

## Genetic endocrinology of aging

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The endocrine system in man undergoes major changes during the aging process. Three hormonal systems show abrupt or gradual decreases in serum hormone concentrations: estrogen (in menopause), testosterone (in andropause), DHEA (in adrenopause), and GH/IGF-I (in somatopause). This decrease in hormone levels occurs in parallel with the appearance of characteristic changes in aging organs. The availability of hormone replacement of all hormones mentioned, as well as the proven clinical effectiveness of such replacement in (young) adults with selective deficiencies in these hormones, has raised hopes that the application of these hormone replacement strategies prevents or delays the aging process. However, such beneficial effects remain largely unproven, and their safety uncertain. In recent years it has become clear that the “set-point” of serum IGF-I levels, and of estrogen- and androgen receptor sensitivity is largely genetically determined commonly occurring polymorphisms in the IGF-I gene, and the estrogen- $\alpha$  and androgen-receptor determine an individual’s sensitivity to steroid hormones, and of his/her personal “normal” hormone concentration within the broad normal range. Studies will be presented, which suggest that the combination of the measurement of an individual’s serum hormone concentration, with DNA examination for polymorphisms in some endocrine receptors result in a much more “personalized” use of hormone replacement therapy, in which indication, prescribed dose, expected beneficial end-points and potential adverse effects can be better predicted.

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