Trans-gender Medicine & the Endocrinology of gender

David Price

Trans female 38 years

- She knew she “was in the wrong body” from her earliest memories
- Married and divorced
- Living as a woman since 2015
- Uncertain if she wanted reassignment surgery
- Aspiring professional performer
  - Concerned about receding hair line
- Seen in Tavistock Clinic London
  - Approved for hormone Rx

Trans female 38 years

- Very unhappy about delays
- Started on triptorelin and estradiol valerate
- Followed up in clinic

Gender dysphoria

Terminology

- Trans-female
- Trans-male
- Cis-gender
- Gender neutral
- Gender fluid
- Intersex states
- Gender phenotype
- Gender perception

“Gender is not accurately captured by the traditional male and female dichotomy of sex. Instead, it is a complex social system that structures the life experience of all human beings”

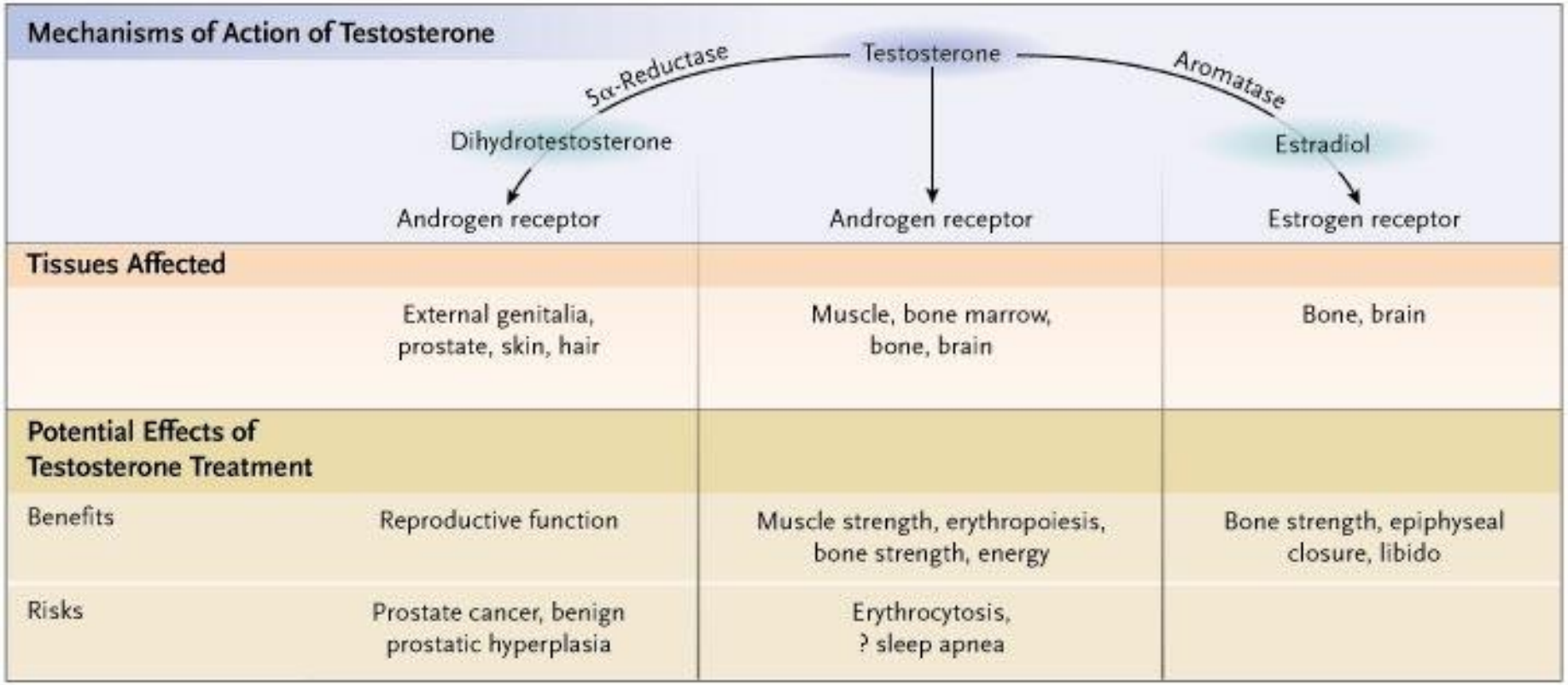
Heise et al Lancet 2019

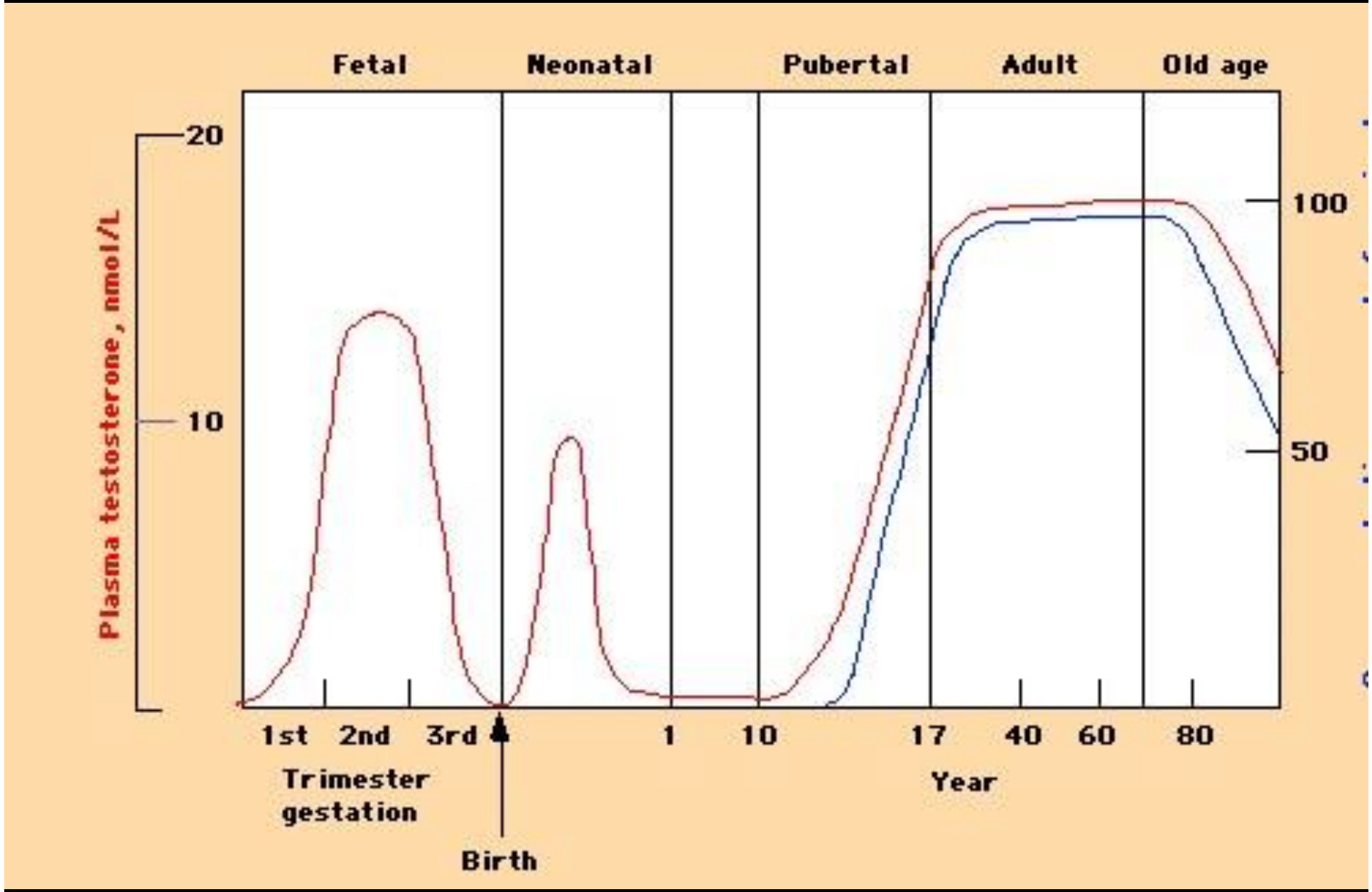
Gender dysphoria

- Discordance between gender phenotype and gender perception
- 90% male to female in UK
- What determines gender phenotype and gender perception?

NB: Intersex states, sexuality and transvestitism are separate issues.


AYUNTAMIENTO
DELEGADO GUBERNATIVO
(C) MARK TOMLINSON


Mechanisms of Action of Testosterone
Testosterone
5α-Reductase
Aromatase
Dihydrotestosterone
Estradiol
Androgen receptor
Androgen receptor
Estrogen receptor
Tissues Affected
External genitalia, prostate, skin, hair
Muscle, bone marrow, bone, brain
Bone, brain
Potential Effects of Testosterone Treatment
Benefits
Reproductive function
Muscle strength, erythropoiesis, bone strength, energy
Bone strength, epiphyseal closure, libido
Risks
Prostate cancer, benign prostatic hyperplasia
Erythrocytosis, ? sleep apnea


Fetal
Neonatal
Pubertal
Adult
Old age
Plasma testosterone, nmol/L
20
10
100
50
1st
2nd
3rd
1
10
17
40
60
80
Trimester
gestation
Year
Birth

Androgen insensitivity syndrome

Gender phenotype

- Exposure to neonatal androgens central to development of male neonatal phenotype (external genitalia)
  - Animal model data
  - Male foetuses exposed to antiandrogens are feminised (Wolf 2002)

- Process completed at puberty
- In the absence of androgens the phenotype will be female

Gender Identity

Discordant Sexual Identity in Some Genetic Males with Cloacal Exstrophy Assigned to Female Sex at Birth

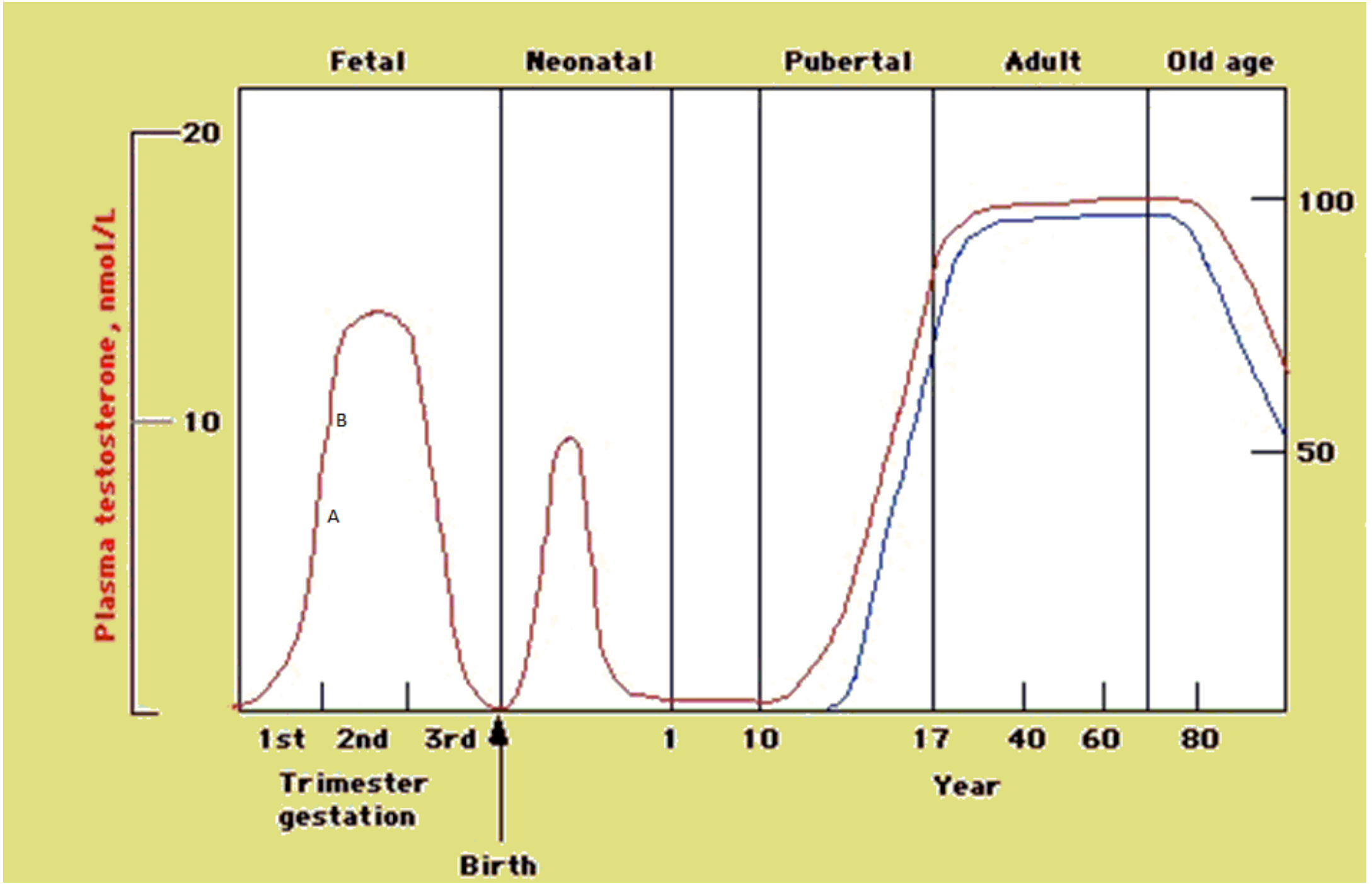
William G. Reiner and John P. Gearhart

NEJM Jan 22nd 2004

- 14 reassigned female identity as neonates
  - Surgery included orchidectomy
- Follow up at 5 to 16 years
- 8 of 14 subjects assigned to female gender declared themselves male
- 2 raised as males remained male
- All 16 had moderate-to-marked interests & attitudes considered typical of males

Gender identity

- Neonatal exposure to androgens has a central role
- More evidence comes from CAH
  - 50-60% identify as male (Meyer-Bahlberg et al 2004; Cohen-Ketteniset al 2005)
- Other factors also contribute
- Most individuals with gender dysphoria do not have any disorder of sexual development or chromosomal abnormality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Puberty

- Skeletal changes
- Increased muscle mass
- Facial, body, pubic and axillary hair
- Male pattern hair loss
- Changes to larynx and voice
- Behavioural changes

Changes at puberty

- Many irreversible
- Phenotypic appearance better if puberty blocked
  - An ethical and medico-legal minefield
  - September 2021 Court of Appeal overturned ban on treating under 16s
  - Endocrine Society (US) 2017 recommended against puberty blocking
- Some changes persist after transition
  - Skeletal changes
  - Muscle mass (to a degree)

- Trans-female athletes have advantage despite prolonged androgen suppression
- IOC previously required trans athletes have suppressed androgens
- 2021 issued “Framework on Fairness”
  - Delegated responsibility to sporting bodies
  - “any resrictions ….. demonstrate consistent, unfair, disproportionate competetive advantage in performance and/or an unpreventable risk to the safety of other athletes”
- World rugby 2021 banned trans women playing women’s rugby

Management of gender dysphoria

- 4 centres in England and Wales
  - London, Leeds, Exeter & Cardiff

- Triadic therapy, 3 stages-
  - Social gender role change
  - Hormone treatment
  - Gender reassignment surgery

Hormone therapy: male to female
A crucial stage on a long and difficult journey

- Reduction of androgens
  - GnRH agonists eg triptorelin
    - Initial stimulation of testosterone blocked by cyproterone
    - Can produce androgen deficiency
  - Alternatives- cyproterone, spironolactone

- Oestrogen replacement
  - Estradiol valerate
  - Aim to achieve serum estradiol levels 400-600 pmol/l

Hormone therapy: male to female

- Changes in 3-12 months
- Reduced facial and body hair
- Reduced libido
- Redistribution of body fat
- Scalp hair loss arrests
- Breast development up to 2 years

Hormone therapy: male to female
Adverse effects

- Thromboembolic disease

- Prolactinomas
- Breast cancer
- Vascular disease
- Gall stones
- Reduced libido

Reduced risk of prostate cancer

Causes of death?

Hormone therapy: female to male

Testosterone, parenteral or transdermal

- Oily skin, acne
- Facial and body hair growth
- Increased muscle mass and strength, fat redistribution
- Cessation of menses
- Deepening of voice
- Clitoral enlargement

Hormone therapy: female to male

Monitoring

- Aim to achieve serum levels in normal (male) range
- Haematocrit
- ? Mastectomy

- Cessation of menses
  - If menses continue consider a progesterone, GnRH agonist or endometrial ablation

Hormone therapy: female to male
Adverse effects

- Erythrocytosis
- Liver dysfunction
- IHD
- Hypertension
- Breast and uterine cancer

Trans female 38 years

6 months later

- Early breast development
- Reduced facial hair
- Improved mood and persona

Gender dysphoria

Complex condition in which there is discordance between-

- gender phenotype
  - Which is determined by androgen exposure in utero

    and
- gender perception
  - Which is multifactorial but in utero androgens have a key role
- Androgens may have these effects at different times in fetal development

Management of gender dysphoria

- Requires specialist centres with the appropriate multidisciplinary team to undertake assessment & counselling and provide support
- Hormonal management
  - Female to male relatively straightforward
  - Male to female more complex
  - Both are associated with potential risks and require long-term monitoring
- Results can be very rewarding