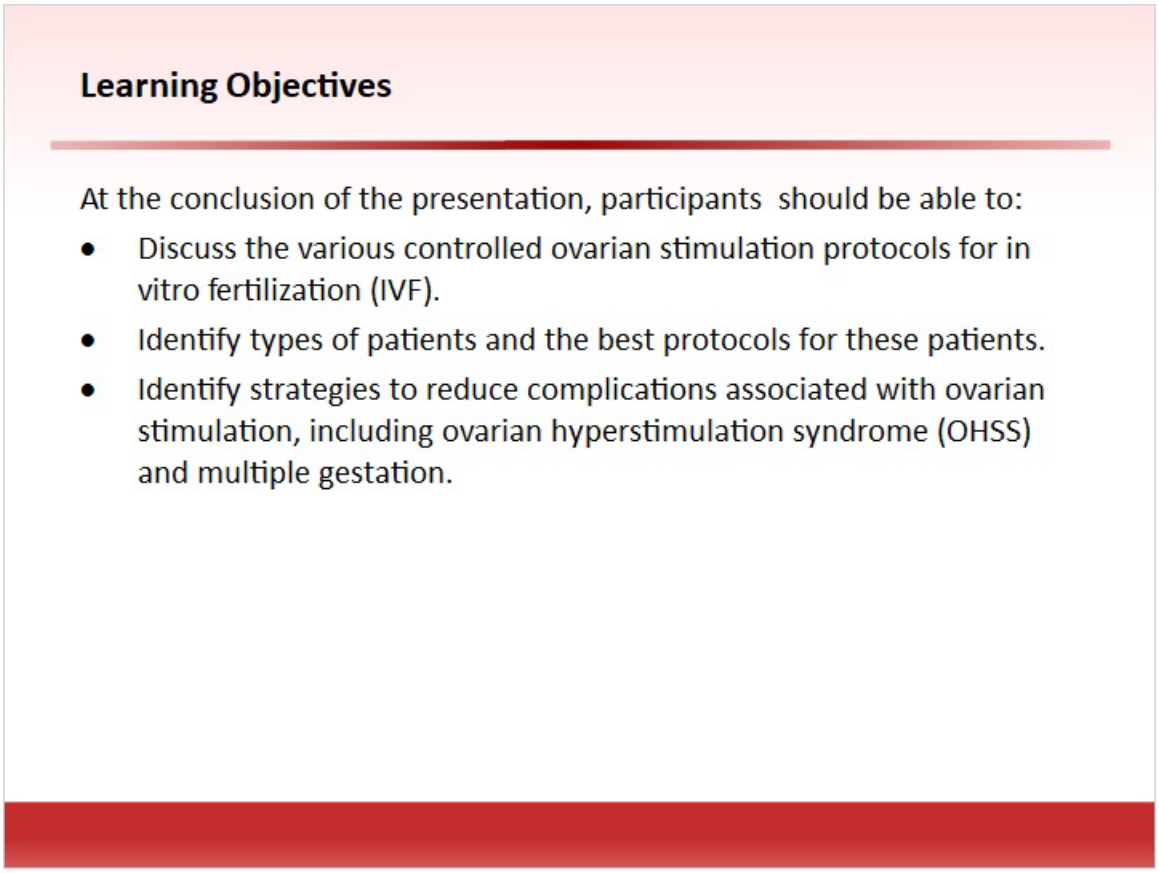
LABCC100 Lesson 11

1.1 Ovarian Stimulation Protocols

Notes:

Welcome to the American Society for Reproductive Medicine's eLearning modules. The subject of this presentation is Ovarian Stimulation Protocols.

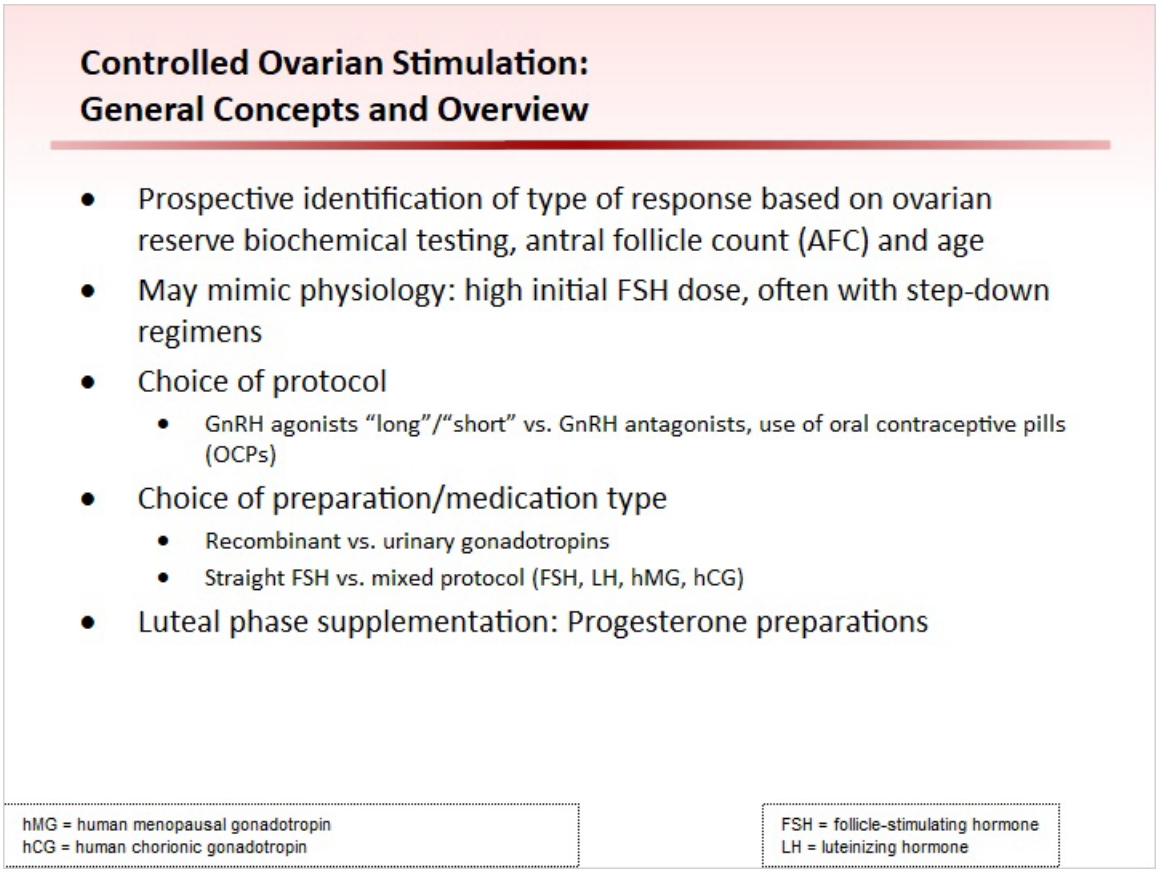
1.2 Learning Objectives



Notes:

At the conclusion of the presentation, participants should be able to:
Discuss the various controlled ovarian stimulation protocols for in vitro fertilization (IVF).
Identify types of patients and the best protocols for these patients.
Identify strategies to reduce complications associated with ovarian stimulation, including ovarian hyperstimulation syndrome (OHSS) and multiple gestation.

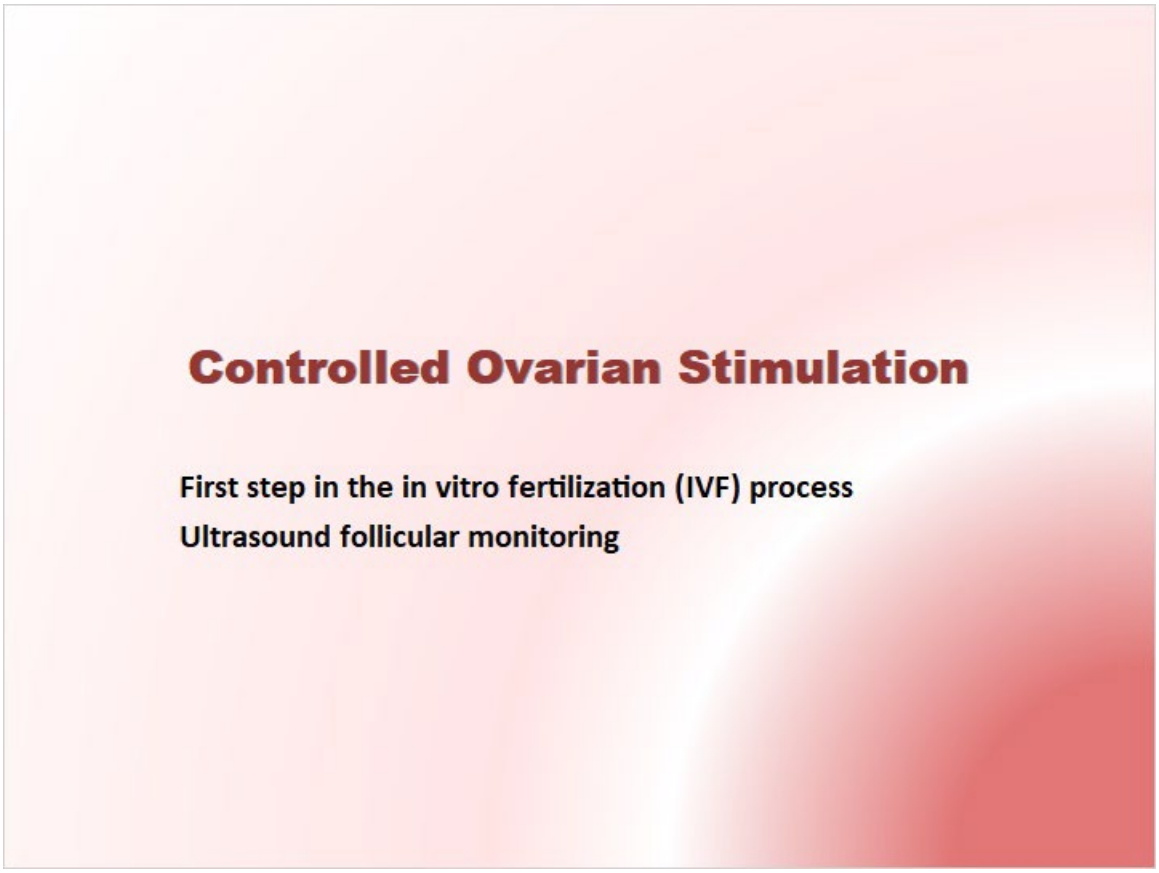
1.3 Controlled Ovarian Stimulation:



Notes:

Many clinics use some method to prospectively identify the type of ovarian response to stimulation. These include ovarian reserve biochemical testing, antral follicle count (AFC), and age. The goal of controlled ovarian stimulation is to mimic natural physiology with a high initial follicle-stimulating hormone (FSH) dose and often various step-down regimens. There are several choices of protocols including gonadotropin-releasing hormone (GnRH) agonists with "long" or "short" protocols vs. GnRH antagonists, and use of oral contraceptive pills (OCPs).
There are also choices in the type and preparation of medication: recombinant vs. urinary gonadotropins, straight FSH vs. a mixed protocol with FSH, luteinizing hormone (LH), human menopausal gonadotropin (hMG), and human chorionic gonadotropin (hCG). Finally, there are various progesterone preparation options for luteal phase supplementation.

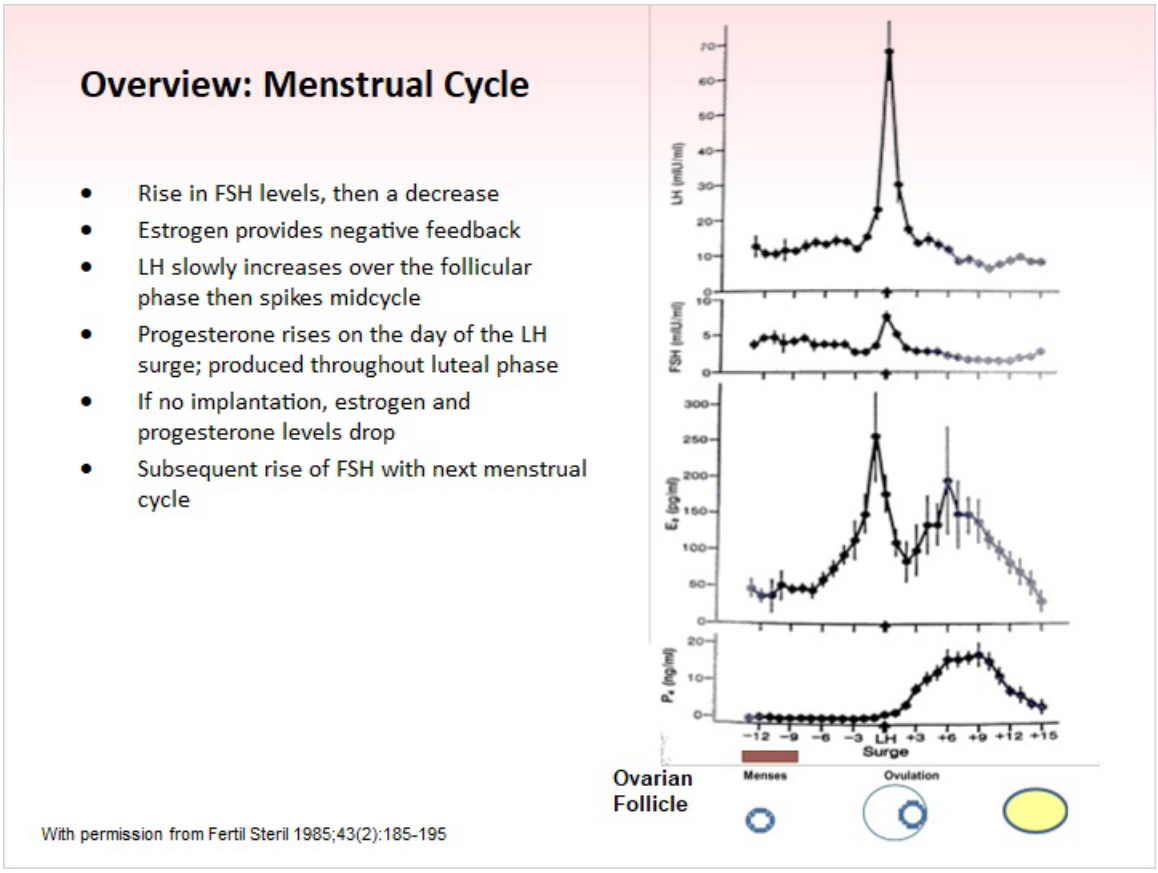
1.4 Controlled Ovarian Stimulation



Notes:

This section will cover controlled ovarian stimulation, the first step in the IVF process and the role of ultrasonographic follicular monitoring.

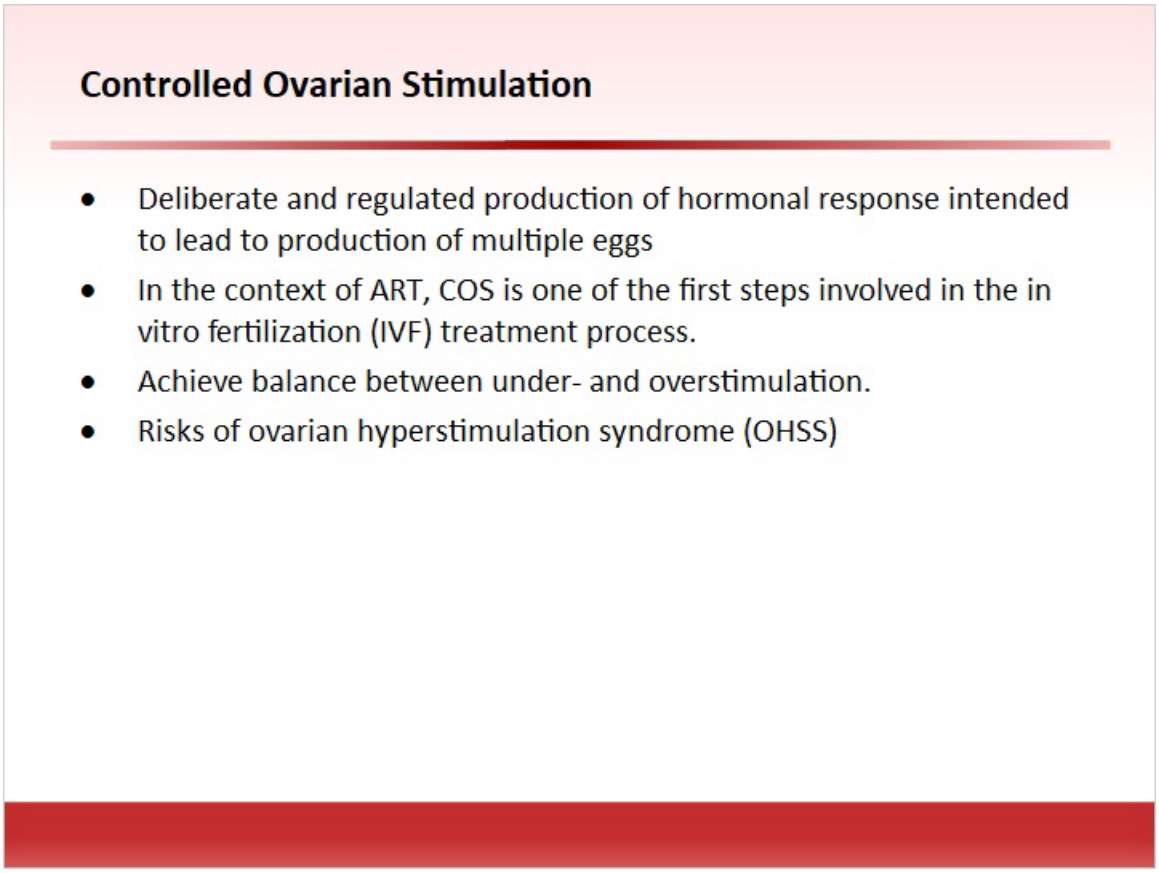
1.5 Overview: Menstrual Cycle



Notes:

A typical 28-day menstrual cycle begins with a rise in FSH levels that then decrease as estrogen from the developing follicle provides negative feedback. LH slowly increases over the follicular phase, but then spikes midcycle, resulting in maturation of the oocyte and ovulation. Progesterone rises on the day of the LH surge and is produced by the corpus luteum throughout the luteal phase. Progesterone is essential for implantation. If implantation does not occur, both estrogen and progesterone levels drop with the demise of the corpus luteum. This causes the subsequent rise of FSH that begins the next menstrual cycle.

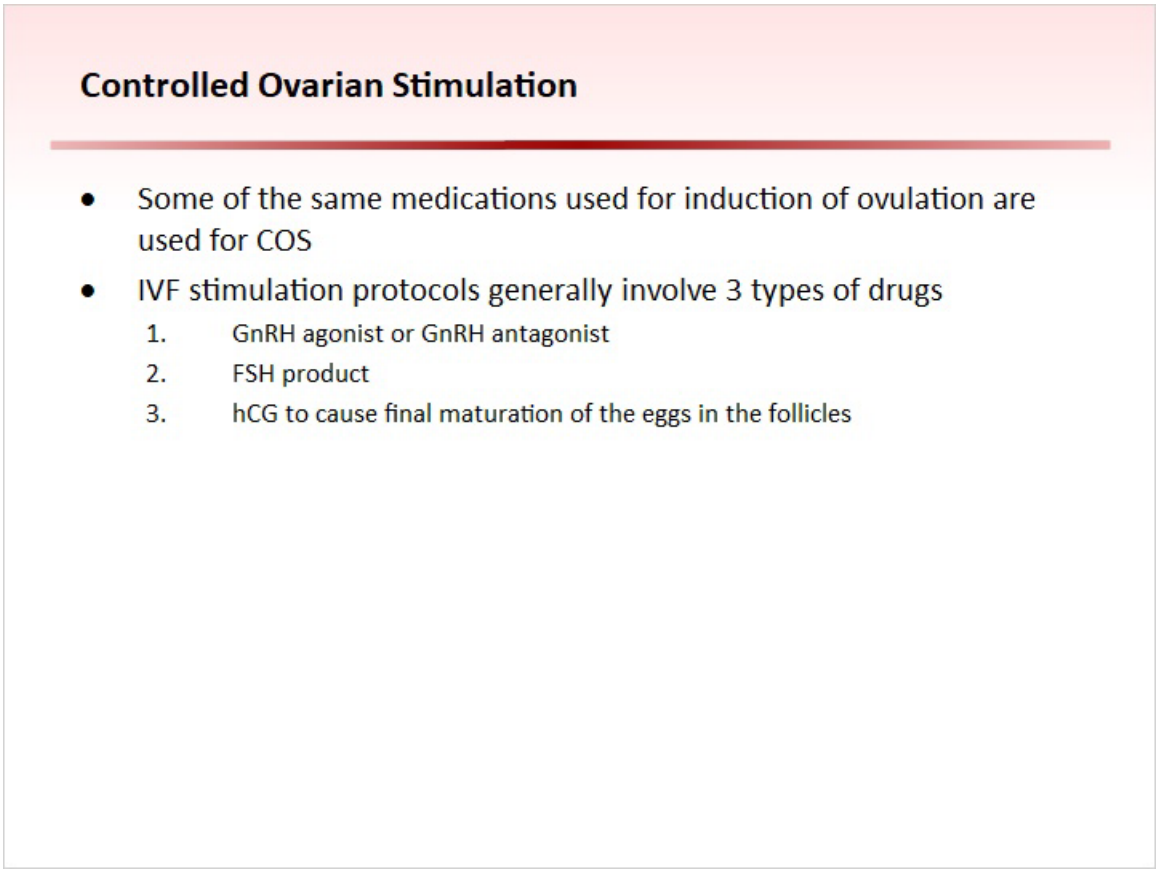
1.6 Controlled Ovarian Stimulation



Notes:

Controlled ovarian stimulation (COS) is the deliberate and regulated production of a hormonal response intended to lead to the production of multiple eggs. In the context of ART, COS is one of the first steps involved in the in vitro fertilization treatment process. The protocols for IVF are designed to create a balance between under- and overstimulation. The goal is to achieve adequate numbers and quality of oocytes leading to a normal singleton birth while maximizing the total reproductive potential of the cycle. The most serious complication that may arise from COS from IVF procedures is ovarian hyperstimulation syndrome (OHSS).

1.7 Controlled Ovarian Stimulation



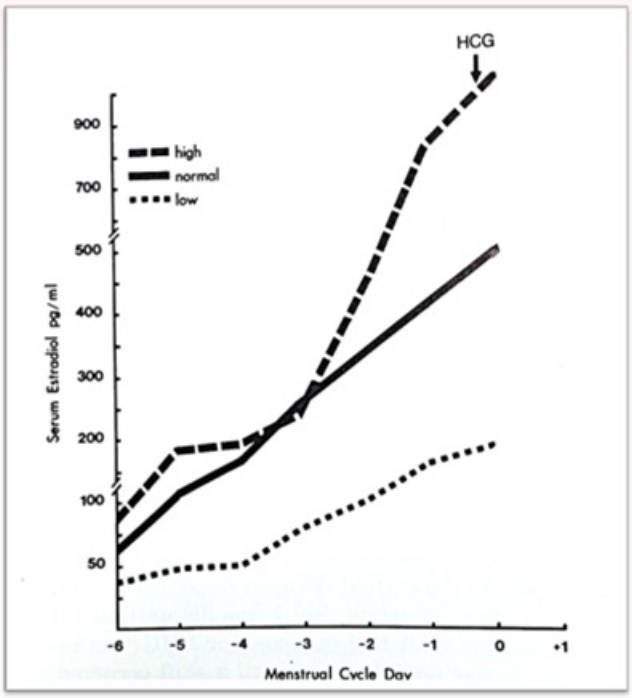
Notes:

Some of the same medications used for induction of ovulation are used for COS.
IVF stimulation protocols generally involve the use of 3 types of drugs.
The purpose of the GnRH agonist (or antagonist) is to suppress release of LH from the woman's pituitary gland during the ovarian stimulation process. A woman's natural LH surges would cause premature ovulation of the eggs.
FSH products stimulate development of multiple follicles (cystic structures that contain eggs) in the ovaries by rescuing eggs that would normally undergo atresia in a natural cycle.
hCG is used to cause final maturation of the eggs in the follicles.

1.8 Types of Response to COS

Types of Response to COS

- Hyper-responders
- Normal responders
- Low responders

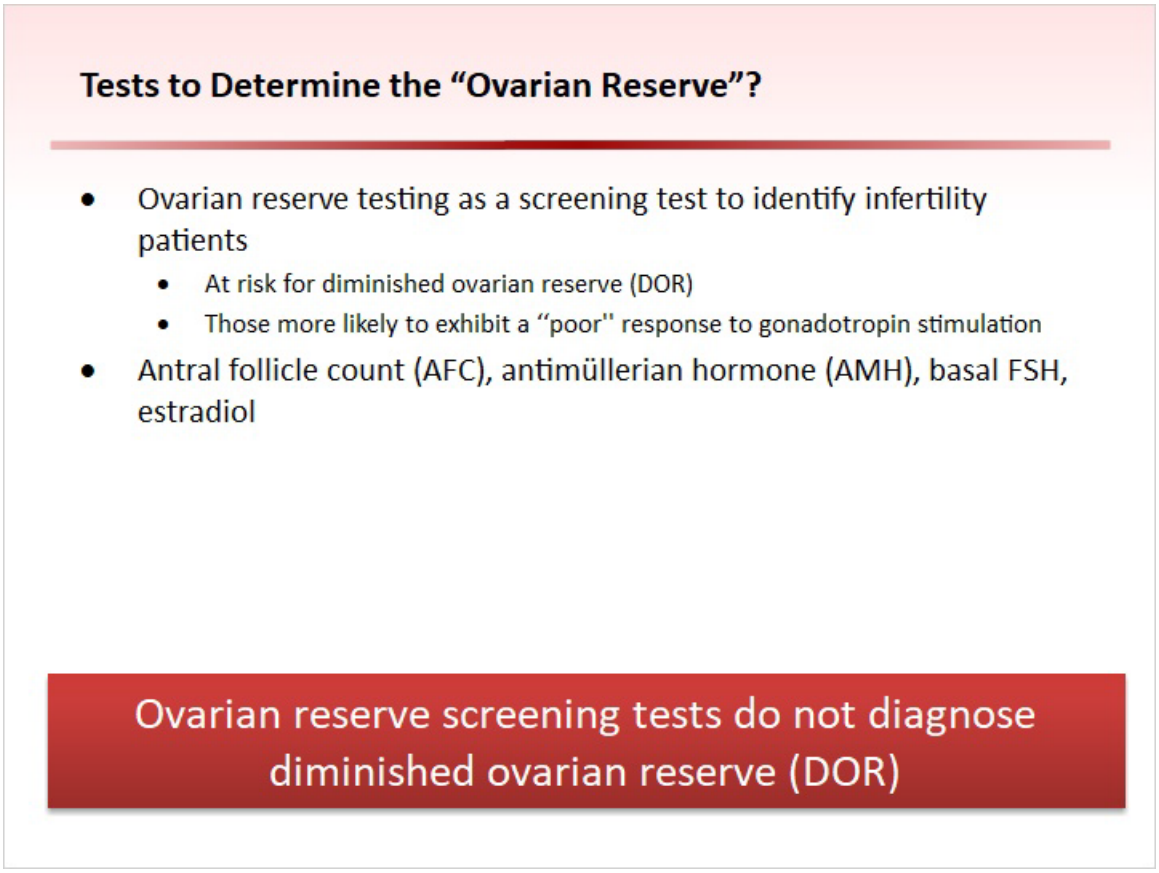


Adapted With permission from Fertil Steril.1983 Feb;39(2):167-73.
Human menopausal gonadotropin/human chorionic gonadotropin follicular maturation for oocyte aspiration: phase I, 1981.
Garcia JE, Jones GS, Acosta AA, Wright G Jr.

Notes:

The IVF stimulation protocol should be individualized to the patient. It has long been noted that women differ by their types of response to controlled ovarian stimulation. Some are hyper-responders and are at risk for hyperstimulation, especially those with polycystic ovary syndrome (PCOS) and young women. Good-prognosis patients fall into the category of normal ovarian responders. A low response suggests ovarian aging; this is common in women of advanced maternal age and may be associated with poor IVF outcomes. The follicular response is as important as the estradiol level in identifying each type of response shown here.

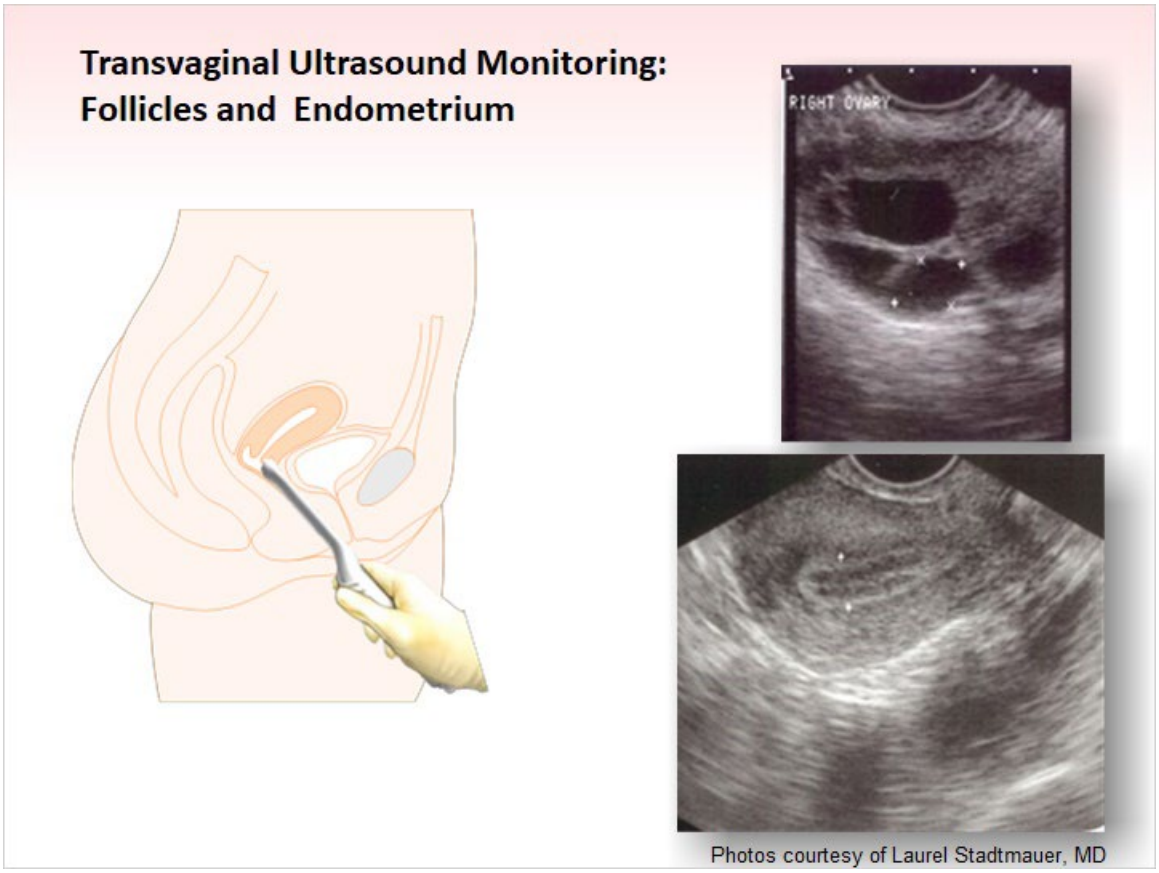
1.9 Tests to Determine the "Ovarian Reserve"?



Notes:

Historically, ovarian reserve testing has been used to identify infertility patients at risk for diminished ovarian reserve. However, it may also identify patients at risk for an exaggerated or over-response. While ovarian reserve testing does identify patients who are more likely to exhibit a "poor" response to gonadotropin stimulation, it is not as good at predicting pregnancy outcomes. There is no single ideal test. The AFC and AMH are considered the most consistent and reliable tests. Basal FSH and estradiol levels are considered good indicators as well.

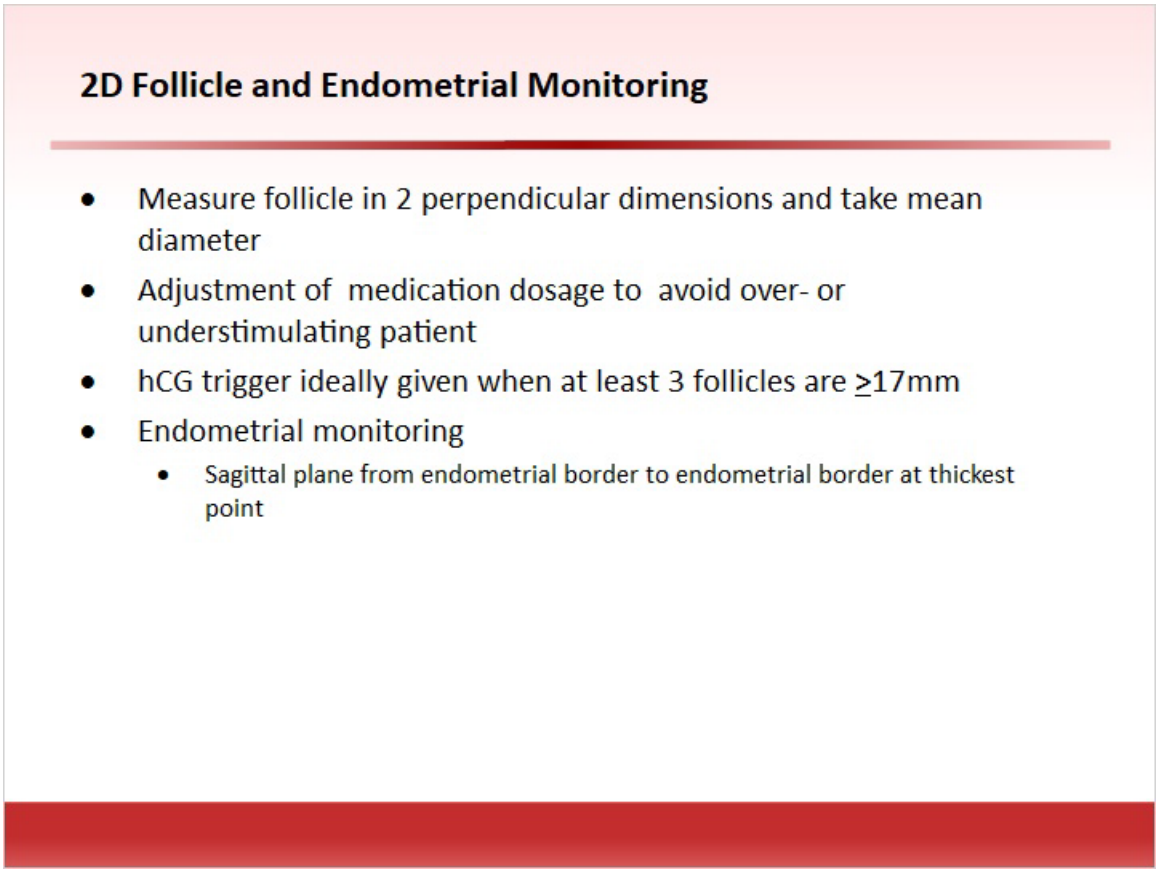
1.10 Transvaginal Ultrasound Monitoring:



Notes:

Transvaginal ultrasound monitoring of follicles and endometrium is the standard for nearly all IVF stimulations.

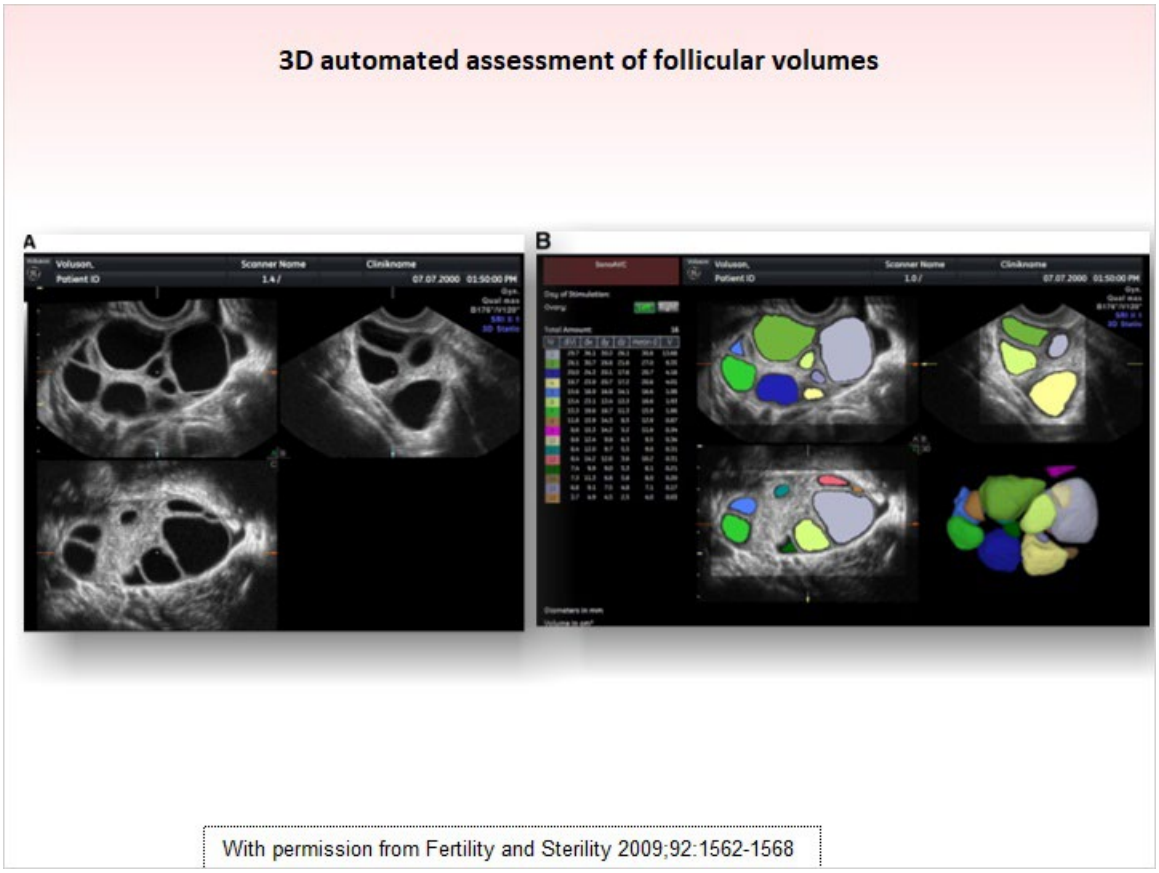
1.11 2D Follicle and Endometrial Monitoring



Notes:

The mean follicle diameter is determined by 2 perpendicular dimensions. Medication dosage is adjusted to avoid over- or understimulating the patient. The ideal follicle size for administering the hCG trigger is >12 mm with the largest 3 follicles at least 17 mm in diameter. The endometrium is measured in the sagittal plane from endometrial border to endometrial border at the thickest point.

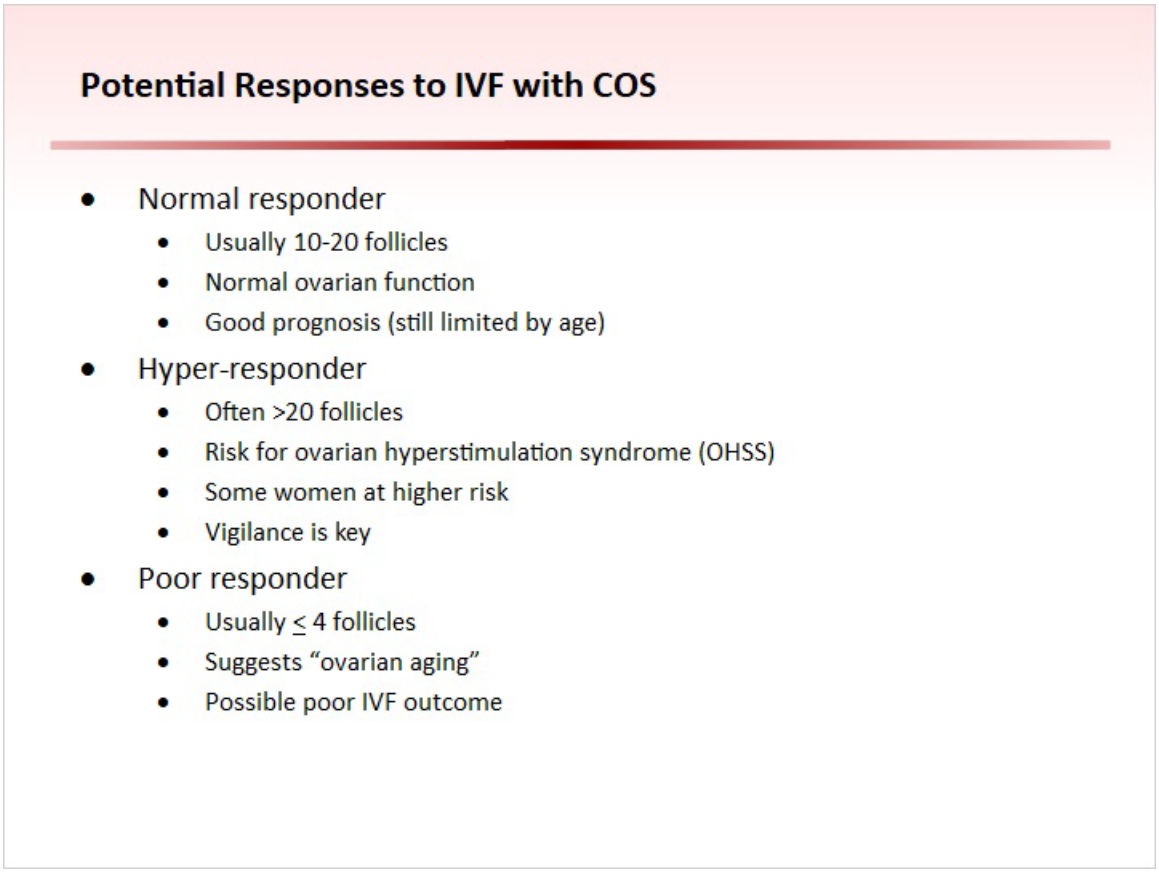
1.12 3D automated assessment of follicular volumes



Notes:

Software is available using 3-dimensional technology that provides automated assessment of follicle volume and may save time in monitoring. Follicle diameters and volumes are calculated automatically and color-coded. Shown here are comparisons of 2D with the 3D automated measurements.

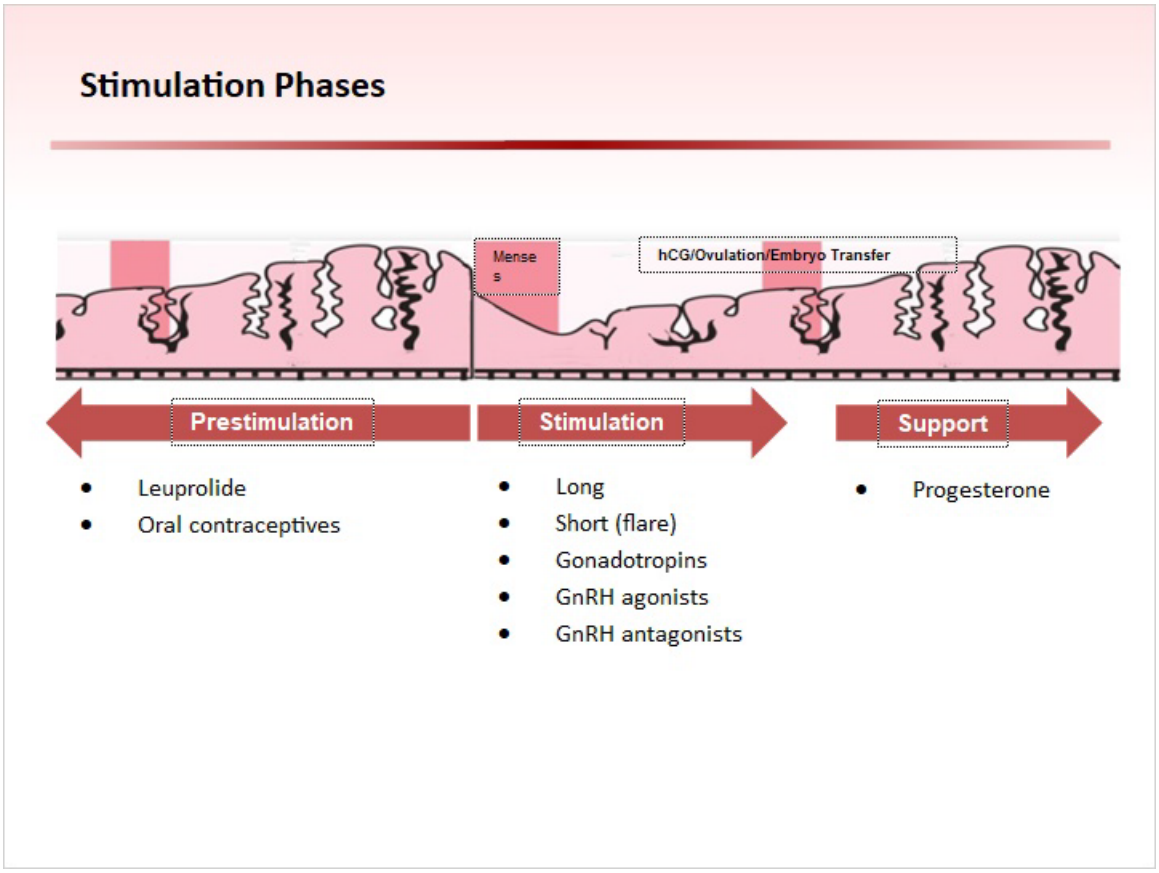
1.13 Potential Responses to IVF with COS



Notes:

A normal response to standard IVF stimulation indicates normal ovarian function and, generally, a good prognosis, although this is still limited by a woman's age. Some women are "hyper" responders and are at risk for ovarian hyperstimulation syndrome. While certain characteristics, such as PCOS, high AMH/AFC, young age, and thin body habitus do increase the risk for hyper-response, hyperstimulation generally cannot be predicted and vigilance is key. A low response suggests "ovarian aging" common in women of advanced maternal age and may be associated with poor IVF outcome.

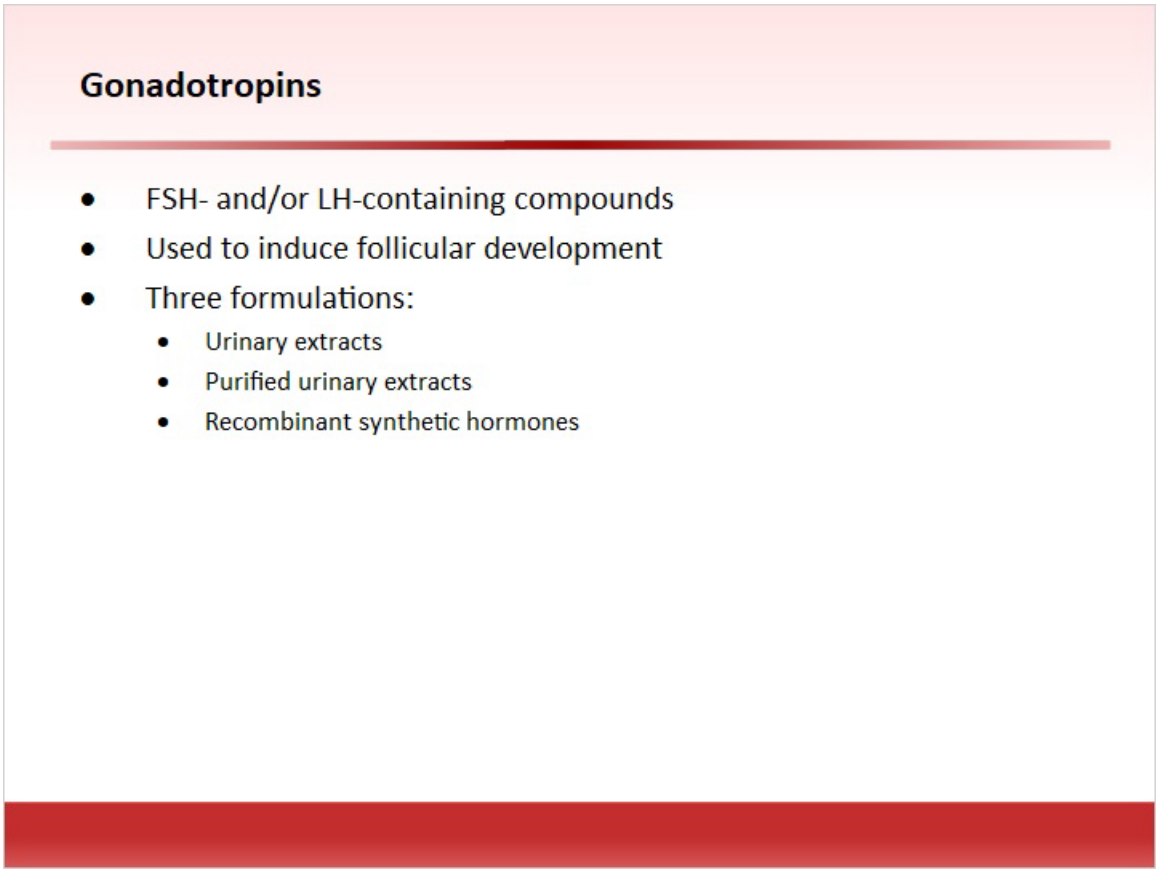
1.14 Stimulation Phases



Notes:

There are three basic phases of stimulation for an in vitro fertilization cycle: prestimulation, stimulation, and support. In the prestimulation phase, ovarian activity is suppressed with leuprolide or with oral contraceptives in the previous cycle. The stimulation phase begins with the administration of gonadotropins to stimulate ovarian follicle growth; this is usually, but not always, during menses. Various long or short protocols that include GnRH agonists or antagonists are used depending on the ovarian reserve. Once optimum follicle size is reached, hCG is given and oocytes are retrieved 36 hours later. The support phase typically begins prior to embryo transfer using progesterone to provide hormonal support to the endometrium.

1.15 Gonadotropins



Notes:

Several medications are commonly used in these cycles. Gonadotropins are FSH- and/or LH-containing compounds that are used to induce ovarian follicular development. They come in three formulations: urinary extracts, purified urinary extracts, and recombinant synthetic hormones.

1.16 Human Menopausal Gonadotropin (hMG)

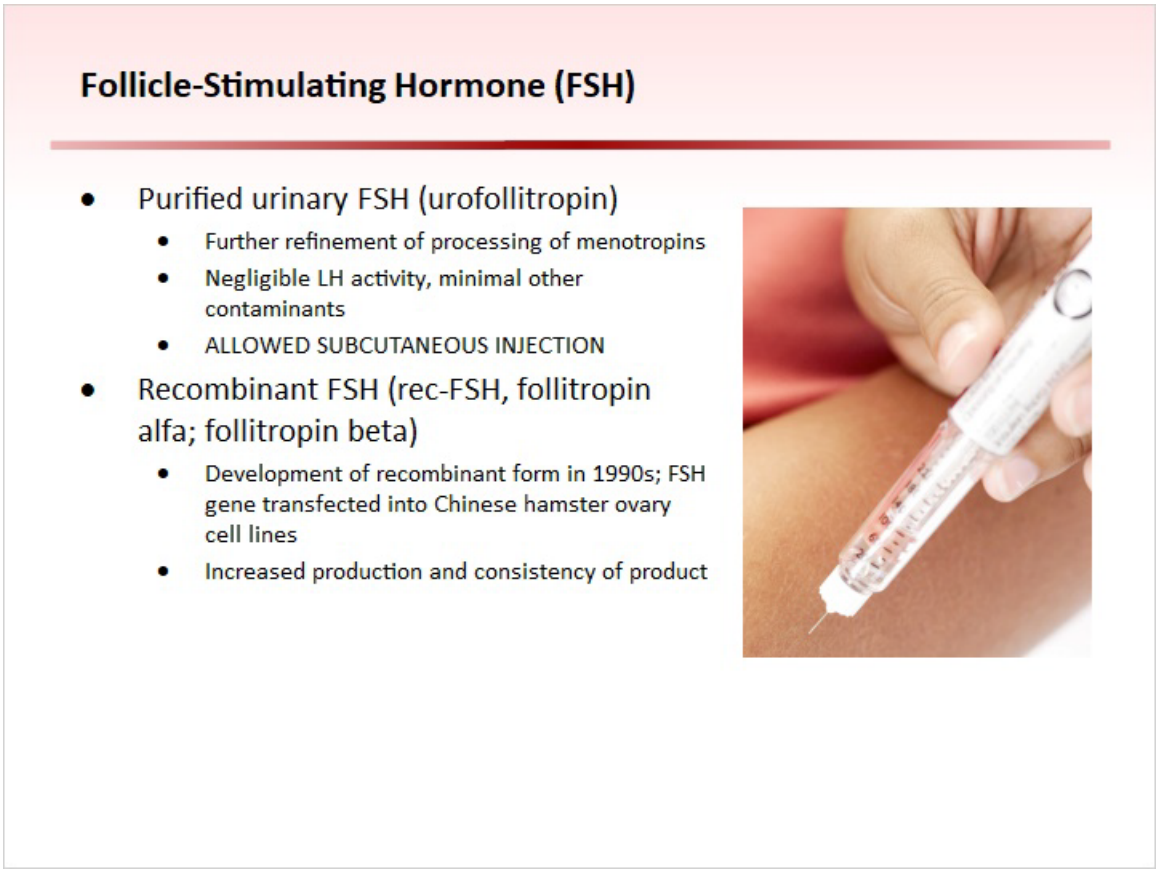
Human Menopausal Gonadotropin (hMG)

- First preparation of gonadotropins for clinical use, "menotropins"
- Extracted from urine of postmenopausal women
- Contains FSH and LH
- hCG added to equalize LH activity
- 75 IU of FSH and LH activity
- "Rescue" of follicles to increase cohort size

Notes:

Human menopausal gonadotropin was the first preparation of gonadotropins available for clinical use. These "menotropins" were extracted from the urine of postmenopausal women, and contain FSH and LH. Improved purification methods to extract the hormones from the urine allowed for standardization of the product to 75 IU of FSH and LH activity; hCG was added to equalize the LH activity.
The FSH and LH within hMG function as native hormones and induce follicular growth. When used for controlled ovarian stimulation, the additional amounts of gonadotropins "rescue" follicles that would normally die off, thus increasing the cohort size for that cycle of treatment.

1.17 Follicle-Stimulating Hormone (FSH)

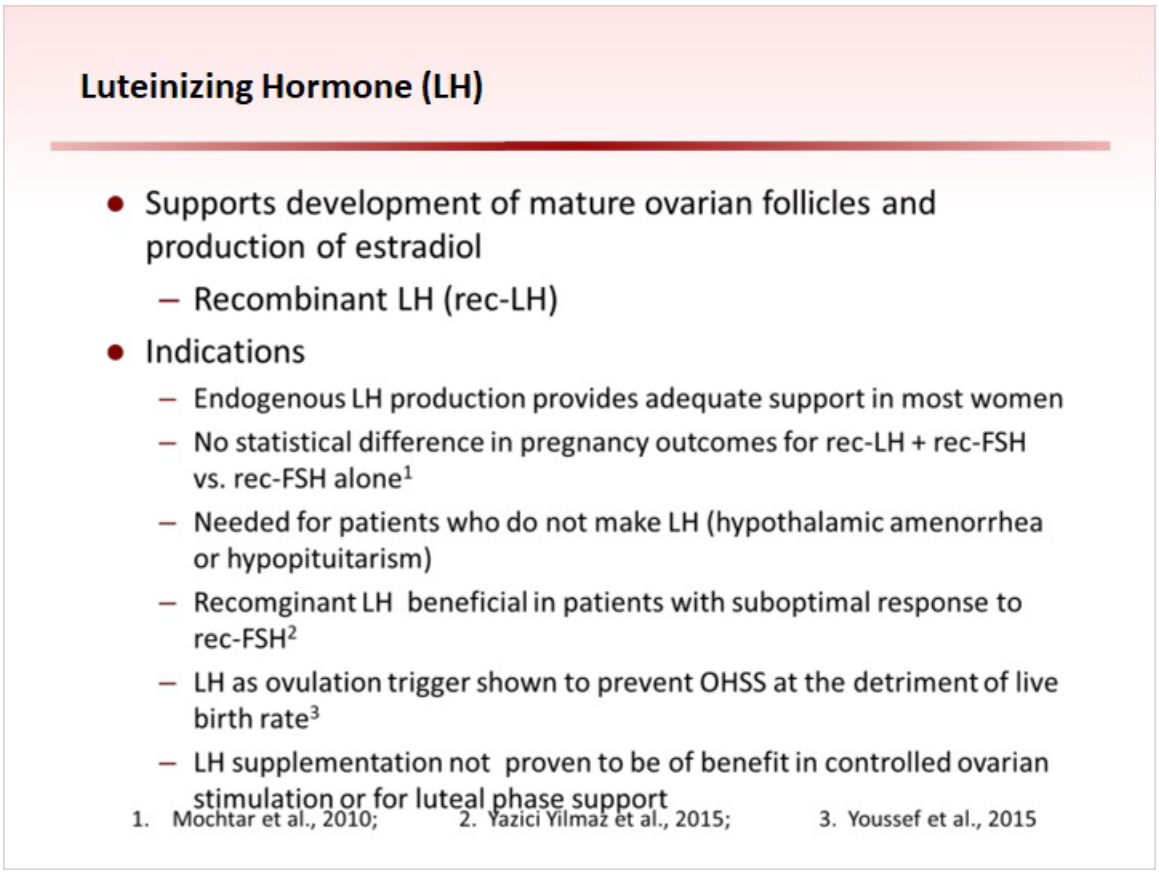


Notes:

Follicle stimulating hormone binds FSH receptors and promotes follicular growth and development and production of estradiol from granulosa cells. It can be given in isolation, as opposed to being combined with LH in hMG, as long as the patient is making endogenous LH. Patients with hypothalamic amenorrhea, for example, will need LH supplementation.

FSH is available in 2 injectable forms: purified urinary FSH (urofollitropin) and recombinant FSH (follitropin). Purified urinary FSH has negligible LH activity and only minimal other urine protein contaminants. A major shift in gonadotropin pharmacotherapy was made in the 1990s with the development of recombinant FSH. Recombinant FSH was developed by transfecting the FSH gene into a Chinese hamster ovary cell line. This allows for FSH to be produced in a lab from cell culture, rather than the processing of postmenopausal urine. The benefits of this type of production include increased availability, consistency of product, and lack of other urinary contaminants. Highly purified urinary FSH is administered as an intramuscular or subcutaneous injection. The recombinant products are given subcutaneously, and are available in vials or multidose pens. The pens ease self-administration and adjustment of dose.

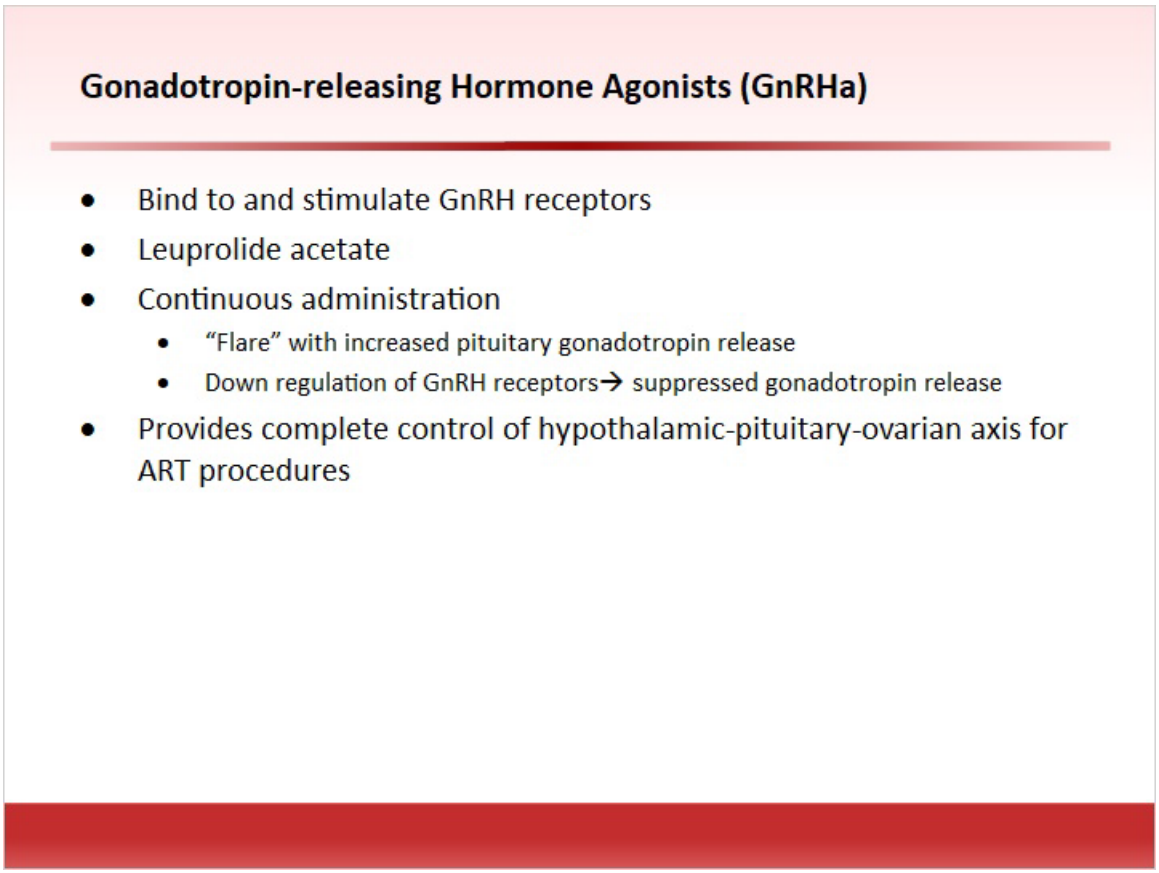
1.18 Luteinizing Hormone (LH)



Notes:

Luteinizing hormone supports the development of mature ovarian follicles and the production of estradiol. Recombinant LH is also available. It is produced in the same fashion as recombinant FSH, by a transfected Chinese hamster ovary cell line. In most women, endogenous LH production is sufficient to provide adequate LH support during controlled ovarian stimulation. Studies have shown no statistical difference in pregnancy outcomes when recombinant LH and recombinant FSH are co-administered, compared with using recombinant FSH alone in controlled ovarian stimulation cycles. However, it is needed in those patients who do not produce endogenous LH, such as those with hypothalamic amenorrhea or hypopituitarism. The addition of recombinant LH may be beneficial in women who are poor responders. The use of LH as an ovulation trigger has been shown to prevent ovarian hyperstimulation syndrome. LH supplementation has not been proven to be of benefit in controlled ovarian stimulation or for luteal phase support.

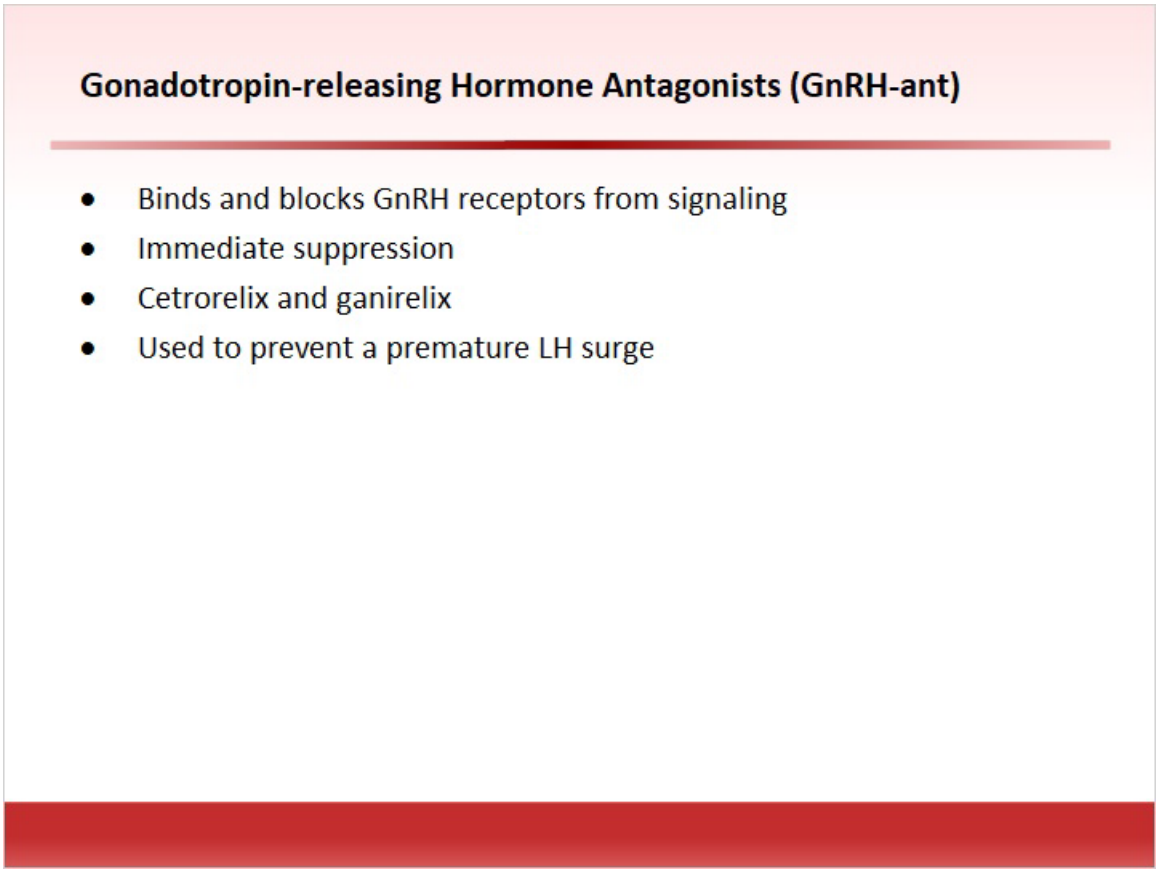
1.19 Gonadotropin-releasing Hormone Agonists (GnRHa)



Notes:

GnRH agonists function by binding to and stimulating the GnRH receptors similar to native GnRH. Leuprolide acetate is the most common GnRH agonist used in ART cycles. With continuous administration of GnRH, first a "flare" results, which is an increased pituitary gonadotropin release in response to the excess GnRH signal. Following this, continued GnRH exposure results in desensitization of the pituitary, and gonadotropin release is suppressed. This provides complete control of the hypothalamic-pituitary-ovarian (HPO) axis for ART procedures.

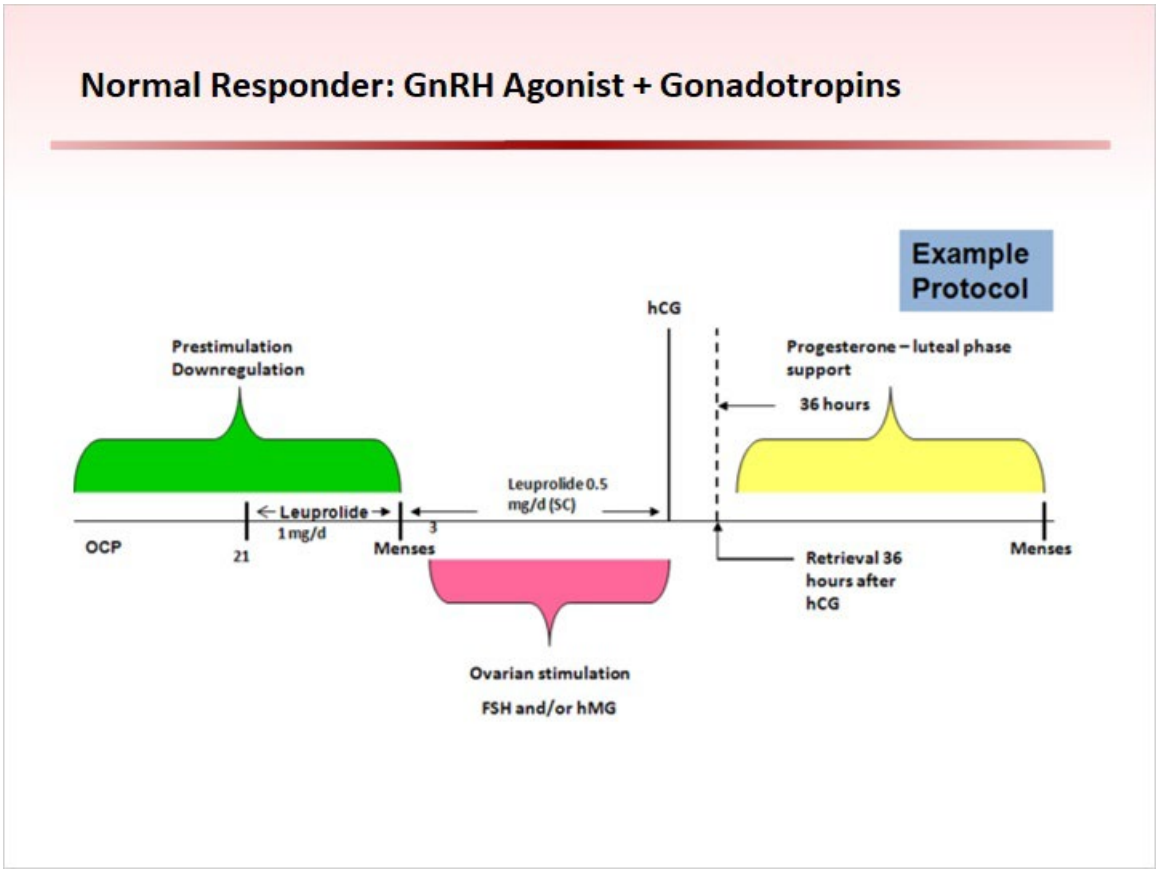
1.20 Gonadotropin-releasing Hormone Antagonists (GnRH-ant)



Notes:

A GnRH antagonist works to antagonize GnRH by binding and blocking GnRH receptors from signaling. Unlike the response to agonists that begins with a flare of FSH and LH release, the response to antagonists is the immediate suppression of gonadotropins. Two products are marketed for use in the United States: cetrorelix and ganirelix. GnRH antagonists have been used for all types of responders with some benefits. Antagonist protocols are shorter and may help reduce the dosage of FSH. They also prevent premature LH surges in women undergoing controlled ovarian stimulation.

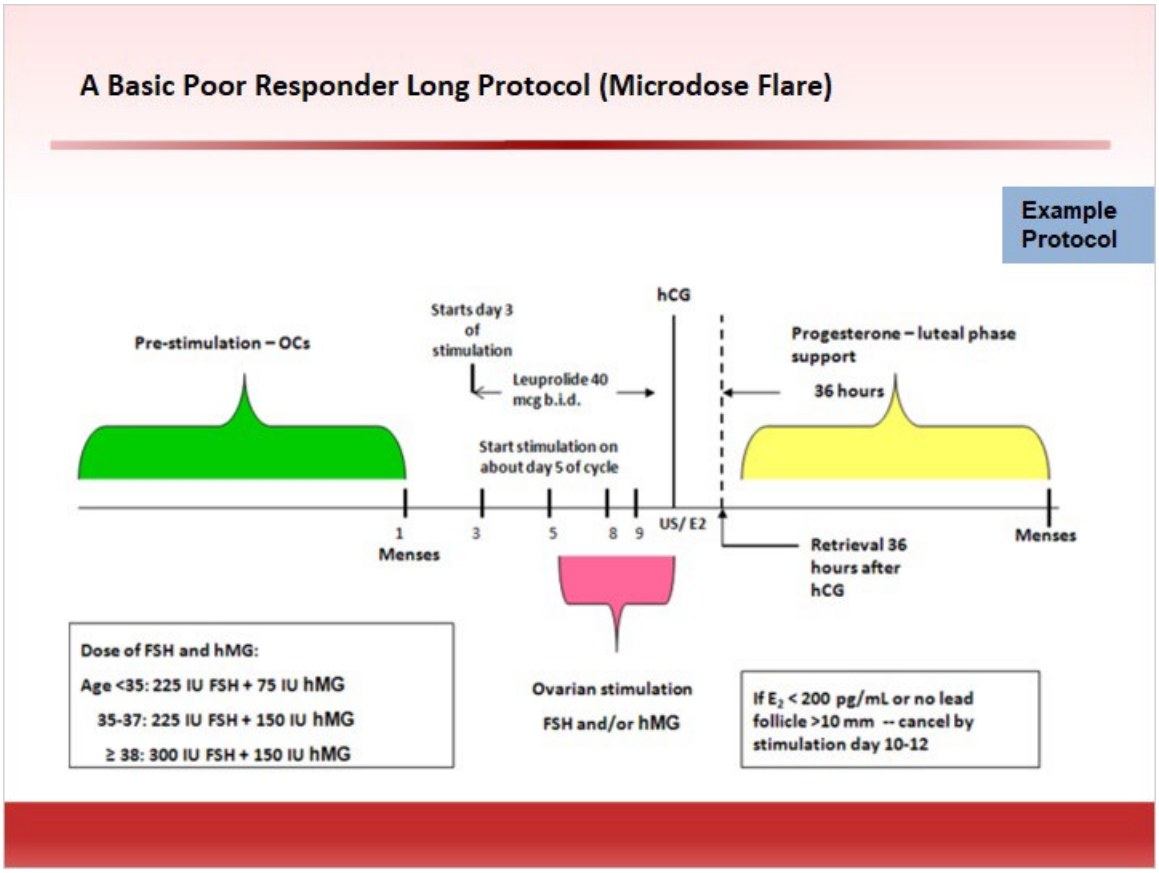
1.21 Normal Responder: GnRH Agonist + Gonadotropins



Notes:

An example of a long-stimulation protocol for a normal responder is shown here. Oral contraceptives may be given during the prior cycle. Beginning after at least 6-7 days of oral contraceptives, leuprolide is given daily for prestimulation down-regulation, and the dosage is decreased once menses begins. Once suppressed, gonadotropins are given daily. When monitoring indicates that follicles are ready, hCG is administered, oocyte retrieval is performed 36 hours later, and luteal phase support begins.

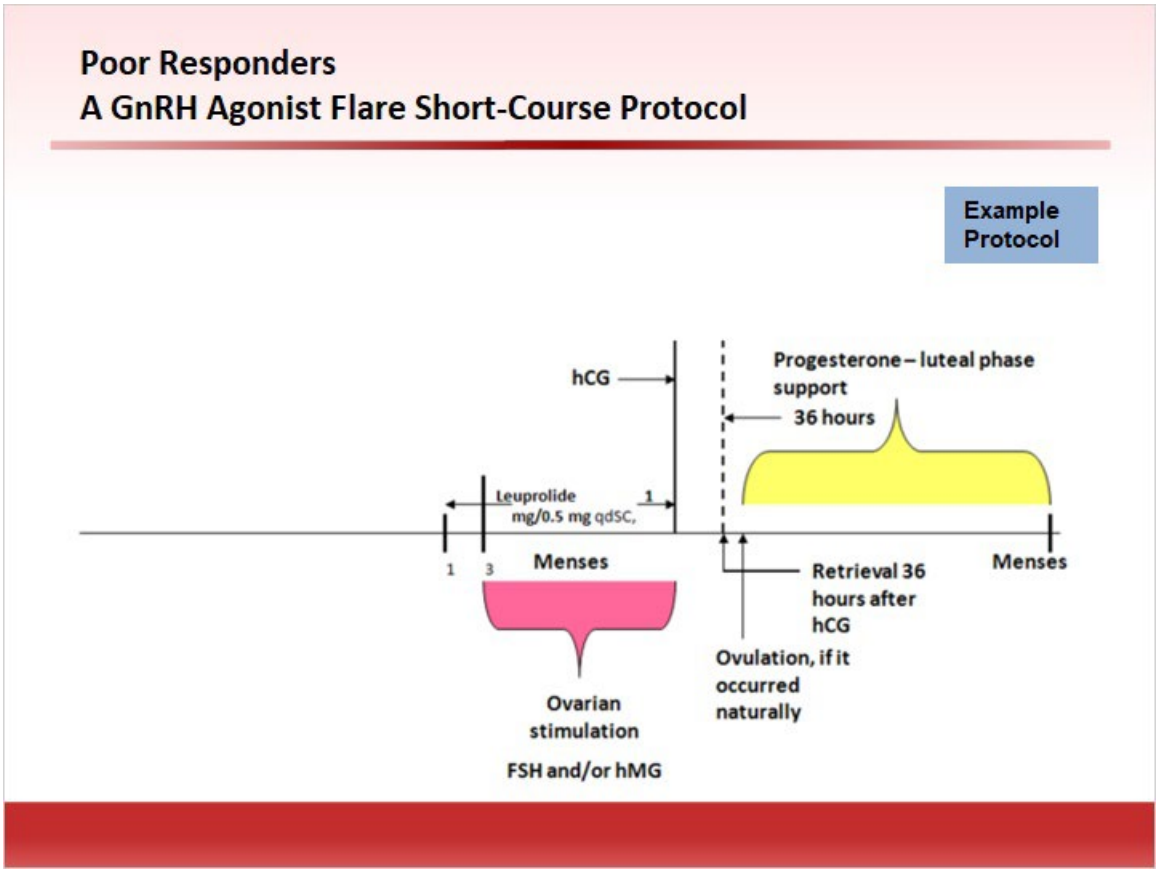
1.22 A Basic Poor Responder Long Protocol (Microdose Flare)



Notes:

Historically, the basic treatment cycle for poor responders begins with down-regulation using oral contraceptives in the prestimulation phase. In the microdose flare protocol shown here, the continuous oral contraceptives are stopped at a time that can be adjusted. Two to 4 days after the last OCP, leuprolide is started in a twice-daily dosing. Stimulation actually begins with the start of the leuprolide which causes a “flare” of endogenous gonadotropin. Gonadotropins are begun after 2 additional days. The approximate starting doses of gonadotropins are related to age but could be adjusted for clinical history as well. The goal is steady growth and development of follicles. It should be noted that OCPs are increasingly not utilized in poor responder protocols.

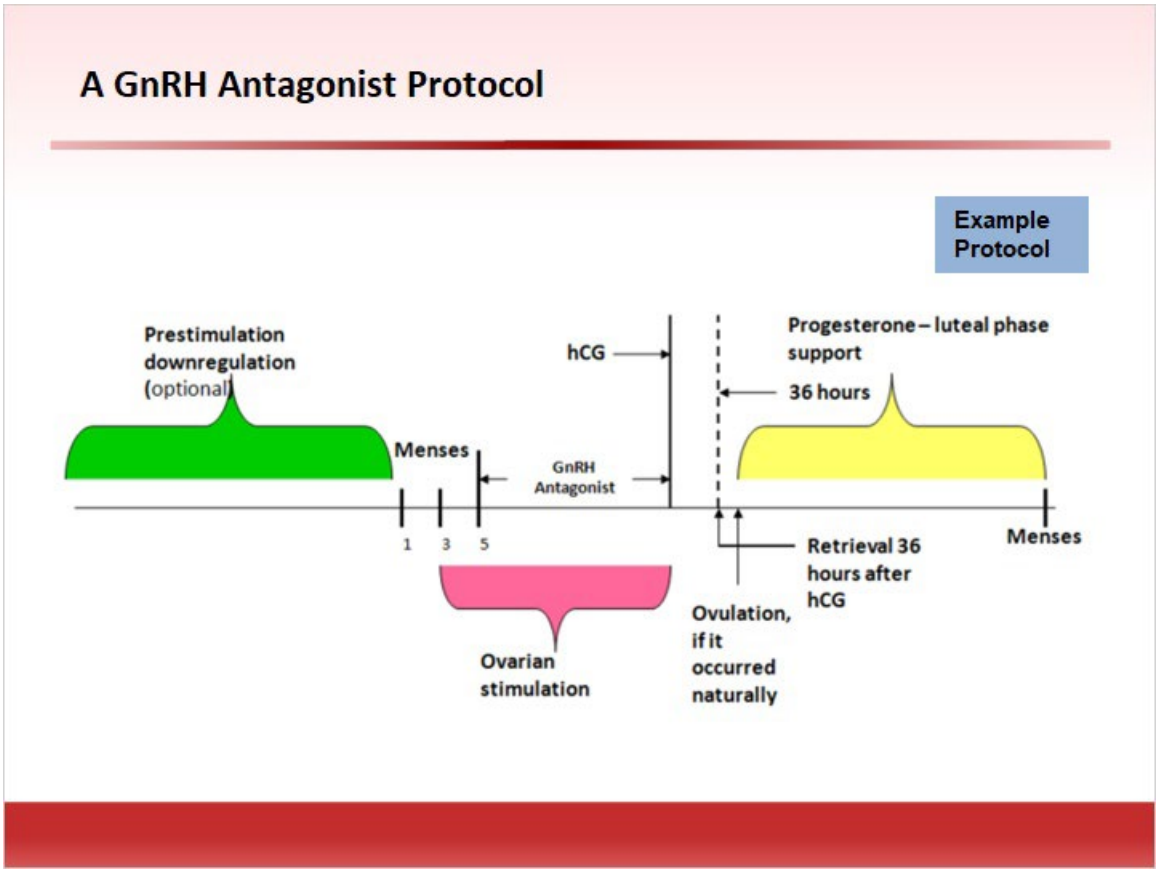
1.23 Poor Responders



Notes:

Women considered poor responders may be oversuppressed on the oral contraceptive protocols. This diagram illustrates the principles of the GnRH agonist flare short-course protocol, with no suppression prior to the cycle. The leuprolide dosage is reduced from 1.0 mg to 0.5 mg daily on cycle day 3. The microdose leuprolide flare protocol takes advantage of a short agonist effect of leuprolide. It will stimulate the release of natural pituitary FSH for several days before beginning its suppressive effect. The increase in ovarian stimulation may maximize the outcomes for the poor responders.
The option of stopping leuprolide the day gonadotropins are started helps avoid oversuppressing the ovaries. Despite discontinuation of the leuprolide, premature ovulation usually does not occur.

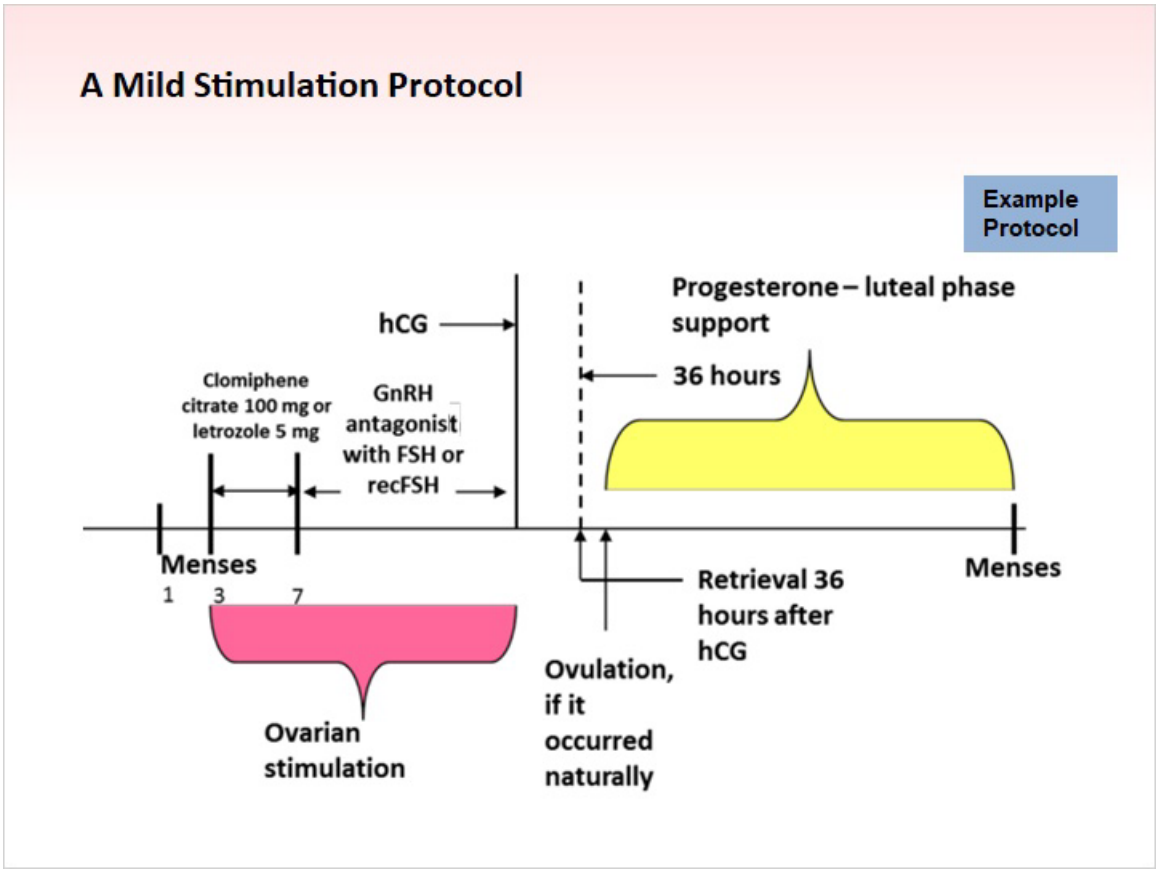
1.24 A GnRH Antagonist Protocol



Notes:

Another type of stimulation protocol is the GnRH antagonist cycle, illustrated here. An optional prestimulation suppression is achieved with oral contraceptives. Gonadotropins are given beginning at least by day 2 or 3, and the GnRH antagonist is started typically on day 6 with a fixed protocol and based on follicle size in a variable protocol. It is continued until hCG is given.

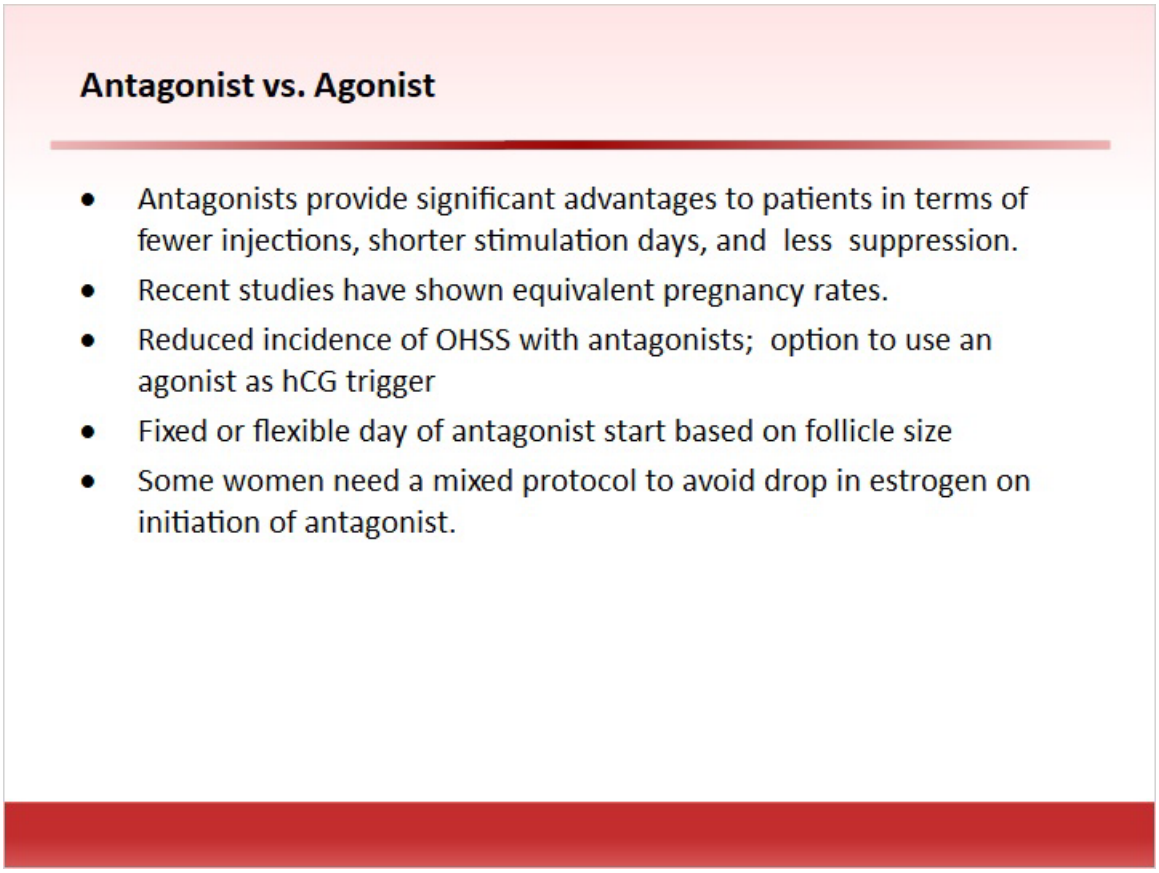
1.25 A Mild Stimulation Protocol



Notes:

Mild stimulation protocols can be an option for young normal responders with tubal factor or poor responders who do not produce more than a few follicles with maximum stimulation. Stimulation can be initiated with either clomiphene citrate or letrozole for 5 days followed by gonadotropins, or with low-dose gonadotropins alone. The GnRH antagonist is used to prevent premature ovulation.

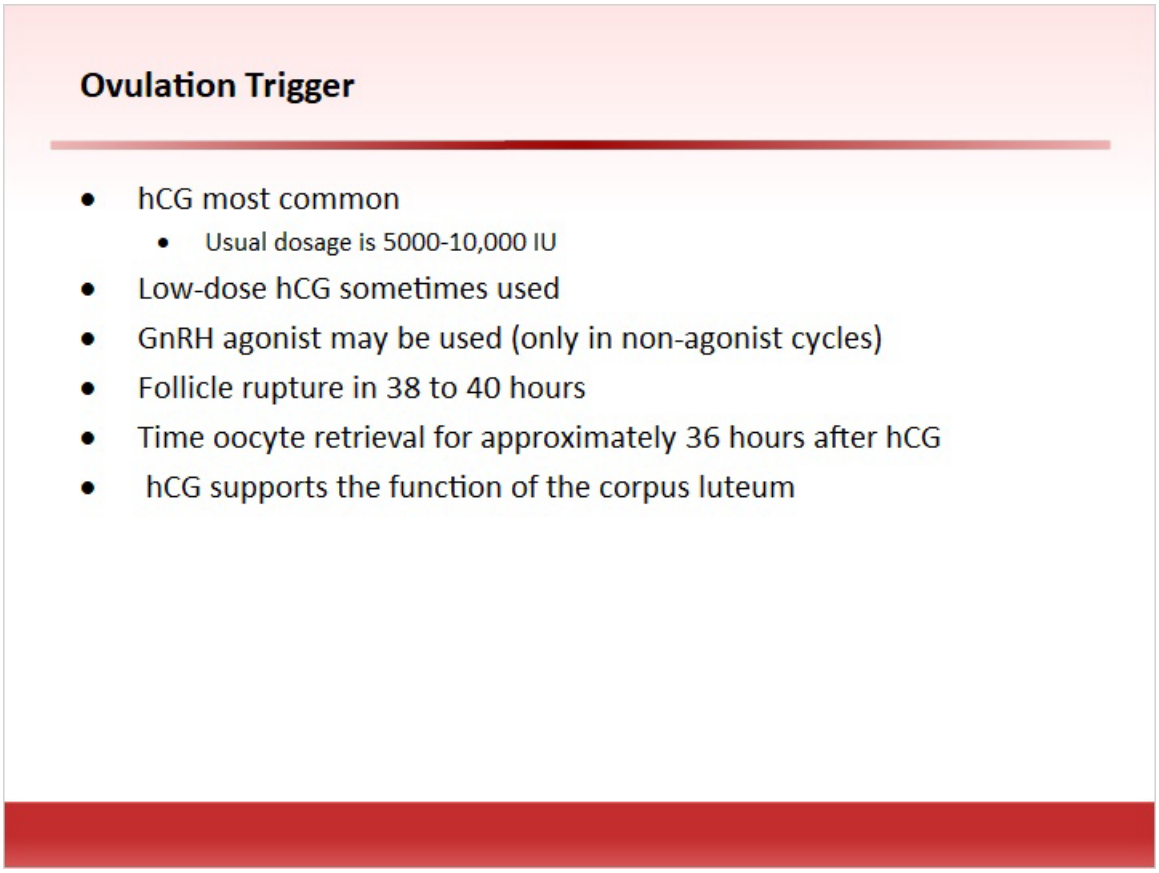
1.26 Antagonist vs. Agonist



Notes:

These are some crucial points comparing agonist and antagonist protocols. Generally, antagonists provide significant advantages to patients in terms of fewer injections, shorter stimulation days, and less suppression. Pregnancy rates for both treatments need to be continually monitored, but recent studies have shown equivalence. The incidence of OHSS is less with antagonists with an option to use an agonist as hCG trigger. The day the antagonist is started can be fixed or flexible based on follicle size. Some women need a mixed protocol to avoid a drop in estrogen on initiation of antagonist.

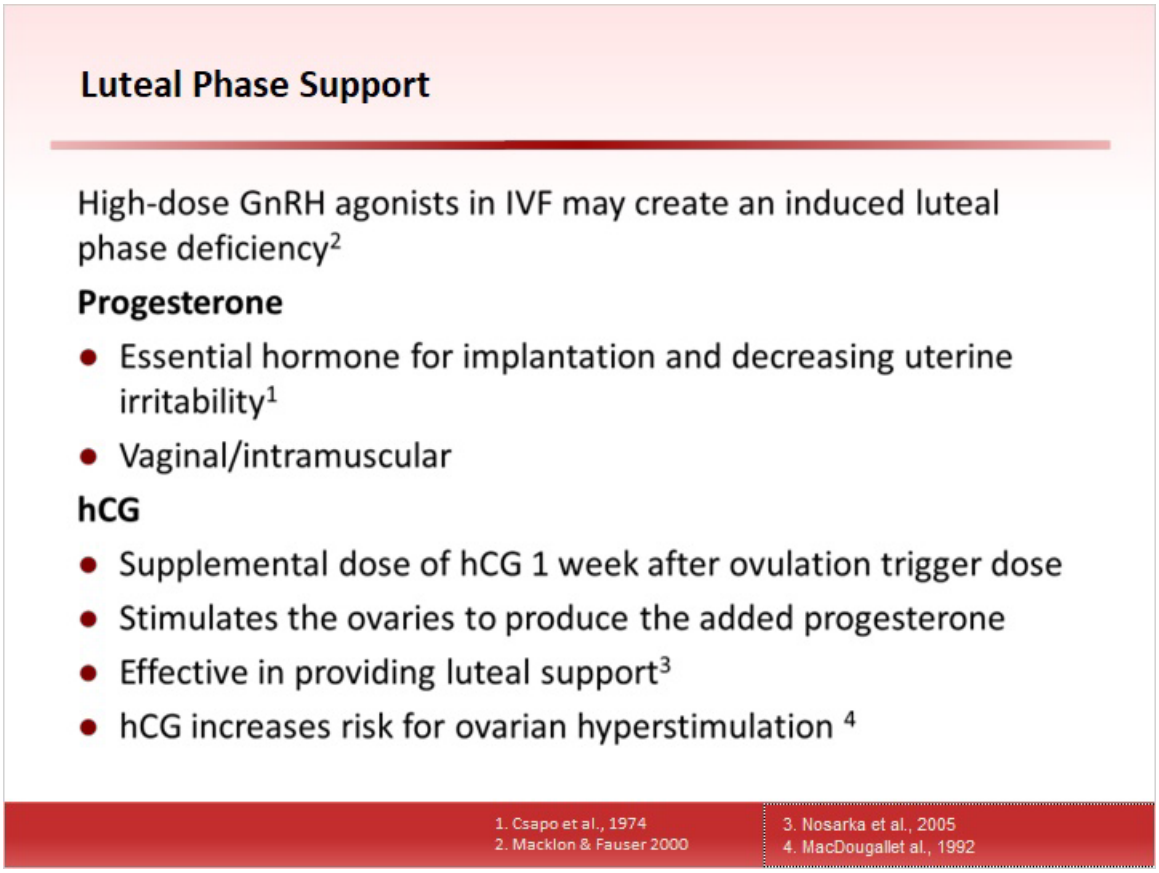
1.27 Ovulation Trigger



Notes:

When follicles have reached optimum size, hCG is administered as a trigger for ovulation to occur 38 to 40 hours later. The usual dosage is 5,000 to 10,000 units. For IVF cycles, oocyte retrieval is thus scheduled in a tight time window before ovulation occurs to maximize the number of mature oocytes, usually about 36 hours after trigger. hCG also supports the function of the corpus luteum. As noted previously, if a GnRH agonist has not been used in the cycle, it may be given as the trigger to lessen the risk of ovarian hyperstimulation.

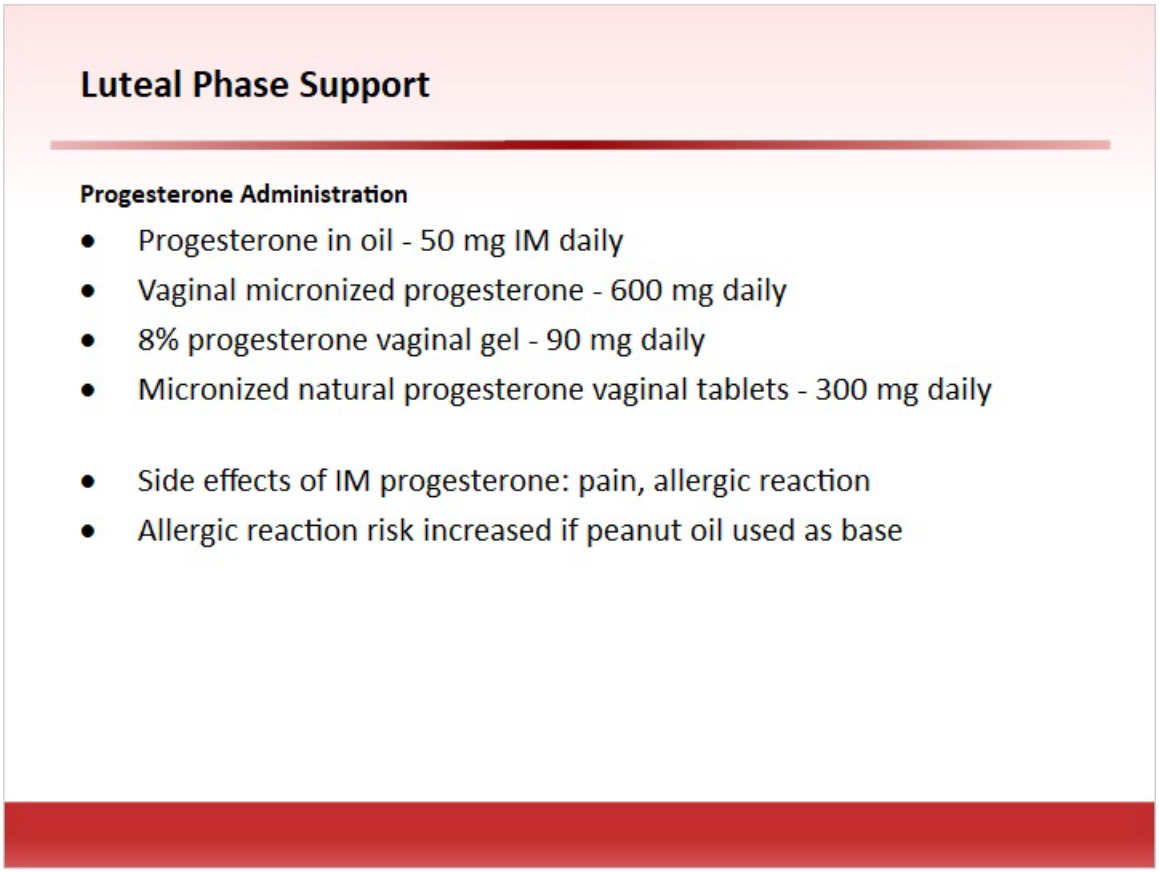
1.28 Luteal Phase Support



Notes:

Once ovulation is triggered, nearly all women in controlled ovarian stimulation cycles require luteal phase support. High-dose GnRH agonists in IVF may create an induced luteal phase deficiency.
Progesterone is an essential hormone to aid in implantation and decrease uterine irritability. Progesterone has been shown to be effective when given intramuscularly or vaginally. The effectiveness of oral progesterone is not as clear.
Alternatively, a supplemental dose of hCG 1 week after the ovulation trigger dose can assist in luteal phase support. Administration of 250 mcg of recombinant hCG subcutaneously or 2,500-5,000 IU of hCG intramuscularly may be repeated 1 week after the initial trigger dose. This therapy ideally uses the patient's ovaries to produce the added progesterone. Meta-analysis data demonstrate that hCG and progesterone are both effective in providing luteal phase support. However, hCG increases the risk for ovarian hyperstimulation and thus is used infrequently in the United States.

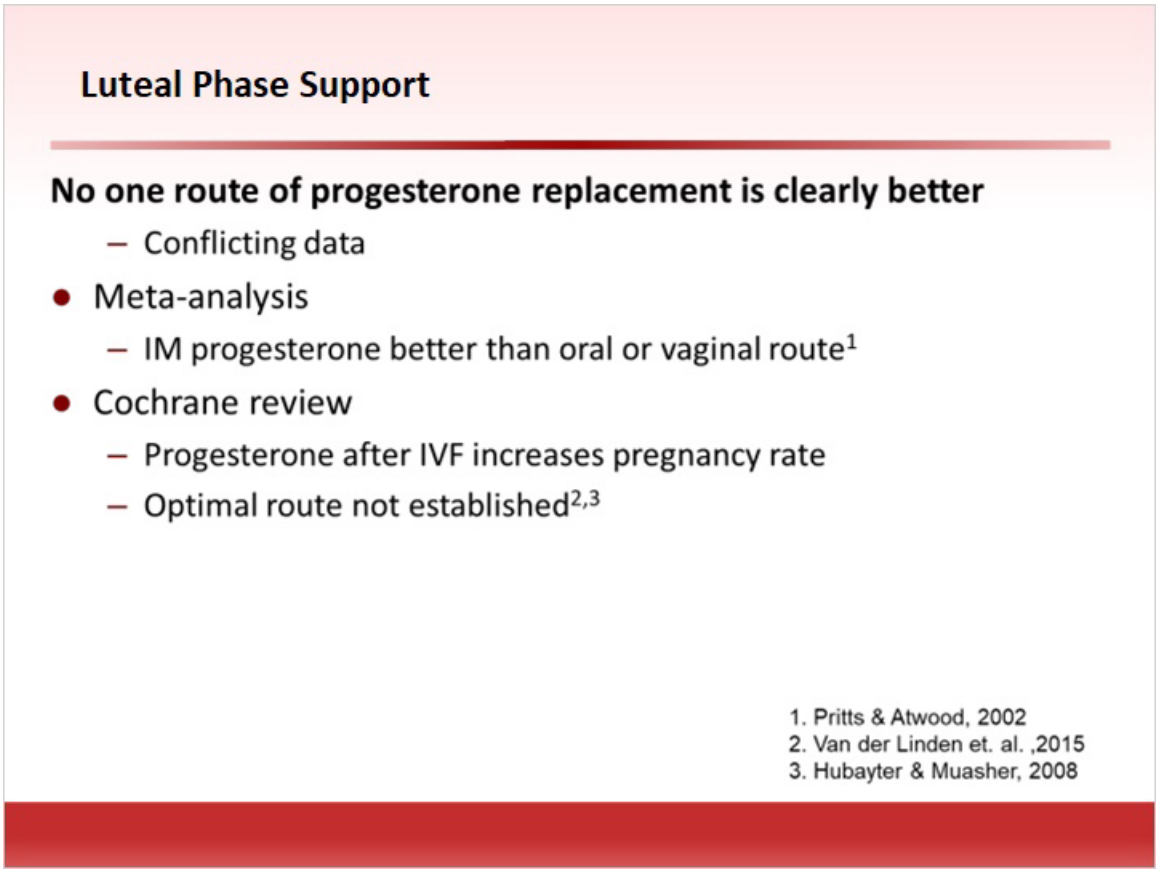
1.29 Luteal Phase Support



Notes:

Progesterone may be administered in several ways: progesterone in oil, 50 mg IM daily; vaginal micronized progesterone, 600 mg daily; 8% progesterone vaginal gel, 90 mg daily; or micronized natural progesterone in vaginal tablets, 300 mg daily. Side effects of intramuscular progesterone include pain and allergic reaction. Also the risk of allergic reaction is increased if peanut oil is used as a base for the hormone in oral or injectable forms. Localized irritation may also occur. The efficacy of oral preparations has not been clearly demonstrated. While controversial, some groups add estradiol to their progesterone regimen.

1.30 Luteal Phase Support



Notes:

Generally, progesterone in any form is better than no luteal support. However data do not show that one route is clearly better than others. A meta-analysis of randomized studies showed IM progesterone was better than the oral or vaginal route. A Cochrane review demonstrated that progesterone after IVF increases the pregnancy rate and that the optimal route of progesterone has not been established.

1.31 Risks of Ovarian Stimulation Medications

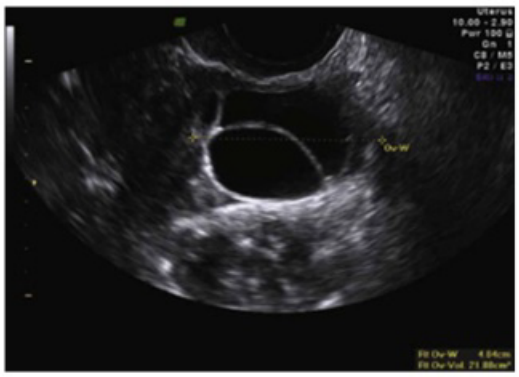
Notes:

Ovarian hyperstimulation syndrome is a significant risk of treatment with ovarian stimulation medications.

1.32 Ovarian Hyperstimulation Syndrome (OHSS)

Ovarian Hyperstimulation Syndrome (OHSS)

- Exaggerated response to ovarian stimulation
- Most common with gonadotropin use
- Very rare with clomiphene
- Can vary in intensity and is usually self-limited
  - Often worse in conception cycles
- Increased permeability of capillaries shifting fluid from intravascular to extravascular space.

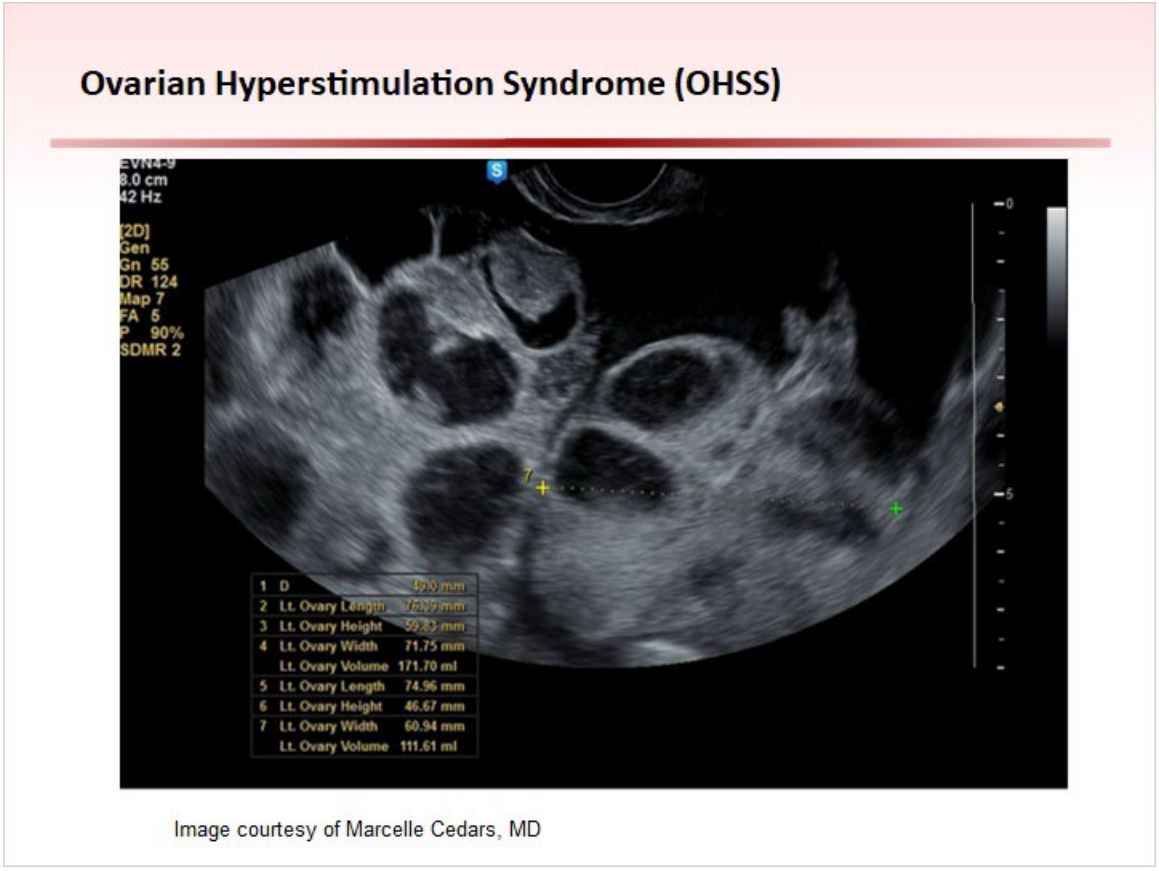


With permission from Fertil Steril. 2008 Nov;90(5):2004.e15-7

Notes:

Ovarian hyperstimulation syndrome has been mentioned throughout this module. This is a significant medical condition resulting from an exaggerated response to ovarian stimulation. It occurs most often with gonadotropin use and is rare with other agents, such as clomiphene. OHSS varies in intensity and is usually self-limited. However, it is often worse if the patient conceives on that cycle. The basic pathophysiology of this condition is an increased permeability of capillaries shifting fluid from intravascular to extravascular space.

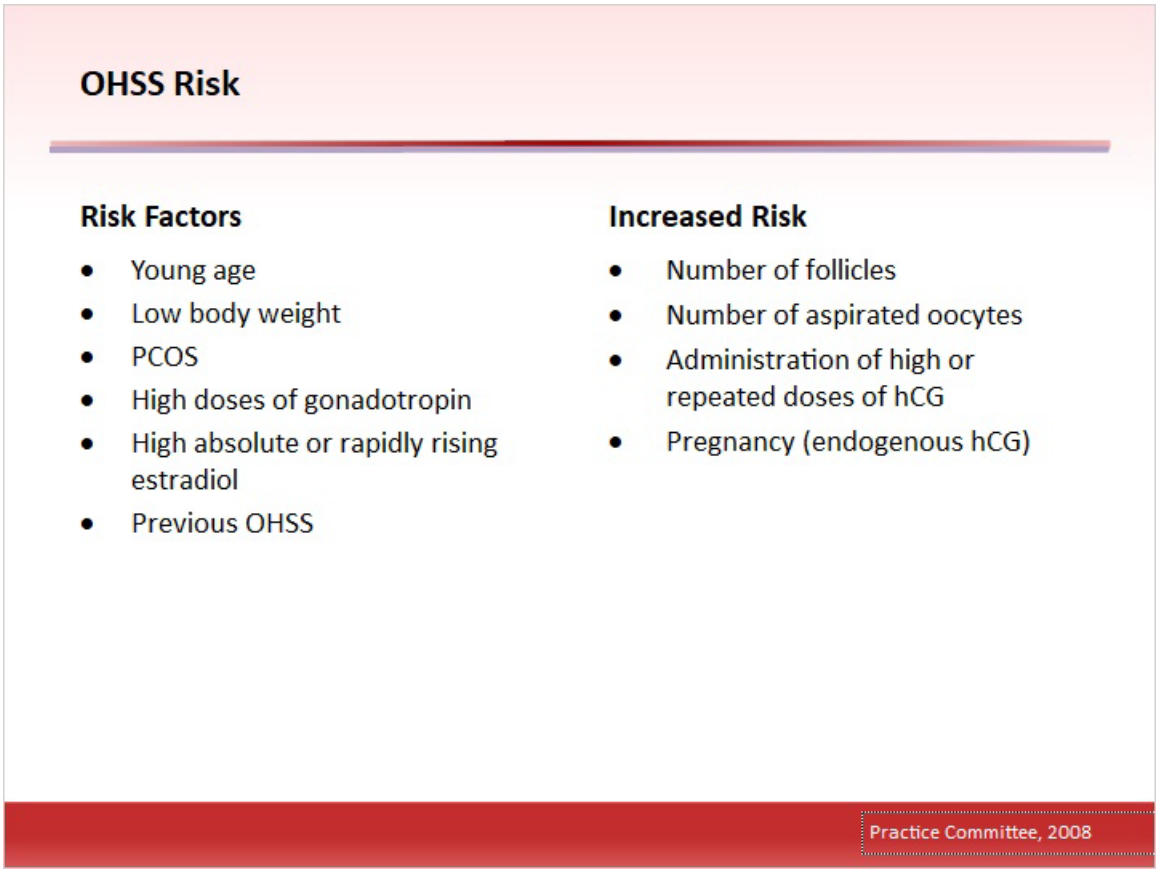
1.33 Ovarian Hyperstimulation Syndrome (OHSS)



Notes:

This ultrasound image shows enlarged ovaries and free fluid in the cul de sac.

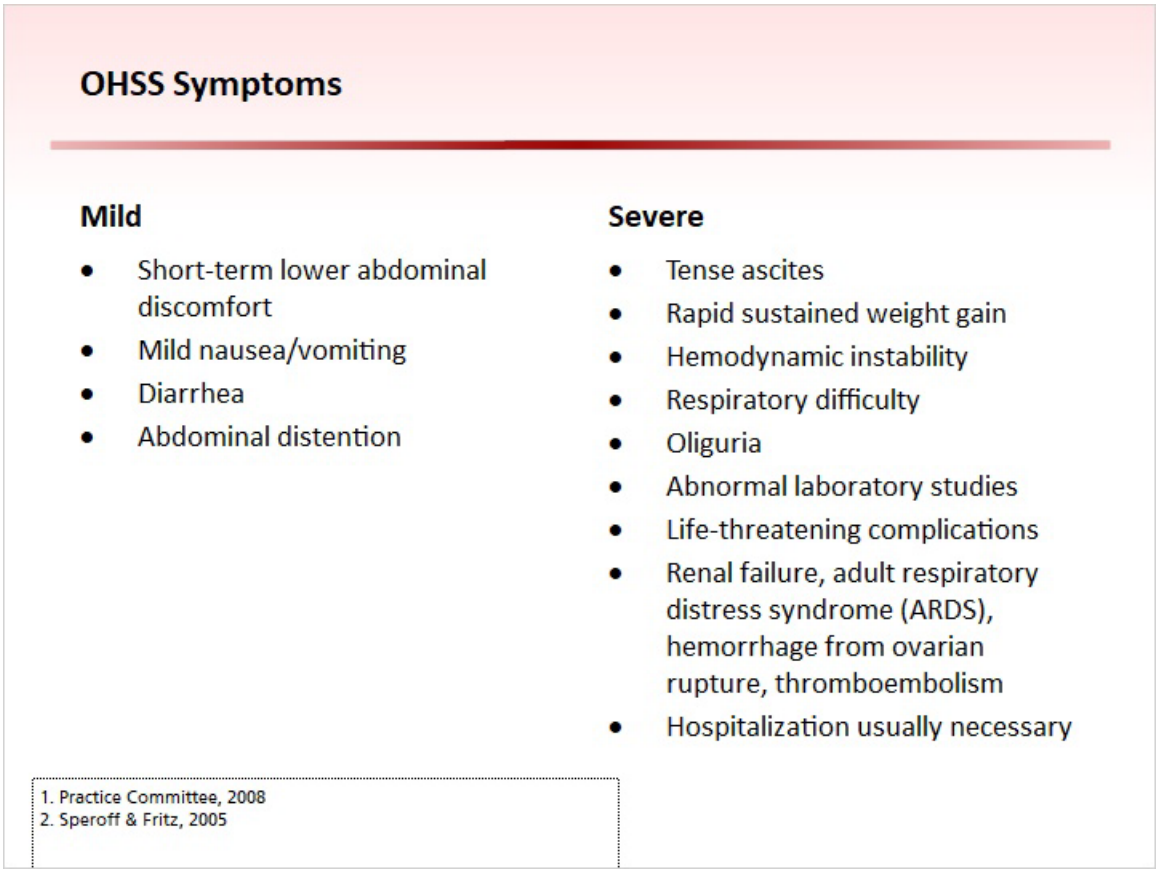
1.34 OHSS Risk



Notes:

Risk factors for OHSS include young age, low body weight, presence of PCOS, use of high doses of gonadotropin, high absolute or rapidly rising estradiol levels, and previous hyperstimulation episodes. Note that risks persist after embryo transfer if the patient has a high number of follicles and aspirated oocytes, as well as many larger follicles before hCG. Having multiple small follicles increases the risk as well. Risk also increases with administration of high doses or repeated doses of hCG. Conception, with the natural production of hCG, increases the likelihood, duration, and severity of symptoms.

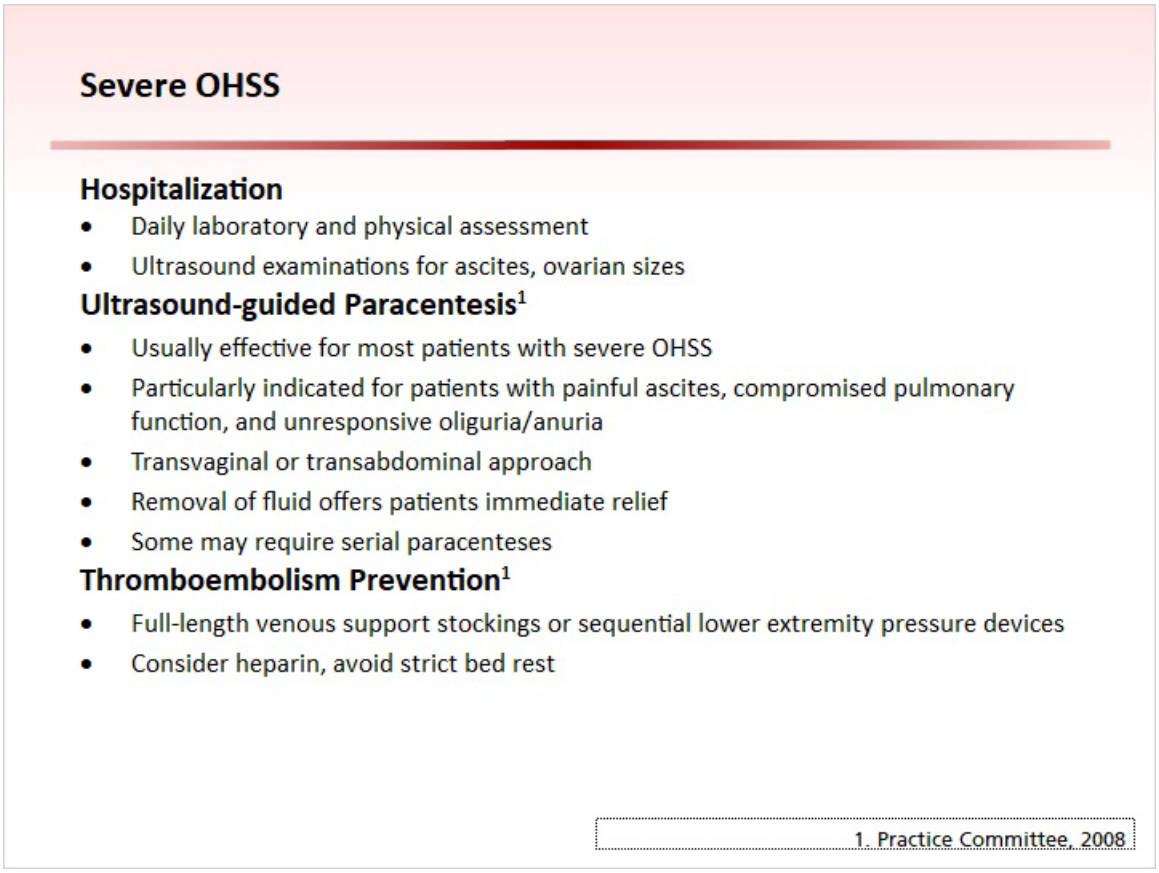
1.35 OHSS Symptoms



Notes:

Early OHSS symptoms can be mild and are self-limited, typically going away in a few days. Mild symptoms include short-term lower abdominal discomfort, mild nausea, vomiting, diarrhea, and abdominal distention. More severe symptoms may be associated with a drop in blood pressure and tachycardia. It may be difficult for the patient to breathe due to her distended, fluid-filled abdomen. Her urine output will decrease and laboratory studies may show increased hematocrit, hyponatremia, and hypokalemia, as well as abnormal liver function tests. Life-threatening complications, although rare, include renal failure, adult respiratory distress syndrome (ARDS), hemorrhage from ovarian rupture, and thromboembolism. Emphasis is on prevention so that severe OHSS is avoided.

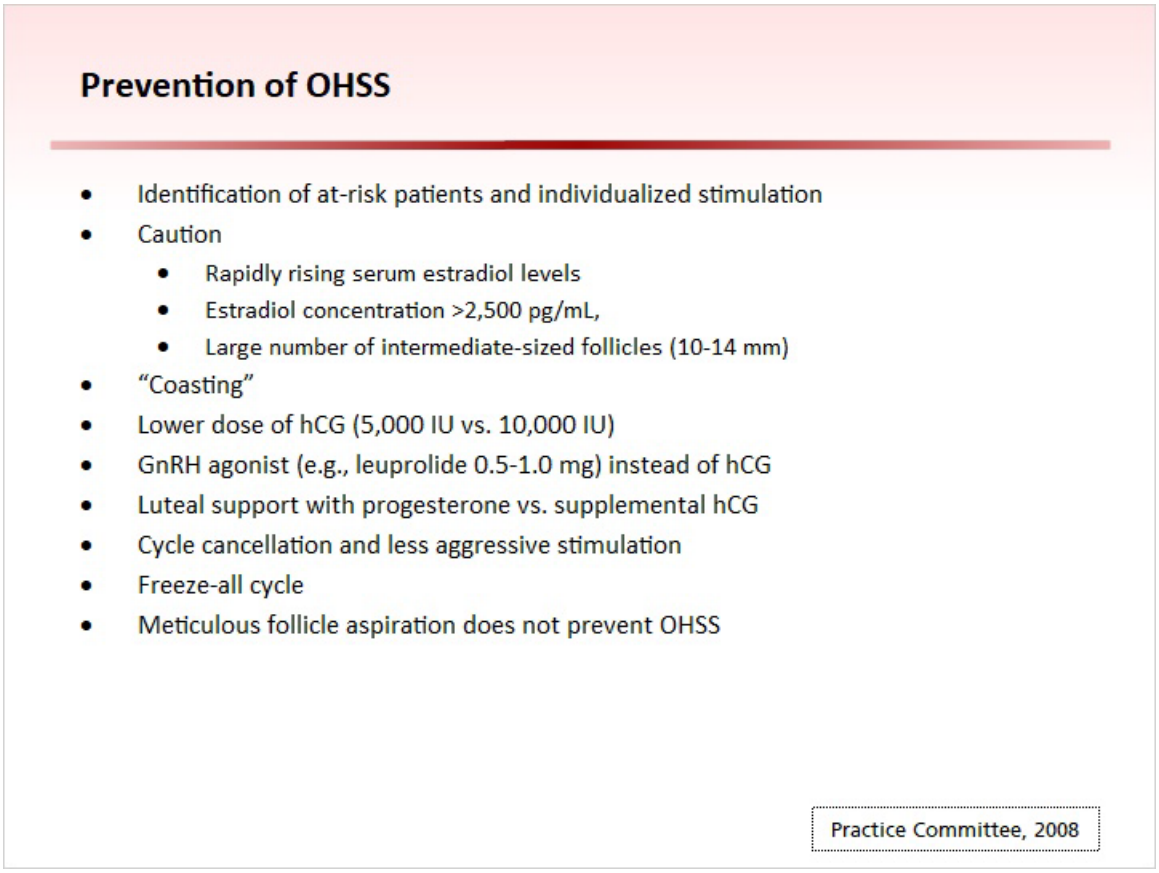
1.36 Severe OHSS



Notes:

Severe illness may require hospitalization with daily assessment of laboratory and clinical status and ultrasound examinations to assess ascites and ovarian size. Ultrasound-guided paracentesis is usually effective in most patients with severe OHSS and is particularly indicated for patients with painful ascites, compromised pulmonary function, or oliguria/anuria that does not improve with appropriate fluid management. A transvaginal or transabdominal approach may be used, under gentle ultrasound guidance. Abdominal examination should be done gently due to the risk of ovarian follicle cyst rupture resulting in intra-abdominal bleeding. The optimal volume of fluid and the interval for fluid removal are not well established, but removal of fluid offers patients immediate relief. Serial paracenteses may be required for some women. Thromboembolism is a serious complication of ovarian hyperstimulation syndrome, and preventive measures should be taken for all hospitalized women, including use of full-length venous support stockings or sequential pressure devices. Some women may require heparin therapy, and strict bed rest should be avoided when possible.

1.37 Prevention of OHSS

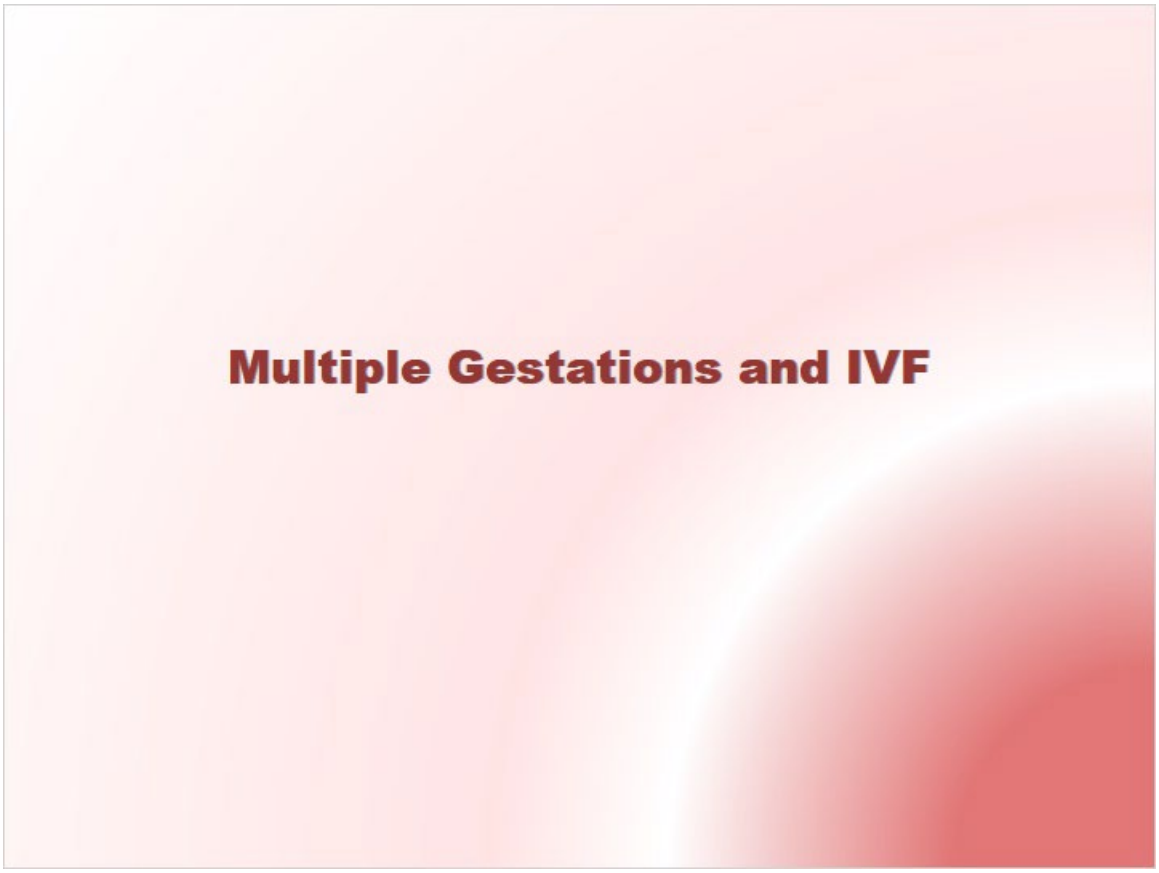


Notes:

Keys to preventing OHSS are experience with the medications and recognizing risk factors. Stimulation therapies should be highly individualized, carefully monitored, and use the minimum dose and duration necessary to achieve the therapeutic goal. Caution is indicated when any of the following are present: rapidly rising serum estradiol levels, an estradiol concentration >2,500 pg/mL, and the emergence of a large number of intermediate-sized follicles (10-14 mm).
"Coasting" or withholding further gonadotropin stimulation and delaying hCG administration until estradiol levels plateau or decrease significantly can reduce risks of OHSS. Available evidence suggests that doing so does not adversely affect IVF outcomes unless is it prolonged (3 days). Given the evidence of the pivotal role of hCG in the development of OHSS, a lower dose of hCG (5,000 IU vs. 10,000 IU) may be prudent for patients judged to be at high risk for OHSS. Alternatively, a GnRH agonist (e.g., leuprolide 0.5-1.0 mg) may be used instead of hCG to stimulate an endogenous LH surge for cycles that did not have a previous down-regulation. Luteal support with progesterone rather than supplemental hCG doses may further reduce risks of OHSS. When symptoms of OHSS emerge prior to ovulation trigger, cycle cancellation and less aggressive stimulation in a subsequent cycle should be considered seriously. Freezing all

embryos in cycles predicted to result in severe OHSS is another strategy to avoid or treat OHSS as it eliminates the risk from continued stimulation by the endogenous hCG of a pregnancy.
Although evidence indicates that meticulous follicle aspiration will reduce corpus luteum progesterone production, this technique cannot be relied on to prevent OHSS from developing or progressing.

1.38 Multiple Gestations and IVF



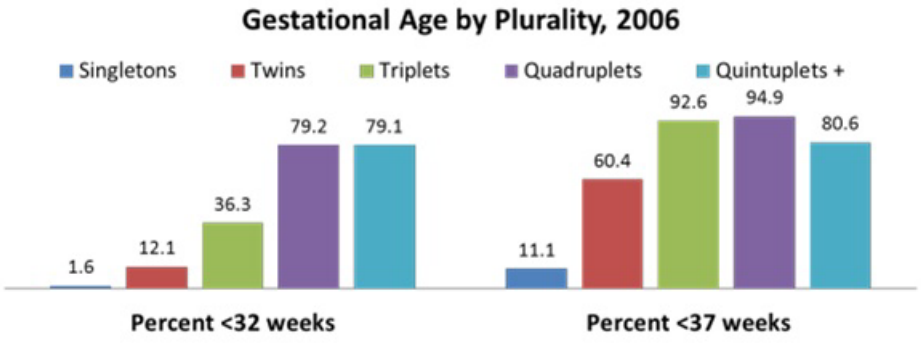
Notes:

While multiple gestation, that is, a conception with twins or more, is not really a risk of ovarian stimulation with IVF, it is a consequence of increased embryo transfer number and will be discussed here.

1.39 Multiple Gestation

Multiple Gestation

- All multiple gestations have increased maternal, fetal, and neonatal morbidity and mortality
- Risks increase as number of fetuses increases
- Increased OHSS risk
- Educate patients to the risk of multiples, including twins!

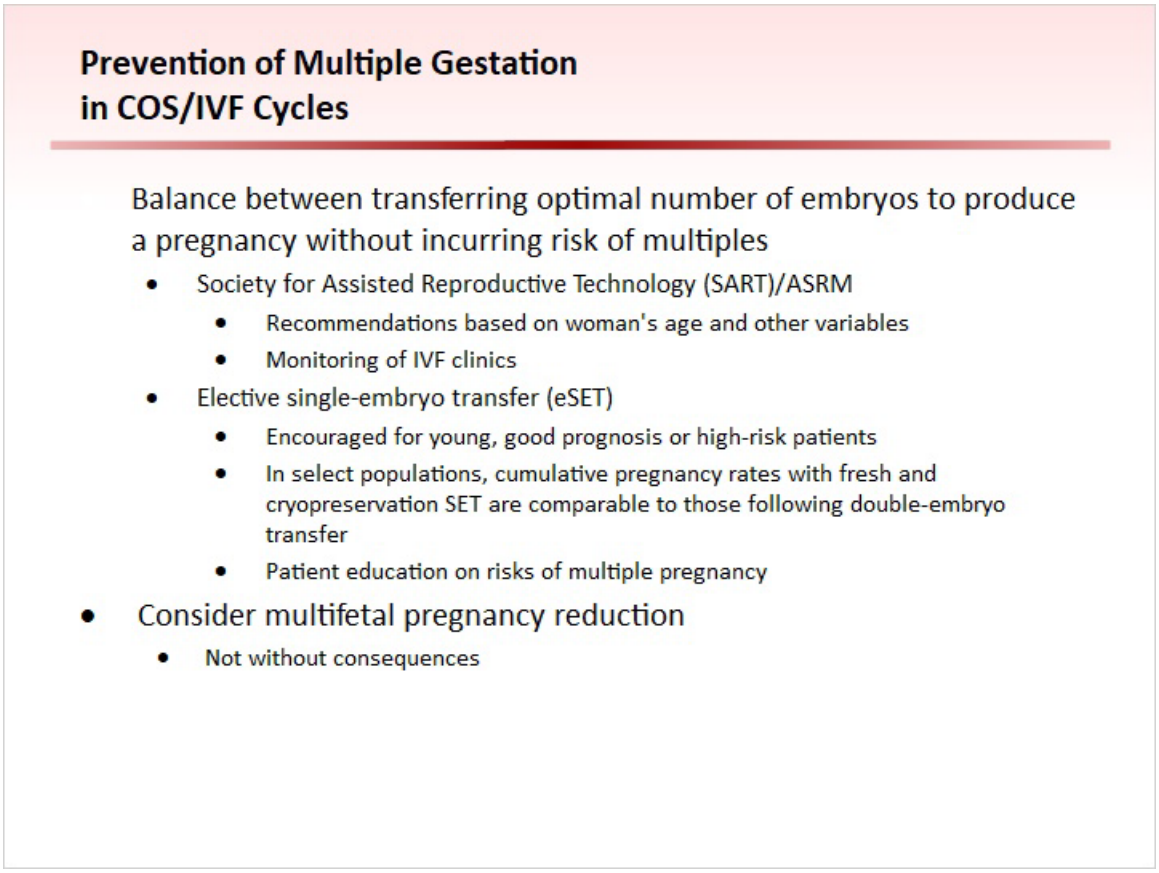


Martin et al., 2009

Notes:

All multiple gestations, including twins, have increased maternal, fetal, and neonatal morbidity and mortality. Generally, risks increase as the number of fetuses increases. Conceptions with multiple embryos are at increased risk for OHSS as well. It is important to educate patients about the risk of multiples with infertility treatment, including the risk of twins. The average gestational age of twins at delivery is 35 weeks.

1.40 Prevention of Multiple Gestation



Notes:

The goal of IVF is to create embryos that will be able to be transferred back to the uterus. The Society for Assisted Reproductive Technology (SART) is the professional organization that monitors stimulation results of IVF. Recommendations from SART have been made based on the woman's age that inform the practitioner how many embryos should be transferred. SART may audit IVF programs that have a high-order multiple pregnancy rate that is more than 2 standard deviations above the mean rate for all SART reporting clinics for 2 consecutive years. These recommendations apply to fresh and frozen/thawed-embryo transfers.

Elective single-embryo transfer (eSET) is an effective strategy for reducing the risk of multiple pregnancy with ART. In select populations, cumulative pregnancy rates with fresh and cryopreservation SET are comparable to those following double-embryo transfer. Education regarding the risks of multiple pregnancy leads to increased acceptance of eSET. When other strategies fail and treatment results in a high-order multiple pregnancy, multifetal pregnancy reduction offers an option for reducing the risk for the remaining fetuses.

1.41 SART Guidelines - 1st IVF Attempt

SART Guidelines - 1st IVF Attempt

	Age			
Prognosis	<35	35-37	38-40	41-42
Cleavage stage embryos				
Euploid	1	1	1	1
Other Favorable[b]	1	1	≤ 3	≤ 4
Embryos not [a] or [b]	≤ 2	≤ 3	≤ 4	≤ 5
Blastocysts				
Euploid[a]	1	1	1	1
Other Favorable[b]	1	1	≤ 2	≤ 3
Embryos not [a] or [b]	≤ 2	≤ 2	≤ 3	≤ 3

[a]Demonstrated euploid embryos, best prognosis

[b]Other Favorable = Any ONE of these criteria: *Fresh cycle*: expectation of 1 or more high-quality embryos available for cryopreservation or previous live birth after an IVF cycle; *FET cycle*: availability of vitrified day-5 or day-6 blastocysts, euploid embryos, 1st FET cycle, or previous live birth after an IVF cycle.

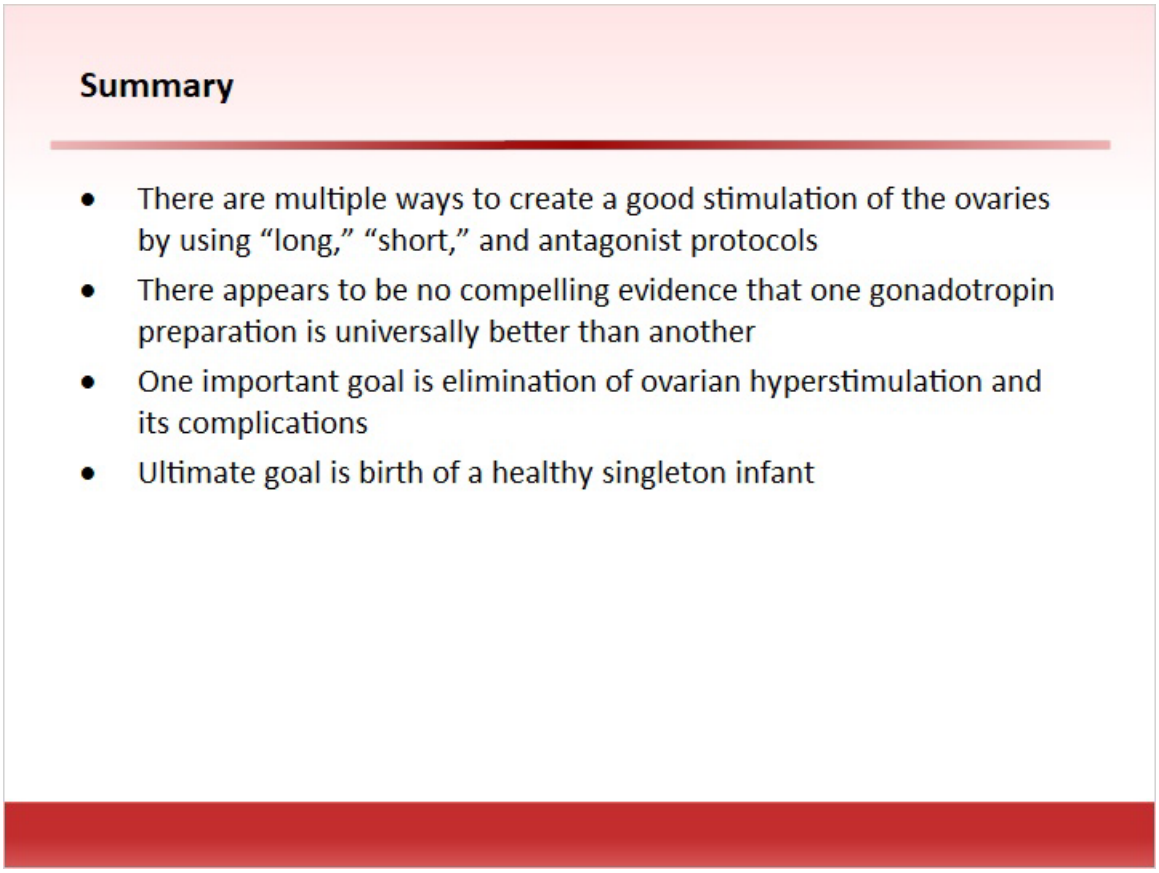
**Please note that justification for transferring additional embryos beyond recommended limits should be clearly documented in the patient's medical record.

Fertil Steril 2017;107:901–3.

Notes:

SART has made recommendations to decrease the chances of twins and high-order multiple pregnancy in IVF cycles.

1.42 Summary



Notes:

In summary, there are multiple ways of creating a good stimulation of the ovaries by using “long,” “short,” and antagonist protocols. There appears to be no compelling evidence that one gonadotropin preparation is universally better than another. One important goal is the elimination of ovarian hyperstimulation and its complications. The ultimate goal is the birth of a healthy singleton infant.

1.43 Thank you!

Notes:

Thank you for participating in this educational activity.