In the name of Allah

# *Induction Ovulation with Gonadotropins*

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## GONADOTROPIN THERAPY

- Introduction into clinical practice in 1961
- Extracted from the urine of postmenopausal women (human menopausal gonadotropins [hMG])
- Ratio of luteinizing hormone (LH) to follicle-stimulating hormone (FSH) bioactivity is 1:1
- Central role in ovulation induction

- ✓ *Since 1996, recombinant human FSH (rhFSH, >99 percent purity) has been available*

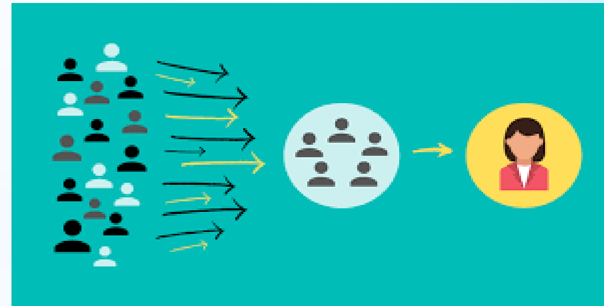
- ✓ *Recombinant preparations are appealing due to:*

- *Ease of administration (subcutaneous rather than intramuscular)*
- *Purity*
- *Batch-to-batch consistency*

## ➢ *Gonadotropin therapy:*

- ✓ *Exogenous gonadotropin: complex and expensive & are best carried out by experienced clinicians*
- ✓ *FSH, LH, HMG*
- ✓ *Assessment of fallopian tube patency before initiating*
- ✓ *high risk for OHSS*

## ▪ *Candidates:*



✓ ***PCOS women who have not ovulated or conceived with weight loss, clomiphene, or letrozole therapy***

✓ ***Hypogonadotropic anovulatory women with hypopituitarism or women with hypothalamic amenorrhea***

- ***Pretreatment evaluation:***

- ✓ ***Complete history and physical examination***
- ✓ ***Laboratory testing***
- ✓ ***Pelvic examination or a pelvic ultrasound to rule out ovarian cysts***
- ✓ ***Semen analysis of the partner***
- ✓ ***HSG***

- *Preparations*

*hMG OR FSH*

- ✓ *no differences in clinical pregnancy or live-birth rates for rFSH and urinary-derived gonadotropins*

- ✓ *no differences in the rates of ovarian hyperstimulation syndrome (OHSS) between rhFSH and urinary-derived gonadotropins*

- *Hypogonadotropic hypogonadal women need FSH & LH*

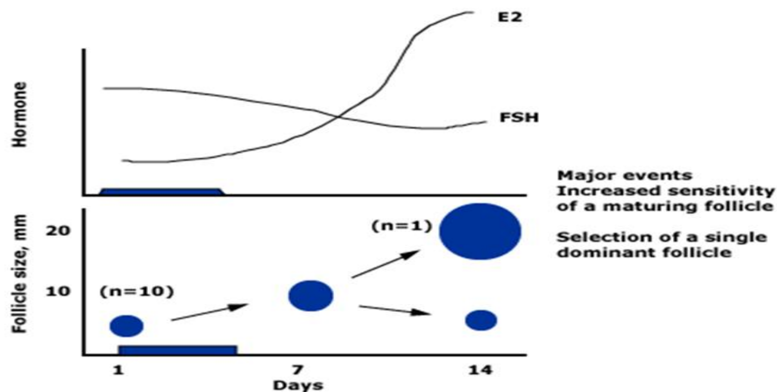
- *Long-acting rhFSH preparations are currently registered in some countries for use in in vitro fertilization (IVF)*

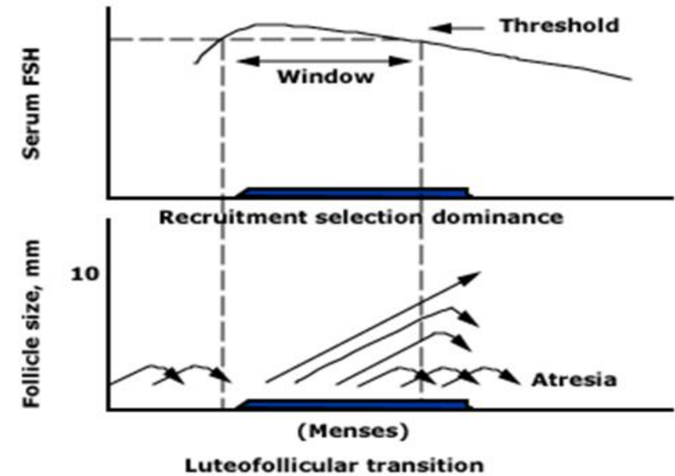
## *Protocols:*

- ✓ *The aim of ovulation induction with gonadotropins: formation of a single dominant follicle*

- ✓ *Because ovarian sensitivity to FSH stimulation varies among individual women, specific treatment and monitoring protocols are needed to achieve development of a single follicle when exogenous gonadotropin is administered*

- ***In spontaneous cycles, this is achieved at the beginning of the cycle by a transient increase in serum FSH concentrations above the threshold value***




- ***Concentrations then decrease due to negative feedback, preventing more than one follicle from undergoing preovulatory development***

- ***In the conventional gonadotropin protocol, the starting dose of FSH is 150 international units/day***

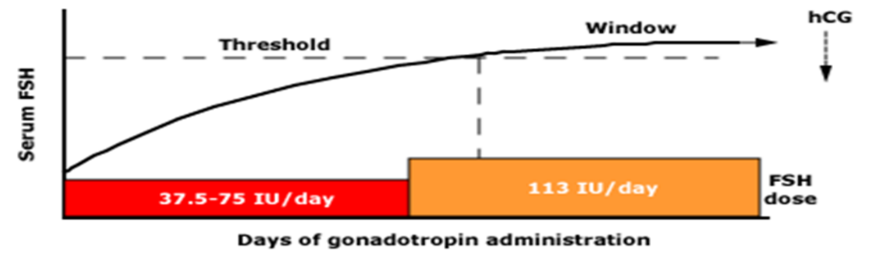
- ***This regimen is associated with a multiple pregnancy rate of up to 36 percent, and ovarian hyperstimulation occurs in up to 14 percent of treatment cycles***

- *In PCOS:*

✓ *Low-dose, step-up protocol*

✓ *Low-dose, step-down protocol*

## In PCOS:



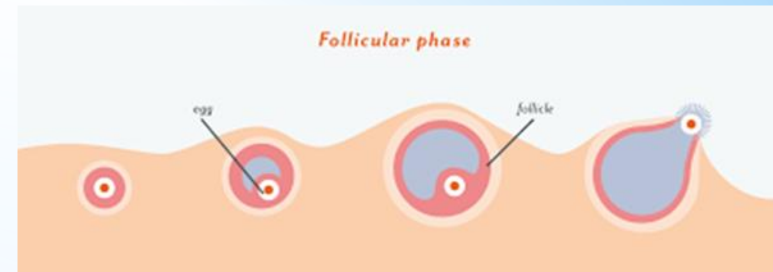

- ✓ *Low-dose, step-up protocol designed to minimizing excessive stimulation and the risk of development of multiple follicles*
- ✓ *Initial subcutaneous or intramuscular dose of FSH is 37.5 to 75 IU/day*
- ✓ *Dose be increased only if, after 14 days, no response is documented on ultrasonography*
- ✓ *37.5 IU then are given at weekly intervals up to a maximum of 225 IU/day*
- ✓ *hCG can be given to trigger ovulation*

- ***Low-dose, step-down protocol of ovulation induction mimics more closely the physiology of normal cycles***
- ***Therapy with 150 IU FSH/day is started shortly after bleeding and continued until a dominant follicle (>10 mm) is seen on transvaginal ultrasonography***
- ***Dose is then decreased to 112.5 IU/day followed by a further decrease to 75 IU/day three days later, which is continued until hCG is administered to induce ovulation***

## *Monitoring:*

- ✓ *TVS to measure follicular diameter*
- ✓ *During late follicular phase*
- ✓ *Every two or three days*
- ✓ *If three or more follicles larger than 15 mm are present, stimulation should be stopped, hCG withheld, and use of a barrier contraceptive advised in order to prevent multiple pregnancies and ovarian hyperstimulation*

## Ovulatory triggers:




- ✓ *hCG is given as an ovulatory trigger on the day that at least one follicle appears to be mature (follicle diameter of 18 mm)*
- ✓ *Both urinary and recombinant hCG preparations are available*
- *250 mcg of recombinant hCG appears to be equivalent to the standard doses of urinary hCG (5000 units)*
- *GnRh Agonist*
- *Recombinant LH*

- ***Multiple gestation***

- ***Ovarian hyperstimulation syndrome***

Best
Wishes