

Androgen Use, Misuse and Abuse



HEALTHY MALE
Generations of healthy Australian men

The general practitioner's role

General practitioners have a role in identification of androgen abuse and the management of its cessation, usually under the guidance of an experienced endocrinologist.

Overview

The extent of androgen abuse is unknown, however, it is estimated that lifetime use in the general population is probably 1-5% globally, with prevalence at least 50 times higher in men than women¹. Two percent of Australian secondary school students report using performance and image enhancing drugs (including androgens²).

Androgen abuse often involves massive doses and multiple drugs taken simultaneously that provide a vastly higher level of androgen action than required for physiological replacement in legitimate androgen deficiency¹.

Commonly abused androgenic substances^{1,3}

Substance	Common or brand name	Route
Boldenone undecylenate	Equipoise, Parenabol	IM
Clostebol acetate	Steranabol	IM
Chlorodihydrodromethyl-testosterone	CDMT	Oral*
Dihydrotestosterone		Oral*, transdermal, IM
Drostanelone propionate	Dromostanalone, Masteron	IM
Fluoxymesterone	Halotestin, Ultandren	Oral*
Formebolone	Esiclone	Oral*
Mesterolone	Proviron	Oral*
Metandienone	Methandrosteneolone, Dianabol	Oral*
Methenolone acetate	Primabolon	IM
Methyltestosterone	Android, Metandren, Testred	Oral*
19-Nortestosterone	Nandrolone, Deca-Durabolin	IM
Oxandrolone	Anavar	Oral*
Oxymetholone	Anadrol	Oral*
Stanozolol	Winstrol	Oral*
Testosterone	Sustanon, Testo depot, Nebido	IM
Tetrahydrogestinone	THG, The Clear	Oral*
Trenbolone ethanate	Trenabol, Parabolan	IM

* All orally taken androgenic compounds are alkylated and therefore hepatotoxic.

Definitions⁴

Legitimate androgen uses

Testosterone replacement for androgen deficiency due to pathological hypogonadism

- Primary testicular failure (hypergonadotrophic hypogonadism)
 - Klinefelter syndrome and other genetic disorders
 - Testicular trauma, torsion, infection or excision (orchidectomy)
 - Testis atrophy
- Secondary testicular failure (hypogonadotropic hypogonadism)
 - Congenital cause (e.g., Kallman's syndrome and variants)
 - Acquired (prolactinoma, pituitary disease, surgery, radiotherapy)
- Gender affirming treatment of transgender and gender diverse people⁵
- Delayed puberty

Pharmacological use for non-androgen deficiency

(Typically using synthetic androgen receptor modulators rather than testosterone).

- Osteoporosis (including corticosteroid-induced bone loss)
- Anaemia (due to bone marrow or renal failure)
- Advanced breast cancer
- Cachexia or wasting
- Burns
- Hereditary angioedema

Research

- Functional low testosterone, chronic disease and ill health
- Male contraception

Androgen misuse

Use without valid medical indication or despite contraindication

- Male infertility
- Sexual dysfunction (in absence of androgen deficiency due to pathological hypogonadism)
- "Low T (testosterone)", "late-onset hypogonadism", "male menopause", "andropause", functional hypogonadism
- Non-specific symptoms (e.g., lethargy, tiredness)
- Aging

Androgen abuse

Use without medical indication

- Physical performance (e.g., increased strength, endurance, recovery)
- Physical appearance (e.g., increased muscle mass)
- Occupational (e.g., security staff, police, armed forces)

Compounds commonly used in combination with androgens³

Androgen abuse often involves administration of multiple substances ("stacking") and various dosing regimens. Cycles of use, lasting for several weeks or months (interspersed with periods of abstinence, for "recovery") are usual, with an entrenched but incorrect belief that it is possible to maximise anabolic effect while minimising androgenic impact³. This is biologically implausible given the action of androgens through a single type of androgen receptor.

The below list of medications, commonly used in combination with androgens, is for information only, not as an endorsement of clinical use. At least one of the following applies to these drugs:

- There is no evidence to support use in the context of androgen misuse or abuse or for performance or image enhancement
- Usage is 'off label'
- Safety is uncertain
- Rationale is based on poor understanding of complex endocrinological mechanisms.

Substance	Details
Clenbuterol	A veterinary β 2-adrenergic receptor agonist, used to increase muscle mass and reduce body fat
Ephedrine, Synepherine	Used to reduce body fat
Growth hormone	Used for its anabolic and lipolytic properties, and its potential to reduce muscle and tendon rupture
Growth hormone releasing hormones/peptides (e.g. Modified GRF(1–29), Sermorelin, Ipamorelin, GHRP-2), HGH analogues (e.g. HGH Fragment 176–191)	Falsely claimed to increase muscle mass and do not increase GH levels
Human chorionic gonadotropin (hCG)	Used to promote testicular testosterone production
Recombinant human luteinising hormone (rLH)	May be promoted for stimulation of the testes but it is difficult to manufacture and exceedingly expensive, so marketed preparations are likely to be fake
Insulin-like Growth Factor-1 (IGF-1)	Used to increase muscle mass
Clomiphene citrate and aromatase inhibitors	Used to prevent gynaecomastia, promote testes growth and/or hasten recovery of the suppressed HPT axis
Insulin	Used (often in combination with growth hormone) to increase glucose uptake by muscle and adipose tissue, and inhibit protein breakdown
Prohormones (e.g., androstenedione, dihydroepiandrosterone)	Used as substrate for androgen production
Thyroid hormone (synthetic T3, T4 or natural extracts)	Used to increase metabolism, thereby reducing body fat
Prescription drugs (e.g., sedatives, analgesics, anti-inflammatories, PDE5 inhibitors, antidepressants, diuretics)	Used to treat unwanted side effects of androgen abuse
Illicit drugs (amphetamine, cocaine, cannabis, heroin)	May be used to lose or maintain weight, relax, or relieve pain.

Antiandrogens (clomiphene, tamoxifen) and aromatase inhibitors (letrozole, anastrozole, exemestane) are used in an attempt to reduce the risk or extent of androgen-induced gynaecomastia. This is often unsuccessful, and these drugs have inherent adverse effects such as bone loss and increased thromboembolic risk.

These drugs, together with injectable hCG, are also used as "post-cycle therapy" in an attempt to reverse the androgen-induced suppression of sperm and testosterone production. However, there is no evidence these regimens restart the reproductive system.

Sources of androgens and other substances

The Internet is a common source of androgens and other drugs used in combination, but there is concern about the actual content, purity and safety of any agents obtained in this way⁶.

People who misuse or abuse androgens may attempt to obtain prescriptions from doctors⁷, whose compliance would constitute professional misconduct.

Dietary supplements

Contamination of protein supplements with biologically active androgens^{8,9,10} can result in an identical clinical and biochemical picture to androgen abuse. Close examination of products acquired through gyms or the Internet is required.

The Australian Institute of Sport classifies dietary supplements according to scientific and practical considerations related to safety, efficacy and permissibility, and provides guidance for choosing safe products¹¹.

Patients should be advised to eat healthy food rather than use supplements. Supplements do not contain all the nutrients contained in whole foods and cannot compensate for a poor diet¹².

Diagnosis of androgen abuse

An effective means of knowing if a patient is abusing androgens is to ask them¹, after establishing a trusting, non-judgemental relationship. For patients suspected of androgen abuse, or who seek treatment for androgen abuse or its side effects, an appropriate medical history, physical examination and laboratory tests should be undertaken.

Typically, serum LH, FSH and SHBG will be suppressed. Serum testosterone levels will vary. High levels will be obtained if testosterone administration is recent. Low levels will occur if synthetic androgens (which are not detected by testosterone immunoassays) are used, or during the withdrawal phase when hypogonadotropic hypogonadism is induced.

Medical history

Social factors

- Education level
- Profession or occupation
- Sports and recreational activities (gym or other athletic activities, professional training)
- Marital and fertility status
- Support network
- Alcohol and other drug use
- Other types of abuse

Medical and psychological factors

- Puberty
- Prior reproductive pathology
- Presenting complaint(s)
- Psychiatric health
- Sleep
- Sexual function and reproductive health
- Current diseases
- Current medications
- Current dietary supplement use
- Allergies/hypersensitivity
- Family history (especially prostate and cardiovascular disease)

Physical examination

- General appearance (height, weight, body mass index, muscularity)
- Testicular size and consistency, or cliteromegaly
- Skin (acne, stretch marks)
- Chest (gynaecomastia)
- Hair (premature baldness, body hair)
- Abdomen (hepatic enlargement)
- Heart and lungs (pulse, blood pressure, signs of heart failure, cardiac murmurs)
- Neurological
- Musculoskeletal

Investigations

Laboratory tests

- Reproductive hormones (testosterone, sex hormone binding globulin, luteinising hormone, follicle stimulating hormone)
- Other hormones, when considering hypothalamo-pituitary-adrenal function (insulin-like growth factor-1, thyroid stimulating hormone, T3, T4, prolactin)
- Liver function (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, bilirubin)
- Routine biochemistry and haematology (renal function, glucose, full blood count, lipids)

Imaging

- Liver scan, MRI or CT scan – rarely required unless suspicion of hepatic dysfunction (fatty liver, peliosis or tumor)

Physical signs of androgen abuse

- Rapid and significant weight gain (approx. 10 kg in 2-3 months)
- Muscular physique (disproportionate muscle growth around chest, neck and shoulders)
- Preoccupation with physical fitness, diet or gym attendance dominating lifestyle
- Severe acne (mainly on back, shoulders and chest)
- Stretch marks (usually between biceps and pectoral muscles, possibly back and thighs)
- Excess body hair and/or accelerated baldness
- Hypertension
- Injection site swelling, tenderness, redness
- Tendon and muscle tears
- Abnormal blood lipids
- Abnormal liver function

Male-specific physical signs of androgen abuse

- Gynaecomastia
- Erectile dysfunction
- Subfertility
- Testicular atrophy

Female-specific physical signs of androgen abuse

- Deeper voice
- Increased growth of facial and body hair
- Abnormal menstruation
- Clitoral enlargement

Psychological signs of androgen abuse

- Aggression
- Impulsivity
- Altered libido
- Anxiety
- Dysphoria
- Depression
- Empathy disorder
- Jealousy
- Muscle dysmorphia
- Mood instability
- Panic attack
- Psychosis
- Reduced mentalising capacity
- Sleep disorders
- Suicidal ideation
- Suicide attempt
- Violence
- Worry

Adverse psychological effects of androgen abuse

- Irritability
- Nervousness
- Aggressiveness
- Recklessness
- Self-aggressiveness
- Dependence
- Withdrawal syndrome
- Depression
- Suicidal ideation

Adverse physical effects of androgen abuse

Haematological system

- Polycythaemia

Cardiovascular system

- Dyslipidaemia
- Coronary heart disease
- Myocardial infarction
- Hypertension
- Abnormal ECG
- Arrhythmia
- Left ventricular hypertrophy
- Hypertrophic cardiomyopathy
- Dilated cardiomyopathy
- Heart failure
- Sudden cardiac failure

Hepatic system

- Cholestasis
- Hyperbilirubinaemia
- Steatosis
- Peliosis
- Adenomas
- Hepatocellular carcinoma
- Liver coma

Integumentary system

- Acne
- Striae distensae
- Profuse sweating
- Alopecia
- Hirsutism

Renal system

- High creatinine
- High cystatin C
- Glomerulosclerosis
- Cholemic nephrosis (bile cast nephropathy)
- Renal failure

Reproductive system

Male

- Decreased testis volume
- Impaired spermatogenesis
- Infertility
- Low libido
- Erectile dysfunction
- Gynaecomastia
- Hypogonadism

Female

- Anovulation
- Amenorrhoea
- Dysmenorrhoea
- Infertility

Management of androgen abuse

There are no clinical trials of managing patients from the public who abuse androgens¹³, so information to guide practice¹⁴ is limited to that from observational studies^{15, 16, 17}.

Treatment usually requires a multidisciplinary approach involving the combined efforts of the general practitioner, endocrinologist and psychologist. A formal care plan could facilitate this approach and would also facilitate patient education for long-term behaviour change. The focus of care should be for the expeditious and permanent cessation of this dangerous lifestyle choice.

A supportive approach that is analogous to that used for other licit and illicit social drugs (e.g., alcohol, caffeine, cocaine) and behavioural disorders (e.g. anorexia nervosa, muscle dysmorphia) is the best option. Encouragement and advice that reproductive function will recover with time, and that patience is necessary, may be helpful.

Referral for psychological assessment and possible therapy may benefit patients who abuse androgens because of body image issues¹⁸.

Patients who are unwilling to cease androgen abuse should be advised of the adverse effects of continued use, focussing on the potential consequences for their fertility and long-term cardiovascular health. They should be counselled about the health risks associated with the use of potentially unknown substances and self-injecting.

Medical practitioners should not allow themselves to become resources for ongoing drug supply, including medications used in this subculture (e.g., antiestrogens, hCG), or to facilitate continuation of androgen abuse. The development of a trusting clinician-patient relationship may facilitate discontinuation of androgen abuse. A care plan should be established, aimed at cessation, ideally performed by a supportive team with endocrine and psychological expertise.

Discontinuing androgen abuse

People who abuse androgens develop psychological and physical dependence. Withdrawal symptoms from discontinuation of androgen abuse include decreased sexual drive and a flu-like syndrome consisting of fatigue, headache, musculoskeletal pain and insomnia, followed by depression¹⁹. These features are like those from withdrawal from caffeine or benzodiazepines, less severe than those from withdrawal from nicotine, and without the potential fatality of withdrawal from alcohol, amphetamines or opiates.

There is no legal pathway for the prescription of testosterone or synthetic androgens without a legitimate medical indication.

Fertility recovery

Many men who abuse androgens seek assistance with discontinuation because of infertility. Cessation of androgen abuse often allows recovery of fertility within 6-18 months^{20, 21}. Recovery of endogenous gonadotrophins, testosterone and spermatogenesis, may take many months with the duration of recovery depending mainly on the time since cessation. The outlook for recovery of fertility and testosterone production is generally very good but prolonged.

Ad hoc treatment with anti-estrogens, aromatase inhibitors or hCG lacks any sound evidence basis for safety and efficacy. If there is claimed urgency for restoration of spermatogenesis (e.g. restoration of fertility for a man with a female partner of advanced age), consultation with an experienced endocrinologist is essential because potential treatment may be subject to restrictions based on 'off label' uses and/or uncertain safety considerations.

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This resource was produced in response to requests from Australian General Practitioners, for information to help them respond to androgen abuse. Healthy Male supports GPs in their goal of helping patients to cease this damaging behaviour.

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