Androgen deficiency (AD)

- Androgen deficiency is common, affecting 1 in 200 men under 60 years.
- The clinical presentation may be subtle and its diagnosis overlooked unless actively considered.

The GP’s role

- GPs are typically the first point of contact for men with symptoms of AD.
- The GP’s role in the management of AD includes clinical assessment, laboratory investigations, treatment, referral and follow-up.

Diagnosis

Medical history

- Change in general well-being or sexual function**
- Degree of virilisation
- Prescription or recreational drug use
- Co-existent medical illness*

* Pituitary disease, thalassaemia, haemochromatosis. ** AD is an uncommon cause of ED. However, all men presenting with ED should be assessed for AD.

Examination and assessment of clinical features of AD

Pre-pubertal onset – Infancy
- Micropenis
- Small testes

Peri-pubertal onset – Adolescence
- Late/incomplete sexual and somatic maturation
- Small testes
- Failure of enlargement of penis and skin of scrotum becoming thickened/pigmented
- Failure of growth of the larynx
- Poor facial, body and pubic hair
- Gynaecomastia
- Poor muscle development

Post-pubertal onset – Adult
- Regression of some features of virilisation
- Mood changes (low mood, irritability)
- Poor concentration
- Low energy (laziness)
- Hot flushes and sweats
- Decreased libido
- Reduced beard or body hair growth
- Low semen volume
- Gynaecomastia
- Reduced muscle strength
- Fracture (osteoporosis)
- Erectile dysfunction (uncommon)

Laboratory assessment of AD

- Normal range serum total testosterone 8–27 nmol/L
- Two morning samples of serum total testosterone*, taken on different mornings.
- Guidelines for the diagnosis of AD in men aged 40+:
  - Testosterone <8 nmol/L**
  - Testosterone 15 nmol/L** and LH >1.5 times upper limit of eugonadal reference range for young men

* If a second total testosterone sample is indicated, a LH level should also be ordered. ** These criteria apply to men without underlying pituitary or testicular pathology.

Other investigations

- SHBG/calculated free testosterone (selected cases – obesity, liver disease)
- Semen analysis (if fertility is an issue)
- Karyotype (if suspicion of Klinefelter’s syndrome, 47XXY)

Investigations if low total testosterone with normal or low LH/FSH:
- Serum prolactin (prolactinoma)
- Iron studies (haemochromatosis)
- MRI (various lesions)
- Olfactory testing (Kallmann’s syndrome)
Klinefelter’s syndrome

- Is the most common genetic male reproductive disorder (1 in 650 men)
- Is the most common cause of hypogonadism
- Reproductive features: small firm testes <4 mL, infertility, failure to progress through puberty, gynaecomastia, eunuchoidal proportions, diminished or absent body hair, decreased skeletal muscle mass
- Other: learning difficulties & behavioural problems, particularly in adolescence

Refer to Clinical Summary Guide 10

Clinical notes and contraindications

- Absolute contraindications to TRT are known or suspected hormone-dependent malignancies (prostate or breast) or haematocrit >55%
- Relative contraindications include haematocrit >52%, untreated sleep apnoea, severe obstructive symptoms of BPH and advanced congestive heart failure
- Fertility: Exogenous testosterone results in suppression of spermatogenesis in eugonadal men. For men with secondary causes of AD, and in whom fertility is desired, gonadotropin therapy should be instituted
- Low-normal serum testosterone common in obesity or other illness may not reflect AD. Address underlying disorders first
- Withhold treatment until all investigations are complete
- Certain adverse effects must be prospectively sought, especially in older men, including polycythemia and sleep apnoea, however the testosterone preparations discussed do not cause abnormal liver function

Causes of hypogonadism (AD)

Testicular (primary)
- Chromosomal: Klinefelter’s syndrome (most common cause)
- Undescended testes
- Surgery: bilateral orchidectomy
- Trauma
- Infection: mumps orchitis
- Radiotherapy/chemotherapy/drugs (spironolactone, ketoconazole)
- Systemic disease: haemochromatosis, thalassaemia, myotonic dystrophy

Hypothalamic-pituitary (secondary)
- Idiopathic hypogonadotrophic hypogonadism: Kallmann’s syndrome
- Pituitary microadenoma (<1 cm) or macroadenoma (>1 cm)
  - functional or non-functional: in men typically macroprolactinoma
- Other causes of hypothalamic pituitary damage: surgery, radiotherapy, trauma, infiltrative disease such as haemochromatosis

Follow-up

Monitoring TRT is essential
- Testosterone levels: results should be interpreted in context of the treatment modality being used
- Prostate: DRE and PSA, as per standard guidelines
- Cardiovascular risk factors: blood pressure, diabetes, lipids, as per guidelines
- Osteopenia/osteoporosis (fractures): bone density-DEXA
- Polycythemia: haemoglobin and haematocrit, pre-treatment, at 3 and 6 months, and annually thereafter
- Sleep apnoea: clinical assessment for presence of sleep apnoea (polysomography)

Specialist Referral

- Refer to an endocrinologist to plan long-term management of AD
- Refer to a fertility specialist as needed
- Refer to a paediatric endocrinologist if >14.5 years old with delayed puberty