

Hyperestrogenism

(Estrogen Toxicity)

Basics

OVERVIEW

- “Hyperestrogenism” refers to a condition in which excessive estrogen is present in the body
- A syndrome characterized by high serum concentration of estrogens (estradiol, estriol, or estrone)
- Estrogens are hormones that are produced by the female (ovary, placenta), male (testicles), by both sexes (adrenal glands), and by some plants; most commonly recognized as a female sex hormone that is responsible for normal sexual behavior and development and function of the female reproductive tract; in the male, estrogens are responsible for Leydig cell function, which produce testosterone
- Hyperestrogenism may occur as a result of excessive estrogen secretion in the body or administration of estrogen-containing medications, such as diethylstilbestrol or estriol

SIGNALMENT/DESCRIPTION OF PET

Species

- Dogs

Mean Age and Range

- Older female dogs (secondary to tumors of the ovaries; follicular ovarian cysts, in which the area containing the egg [known as the “follicle”] in the ovary develops, but ovulation does not occur normally)
- Young female dogs (secondary to follicular ovarian cysts)
- Older male dogs (secondary to tumors of the testicles)
- If from exposure to estrogenic medications, all ages, breeds, genders; toy breed exposure to owner transdermal hormone replacement therapy patches

SIGNS/OBSERVED CHANGES IN THE PET

- Attractive to intact male dogs (intact male dogs are capable of reproducing)
- Infertility
- Prolonged heat (specifically proestrus and estrus) in females
- Decreased libido in males
- Impulse to engage in sexual behavior (known as “nymphomania”)
- Bleeding from the vulva (the external genitalia of females) and enlargement of the vulva; excessive licking of the vulva
- Blood in the urine (known as “hematuria”), in association with benign prostatic enlargement (known as “benign prostatic hyperplasia” or “BPH”) or low platelet count (known as “thrombocytopenia”) that may result from effect of estrogen on bone marrow; “platelets” and “thrombocytes” are names for the normal cell fragments that



originate in the bone marrow and travel in the blood as it circulates through the body; platelets act to “plug” tears in the blood vessels and to stop bleeding

- Skin—non-itchy, symmetrical hair loss (known as “endocrine alopecia”); “stud dog tail”; darkened skin (known as “hyperpigmentation”)
- Reproductive abnormalities in females—fluid buildup of the vulva (the external genitalia of females); enlargement of the vulva; discharge from the vulva; enlargement or development of the mammary glands (known as “gynecomastia”)
- Reproductive abnormalities in males—tumor or mass in the testicles; difference in size of the testicles; decrease in size of the testicles (known as “testicular atrophy”); enlarged prostate; excessive development of the male mammary glands (known as “gynecomastia”)
- Pale gums and other moist tissues of the body (known as “mucous membranes”)
- Small, pinpoint areas of bleeding (known as “petechia”)
- Fever (due to secondary bacterial infection in association with low white-blood cell counts [known as “neutropenia”] that may result from effect of estrogen on bone marrow)
- Depression

CAUSES AND RISK FACTORS

- Follicular ovarian cysts, in which the area containing the egg (known as the “follicle”) in the ovary develops, but ovulation does not occur normally
- Tumors of the ovaries
- Tumors of the testicles (specifically Sertoli cell tumor, but also may occur secondary to Leydig and interstitial cell tumors)
- Administration of estrogen-containing medications or exposure to estrogen-containing medications
- Small dogs (for example, toy-breed dogs) are at increased risk of exposure to transdermal hormone replacement therapy being used by their owners; these patches often are applied to the forearm of the person and the small dog is exposed as a consequence of being held frequently

Treatment

HEALTH CARE

- Discontinue administration of estrogen-containing medications, if applicable
- Avoid exposure to estrogen-containing medication (such as transdermal hormone replacement therapy), if applicable

SURGERY

- Treatment of choice for excessive levels of estrogen (hyperestrogenism) in the intact female and male is surgical neutering; perform a “spay” or “ovariohysterectomy” for females and perform a “neuter” or “castration” for males
- Surgical removal of only one ovary containing a tumor for females or one testicle containing a tumor for males may be considered in valuable breeding dogs; effects of prolonged high levels of estrogen on the uterus or remaining testicle may decrease fertility even if the abnormal gland has been removed, making prognosis for fertility guarded

Medications

Medications presented in this section are intended to provide general information about possible treatment. The treatment for a particular condition may evolve as medical advances are made; therefore, the medications should not be considered as all inclusive

- Administration of antibiotics and blood products, as needed for the individual pet
- Medications (such as synthetic erythropoietin, darbopoietin, granulocyte stimulating factor) may be considered to stimulate production of red-blood cells and/or white-blood cells in the bone marrow; lithium reportedly has been of benefit in cases of estrogen-induced lack of production of blood cells (known as “bone-marrow aplasia”)
- Gonadotropin-releasing hormone (hormone that causes release of luteinizing hormone from the pituitary gland; “luteinizing hormone” is a female hormone that stimulates the ovarian follicle to develop and rupture to allow release of the egg and to produce progesterone)—unlikely to induce ovulation in cases of follicular ovarian cysts

Follow-Up Care

PATIENT MONITORING

- Repeat serial complete blood count (CBC) analyses—to evaluate response to therapy and progression of disease if bone marrow cell production
- Repeat serial bone-marrow evaluations may be done—to evaluate bone-marrow response including production of red-blood cells, white-blood cells, and platelets; signs of regeneration of blood cells may not occur for weeks to months
- Iron supplementation may be done to support regeneration of red cells
- If using red cell stimulating drugs such as darbopoietin, red and white cell regeneration will be closely monitored
- Clinical signs of male feminization syndrome should resolve within 2–6 weeks after surgical removal of a tumor of the testicles

POSSIBLE COMPLICATIONS

- Decreased production of blood cells by the bone marrow (known as “bone-marrow hypoplasia”) or lack of production of blood cells (known as “bone-marrow aplasia”)
- Death

EXPECTED COURSE AND PROGNOSIS

- Lack of resolving low blood-cell counts and continued lack of response of the bone-marrow 3 weeks after surgical removal of ovarian or testicular tumors or removal of follicular ovarian cysts (in which the area containing the egg [known as the “follicle”] in the ovary develops, but ovulation does not occur normally)—associated with a grave prognosis

Key Points

- Excessive levels of estrogen in the body (hyperestrogenism) may cause several conditions, many of which are serious or even potentially life-threatening
- Complications include decreased production of blood cells by the bone marrow (bone-marrow hypoplasia) and lack of production of blood cells (bone-marrow aplasia)