ANDROLOGY AUSTRALIA

ANDROGEN DEFICIENCY

DIAGNOSIS AND MANAGEMENT

CLINICAL SUMMARY GUIDE 4

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

Androgen Deficiency and the Ageing Male

- Ageing is associated with a 1% decline per year in serum total testosterone starting in the late 30's
- The decline may be more marked in men who have obesity
- Some estimates suggest that AD affects 1 in 10 men over 60 years
- Acute and chronic illness result in decreased serum testosterone and may present with AD-like symptoms
- The role of Testosterone Replacement Therapy (TRT) in older men with modest declines in serum testosterone remains controversial
- The most consistent effects of TRT are on:
  - body composition
  - selected aspects of mood and cognition
  - libido
- Studies of men with age related AD have not shown any significant improvement in sexual function (erectile function) with TRT
- The use of TRT for ageing men who do not meet the established criteria (PBS guide) is not recommended
- Older men treated outside of guidelines should be informed that long-term risks/benefits are not yet documented

Diagnosis

Medical history

- ❑ Undescended testes
- ❑ Surgery of the testes
- ❑ Pubertal development
- ❑ Previous fertility
- ❑ Genito-urinary infection
- ❑ Co-existent medical illness*
- ❑ Change in general well-being or sexual function**
- ❑ Degree of virilisation
- ❑ Prescription or recreational drug use

Refer to Clinical Summary Guides 1-3

* Pituitary disease, thalassemia, 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 growth of the larynx
- Genital (failure of enlargement of penis and skin of scrotum becoming thickened/pigmented)
- Poor muscle development
- Poor facial, body and pubic hair
- Gynaecomastia

Post-pubertal onset – Adult
- Regression of some features of virilisation
- Mood changes (low mood, irritability)
- Poor concentration
- Low energy (lethargy)
- 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 8-27nmol/L
- Two morning samples of serum total testosterone*, taken on different mornings.
- Guidelines for the diagnosis of AD in men aged 40+:
  - Testosterone <8nmol/L**

  OR
  - Testosterone 8-15nmol/L** and LH >1.5 x 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)

Management

Assessment of treatment indications

PBS-approved indications for the prescription of testosterone are:

- Micropenis, pubertal induction, or constitutional delay of growth or puberty, in males <18 years
- AD in males with established pituitary or testicular disorders
- AD (confirmed by at least 2 morning samples) in males aged 40+ who do not have established pituitary or testicular disorders other than ageing

Testosterone replacement therapy (TRT)

Treatment options	Dosage
Injections (IM)	
Sustanon®, Primoteston®	250mg every 2-3 weeks
Reandron®	1000mg every 12 weeks range: 10 - 14 weeks (loading dose 6 weeks after initiating therapy e.g. 0, 6, 18, 30 weeks)
Subcutaneous implants	
Organon	3-4 x 200mg pellets every 4-6 months
Transdermal patch	
Androderm®	5mg applied nightly
Transdermal gel	
Testogel®	50mg/5g applied daily
Transdermal cream	
Andromen®, Andromen Forte®	2% or 5% (2-6cm) applied daily
Oral undecanoate	
Andriol Testocaps®	160-240mg in 2-3 divided doses daily

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
- **Osteopaenia/osteoporosis (fractures):** bone density-DEXA
- **Polycythaemia:** 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

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

Hypothalamo-pituitary (secondary)

- Idiopathic hypogonadotrophic hypogonadism: Kallmann's syndrome
- Pituitary
  - Macroadenoma: non functional
  - Microadenoma: prolactinoma
  - Panhypopituitarism: post surgery or radiotherapy
- Haemochromatosis, thalassaemia

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 <4mls, 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 hematocrit >55%
- **Relative contraindications** include hematocrit >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

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