WORLD ANTI-DOPING AGENCY
play true

FMSI FEDERAZIONE MEDICO SPORTIVA ITALIANA

Athlete Biological Passport Symposion
Rome, Nov. 5 – 7, 2018

Diseases / conditions affecting the steroid profile in blood

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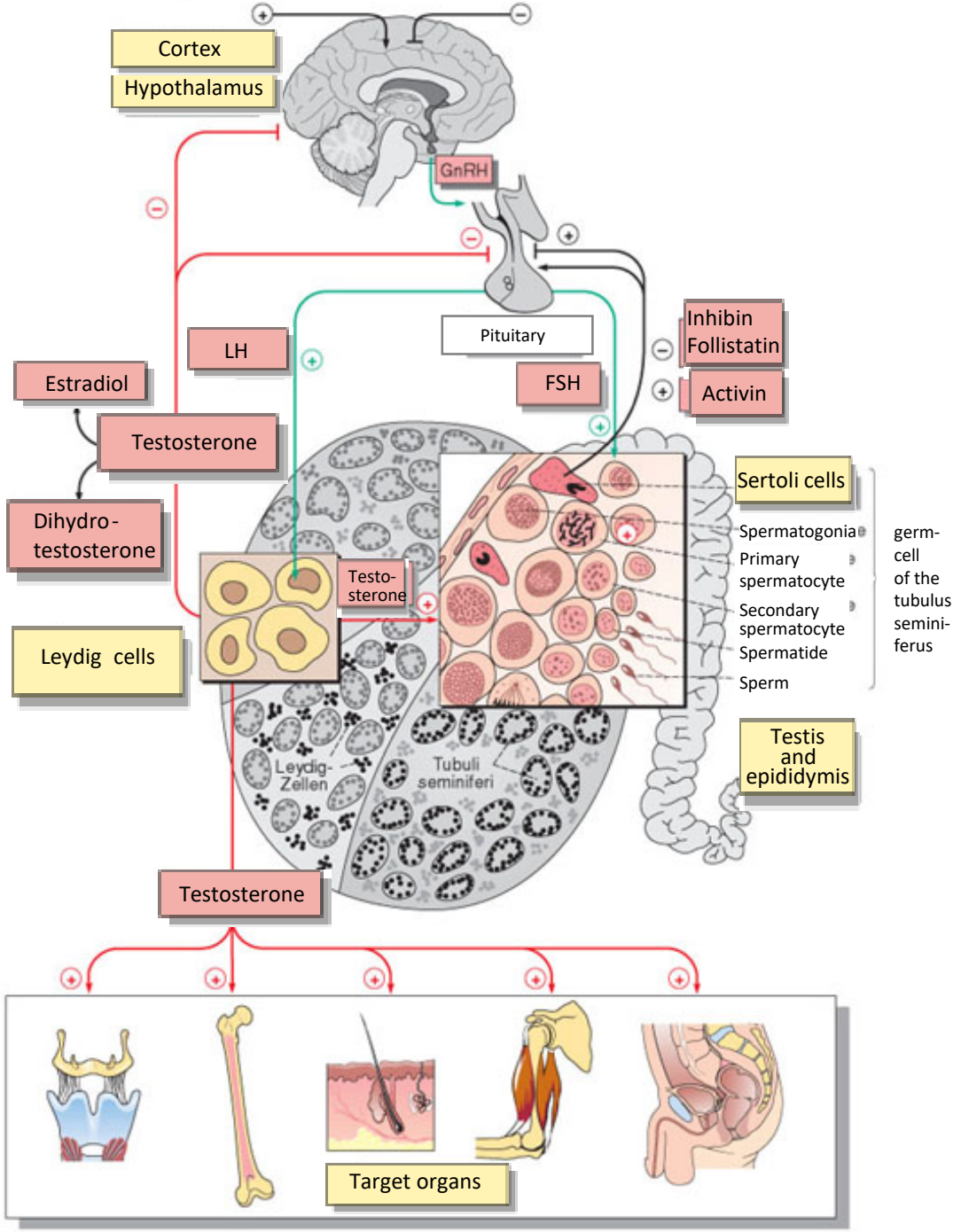
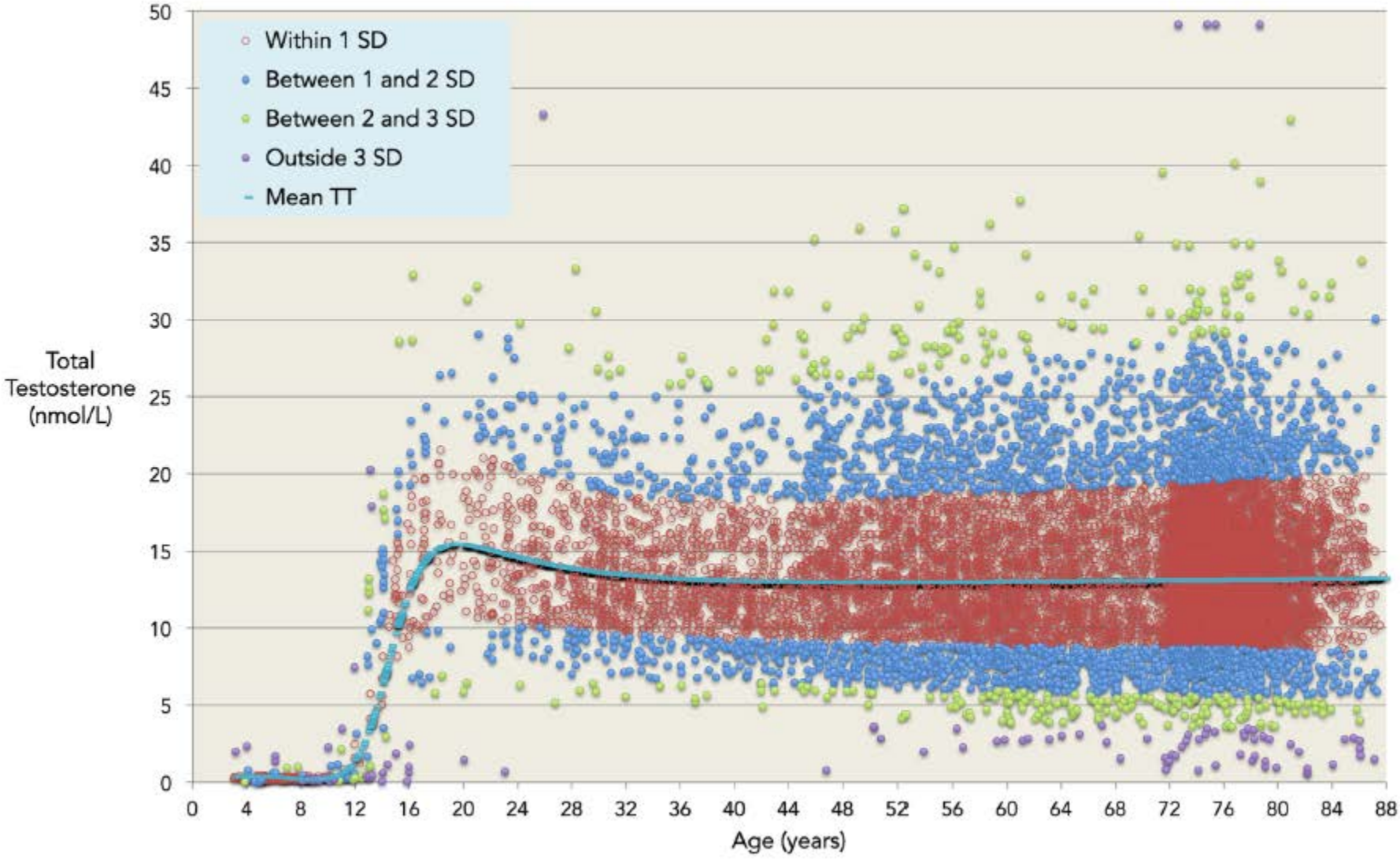


Nieschlag, Behre,
Nieschlag (eds)
Andrology 3rd ed
Springer 2010

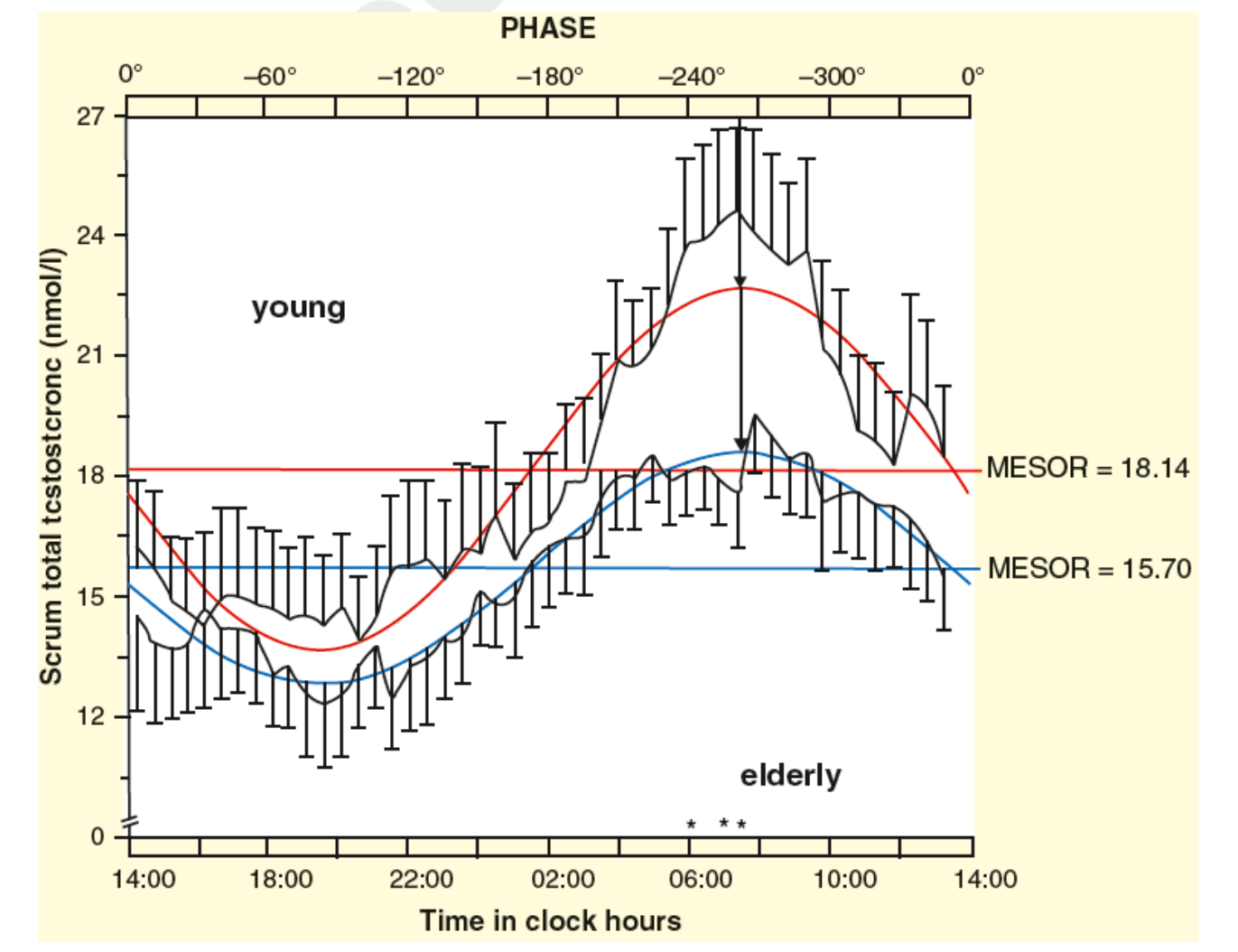
F 1550 G

Total testosterone in 10,098 males, 3 to 88 years:

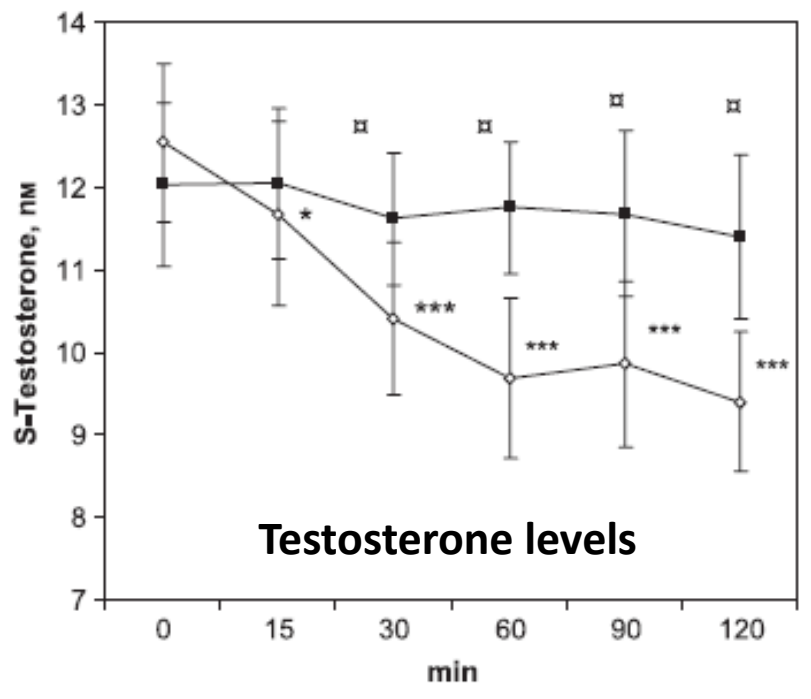


(Kelsey et al., PLoS ONE 9: e109346, 2014)

Circadian rhythm of serum total testosterone in 10 young (23-33 yrs) and 8 elderly men (55-64 yrs)

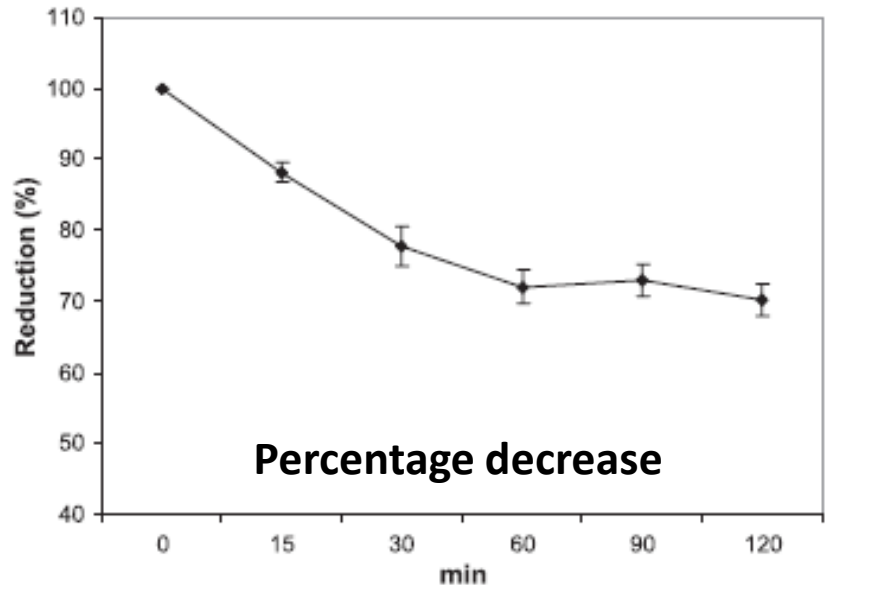


(Diver et al. Clin. Endocr. 58: 710, 2003)



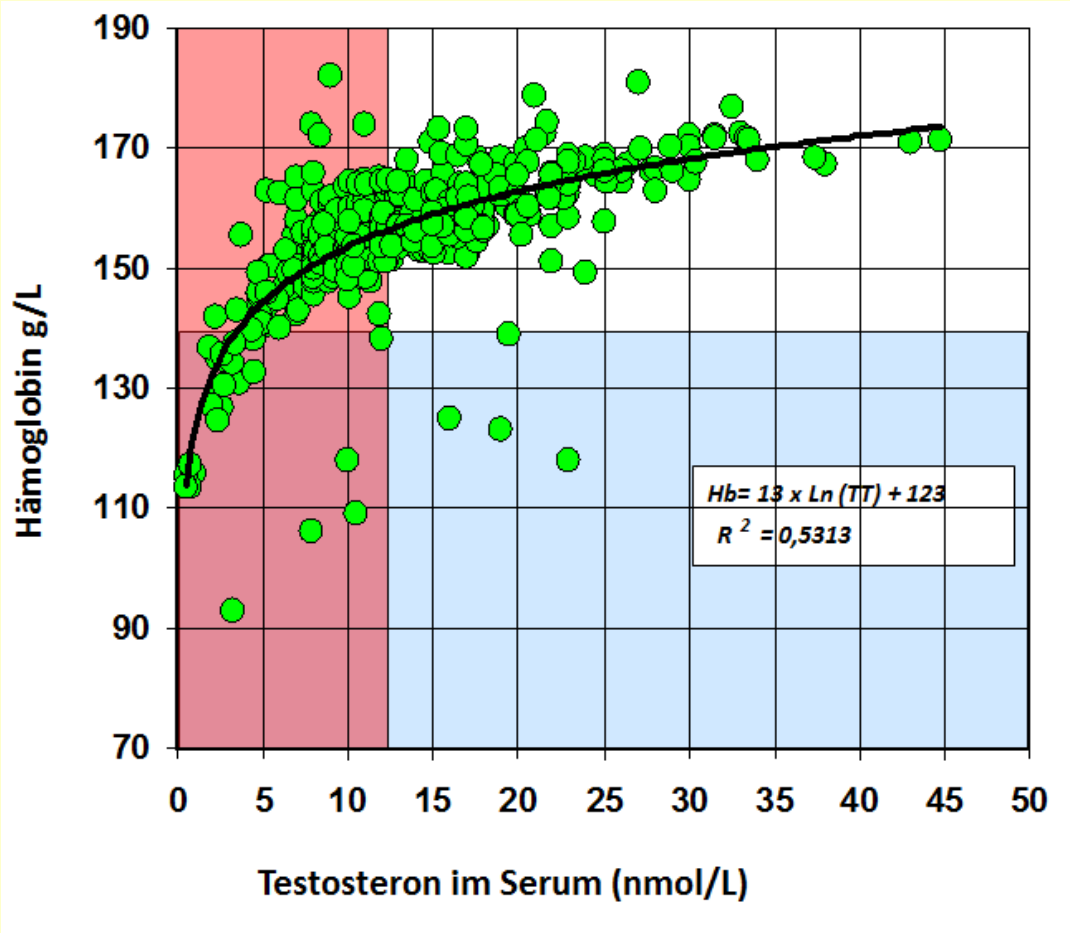
Serum testosterone in 11 healthy men (37 – 51 yrs) after an overnight fast (●) or following a 550 kcal breakfast (o):

A meal may decrease testosterone by 30 %!



(Lehtihet et al. Andrologia 44: 405-410, 2012)

Testosterone and hemoglobin in 434 aging men

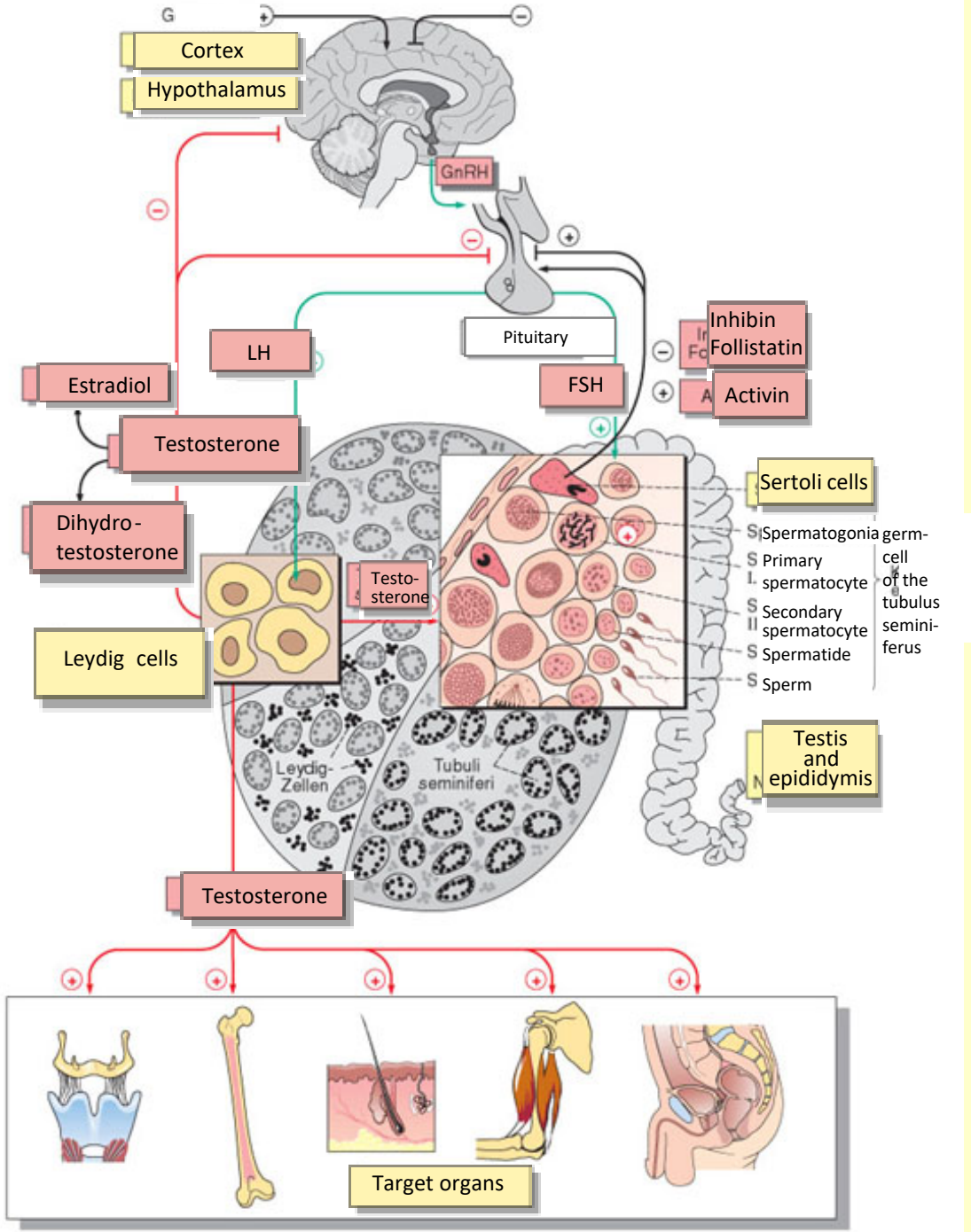


(Zitzmann & Nieschlag JCEM 92: 3844 – 53, 2007)

Secondary (hypogonadotropic) hypogonadism

Late-onset hypogonadism (LOH)

Primary hypogonadism



Nieschlag, Behre, Nieschlag (eds) Andrology 3rd ed Springer 2010

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Classification of male hypogonadism

Primary hypogonadism

Klinefelter syndrome 47,XXY

XX-Male syndrome

Gonadal dysgenesis

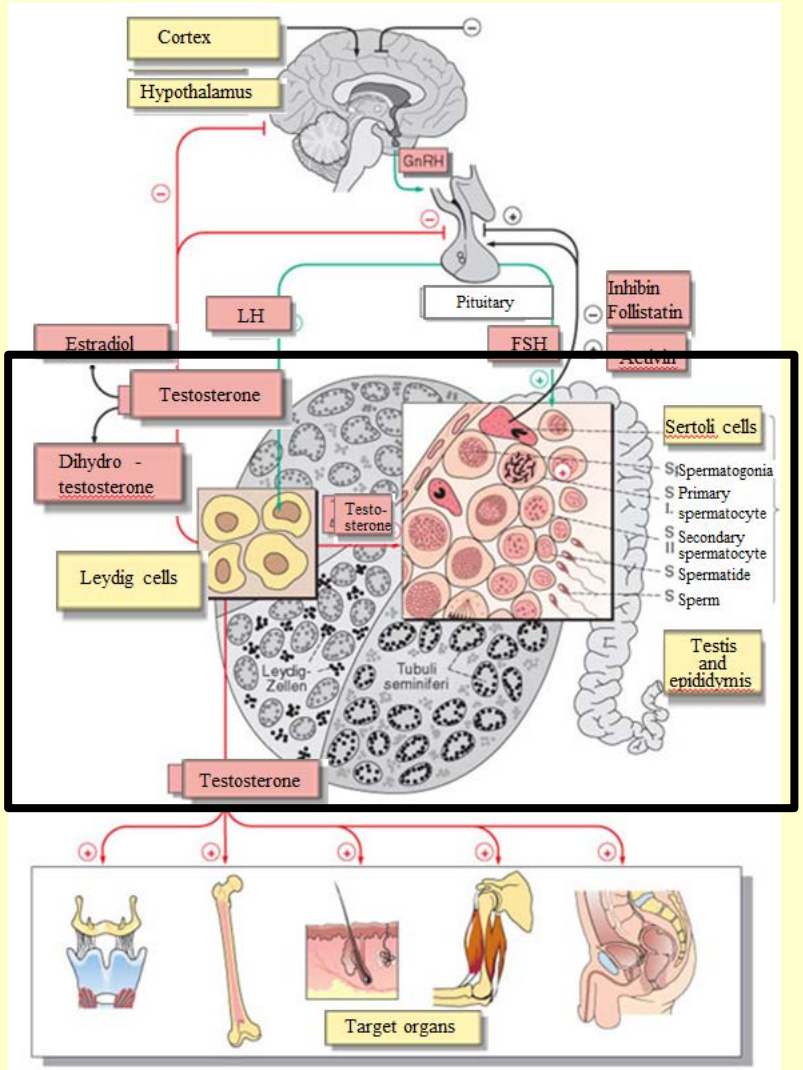
Anorchia, congenital or acquired

e.g. trauma, torsion, tumor

Maldescended/cryptorchid testes

Orchitis, resulting in testicular atrophy

Radiation or chemotherapy



(Nieschlag, Behre, Nieschlag (eds) Andrology 3rd ed Springer 2010)

Phenotype of patients with Klinfelter syndrome

Incidence: 1 in 500 men
47,XXY karyotype
Small testes
Azoospermia
Gynecomastia

72 years

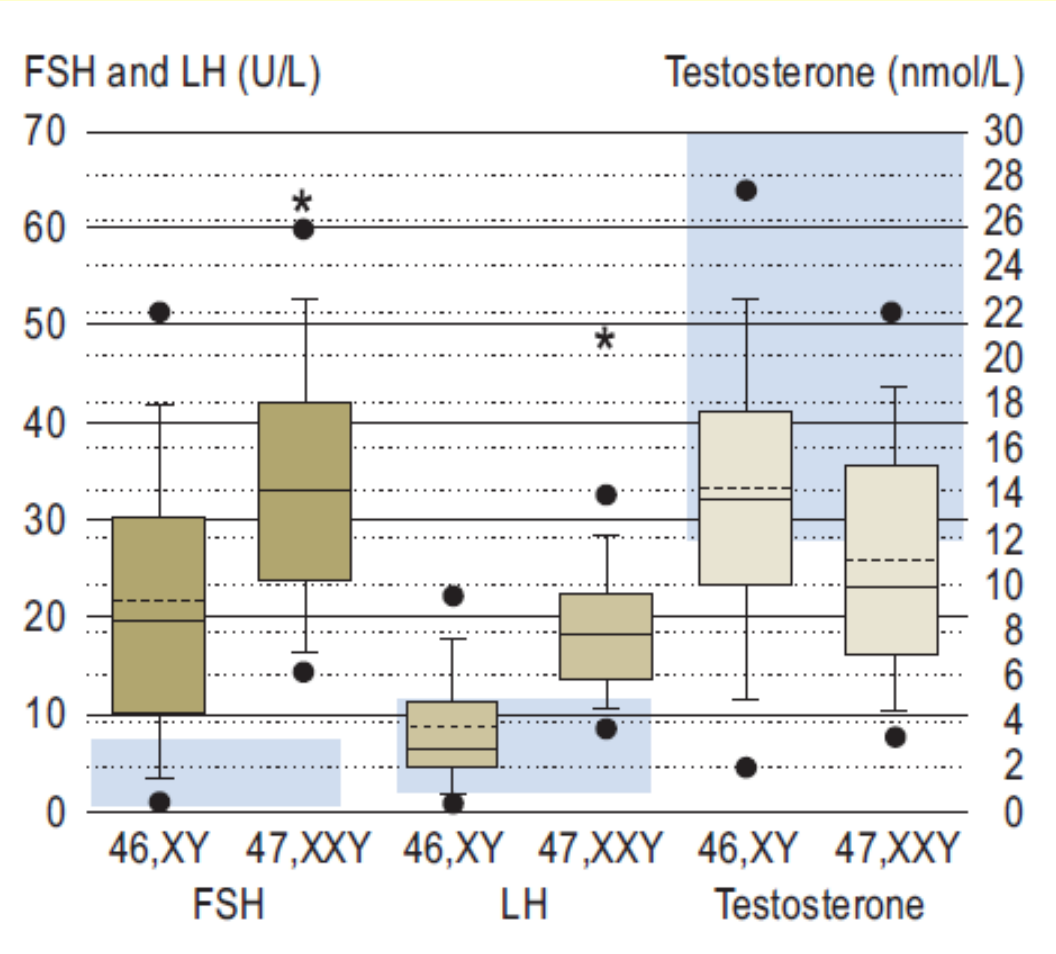
40 years

30 years

15 years

F 2590

Hormone concentrations in 228 Klinefelter patients and 224 infertile patients with normal karyotype



normal range

(Nieschlag, Dtsch Ärztebl Int 110: 347-353, 2013)

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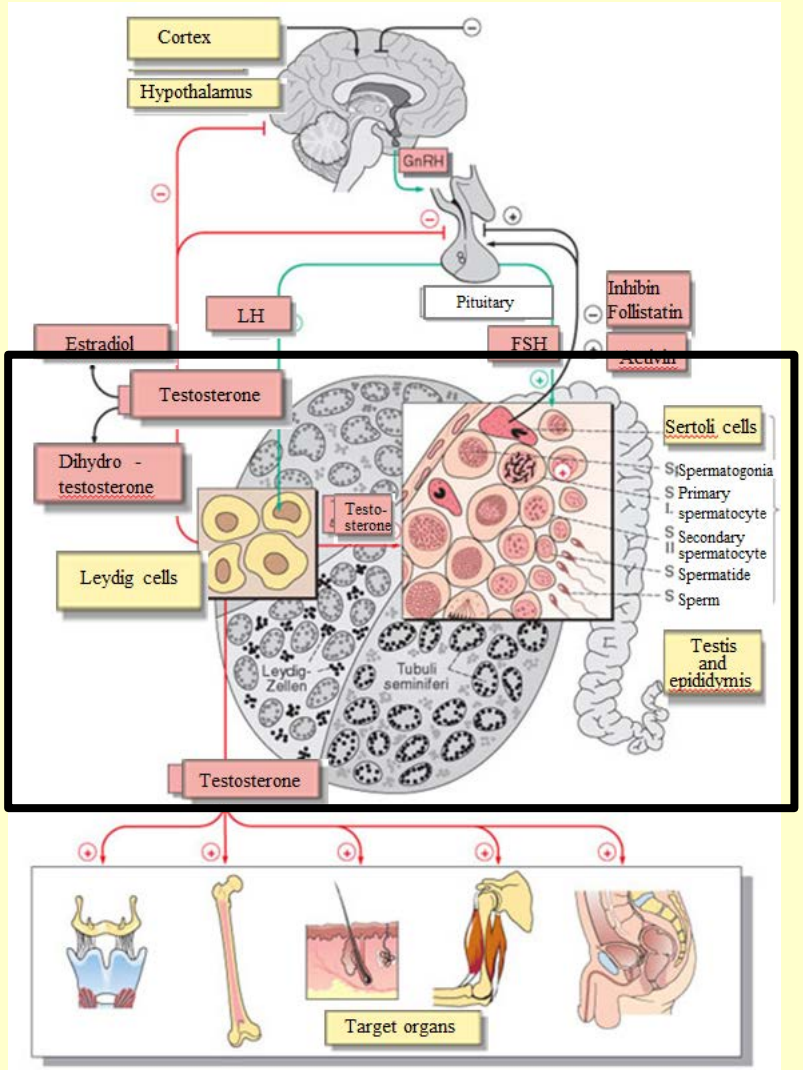
Radiation or chemotherapy

All disorders result in low T, except some testicular tumours may cause elevaterd T and E2.



Leydig cell tumours

Gynecomastia
Loss of libido
Erectile dysfunction
Testicular tumour
Elevated T and E2

Testicular ultrasonography showing a Leydig cell tumour

Leydig cell tumours cause elevated T and E2, but low gonadotropins.

Seminomas and choriocarcinomas *may* secrete hCG and elevate T.

Classification of male hypogonadism

Secondary hypogonadism

Isolated hypogonadotropic hypogonadism (IHH) and Kallmann syndrome

Brain trauma

Pituitary tumor

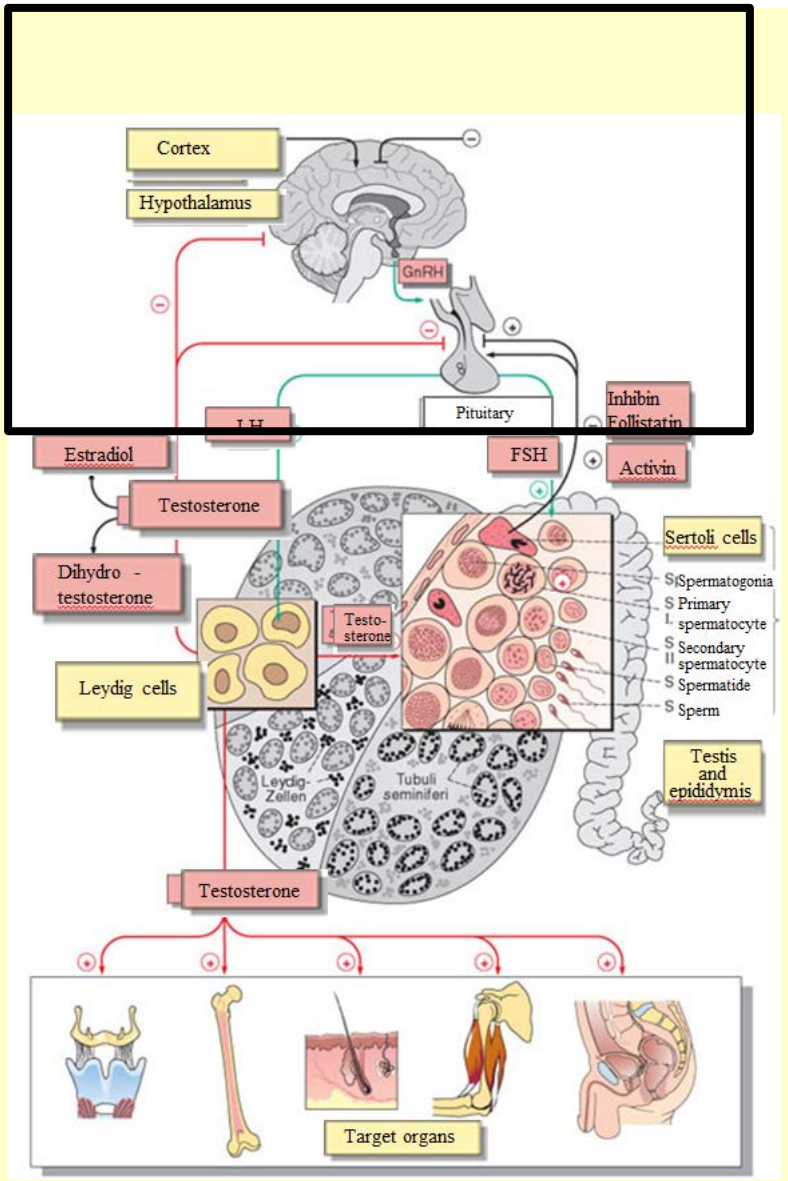
Pituitary infections

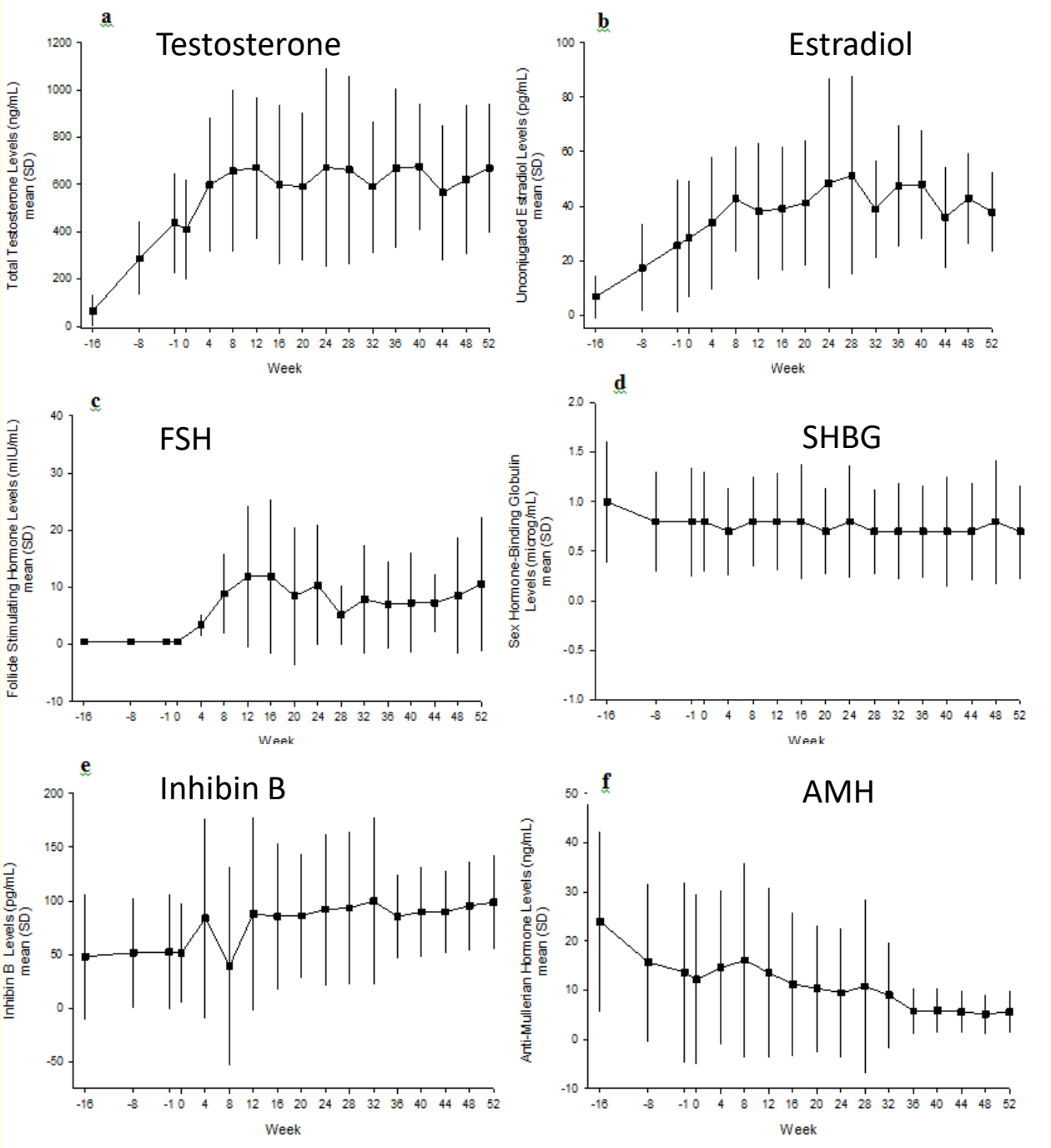
Pituitary hemochromatosis

Hypopituitarism (= multiple pituitary hormone deficiency (MPHD)

Hyperprolactinemia

Congenital Adrenal Hyperplasia (CAH)





Trial of hCG and corifollitropin alfa (long-acting rFSH) in 17 patients with hypogonadotropic hypogonadism for 16 and 52 weeks.

(Nieschlag et al. Reprod Biol Endocrinol 15: 17, 2017)

33 year old patient with Kallmann syndrome before and under substitution therapy.

Signs of masculinization are clearly visible.

Classification of male hypogonadism

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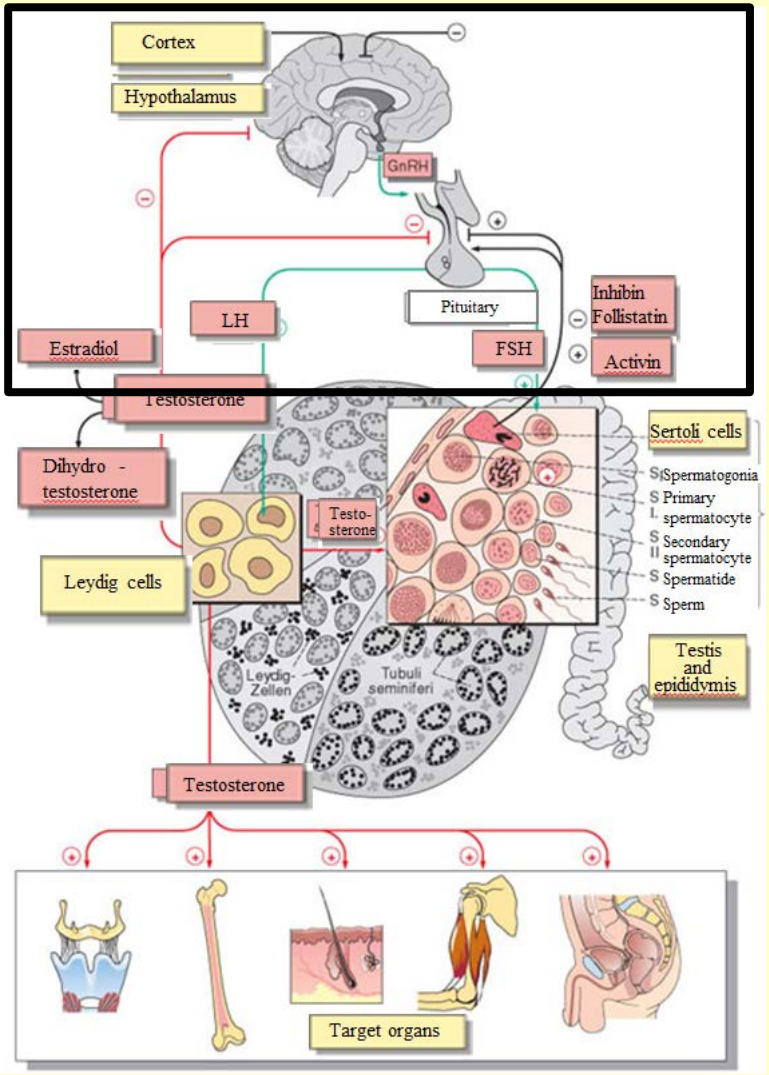


All disorders result in low T, except CAH: increased T and 17OHP

WADA TUE Physician Guidelines 2016

differentiates between organic and functional hypogonadism / androgen deficiency

Organic: **„There is a pathological physical change in the structure of an organ or within the hypothalamic-pituitary-testicular axis“ i. e. „long-lasting or permanent“.**

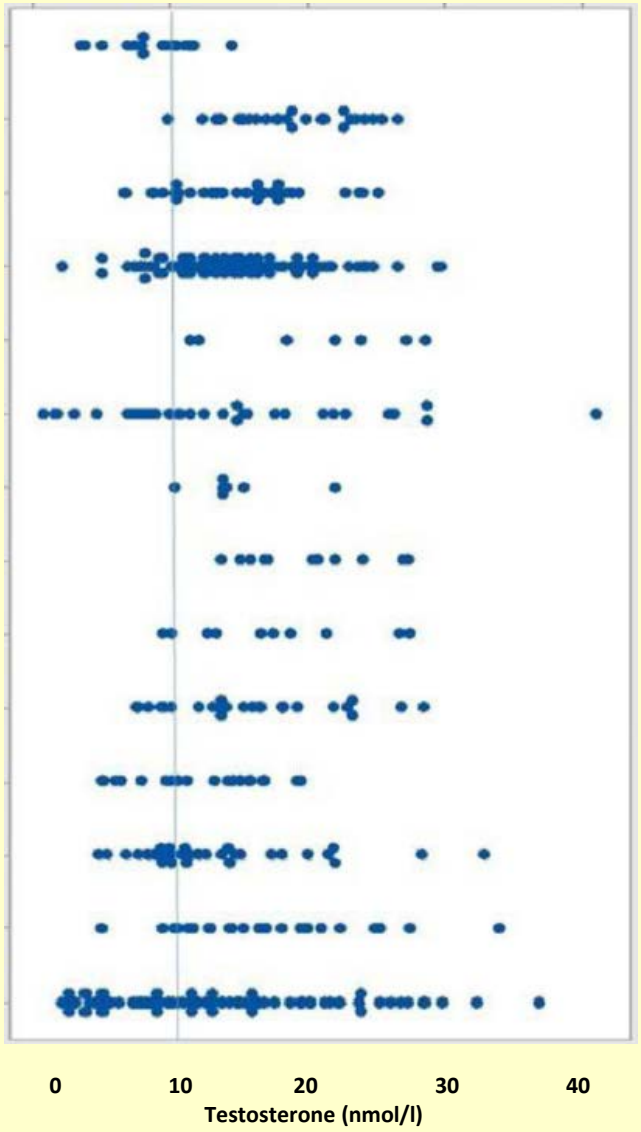
Functional: **„There is no observable pathological change in the structure of an organ or within the hypothalamic-pituitary-testicular axis“ i. e. „potentially reversible“.**

Functional causes of hypogonadism / androgen deficiency

1. Severe emotional stress
2. Morbid obesity
3. Overtraining, malnutrition, eating disorders
   „Male Athlete Triad“
4. Medication e. g. androgens, SARMs, glucocorticoids, progestins, estrogens, medication-induced hyperprolactinaemia
5. Chronic systemic illness, e. g. chronic organ failure, diabetes mellitus, malignancy, rheumatic disease, HIV-infection, Crohn‘s disease, inherited metabolic storage disease
6. Const. Delayed puberty
7. Alcohol excess
8. Aging/Late-onset hypogonadism (LOH)

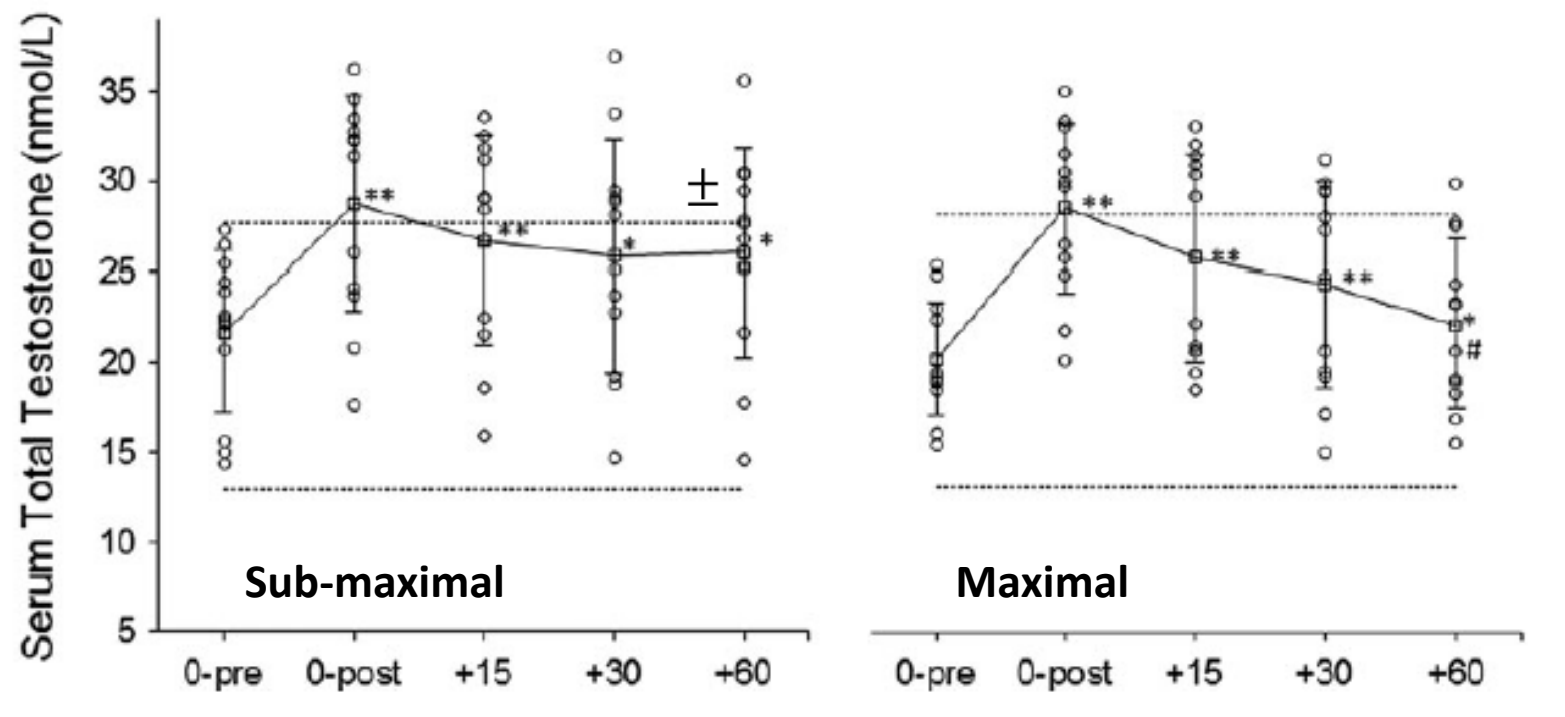
Serum T values from 445 elite male athletes grouped according to disciplenes

Power Lifting
Basketball
Football
Swimming
Canoeing
Rowing
Cross Country Skiing
Alpine Skiing
Weight Lifting
Judo
Bandy
Ice Hockey
Handball
Track and Field

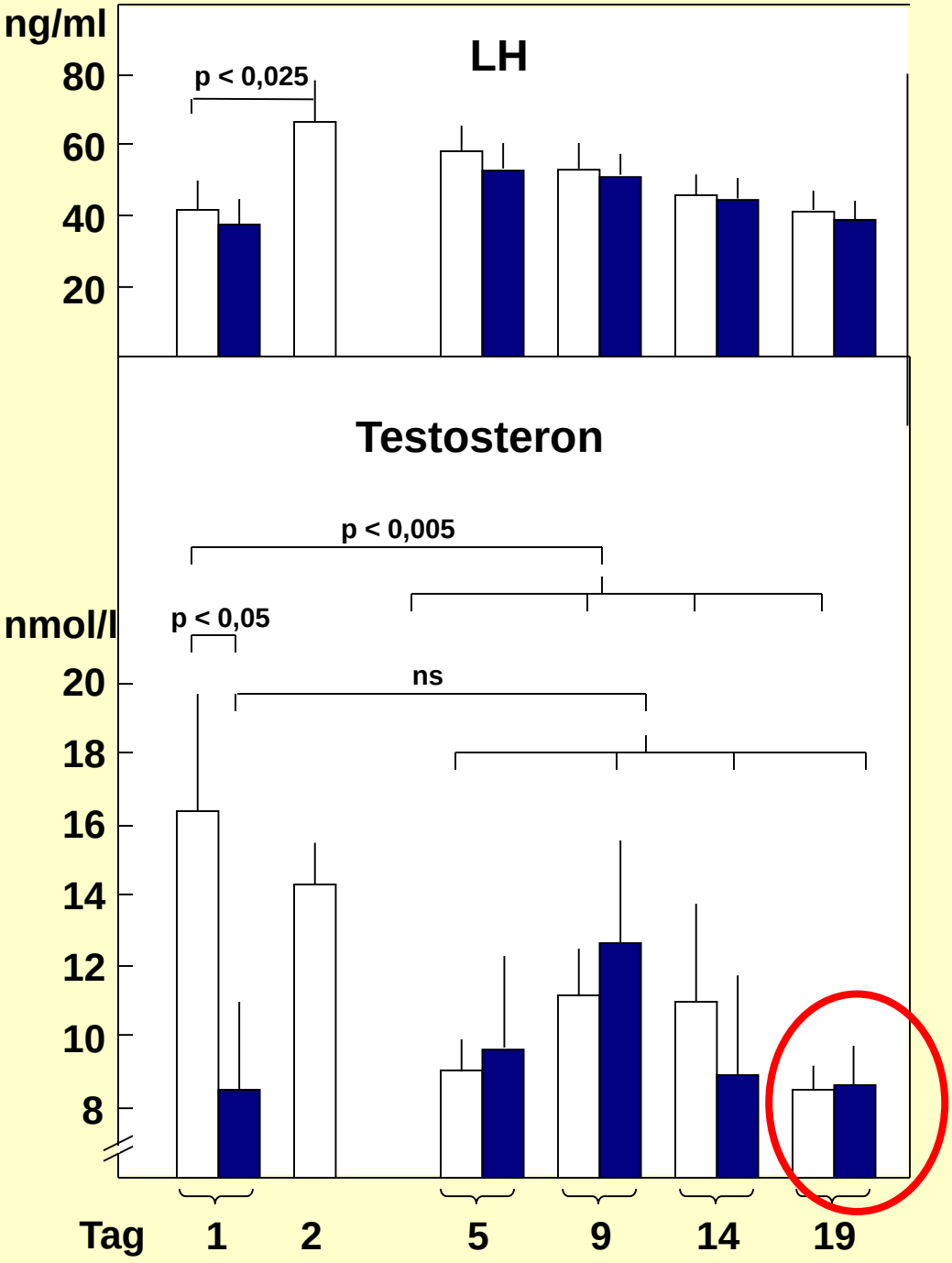


(Sönksen et al Clin Diab Endocrinol 4: 3, 2018)

Serum testosterone in 12 men before and after a 30 min sub-maximal exercise and a maximal exercise until exhaustion (22.3 ± 2.4 min) (2 weeks between tests)



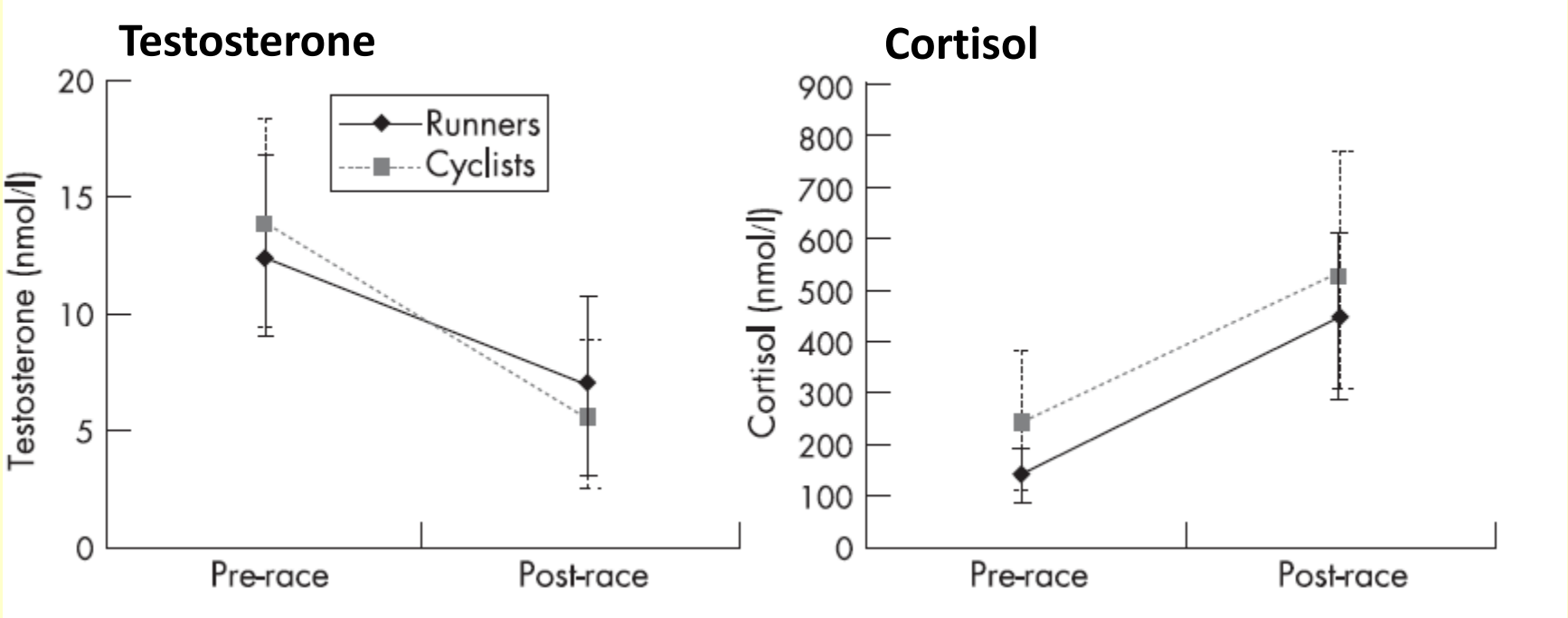
(Sgrò …. Di Luigi J Endocrinol Invest 37: 13-24, 2014)



LH and T in 5 athletes during a 20-day 1100 km run through Germany before ☐ and after ■ the daily stretch of 45 – 65 km.

(Schürmeyer, Jung & Nieschlag Int. J. Androl. 7, 276, 1984)

Testosterone and cortisol levels in 6 runners and 10 cyclists before and after a 160 km race across frozen Alaska:
(Finish times: runners 34 ± 6 h, cyclists 22 ± 6 h)



(Kraemer et al. Br J Sports Med 42: 116-120, 2008)

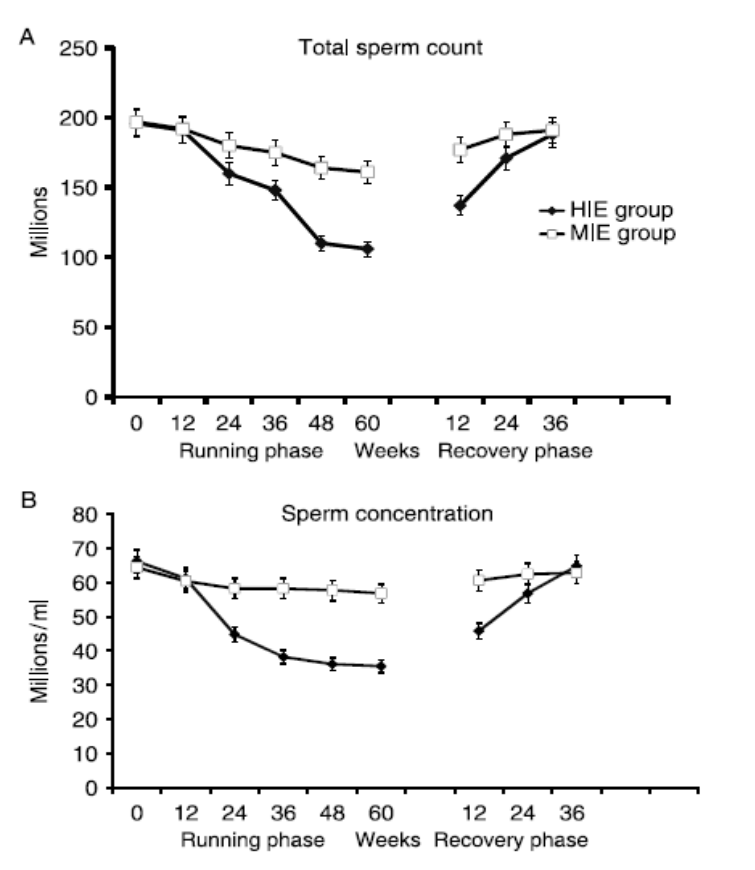
Effect of treadmill running on male fertility parameters :

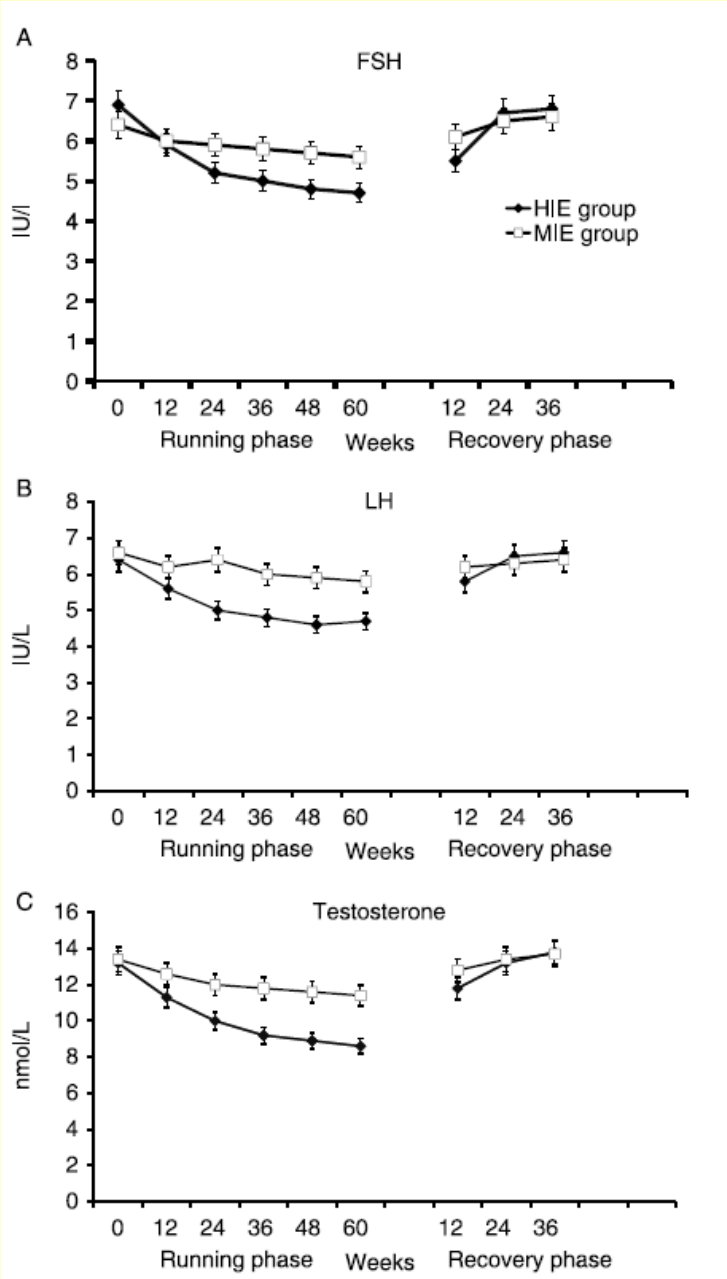
5 sessions per week for 60 weeks.

HIE group = high intensity (n=143)

MIE group = moderate intensity (n=143)

(Safarinejad et al- J Endocrinol 200:259-271, 2009)





Exercise-Induced Hypogonadism

(Hackney & Aggon J Biochem Physiol 2018 epub)

Historical overview of testosterone preparations available for clinical use.

1940

1954

1992

1995

2008

1977 2006

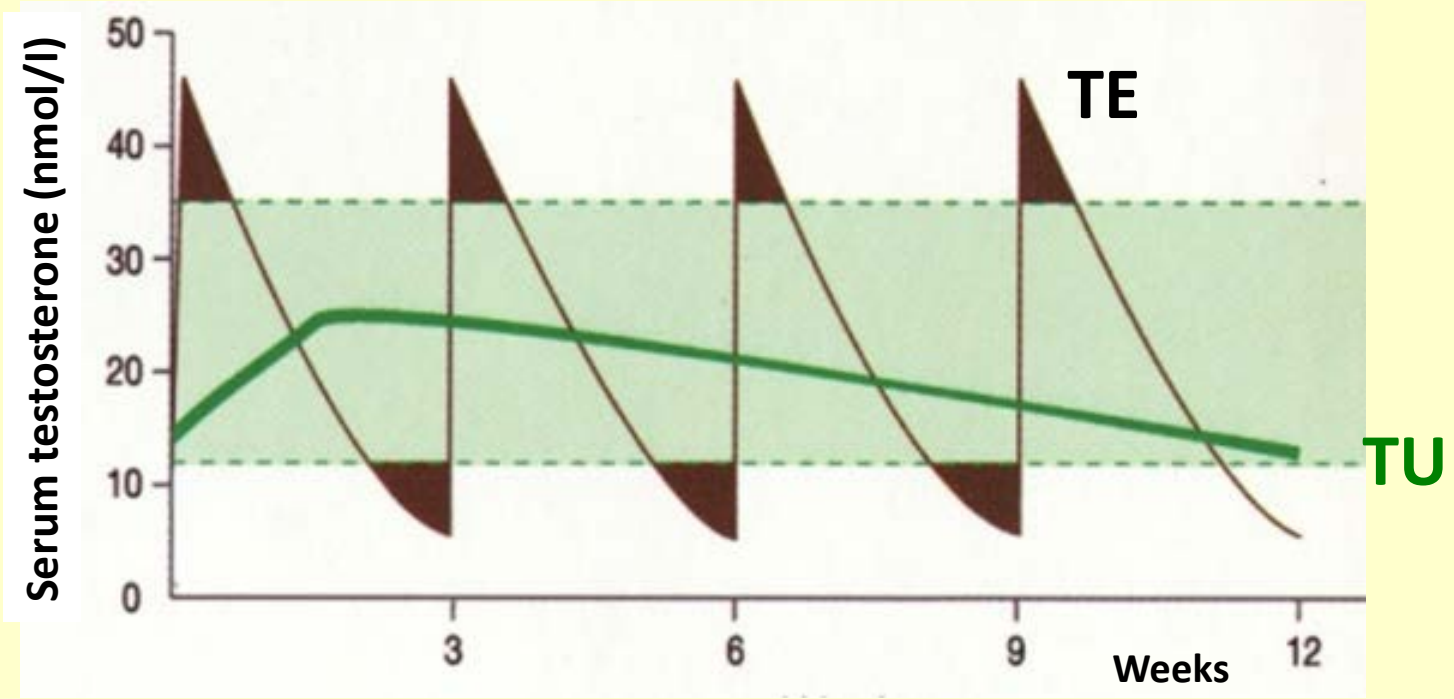
since 2002

since 2004

2004

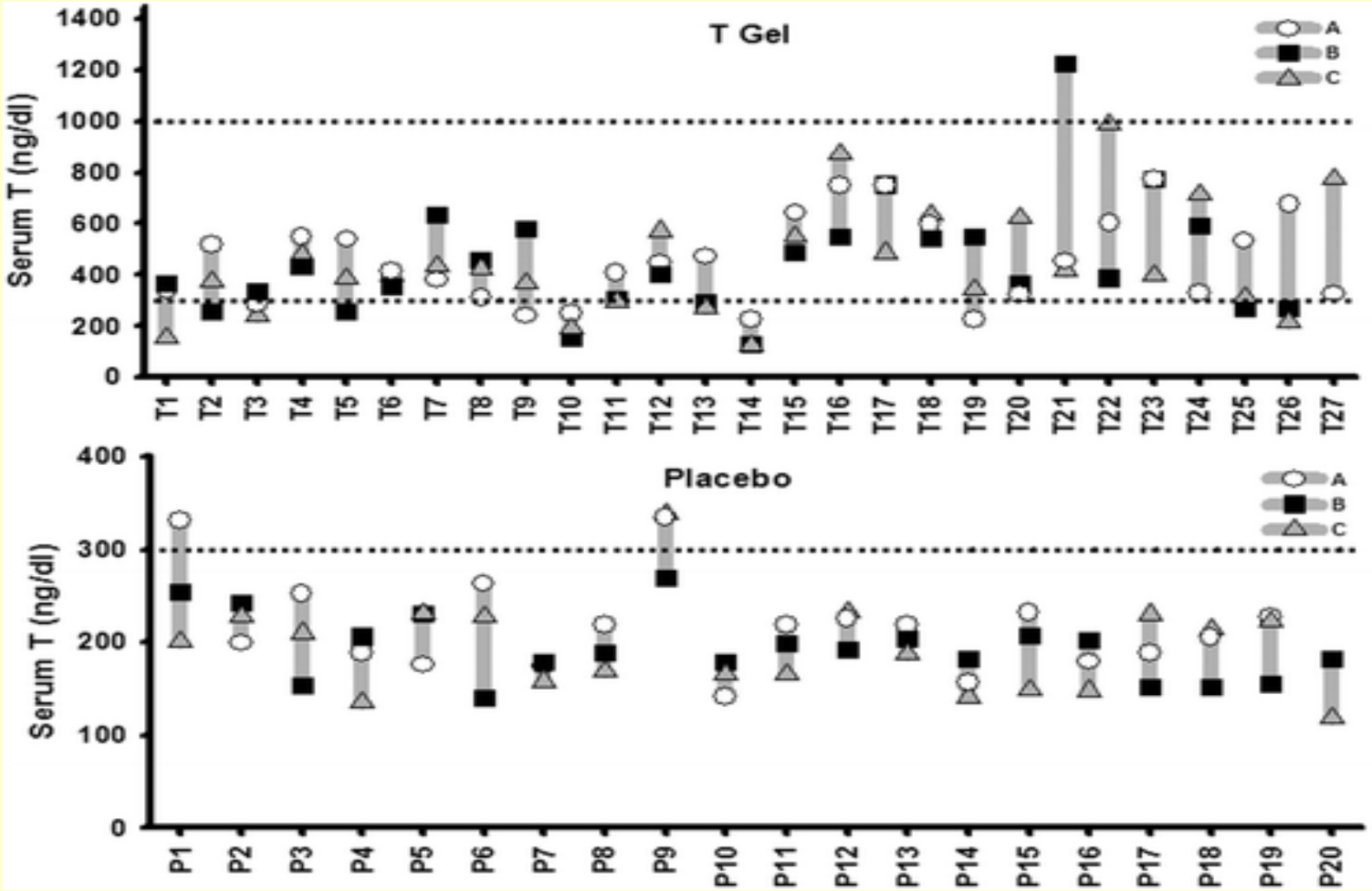
since 2004
USA 2014

Serum testosterone levels under 4 x 250 mg testosterone enanthate (TE) or 1 x 1000 mg testosterone undecanoate (TU)



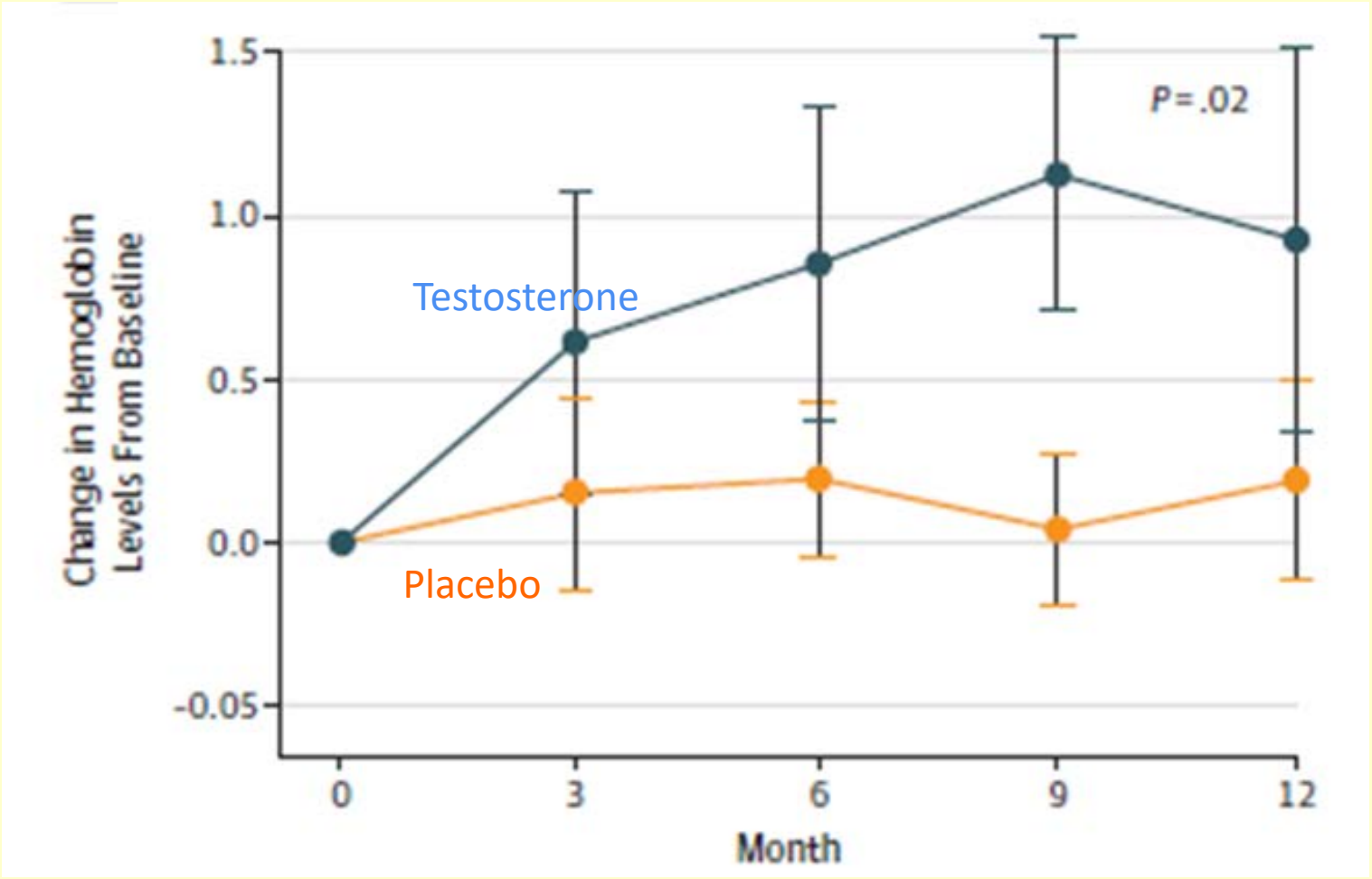
(compiled from Nieschlag, Behre, Nieschlag „Testosterone“ 4th ed 2012)

Serum testosterone levels in 27 LOH patients 2 hours after application of AndroGel 1 % and in 20 patients receiving placebo on 3 different days (A, B and C)

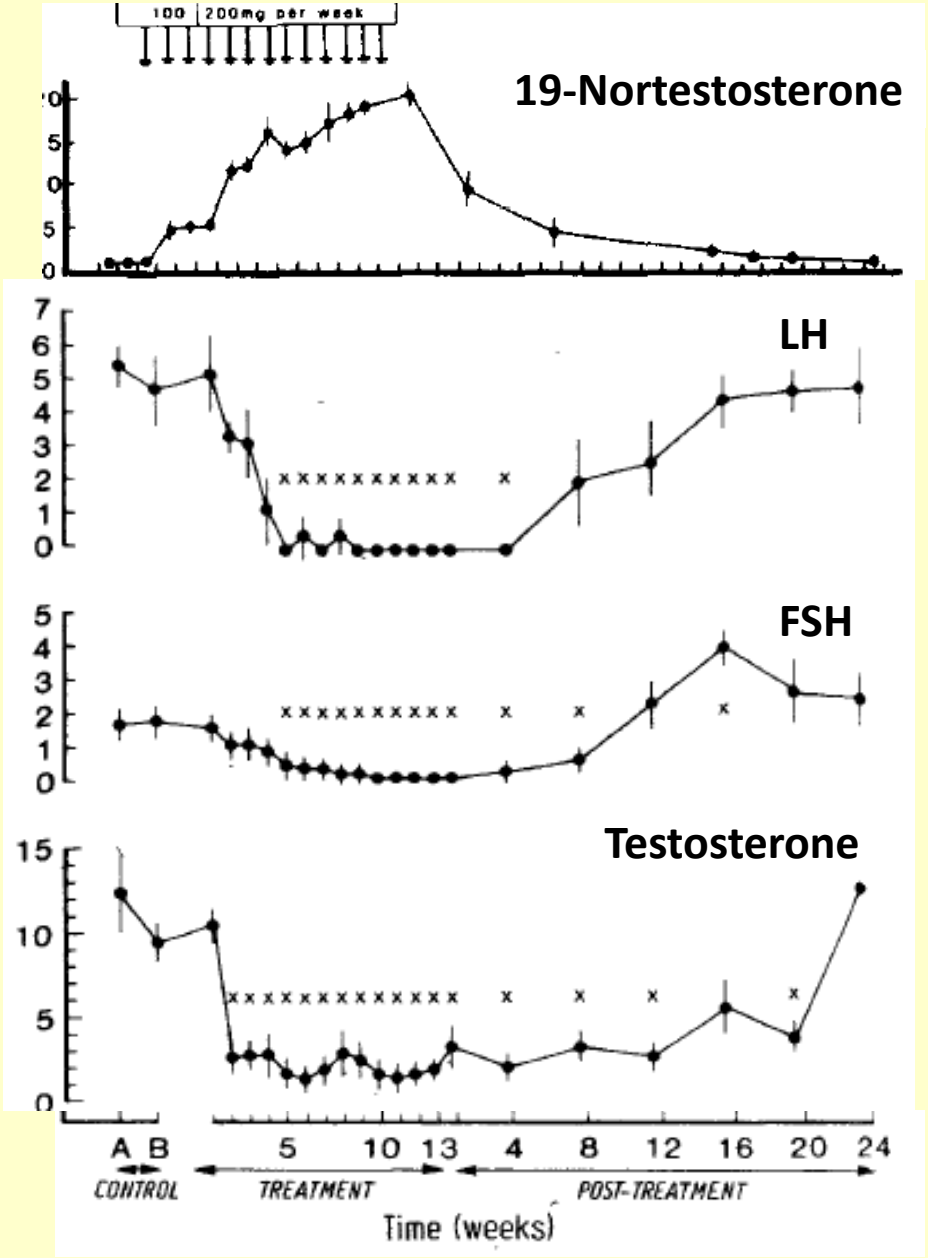


(Swerdloff et al. JCEM 100:3280-87, 2015)

Effect of testosterone (n=27) vs placebo (n=35) treatment for 12 months in aging men with unexplained anemia.



(Roy et al. JAMA Intern Med. 177: 480-490, 2017)



Effect of weekly injections of 19-nortestosterone* on serum hormone levels in 5 volunteers

.

* 1000 mg 19-nortestosterone-hexoxyophenylpropionate for 3 weeks followed by 200 mg weekly injections for 10 weeks

(Schürmeyer…..Nieschlag Lancet i, 417-420, 1984)

Diseases / conditions affecting the testosterone profile in blood

Men

- Lower testosterone
- Elevated testosterone

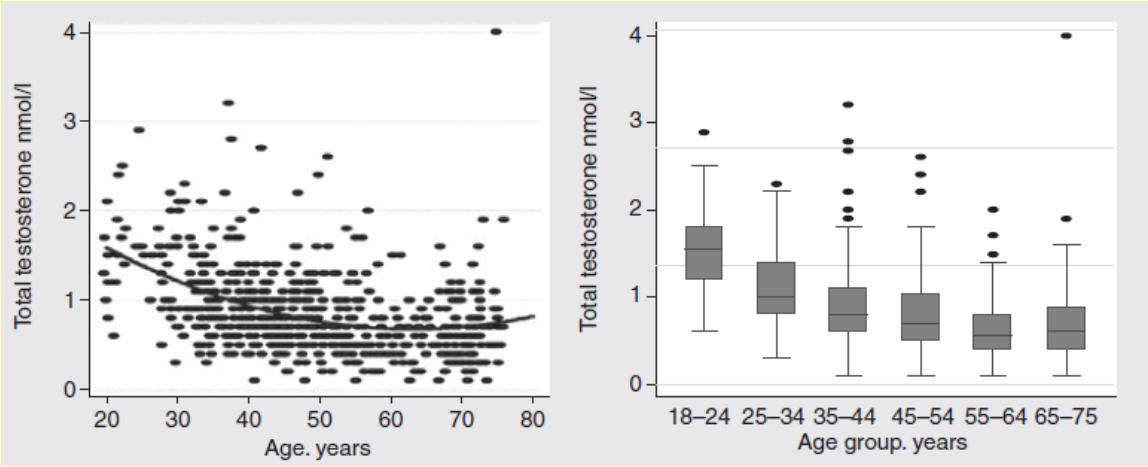
Women

- **Lower testosterone**
- **Elevated testosterone**

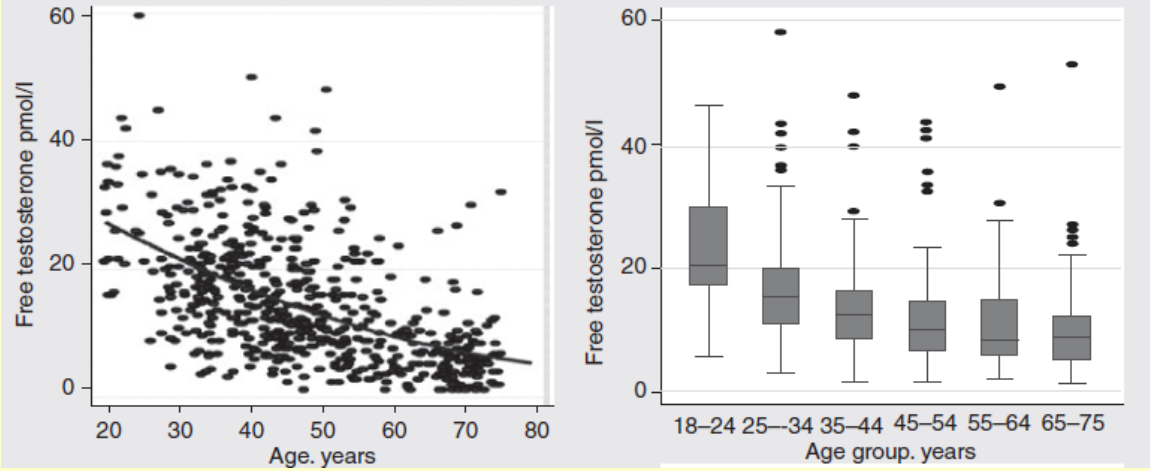
Disorders of Sex Development (DSD)

Total and free testosterone in normal women, 18 to 75 years old.

total T



free T



Davis SR in: Nieschlag & Behre (eds.) Testosterone : action, deficiency, substitution. 4th ed. Springer, 494-516, 2012

Testosterone levels in women

Testosterone excess in women

- **Polycystic Ovary Syndrome (PCOS)**
  hirsutism, acne, anovulation
- **Congenital Adrenal Hyperplasia (CAH)**
  small stature, hirsutism, anovulation
- **Androgen-secreting ovarian tumours**
- **Androgen-secreting adrenal tumours**

Low testosterone in women

- **Turner‘s syndrome (45,X)**
- **Bilateral oopherectomy**
- **Premature ovarian failure (POF)**
- **Adrenal insufficiency (Addison‘s disease)**

Disorders of Sex Development (DSD)

Congenital variants of biological Anlagen resulting in ambiguous categories to which neither „male“ nor „female“ are strictly applicable.

Disorders of Sex Development = DSD
Hughes et al. The Chicago Consensus 2006
(Arch Dis Child 91: 554 – 562, 2006)

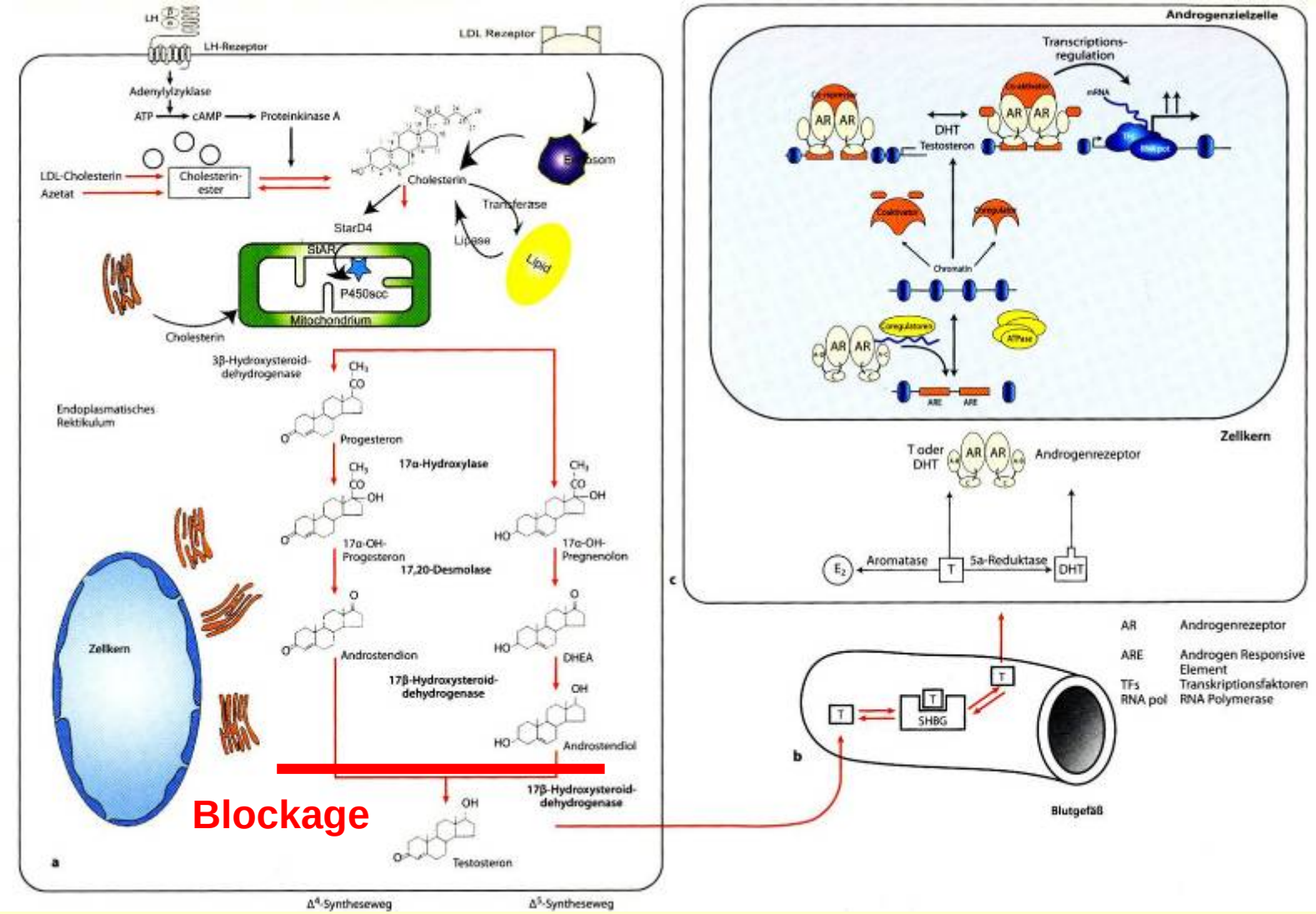
Formerly: Intersexuality

Incidence of 46, XY DSD among elite female athletes

- 849 athletes from 163 countries participating in the 2011 IAAF World Championships in South Korea
- 168 on oral contraceptives
- 5 detected as Anabolic Androgenic Steroid abusers
- 5 cases of 46, XY DSD
  i.e. 7 per 1000 women
  = 140 times more than in general population!

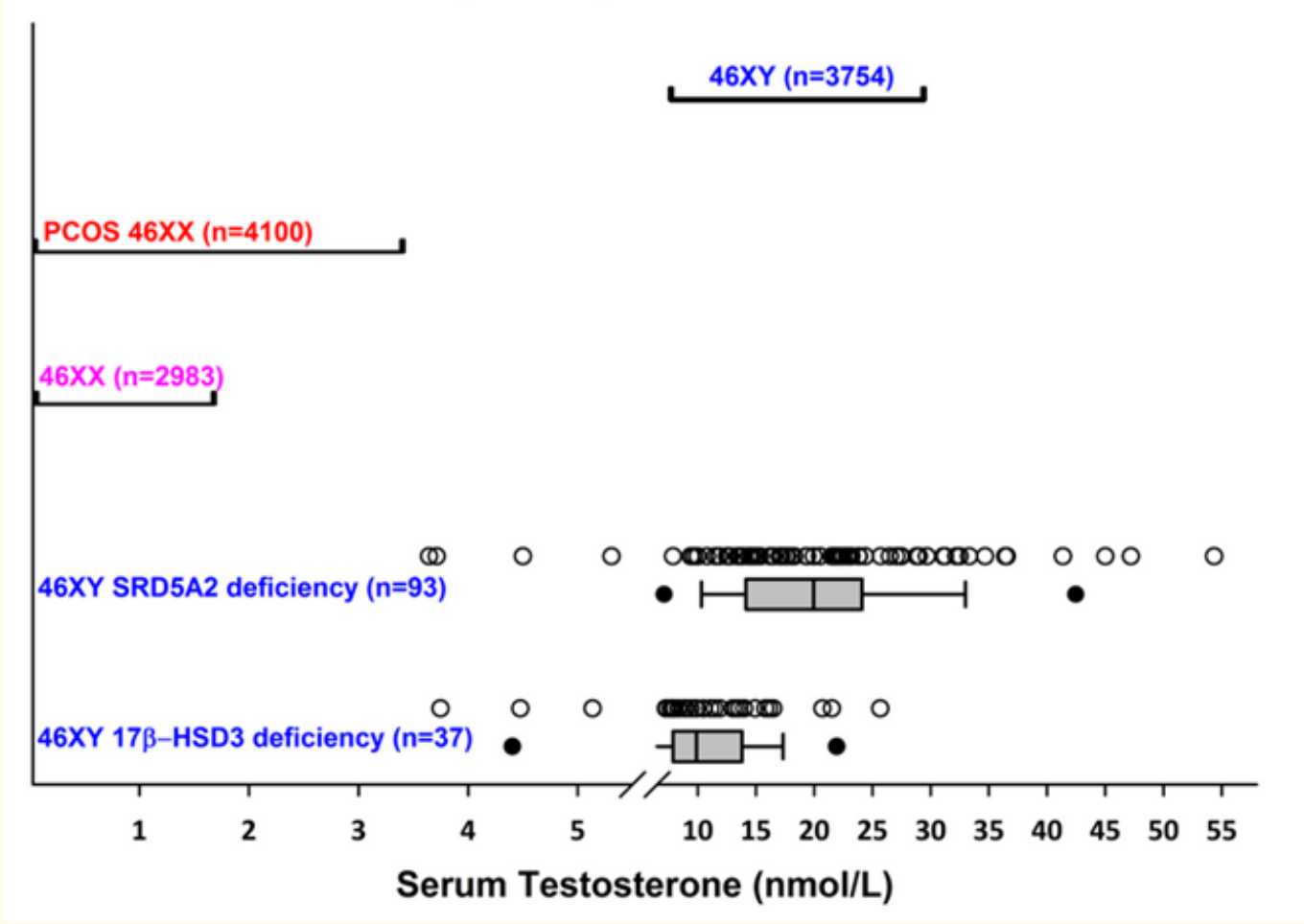
(Bermon et al. J Clin Endocr Metab 99:4328-35, 2014)

Testosterone biosynthesis, transport and intracellular action: Effect of 17ß-hydroxysteroid dehydrogenase defect.



(Nieschlag et al „Andrology“ 3rd ed. Springer 2010)

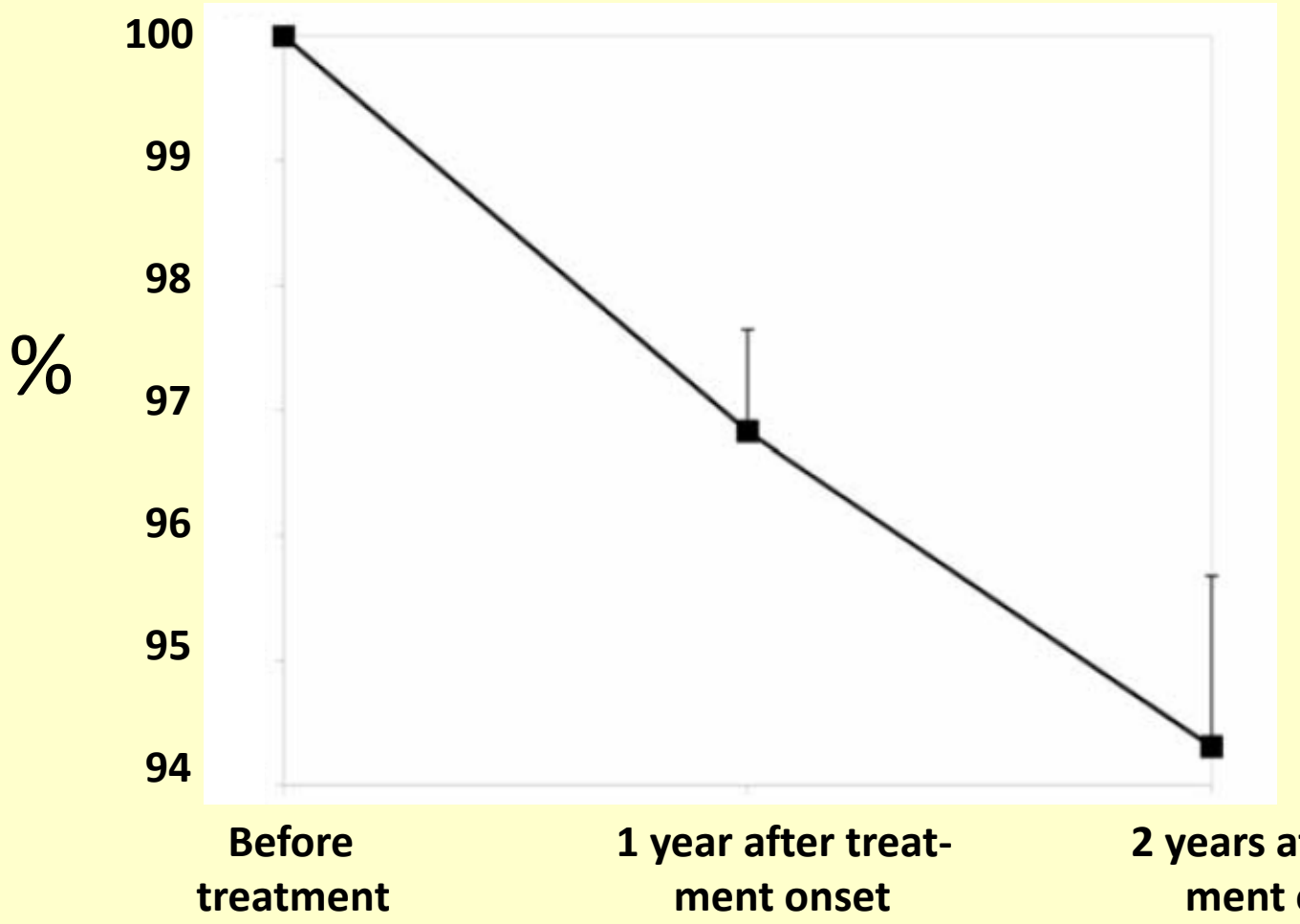
Serum testosterone (by LC-MS)
in normal men and women as well as in PCOS and 46,XY DSD patients



(adapted from data in Handelsman et al Endocrine Reviews 39: 803-829, 2018)

Best chronometric performance in 3 hyperandrogenic female distance runners with disorders of sex development before and under testosterone-lowering therapy

(Bermon, Curr Opin Endocrinol Diabetes Obes. 24: 246-251, 2017)



Diseases / conditions affecting the testosterone profile in blood
- Summary -

♂

T shows a diurnal rhythm, high levels in the morning, low in the evening.

Hypogonadism of all forms is characterized by low T, except in some testicular tumors and in CAH.

Short exercise increases T, exhaustive long exercise lowers T (= exercise-induced hypogonadism).

AAS lower gonadotropins and T.

♀

T can be above the normal range in PCOS, CAH, adrenal and ovarian tumors.

DSD

46,XY DSD phenotypic females have T levels above the normal female range.