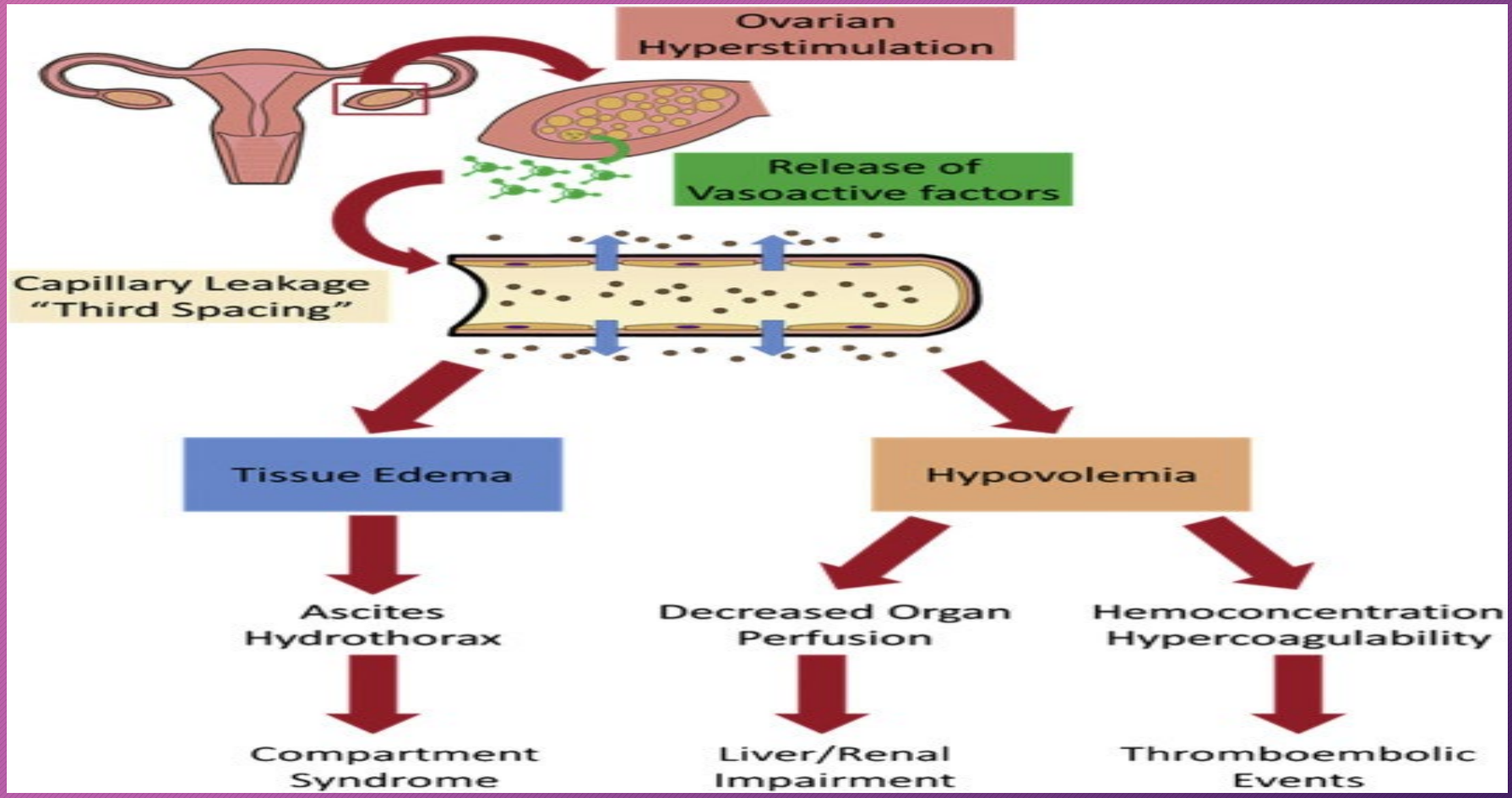
Ovarian Hyperstimulation Syndrome(OHSS)

Definition

- OHSS is an exaggerated ovarian response to ovulation induction, particularly in the setting of IVF. OHSS is the most serious iatrogenic complication of COH for ART.
- It can be strictly defined as the shift of serum from the intravascular space to the third space, mainly to the abdominal cavity, in the context of enlarged ovaries due to follicular stimulation.
- In its very severe form, OHSS is a life-threatening condition


Ovarian Hyperstimulation
Release of Vasoactive factors
Capillary Leakage "Third Spacing"
Tissue Edema
Hypovolemia
Ascites Hydrothorax
Decreased Organ Perfusion
Hemoconcentration Hypercoagulability
Compartment Syndrome
Liver/Renal Impairment
Thromboembolic Events

Epidemiology

The incidence of **moderate** and **severe** OHSS while undergoing IVF has **decreased** in the last decade due to modern approaches in prevention strategies:

It occurs when :

- the ovaries are hyper stimulated and enlarged due to fertility treatments .(in exogenous gonadotropin administration).

Rare Cases of OHSS (in the absence of exogenous gonadotropin administration)

1. OHSS after Tx with CC
   - Severe form in PCO patient
   - Conception after CC Tx

2. In spontaneous pregnancy
   - Multiple gestations –Molar pregnancy
   - A patient with PCO
   - A hypothyroid patient with Down's syndrome
   - normal females with ascites and pleural effusion → R/O advanced ovarian cancer →exploratory laparotomy
   - spontaneous recurrent familial OHSS
     - They had a similar condition in their previous pregnancies
     - They had a *FSHr mutant* → ↑ sensitivity to hCG and TSH, ↑ in basal activity

In these cases, OHSS may be the consequence of :

- the **high production** of **endogenous** gonadotropins (hCG) or gonadotropin-like molecules (TSH)

or

- enhanced **sensitivity** to endogenous gonadotropins (mutations in the FSH receptor).

Pathogenesis

- The pathophysiology of OHSS is not fully understood, but increased capillary permeability with the resulting loss of fluid into the third space is its main feature.

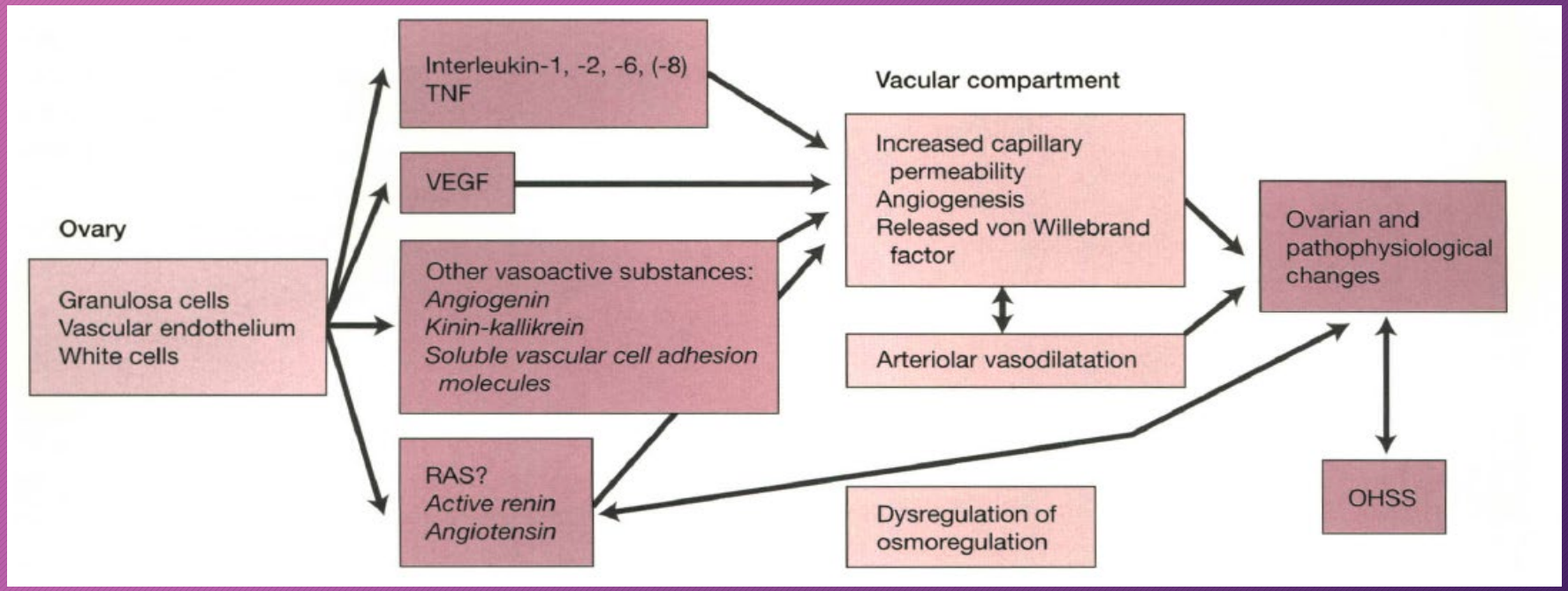
- In the susceptible patient, hCG administration for final follicular maturation and triggering of ovulation is the pivotal stimulus for OHSS, leading to :
  - overexpression of VEGF in the ovary
  - release of vasoactive-angiogenic substances
  - increased vascular permeability
  - loss of fluid to the third space

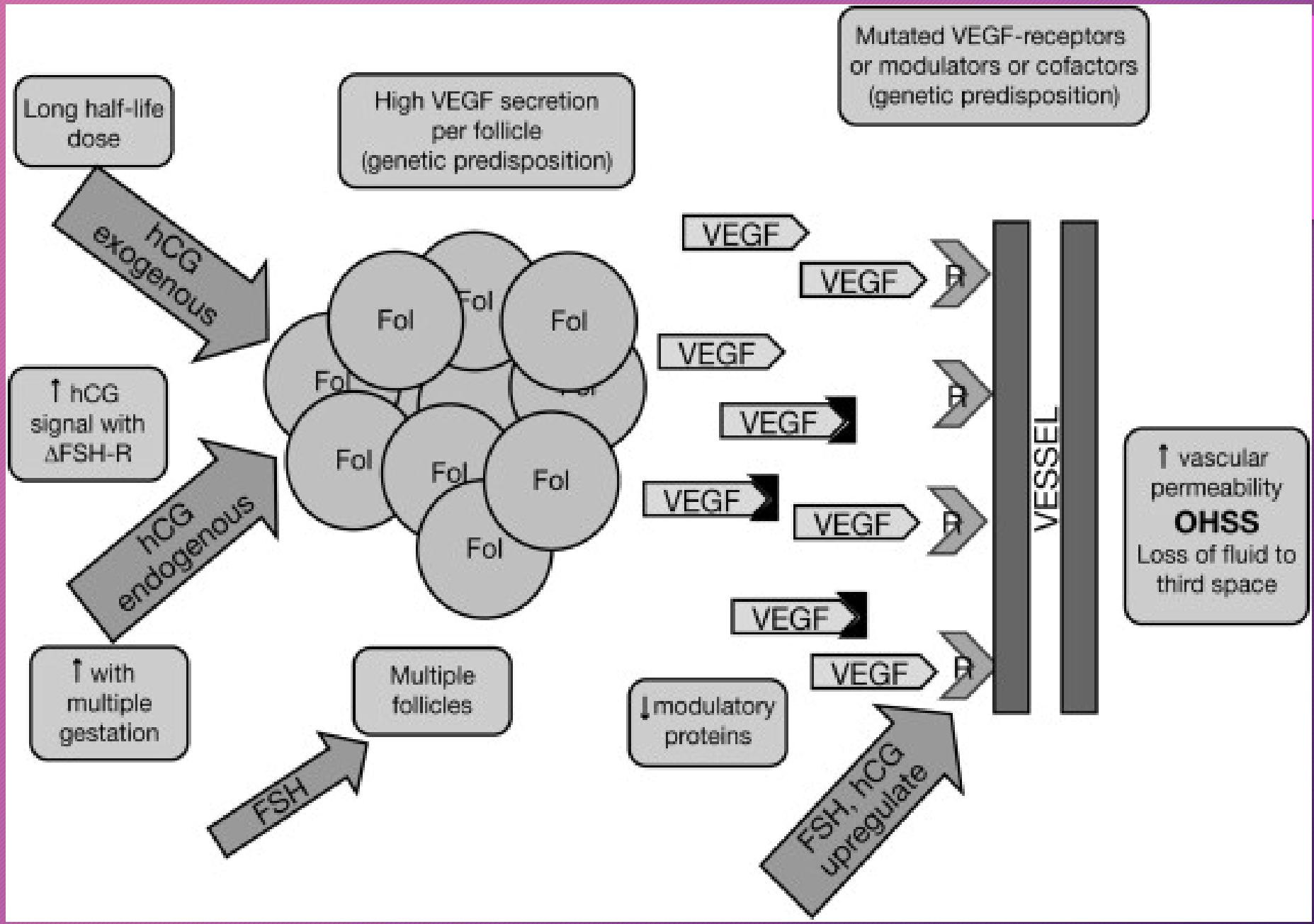
- A number of substances have been proposed as the cause of increased vascular permeability post-hCG administration, but VEGF appears to play the main role.

Etiology of OHSS

- Exact etiological factor is unknown
- Characteristic feature of OHSS:

  ↑ capillary permeability → fluid shift from the intravascular to extravascular spaces due to ↑ ovarian secretion of vasoactive substances




Long half-life dose
hCG exogenous
↑ hCG signal with ΔFSH-R
hCG endogenous
↑ with multiple gestation
High VEGF secretion per follicle (genetic predisposition)
Fol
Multiple follicles
FSH
Mutated VEGF-receptors or modulators or cofactors (genetic predisposition)
VEGF
VEGF-R
VESSEL
↓ modulatory proteins
FSH, hCG upregulate
↑ vascular permeability
OHSS
Loss of fluid to third space

VEGF (Vascular endothelial growth factor)

- a member of the family of heparin-binding proteins .
- act directly on endothelial cells to induce proliferation and angiogenesis.
- VEGF mRNA and protein are expressed by granulosa and theca cells **late** in follicular development and **after ovulation**.
- Studies on **ascitic fluid** from patients with severe OHSS have demonstrated that VEGF is the major capillary permeability agent.
- VEGF **serum concentrations** are positively correlated with the risk of developing OHSS and with the severity of its form.
- patients who get pregnant after oocyte donation do not have OHSS, despite high free VEGF levels.

Classification of OHSS

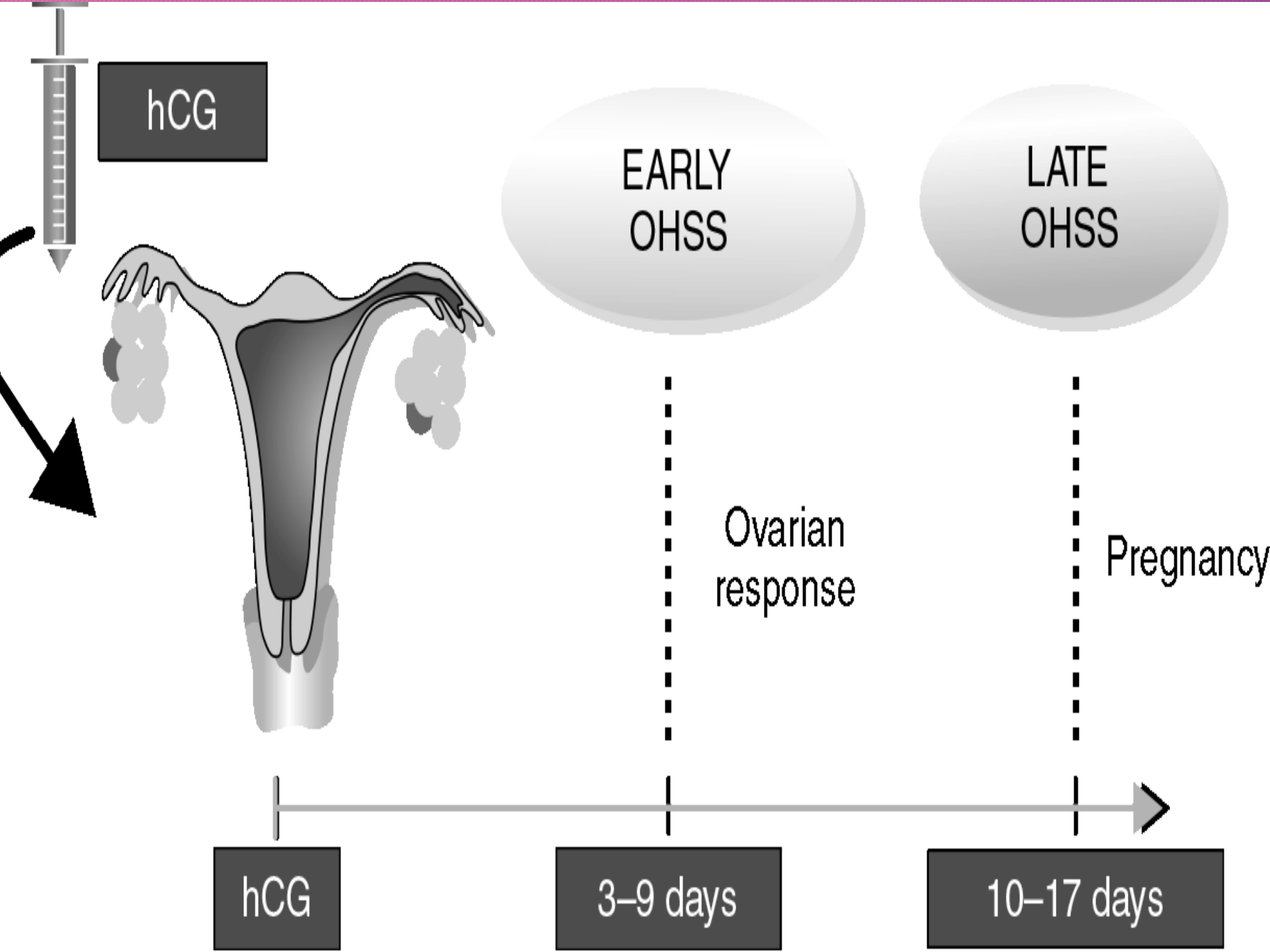
Classification of OHSS Onset

Early onset

- Occurs 3-9 days following the hCG trigger
- Is associated with the administration of exogenous HCG.
- is usually mild to moderate

Late onset

- Occurs at least 9 days after the hCG trigger
- Is the result of endogenous hCG from the pregnancy
- tends to be more severe with multiple gestation


hCG
EARLY OHSS
LATE OHSS
Ovarian response
Pregnancy
hCG
3–9 days
10–17 days

OHSS

Classification

Classification of OHSS

1-Mild:20-33%

2-Moderate: 3-6%

3-Severe:clitical: 0.1-2%

4-critical

Ovarian hyperresponder

2-4=OHSS

Classification of OHSS Severity

Mild	Moderate	Severe	Critical
▪ Bloating ▪ Nausea ▪ vomiting ▪ diarrhea ▪ Abdominal distention (Ovaries ≤ 5 cm) no biochemical abnormalities	❑ Vomiting ❑ Abdominal pain ❑ U/S evidence of ascites ❑ Hct >41% ❑ WBC>10000/m ❑ hypoproteinemia ❑ Ovaries 5-12 cm ❑ increase in weight of more than 3 kg (6.6 lbs) may be an early sign of moderate OHSS (update)	• Massive ascites • gain as much as 15 to 20 kg (33 to 44 lbs) over 5 to 10 days • Hydrothorax • Hct >45%(>55) • WBC >15 000/mm3 (>25) • Cr 1–1.5 mg/dl(>1.6) • Cr cl ≥50 ml/min • Hepatic dysfunction transaminases are increased • Anasarca • Ovaries >12cm • Hypovolemia • Oliguria • Hypo Na • Hyper K • Hypotension	○ Tense ascites ○ Hypoxemia ○ Pericardial effusion ○ Hct >55% ○ WBC >25 000/mm3 ○ Oliguria /Anuria ○ Cr >1.5 mg/dl ○ Cr cl <50 ml/min ○ Renal failure ○ cardiac arrhythmia ○ respiratory insufficiency ○ Thromboembolic phenomena ○ ARDS ○ Ovaries variably enlarged ○ Sepsis ○ DIC ○ Death

Risk Factors Associated with OHSS

High risk	Low risk
▪ Young (<35 years old) =(Although younger age and low body weight have been reported as possibly associated with OHSS, neither is a good predictor of risk ▪ Polycystic-appearing ovaries ,Necklace sign ▪ Previous OHSS ▪ High serum estradiol (ART>4000, OI>1700 pg/ml) ▪ Multiple stimulated follicles (ART >20, OI >6) (≥ 13 sized≥ 11mm in GnRH-ant) ▪ **Pregnancy** ▪ **hCG l**uteal supplementation ▪ **GnRH-agonist** down regulatory **protocol** ▪ Basal **AMH >3.3** ng/mL and **AFC >8**=update ▪ **increasing number of oocytes retrieved in IVF cycle** =update	○ Older (>35 years old) ○ Hypogonadotropic ○ Heavy build ○ Low serum estradiol ○ Poor response to gonadotropins ○ Few AFC ○ Elevated baseline FSH ○ Progesterone or no luteal supplementation ○ Clomiphene citrate and/or hMG protocol

DIAGNOSIS

❑clinical history :

- history of ovarian stimulation followed by administration of hCG.
- The number of collected oocytes, peak serum estradiol, and number of transferred embryos are **predictors** of the presence of OHSS.

❑transvaginal ultrasound(update)

Once the diagnosis of OHSS is made, disease severity should be classified as mild, moderate, severe, or Critical.

Complications of OHSS

- Vascular complications
- Hemoconcentration
- Thromboembolic complications
- Myocardial infarction
- Liver dysfunction
- Respiratory complications
- Renal complications
- Gastrointestinal complications
- Benign intracranial tension
- Obstetric complications
- Ovarian torsion

Keys to prevention

- Recognition of risk factors for OHSS
- Extensive clinical experience with drugs used for ovarian stimulation
- Use of individualized ovarian stimulation regimens for assisted reproduction.

prevention

- Gonadotropin (dose and type)
- Monitoring
- protocol of GnRH (agonist or antagonist)
- Coasting
- Withholding hCG (cycle cancellation)
- Using lower dose hCG or GnRH agonistfor final oocyte maturation
- Pretreatment with metformin in women with PCOS (prior to IVF for reducing the risk of OHSS).
- Luteal phase support : We suggest progesterone regimens over hCG regimens. An alternative approach has been to administer intermittent, low doses of hCG.
- IVM
- Embryo cryopreservation(Women with PCOS who undergo IVF have lower rates of OHSS with the transfer of frozen rather than fresh embryos) was associated with a lower incidence of OHSS.
- Dopamine agonists(Cabergoline-Quinagolide)

prevention

- Intravenous albumin (We do not suggest the routine use)
- Low-dose aspirin — Two studies suggest that low-dose aspirin may be associated with a lower risk of OHSS. However, we do not suggest its use at this time. The use of aspirin for OHSS prevention has been investigated by two randomized trials . These studies found a lower incidence of OHSS in patients treated with a daily dose of 100 mg aspirin from the first day of stimulation until the day of the pregnancy test/detection of embryonic cardiac activity. Indeed, mechanism at the base of OHSS consists in a releasing of substances (histamine, serotonin, platelet-derived growth factor, lysophosphatidic acid) due to an activation of platelet by VEGF. Given this, aspirin has been suggested to have a potential role in reduction of OHSS risk .
- the use of IV calcium (10 mL of 10% calcium gluconate in 200 mL normal saline) around the day of oocyte retrieval and thereafter has been investigated as a strategy to reduce OHSS. Calcium is described to inhibit the secretion renin mediated by cAMP resulting in a reduction of angiotensin II and subsequent decrease of VEGF production. A RCT compared the use IV calcium and normal saline in 200 women at risk for OHSS reporting higher incidence of moderate and severe OHSS in women treated with normal saline , without impact on clinical pregnancy or ongoing pregnancy rate between the groups. In addition, evidence suggests that IV calcium is as effective as cabergoline in lowering the OHSS risk in PCOS women and in its prevention

protocol of GnRH agonist or antagonist(to prevent the endogenous LH surge)

We suggest the use of GnRH antagonists rather than GnRH agonists in women at high risk for OHSS.

- The use of GnRH agonists is associated with a higher incidence of OHSS, probably due to enhanced follicular recruitment.
- the use of GnRH antagonists may result in lower pregnancy rates when compared with GnRH agonist therapy.

Ovarian stimulation protocol

- Gonadotropin dose :
  - correlate with **OHSS severity**
  - The current approach : to dosing based upon patient variables such as age, AMH, AFC, and previous ovarian response. This approach typically uses lower doses than fixed ovarian stimulation protocols.
  - in patients at risk, the starting dose of gonadotropins should be decreased (to 100 to 150 international units) .

there is currently no consensus on the ideal dosing approach that optimizes pregnancy rates yet minimizes OHSS risk.

- type of gonadotropin preparation (hMG versus rFSH versus uFSH) does not appear to affect the risk of OHSS.

Ovulatory triggers

- Low versus standard-dose hCG(would be associated with lower risks of OHSS) by decreasing VEGF secretion by granulosa cells.

- Recombinant LH/recombinant hCG:(pooled data from three trials comparing rlh(10h) and urinary hCG(24-36h) showed no difference in achieving final follicular maturation in IVF, with similar pregnancy and OHSS rates.

- GnRH agonist trigger(In GnRH antagonist cycles, the administration of a GnRH agonist at the end of ovarian stimulation induces an endogenous rise in both LH and FSH concentrations and effectively triggers oocyte maturation. This is a useful approach in high-risk patients, **preventing both early and late forms of OHSS**.in two settings:

  - Women at high risk for OHSS (development of multiple follicles during ovarian stimulation [>20 follicles over 10 mm])
  - Women undergoing ovarian stimulation who plan to donate oocytes to recipients, or women undergoing fertility preservation cycles (eg, women planning to freeze their oocytes or embryos for future use)

Monitoring

using both :

- transvaginal ultrasound (TVUS) (for follicular number and size)
- serum E2 concentrations.

Modifying treatment when indicators for increasing OHSS risk develop:

- Serum E2 >3500 pg/mL
- many intermediate-sized follicles (more than 20 follicles >10 mm) .

Coasting

Coasting refers to **withholding gonadotropin** therapy while continuing pituitary suppression with a GnRH agonist or antagonist until serum E2 levels fall into a range acceptable for hCG administration .

The larger follicles can continue their growth and maturation when FSH is stopped;
the smaller follicles have a greater FSH requirement and therefore undergo atresia.

We typically start coasting when the dominant follicles are ≥16 mm and serum E2 levels are >3500 pg/M l.
Once initiated, daily TVUS and serum E2 measurements should be performed;
administration of hCG should be withheld until serum E2 falls below 3500 pg/mL.

Coasting for **greater than three days** (but not up to three days) has a modest adverse effect on pregnancy rates ,Therefore, we consider **cycle cancellation** if E2 levels have not fallen by the fourth day of coasting.

This approach is less common now because of the availability of GnRH antagonists.

Although we agree with trying this approach in high-risk cycles, available data are conflicting on its impact on preventing OHSS.

In vitro oocyte maturation(IVM)

- an experimental technique that consists of the in vitro conversion of oocytes at the germinal vesicle stage to oocytes at the metaphase II stage.
- To be successful, this technology must include nuclear and cytoplasmic maturation of the oocyte and give rise to embryos that have a developmental potential that is similar to embryos obtained from standard IVF or from spontaneously in vivo matured oocytes.
- Initial studies with IVM resulted in **low fertilization rates** and **suboptimal embryonic quality** . However, preliminary studies in women with PCOS suggest that IVM is associated with a **lower OHSS rate** but also a **lower live birth rate** than IVF using a GnRH antagonist protocol .
- **This technique is not yet used clinically**.

Intravenous albumin

- mechanism of action of prophylactic intravenous : increase plasma oncotic pressure, maintain intravascular volume, and bind to and inactivate ovarian mediators (eg, VEGF) involved in the development of OHSS .

- benefit of intravenous albumin for reducing the occurrence of severe OHSS in high-risk women.
- We do not suggest the routine use of intravenous albumin or other volume expanders for the prevention of OHSS.

- Intravenous albumin has also been used for intravenous hydration in the management of severe OHSS.

- A second volume expander, hydroxyethyl starch, was associated with a reduction in OHSS rates compared with placebo in three trials , but the safety of this product has not been well established.

Dopamine agonists

- In females at high risk for OHSS undergoing ovarian stimulation, the rate of developing moderate and severe OHSS can be significantly reduced with cabergoline (0.5 mg/day orally), **beginning** on the day of hCG administration or oocyte retrieval.

- Dopamine agonists inhibit VEGF receptor phosphorylation and thereby decrease vascular permeability, and a number of studies have reported that either dopamine or dopamine agonists reduce the risk of OHSS in women undergoing controlled ovarian stimulation.

- Cabergoline
- Quinagolide: another dopamine agonist, appears to reduce the risk of early onset severe OHSS.

Treatment

Management of OHSS : Mild OHSS

- self-limited
- outpatient
- conservatively with a goal of relieving symptoms.
- Only oral analgesics(acetaminophen rather than NSAIDs)
- avoidance of heavy physical activity
- Intercourse is best avoided (risk of ovarian rupture)
- Explaining the signs and symptoms of progressive illness
- Mild OHSS **can progress** to become moderate or severe, particularly if pregnancy has occurred.

- females with mild disease should be observed for:
  - worsening abdominal pain
  - weight gain (>1 kg/day)
  - increasing abdominal girth

for at least **two weeks** or **until menstrual bleeding occurs.**

Management of OHSS : Moderate OHSS

- Outpatient management
- Persistent or worsening symptoms or ascites signal **progressing** illness
- Required treatment with anti-emetics and more potent oral analgesics
- Daily monitoring of weights , abdominal circumference measurements and urinary frequency
- Serial clinical examinations to detect increasing ascites
- Serial laboratory evaluation of hematocrit, electrolytes, and serum cr , serum albumin, and liver enzymes
- Oral fluid intake ≥ 1 L/day(1-2L) (electrolyte supplemented drinks)
- No heavy physical activity (risk of ovarian torsion)
- Avoid sexual intercourse.
- Light physical activity is preferable to bedrest (risk for thromboembolism)
- **Diuretics** are contraindicated because they can worsen decreased intravascular volume.

Medical treatment of **severe** OHSS

goals :

- correcting the disturbed fluid and electrolyte balance
- relieving secondary complications of ascites and hydrothorax
- preventing thromboembolic phenomena.

maintaining intravascular blood volume:

- **isotonic crystalloid solutions** (eg, normal saline, Ringer's lactate) are typically used for intravenous hydration in patients with severe OHSS

- some clinicians use **intravenous albumin** in critically ill, volume-depleted patients.

available evidence suggests that intravenous albumin provides no additional benefit when compared with crystalloid solutions.

We suggest **thromboprophylaxis** in all hospitalized patients with OHSS.

monitored for signs of infection:

Bacterial peritonitis has been described in occasional patients .

other potential sources of infection include indwelling catheters and procedures to drain pleural and ascitic fluid.

If bacterial infection is suspected, we suggest broad-spectrum empiric **antibiotic** therapy while awaiting culture results.

We typically use a third- or fourth-generation cephalosporin in combination with metronidazole.

Critical OHSS

- Assessment of fluid balance (daily or more often)
- Weights and measurement of abdominal circumference
- CBC, Electrolytes, BUN, Cr
- Serum hCG measurements (to determine if patient has conceived)
- Invasive monitoring of central venous pressure
- **Pelvic ultrasound** as needed to evaluate ovarian size and ascites
- Chest radiograph and echocardiogram when pleural or pericardial effusion is suspected (as often as needed)

Hospital admission

- Inadequate pain relief
- Severe OHSS :
  - Severe abdominal pain or peritoneal signs
  - severe oliguria/anuria
  - hypotension, severe electrolyte imbalance
  - Intractable nausea and vomiting
  - Tense ascites
  - Dyspnea or tachypnea
  - Dizziness or syncope
  - Hemoconcentration (HCT> 45%)(>55)
  - leukocytes >25,000/L
  - Severe hyponatremia (Na<135 mEq/L) or hyperkalemia (K>5 mEq/L)
  - Abnormal renal functions (Cr> 1.2 mg/Dl(1.6); Cr Cl<50 ml/min)
  - Abnormal liver functions (↑ transaminases)

inpatient care for hospitalized women

- Frequent evaluation of VS
- Daily weights - abd circumference
- Fluid I&O
- CXR and echocardiogram (if pleural or pericardial effusion is suspected)
- Pulse oximetry (pulmonary symptoms)
- Serial HCT, electrolytes, renal and liver function studies
- IV fluid management (restore an effective plasma vol but not ↑ extravascular fluid)
  - Initial rehydration
  - Maintenance therapy in the lowest vol (for adequate U/O and relieve hemoconcentration)
  - Saline is preferable to lactated Ringer's solution (to avoid hyponatremia)
  - Alb (25%; 50-100 g, slow infusions ,over 4 hr, at 4-12 h intervals) can effectively expand plasma volume (when saline fails)

Continued …

- Diuretics can be considered to improve weight gain and oliguria , only after hypovolemia has been corrected (premature or excessive use of diuretics is counterproductive)
- IV fluid support can be reduced substantially after diuresis begins and oral intake is re-established
- Hyperkalemia may require specific treatment to move potassium into the intracellular space (insulin/glucose, sodium bicarbonate) or to prevent cardiac dysrhythmias (calcium gluconate)

- Ultrasound-guided paracentesis
- Thoracentesis: persistent bilateral or severe pleural effusions symptoms
- Severe hemoconcentration:
  - ✓ full-length venous support stockings
  - ✓ prophylactic heparin therapy (5,000 units q12 hr)
- Clinical signs and symptoms of thromboembolism:
  - ✓ Additional diagnostic measures
  - ✓ Therapeutic anticoagulation when the diagnosis is confirmed or strongly suspected

Indications for ICU Admission in OHSS

- Hyperkalemia
- Renal failure
- Respiratory failure
- Thromboembolic disease

paracentesis OR culdocentesis

- Transabdominal – Transvaginal
- even on an outpatient basis
- In females with : tense Painful ascites
  Oliguria that does not respond to fluid management

  orthopnea, Pulmonary symptoms
  rapid increase of abdominal fluid
  any other sign that may indicate progression of illness
- The volume of fluid to be removed is not well established, but **after aspiration of 500 mL of ascitic fluid, patients typically report resolution of abdominal discomfort.**
- Removal of **more than 4 liters** of fluid is not recommended.
- **Blind paracentesis** should not be done, because of the potential risk of bowel or vessel puncture.

Indications for Laparotomy

- Experienced surgeon Only if :
  - Hemorrhage
  - Torsion
  - Rupture
  - Ectopic
- Only hemostatic

Dopamine agonists (DA)

- Less is known about the efficacy of DA for the treatment of OHSS once it is established. However, **some small studies suggest it may diminish clinical symptoms and severity**.

Prophylaxis for thromboembolic events

- All hospitalized patients with OHSS.

- Females with OHSS being managed as outpatients with two to three additional risk factors (in addition to OHSS):

✓ age >35 years
✓ Obesity
✓ Immobility
✓ elevated hematocrit
✓ personal or family history of thrombosis
✓ thrombophilias
✓ pregnancy

For those in whom **bed rest** is suggested, an intermittent pneumatic compression device is typically recommended.

- We use prophylactic low molecular weight heparin, 20 mg subcutaneously every 12 hours, or heparin 5000 units subcutaneously every 12 hours .

Prophylaxis for thromboembolic events

- arterial (25 %) or venous (75 %)
- may lead to permanent neurologic injury or death
- have been reported in :
  - internal jugular
  - Subclavian
  - axillary
  - mesenteric vessels
- Some experts advise that women with an **underlying thrombophilia (eg, antithrombin III deficiency, factor V mutation, and protein C or S deficiency)** should receive prophylaxis (such as low-dose heparin therapy) prior to ovulation induction, to prevent thromboembolic complications

Because thromboembolic complications are rare, we do not suggest routine screening for thrombophilia in women planning to undergo ovarian stimulation.

Resolution and prognosis

- The pathophysiological process of OHSS is self-limited, and increased vascular permeability regresses spontaneously.

- Those who have not conceived recover over 10 to 14 days from the onset of initial symptoms. Third-space fluid begins to re-enter the intravascular space, hemoconcentration reverses, and natural diuresis ensues.

- **Clinical evidence of resolution includes:**
  - Normalization of hematocrit
  - Progressive reduction of ascites on ultrasound
  - Alleviation of clinical symptoms

Resolution and prognosis

- If pregnancy occurs, Pregnancy increases the risk, duration, and severity of OHSS (due to the persistent stimulation by endogenous hCG).

- Pregnancy outcomes with OHSS vs without OHSS:
  - Higher rates of biochemical losses
  - Similar rates of clinical losses

- Some studies have suggested that OHSS pregnancies are associated with a **higher rate of** miscarriage and later complications, such as gestational diabetes and pregnancy-associated hypertension.

in a retrospective chart review of females undergoing IVF, similar rates of gestational diabetes and preeclampsia were seen in those who did and did not develop OHSS


Thank you for your generosity and continued support.
Thank You

changes of plasma D-dimer level and the role of its test in the pathogenesis of OHSS

Plasma D-dimer levels were significantly higher in the four groups with early onset of symptomsthan in the normal group.

With increasing symptoms of OHSS, D dimer levels gradually increased in all four groups.

There was a significant positive correlation between symptoms and D-dimer levels.

When OHSS symptoms improved or healed based on the patient's clinical manifestations and laboratory parameters, the D-dimer levels of patients with moderate and severe symptoms remained significantly higher than the normal range .

The D-dimer levels in the improved stage in moderate and severe groups were significantly higher than those in the early stage.

Conclusions….

According to elevated D-dimer levels, we can more accurately predict the severity of OHSS in the early stage.

with further increases in D-dimer levels along with symptoms, we can more precisely determine the prognosis of patients.

Overall, 140 patients were divided into four groups based on OHSS status: normal, mild, moderate, and severe. All patients were hospitalized because of embryo transfer or OHSS. We retrospectively analyzed their clinical data, hormone levels, ovulation induction agents, and plasma D-dimer levels during the occurrence of OHSS and improved stages.

- Results: Plasma D-dimer levels were significantly higher in the four groups with early onset of symptoms ($P<0.05$; reference value, 0–0.5 μg/mL) than in the normal group. With increasing symptoms of OHSS, Ddimer levels gradually increased in all four groups. There was a significant positive correlation between symptoms and D-dimer levels ($\gamma=0.575$; $P<0.05$), and the 95% confidence intervals of the three OHSS groups were 0.71–1.41 μg/mL (mild group), 1.65–2.26 μg/mL (moderate group), and 2.24–3.62 μg/mL (severe group). The cross-interval between the different groups of OHSS symptoms was minimal. When OHSS symptoms improved or healed based on the patient's clinical manifestations and laboratory parameters, the D-dimer levels of patients with moderate and severe symptoms remained significantly higher than the normal range ($P<0.05$). The D-dimer levels in the improved stage in moderate and severe groups were significantly higher than those in the early stage ($P<0.05$).
- Conclusions: According to elevated D-dimer levels, we can more accurately predict the severity of OHSS in the early stage. Additionally, with further increases in D-dimer levels along with symptoms, we can more precisely determine the prognosis of patients.