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Information on Ovarian stimulation

Patient leaflet

based on the ESHRE guideline on Ovarian stimulation

Version 2025

www.eshre.eu

Introduction

This booklet is for you if you are:

- Initiating or considering ovarian stimulation for IVF/ICSI
- Initiating or considering ovarian stimulation for egg freezing

This booklet is intended for patients but may also be useful for their family members and caregivers.

This booklet aims to

- Provide information on what ovarian stimulation is
- Provide information on most frequently asked questions about ovarian stimulation.

Content

This booklet and the information presented are entirely-based on the evidence-based Guideline on Ovarian stimulation. All the information and recommendations in the guideline are built upon the best available evidence from research. Where there is insufficient evidence from research, a group of experts has formulated recommendations based on their clinical expertise. The experts also formulated areas of research to improve knowledge about best practice in ovarian stimulation.

More information is available in the last pages of this booklet, including a list of medical and research terms and their meanings. The full guideline is available on the website of ESHRE (www.eshre.eu/guidelines).

What is Ovarian stimulation?

Why is IVF/ICSI done?

IVF or ICSI treatment may be recommended if:

- Sperm quality is very low
- The fallopian tubes are blocked
- Ovulation does not happen regularly
- Or no clear reason is found (sometimes age plays a role)

IVF/ICSI treatment has **four main steps**:

1. Stimulating the ovaries to produce several eggs
2. Egg retrieval
3. Fertilising the eggs in the laboratory
4. Transferring an embryo into the uterus

The ESHRE guideline on Ovarian stimulation is focussed on the first step: stimulating the ovaries to produce several eggs.

Why are the ovaries stimulated?

In a natural cycle, usually **only one egg** matures, which is released from the ovary during ovulation.

In IVF, we aim to collect **several eggs** because:

- Not every egg fertilises
- Not every fertilised egg becomes a good embryo
- Having more eggs increases the overall chance of success

How are the ovaries stimulated?

Ovarian stimulation for IVF or ICSI is usually a 4-step process

1. Preparing the ovaries

Before stimulating the ovaries, doctors often use medication (like injections or nasal sprays) to temporarily "quiet down" your natural hormone signals. This is what doctors call "pituitary suppression". There are different medications to achieve this, often referred to as "protocols", such as long protocol, short protocol, antagonist protocol,...

This step makes sure your doctor has more control over when your eggs mature, so they can collect them at just the right time.

2. Stimulating the ovaries

To stimulate the ovaries, you take daily injections of a hormone called **FSH (follicle stimulating hormone)** for about 1-2 weeks. This encourages several follicles (tiny sacs that hold eggs in your ovary) to grow at the same time.

3. Final egg maturation

When the follicles are large enough (about 18–20 mm), you receive one final hormone injection, also known as the **"trigger" injection**. This helps the eggs finish maturing so that they are ready to be collected. Eggs that are not matured are not suitable for fertilisation and development into embryos.

4. Egg retrieval

Before the matured eggs can be released spontaneously by your ovaries (ovulation), the eggs are collected during a short procedure called an egg retrieval (or pick-up). The eggs are then fertilized in the lab with sperm to create embryos, which can later be transferred into your uterus.

Why must spontaneous ovulation be prevented during stimulation?

Your body could release the eggs too early. If that happens, the eggs are lost.

Frequently asked questions (FAQ)

How should I prepare before starting stimulation?

1. Have your ovarian reserve tested

Before starting, your doctor will usually check your ovarian reserve. There are two reliable tests:

- **AMH (Anti-Müllerian Hormone)**— a blood test
- **AFC (Antral Follicle Count)**— an ultrasound count of small follicles in your ovaries

Ovarian reserve tests help the doctor to estimate:

- How strongly your ovaries may respond to the hormone (FSH) stimulation
- Your risk of a low or high response to the hormone (FSH) stimulation
- What would be a safe starting dose of hormones (FSH) for you

In case of a low response, meaning three or fewer follicles (tiny sacs that hold eggs in your ovary) or eggs, the chances of success may be lower (especially if your age is over 35 years)—because not every egg will necessarily fertilize or turn into an embryo. On the other hand, if there are more than 18 follicles or eggs, there is a risk of a serious side effect called ovarian hyperstimulation syndrome (OHSS). It's helpful to know ahead of time if you're likely to have a low or high number of eggs. That way, your doctor can adjust your hormone dose to get the best possible result, and you'll have a better idea of what result to expect from the treatment.

Important:
These tests **do not predict pregnancy**. They only predict egg numbers.

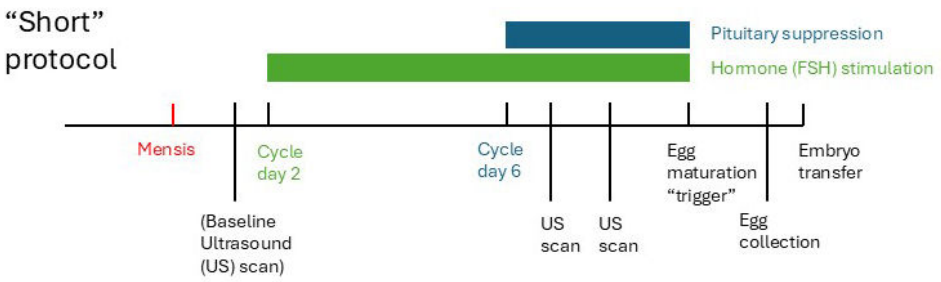
2. Understand your treatment protocol

As explained above, the ovarian stimulation process consists of different parts. Yet these parts take place in the same period of op approximately two weeks. Your treatment protocol will most likely contain a medication to temporarily "quiet down" your natural hormone signals (pituitary suppression) in combination with hormone medication (follicle stimulating hormone or FSH) to encourage the growth of several follicles at the same time.

For pituitary suppression, several medications are available, also referred to as "protocols". Most patients today receive the **GnRH antagonist ("short") protocol**, because it:

- Is safer because there is a lower risk of ovarian hyperstimulation syndrome (OHSS)
- Gives similar pregnancy chances compared to older protocols.

Here you can see a picture of the SHORT Protocol:



There are also different FSH medications available, all containing FSH, often in combination with luteinizing hormone (LH).

You can ask your doctors:

- Which protocol am I using?
- Why is it suitable for me?
- When do I start each medication?

3. Follow your medication plan carefully

You will usually take:

- Daily FSH injections
- A medication for pituitary suppression
- One trigger injection before egg collection

Tips:

✓ Set daily reminders
✓ Ask for a clear written calendar
✓ Practice injections if needed

How does the doctor choose my dose for the hormone stimulation?

The goal is balance:

- Not too few eggs
- Not too many eggs
- Keep the treatment safe

The usual target is about **8–15 eggs**.

Your starting dose depends on:

- AMH or AFC
- Age

- Body weight (BMI)
- Previous response (if you had IVF before)

Important:
Higher doses of hormones (FSH) do **not** improve egg quality, and pushing the dose too high does not increase success, but instead will produce many eggs that are not fit to become a baby.

Which test is better: AMH or AFC?

Before starting, your doctor will usually check your ovarian reserve. There are two reliable tests:

- **AMH (Anti-Müllerian Hormone)**— a blood test
- **AFC (Antral Follicle Count)**— an ultrasound count of small follicles in your ovaries

Both tests are equally good.

- You do not need both.
- There is no clear evidence that one is superior.

What is considered a low or high response?

A low or high response can refer to the result of the ovarian reserve testing by AMH or AFC (see above) before ovarian stimulation. This is the predicted ovarian response.

During ovarian stimulation, the growth of the follicles (tiny sacs that hold eggs in your ovary) is monitored by ultrasound. This is observed ovarian response.

- Low response: three or fewer follicles
- High response: more than 18 follicles

The categorisation of a low or high response can also be made based on the results in a previous IVF cycle.

- Low response: three or fewer eggs
- High response: more than 18 eggs

A low response, meaning three or fewer follicles (tiny sacs that hold eggs in your ovary) or eggs, the chances of success may be lower (especially if your age is over 35 years)—because not every egg will necessarily fertilize or turn into an embryo. On the other hand, if there are more than 18 follicles or eggs, there is a risk of a serious side effect called ovarian hyperstimulation syndrome (OHSS).

Sometimes it can happen that the growth of the follicles during ovarian stimulation is not in line with the predicted ovarian response. This is often called an unexpected low or high response to ovarian stimulation.

A high response increases the risk of OHSS but does not improve success rates.

What is my real chance of pregnancy?

This is one of the most important questions.

AMH and AFC predict egg numbers — **not pregnancy**.

The most important factor influencing chances of pregnancy and a healthy baby is your age.

Age mainly determines egg quality. Medication cannot reverse age-related changes.

Egg number helps — but only up to a point.

- Very low numbers may reduce overall chances, especially if your age is over 35 years.
- Around 8–15 eggs is often optimal.
- Very high numbers do not further increase live birth chances, and brings risks of the OHSS

Other factors also matter:

- How embryos develop (which cannot be predicted beforehand)
- IVF Laboratory quality
- Whether fresh and frozen transfers are included

Doctors should give realistic ranges — not exact guarantees.

Why do I sometimes need to take a contraceptive pill before stimulation?

Pretreatment with a contraceptive pill may be used to:

- Synchronise follicle growth
- Help schedule the cycle for practical reasons

This does **not** increase pregnancy chances. It mainly helps with timing.

What is the difference between the long and short protocol?

To prevent spontaneous ovulation, you receive additional medication to temporarily block the natural LH surge (the hormone that causes ovulation). This is usually done using:

- A **GnRH antagonist protocol** (most common today)
- Or a **GnRH agonist protocol** (older "long protocol")

There is also a newer approach using progesterone tablets (PPOS). With this method, all embryos must be frozen and transferred later. This is why the PPOS protocol is only recommended in cases where freezing of all eggs or embryos was already planned, such as in case of an expected high response to ovarian stimulation or egg freezing for fertility preservation.

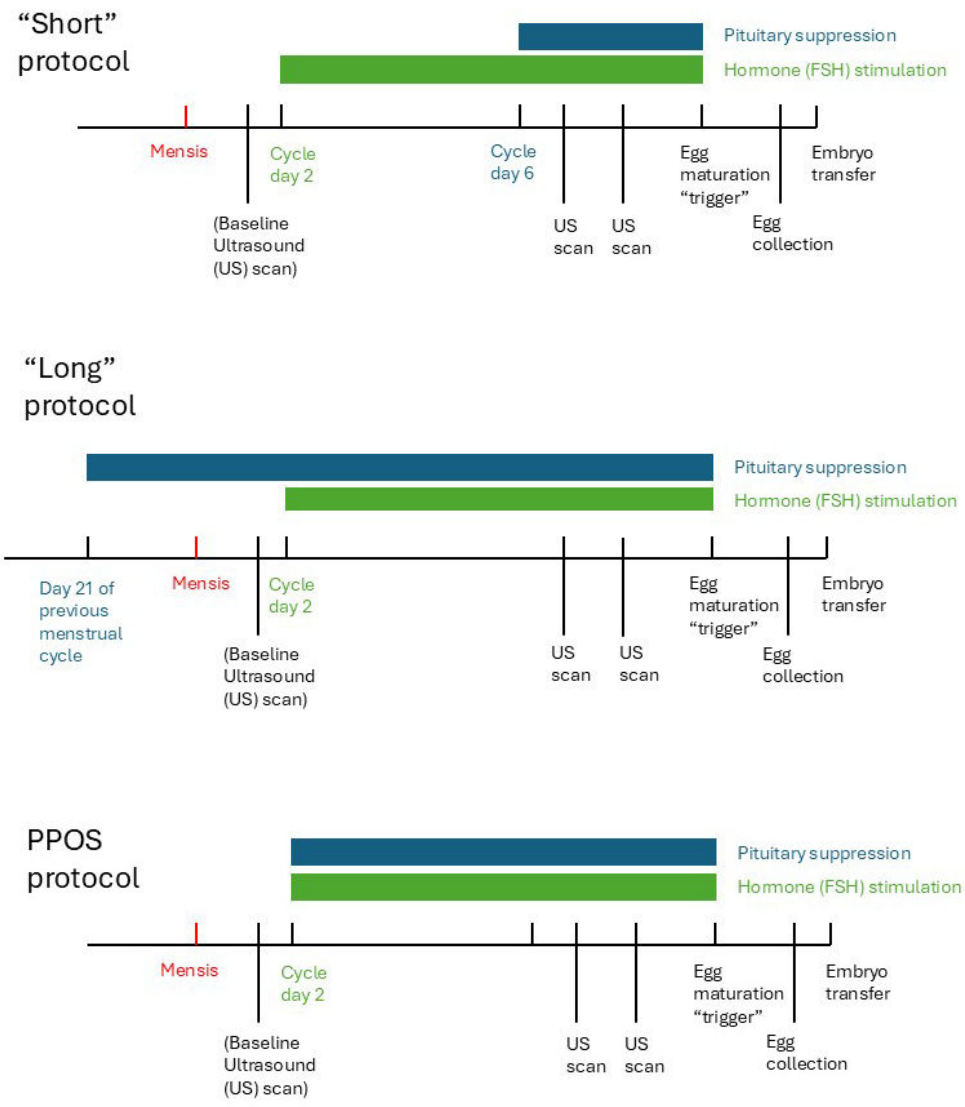
Long protocol (GnRH agonist)

- Older method
- Slightly higher OHSS risk
- Not first choice today

Short protocol (GnRH antagonist)

- Most commonly used
- Lower OHSS risk
- Same pregnancy chance

As an illustration, this is a schematic overview of the protocols:



Which FSH medication is best?

There are also different FSH medications available, all containing FSH, often in combination with luteinizing hormone (LH).

- Recombinant FSH (rFSH): contains only FSH
- Highly purified FSH: contains negligible amount of LH
- Purified FSH: contains <5% LH
- Human Menopausal Hormone: contains 50% LH like activity (hCG is often added)

All of these FSH preparations have been shown to be equally effective. There is no single "best" FSH drug.

Adding LH to recombinant FSH does not improve outcomes.

Your doctor will choose based on your specific situation.

Why do I need ultrasounds? Do I need blood tests?

It is important to monitor the growth of the follicles during the stimulation, therefore you will have:

- Always 2–3 ultrasound scans within the two week period of the stimulation
- Sometimes blood tests

Blood tests are mainly used:

- To assess OHSS risk (estradiol)
- To check progesterone on trigger day to decide on aiming for a fresh embryo transfer

In many cases, ultrasound monitoring is sufficient.

Are IVF "add-ons" useful?

According to the ESHRE guideline, most add-on treatments during stimulation are **not recommended**, because there is no strong, convincing evidence that they improve live birth rates.

Examples of add-ons that are NOT recommended:

- Metformin
- Growth hormone
- Testosterone
- DHEA
- Aspirin
- Sildenafil

Add-ons can increase cost and complexity without proven benefit. For some of these add-ons, it is also unclear if they are safe to use during ovarian stimulation, such as growth hormone.

ESHRE has developed a separate Good practice recommendations paper on Add-ons in IVF/ICSI, which can be found here: https://www.eshre.eu/guideline/add-ons

The Council of Europe has also developed a patient booklet on Add-ons in medically assisted reproduction, which can be found here: https://www.edqm.eu/en/-/edqm-publishes-booklet-on-add-ons-in-medically-assisted-reproduction-treatments

If I am undergoing ovarian stimulation for egg freezing, how many eggs should I freeze?

There is no guaranteed number, but your age matters most.

Approximate targets used in practice:

- Under 35 years: 10–15 eggs
- 35–38 years: 15–25 eggs
- Over 38 years: 25–30 or more

These numbers increase the probability of at least one live birth — but do not guarantee it.

What is OHSS?

OHSS (Ovarian Hyperstimulation Syndrome) happens when the ovaries over-respond to the hormone (FSH) stimulation.

It can cause:

- Swollen abdomen
- Fluid buildup
- Blood clots (rare but serious)
- Breathing problems

Severe OHSS occurs in about 1–2% of IVF cycles.

Modern prevention includes:

- Individualised dosing of the hormone (FSH) stimulation
- Using the “short” protocol, because it gives the option to create an endogenous LH peak using the so-called Agonist trigger for the final maturation of the eggs, instead of the standardly used hCG.
- Freezing all eggs or embryos
- Medication after the egg retrieval

With these strategies, most severe OHSS cases can be prevented.

Will my cycle be cancelled if I have a high response (to prevent OHSS)?

Cancellation completely avoids pregnancy-related worsening of OHSS, but it is usually not necessary because other preventive measures, such as freezing all the eggs, are very effective.

In rare cases of extremely high response (for example, more than 25–30 follicles), the preventative measures are not enough to avoid or reduce the risk of developing OHSS. In this instance, it is safer for you to cancel the cycle.

Will my cycle be cancelled if I have a low response?

When ovarian reserve tests have predicted that you might have a low response to ovarian stimulation, or you experienced a low response in a previous IVF cycle, observing a low response in your current IVF cycle is not a valid reason to cancel the cycle.

If your ovarian reserve test predicted a normal or even high response, and you experience a low response during the ovarian stimulation, your doctor may propose to cancel the cycle.

Final Key Message

The goal of ovarian stimulation is:

Safe, balanced, and individualised treatment — not "as many eggs as possible."

Age remains the strongest factor influencing pregnancy chances.

Your treatment plan should be tailored to you, with realistic expectations and safety as top priorities.

Where can I find more information or support?

More detailed information on each of the topics in this booklet can be found in the clinicians' edition of the guideline on the ESHRE website (www.eshre.eu/guidelines).

For more detailed information or support, you can contact your doctor or a patient organisation.

For contact details of national patient organisations for infertility, you can ask your doctor, or contact **Fertility Europe** (www.fertilityeurope.eu)

About this booklet

This booklet aims to involve patients in healthcare improvement by informing them about current standards of care, and by enabling them to make informed decisions on their health, supported by the best available evidence.

How this booklet was developed

This booklet was written by Prof. Dr. Broekmans and revised by Nathalie Le Clef (methodological expert). All the information provided is based on the recommendations in the ESHRE guideline on Ovarian stimulation.

Who developed the ESHRE guideline?

The ESHRE guideline on Ovarian stimulation, was developed by a multidisciplinary guideline development group including fertility specialists, an andrologist, a nurse/midwife, a patient representative and a research specialist.

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Glossary (explanation of medical or research terms)

FSH: Follicle stimulating hormone. Follicle-stimulating hormone (FSH) is a hormone your pituitary gland makes and releases that plays a role in sexual development and reproduction. It affects the function of ovaries. FSH stimulates follicles on the ovary to grow and prepare the eggs for ovulation.

Follicle: tiny sacs that hold eggs in your ovary

Intracytoplasmic sperm injection (ICSI): a more specialised form of IVF, where one sperm is injected into the egg.

In vitro fertilization (IVF): a technique by which eggs are collected from a woman and fertilised with a man's sperm outside the body. Usually, one embryo is transferred into the womb, in exceptional circumstances two embryos can be transferred. If an embryo implants successfully, it results in a pregnancy.

LH: Luteinising hormone. This hormone is also produced by the pituitary gland, and works alongside of FSH. In the first several days of your cycle, LH helps grow your ovarian follicles. A surge in LH causes your ovary to release an egg around the second week of each menstrual cycle.

Ultrasound: High frequency sound waves used to provide images of the body, tissues and internal organs.

Disclaimer

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This booklet is in no way intended to replace, dictate or fully define evaluation and treatment by a qualified physician. It is intended solely as an aid for patients seeking general information on issues in reproductive medicine.

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