HYPERESTROGENISM
Hyperestrogenic State, Estrogen Excess
An excessive amount of estrogenic activity in the body.

Diagnosis
♂ Male & Female

Related Diagnoses:
Endometriosis

About Hyperestrogenism

Hyperestrogenism is a medical condition characterized by an excessive amount of estrogenic activity in the body. Estrogen excess may cause hyperplasia (excessive growth) or transformation of endometriosis (abnormal growth of inner uterine layer outside the uterus) into cancer.

Hyperestrogenism can arise from:
- endogenous causes such as ovarian tumors, genetic conditions such as aromatase excess syndrome (also known as familial hyperestrogenism)
- exogenous causes such as overconsumption of exogenous sources of estrogen, including medications used in hormone replacement therapy and hormonal contraception

Liver cirrhosis is another cause, though through lowered metabolism of estrogen, not oversecretion or overconsumption like the aforementioned.

Aromatase excess syndrome (AES or AEXS), also sometimes referred to as familial hyperestrogenism or familial gynecomastia (enlargement of male breast), is a rare genetic and endocrine syndrome which is characterized by an overexpression of aromatase, the enzyme responsible for the biosynthesis (production by a living organism) of the estrogen sex hormones from the androgens, in turn resulting in excessive levels of circulating estrogens and, accordingly, symptoms of hyperestrogenism. It affects both sexes, manifesting
itself in males as marked or complete phenotypical feminization (with the exception of the genitalia; i.e., no pseudohermaphroditism) and in females as hyperfeminization (development of female sexual characteristics).

Diagnosis of hyperestrogenism is presumptive based on estrogen test. An estrogen test measures the amount of each type of estrogen (estradiol, estriol, and estrone) present in a blood or urine sample (Tab. 1).

An estrogen receptor test is a laboratory test to find out if cancer cells have estrogen receptors (proteins to which estrogen will bind). If the cells have estrogen receptors, they may need estrogen to grow, and this may affect how the cancer is treated.

Treatment must be individualized from case to case. It may consist of hormone medications or surgery in the case of tumour.

**Associated diseases**

- endometrial cancer
- ovary cancer
- breast cancer
- liver cirrhosis
- hyperplasia

**Complications**

If left untreated, hyperestrogenism may increase the risk of estrogen-sensitive cancers such as breast cancer later in life. Hyperestrogenism, caused either by endogenous or exogenous sources, is a significant risk factor for the development of cancer from endometriosis (abnormal growth of uterine lining).

**Risk factors**

- obesity
- hormonal contraceptives
- family history

**Impact on fertility**

**Male fertility**

Estrogen especially estradiol is necessary for creating a healthy sperm. In case of high level of estrogen, sperm levels in semen may fall.

The function of estradiol varies depending on the cells in which it is being
produced. In testicular cells, estradiol is known to regulate numerous aspects of spermatogenesis (the process in which sperms are produced). Estradiol is involved in the modulation of cell communication of Sertoli cells (cell of the testicles that is part of a seminiferous tubule and helps in the process of spermatogenesis) and in the regulation of Leydig cell (cells in testicles which are producing testosterone) function.

In the efferent ductules (connect the rete testis with the initial section of the epididymis), estradiol is involved in the reabsorption of fluids, thus, affecting sperm concentration, motility and morphology.

Any disruption in processes of sperm development or their transport to the uterus due to high levels of estrogen can lead to fertility problems. There is lower possibility of natural conception, because the sperm is no able to reach the egg inside the fallopian tube, where the fertilization occurs.

Female fertility

High levels of estrogen, may negatively impact the growing follicles, oocytes, and the endometrium, thus reducing the chances of a successful pregnancy for poor responders.

Estradiol levels in female may provide useful information for the evaluation of ovarian reserve. High levels may show poor ovarian reserve (a condition of low fertility characterized by low numbers of remaining oocytes in the ovaries). With low count of oocytes, there is lower possibility to conceive naturally.

Prevention

One way to prevent high estrogen could be to control your weight through a healthy diet and regular exercise.

Symptoms

Signs of hyperestrogenism may include heightened levels of one or more of the estrogen sex hormones (usually estradiol and/or estrone), lowered levels of follicle-stimulating hormone and/or luteinizing hormone (due to suppression of the hypothalamic–pituitary–gonadal axis by estrogen), and lowered levels of androgens such as testosterone (generally only relevant to males).

Symptoms of the condition in women may consist of menstrual irregularities,
amenorrhea, abnormal vaginal bleeding, and enlargement of the uterus and breasts. It may also present as isosexual precocity (puberty occurring at an unusually early age with appropriate sexual features) in children and as hypogonadism (diminished function of gonads), gynecomastia (enlargement of male breast), feminization (hormonally induced development of female sexual characteristics), impotence, and loss of libido in males.

**Therapies**

**Self therapy**

**Healthy lifestyle**

Balanced diet and getting regular exercise could help to lose or maintain your weight, reducing risk of hyperestrogenism.

There is some evidence that eating a diet which is very high in fat could increase the amount of estrogen, whereas going vegetarian could reduce estrogen levels. Cutting back on sources of animal fats, such as red meat and cheese, could help to manage hyperestrogenism. Meanwhile, eating soy could reduce the effects of estrogen on the body.

**Conventional medicine**

Treatment of hyperestrogenism may consist of surgery in the case of tumors, lower doses of estrogen in the case of exogenously (externally)-mediated estrogen excess, and estrogen-suppressing medications like gonadotropin-releasing hormone (GnRH) analogues and progestogens. In addition, androgens may be supplemented in the case of males.

**Pharmacotherapy**

**Aromatase inhibitors, antiestrogens**

Aromatase inhibitors and antagonadotropins reduce the production of estrogen, while the term "antiestrogen" is often reserved for agents reducing the response to estrogen.

Aromatase is the enzyme that synthesizes (produces) estrogen. As breast and ovarian cancers require estrogen to grow, aromatase inhibitors are
taken to either block the production of estrogen or block the action of estrogen on receptors.

Antiestrogens prevent estrogens like estradiol from mediating their biological effects in the body. They act by blocking the estrogen receptor and/or inhibiting or suppressing estrogen production. Antiestrogens are one of three types of sex hormone antagonists, the others being antiandrogens and antiprogestogens.

**Surgical therapy**

**Removal of the hormone-active tumor**

The surgical indication is recommended for ovarian tumors and in some situations of ovarian cystic lesions.

**Assisted reproduction**

If infertility persists after the treatment, assisted reproductive technologies (ART) give an option. Assisted reproductive technology is the technology used to achieve pregnancy in procedures such as fertility medication, artificial insemination, in vitro fertilization (IVF) and surrogacy. It is reproductive technology used primarily for infertility treatments, and is also known as fertility treatment.

Since high estrogen levels may be the cause of poor ovarian reserve, the fertility should be impaired. Treating patients with poor ovarian response remains one of the biggest challenges in reproductive medicine because it is accompanied with the reduction in quantity and quality of oocytes in women of reproductive age. It is usually a problem of advanced reproductive age patients; however previous ovarian surgery, pelvic infections, and environmental factors or genetic factors may be associated with it in younger patients as well.

One of the fundamental steps to reach the success is still related to the number of eggs obtained after hormonal stimulation by gonadotropins in combination with GnRH analogues. In patients defined “poor responders,” the limited number of obtained eggs remains the main problem in optimizing the live birth rates. In fact, as a result of a lower number of oocytes retrieved, there are fewer embryos to select and transfer and subsequently these patients have lower pregnancy rates per transfer and lower cumulative pregnancy rates per started cycle compared with normal responders.

Different strategies are applicable for poor responder involving oocyte
cryopreservation (preservation by freezing). Some authors have recently suggested obtaining a large cohort of oocytes in these patients by accumulating vitrified oocytes over several stimulation cycles creating a similar situation as in normal responder patients. According to the results presented in the study, it could be possible to obtain higher live birth rate per patient treated and potentially to reduce the dropout. Moreover, oocyte cryopreservation can also be used to preserve the fertility of all those women at risk to lose their ovarian potential over the time.

Infertility induced by surgery to remove tumor in reproductive system may be overcome by treatments involving assisted reproductive technologies, such as intrauterine insemination (IUI) or IVF. If assisted reproductive treatments involving IVF are needed thereafter, the ovaries are often difficult to access for ovum pickup. Ovarian stimulation in connection with subsequent cryopreservation of oocytes or embryos before cancer treatment is thus indicated in such cases. However, even if ovarian function is preserved, or oocytes or embryos have been cryopreserved, irradiation of the uterus may cause irreversible damage. Although cases of good obstetric outcome have been reported after fertility preservation among women with a heavily irradiated uterus, unsuccessful results should be expected and in many cases surrogacy will be necessary.

Find more about related issues

**Diagnoses**

**Endometriosis**
A state in which pieces of the tissue alike to the lining of the uterus (endometrium) grow in other parts of the body.
Learn more at: [www.fertilitypedia.org/therapy/diag/endometriosis](http://www.fertilitypedia.org/therapy/diag/endometriosis)

**Risk factors**

**High level of estrogen**
A medical condition characterized by an excessive amount of estrogenic activity in the body.
Learn more at: [www.fertilitypedia.org/therapy/rf/high-level-of-estrogen](http://www.fertilitypedia.org/therapy/rf/high-level-of-estrogen)

**Low level of FSH**
A condition with low serum follicle–stimulating hormone (FSH) concentration.
Learn more at: [www.fertilitypedia.org/therapy/rf/low-level-of-fsh](http://www.fertilitypedia.org/therapy/rf/low-level-of-fsh)
**Low level of testosterone**
An abnormally low testosterone production which may occur because of testicular or hypothalamic-pituitary dysfunction.
Learn more at: [www.fertilitypedia.org/therapy/rf/low-level-of-testosterone](http://www.fertilitypedia.org/therapy/rf/low-level-of-testosterone)

### Therapies

**Egg donation**
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: [www.fertilitypedia.org/edu/therapies/egg-donation](http://www.fertilitypedia.org/edu/therapies/egg-donation)

**ICSI**
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: [www.fertilitypedia.org/edu/therapies/icsi](http://www.fertilitypedia.org/edu/therapies/icsi)

**Sperm donation**
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: [www.fertilitypedia.org/edu/therapies/sperm-donation](http://www.fertilitypedia.org/edu/therapies/sperm-donation)

**Standard IVF**
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used.
Learn more at: [www.fertilitypedia.org/edu/therapies/standard-ivf](http://www.fertilitypedia.org/edu/therapies/standard-ivf)

### Gallery

**Tab**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>Reference range</th>
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<tbody>
<tr>
<td>Female</td>
<td>20 - 29</td>
<td>149 pg/mL</td>
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<td>30 - 39</td>
<td>210 pg/mL</td>
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<tr>
<td></td>
<td>&gt; 40</td>
<td>152 pg/mL</td>
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<tr>
<td>Low estrogen</td>
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<tr>
<td>High estrogen</td>
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</tr>
<tr>
<td>Male</td>
<td>-</td>
<td>15 – 60 pg/mL</td>
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Sources


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“Assisted reproductive technology (https://fertilitypedia.org/edu/therapies/assisted-reproductive-technology)” —sourced from Fertilitypedia licensed under CC BY-SA 4.0


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