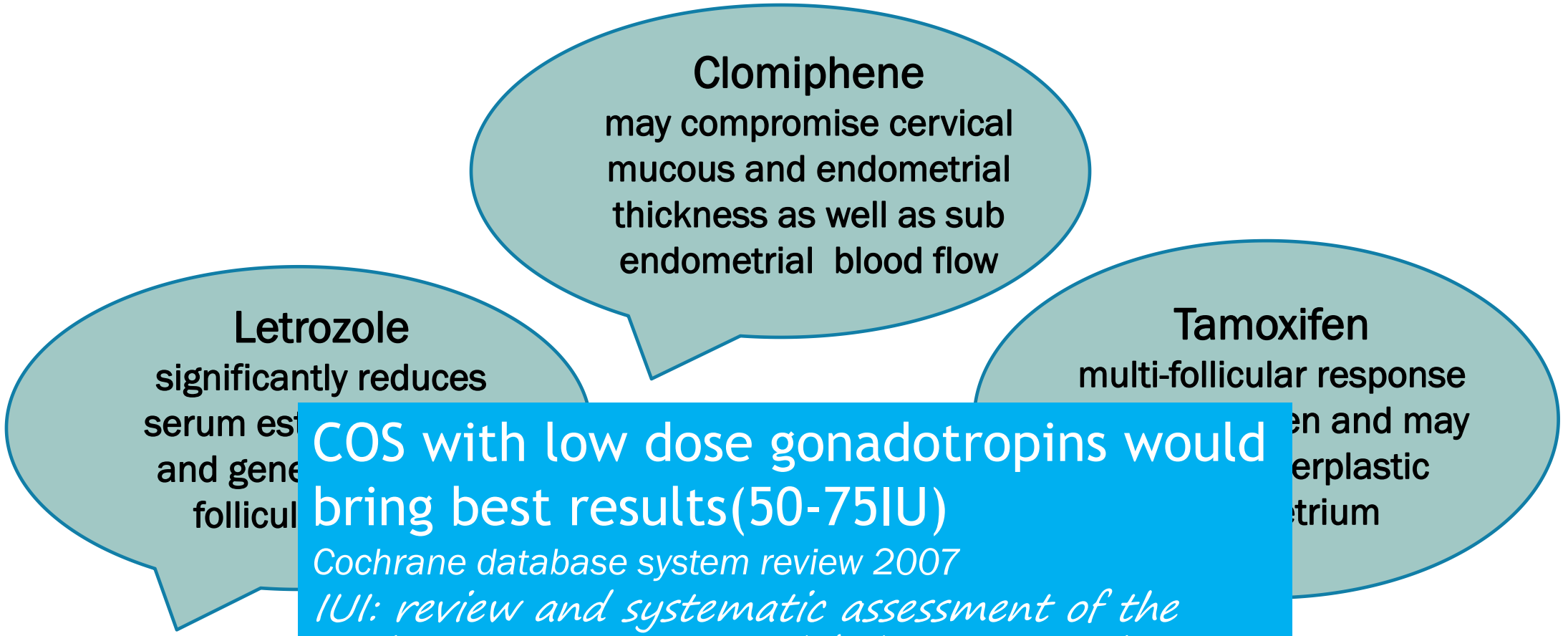
1. Clomiphene: Day 3 to 7 for 5 days 100 mg/day

2. Tamoxifen: Day 3 to 7 for 5 days 40 mg/day

3. Letrozole: Day 3 to 7 for 5 days 2.5 to 5mg/day

4. Gonadotropins: Daily dosing starting with 50 to 75 units/day from day 3 or 4 of cycle till dominant follicle is made

Effect of oral and injectable drugs to enhance ovulation in Unexplained Infertility



COS with low dose gonadotropins would bring best results(50-75IU)

Cochrane database system review 2007

IUI: review and systematic assessment of the evidence that supports global recommendations Human Reproduction Update, Volume 24, Issue 3,

OS protocols : anti-oestrogens vs gonadotrophins for IUI for sub-fertility

43RCTs, n=3957

- CC with letrozole: no significant difference (OR 1.2)
- Gonadotrophins versus CC: Significant higher PR with gonadotrophins (OR 1.8)
- Different gonadotrophins: no significant difference
- No evidence of benefit in doubling the dose of gonadotrophins(OR 1.2), multiple pregnancy rates and OHSS rates increased.

Cochrane Jan 21 2009 (up to date: January 23, 2007)

R- FSH versus U- gonadotrophins (HMG, P-FSH, HP- FSH) for ovarian stimulation in ART

- 42 RCTs, n=9606
- R-FSH with U- gonadotrophins: no difference in live birth rate, OHSS or any other outcomes.
- r-FSH with P-FSH or HP-FSH: No difference in live birth rate
- r-FSH with HMG/HP-HMG: Lower live birth rate in the rFSH group though differences were insignificant. (OR 0.84)

Conclusion: all gonadotrophins equally effective and safe, and further trials unwarranted. Choice of gonadotrophin should depend on availability, convenience and costs.

- Cochrane Feb 16, 2011(up to date: October 20, 2010)

THE STARTING DOSE FOR GONADOTROPIN IS BASED ON

- Age
- Body mass index (BMI)
- Presence of underlying PCOS
- Test for ovarian reserve indicating poor reserve
- Previous history of high response or poor response

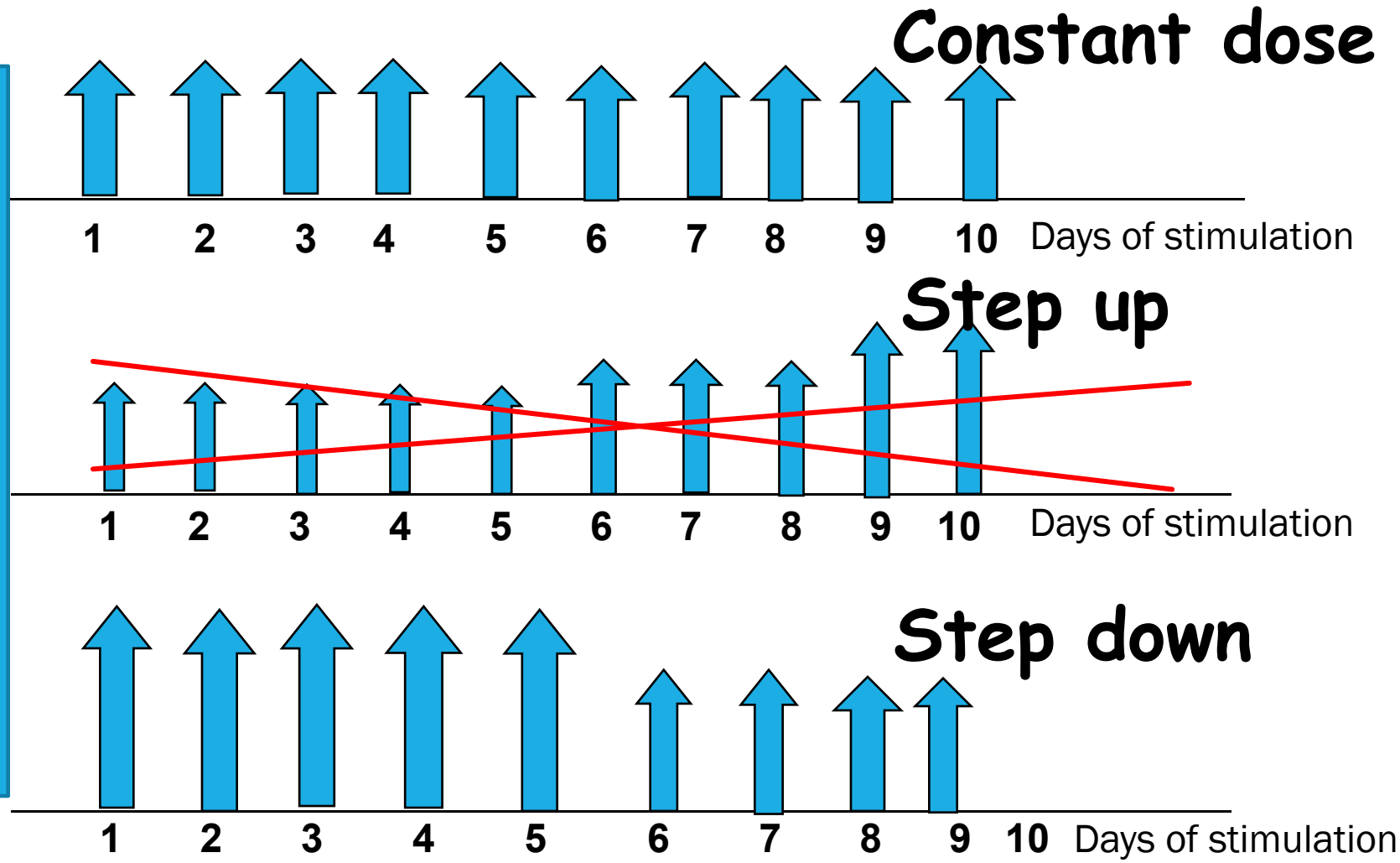
Normal or hyper responders starting dose of 75 or 50 /62.5 IU

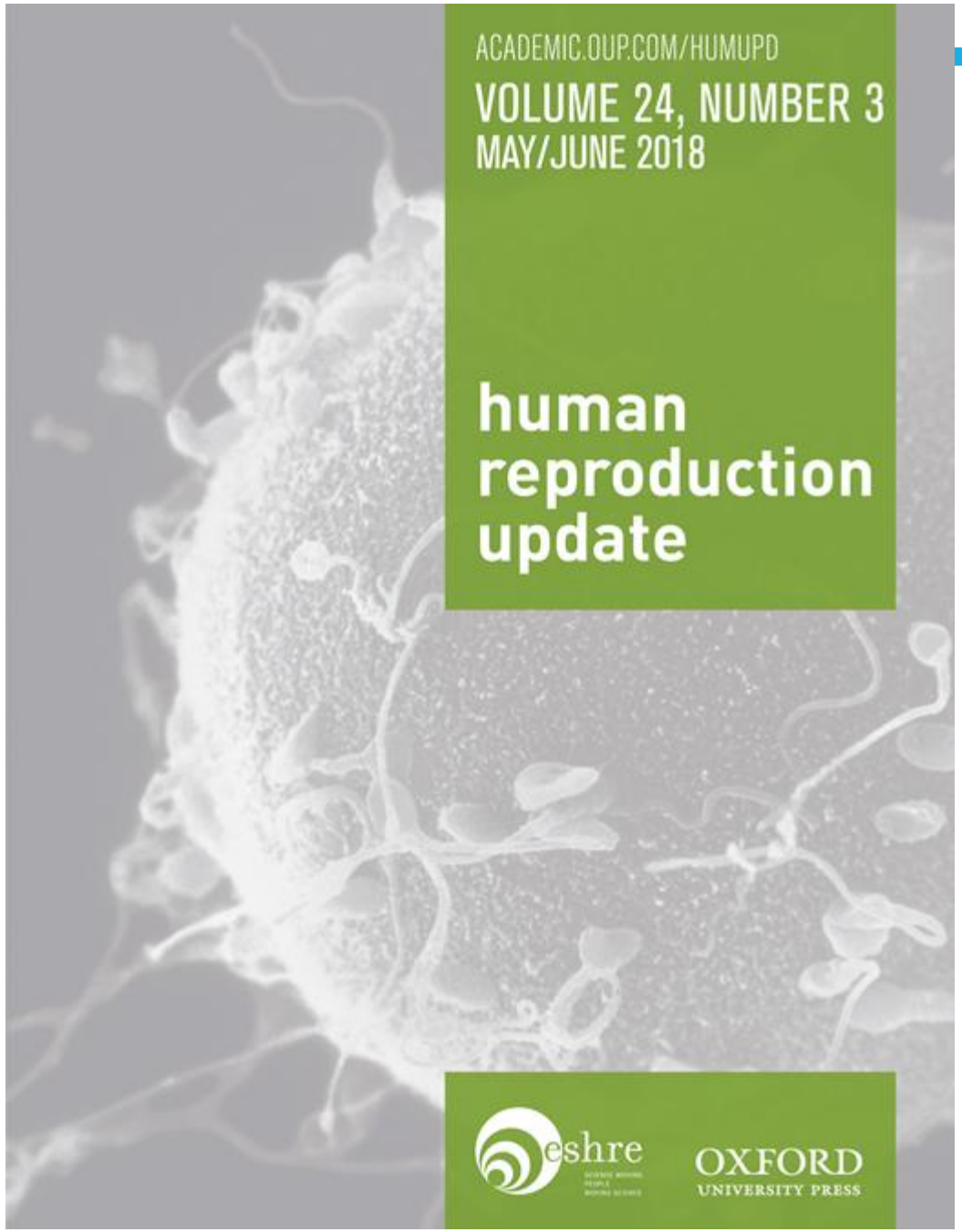
Poor responders starting dose of 100 or 150 IU

Gonadotropin regimes for unexplained infertility

USG monitoring
Day 2/3
Day 7/8
Day10/11

Urine LH test +ve
IUI 24 hours later
Or
hCG trigger
5000iu
IUI 40-48hours later





IUI: review and systematic assessment of the evidence that supports global recommendations

Ben Cohlen, Aartjan Bijkerk, Sheryl Van der Poel, Willem Ombelet Author Notes

Human Reproduction Update, Volume 24, Issue 3, May-June 2018, Pages 300–319, https://doi.org/10.1093/humupd/dmx041

12. How can you prevent multiple pregnancies and ovarian hyperstimulation syndrome in an IUI programme?	In order to prevent high rates of multiple gestation pregnancies in IUI–OS, IUI should be withheld when more than two dominant follicles >15 mm or more than five follicles >10 mm at the time of HCG injection or LH surge are present.	Moderate
	When gonadotrophins are used in IUI, regiments with 75 IU or lower should be used because higher doses have similar pregnancy rates but increase multiple pregnancy rates.	High

Continued

Table I *Continued*

Clinical questions	Recommendations through assessment of developed PICO question and associated evidence analysis	Strength of the evidence
	Clomiphene citrate or tamoxifen are acceptable alternatives to low dose gonadotrophins for low multiple pregnancy and birth rates and with lesser costs, although at a lower live birth rate than with gonadotrophins.	Moderate
	Addition of GnRH agonist to gonadotrophins in IUI–OS is not recommended because there is no increase in pregnancy rate despite increased multiple pregnancy rates and increased costs.	Moderate
	Good practice point: As an alternative to cycle cancelation, aspiration of excess follicles at the time of HCG injection or LH surge might be additional options for reducing the risk of multiple pregnancy in IUI–OS.	Low

OHSS
&
Multiple pregnancy

Question 12: How can you prevent multiple pregnancies and OHSS in an IUI program?
Draft recommendation

- IUI should be withheld when more than two dominant follicles >15 mm or more than five follicles >10 mm at the time of HCG injection or LH surge are present.

- When gonadotrophins are used in IUI, regiments with 75 IU or lower should be used because higher doses have similar pregnancy rates but increase multiple pregnancy rates.

- Clomiphene citrate or tamoxifen are acceptable alternatives to low dose gonadotrophins for low multiple pregnancy and birth rates and with lesser costs, although at a lower live birth rate than with

- Addition of GnRH agonist to gonadotrophins in IUI–OS is not recommended because there is no increase in pregnancy rate despite increased multiple pregnancy rates and increased costs.
- Good practice point: Alternative to cycle cancellation, aspiration of excess follicles at the time of HCG injection or LH surge might be additional options for reducing the risk of multiple pregnancy in IUI–OS.
- Converting the cycle to IVF should be last resort with freeze all and single frozen embryo transfer

Why is learning the right ovarian stimulation so important?

- Unacceptable high multiple pregnancy rates (MPR) aswell as OHSS after IUI with OS treatment are most often attributed to uncontrolled use of gonadotrophins for OS prior to insemination.

  - ❑ Clinical complication of multiple pregnancy affect the maternal and perinatal morbidity and mortality

  - ❑ Clinical complication of OHSS may lead to intense maternal morbidly at a time when she would have welcomed and enjoyed a pregnancy most

HIGH ORDER PREGNANACY

Maternal physical health: higher incidence of ectopic, heterotopic pregnancy, 1st &2nd trimester miscarriages, higher incidence of hypertension, diabetes, cholestasis, chest complications and physical discomfort

Fetal complication: High risk of prematurity, intra uterine growth restriction, congenital malformations, discordant growth, perinatal death, life long neurological deficits

PREVENTION OF MULTIPLE PREGNANCIES AND OVARIAN HYPERSTIMULATION SYNDROME (OHSS) IN IUI CYCLES

- **Primary measures**
  - Appropriate drug and doses and individualize doses when possible.
  - Attempts to prevent the growth of more than two to three dominant follicles
- **Secondary measure**
  - Cycles cancellation
  - heterosexual couples to abstain from unprotected intercourse.
  - Aspiration of excess follicles at the time of HCG injection or LH surge
  - Conversion to IVF, might be additional options
  - Finally, multifetal reduction can be proposed when multiple

All gonadotropin treated cycles should be closely monitored by regular vaginal ultrasounds

HOW IS AN IVF STIMULATION DIFFERENT FROM IUI OVARIAN STIMULATION NO CONFUSION

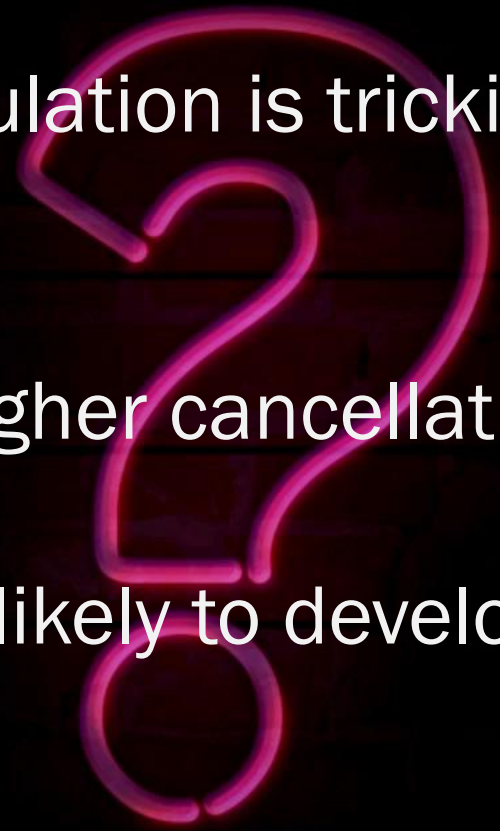
IVF

- Ovarian stimulation with high doses of gonadotropins to get optimum number of oocytes
- GnRH analogs mandatory to prevent cycle cancellation & retrieve all possible oocytes
- Window of oocyte retrieval is approx 1 hour
- OHSS can almost completely be prevented in antagonist cycle with agonist trigger and FET
- Single embryo transfer can eliminate the risk of high order births

IUI

- Very controlled ovarian stimulation required to have not more than 2 dominant follicles
- GnRh does not help to improve outcome instead increases cost
- Window of insemination is 12 – 16 hours post oocyte release
- Early OHSS cannot be prevented even if we withhold IUI and sexual inter course to prevent multiple pregnancy
- Risk of high order pregnancy is always there

RAPID FIRE QUESTIONS



Which gonadotropin stimulation is trickier within the 2 techniques? IUI or IVF

Which technique has a higher cancellation rate? IUI or IVF

Which technique is more likely to develop OHSS despite cancellation? IUI or IVF

In which technique you cannot control multiple pregnancy rates? IUI or IVF

THANK YOU