

Gonadal Steroidogenic Pathway

Hormone Synthesis & Cortisol Steal

Cholesterol

1. LDL (mostly)
2. HDL from dietary sources, and/or
3. de novo fatty-acid synthesis via acetyl CoA (normal adrenal synthesis w/o LDL receptor, e.g. in familial hypercholesterolemia)

★ **StAR-mediated uptake of cholesterol**
StAR expression is stimulated by LH binding its receptor in Leydig cells (testis) and theca cells (ovaries)

Stimulated by LH in theca cells

P450_{scc}

Pregnenolone

3β-HSD

Progesterone

P450_{aldo}

Deoxycorticosterone

18-O-Corticosterone

Aldosterone

170H-Pregnenolone

3β-HSD

170H-Progesterone

21-Hydroxylase

11-Deoxycortisol

11β-Hydroxylase

Cortisol

Natural Process: In states of stress, the body shunts pregnenolone down the pathway to become **cortisol**.

✗ **Pregnenolone Steal / Cortisol Steal:** When chronic stress persists, resources are continuously pulled away from the pathways that produce the hormones **testosterone**, **estrogen** and **aldosterone**.



Occurs in Adrenal Glands

DHEA-S

SULT2A1

- Stimulates**
1. Stimulates androgen secretion;
 2. serum levels reflect DHEA levels if SULT2A1 is active;
 3. occurs in zona reticularis

DHEA

3β-HSD major pathway

Androstenedione

Occurs in Gonads

17β-HSD stimulated by FSH in granulosa cells

Testosterone

5α-reductase

Dihydrotestosterone

Estrone

17β-HSD

Estradiol

Testosterone to Estrogen Conversion

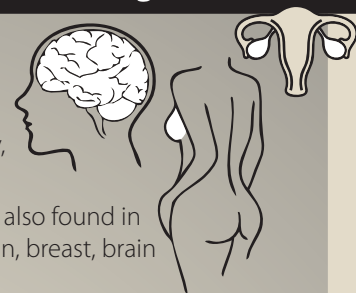
*Aromatase Activity

Conversion of androgens (theca cells) into estrogens (granulosa cells) of the ovary, is carried out by **aromatase**.

Aromatase and 17β-HSD are also found in peripheral tissues such as skin, breast, brain and blood vessels.

In males, most aromatase activity occurs in adipose tissue.

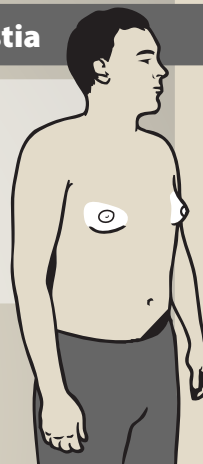
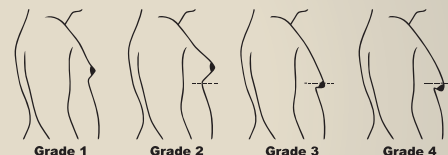
A hormone imbalance in men can lead to **Gynecomastia**.



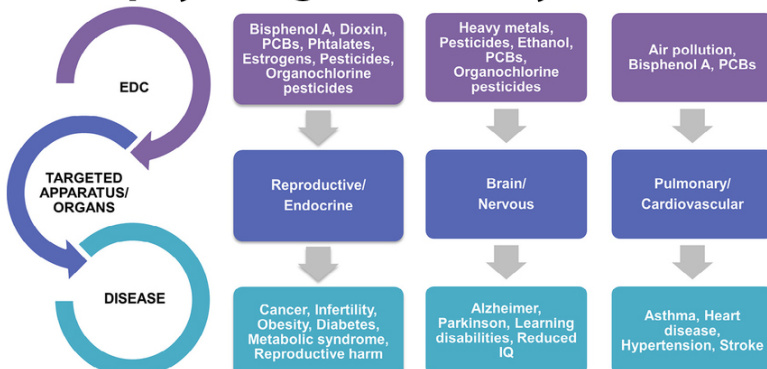
Gynecomastia

Gynecomastia is an enlargement or swelling of breast tissue in males.

It is most commonly caused by male estrogen levels that are too high, or are out of balance with testosterone levels.



Pathophysiological Pathways of EDCs



reference: www.researchgate.net/figure/List-of-the-main-pollutants-classified-as-endocrine-disruptors-and-related-effects-on_fig1_301772387

