Recognition and diagnosis of androgen excess

Educational Slide Kit
Module 2
1. Which of the following could be a non-hormonal cause of acne?

A. Genetic predisposition
B. Medication use
C. Cosmetics
D. All of the above
2. What is SAHA syndrome?

A. SAHA – Skin, Acne, Hyperandrogenism, Alopecia
B. Simultaneous presentation of seborrhea, acne, hirsutism and alopecia
C. SAHA - Serum, Androgens, Hair loss, Acne
D. Simultaneous presentation of specifically distributed acne and hirsutism in androgen excess
3. In addition to androgen-secreting tumours which of the following conditions can also cause androgen excess

A. Polycystic ovary syndrome (PCOS)
B. Thyroid dysfunction
C. Non-classic congenital adrenal hyperplasia (NCAH)
D. All of the above
4. Why is early recognition and treatment of androgen excess important?

A. Hyperandrogenic skin symptoms cause significant quality of life and psychological impairment
B. Androgen excess due to biochemical hyperandrogenism may have a long-term impact on general health
C. Androgen excess represents a significant health economic burden
D. All of the above
Module content

• Challenges in the recognition of androgen excess
• Rationale for early diagnosis and treatment
• A diagnostic pathway:
  • Ask, Assess, Consider, Test
• Further investigations
• Resources
Challenges in the recognition of androgen excess
Global and ethnic differences in prevalence and primary presentation of androgen excess\textsuperscript{1,2}

- Women in far-East Asia present less frequently with hirsutism than Western women\textsuperscript{1}
- Thickness of body hair is greater in Caucasian women than Asian women\textsuperscript{2}
- Increased risk of insulin resistance in African-American women\textsuperscript{2}

Women can present with a combination of non-specific symptoms\textsuperscript{1,2}

In some cases, women present with all four hyperandrogenic skin symptoms, described as the \textbf{SAHA syndrome}\textsuperscript{3,4}

Sometimes skin symptoms are mistakenly seen as just a cosmetic problem

- Women with hirsutism and some practitioners, still believe this abnormality to be primarily a cosmetic disturbance\(^1\)
- Many women therefore seek help from a beautician, cosmetologist or electrologist in preference to a physician\(^2,3\)
- Acne can be seen as an ‘adolescent problem’ that will resolve with age\(^4\)

Not all acne is specific to a disorder of androgen metabolism

<table>
<thead>
<tr>
<th>Hormonal influences</th>
<th>Non-hormonal influences</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Menstrual cycle</td>
<td>• Genetic predisposition</td>
</tr>
<tr>
<td>• Pregnancy (+/- effect)</td>
<td>• Medication use (e.g. iodine, lithium, isoniazid, phenytoin, cyclosporine)</td>
</tr>
<tr>
<td>• Polycystic ovary syndrome (PCOS)</td>
<td>• Cosmetics (e.g. oil- or cocoa butter-containing products)</td>
</tr>
<tr>
<td>• Androgen excess is the cause of acne in approximately 1 in 6 women¹</td>
<td>• Competitive sport</td>
</tr>
<tr>
<td>• Hormone treatment (e.g. oral contraceptives)</td>
<td>• Lifestyle aspects (e.g. smoking or diet, the latter possibly related to consumption of dairy products or foods with a high glycemic index)</td>
</tr>
<tr>
<td></td>
<td>• Pressure or friction on the skin (e.g. bike helmet straps)</td>
</tr>
</tbody>
</table>

Although hirsutism is a recognised marker of androgen excess...¹

...less frequently, it can also be caused by ovarian or adrenal dysfunction²,³

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Frequency (%)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polycystic ovary syndrome (PCOS)</td>
<td>71</td>
</tr>
<tr>
<td>Idiopathic hyperandrogenism</td>
<td>15</td>
</tr>
<tr>
<td>Idiopathic hirsutism</td>
<td>10</td>
</tr>
<tr>
<td>Non-classic congenital adrenal hyperplasia (NCCAH)</td>
<td>3</td>
</tr>
<tr>
<td>Androgen-secreting tumors</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Assessment of skin symptoms is not always straightforward\(^1\)

- Women may present in a variety of settings.
- Use of validated assessment tools outside dermatology or clinical trial settings is rare\(^2\).
- When they are used, confirmation of hirsutism for example can be further complicated by:\(^1\)
  - The semi-quantitative approach of the modified Ferriman-Gallwey (mF-G) scale\(^1\)
  - High inter-observer variability
  - Lack of consensus regarding the score that defines hirsutism
- Self-care such as shaving or waxing may limit full assessment of severity

Rationale for early diagnosis and treatment
Why is early recognition and treatment of androgen excess important?

- Hyperandrogenic skin symptoms cause significant quality of life and psychological impairment\(^1\)\(^-\)\(^4\)
- Androgen excess due to biochemical hyperandrogenism may have a long-term impact on general health\(^5\)

Androgen excess therefore represents a significant health economic burden\(^6\)

A diagnostic pathway – Ask, Assess, Consider Test
Four key steps in the recognition and diagnosis of androgen excess

1. ASK
2. ASSESS
3. CONSIDER
4. TEST
1. ASK

What to ask\textsuperscript{1,2}

- Previous or ongoing treatment and/or self care (e.g. use of make-up, shaving, waxing)
- Detailed history of menstrual pattern\textsuperscript{1}
- Menstrual irregularity\textsuperscript{1}
- Ovulatory dysfunction
- Detailed family history of similar disorders\textsuperscript{2}

Why?

Make-up or regular waxing or shaving can disguise the symptom severity

Hyperandrogenic skin symptoms and menstrual or ovulatory dysfunction could indicate polycystic ovary syndrome (PCOS)

2. ASSESS

Seborrhea  
Alopecia  
Hirsutism  
Acne

Body mass index (BMI)  
Waist/height ratio (WHR)  
Blood pressure (BP)

Clinical signs of acne include greasy skin, altered keratinisation, inflammation, and bacterial colonisation by *P Acnes*.  

| Comedonal acne | Papulo-pustular acne | Nodular acne |

*For assistance with the identification of acne due to androgen excess, please see the AWARE ‘Educational manual: Female acne for non-dermatologists’*

Hirsutism is evaluated and quantified by the modified Ferriman-Gallwey score\textsuperscript{1-4}
Emotional wellbeing

Quality of life

Long-term health

• A number of conditions can cause androgen excess
  - Polycystic ovary syndrome (PCOS)
  - Thyroid dysfunction
  - Androgen-secreting tumours
  - Non-classic congenital adrenal hyperplasia (NCAH)

• Other potential causes of skin symptoms of androgen excess
  - Androgenic medications
  - Skin irritants
  - Genetic predisposition
Confirming the cause of androgen excess\(^1-3\)

**Laboratory tests to exclude other disorders:**
- Serum thyroid stimulating hormone (TSH)
- Serum prolactin
- Serum 17-hydroxyprogesterone (OHP)

**Confirm PCOS**
- Serum testosterone
- Ultrasound ovarian morphology

**Confirm severity of dysfunction**
- Anti-Mullerian hormone (AMH)
- Sex hormone binding globulin (SHBG)
- Metabolic tests

Also important to assess:
Quality of life

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Essentials for the identification of androgen excess in women of reproductive age

1. **ASK**

**What to ask?**
- Previous treatment and/or self care (e.g. use of make-up, shaving, waxing)
- Menstrual irregularity (intervals <21 days or >35 days; prolonged or heavy menstrual bleeding)
- Ovulatory dysfunction (irregular intervals, intervals of <21 or >35 days, or delayed ovulation)

**Why?**
- Make-up or regular waxing or shaving can disguise the symptom severity
- Hyperandrogenic skin symptoms and menstrual or ovulatory dysfunction could be PCOS

2. **ASSESS**

**What to assess?**
- Clinical presence of skin symptoms such as acne, hirsutism, seborrhea and alopecia
- Biochemical evidence of elevated androgens
- Body mass index (BMI)
- Waist/height ratio (WHR)
- Blood pressure (BP)

**Why?**
- Androgen excess can present as:
  - **Clinical hyperandrogenism** - the pilosebaceous unit has increased sensitivity to normal serum androgen levels
  - **Biochemical hyperandrogenism** - excessive production and/or secretion of androgens which may be of ovarian or adrenal origin and a symptom of PCOS
  - Central obesity and preventable diseases associated with metabolic syndrome may indicate PCOS as the cause of androgen excess

3. **CONSIDER**

**What to consider?**
- Emotional wellbeing
- Quality of life
- Long term health
- Hyperandrogenic skin symptoms are associated with significant quality of life and psychological impairment
- Androgen excess may lead to increased risk of metabolic syndrome and endometrial hyperplasia or malignancy if left untreated, particularly if there is accompanying anovulation or PCOS

4. **TEST**

**What to test?**
- Thyroid stimulating hormone (TSH)
- Prolactin
- Quality of life
- Thyroid dysfunction, pituitary tumours and non-classic congenital adrenal hyperplasia (NCAH) are all potential causes of androgen excess

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Risk factors prompting further investigation

• Suspicion of androgen-secreting tumour
• Undiagnosed bleeding
• Severe psychological morbidity for example, severe anxiety and/or depression
• Scarring acne
• Fertility problems
Some practical reminders
Remember...

• The cause of androgen excess is not always detectable using biochemical tests

• In some cases, clinical symptoms result from the hypersensitivity of skin tissue to normal androgen levels.
  
  • However, the clinical symptoms causing psychological distress or impaired quality of life should still be addressed

• Menstrual irregularity can be a good indicator of PCOS, particularly in combination with clinical hyperandrogenic skin symptoms
Conclusions

• There are a number of **challenges in the recognition** of androgen excess, including:
  • Global and ethnic differences in prevalence and primary presentation\(^1,2\)
  • Presentation of a combination of non-specific symptoms\(^3,4\)
  • Difficulty assessing skin symptoms\(^2,5\)

• **Early recognition and diagnosis** of androgen excess is important
  • It allows prompt treatment of hyperandrogenic skin symptoms and can lead to improvements in quality of life and psychological wellbeing\(^6-10\)

• Despite the challenges, there are **tools and resources available** to help aid awareness and aid diagnosis

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Tools and resources available to aid awareness & diagnosis of AE

Find further FREE educational materials from 'The Global AWARE Group' on the European Menopause & Andropause Society website: https://www.emas-online.org/nonemaseducationalmaterials
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1. NHS choices. Acne – causes Available at: http://www.nhs.uk/Conditions/Acne/Pages/Causes.aspx (Last reviewed April 2016)
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FREE resources to download

The AWARE group is a panel of independent physicians with an expert interest in androgen excess in women. Formation of the AWARE group and its ongoing work is supported and funded by Bayer AG.