

Reproductive

Estrone

Analyte Information



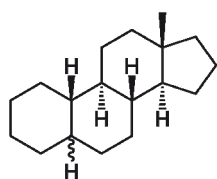


Estrone

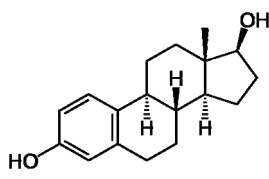
Introduction

Estrone (E1) is one of the three major naturally-occurring estrogens. It is the aromatized C₁₈-steroid with a 3-hydroxyl group and a 17-ketone. Its chemical name is 3-hydroxy-1,3,5 (10)-estratrien-17-one, its summary formula is C₁₈H₂₂O₂ and its molecular weight (Mr) is 270.4 Da. As with the other estrogens, it is a derivative of the hydrocarbon estrane with an aromatic ring and an 18-carbon molecule. The structural formulas of estrone and the two other principal estrogens — estradiol (E2) and estriol (E3) — are shown in Fig.1.

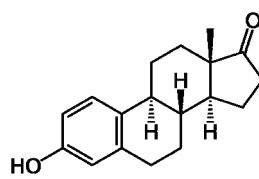
Fig.1: Structural formulas of estrane and its derivatives estrone, estradiol and estriol.



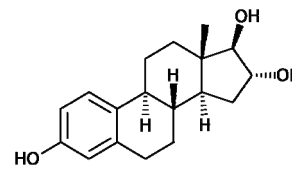
Estrane



Estradiol



Estrone



Estriol

There are also several other names for this compound, including: oestrone, 1,3,5(10)-estratrien-3-ol-17-one, and folliculin.

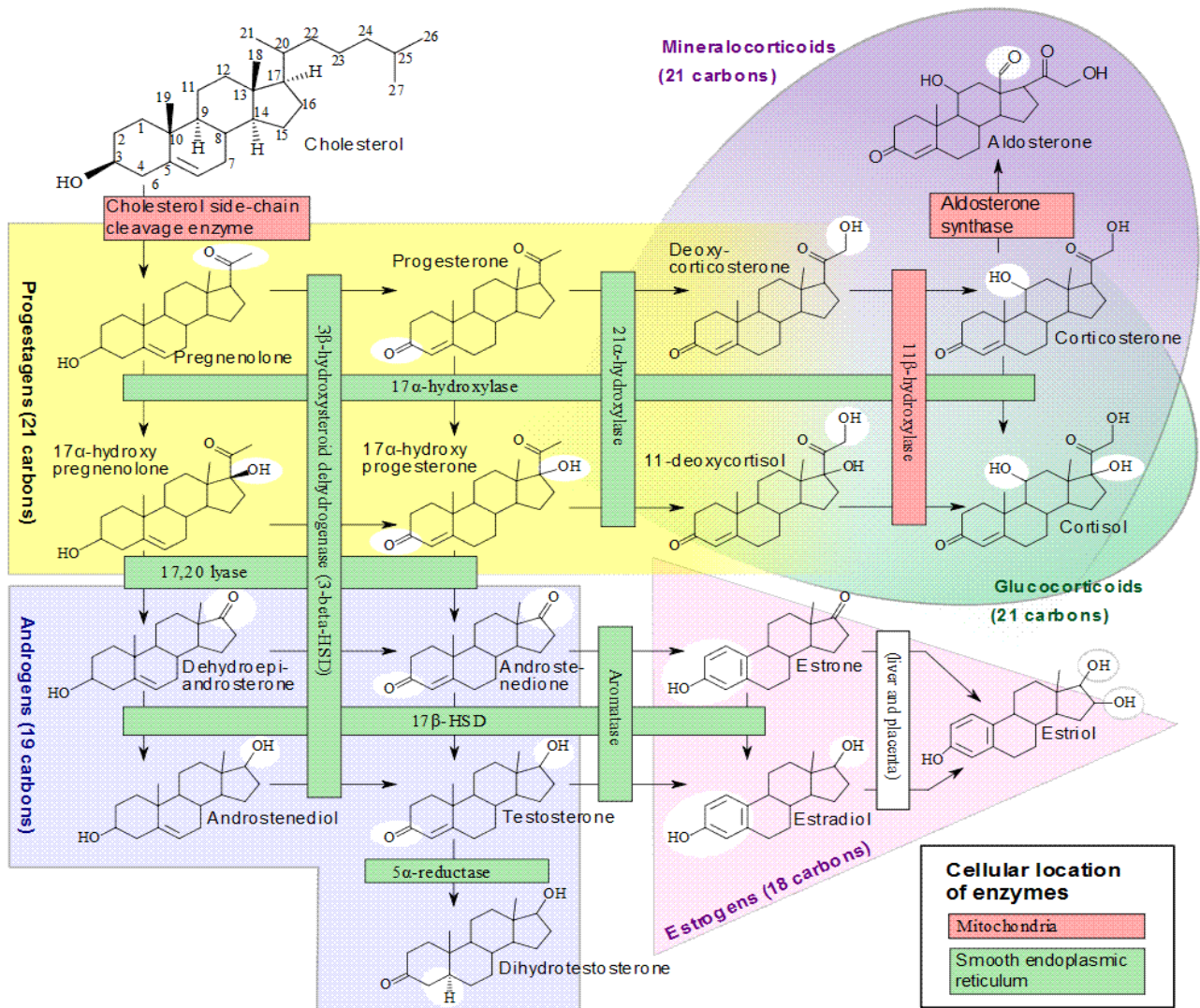
Biosynthesis

Estrone is produced primarily from androstenedione, which originates in either the adrenal cortex or the gonads^{1,2}. Its production differs during the follicular and luteal phases of the menstrual cycle.

Estrone may also be derived via reversible conversion of estradiol or estrone sulphate (estrone-3 sulfate)⁶. Estrone sulphate itself is not biologically active, but may serve as a circulating reservoir for the formation of estrone and estradiol in various tissues.



Fig.2: Steroidogenesis



In ovulating women, the estrone precursor androstenedione is secreted by both the adrenal glands and the ovaries. Ovarian theca cells secrete androstenedione, which is converted to estrone and then estradiol by granulosa cells. Thus, ovaries produce large amounts of estradiol and small amounts of estrone.



Most estrone originates from peripheral conversion of estradiol and from the aromatisation of androstenedione. This conversion takes place mainly in adipose tissue. Overall estrone production is lower than that of estradiol.

In prepubertal children, men and postmenopausal women, the major portion of estrone is derived from peripheral tissue conversion of androstenedione.

During pregnancy, large amounts of estrone are synthesized in the placenta from dehydroepiandrosterone sulfate (DHEA-S), which originates in both maternal circulation and the fetal adrenal gland.

Metabolism

Estrone may undergo reversible conversion to estradiol or estrone sulfate.

In addition, it may be converted to various conjugates via sulfonation, glucuronidation and O-methylation. The main site of degradation is the liver, but these reactions also take place in estrogen target tissues such as those of the breast, ovary and uterus. Several enzymes are employed, including various cytochrome P-450 enzymes, catechol-O-methyltransferases (COMT), sulfonylesterases, and UDP-glucuronosyltransferases (UGTs).

Thus estrone may be metabolized to estrone-3 sulphate or estrone-17 glucuronide, or processed via the 2-, 4- or 16 α -hydroxylation pathways to form 2-hydroxyestrone, 4-hydroxyestrone or 16 α -hydroxyestrone.

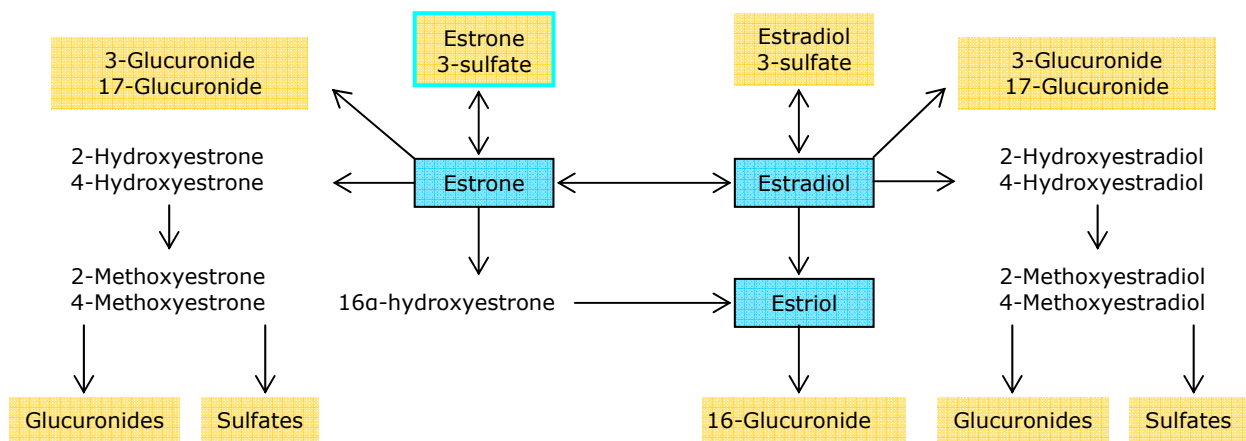
2-Hydroxyestrone and 4-hydroxyestrone are then methylated to 2-methoxyestrone and 4-methoxyestrone, and are finally glucuronidated.

16 α -hydroxyestrone undergoes a similar degradation process, but may also be metabolized into estriol.

In conjugated form, estrogens are water-soluble and do not bind to transport proteins. Therefore the conjugated forms are readily excreted in bile, feces and urine. The glucuronide conjugates are excreted in urine more rapidly than are the sulfates.



Fig.3: Metabolism of estrone and other estrogens



Physiological Function

Estrogens are responsible for the development and maintenance of the female sex organs and female secondary sex characteristics. In conjunction with progesterone, they also participate in the regulation of the menstrual cycle, breast and uterine growth, and in the maintenance of pregnancy.

They are also important to many other, non-gender-specific processes, including growth, nervous system maturation, bone metabolism and remodeling, and endothelial responsiveness. The two major biologically active estrogens in nonpregnant humans are estrone (E1) and estradiol (E2).

A third bioactive estrogen, estriol (E3), is the main pregnancy estrogen, but plays no significant role in nonpregnant women or men.

Estrone is only 20-80% as potent as estradiol. However, its potency varies in different tissues of the body (e.g., brain, bone and endometrium).

In ovulating women, concentrations of estradiol are higher than those of estrone, further contributing to the former's predominance as the most bioactive estrogen.



Ovarian production of estradiol ceases in menopause, allowing estrone synthesized from adrenal androgens to become the most important estrogen in circulation. Among other functions, the estrogenic effects of estrone in postmenopausal women help to maintain bone mineral content.

Estrogens and other hormones are given to postmenopausal women in order to prevent osteoporosis, as well as to treat symptoms of menopause such as hot flashes, vaginal dryness, urinary stress, incontinence, chilly sensations, dizziness, fatigue, irritability and sweating. Unfortunately, it has been found that hormone intake during hormone replacement therapy (HRT) is connected with an increased risk of breast cancer, heart attacks and strokes.

The current recommendations for postmenopausal female hormone replacement are to administer therapy in the smallest possible effective doses for as briefly as possible. Ideally, E2 and E1 levels are held below or near the lower limit of the premenopausal female reference range.

Levels

In ovulating women, blood estrone concentration patterns mirror those of estradiol throughout the menstrual cycle, but at one-third to one-half of the amount⁴. During the follicular phase of the menstrual cycle, estrone exhibits a slight increase. Subsequently, production of estrone (as well as other estrogens) rises dramatically, peaking around day 12. This peak is of short duration, and levels fall by day 16. A second peak occurs around day 22; in the absence of fertilization, production then decreases again.

Estrone levels increase at significantly during pregnancy.

Although follicular function (and hence estradiol production) declines during menopause, estrone continues to be produced from androstenedione of adrenal origin. Thus, estrone becomes the predominant estrogen in postmenopausal women.

Estrone levels follow a diurnal rhythm in both men and non-pregnant women. In blood, estrone is bound primarily to albumin, rather than to SHBG.

Typical estrone levels⁷ of pubertal and adult males and females are given in table 1.

For each assay, the relevant reference values are shown in the appropriate Instructions for Use (IFU).



Tab.1: Typical estrone levels

Specimen (serum)	Reference interval (pg/mL)
Children (1 – 10 years):	<15
Puberty Tanner stage:	
Stage I	
male:	5 – 17
female:	4 – 29
Stage II	
male:	10 – 25
female:	10 – 33
Stage III	
male:	15 – 25
female:	15 – 43
Stage IV	
male:	15 – 45
female:	16 – 77
Stage V	
male:	20 – 45
female:	29 – 105
Adults male:	15 – 65
Adults female	
Early follicular phase:	15 – 150
Late follicular phase:	100 - 250
Luteal phase:	15 - 200
Postmenopausal:	15 – 55


Equation for the conversion of units : 1 ng/mL x 3,700 = pmol/L




Diagnostic utility – prospects and possibilities

Serum estrone level is a useful indicator in estrogen status assessment. Altered estrone levels may be found in a broad spectrum of clinical states, including:

Elevated estrone levels

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- PCOS (polycystic ovary syndrome)
 - androgen-producing tumors
 - estrogen-producing tumors
 - obesity with increased tissue production of E1
 - liver diseases
 - testicular feminization
 - precocious puberty
 - hyperthyroidism

Decreased estrone levels

- 
- primary ovarian failure
 - Turner syndrome
 - hypopituitarism
 - hypogonadism



Diagnostic utility – practical applications

Monitoring of female hormone replacement therapy in postmenopausal women

Estrone is measured together with estradiol in order to establish and monitor dosing.

Diagnosis of precocious puberty

The GnRH stimulation test is the “golden standard.” Estrone is used as a supplementary determination,

Diagnosis of delayed puberty

Estrone is measured together with LH/FSH and estradiol.

Diagnosis of suspected sex steroid metabolism disorders, e.g. aromatase deficiency

Estrone is measured together with other steroids.

Fracture risk assessment of postmenopausal women, and, to a lesser degree, older men

Supplementary test to clinical assessment, imaging studies, bone mineral density measurement and bone marker determination

Monitoring antiestrogen therapy with aromatase inhibitor

Estrone is measured together with estradiol.

Diagnosis of gynecomastia in adults

Estrone is measured together with estradiol, testosterone and adrenal androgens. Causes of this condition may include:

- Androgen-producing tumors, with secondary elevation of estrone due to aromatization
- High androgen levels caused by androgen intake, with secondary elevation due to aromatization
- Obesity with increased tissue production of estrone
- Decreased clearance in liver disease

Irregular or absent menstruation with normal or increased estradiol

Estrone is measured together with estradiol, testosterone, DHEA-S, androstenedione, SHBG and AMH. Causes of this condition may include:

- PCOS
- Androgen-producing tumors
- Estrogen-producing tumors



References

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