Chapter

Introductory Chapter: Estrogen – Sex Steroid Hormone in Ovary and beyond

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1. Introduction

1.1 Non-reproductive health effects of sex steroid hormones

Estrogens are members of the estrane family of sex steroid hormones essential to reproductive and ovarian function. Estranes are derived from cholesterol (specifically low-density lipoprotein) and undergo a series of enzymatic modifications to reduce the number of carbons contained in the molecule from 27 (cholestanes) to 18 (estranes) [1]. The movement of cholesterol from the mitochondrial outer membrane of the cell to the inner membrane is the rate-limiting step for steroidogenesis and estrogen production.

Estrone, estradiol, estriol, and estetrol are all estrogens in the estrane family and vary according to molecular structure and biological activity. Estrone (E1) has only one hydroxyl group and is mainly produced by peripheral aromatization from androgens. Of the estranes, estrone is predominant in postmenopausal women. In terms of bioactivity, estrone is a weak estrane. Estradiol (E2) has two hydroxyl groups and is the main estrane found in reproductive age persons with ovaries. Estradiol is also produced by the testes, liver, adrenal glands, breasts, and placenta. Estradiol has high bioactivity and rapidly declines with ovarian aging and menopause. Estriol (E3) has three hydroxyl groups and is the main estrane of pregnancy. Estriol is derived from androstendione, estrone, and estradiol. Although estriol has a lower affinity to the sex hormone binding globulin and higher bioavailability, it is a weaker estrange than estradiol [2]. With four hydroxyl groups, estetrol is produced solely through the fetal liver by 15 alpha and 16 alpha hydroxylation. Estetrol is a metabolite of estriol and estradiol and is found in serum and urine with peak levels at the end of pregnancy [3].

For reproductive function, estradiol is mediated through the hypothalamic–pituitary-gonadal axis. Gonadotropin-releasing hormone is released in a pulsatile fashion from the hypothalamus to stimulate follicle-stimulating hormone (FSH) from the anterior pituitary. FSH then stimulates gonads for folliculogenesis in the ovary and spermatic production in the testes.

Estrogen action is mediated through estrogen receptor signaling. Estrogen action can occur through genomic effect (estrogen receptor complex binding to DNA promoter) and non-genomic effect (no direct binding of estrogen receptor complex to DNA) [4]. Various signaling pathways are involved with the G-protein estrogen receptor including nuclear factor-kappa B, hippo, mitogen-activated protein kinase,

phosphatidylinositol 3-kinase, and extracellular regulated kinase. These pathways are involved in many disease processes outside of the reproductive tract.

Estrogens – Recent Advances provides an in-depth look at the role of estrogen and the multiple organ systems it affects. As most are familiar with the role of estrogen in the ovary and uterus, this book moves beyond these organs to explore estrogen's effect on cancers, prostate, oral mucosa, and olfactory mucosa to provide an excellent review of the sex steroid hormone. By understanding the extensive role of estrogen in multiple organ systems, we may uncover novel management and treatment options for individuals in the future.

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