The role of testosterone and hypogonadism

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History

- 8th century AD
  - Chinese used testicular extracts to treat impotence

- 1889
  - Brown-Sequard used injections of dog and guinea pig testicular extracts

Androgens in Men

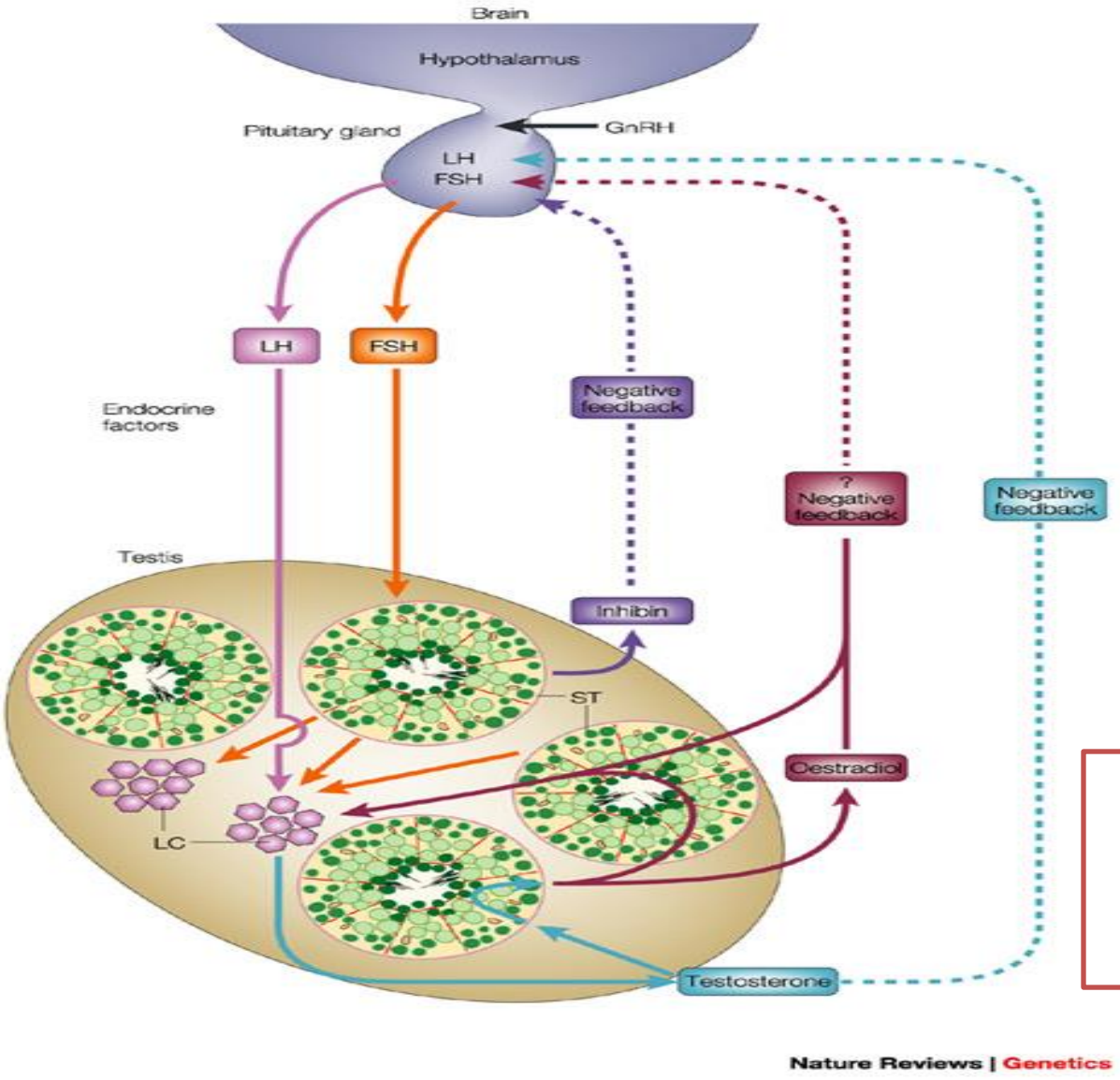
- Testosterone
- Dihydrotestosterone (DHT)
- Androstenedione

Testis OR
peripheral conversion

- Dehydroepiandrostenedione (DHEA)
- DHEAS

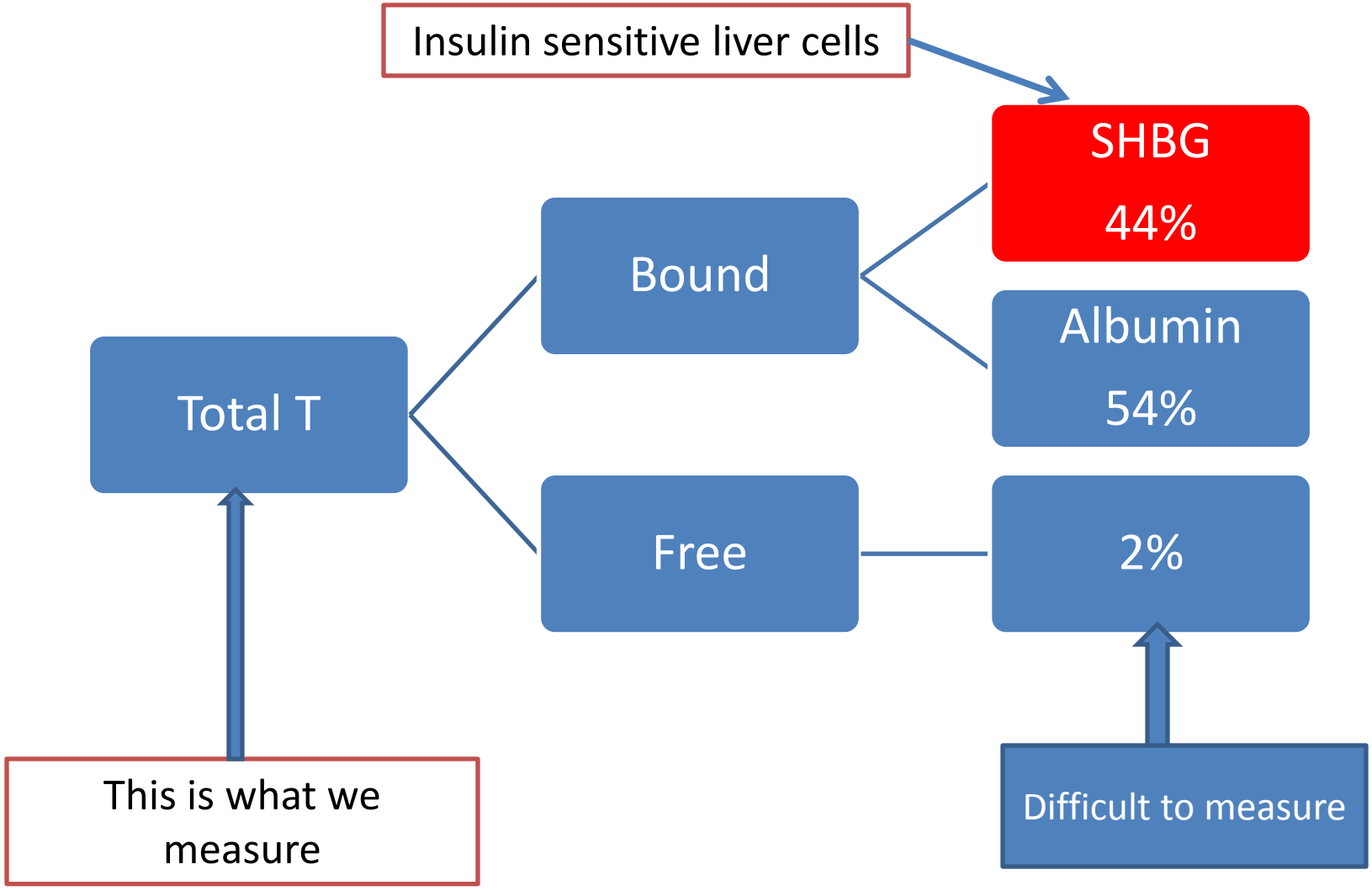
Adrenal gland

Regulation of Testosterone Production

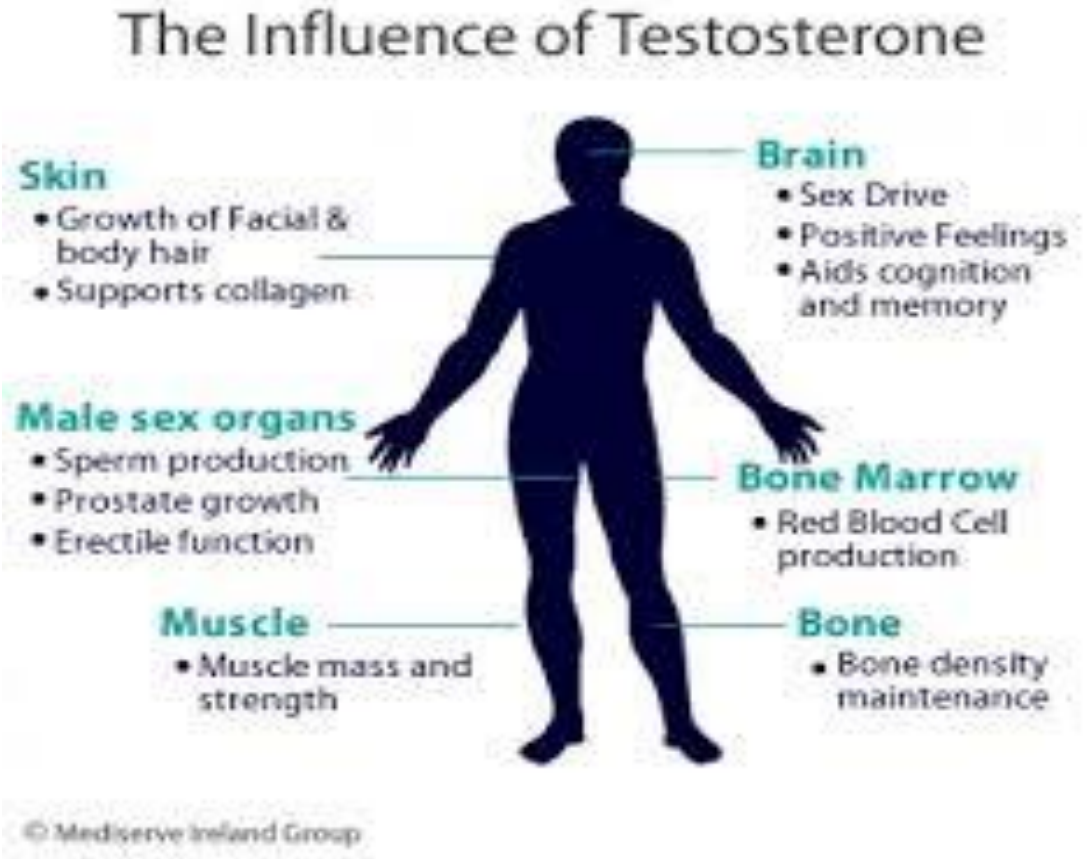


Peak in the morning with nadir in the afternoon [35%]

Circulating Testosterone



Effects of Androgens in Men



Androgen deficient man [late onset hypogonadism]

- Hot flushes
- Loss of body hair
- Fatigue
- Depression
- Reduced bone mass
- Reduced muscle mass
- Erectile dysfunction
- Reduced libido

Conditions associated with low T

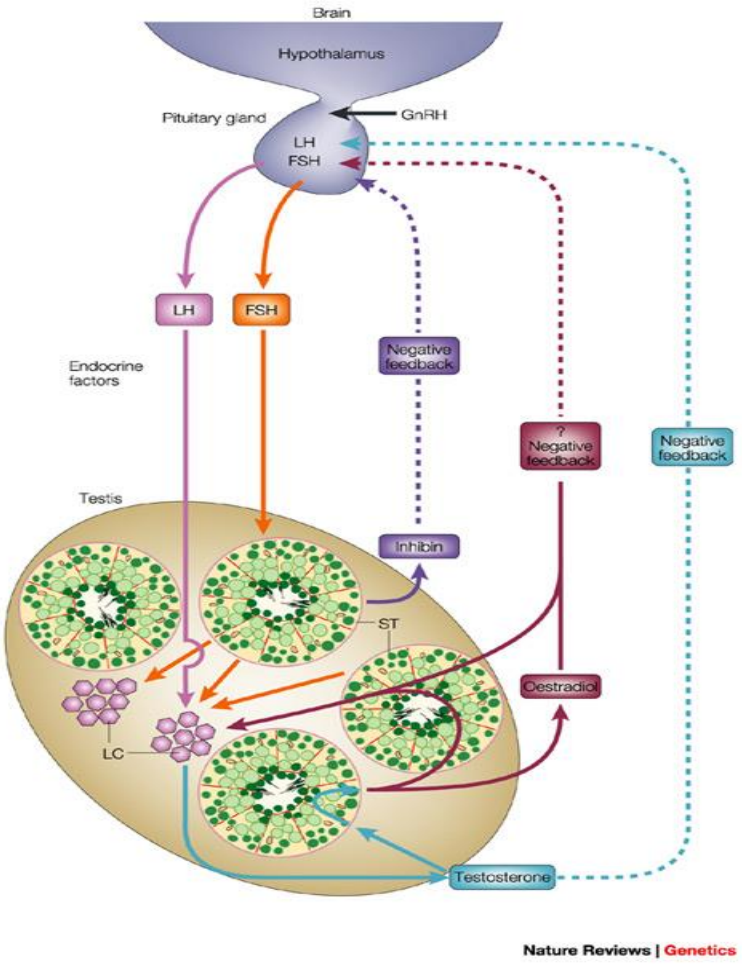
- Acute illness
- Heart failure
- Type 2 DM/obesity
- Chronic diseases: COPD, RA, epilepsy
- Cirrhosis
- CKD
- Advancing age
- Pituitary tumours
- Haemochromatosis
- Primary hypogonadism

Effect of age on testosterone levels

- Total testosterone ↓ from 40 years onwards [2% fall per year]
- SHBG levels ↑ from 40 years onwards
  - Greater fall in free testosterone
- Reliable marker of androgen activity at the level of the tissues is lacking
- Age-specific ‘normal’ ranges lacking

Medications associated with low T

- Decreased LC testosterone production
  - Corticosteroids
  - Alcohol
  - Ketoconazole
- Increased T metabolism
  - Anticonvulsants
- Decreased LH release
  - Anabolic steroids
  - Alcohol
  - Corticosteroids
  - Psychotropic agents

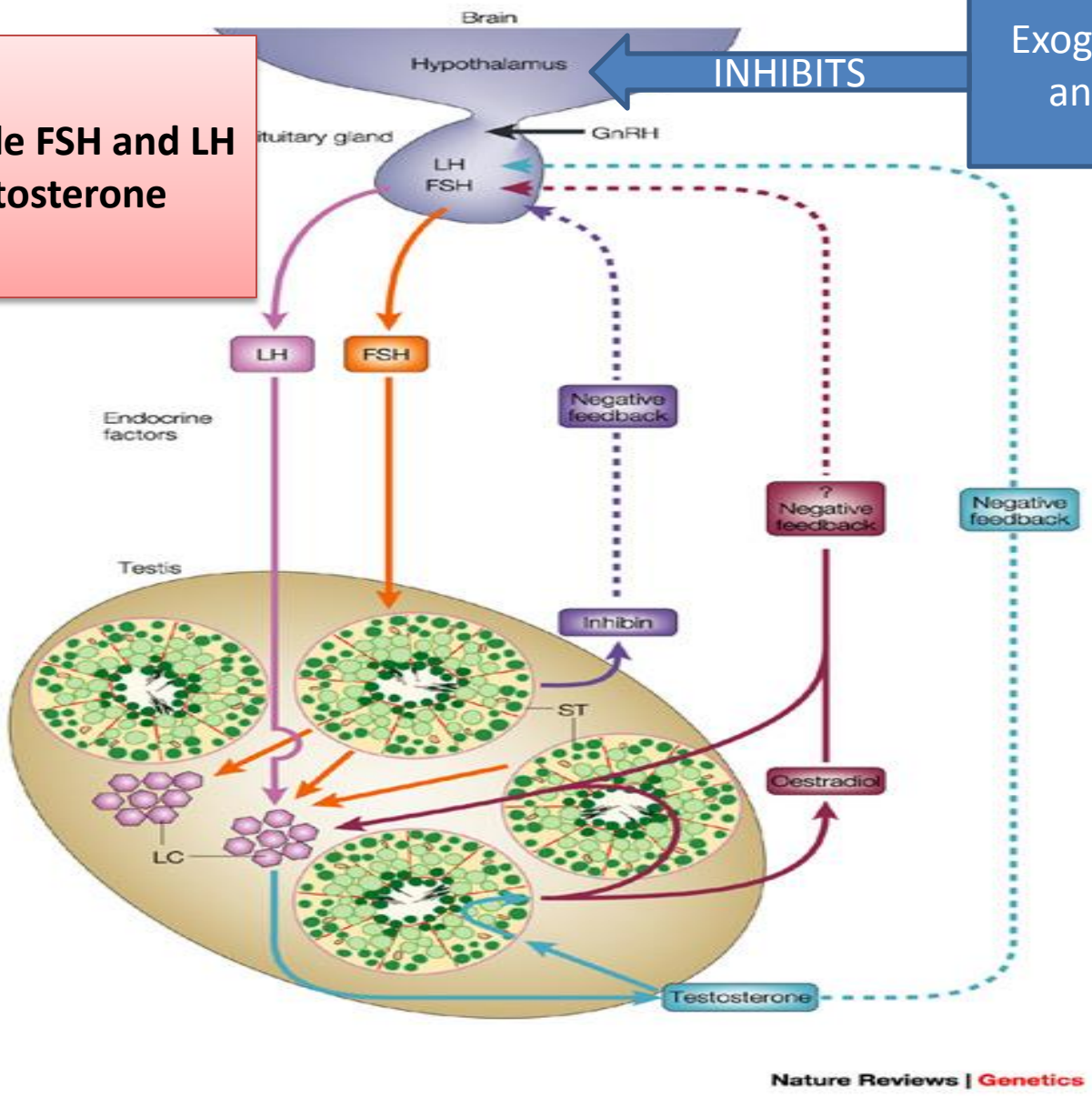


Iatrogenic hypogonadism

Undetectable FSH and LH
Low Testosterone

Exogenous steroids and androgens

INHIBITS



54 year-old man

- ED with loss of libido
- Past Mhx:
  - Type 2 DM since 2003 (BMI = 36)
  - HT
- Non-smoker, alcohol 18 units/week
- **Rx:** Metformin, pioglitazone, losartan, simvastatin
- Serum testosterone [1200] = 7.9 [9-32]

The endocrinologist's dilemma!

- Does this man have 'true' hypogonadism?

- Will he benefit from testosterone replacement?

Does he have ‘true’ hypogonadism?

- History is important
  - Onset of symptoms
  - Local testicular pathology
  - Markers for other pituitary hormone problems
- Examination
  - Absence of secondary sexual characteristics
- Biochemistry and imaging
  - Always measure T in the morning
  - Exclude pituitary disease
  - Ensure causes for primary hypogonadism have not been missed
  - BMD

Type 2 DM and obesity

- Total T is reduced
  - Lower SHBG levels
- Free T is also reduced
  - Direct effect from the HT [GnRH]
- Circadian rhythm is blunted

Hypogonadotrophic hypogonadism

Does he have ‘true’ hypogonadism?

- Once primary hypogonadism and pituitary disease are ruled out:
  - Case rests on finding evidence of hypogonadism clinically

Will he benefit from testosterone replacement?

- Possibly, if there is evidence of deficiency clinically

- If not
  - Literature often contradictory
  - Risks versus Benefits

Benefits versus Risks

Benefits

- Improve ED and libido
- ↑muscle mass
- ↑BMD
- ↓Visceral fat
- Improved mood
- ? QOL improvement

Risks

- Fluid retention
- Gynaecomastia
- Acne/oily skin
- ↑ haematocrit
- ↓ HDL cholesterol
- ↑BP
- ↑ risk of BHP and Ca Prostate
- Behaviour change
- ↓endogenous T production

Thank you for your attention

Questions and discussion