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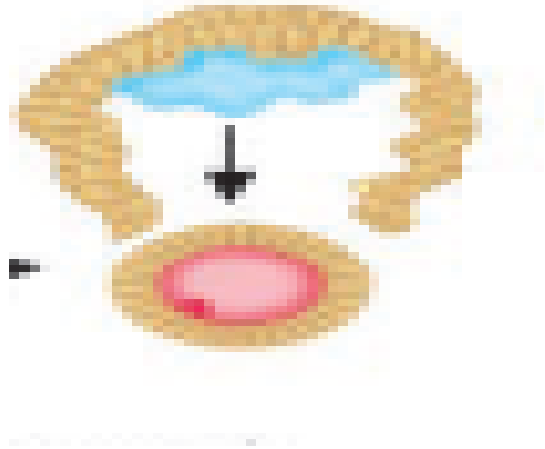
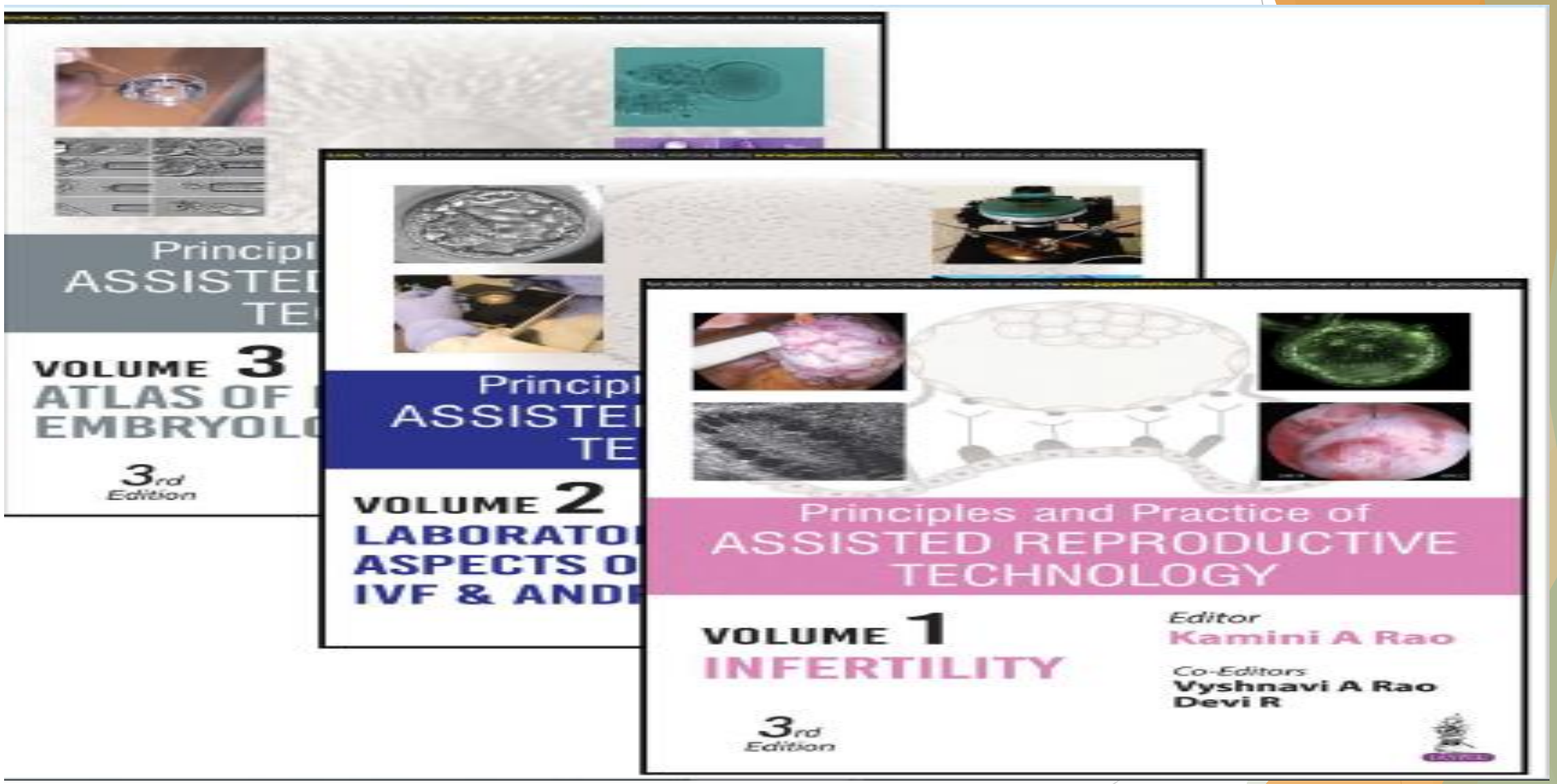
Ovulation Trigger

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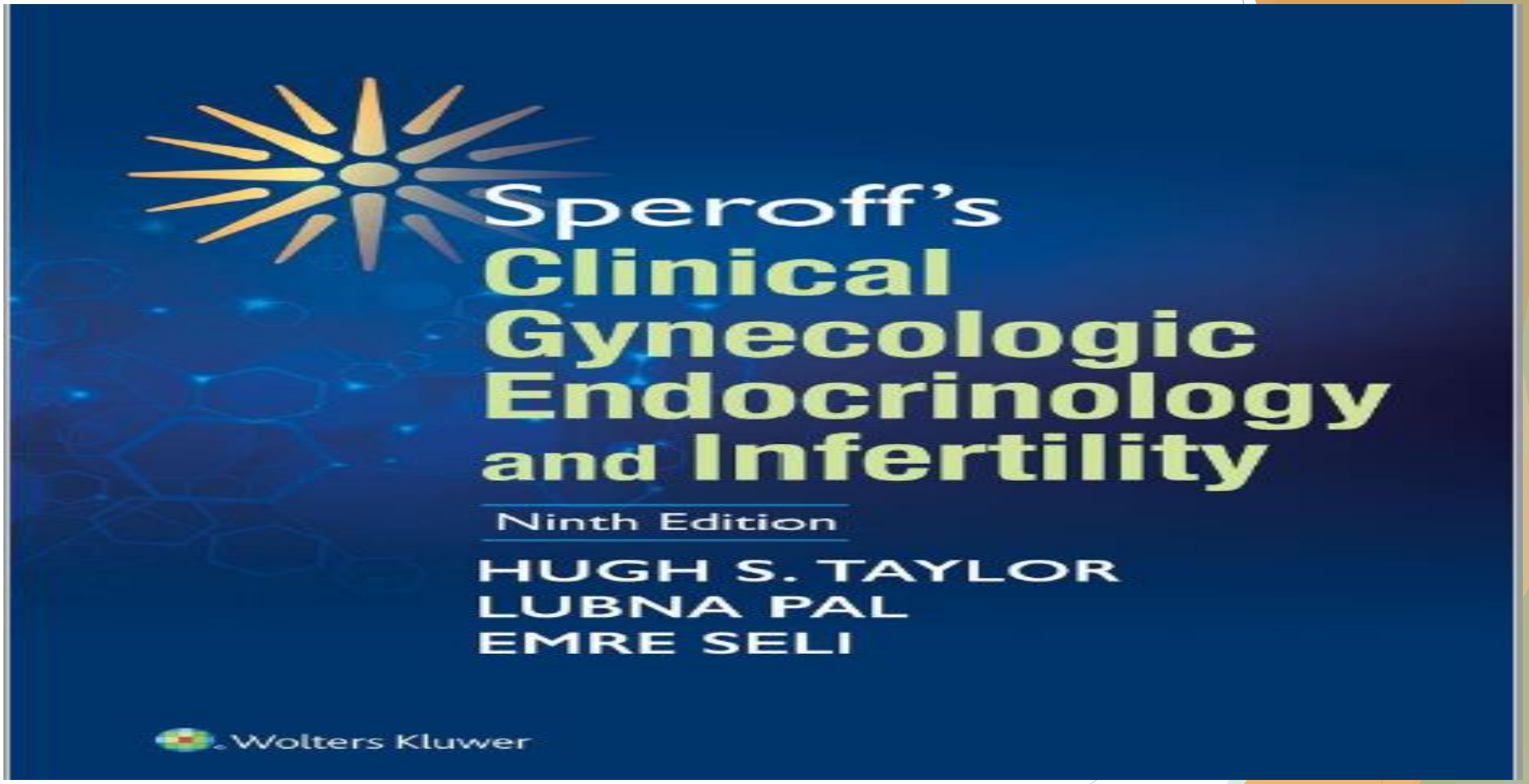
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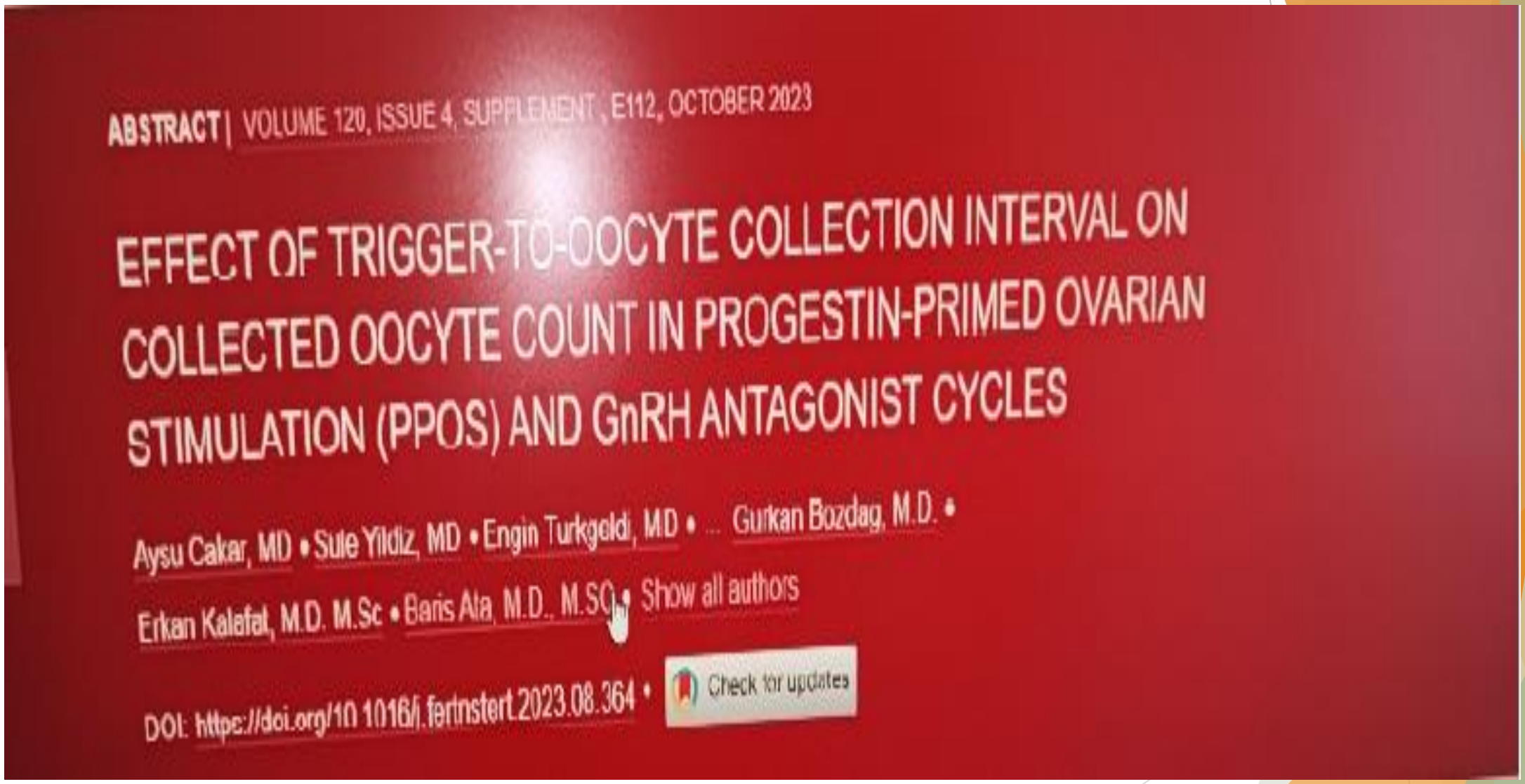
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Aysu Cakar, MD • Sule Yildiz, MD • Engin Turkgeldi, MD • ... Gurkan Bozdag, M.D. •
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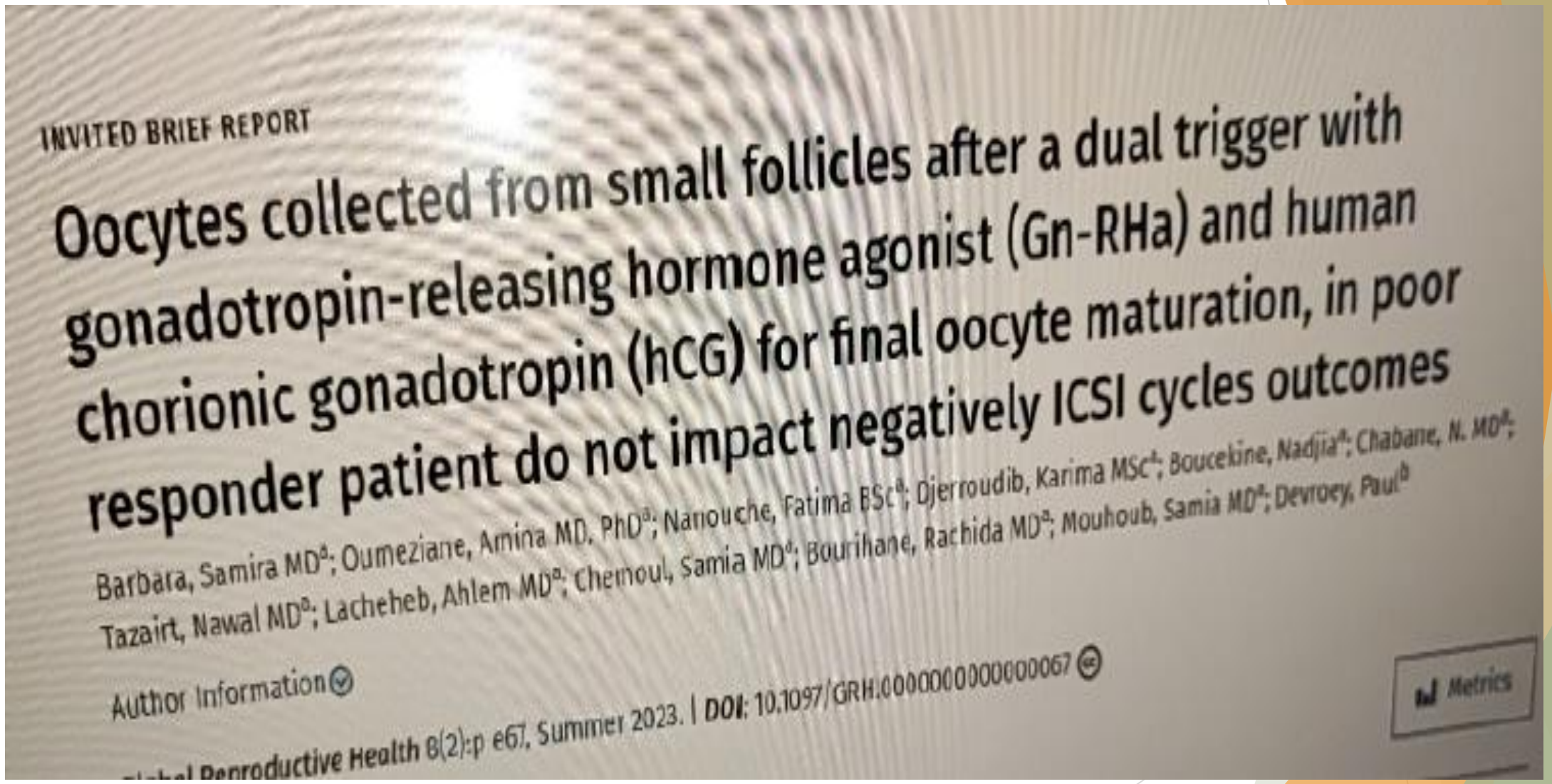

INVITED BRIEF REPORT

Oocytes collected from small follicles after a dual trigger with gonadotropin-releasing hormone agonist (Gn-RHa) and human chorionic gonadotropin (hCG) for final oocyte maturation, in poor responder patient do not impact negatively ICSI cycles outcomes

Barbara, Samira MD[a]; Oumeziane, Amina MD, PhD[a]; Nanouche, Fatima BSc[a]; Djerroudib, Karima MSc[a]; Boucekine, Nadjia[a]; Chabane, N. MD[a]; Tazairt, Nawal MD[a]; Lacheheb, Ahlem MD[a]; Chemoul, Samia MD[a]; Bourihane, Rachida MD[a]; Mouhoub, Samia MD[a]; Devroey, Paul[b]

Author Information

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Metrics

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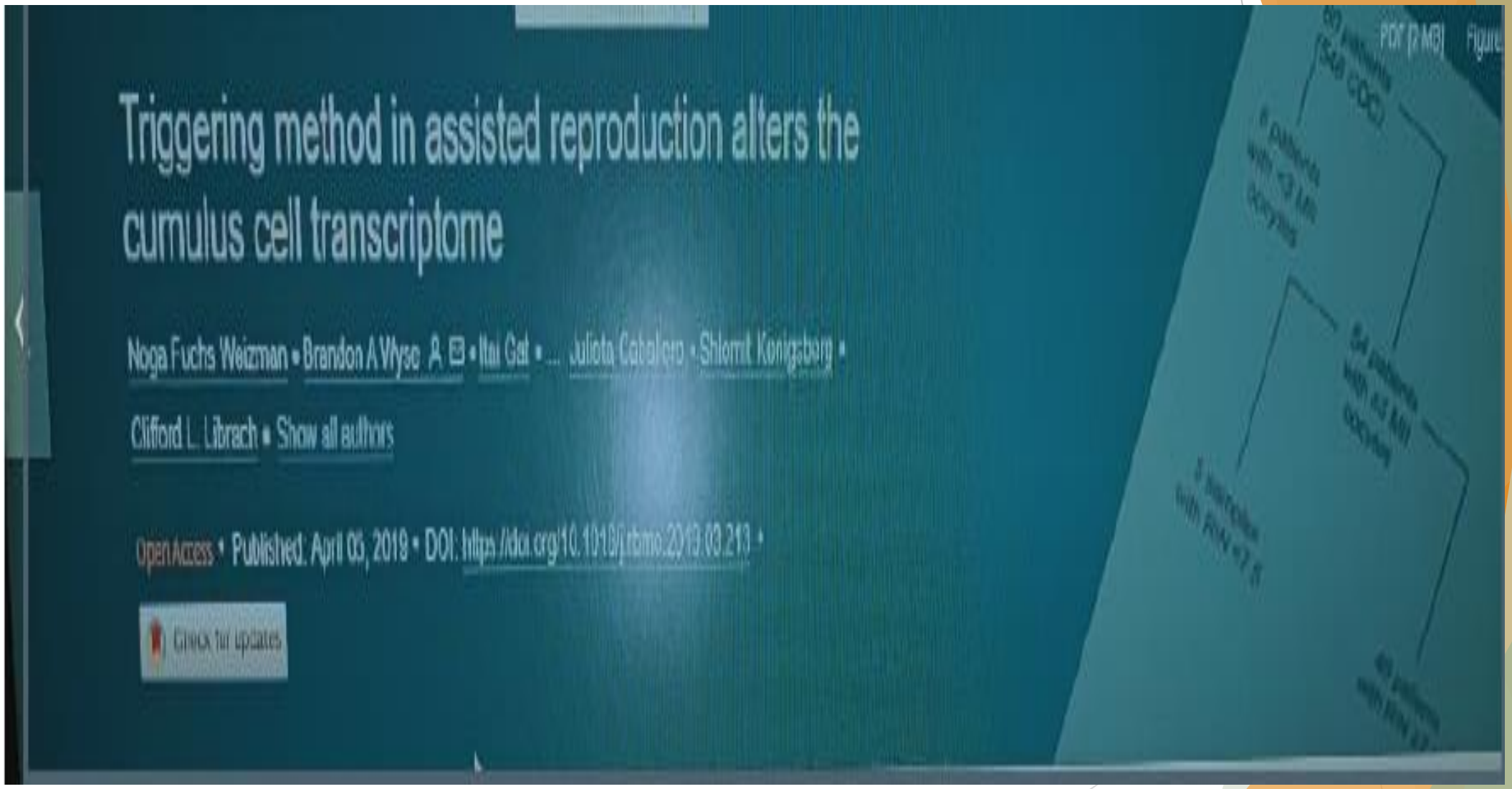
Triggering method in assisted reproduction alters the cumulus cell transcriptome
Noga Fuchs Weizman • Brandon A Wyse • Itai Gat • ... Julieta Cabalero • Shlomit Konigsberg •
Clifford L. Librach • Show all authors
Open Access • Published: April 05, 2019 • DOI: https://doi.org/10.1016/j.rbmo.2019.03.213 •
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RESEARCH Open Access

Low dose human chorionic gonadotropin administration at the time of gonadotropin releasing-hormone agonist trigger versus 35 h later in women at high risk of developing ovarian hyperstimulation syndrome – a prospective randomized double-blind clinical trial

L. L. Engmann[1,4*], B. S. Maslow[2], L. A. Kaye[1], D. W. Griffin[3], A. J. DiLuigi[1,4], D. W. Schmidt[1,4], D. R. Grow[1,4], J. C. Nulsen[1,4] and C. A. Benadiva[1,4]

Abstract

Background: Ovarian hyperstimulation syndrome remains a serious complication during in vitro fertilization cycles if high dose human chorionic gonadotropin (hCG) is used to trigger ovulation in high responder patients. Though much of this risk is mitigated with trigger using gonadotropin releasing-hormone (GnRH) agonist alone, it may result in lower birth rates. GnRH-agonist trigger and adjuvant low dose hCG has been proposed to improve birth rates, but timing of this hCG support to corpus luteum function has never been fully described. In this randomized, prospective trial, we explore differences in live birth rates and incidence of ovarian hyperstimulation syndrome (OHSS) in high-responder patients undergoing in vitro fertilization (IVF) receiving low dose hCG at the time of GnRH-agonist (dual trigger) or hCG adjuvant at the time of oocyte retrieval. Does the timing of hCG support make a difference?

Results: Thirty-four subjects high-responder patients were randomized to receive low-dose hCG at the time of GnRH-agonist trigger (Group 1) and 37 received low-dose hCG at the time of oocyte retrieval (Group 2). There were no differences in the baseline characteristics and outcome of ovarian stimulation between the two groups. There were no differences in the live birth rates between Group 1 and Group 2 by intention-to-treat (14/34, 41.2% versus 21/37, 56.8%, $p = 0.19$) or per-protocol (14/26, 53.8% versus 19/31, 61.3%, $p = 0.57$) analyses. There was a slightly higher incidence of OHSS in Group 2 compared to Group 1 although the difference was not statistically significant (3/31, 9.7% versus 1/26, 3.8%). All the cases of OHSS in Group 2 were moderate while the one case of OHSS in Group 1 was mild.

(Continued on next page)

In a natural cycle

Early rise in follicle-stimulating hormone (FSH) level which results in follicular growth.

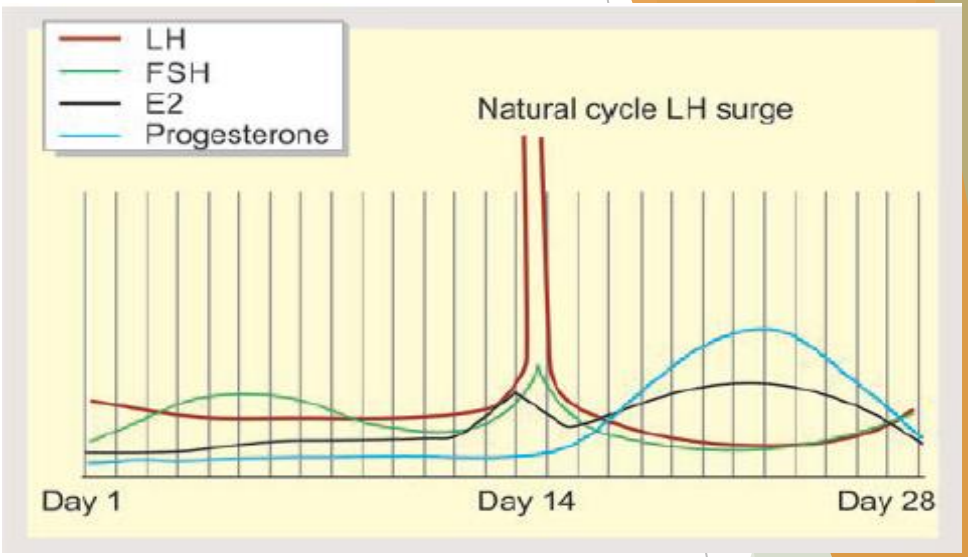
Rise in the level of serum estrogen .

Negative feedback on the production of FSH from the HPO axis.

Estrogen rises subsequently causing midcycle LH surge .

Oocyte maturation and release .

Ovulation



10-12 hours after LH peak.

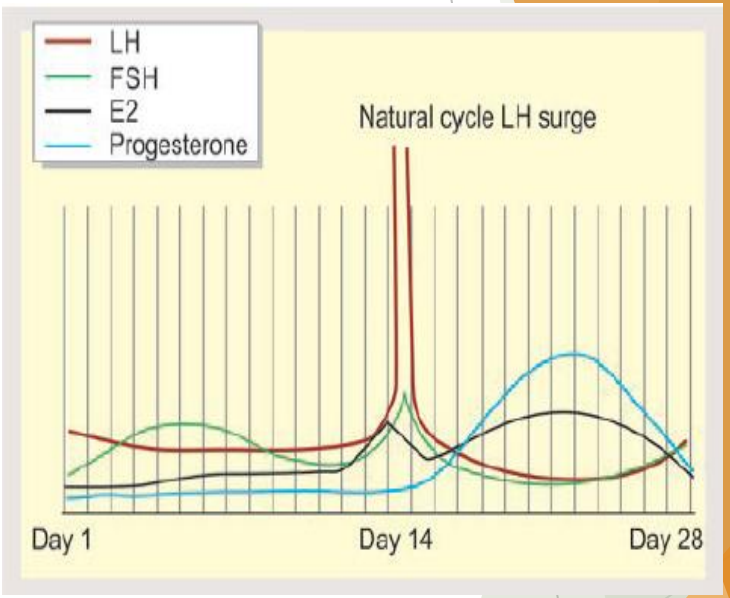
24-36 hours after peak serum estradiol levels.

Onset of LH surge appears to be the most reliable indicator of ovulation occurring 34-36 hours prior to follicular rupture.

In an ovulatory cycle,

LH surge is caused by estrogen released from preovulatory follicles, which causes luteinization of granulosa cells

Oocyte maturation and release result of positive feedback by high levels of estrogen (>300 p g /mL for >48 hours) which leads to LH surge from pituitary.

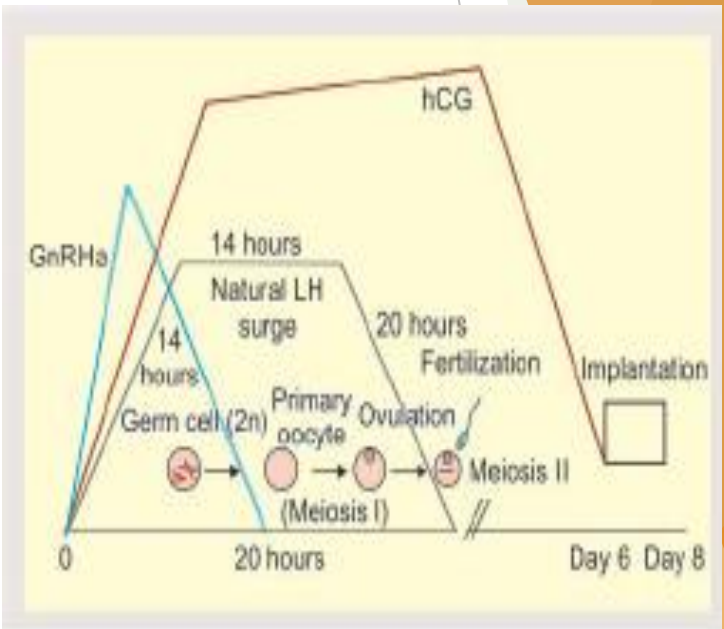


The LH surge lasts for about 48–50 hours and comprises of three phases:

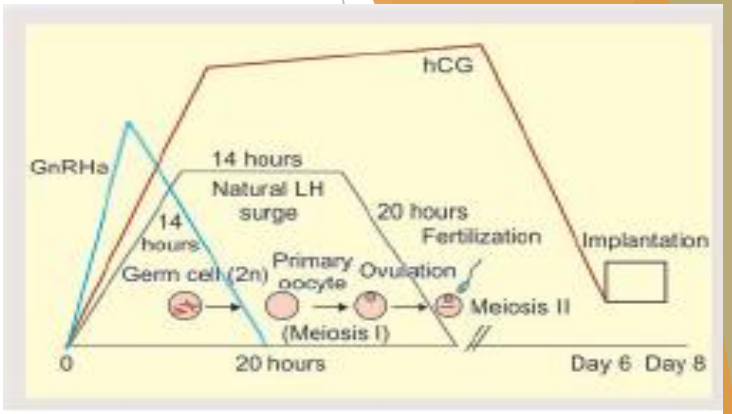
1. Ascending phase—14 hours

2. Plateau phase—14 hours

3. Descending phase—20 hours.



Luteinizing hormone surge



- Germinal vesicle breakdown
- Resumption of meiosis in oocyte
- Luteinization of granulosa cells and secretion of progesterone
- Expansion of cumulus and loss of gap junctions between cumulus cells and oocyte

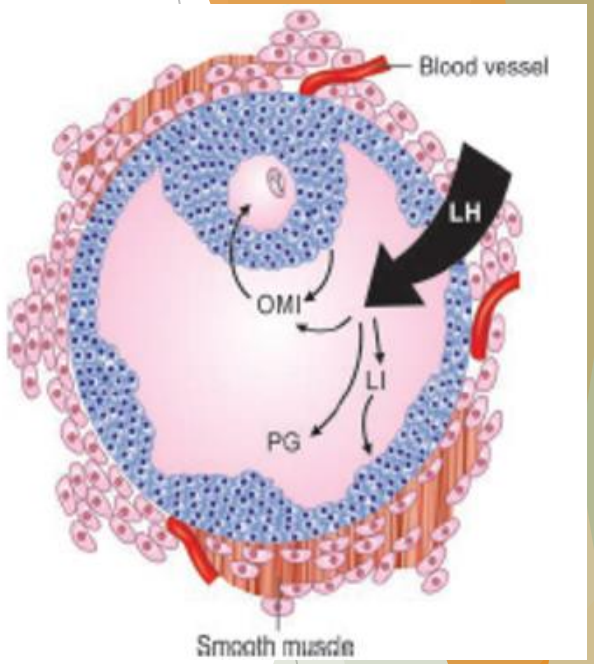
.

Luteinizing hormone surge

■ Secretion of prostaglandin and other eicosanoids essential for follicular rupture

■ With LH surge, levels of progesterone in follicle rise up until the time of ovulation.

■ Progesterone increases distensibility of follicular wall and causes preovulatory FSH surge by positive feedback mechanism from pituitary.



Follicle-stimulating hormone surge

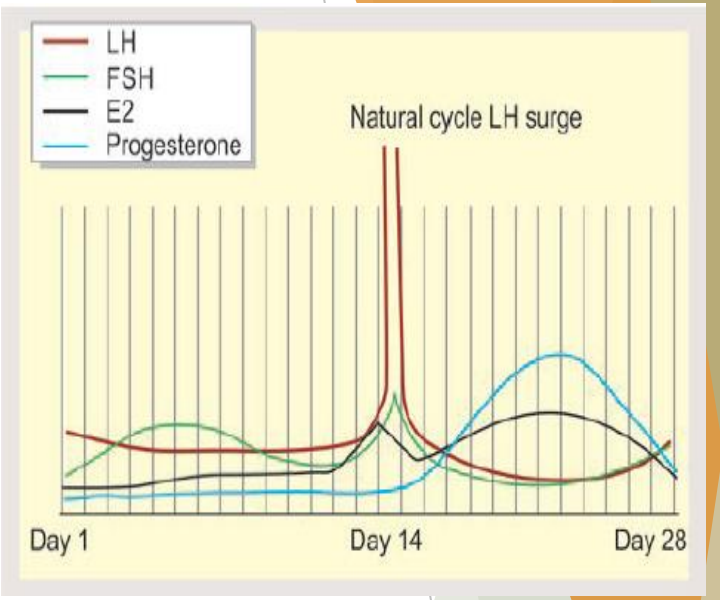
Cumulus expansion

Resumption of meiosis

Promotion of nuclear maturation

Induction of LH receptors on granulosa and cumulus cells

Functioning of corpus luteum

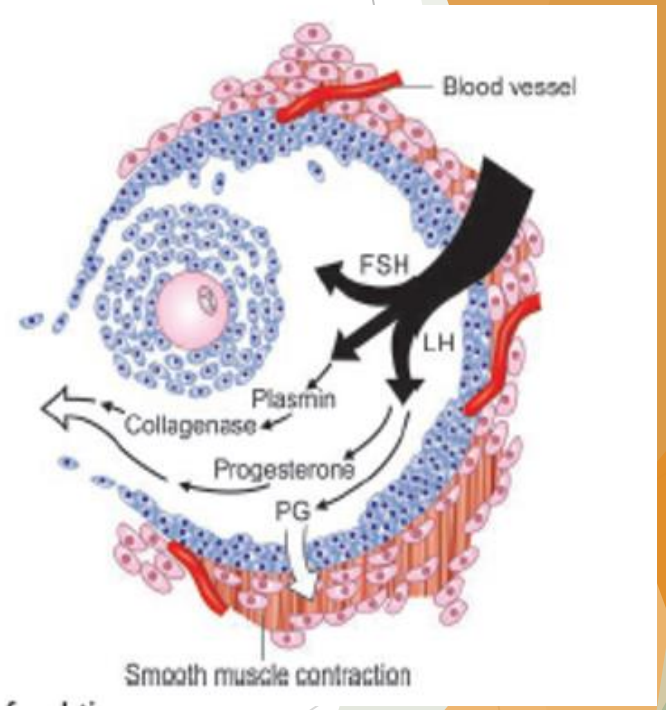


Follicle-stimulating hormone, LH, and progesterone

Stimulate the activity of proteolytic enzymes digestion of collagen in follicular wall and increasing its distensibility

Nuclear maturation (resumption of meiosis) & cytoplasmic maturation

Release of the developmentally competent oocyte from follicle.



Ovulation triggers are responsible for triggering the process of ovulation and also help in final maturation of the oocyte.

- Human chorionic gonadotropin (HCG)
- Gonadotropin-releasing hormone agonist (GNRHa)
- Recombinant luteinizing hormone (r-LH)
- Kisspeptins (KPs)
- Combining small dose of hCG with GnRHa (dual trigger)
- FSH with HCG

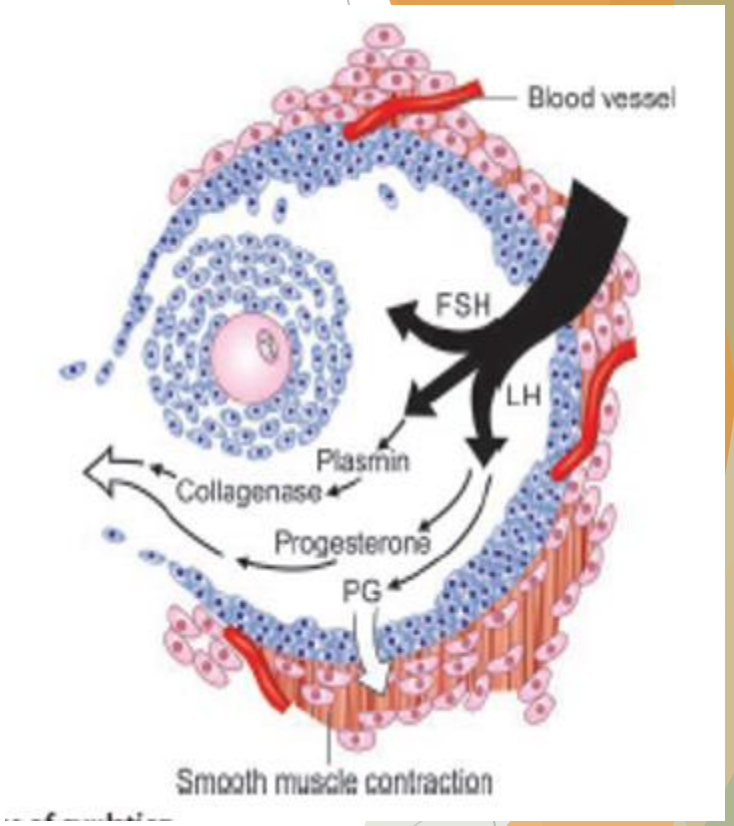
■ **Oocyte arrest in prophase 1 of meiosis** is maintained by elevated levels of cyclic cAMP in the oocyte which transported inside oocyte from cumulus or somatic cells through gap junctions

■ **LH and FSH surge** results in cumulus expansion and disruption of these gap junctions, resulting in low concentrations in cAMP in the oocyte. This results in the germinal vessel breakdown and resumption of meiosis

Follicular rupture

- Changes in the cumulus and matrix

- Increase in plasminogen activator mediated by FSH and LH in granulosa cells to activate plasminogen to plasmin which in turn activates collagenase to disrupt follicular wall

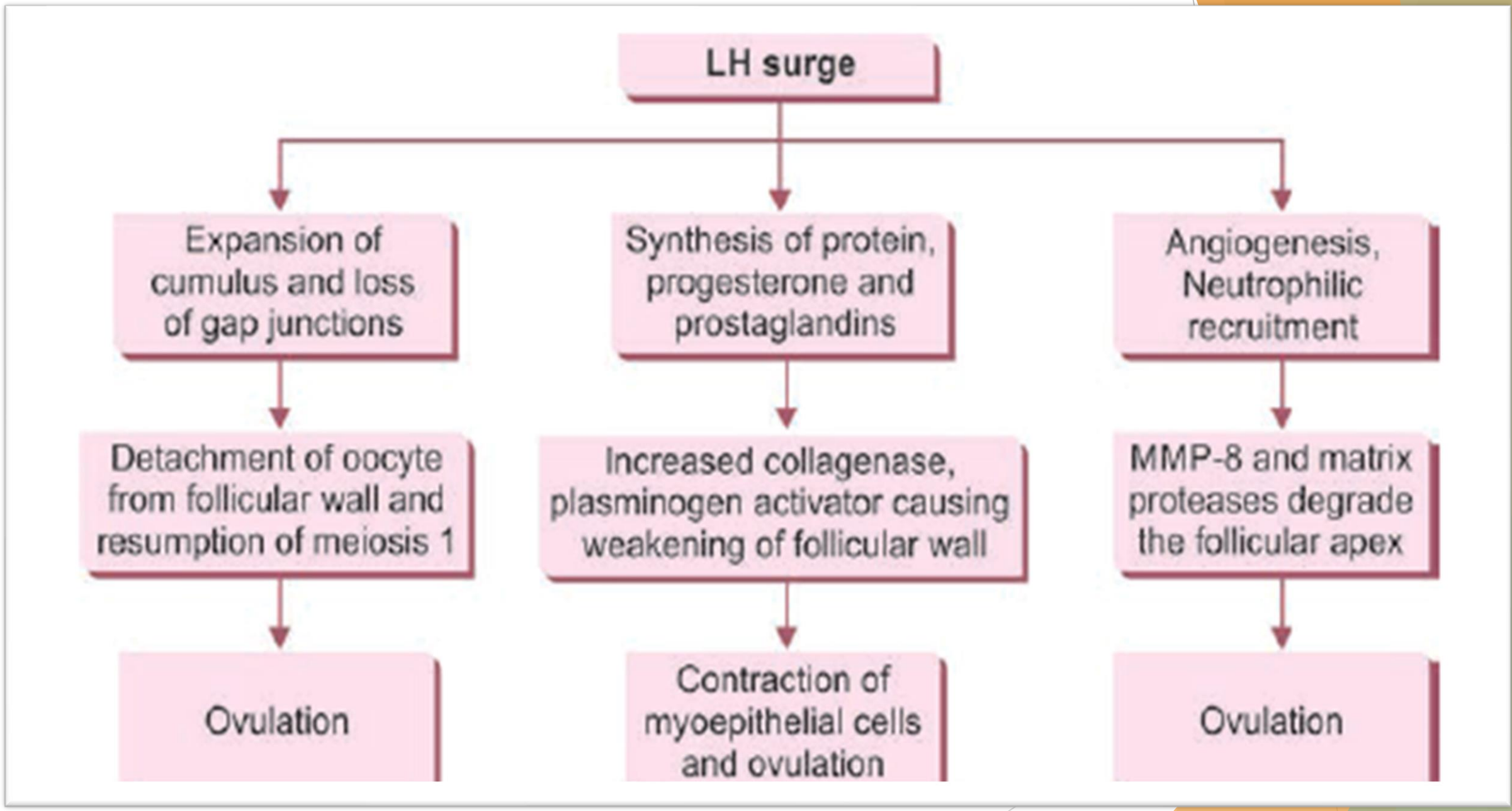


- Proteolytic digestion of tunica and basement membrane
- Follicular vascular and membrane remodeling
- Appearance of more inflammatory cells such as neutrophils in the follicular wall

■ **Prostaglandin being E2 and F2 α synthesized by cumulus cells, which causes cumulus expansion, resumption of oocyte meiosis, and extrusion of oocyte-cumulus complex from ruptured follicle by contraction of smooth muscle cells**

■ **Apoptosis of the epithelial cells over the apex or stigma mediated by matrix metalloproteinases enzymes which are activated in response to LH**

■ **Rise in intrafollicular pressure and contractions of the myoepithelial cells will result in the rupture of the follicle with extrusion of the mature oocyte**[7]


LH surge
Expansion of cumulus and loss of gap junctions
Synthesis of protein, progesterone and prostaglandins
Angiogenesis, Neutrophilic recruitment
Detachment of oocyte from follicular wall and resumption of meiosis 1
Increased collagenase, plasminogen activator causing weakening of follicular wall
MMP-8 and matrix proteases degrade the follicular apex
Ovulation
Contraction of myoepithelial cells and ovulation
Ovulation

In natural cycle, midcycle LH surge induces follicular rupture and ovulation. In stimulated ART cycles, LH surge is deliberately suppressed by gonadotropin-releasing hormone (GnRH) analogs to prevent follicle rupture before oocyte retrieval. **Hence, administration of trigger for final oocyte maturation is essential**.

Various Pharmacological Options for Ovulation Trigger

- Urinary human chorionic gonadotropin (u-hCG)
- Recombinant human chorionic gonadotropin (r-hCG)
- Recombinant luteinizing hormone (r-LH)
- Gonadotropin-releasing hormone agonists (GnRH agonist)
- Dual trigger (h HCG + GnRH Agonist)
- KPs.
- FSH+HCG

Human Chorionic Gonadotropin

■ As a result of structural differences and posttranslational modifications, HCG is more stable, has a longer half-life, and has greater receptor affinity than LH, thus making it more biologically active.

■ After subcutaneous administration, HCG has significantly longer half-life in comparison to LH.

■ Although HCG has LH-like activity, it does not reconstitute midcycle FSH surge.

Human Chorionic Gonadotropin

■ Due to above mentioned pharmacokinetic properties and because of sustained luteotropic effect, development of multiple corpus luteum, and supraphysiological levels of estradiol and progesterone synthesis, HCG is notorious in producing OHSS.

■ Minimal effective doses of u-HCG used to trigger oocyte maturation were studied as 2,000 IU, 5,000 IU, and 10,000 IU.

Human Chorionic Gonadotropin

- In a randomized controlled trial (RCT) study involving 80 polycystic ovary syndrome (PCOS) patients stimulated with rFSH and antagonist being added on day 6 of stimulation, no significant difference was noted in terms of ongoing pregnancy rates, severe OHSS, or number of oocytes retrieved in 2,000 IU, 5,000 IU, and 10,000 IU groups.

Human Chorionic Gonadotropin

- Urinary products still remain the first choice as they are cheap and easily available.

- 250 µg r-HCG = 5,000 IU u-HCG.

- ESHRE guideline 2019 for ovarian stimulation for IVF/intracytoplasmic sperm injection (ICSI): Use of recombinant and urinary HCG is equally recommended for triggering final oocyte maturation during ovarian stimulation protocols.

Recombinant Luteinizing Hormone

Advantages

- More physiological
- Risk of ovarian hyperstimulation syndrome is almost nil

Disadvantages

- Very high doses of r-LH is required to induce ovulation (15,000–30,000 IU)
- Not cost-effective
- Limited literature to support its use

Recombinant Human Chorionic Gonadotropin

The Cochrane meta-analysis reported no difference in live birth rate, moderate OHSS, and number of oocytes retrieved between r-LH and u-HCG when used for triggering final oocyte maturation.

Another RCT done including 49 women with poor ovarian reserve to compare r-LH and u-HCG showed that there is no statistically significant difference in cycle

Recombinant Human Chorionic Gonadotropin

Farrag et al. showed that r-HCG increases the rate of metaphase II (MII) oocytes with mature cytoplasm compared to u-HCG.

However, many RCTs have shown that r-HCG and u-HCG are equally effective.

Gonadotropin-releasing Hormone Agonist

Activates GnRH receptors.

Causing increase in the levels o FSH and LH.

It mimics a natural midcycle FSH and LH surge This is called “flare effect”.

This effect is used to obtain oocyte maturation.

Gonadotropin-releasing Hormone Agonist

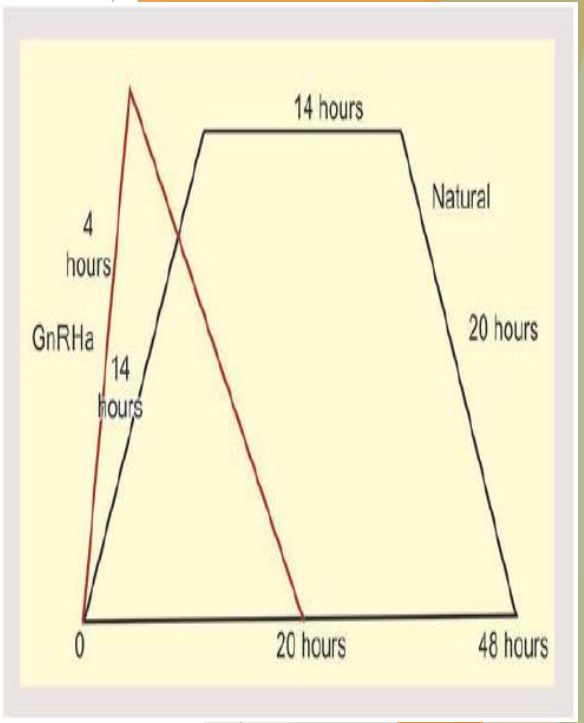
- GnRH agonist is derived from native GnRH by substitution of amino acids at 6th and 10th positions.

- These modifications result in alteration of enzymatic cleavage and potency of the molecule.

- Native GnRH is a decapeptide .

- Dose of agonists as trigger: Triptorelin 0.2 mg, leuprolide 1–1.5 mg, and buserelin 0.5 mg.

Gonadotropin-releasing Hormone Agonist



ESHRE guideline 2019 recommends choosing dosage of triptorelin ranging from 0.1 to 0.4 mg.

■ Some studies have used higher dose and others two doses 12 hours apart.

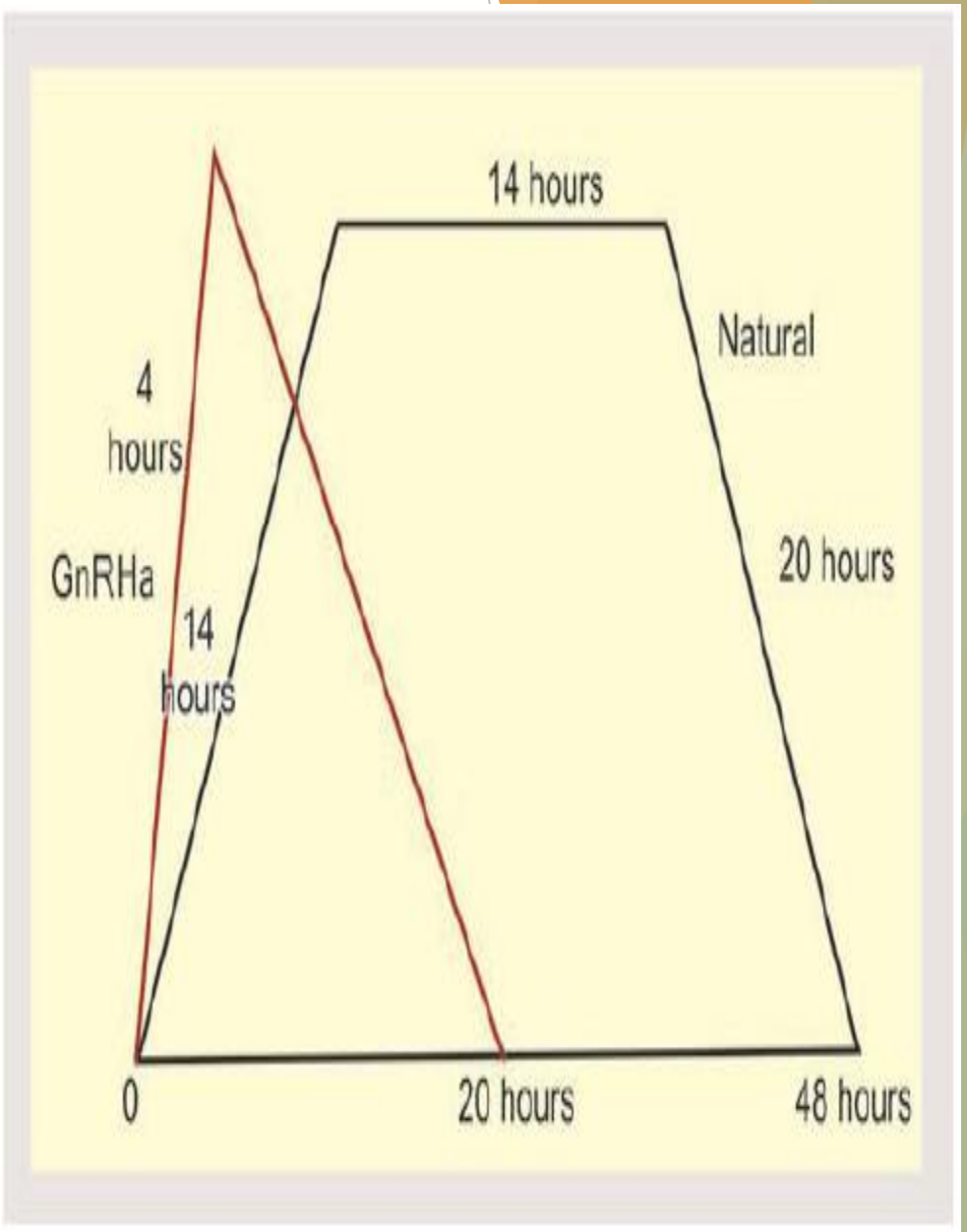
■ A single dose of 1 mg of leuprolide yields optimal mature oocyte yield.

Gonadotropin-releasing Hormone Agonist

■ The surge induced by a GnRH agonist is short-lasting and consists of two phases:

1. A short ascending limb (4 hours)

2. Long descending limb (20 hours), in total of 24–36 hours as compared to 48 hours in a natural cycle



- **GNRHa trigger is as effective as hCG in**

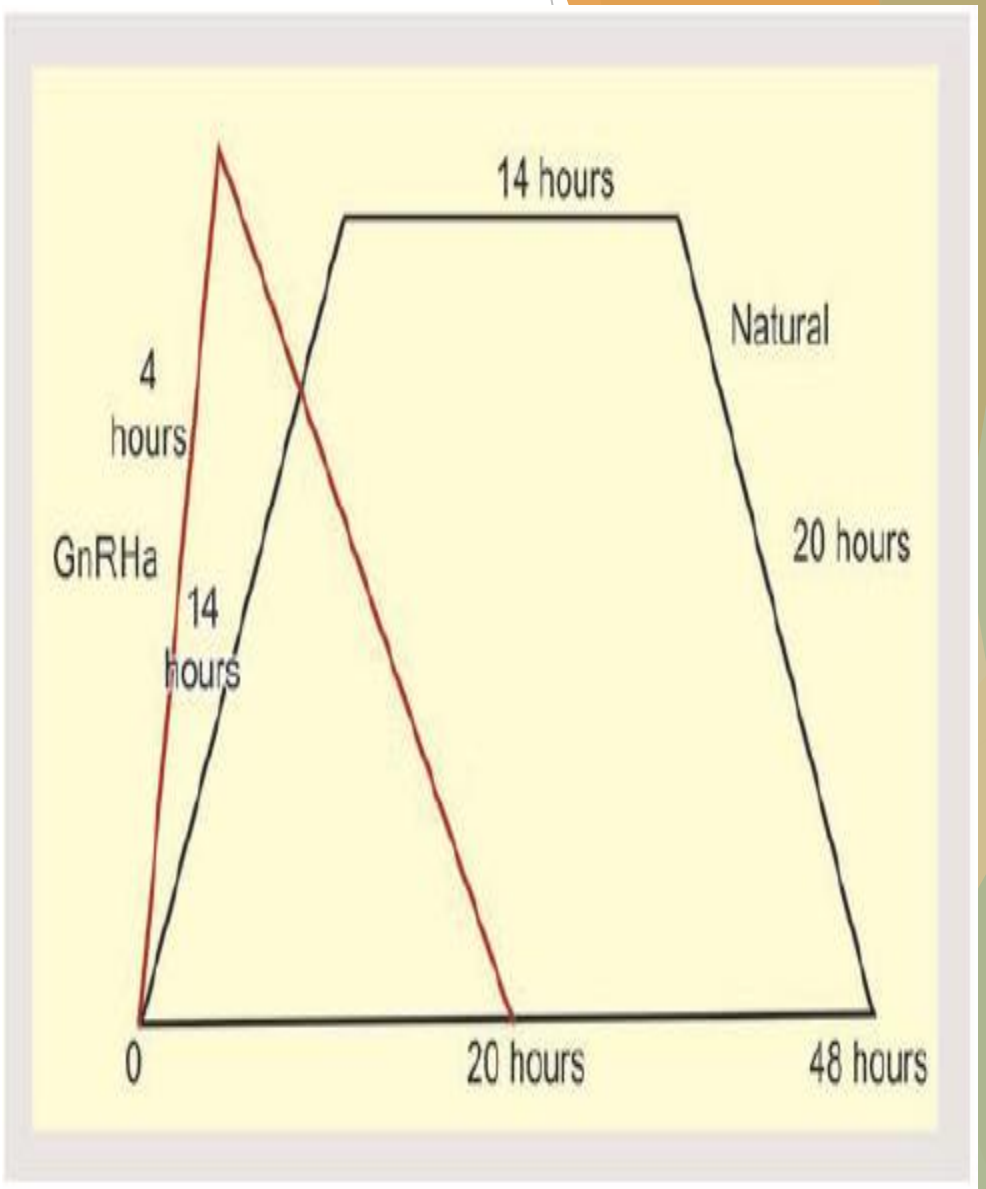
Inducing final follicular maturation
Inducing FSH surge

- **There is no difference in oocyte and embryo quality when compared to HCG with almost elimination of OHSS.**

■ But reduction in clinical pregnancy rates with GnRH agonist and conventional luteal support as compared to HCG in normal responders was noted in meta-analysis comparing 10,000 IU urinary HCG and 0.2 mg triptorelin.

■ The drawback of a GNRHa trigger is early corpus luteolysis and inadequate steroidogenesis

■ **The drawback of a GNRHa trigger is early corpus luteolysis and inadequate steroidogenesis**



Indications for Gonadotropin-releasing Hormone Agonist Trigger

- **Oocyte donors**
- **Fertility preservation**
- **Risk of OHSS**
- **Preimplantation genetic diagnosis**
- **Prematurely elevated progesterone prior to trigger.**

How to Predict Gonadotropin-releasing Hormone Agonist Trigger Failure?

- Failed oocyte maturation after GnRH trigger often detected with low serum LH on the day after trigger

- GnRH agonist trigger needs to be avoided in patients with preexisting hypothalamus-pituitary axis dysfunction and also with a pretrigger LH <0.5 IU/L.

- Predicting probability of EFS after GnRH trigger is important as to decide whether to proceed with retrieval or whether rescue dose of HCG is needed.

■ **Serum LH and progesterone levels measured 12 hours after trigger can indicate failed endogenous response to trigger injection and need for intervention.**

■ **If no LH surge and/or progesterone rise noted after GnRH trigger, repeat trigger with HCG and oocyte retrieval after 35 hours later is indicated.**

■ If suboptimal LH rise with value <15 IU/L is noted, repeat trigger with HCG as soon as possible and oocyte retrieval as planned or cancellation of cycle is indicated.

■ Also, unilateral follicle aspiration and if no oocytes are obtained, HCG trigger and oocyte retrieval after 34 hours can be done.

Luteal Phase Support after Gonadotropin releasing Hormone Agonist Trigger

Luteal Support with Progesterone and Estrogen

Recombinant Luteinizing Hormone for Luteal Support

Human Chorionic Gonadotropin at the Time of Oocyte Retrieval

Very Low-dose HCG for Luteal Support

PREDICTORS OF SUCCESS AFTER GONADOTROPIN-RELEASING HORMONE AGONIST TRIGGER

One study revealed that peak E2 >4,000 p g/mL and raised levels of LH on the day of trigger improved pregnancy rates after GnRH agonist trigger. Pregnancy rate in this group was 53.6% compared to 38.1% in the group that had E2 <4,000 p g/mL.

In the group with E <4,000 pg/mL, dual trigger with GnRH agonist trigger and low-dose HCG 1,000 IU had higher rate pregnancy rates than GnRH agonist trigger alone.

In all those with E >4,000 pg/mL,
supplementation with E2 and progesterone alone is sufficient in luteal phase
or freeze all embryos can be done.

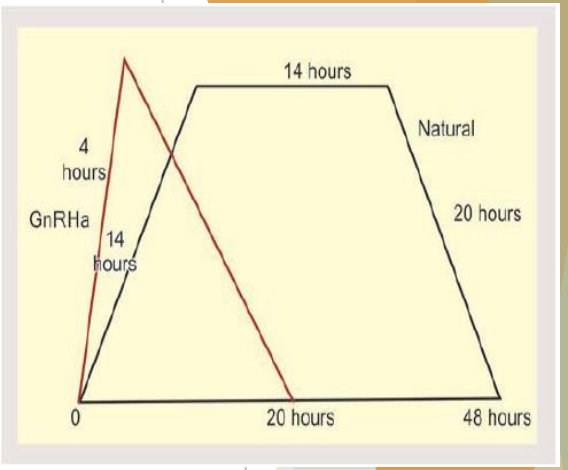
those with E <4,000 pg/mL, adjuvant low-dose HCG in luteal phase improves pregnancy rates.

Number of follicles on the day of trigger will also determine if 1,500 IU of HCG has to be given on the day of oocyte retrieval after agonist trigger.

Seyhan et al. suggested that all **women with 10–14 mm follicles of >18** in number should not be given HCG bolus as the risk of OHSS is 26% and embryos should be cryopreserved.

Few other studies also suggested that **women with >25 follicles of greater than 11 mm in diameter** should not be given HCG bolus and cryopreservation of embryos should be done.

OVARIAN HYPERSTIMULATION SYNDROME IN GONADOTROPIN-RELEASING HORMONE AGONIST TRIGGER



Because of short duration of LH surge and
Early corpus luteolysis
Risk of OHSS is negligible after GnRH agonist trigger.

ESHRE guideline 2019 strongly recommends triggering with GnRH agonist for final oocyte maturation to reduce risk of early onset OHSS in patients at risk of OHSS.

Few cases of OHSS with use of GnRH agonist trigger have been reported which is thought to be due to low dose of HCG(dual trigger).

Very few cases of OHSS with use of GnRH agonist alone have been reported which has been attributed to activating mutations in GnRH or FSH receptor.

Dual Trigger

Dual trigger which includes triggering of the final oocyte maturation by a combination of a GNRHa together with a low-dose HCG (1,000–2,500 IU) was first described by Shapiro.

Dual Trigger

■ Increase in the level of LH was found in the dual trigger soon after trigger along with a surge in FSH compared with HCG trigger. There was no major difference in the number of MII oocytes, or the number of two pronuclei oocytes.

■ The risk of OHSS was almost eliminated by using GNRHa trigger and proper luteal function was also modified by the added HCG when dual trigger was used.

Dual Trigger

■ The combined surge of FSH and LH in dual trigger is particularly useful in patients with immature oocytes and EFS in the previous IVF cycles.

■ Dual trigger may aid in implantation, clinical pregnancy, and live birth rates when used in normal responder patients in an antagonist cycle.

Kisspeptins

■ Exogenously administering of KPs has been found to result in release of gonadotropins particularly in cases of hypothalamic amenorrhea.

■ When given in the periovulatory phase, exogenous KP has been shown to induce a 3–4-fold increase in LH secretion.

■ In women undergoing ART, KPs were capable of eliciting an effective LH surge that resulted in successful oocyte maturation and live birth.

■ KPs, therefore, may offer a completely different, “natural” concept for ovulation induction in ART without the risk of OHSS.

Empty Follicle Syndrome

INTRODUCTION

Empty follicle syndrome (EFS), a rare but frustrating complication of IVF leading to cycle cancellation.

This rare event is responsible for substantial stress and anxiety to both the patients and the clinician during an IVF

DEFINITION

Empty follicle syndrome is no oocytes are retrieved :

Despite repeated aspiration and flushing

After an apparently adequate ovarian response to stimulation

Evidenced by serial ultrasound and adequate steroidogenesis.

INCIDENCE

Uncertainty of its existence and variability in the inclusion criteria across different studies

Also lack of the HCG concentration threshold, to distinguish between genuine and false EFS

The choice of the patient population

0.045 to 7% of IVF cycles

Empty Follicle Syndrome

Genuine empty follicle syndrome

False empty follicle syndrome

Genuine empty follicle syndrome False empty follicle syndrome

Failure to retrieve oocytes from mature ovarian follicles

After triggering apparently normally developed follicles,

Optimal beta HCG levels (HCG trigger)on the day of oocyte retrieval

The presence of optimal LH levels 12 hours post agonist trigger

False empty follicle syndrome

Low beta HCG levels

Due to an error in administration

Due to reduced bioavailability of the HCG

Inappropriately administered agonist trigger (e.g., hypogonadotropic hypogonadism group)

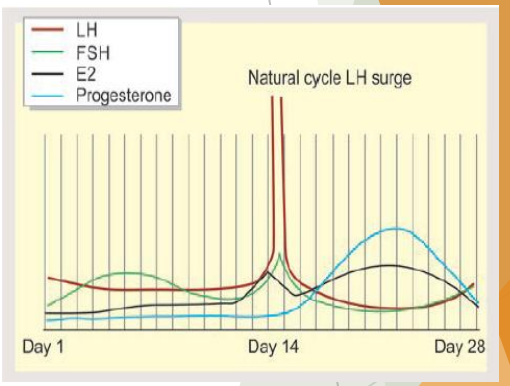
Most common among EFS

Cycle can be rescued with a repeat trigger

Pathophysiology of False Empty Follicle Syndrome Following HCG Trigger

Inadequate or Absent Luteinizing Hormone Surge

- ***Errors in administration of the trigger:***
- ***Error in timing of the injection:***



Luteinizing hormone surge effect is fully displayed after 34–38 hours from injection, with a peak effect at about 36 hours.

- ***Improper timing of the oocyte retrieval***

  if oocyte retrieval is performed too early (before 34 hours from the injection), or too late(after 38 hours, when the largest follicles have already spontaneously ovulated).

- ***Manufacturing defects and potency defects***

■ *Low bioavailability due to variation in the absorption or clearance:*

Subcutaneous administration of HCG injection in women with history of bariatric surgery may alter the absorption due to abdominal skin redundancy. In such patients intramuscular injections are preferred.

■ *Ovarian low bioavailability of HCG:*

It may result in a unilateral EFS, as in ovarian torsion occurring between the time of trigger and follicular aspiration. Oocytes can be aspirated from the unaffected ovary.

Pathophysiology of False Empty Follicle Syndrome Following GNRHa Trigger

- ***Wrong trigger***

  Hypogonadotropic hypogonadism (WHO type 1 anovulation) or in antagonist protocol.

- ***Inadequate response to agonist trigger:***

  Administering an agonist trigger in a woman with overly suppressed pituitary.

Pathophysiology of Genuine Empty Follicle Syndrome

Pathophysiology of GEFS is still poorly understood.

ZP mutations ; prevents zone pellucida formation.(defective oogenesis, folliculogenesis and subsequently impaired fertilization and implantation).

The anti-ZP autoantibodies can induce GEFS.

Dysfunctional Folliculogenesis

the granulosa cells of recurrent EFS have an increased expression proapoptotic genes and a significant reduction in transcripts

As a result , oocytes may be lost in the late folliculogenesis due to apoptosis.

Pathophysiology of Genuine Empty Follicle Syndrome

Dysfunctional Folliculogenesis

- ***Ovarian aging***:

  poor ovarian response and failure to retrieve oocytes , suggesting EFS may represent an advanced stage of ovarian aging, characterized by residual responsiveness of the granulosa cells while the oocytes fail to develop adequately.

- **Faulty oocyte development and maturation**

- ***Receptor polymorphism***

■ **Strong attachment of the cumulus cell complexes to the follicular wall, dysfunctional signaling between the cumulus cells and the oocyte**.

■ ***Receptor polymorphism:***

Novel mutation in LH/HCG receptor (LHCGR) was identified in two sisters with GEFS which is inherited as a recessive trait. mutation

A pericentric inversion in a fragile site of chromosome2 (site 46, XX, inv(2) (p11q21) has been identified in a woman who had repeated GEFS.

Human Chorionic Gonadotropin Trigger

Acts directly on the ovary. So, EFS in case of an HCG trigger can be said to be attributed to abnormal folliculogenesis or to the response of the ovary to the triggering stimulus or errors in administration of the trigger(dose, route, timing).

Pathophysiology of EFS with Various Triggers

Gonadotropin-releasing Hormone Agonist Trigger

Inability of the pituitary to release LH sufficient to trigger ovulation

Failure of the receptors LH on the ovary

Polymorphism of the LH β subunit gene.

- ***Hypogonadotropic hypogonadism patients (WHO Type 1)***

  Endogenous follicle stimulating hormone (FSH) and LH <1.2 IU/L.

■ **EFS in a patient with borderline hypothalamic pituitary dysfunction, but with gonadotropin levels just above the hypogonadotropic hypothalamic level**.

The lower production of LH allow for follicular development and initial luteinization, but insufficient to complete cumulus cell expansion and its loosening from the follicular wall. Hence, depending upon the degree of response of the pituitary to the agonist trigger, a GEFS or FEFS may occur.[6]

■ **A temporary state of hyposensitivity of the pituitary to the agonist trigger may exist in some cycles, so in such cases an HCG trigger may recover mature oocytes**.

■ ***Patients with GnRH receptor polymorphism:***

These women need a high dose of the agonist to activate the receptor.

■ **Women with a variant LH β gene polymorphism, especially the homozygous form, have the less bioactive LH molecule and so are at risk for a blunted response after an agonist trigger.**

RISK FACTORS FOR EMPTY FOLLICLE SYNDROME

- Previous history of EFS
- Advanced age with poor ovarian reserve (37.7 ± 6 years vs 34.2 ± 6 years, p <0.001).
- Ovarian resistance to various stimulations
- Obesity

■ Longer duration of infertility (8.8 ± 10.6 years vs. 6.3 ± 8.4 years, p <0.05)

■ Higher baseline FSH levels (8.7 ± 4.7 IU/L vs. 6.7 ± 2.9 IU/L, p <0.001)

■ Lower estradiol levels on the day of trigger (499.9 ± 480.9 Pg/mL vs. 1,516.3 ± 887.5 pg/mL, p <0.001).

DIAGNOSIS AND PREVENTION

Detecting HCG in urine

HCG in follicular fluid(using a rapid home pregnancy kit)

Blood (>40 mIU/L).

Presence of HCG in these samples more likely suggests a GEFS and the absence or suboptimal values of HCG suggests FEFS.

For an agonist trigger,

12-hour post-trigger LH concentration at or near 15 mIU/mL is used as a threshold between adequate and inadequate response to the GnRHa trigger.

A 12 hour post-trigger progesterone concentration (progesterone level >3.5 ng/mL 8–12 hours after trigger) can be a complementary indicator of trigger response over LH alone.

Luteinization of the follicle releases progesterone.

Patients with a higher number of follicles will have higher values of progesterone.

Elevated post- triger progesterone concentration associated with a borderline or even low LH concentration can still result in successful oocyte retrieval.

But, conversely, low post-trigger progesterone concentration associated with LH concentration>15 mIU/mL might suggest an inadequate response.

MANAGEMENT OF EFS IN THE CURRENT CYCLE

- ***Re-administering HCG and reaspiration in a case of FEFS:***

rescue dose of HCG in cases of FEFS

During the second retrieval attempt, 24–36hours later, follicles from the previously aspirated ovary should be reaspiration.

Mucification of the cumulus cells in response to circulating HCG allows dissociation of the cumulus–oocyte complex, and collection with a second aspiration may be possible. The rescue dose maybe of a higher dose or from a different batch of urinary h HCG or switched to recombinant HCG. A recent review of literature has documented that 42.8% of cycles (6 out of 14) rescued with repeat HCG resulted in a healthy liveborn fetus.

. Mucification of the cumulus cells in response to circulating HCG allows dissociation of the cumulus–oocyte complex, and collection with a second aspiration may be possible.

The rescue dose may

Higher dose or from a different batch of urinary HCG switched to recombinant HCG.

A recent review of literature has documented that 42.8% of cycles (6 out of 14) rescued with repeat HCG resulted in a healthy live born fetus.[9]

MANAGEMENT OF SUBSEQUENT CYCLESAFTER EMPTY FOLLICLE SYNDROME

- Check for possible risk factors before the start of the stimulation.

- Triggering the next cycle with recombinant HCG or recombinant LH.

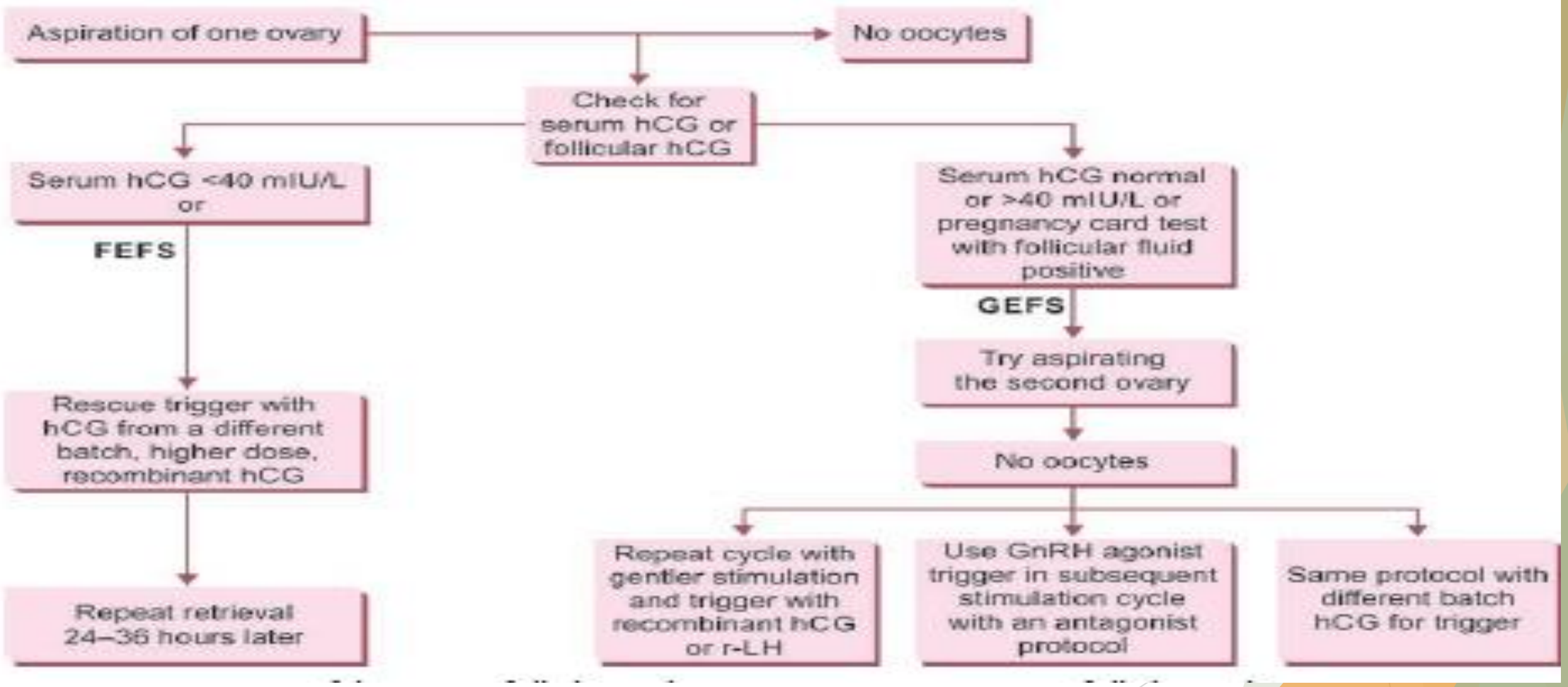
- Gonadotropin-releasing hormone agonist trigger(GNRHa trigger). Agonist trigger to induce, the more physiological LH surge, in an antagonist cycle has been proposed as one of the strategies to prevent EFS.

- Dual triger.

■ *Delayed retrieval if there was an error in timing*:

It maybe hypothesized that cumulus expansion, which allows the oocyte to detach from the follicular wall, may also require longer time periods in certain patients.

Flowchart 1: Management of empty follicle syndrome.




Thank You