Essential blood testing in the patient using androgenic anabolic steroids:
a clinical practice guideline for primary care

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Introduction

As society's emphasis on physical appearance intensifies, individuals are increasingly turning to image- and performance-enhancing drugs (IPEDs) to help them surpass their genetic potential.[1] GPs are no strangers to these people; indeed, it is estimated that over 1 million people in the UK are using IPEDs, such as androgenic anabolic steroids (AAS),[2] and the current authors' unpublished audit data from West Yorkshire, UK, demonstrated that around 20% of all patients presenting to primary care with hypogonadism was secondary to cessation of AAS. However, the conventional assumption that one can readily identify users of AAS based on their physical appearance alone is becoming obsolete. Indeed, exploring biomarkers, behavioural patterns, and psychological indicators will significantly improve the accurate identification of these patients.[2] The following recommendations have been developed by a multidisciplinary team involving both primary and secondary care. By integrating evidence-based data from sources including *BMJ Best Practice* and other original publications, alongside the current authors' expert opinion and experience with users of AAS, these guidelines provide a simple, pragmatic approach to management of these individuals.[3]

Why do we need to identify users of AAS?

In the absence of clinical context, interpretation of blood abnormalities can lead to inappropriate or unwarranted referrals to secondary care, stretching an already burdened healthcare system. Moreover, these patients may then be subject to unnecessary investigations, for example, an extensive liver or pituitary screen.

Presentation of patients using AAS

Users of AAS may develop none, some, or a sequelae of clinical signs and symptoms described in Box 1. Typically, they view their steroid use in a positive, health-promoting context, and are unlikely to attribute this with any deleterious effect.[4] This likely accounts for their resilience in disclosing the relevant information

Box 1. Clinical signs of AAS use

Clinical factor	Details
Consumption of nutritional supplements	Many users of AAS will simply refer to their usage by referencing protein shakes, for example.
Increased weight gain and muscular build	Steroid use results in fast gains with significant increases in lean body mass, which contributes to increased muscle mass
Increased appetite	Common with chronic use
Aggression and mood swings	Aggression, hostility, mood swings, and irritability (also known as 'roid rage') are possible with chronic use and maybe more common with certain AAS (that is, trenbolone)
Disproportionate muscular development of upper torso	Due to predominance of androgen receptors in upper body (that is, thorax, neck, shoulder, and upper arms)
Testicular atrophy	Common with chronic use
Acne and/or oily skin	Possible with chronic use
Striae or keloids	Possible with chronic use
Changes in libido/ impotence and infertility	Despite supra-physiological circulating levels of testosterone, suppression of testicular testosterone production results in infertility (reduction in sperm count). Fluctuating hormone levels and raised oestradiol can lead to erectile dysfunction
Cognitive changes	Includes confusion, forgetfulness, and distractibility. Depression and anxiety can develop on cessation of AAS. Steroid use may uncover a narcissistic personality
Gynaecomastia	Possible with acute/chronic use
Enlarged prostate	Possible with chronic use
Muscle and joint issues	Rapid muscle growth and development may lead to musculoskeletal strain. Gout, avascular necrosis, disc herniations, and knee (ligament/meniscal) and elbow injuries are common

AAS = androgenic anabolic steroids.

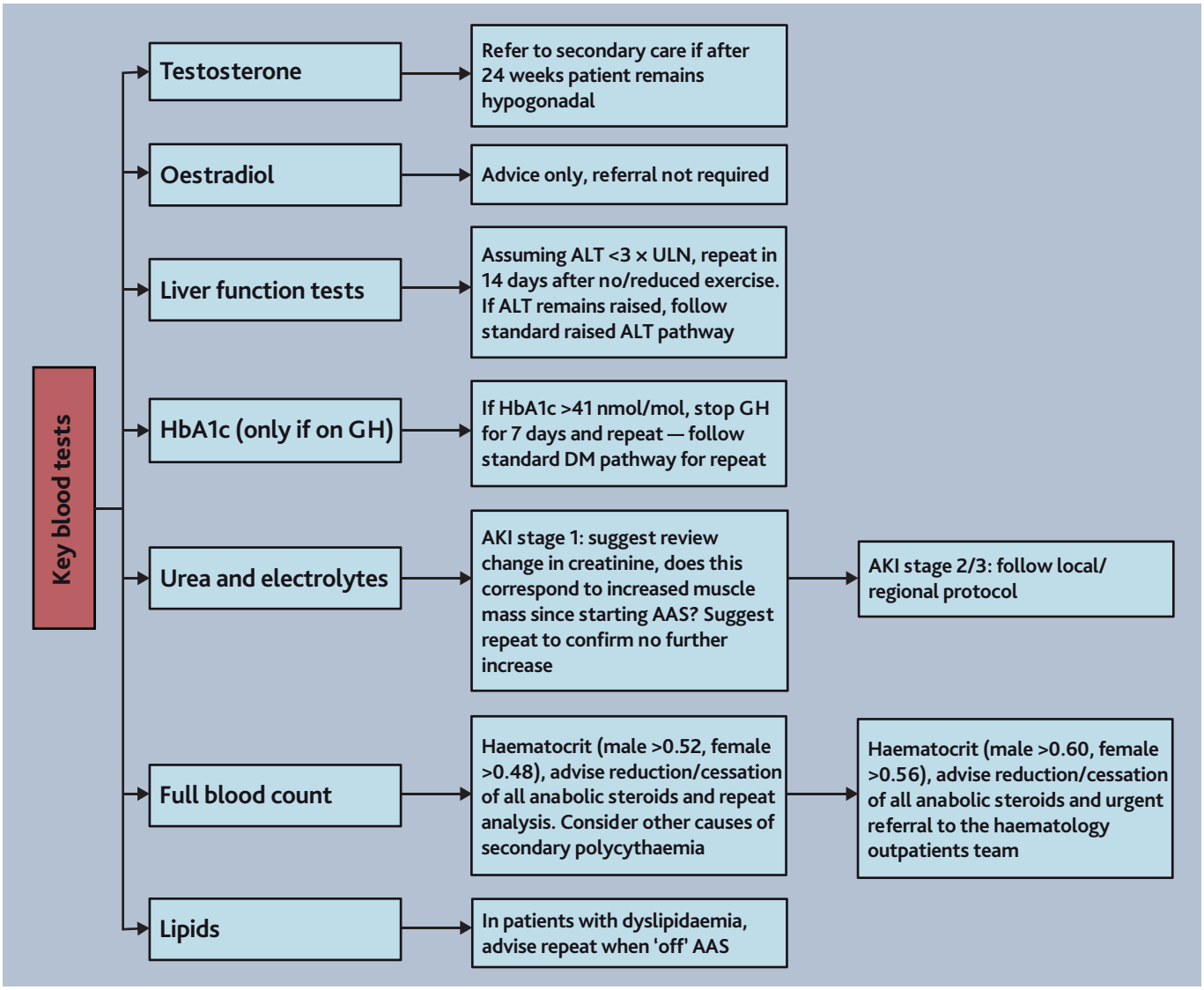

Figure 1. Summary of key blood tests to undertake and follow-up criteria for patients using AAS. AAS = androgenic anabolic steroids. AKI = acute kidney injury. ALT = alanine aminotransferase. DM = diabetes mellitus. GH = growth hormone. ULN = upper limit of normal.

during GP consultations. GPs should be frank when quizzing their patients who present with any of these findings, making it clear that non-disclosure may compromise their care.

Key blood tests to undertake

Testosterone (only to assess degree/severity of hypogonadism)

For patients cycling off AAS this blood test can determine if restoration of the hypothalamic pituitary testicular axis has occurred.

If patients are currently using testosterone there is no requirement to measure testosterone as it is likely to be above the analytical range of the laboratory assay.

Oestradiol

Testosterone is converted to oestradiol *in vivo* through the action of the aromatase enzyme; elevated levels may result in gynaecomastia and changes in libido. Users of AAS may experiment with aromatase inhibitors to decrease blood oestradiol levels.

Liver function tests

Oral steroids are often modified (17 alpha alkylation) to prevent breakdown on first pass through the liver; these esters can cause hepatotoxicity.

HbA1c (if on human growth hormone)

Human growth hormone (HGH) can increase blood glucose leading to diabetes mellitus.

Urea and electrolytes

Hypertensive renal disease secondary to steroid use may be detected. It is suggested that blood pressure also be measured.

Full blood count

Polycythaemia is a well-documented complication of supraphysiological doses of testosterone increasing the individuals' risk of cardiovascular events.

Lipids

Presence of dyslipidaemia (low HDL, high LDL) should be determined to advise on increased risk of cardiovascular complications.

What next if test results are abnormal?

Testosterone

Patients with testosterone <8 nmol/L (or <lower limit of normal for the laboratory) with inappropriately normal/low gonadotropins (that is, hypogonadotropic hypogonadism) regardless of time stated since cessation of AAS should have a repeat blood test in 12 weeks. If testosterone remains low on repeat but has increased (>2 nmol/L) then the patient should have a further repeat in 8–12 weeks. Only after around 24 weeks should the patient be referred to secondary care (endocrinology).[5] It should be noted that suppressed gonadotropins with normal testosterone would suggest continued exogenous use.

Oestradiol

Patients on AAS will likely have elevated oestradiol (>150 pmol/L) due to aromatisation of exogenous testosterone. Referral to secondary care is not warranted and treatment with aromatise inhibitors, although used experimentally by these individuals, should not be advised.

Liver function tests

To minimise detection of non-hepatic sources of raised alanine aminotransferase (ALT), and assuming ALT <3 × upper limit of normal, repeat testing 10–14 days after cessation of heavy weightlifting is recommended.[6] If ALT has normalised, referral is not indicated.

HbA1c

In patients with HbA1c in the pre-diabetic (42–47 mmol/mol)/ diabetic range (≥48 mmol/mol), the patient should be advised to discontinue HGH and testing repeated. Subsequent testing should follow local policy.

Urea and electrolytes/blood pressure

Creatinine is likely to be raised in patients with high muscle mass.

Acute kidney injury

For acute kidney injury (AKI) stage 1, a review change in creatinine should be suggested. Does this correspond to increased muscle mass since starting AAS? A repeat is suggested to confirm no further increase. For AKI stage 2/3, local/regional protocol should be followed.

Chronic kidney injury

As creatinine is likely to be raised, the formula used to estimate glomerular filtration rate may be misleading. This is referenced in NG203 (*Chronic Kidney Disease: Assessment and Management*), which states, *'Interpret eGFR creatinine with caution in adults with extremes of muscle mass, for example, in bodybuilders … underestimation of the GFR.'*[8] Regardless, any patient with chronic kidney disease 3, 4, or 5 should be reviewed as per local policy.

Full blood count

For elevated haematocrit (male >0.52, female >0.48), reduction/ cessation of all anabolic steroids and repeat analysis is advised. Other causes of secondary polycythaemia should be considered, that is, not only all anabolic steroids should be stopped but also smoking and alcohol reduction/cessation should be considered where appropriate.

For extremely raised haematocrit (male >0.60, female >0.56), reduction/cessation of all anabolic steroids is advised and an urgent referral to the haematology outpatients team made.

Lipids

In patients with dyslipidaemia, advise repeat when 'off' AAS. Referral to the lipid team is recommended if the repeat testing demonstrates any of the following:

cholesterol >9 mmol/L or non-HDL cholesterol >7.5 mmol/L

OR

cholesterol >7.5 mmol/L when aged <30 years

OR

triglyceride >10 mmol/L

OR

triglyceride 4.5–9.9 mmol/L WITH non-HDL cholesterol >7.5 mmol/L

Although referral/repeat is not required for HDL, patients with low HDL should be provided with the following information:

- for every 10% reduction in HDL, risk for coronary artery disease increases by 13%;
- low HDL is associated with increased risk for myocardial infarction, stroke, sudden death, restenosis after angioplasty, and severe premature atherosclerotic disease; and
- in patients with low HDL (<0.8 mmol/L), especially in the absence of hypertriglyceridemia, clinical or biochemical investigation of anabolic steroid use is advised.[7]

Summary

Given the escalating trend of AAS usage, particularly among non-bodybuilding individuals, it is imperative that GPs can accurately identify and therefore contextualise abnormal blood test results in these patients. This will prevent inappropriate referrals to secondary care and potentially save unwarranted investigations for the patient. An overview of recommendations is provided in Figure 1.

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