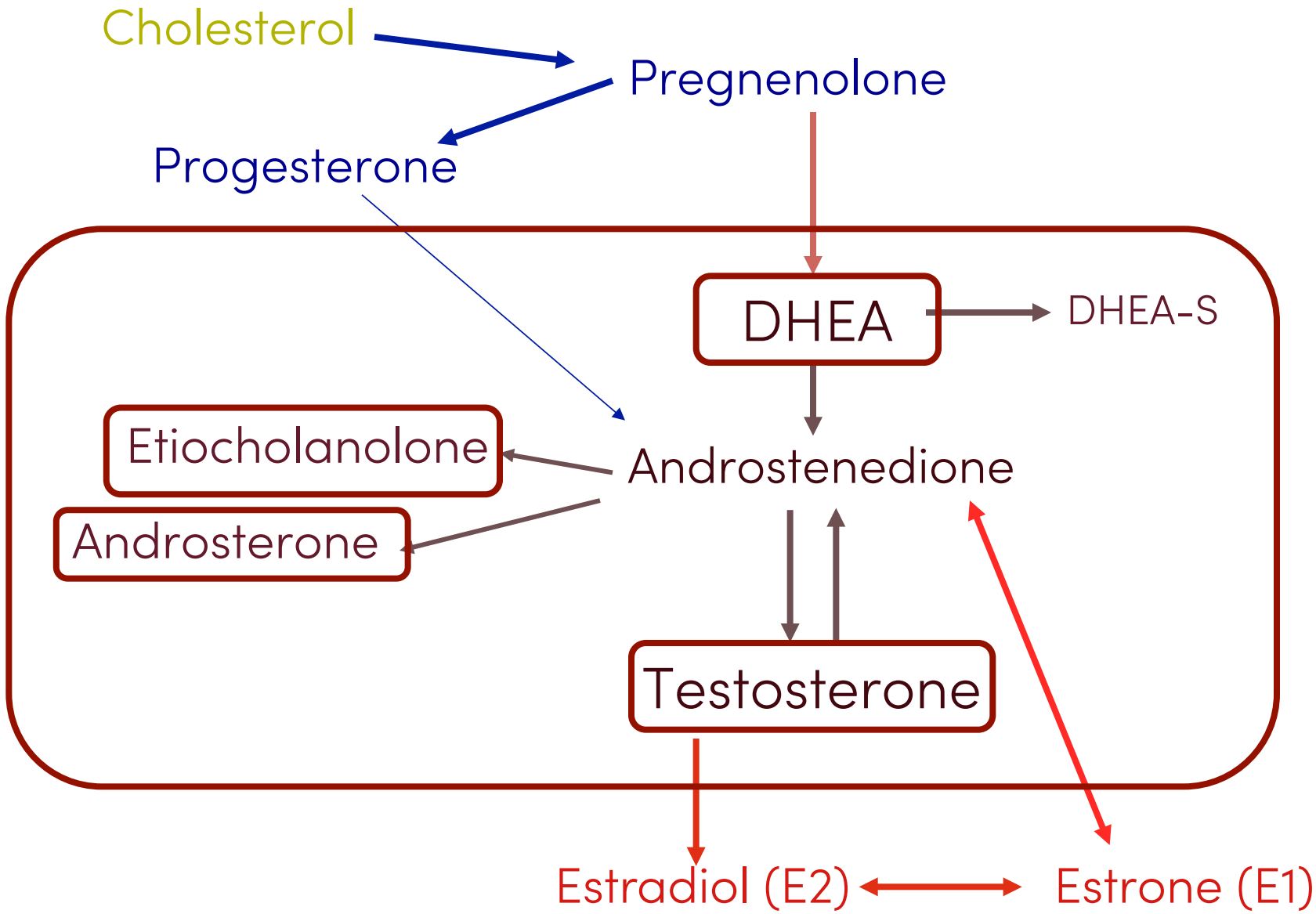
Ovarian Hormone Genesis: Androgens



Estrogens + metabolites	Estradiol (E2) Estrone (E1) Estriol (E3) 2-Hydroxyestrone 2-Methoxyestrone 16-a-Hydroxyestrone 4-Hydroxyextrone Total Potent Estrogens: E2 + E1 Estrogen Ratio: E3/(E2 + E1) 2OH/16aOH Estrone ratio	
Progesterone	Pregnanediol (PD)	
Androgens + metabolites	DHEA Testosterone Etiocholanolone (ET) Androsterone (AN)	Focus on Androgens
Cortico-steroids + Metabolites	Cortisol Cortisone THE THF 5a-THF THE +THF + 5a-THF	

Androgens

DHEA-S (Dehydroepiandrosterone sulphate)

Major product of adrenal (zona reticularis):
3.5 to 20 mg per day!...
Serum concentrations (72 – 186 μg/dL)

DHEA (Dehydroepiandrosterone)

Produced:

- in the adrenal (zona reticularis) (50%) and
- the ovarian theca (20%)

derived from circulating DHEA-S (30%)

6 – 8 mg/day produced
with serum concentrations 0.1 – 1 μg/dL

(0.33 mg/d Estrogen, 37 mg/d progesterone)

- Also produced in the brain

DHEA

It is the most abundant of the circulating steroid hormones

It's a precursor to production of testosterone, estrogens and metabolites.

DHEA has a neuroactive effect and is one possible remedy for anxiety and depression

Principle metabolite is probably etiocholanolone

Remarkably, DHEA acts as a full agonist of ER Beta with a response similar to that of E2 (weaker than E3)

DHEA metabolism to the neurosteroid androsterone: a possible mechanism of DHEA's antidepressant action.

Abstract

BACKGROUND:

Alterations in neurosteroid secretion have been implicated in the efficacy of antidepressants. In a previous study, the adrenal androgen DHEA, a precursor of the neurosteroid androsterone, produced antidepressant and libido-enhancing effects in patients with midlife depression. To investigate the mechanisms underlying DHEA's behavioral effects in this same patient group, we examined plasma levels of four additional neurosteroids implicated in the regulation of affective behavior.

METHODS:

Blood samples were assayed for neurosteroids in men (n = 13) and women (n = 10) with midlife depression who previously participated in a crossover study in which DHEA and placebo were administered for 6 weeks each. Depression severity was measured by the Center for Epidemiologic Studies Depression Scale (CES-D). Plasma levels of androsterone (ADT), allopregnanolone, pregnanolone, and pregnenolone were measured by GC-MS at baseline and week 6 of each treatment phase. Data were analyzed with repeated measures analysis of variance (ANOVA-R) and Bonferroni t tests.

RESULTS:

ADT levels (but not allopregnanolone, pregnanolone, and pregnenolone) increased after DHEA but not after placebo ($F_{2,42} = 3.3$, $p < 0.05$). Post-DHEA ADT levels were higher in women than men [$t_{63} = 2.9$, $p < 0.05$]. However, in both men and women who met criteria for clinical response on the CES-D, baseline ADT levels significantly increased post-DHEA, and the magnitude of the ADT increase post-DHEA treatment was similar in men and women. Consequently, it was the non-responders who accounted for the sex difference in post-DHEA plasma ADT levels, a difference that was driven by values in two women (the only female non-responders).

CONCLUSIONS:

The small sample size notwithstanding, these data emphasize the potential behavioral relevance of ADT in humans, which may include contribution to the antidepressant effects of DHEA.

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DHEA metabolism to the neurosteroid androsterone: a possible mechanism of DHEA's antidepressant action.

Ben Dor R1, Marx CE, Shampine LJ, Rubinow DR, Schmidt PJ.

CONCLUSIONS:
The small sample size notwithstanding, these data emphasize the potential behavioral relevance of androsterone in humans, which may include contribution to the antidepressant effects of DHEA.

Androstenedione & Testosterone

Androstenedione

Produced in the adenal (zona fasciculata) 50% and ovarian stroma 50% (varying thru cycle)

1.4 – 6.2 mg/day, varying with menstrual cycle Serum concentrations (0.5 – 2ng/ml)

Testosterone

The most potent androgen

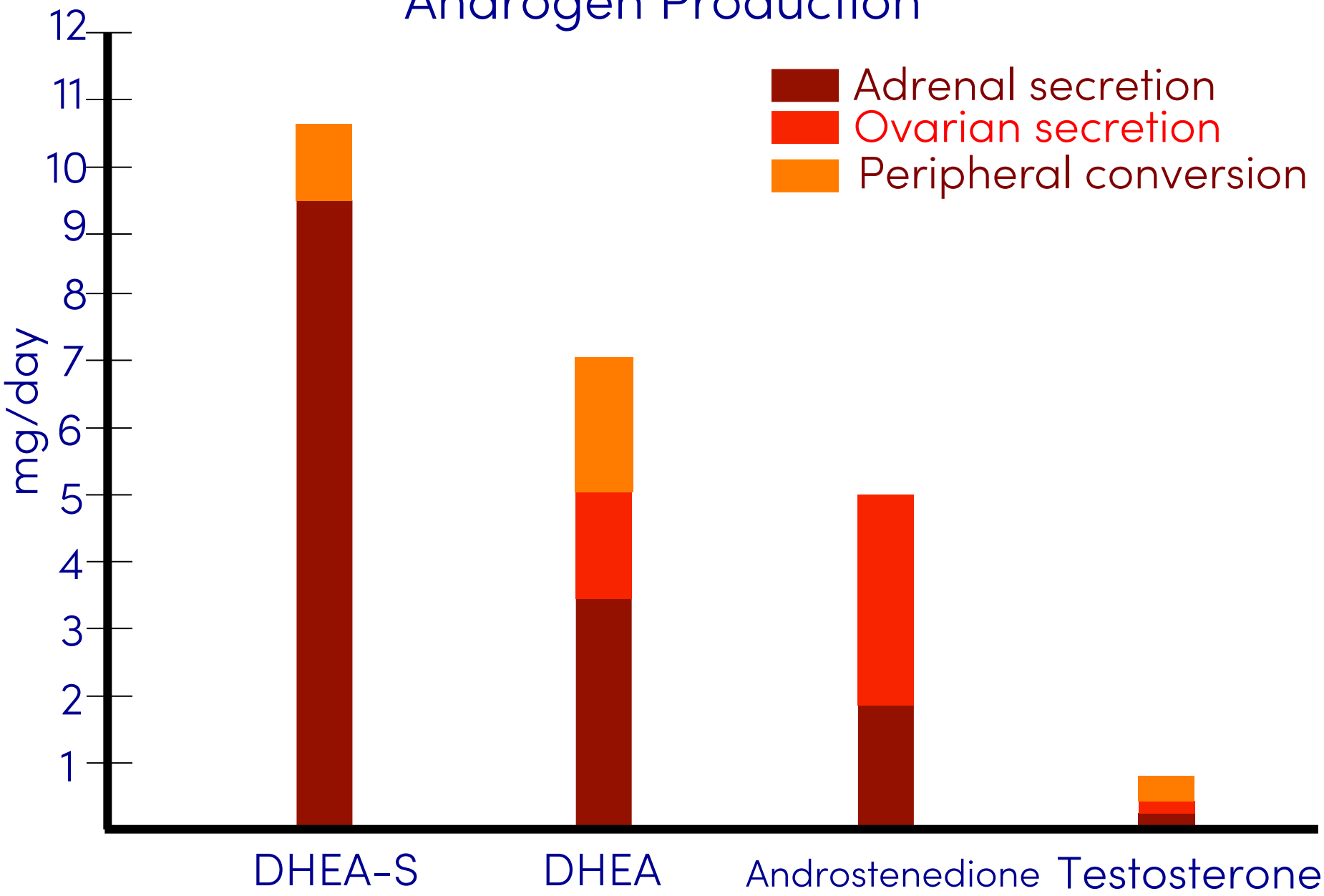
Produced:

- adenal (zona fasciculata) 25%
- ovarian stroma 25%
- from circulating androstenedione 50%
- 0.1 – 0.4 mg/day

Compare: E2 0.3 mg/d, DHEA 7 mg/d

Serum concentrations: 0.2 – 7 ng/ml, and it cycles

Androgen Production *



http://www.glowm.com/resources/glowm/cd/pages/v5/ch002/framesets/003f.html

Testosterone con't

Carried bound in the serum:

- 69%: SHBG (Sex Hormone Binding Globulin)
- 30% albumin

SHBG declines in menopause

- Thus free testosterone can increase

BCP's and oral estrogens increase SHBG

- Transdermal estrogens *do not* increase SHBG
  - … except in excessive dosages

Testosterone levels

- may not change in the beginning of menopause
- or, may already have declined by the beginning
- or may increase in the beginning of menopause!
- but definitely will decline in 1 – 5 years after onset