

What is primary ovarian insufficiency?

Primary ovarian insufficiency (POI) is the medical condition in which the ovaries stop working normally in girls and women before age 40 years. In the past, this condition has also been called *premature ovarian failure*. In these patients, the ovaries stop producing eggs every month and do not produce normal amounts of the usual female hormones (estrogen and progesterone).

What causes primary ovarian insufficiency?

There are many different causes of POI among adolescent girls. These include:

- Genetic or chromosomal disorders: Certain changes to genes or chromosomes may prevent the ovary from forming or functioning normally, which can lead to POI. Some genetic causes are passed down from parent to child and others are not.
- Autoimmune disorders: Autoimmune disorders occur when the body's immune system, which helps to fight infections, becomes confused. In this situation, the infection-fighting cells damage the cells of specific organs in the body. The damage to the cells of a specific organ results in the body making *antibodies* to that organ in your body. These antibodies indicate which organs have been damaged. POI occurs if the immune system targets the ovary.
- Exposure to certain drugs or therapies: POI can occur following chemotherapy, radiation therapy, or certain surgeries.

Sometimes no underlying cause can be found, which is called *idiopathic primary ovarian insufficiency*.

What are the signs and symptoms of primary ovarian insufficiency?

The most common symptom of POI is irregular or absent menstrual cycles (periods). Most commonly, menstrual cycles occur less often and then stop altogether; this is called *secondary amenorrhea*. For some patients, periods never start; this is called *primary amenorrhea*. In younger patients, puberty may never start, or puberty may start but stop progressing normally. Other possible signs and symptoms include mood changes, hot flashes, and/or vaginal dryness.

How is primary ovarian insufficiency diagnosed?

The endocrinologist will review growth and pubertal development, ask about any symptoms your child may be experiencing, ask about family history of fertility, and perform a physical exam including a pubertal assessment. He or she will order blood tests to measure estrogen as well as the pituitary hormones, luteinizing hormone (LH) and follicle stimulating hormone (FSH). Girls with POI will have high levels of LH and FSH and low estrogen. This is because the pituitary gland is trying to push the ovary to make estrogen, but the ovary is not able to respond normally. *Anti-Mullerian hormone* (AMH) is another hormone made in the ovary that may be measured; AMH is typically low in POI. Your endocrinologist may also check blood tests to look for other problems that can cause irregular menstrual cycles, affect pubertal progression, or check for other auto-immune disorders.

What other testing may be done after primary ovarian insufficiency is diagnosed?

Once the diagnosis of POI is made, often your endocrinologist will order more tests to try to find out the underlying cause. These may include genetic tests and testing to see if the body is making antibodies against the ovary. Imaging studies, such as a pelvic ultrasound, may also be helpful. Some causes of POI are associated with additional health concerns such as auto-immune thyroid dysfunction or short stature. Your child's doctor may assess for these other health concerns. If there is a known reason for POI, such as a history of receiving chemotherapy, then additional testing may not be needed.

How is primary ovarian insufficiency treated?

POI is treated by replacing the hormones usually made by the ovaries, estrogen and progesterone. These hormones come in different forms including a pill ("birth control pill") or a patch. Your child's endocrinologist will talk to you about which form may be best for your child. Most girls will receive hormone replacement until they reach an age when natural menopause would occur, typically around age 50 years. In girls who have not finished puberty, the hormone replacement is specialized to allow puberty to progress and finish.

Why is it important to treat primary ovarian insufficiency?

Hormone replacement therapy is important for the development of the breasts and uterus. Untreated girls with POI have a high risk to develop osteoporosis (brittle bones) and bone fractures. There may also be an increased risk of heart disease in girls with POI. In addition to hormone replacement, your child's doctor will encourage healthy eating and exercise habits to help reduce these risks further. Hormone replacement will not help the ovaries recover normal function and does not treat the underlying cause of POI.

How does primary ovarian insufficiency affect child-bearing?

Because girls and women with POI are not releasing eggs normally, they experience decreased fertility. This means that girls with POI are unlikely to be able to become pregnant or carry a pregnancy without the help of a fertility specialist. Your endocrinologist can talk to you about *fertility preservation* and if that may be an option for your child. Most girls and their parents are devastated to learn of the infertility associated with POI. Loss of fertility impacts self-esteem, gender identity, and future dreams of being a mother. Counseling with a mental health provider is encouraged.