

ESTROGENS PLAY A HIDDEN ROLE IN TUMORIGENESIS

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Abstract: *A balanced quantity of estrogenic compounds is very essential for healthy living for man and woman, The normal level of estrogen in females varies by age and physiological state, such as age, gender, and health history. Estrogen levels fluctuate throughout life of a woman, and it's normal for them to rise and fall. For example, levels rise during puberty and ovulation, and dip during menstruation. Lately, in addition to its involvement in reproductive organs, estrogen regulates non reproductive tissues too. So far reports appeared deals with estradiol causing cancers in reproductive organs only but indications are there other organs too if not direct involvement, estrogens are involved indirectly in prostate, lung and colorectal cancers.*

Keywords: Estrogens, Hormonal imbalance,

INTRODUCTION

Estrogenic compounds are very essential for our body functions. There are various sources of these compounds: Nature produced phytoestrogens, environment has xenoestrogen, scientists have synthesized estrogenic molecules in the laboratory and ovary synthesizes true estrogens from cholesterol what we eat in our diet [1]. Estrogens which are produced by the ovaries are one group of the most essential sex steroid hormones; they are responsible for the proliferation, development and regulation of the female reproductive system [2-4]. Phytoestrogen are very useful for mankind [1], where as environmental estrogenic molecules [5,6] played havoc in human life. Most of the synthetic estrogenic hormones are used in pharma and cosmetic industries [7,8].

Complex relationship between estrogen and microbiota: Because of low levels of estrogens, the post-menopausal women suffer a diverse range of clinical disorders in the brain, gut, and the female reproductive tract. Estrogens are one of the principal regulators of microbiota. In the recent years the role of microbiota in estrogen-modulated diseases was studied extensively [9]. The gut microbiota regulates estrogens through secretion of β -glucuronidase, an enzyme that deconjugates estrogens into their active forms.

Microbes and estrogens: A healthy vagina has certain bacteria and other microbes [10]. Usually, there are many different kinds of microbes, and they all live in balance in the body. This hormonal imbalance affects the balance of microbes in the vagina [11].

This is called vaginal atrophy (Fig. 1)

The loss of estrogen around menopause changes the quality and quantity of microbes in vagina, leaving more bad bacteria than good. Because of this the vagina is inflamed. It might be swollen, itchy, or sore. It might even smell strange or make an unusual discharge. If the vulva is also affected, it is called vulvovaginitis. When this happens, one microbe can grow too much, or an unwelcome microbe can take hold and cause an infection. This can lead to vaginitis low estrogen levels cause. It usually happens after menopause or surgical removal of the ovaries.

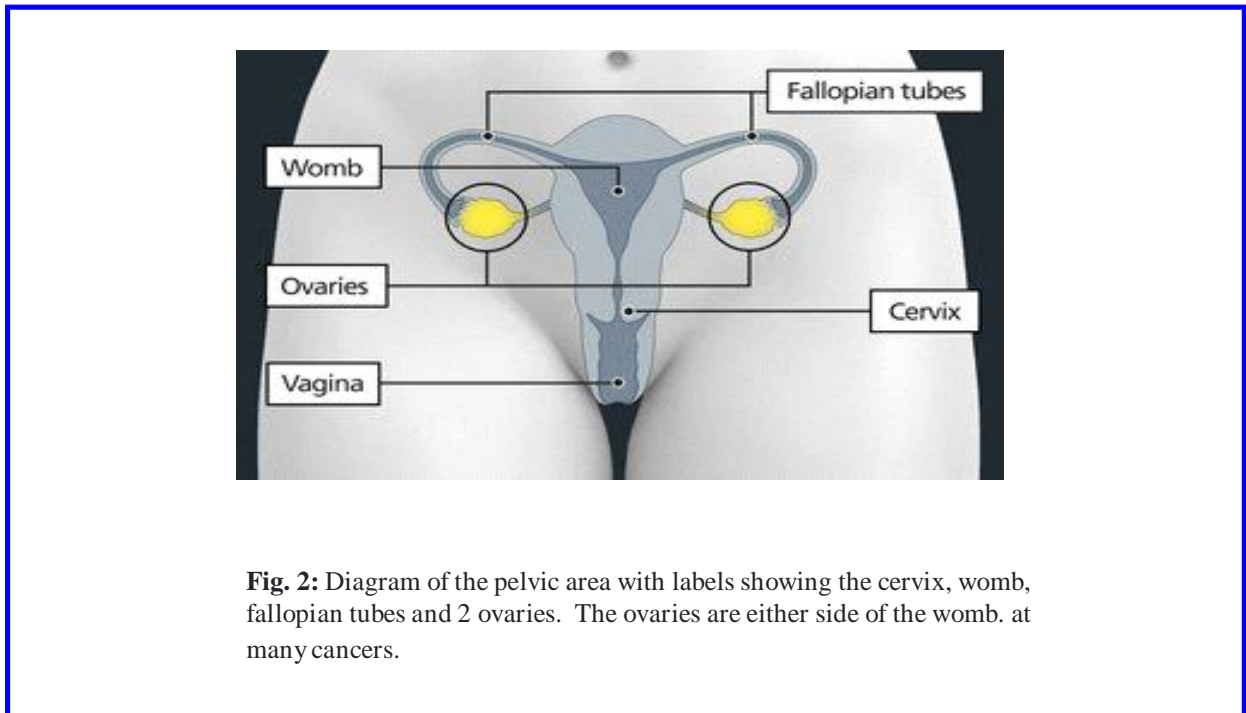
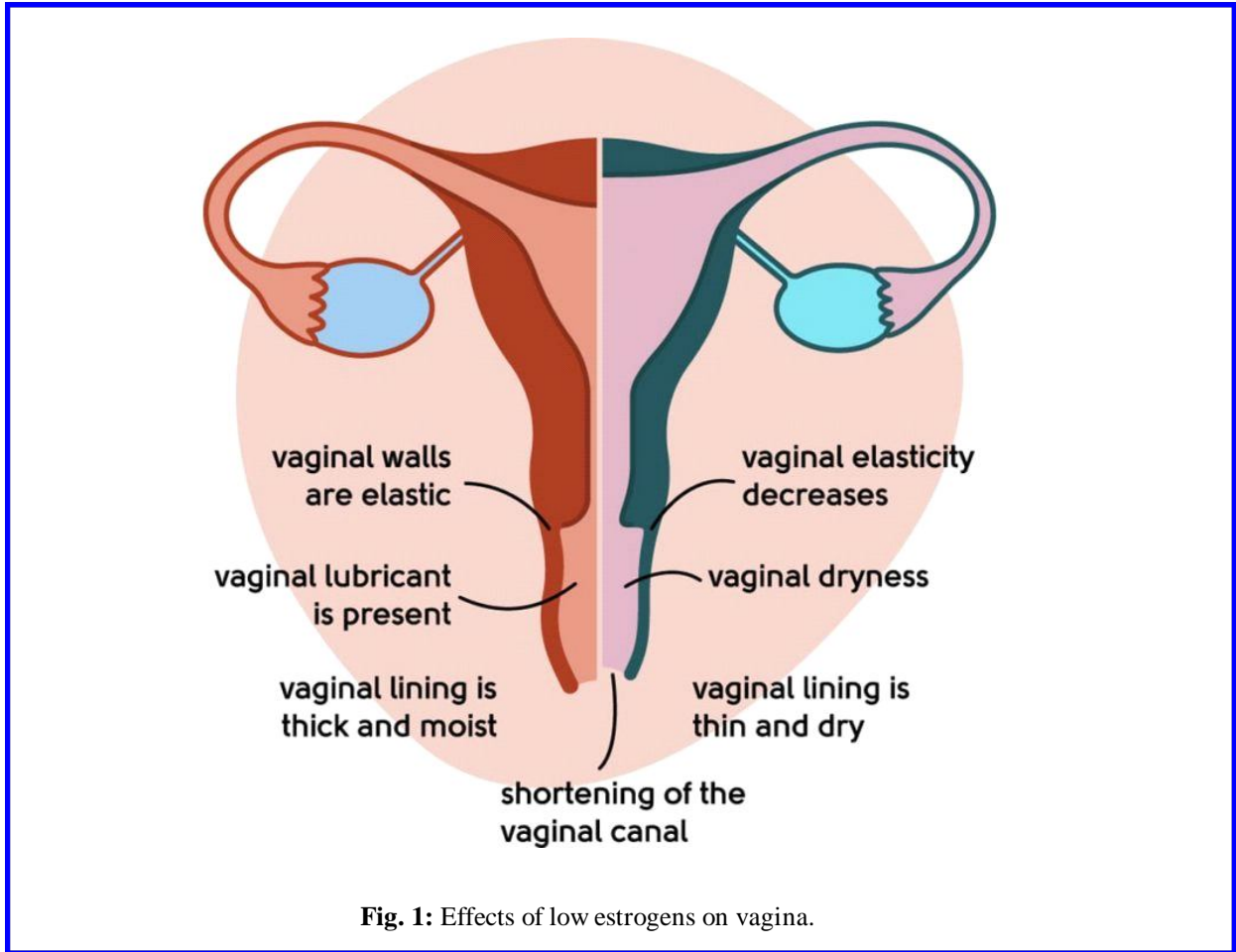
Pregnancy induces several immunological, hormonal, and metabolic changes necessary for the normal development of the foetus and for the timely onset of labour and successful delivery. The rise in estrogens and progesterone during pregnancy alters gut function and microbiota composition, increasing vulnerability to pathogens. The gut microbiota progressively changes with each trimester of pregnancy; the composition is most commonly dominated by Firmicutes as in obese populations. The concept of embryonic development in a sterile uterus has been challenged and now the existence of microbiota of the placenta, amniotic fluid, and the foetal gut is considered in normal, uncomplicated pregnancies. The maternal microbiota is recognized as a key determinant of a range of important maternal and child health outcomes, and together with perinatal factors influences the infant microbiota.

Hormonal imbalances: Throughout our life hormone levels changes in phase manner, there may be dramatic changes and fluctuations in hormones during puberty, pregnancy and menopause in woman's life. Hormonal imbalances occur when there is too much or too little of a hormone in the blood. Hormonal imbalance can affect many body functions. Low hormones levels, especially estrogen can cause thinning, drying, and inflammation of vaginal walls. Many factors can trigger a hormone imbalance, some of them are due to normal physiological processes such as, puberty, pregnancy, and menopause; some of them may be due to pathological as chronic stress, autoimmune

conditions and others may be due to medical conditions, such as, certain steroids medications, endocrine gland injury caused by radiation therapy, infection, trauma, excessive blood loss or damage from surgery. However, there are several other reasons why our hormone levels may be irregular at unexpected at times. Some of the most common causes of fluctuating or imbalanced hormone levels include: stress, depression, certain medications and use of steroid. A hormonal imbalance means the body has too little or too much of one or more hormones. A hormonal imbalance can be temporary or chronic, depending on the cause [12,13]. A hormonal imbalance may require medical treatment, especially if the symptoms affect the health and quality of life. Hormonal imbalances can lead to medical conditions like: diabetes, thyroid disease, obesity, acne, infertility, irregular periods, polycystic ovary syndrome, amenorrhea including cancers including tumours, growths or adenomas (noncancerous tumours on the pituitary, parathyroid or adrenal glands) [14].

Pathology of estrogen action: Action of estrogen ranging from regulation of the menstrual cycle and reproduction to modulation of bone density, brain function, and cholesterol mobilization [1,15]. Estrogen plays a role in causing certain cancers especially in those organs which carry estrogen receptors for example breast, ovary and uterus, vagina [16-18]. lately it was reported that not only reproductive tissues but organs such as liver [20] brain and even eye lens epithelium cells [21] have these receptors. Despite the normal and beneficial physiological actions of endogenous estrogen in women, abnormally high estrogen levels are associated with the increased incidence of certain types of cancer [22], especially those of the breast and endometrium. Direct Estrogen-dependent cancers include breast cancer, ovarian cancer and uterine cancer [23]. However, indirectly it also influences prostate, lung and colorectal cancers.

Breast cancer: Estrogens are known to be human carcinogens. In certain conditions Estrogen increase breast cancer risk for example: postmenopausal women are most likely to develop breast cancer, and about 70% of breast cancers are sensitive to



estrogen. high systemic estrogens and a high ratio of circulating estrogen metabolites and parent estrogen are considered as strong risk factors for post menopausal ER+ breast cancer [19]. In postmenopausal women, it has been proved that reduction of the ratio of estrogen metabolites to parental compounds and the reduction of fecal microbiota diversity are associated with an increased risk of breast cancer. This means that estrogen receptors are present on the outside of the cancer cells, allowing the cells to use estrogen as fuel to grow. However, Duke cancer institute researchers unexpectedly finds that estrogens play a role in fuelling the growth of breast cancers without the receptors, as well as numerous other cancers. Appearing Sept. 27 in the journal Science Advances, 2024 the researchers describe how estrogens not only decrease the ability of the immune system to attack tumors, but also reduce the effectiveness of immunotherapies.

Ovarian cancer: Anyone with ovaries can get ovarian cancer, however, cases are reported that even after ovaries removed one can have ovarian cancer. This is because ovarian cancer can also affect fallopian tubes, or the peritoneum. The dysfunctions of estrogen levels and abnormal estrogen synthesis and metabolism may lead to ovarian cancer, and a higher level of circulating E2 causes a higher risk of ovarian cancer. It is also, besides other factors, regulated by estrogens. If a woman started periods at a young age or went through the menopause late (over 55), or have not had a baby will be prone to ovarian cancer—because these things also regulated.

Uterine cancer: It's most common in women who've been through menopause. Most uterine cancer begins in the layer of cells that form the lining (endometrium) of the uterus. Risk factors are related to again related to estrogen such as overweight, starting periods at an early age, and delaying menopause. Uterine cancer is a disease that occurs when cells in the uterus grow out of control. The two main types of uterine cancer are:

* Endometrial cancer: The most common type, which develops in the lining of the uterus.

* Uterine sarcoma: A rarer type, which develops in the muscles or support tissue of the uterus.

Endometriosis: Endometriosis (EMS) is a frequent estrogen-driven disease among women at reproductive age, which is a kind of endometriotic lesions (i.e, endometrial glands and stroma) outside the uterus. Mechanisms of EMS, such as estrogen metabolism, immune inflammation and tumour characteristics, etc. The hyper-estrogen has been implicated as an essential causative factor in EMS [24,25].

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