



PCOS TUTORIALS

*A Post Graduate
Certificate Course in
PCOS Management*

Module 3
PCOS and Cosmetic Issues



Course Directors



Dr. Duru Shah
Founder President
The PCOS Society, India



Dr. Madhuri Patil
Chair, Scientific Committee
The PCOS Society, India

Course Faculty for Module 3



Dr. Rekha Sheth
Vice President, The PCOS Society, India



Module III

PCOS and Cosmetic Issues

Table of Contents

1. Module Overview	3
2. Learning Objectives	3
3. Pre-Test	4
4. Introduction	
• PCOS and Skin: The Relationship	6
5. Prevalence of Cutaneous Manifestations in PCOS	7
6. Types of Cutaneous Manifestations in PCOS	
• Skin Changes and Hormonal Levels: Correlation	8
• Hirsutism	9
• Acne	10
• Alopecia	11
• Acanthosis Nigricans	12
• Acrochordons (Skin tags)	13
7. Pathogenesis of Cutaneous Manifestations in PCOS	
• Hyperandrogenaemia	14
• Hirsutism	15
• Acne	17
• Acanthosis Nigricans	18
• Alopecia	19
8. Grading the Severity of Cutaneous Manifestations	
• Hirsutism	20
• Acne	22
• Acanthosis Nigricans	23
9. Management of Cutaneous Manifestations	
• Hirsutism	24
• Acne and Alopecia	27
10. Conclusion	31
11. Key Points	31
12. Suggested Readings	32

Module Overview

- One in 10 women is affected by polycystic ovarian syndrome (PCOS)
- Hyperandrogenism and insulin resistance are found in PCOS
- They tend to cause dermatologic manifestations in the form of hirsutism, acne vulgaris, androgenic alopecia (AGA), and acanthosis nigricans (AN). These are among the cardinal manifestations of PCOS
- These have a profound effect on the health and quality of life of the women suffering from the cutaneous manifestations
- This module is designed to provide in-depth understanding of the pathophysiology of the cutaneous presentations in PCOS
- Further quantifying the severity of these malformations is important to delineate the appropriate management plan; hence grading systems have been included in this module along with the overview on management of cosmetic issues in PCOS

Learning Objectives

At the completion of this module the participant is expected to be able to :

- Identify the cutaneous manifestations of PCOS
- Understand the pathophysiology of the development of these lesions
- Grade their severity, and
- Develop a management plan for satisfactory clinical outcomes

PCOS and Cosmetic Issues

PRE-TEST

State whether the following statements are True or False.

1. **PCOS has a minimal impact on the aesthetics of the patient.**

True

False

2. **Acne in PCOS patients indicates hyperandrogenism.**

True

False

3. **Acanthosis nigricans is a poor marker of insulin resistance.**

True

False

4. **Alopecia in PCOS occurs due to poor nutrition.**

True

False

5. **Weight reduction is an important management for all aspects in PCOS patients.**

True

False

6. **Adrenal tumors may cause hirsutism.**

True

False

7. **Acne does not respond to conventional therapy if hormonal dysregulation is present.**

True

False

8. Skin tags are unusual in obese PCOS patients.

True

False

9. Contraceptive pills are the mainstay of PCOS management.

True

False

10. Lifestyle modification is of little benefit in the management of cosmetic issues in PCOS patients.

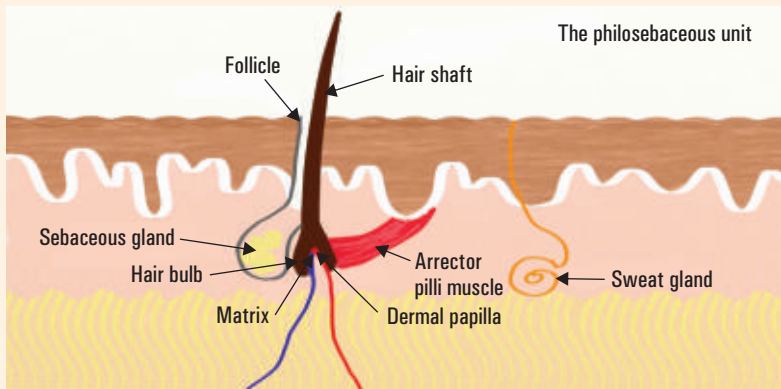
True

False

Answers: 1. False; 2. True; 3. False; 4. False; 5. True; 6. True; 7. True; 8. False; 9. True; 10. False

PCOS and Skin: The Relationship

- Almost 90% patients with PCOS present with skin disorders/ cutaneous manifestations
- Main pathophysiological feature of PCOS: abnormal regulation of steroidogenesis
- Excessive androgen secretion in PCOS results in: hirsutism, acne, seborrhoea and AGA, AN etc.¹



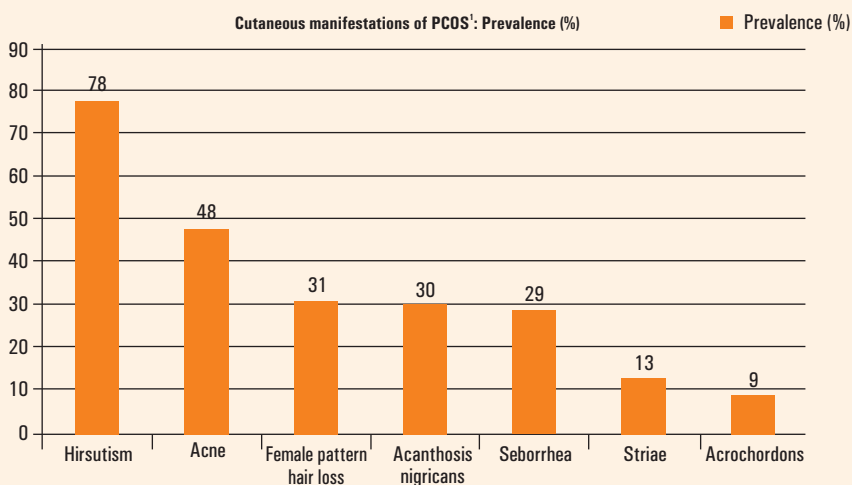
- PCOS refers to a heterogeneous collection of signs and symptoms forming a spectrum of disorders with the disturbance in reproductive, endocrine and metabolic functions.
- It has been observed that PCOS has various skin manifestations and almost 90% of patients with PCOS present with cutaneous signs/symptoms.
- The main pathophysiological process in PCOS points to the ovary being the source of excess androgens, resulting from an abnormal regulation of steroidogenesis.
- Excessive secretion of androgens in PCOS patients results in a series of skin changes including hirsutism, acne, seborrhoea and AGA, AN etc.¹
- The pilosebaceous unit is the target of androgen stimulation, and is responsive to local enzymes and the androgen receptors.²

References:

1. Gowri BV, Chandravathi PL, Sindhu PS, *et al.* Correlation of Skin Changes with Hormonal Changes in Polycystic Ovarian Syndrome: A Cross-sectional Study Clinical Study. *Indian J. Dermatol.* 2015;60(4): 419.
2. Fauser BCJM, Tarlatzis BC, Rebar RW, *et al.* Consensus on women's health aspects of polycystic ovary syndrome (PCOS): The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. *Fertility and Sterility.* 2012;97(1):28–38.

Prevalence of Cutaneous Manifestations in PCOS

- Hirsutism; the most common skin manifestation of PCOS followed by acne and alopecia.
- Patients with hirsutism were found to be younger¹



- A recent Indian study published in Indian dermatology online studied the incidence and prevalence of various skin manifestations in patients with PCOS.
- This study also attempted to correlate these skin manifestations with hormonal changes. The study results showed that hirsutism was the most common skin manifestation of PCOS followed by acne and alopecia.
- The prevalence of skin manifestations of PCOS has been depicted in the figure.
- Acne which is persistent and recurrent indicates hormonal irregularities in women >25 years of age.
- Increased seborrhoea of the skin and pre-menstrual flares of acne in women > 30 years of age depict hyperandrogenemia and end organ sensitivity.^{2,3,4}

References:

1. Keen MA, Shah IH, and Sheikh G. Cutaneous Manifestations of Polycystic Ovary Syndrome: A Cross-Sectional Clinical Study. *Indian Dermatol. Online J.* 2017; 8(2):104–110.
2. Lucky AW. Quantitative documentation of a premenstrual flare of facial acne in adult women. *Arch. Dermatol.* 2004;140(4):423–4.
3. Collier CN, Harper JC, Cantrell WC, et al. The prevalence of acne in adults 20 years and older. *Am. Acad. Dermatol.* 2008;58(1):56–9.
4. Shaw JC, White LE. Persistent acne in adult women. *Arch. Dermatol.* 2001;137(9):1252–3.

Skin Changes and Hormonal Levels: Correlation

- High fasting insulin levels was the most common hormonal abnormality seen in both acne and hirsutism
- AGA was associated with high testosterone levels

Skin manifestation	FSH (%)	LH (%)	TSH (%)	Fasting insulin (%)	PRL (%)	Testosterone (%)	DHEA-S (%)	SHBG (%)
Hirsutism	7	9	4	30	4	21	21	4
Acne	5	15	5	28	3	23	18	3
AGA	4	15	0	23	4	31	19	4
Seborrhea	4	15	2	28	4	24	21	2
Acanthosis nigricans	5	14	0	33	5	24	19	0
Acrochordons	6	13	0	27	7	20	20	7

FSH: Follicle stimulating hormone; LH: Luteinizing hormone; TSH: Thyroid stimulating hormone; DHEA-S: Dehydroepiandrostenidione; SHBG: Sex hormone binding globulin; AGA: Androgenetic alopecia; PRL: Prolactin

- An Indian study by Gowri *et al.* aimed to understand the correlation of skin manifestations with hormonal changes in patients with PCOS.
- It was seen that fasting insulin levels was the most common hormonal abnormality seen in both acne and hirsutism.
- Acne was associated with increase in fasting insulin in 28% of patients, testosterone in 23%, Dehydroepiandrostenidone (DHEA-S) in 18% and Lueteinizing hormone (LH) in 15%.
- AGA was associated with high testosterone levels.
- AGA showed increase in testosterone by 31%, fasting insulin by 23%, DHEA-S by 19%.
- Seborrhea showed increase in fasting insulin by 28%, testosterone by 24% and DHEA-S in 21%.
- AN showed increased fasting insulin level in 33%, increased testosterone in 24% and DHEA-S in 19%.
- Acrochordons showed increased fasting insulin levels in 27% whereas 20% showed rise in both testosterone and DHEA-S.¹

Reference:

1. Gowri BV, Chandravathi PL, Sindhu PS, *et al.* Correlation of Skin Changes with Hormonal Changes in Polycystic Ovarian Syndrome: A Cross-sectional Study Clinical Study. *Indian J. Dermatol.* 2015;60(4):419.

Cutaneous Manifestations of PCOS: Hirsutism

- Hirsutism is usually manifested by excessive facial and/or body hair.
- It is the most frequent clinical manifestation seen in 60% of the women with PCOS.¹



- Hirsutism is defined as excessive terminal hair growth in androgen-dependent areas in women.
- It is the most frequent clinical manifestation seen in 60% of the women with PCOS.¹
- In PCOS patients, hirsutism may result from the combined influence of increased androgen production, increased circulating free testosterone, or greater androgen activity within the pilosebaceous unit.
- Systemic conditions such as hypothyroidism and growth hormone therapy may also be associated with hirsutism.
- Ovary is the primary source of androgen overproduction; however, adrenal androgens are increased in about 30% of cases.
- In addition, this increased androgen output is enhanced by elevated levels of serum free testosterone due to decreased sex hormone-binding globulin (SHBG) levels, particularly in obese women.
- Differential diagnosis of hirsutism includes: hyperthecosis, nonclassic adrenal hyperplasia, Cushing syndrome, thyroid dysfunction, and ovarian and adrenal androgen-secreting tumors.²
- Drugs causing hypertrichosis include acetazolamide, anabolic steroids (eg, danazol, nandrolone, stanozolol), androgenic progestogens or oral contraceptive pills (OCPs) containing progestogen (eg, norethindrone and levonorgestrel found in first- and second-generation OCPs), cyclosporine, diazoxide, glucocorticoids, drugs containing heavy metals, minoxidil, penicillamine, phenytoin, tamoxifen, and thyroxine.
- Drug-induced hypertrichosis is reversible upon discontinuation of the drug. In certain cases where the medication needs to be continued, use of laser hair reduction methods can be beneficial.³

References:

1. Marques AR, Silva C, Colmonero S, *et al* . Diabetes Mellitus and Polycystic Ovary Syndrome: Beyond A Dermatological Problem. *Diabetes Case Rep*. 2016;1:113.
2. Fauser BCJM, Tarlatzis BC, Rebar RW, *et al*. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. *Fertility and Sterility*. 2012;97(1):28–38.
3. Rosenfield RL. Clinical practice. Hirsutism. *N. Engl. J. Med*. 2005; 353(24):2578–88.

Cutaneous Manifestations of PCOS: Acne

- Facial Acne is seen in most women with PCOS
- About 50% of women with PCOS demonstrate lesions on the neck, chest, and upper back¹



- Acne results from the formation of comedones, due to sebum accumulation along with desquamated follicular epithelial cells, which allows colonization by the bacterium *Propionibacterium acnes*.
- Inflammation of comedones may lead to the development of papules, pustules, and nodules.
- Androgens may worsen acne formation by increasing sebum production within the pilosebaceous unit .
- It has been observed that about 50% of women with acne do not have clinical or biochemical evidence of hyperandrogenism.
- Conversely, in many women with PCOS hirsutism may not be associated with acne.
- These differences may be due to local androgen bioactivity.
- It has been suggested that:
 - o Androgen levels within skin are more important mediators of acne than circulating levels
 - o Androgen receptors may exhibit variable sensitivity to androgens.¹

Reference:

1. Fauser BCJM, Tarlatzis BC, Rebar RW, *et al.* Consensus on women's health aspects of polycystic ovary syndrome (PCOS): The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. *Fertility and Sterility*. 2012;97(1):28–38.

Cutaneous Manifestations of PCOS: Alopecia

- Alopecia: Male-pattern (affecting the fronto-temporo-occipital scalp) or female-pattern (Christmas tree pattern)¹
- AGA shows a wide variation in prevalence range among PCOS patients, ranging between 3.2%–34.8%²



- Alopecia can represent as male-pattern (affecting the fronto-temporo-occipital scalp) or female-pattern (affecting the crown, typically manifesting early as a midline part widened in a "Christmas tree" pattern).¹
- AGA is a form of nonscarring hair loss characterized by miniaturization of mature terminal scalp hairs into thin vellus hair follicles that do not reach full length.
- In AGA androgen-responsive hair follicles shorten the anagen (growth) phase, resulting in fewer and finer hairs.
- AGA is associated with variable degrees of biochemical androgenemia.
- AGA is associated with other cutaneous markers of androgen excess, including hirsutism and acne.
- It is seen that there is decreased SHBG in subjects with AGA and PCOS than in those with PCOS alone.

References:

1. Rosenfield RL. Definition, clinical features and differential diagnosis of polycystic ovary syndrome in adolescents. UpToDate. Available at: https://www.uptodate.com/contents/definition-clinical-features-and-differential-diagnosis-of-polycystic-ovary-syndrome-in-adolescents?source=search_result&search=PCOS&selectedTitle=4~150. Last accessed: 19th June 2017.
2. Quinn M, Shinkai K, Pasch L, *et al.* Prevalence of androgenic alopecia in patients with polycystic ovary syndrome and characterization of associated clinical and biochemical features. *Fertility and Sterility*. 2014;101(4):1129–1134.

Cutaneous manifestations of PCOS: Acanthosis Nigricans

- AN is a marker of insulin resistance²
- AN is seen in about 30% of hyperandrogenic women³



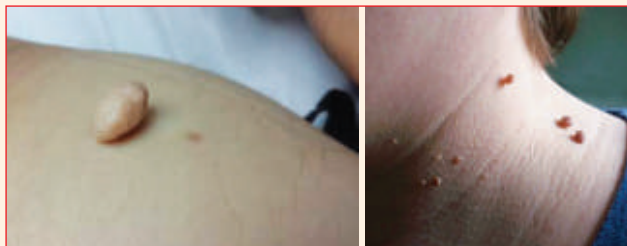
- AN refers to velvety, brown, thickened plaques with accentuated skin markings in intertriginous areas such as the axillae, groin, anogenital region, and inframammary region.
- It has been observed that obese patients with AN had markedly higher fasting plasma insulin levels than obese patients without this condition.¹
- AN is an indicator of insulin resistance and may be the presenting complaint of patients with PCOS.
- Among women with PCOS, acanthosis nigricans may be a marker of increased risk for endocrine and metabolic abnormalities.²

References:

1. Marques AR, Silva C, Colmonero S, *et al.* Diabetes Mellitus and Polycystic Ovary Syndrome: Beyond A Dermatological Problem. *Diabetes Case Rep.* 2016;1:113.
2. Sander I. Acanthosis nigricans. UpToDate. 2017. Available at: https://www.uptodate.com/contents/acanthosis-nigricans?source=see_link. Last accessed: 19th June 2017
3. Pannil M. Polycystic Ovary Syndrome: An Overview. *Advanced Practice Nursing eJournal.* 2002;2(3)

Cutaneous Manifestations of PCOS: Acrochordons (Skin tags)

- Multiple skin tags are frequently found in obese individuals and those with diabetes¹
- Acrochordons are associated with pregnancy, acromegaly, intestinal polyps, dyslipidaemia and syndromes such as PCOS²

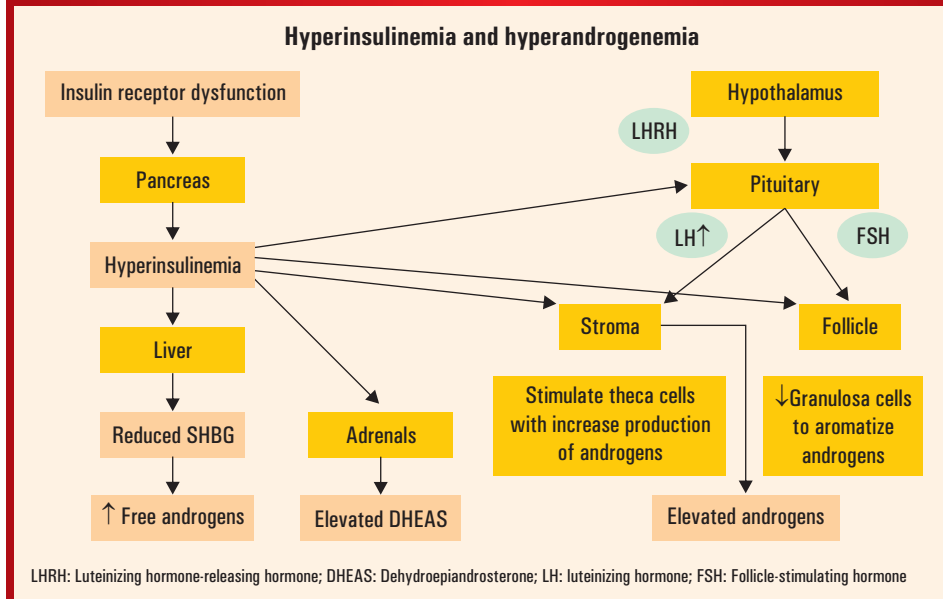


- Acrochordons (skin tags) appear as soft, pedunculated, flesh-colored to tan papules, usually ranging from 1 to 5 mm in diameter.¹
- They are commonly seen in areas that are exposed to a high degree of friction, such as the sides of the neck and axillae.
- The proliferation of fibroblasts that occurs in skin tags is due to hyperinsulinemia, via activation of the insulin-like growth factor (IGF-1) receptors present on their surfaces.²
- A sudden increase in the number of skin tags serves as a marker of developing insulin resistance.

References:

1. Azziz R, Nestler JE and Dewailliy D. Androgen excess disorders in women with polycystic ovary syndrome and other disorders. Second edition. Chapter 14. Clinical Features of the Polycystic Ovary Syndrome. 155–169. Humana Press. Totowa. New Jersey
2. Barbato MT, Criado PR, Silva AK, *et al.* Association of acanthosis nigricans and skin tags with insulin resistance. *An. Bras. Dermatol.* 2012;87(1):97–104.

Hyperandrogenaemia in PCOS

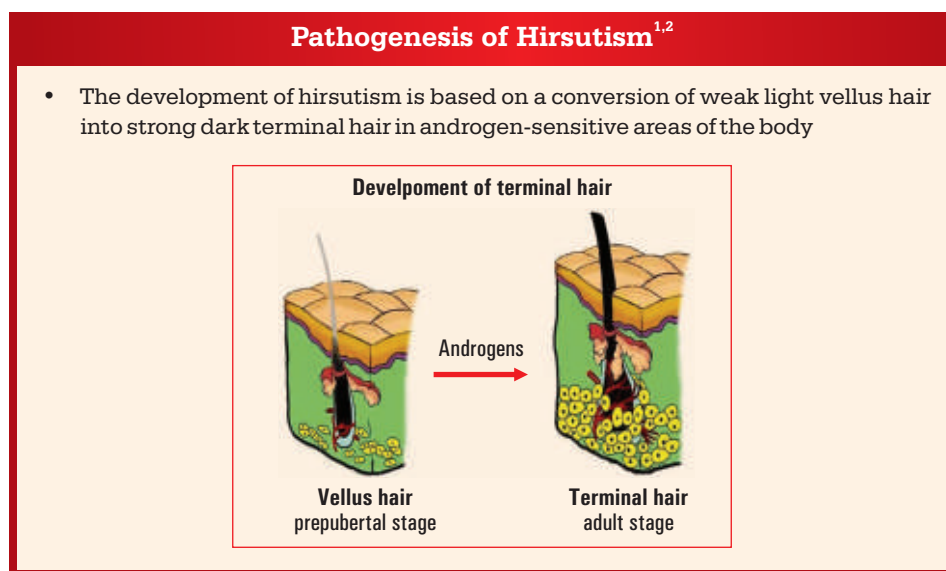


- Hyperandrogenaemia inhibits production of hepatic SHBG.
- Due to decreased SHBG in circulation, more androgens are left unbound and therefore produce a greater clinical response in terms of hirsutism, acne, and other manifestations of androgen excess.
- Hyperandrogenism can result in glucose intolerance and elevated levels of insulin.
- It is a well known fact that hyperinsulinaemia begets hyperandrogenism.
- Insulin may increase androgen synthesis by various mechanisms:
 - Increasing ovarian androgen synthesis by interacting with its own receptor or with the receptor for IGF-1, thereby increasing cytochrome P450c17-alpha enzyme activity.
 - Insulin amplifies the LH response of granulosa cells, thereby causing an abnormal differentiation of these cells with premature arrest of follicular growth thus causing an ovulation. It may also change the ovarian response to LH.
 - It also suppresses hepatic production of SHBG, which increases free testosterone levels.
 - Insulin alters normal folliculogenesis by increasing intra-ovarian androgens.

- Obesity is known to increase androgen, insulin & leptin levels, insulin resistance and risk of early pregnancy loss. Adipose tissue dysfunction may be the central factor in the pathogenesis of PCOS. There is a complex interaction between the pituitary gland, pancreas and ovary that results in the changed hormonal secretion pattern.¹

References:

1. Patil M. Pathophysiology of PCOS. The PCOS Society of India Newsletter. *PANDORA*. 2016;1: 6–8.



- Vellus hair is the type of hair that is soft, non-pigmented and with a diameter <0.03 mm covering much of the body in men and women.
- Terminal hair is longer, pigmented, and coarser in texture. Women have terminal hair only in the eyebrows, eyelashes, scalp, pubis, and axillae.
- Hirsutism occurs due to the alteration in the hair follicle cycle with a prolongation of the anagen phase with a consequent transformation of vellus into terminal hair.
- These changes occur under the effect of androgens that are triggered and involved in the regulation of sexual hair growth.
- Androgens involved in the regulation of hair follicles are testosterone and dihydrotestosterone (DHT).^{1,2}

References:

1. Kopera D, Wehr E, Obermayer-Pietsch B. Endocrinology of Hirsutism. *Int. J. Trichology*. 2010; 2(1):30–35.
2. Pasquali R, Gambineri A. Treatment of hirsutism in the polycystic ovary syndrome. *European Journal of Endocrinology*. 2014;170: R75–R90.

Aetiology of Hirsutism

Gonadal hyperandrogenism

- Ovarian hyperandrogenism
- PCOS/functional ovarian hyperandrogenism
- Ovarian steroidogenic blocks
- Syndromes of extreme insulin resistance (e.g, lipodystrophy)
- Ovarian neoplasms

Adrenal hyperandrogenism

- Premature adrenarche
- Functional adrenal hyperandrogenism
- Congenital adrenal hyperplasia (nonclassic and classic)
- Abnormal cortisol action/metabolism
- Adrenal neoplasms

Other endocrine disorders

- Cushing's syndrome
- Hyperprolactinemia
- Acromegaly

Peripheral androgen overproduction

- Obesity
- Idiopathic

Pregnancy-related hyperandrogenism

- Hyperreactio luteinalis
- Thecoma of pregnancy

Drugs

- Androgens
- Oral contraceptives containing androgenic progestins
- Minoxidil
- Phenytoin
- Diazoxide
- Cyclosporine

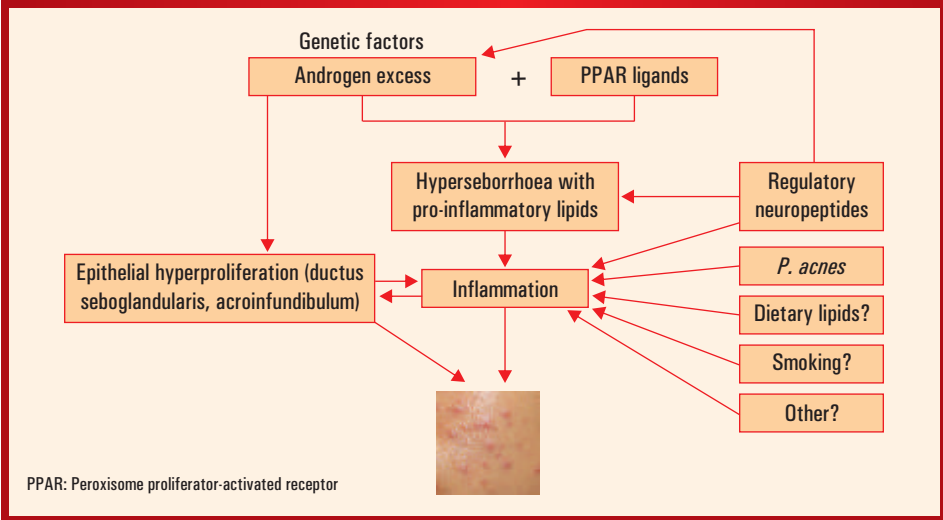
True hermaphroditism

- This slide enumerates the causes of hirsutism¹ other than PCOS
- These causes should be considered in the differential diagnosis of hirsutism

Reference:

1. Ehrmann DA. Alterations In Sexual Function and Reproduction. Chapter 68. 331–335. Harrison's Principles of Internal Medicine. 19th Edition. McGraw Hill Education.

Pathogenesis of Acne in PCOS^{1,2}

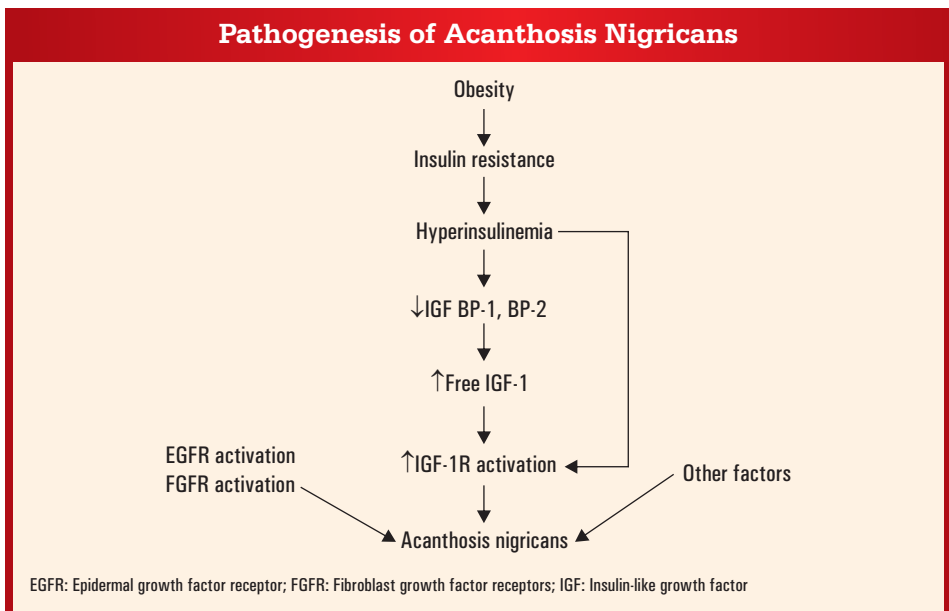


- Androgens cause worsening of acne formation by increasing sebum production within the pilosebaceous unit.
- It is important to note that androgen levels within the skin are more important mediators of acne than circulating levels.
 - The different stages of acne that may be clinically encountered are:
 - The primary lesion of acne is a comedone - these can also be invisible to the naked eye and can be visualised after stretching, palpating the skin.
 - Comedones can remain as they are open - blackhead, closed - whitehead or they can become inflamed and appear as papules, pustules, nodules and cysts.
- Immune response of the host plays an important role in the development of acne.
- Following steps result in the different stages of acne :
 - Altered follicular keratinisation
 - Hyperplasia of sebaceous glands
 - Colonization of *Propionibacterium acnes*, a bacterium which is responsible for the inflammation that occurs in acne.³
- Within the hair follicle, the androgen bioactivity is regulated, partly by 5- α -reductase, which acts to convert free testosterone to the more potent DHT.
- This enzyme has two isoforms: type 1 is found in the sebaceous glands and pubic skin and type 2 is located primarily in the hair follicle, genital skin, and adult scalp.

- The relative activities of these isoenzymes within the hair follicle may be responsible for the variable clinical presentation seen in hyperandrogenic women.
- 5- α -reductase expression is also stimulated by excess androgen, insulin, and insulin-like growth factor, which is likely to contribute to the increased local androgen bioactivity, resulting in the hirsutism and acne seen in PCOS.¹
- Androgens, peroxisome proliferator activating receptor (PPAR) ligands, regulatory neuropeptides along with hormonal and non-hormonal activity and environmental factors cause cascade of processes resulting in the formation of inflammatory acne.²

References:

1. Chuan SS, Chang JR. Polycystic Ovary Syndrome and Acne. *Skin Therapy Letter*. 2010;15(10):1–4.
2. Zouboulis CC, Eady A, Philpott M, et al. What is the pathogenesis of acne? *Experimental Dermatology*. 2005;14(2).
3. Kubba R, Bajaj AK, Thappa et al. Pathogenesis of acne. *Indian J. Dermatol. Venereol. Leprol*. 2009;75 Suppl S1 :5–9

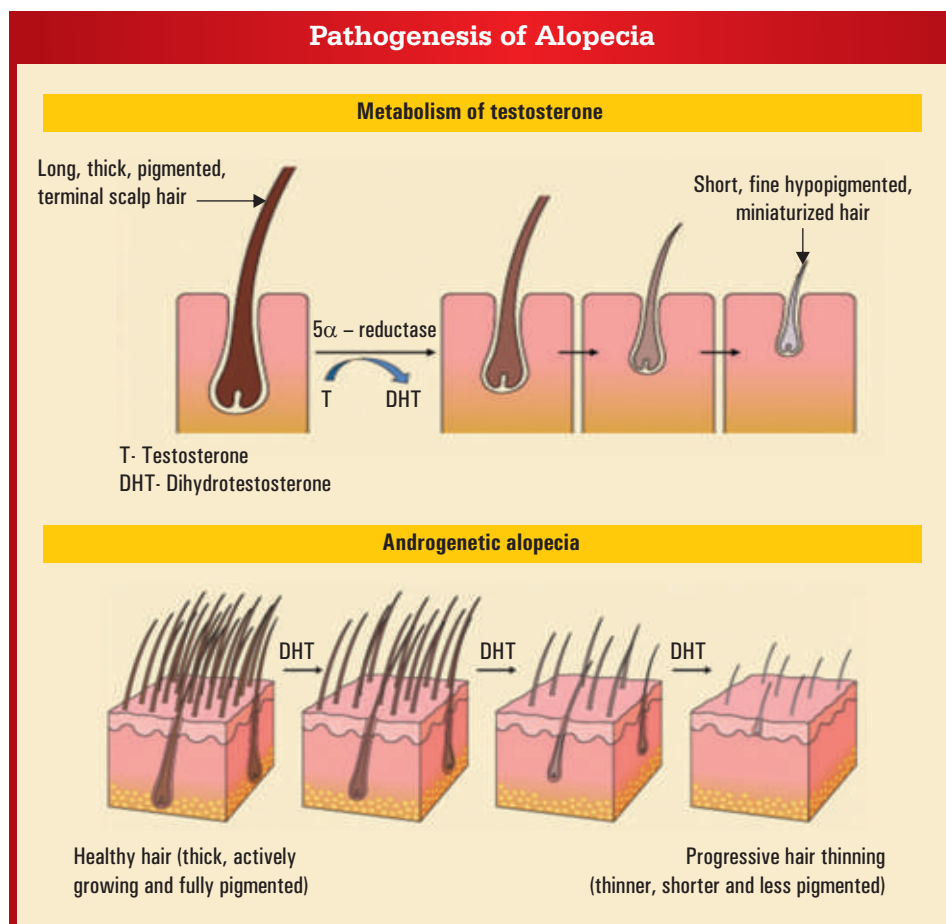


- AN is commonly associated with insulin resistance, including obesity, type 2 diabetes, and PCOS.
- Hyperinsulinaemia plays a central role in the development of AN.
- At high concentrations, insulin can exert more potent growth-promoting effects through binding to insulin-like growth factor 1 receptors (IGF-1Rs).

- Hyperinsulinaemia may also facilitate the development of AN indirectly by increasing the levels of free IGF-1 in the circulation.
- The activity of IGF-1 is regulated by IGF binding proteins (IGFBPs), which increase IGF-1 half life.
- IGFBP-1 and IGFBP-2 are both decreased in obese subjects with hyperinsulinaemia, increasing plasma concentrations of free IGF-1.
- An insulin-induced systemic reduction of IGFBP-1 and IGFBP-2 could increase local levels of free IGF-1, thereby facilitating the development of hyperkeratosis and papillomatosis.¹

Reference:

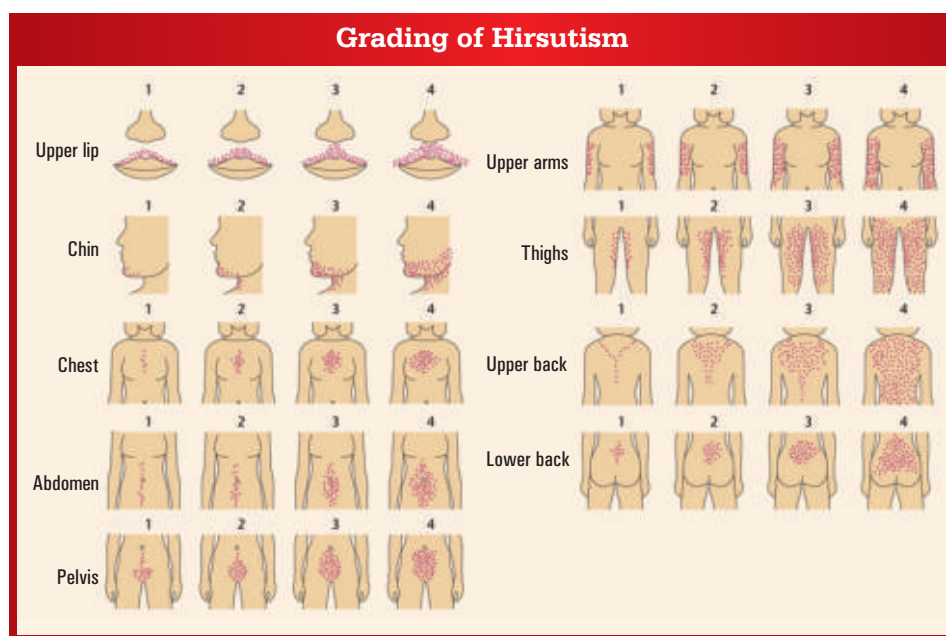
1. Higgins SP, Freemark, Neil SP. Acanthosis nigricans: A practical approach to evaluation and management. *Dermatology Online Journal*. 2008;14(9):2. Available at: <http://escholarship.org/uc/item/7mf6g290>. Last accessed 20th June 2017.



- Hyperandrogenism is a central pathophysiological process in PCOS.
- Excess of androgen, high levels of 5- α -reductase, higher concentration of androgen receptors and lower levels of the enzyme cytochrome p450 result in the shortening of the anagen phase.
- The terminal follicles undergo miniaturization turning into vellus hair.
- These changes are more evident in the frontal and parietal regions.
- Widening of the central partition, receding hairline, thinning of hair over the temporal aspect of the scalp in females is a common finding in a suspected case of PCOS, it can start as early as the 2nd decade of life.
- It may be difficult to distinguish female pattern hair loss with other types of patterned hair loss, associated features of cutaneous hyper-androgenism like acne; seborrhoea etc can serve as a diagnostic indicator.

Reference:

1. Gonçalves de Moura HH, Costa DLM, Bagati E, *et al.* Polycystic ovary syndrome: A dermatologic approach. *An. Bras. Dermatol.* 2011;86 (1).

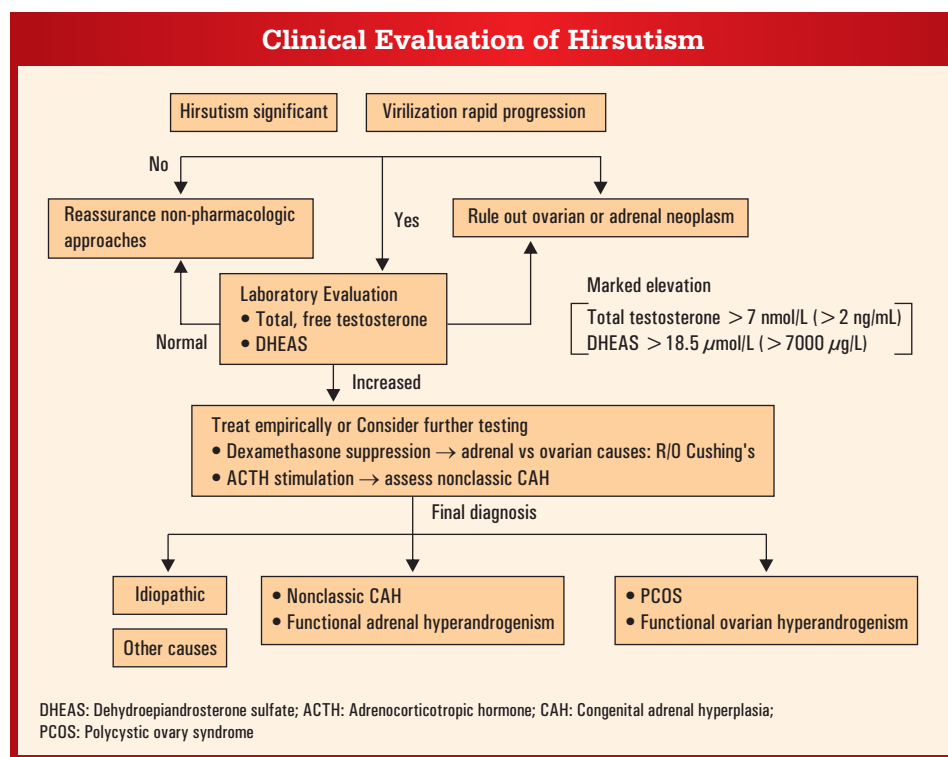


- Grading of hirsutism is done using the modified Ferriman-Gallwey (mFG) score.¹
- A score of 0 (none) to 4 (severe) in nine areas of the body is assigned with a maximum possible score of 36.

- o Scores < 4 indicate mild hirsutism
- o 4–7 indicate moderate hirsutism
- o ≥8 indicate severe hirsutism¹

Reference:

1. Malik S, Jain K, Talwar P, et al. Management of Polycystic Ovary Syndrome in India. *Fertil .Sci. Res.* 2014;1:23–43.



- The algorithm depicted in the slide describes the clinical evaluation in patients with hirsutism.¹

Reference:

1. Ehrmann DA. Alterations In Sexual Function and Reproduction. Chapter 68. 331–335. Harrison's Principles of Internal Medicine. 19th Edition. McGraw Hill Education.

Grading of Acne¹

Table 1: Grading of acne severity: Recommendation of Indian Acne Association

Mild acne (Grade I) Predominance of comedones	Comedones < 30 Papules < 10 No scarring
Moderate acne (Grade II) Predominance of papules	Comedones any number Papules > 10 Nodules < 3 With or without scarring
Severe acne (Grade III) Many nodules	Comedones any number Papules any number Nodules/cysts > 3 With scarring

Table 2: Acne distribution by age groups: Recommendation of Indian Acne Association

Age group	Location of lesions	Type of lesions	Sex
Neonates	Cheeks, chin, eyelids, forehead	Papules and pustules, no comedones	Both
Infants	Full face	Comedones, papules, nodules, scars	Male
Preadolescent	Forehead, upper cheeks, nose	Predominantly comedonal, occasional papule	Both
Adolescent	Full face, seborrhic areas of torso	All types of lesions	Both
Adults	Chin, upper lip, jaws	Papules, excoriated papules	Female

- Acne can be graded as mild, moderate, and severe depending on the number and types of inflammatory lesions as shown in table 1.
- Typically, in girls, acne starts between 12–14 years of age, and in boys between 14–16 years of age.
- The location and type of acne lesions according to the age group, as described by the Indian Acne Association (IAA) has been depicted in the table 2

Reference:

1. Malik S, Jain K, Talwar P, et al. Management of Polycystic Ovary Syndrome in India. *Fertil .Sci. Res.* 2014;1:23–43.

Grading of Acanthosis Nigricans¹

Neck grading in acanthosis nigricans

Neck grading	Description
I	Visible only on close inspection
II	Confined to the base of the skull
III	Extending laterally up to the posterior border of the sternocleidomastoid muscle. This is not visible when the patient is viewed from the front
IV	Visible (encircling the neck) when the subject is viewed from the front

Neck texture grading in acanthosis nigricans

Neck texture grading	Description
0	Smooth to the touch
1	Rough to the touch
2	Coarseness is visible
3	Extremely coarse: "Hills and valleys" are observable on visual examination

Axilla grading in acanthosis nigricans

Classification	Description
0	Absent
1	Clearly present on close visual inspection
2	Mild: Localised to the central portion of the axilla
3	Moderate: Involving the entire axillary fossa
4	Severe: Visible from the front or the back of the unclothed participant, when the arms are left to rest against the patient's side

- The slide depicts neck grading and neck texture grading of AN
- It also shows the axilla grading in AN

Reference:

1. Venkatswami S. Acanthosis nigricans: A flag for insulin resistance. *JEMDSA*. 2014;19(2):68-74

Management of Hirsutism

Lifestyle modifications^{1,2}

- Weight loss
- Balanced diet

Pharmacological management^{2,3}

- Androgen receptor blockade (spironolactone, flutamide, and cyproterone acetate, finasteride)
- Insulin sensitizers (metformin or thiazolidinediones)



- In PCOS patients, lifestyle modifications with respect to diet, exercise, behavioral or combined treatments show improvement in body composition, hyperandrogenism and insulin resistance.¹
- A study showed that 16 weeks of therapy with oral essential amino acids in patients with PCOS resulted in a significant decrease in the levels of fasting insulin, LH, follicle-stimulating hormone (FSH), and total testosterone.²
- Anti androgen: Spironolactone competes with the androgens for the androgen receptor, 5 α -reductase, and SHBG. Dose: 100 mg per day are generally effective for the treatment of hirsutism, higher doses (200–300 mg per day) may be preferable in the very hirsute or obese women.
- Finasteride at doses of 5 mg/day is beneficial for the treatment of hirsutism and female pattern hair loss in women.^{2,3}
- Insulin sensitizers such as metformin improve hyperandrogenaemia and ovulatory function and also prevent pregnancy loss in PCOS.
- OCPs suppress circulating LH and FSH, leading to a decrease in ovarian androgen production.
- Combined oral contraceptives (COCs) with anti-androgenic progestins such as cyproterone acetate, drospirenone, desogestrel are used for the management of hirsutism in PCOS patients.

- Cyproterone acetate decreases circulating testosterone and androstenedione levels through a decrease in circulating LH levels.
- Long-acting Gonadotrophin-releasing hormone (GnRH) agonists suppress the hypothalamic–pituitary–ovarian axis in severely androgenised or hyperinsulinaemic patients. Two to three months of treatment may be required for the full suppressive effect of the agonist to occur and these drugs should be reserved for women who do not respond to combination hormonal therapy or those who cannot tolerate OCs

References:

1. Malik S, Jain K, Talwar P, *et al.* Management of Polycystic Ovary Syndrome in India. *Fertil .Sci. Res.* 2014;1:23–43.
2. Hantash BM. Dermatologic Manifestations of Hirsutism Treatment & Management. *Medscape.* 2017. Available at: <http://emedicine.medscape.com/article/1072031-treatment#d9>. Last accessed 21st June 2017.
3. Agarwal NK. Management of hirsutism. *Indian J. Endocrinol. Metab.* 2013;17(1): S77–S82.

Management of Hirsutism

<p>Hair removal:</p> <p>Depilation</p> <ul style="list-style-type: none"> • Shaving or chemicals <p>Temporary epilation</p> <ul style="list-style-type: none"> • Creams • Waxing • Threading <p>Permanent epilation</p> <ul style="list-style-type: none"> • Electrolysis • Laser¹ 	
--	---

- Depilatories remove hair from the surface of the skin. Depilatory methods include ordinary shaving and the use of chemicals which can irritate the skin and lead to allergic reactions.
- Shaving removes the hair from the surface of the skin as the root is left intact within the skin and is expensive in the long term scenario.
- Temporary epilation involves plucking, waxing, threading etc. Apart from being painful they can also lead to superficial bacterial infections and ingrowth of hair.

- Hair destruction by electrolysis, thermolysis, or a combination of both is performed with a fine, flexible electrical wire that produces an electrical current after it is introduced down the hair shaft, hence destroying it. Multiple sessions are required.
- Permanent hair reduction methods with the use of energy and light based devices is a long term solution and is much more economical than all the above mentioned methods.
- The laser and light based devices target the melanin in the hair root and in multiple sittings convert the terminal thick dark hair in vellus light thin hair.
- These procedures are painless and efficient; they also reduce the ingrowths and chances of infections with waxing etc.
- Women with PCOS who are hirsute respond better to laser hair reduction when under simultaneous treatment for PCOS.

Reference:

1. Hantash BM. Dermatologic Manifestations of Hirsutism Treatment & Management. *Medscape*. 2017. Available at: <http://emedicine.medscape.com/article/1072031-treatment#d9>. Last accessed 21st June 2017

Management of Hirsutism: Recommendations

- In adult women who do not want to conceive it is recommended to use low-dose COCs with anti-androgen progestin (cyproterone acetate, drospirenone, or desogestrel) for the management of hirsutism
- For women with menstrual irregularity + hirsutism, low-dose COCs with anti-androgenic activity (cyproterone acetate, drospirenone, desogestrel) are suggested
- In adolescents/children with hyperandrogenism, obesity and signs of insulin resistance, lifestyle modification is first-line therapy; metformin is second-line therapy with a wait period of 2 years post-menarche in children¹

Important recommendations for the management of Hirsutism in Indian patients have been discussed by Malik S, *et al*–

- Cyproterone acetate has been shown to be more beneficial than other progestins in Indian patients.
- If there is no improvement with COCs or COCs are not tolerated, it is recommended to use spironolactone or finasteride but recommended to stop 6 months before planned pregnancy.

- Risk of thromboembolism with use of COCs can be managed by identifying susceptible patients and/or pausing treatment for 3 months after one year of treatment.
- In adolescents with hyperandrogenism, if glucose intolerance is not established by oral glucose tolerance test (OGTT), metformin should not be started.

Reference:

1. Malik S, Jain K, Talwar P, et al. Management of Polycystic Ovary Syndrome in India. *Fertil .Sci. Res.* 2014;1:23–43.

Management of Acne

Topical applications:¹

- Benzoyl peroxide
- Topical retinoids
- Topical antibiotics

Pharmacological management:²

- COCs
- Anti-Androgens
- Insulin sensitizing agents



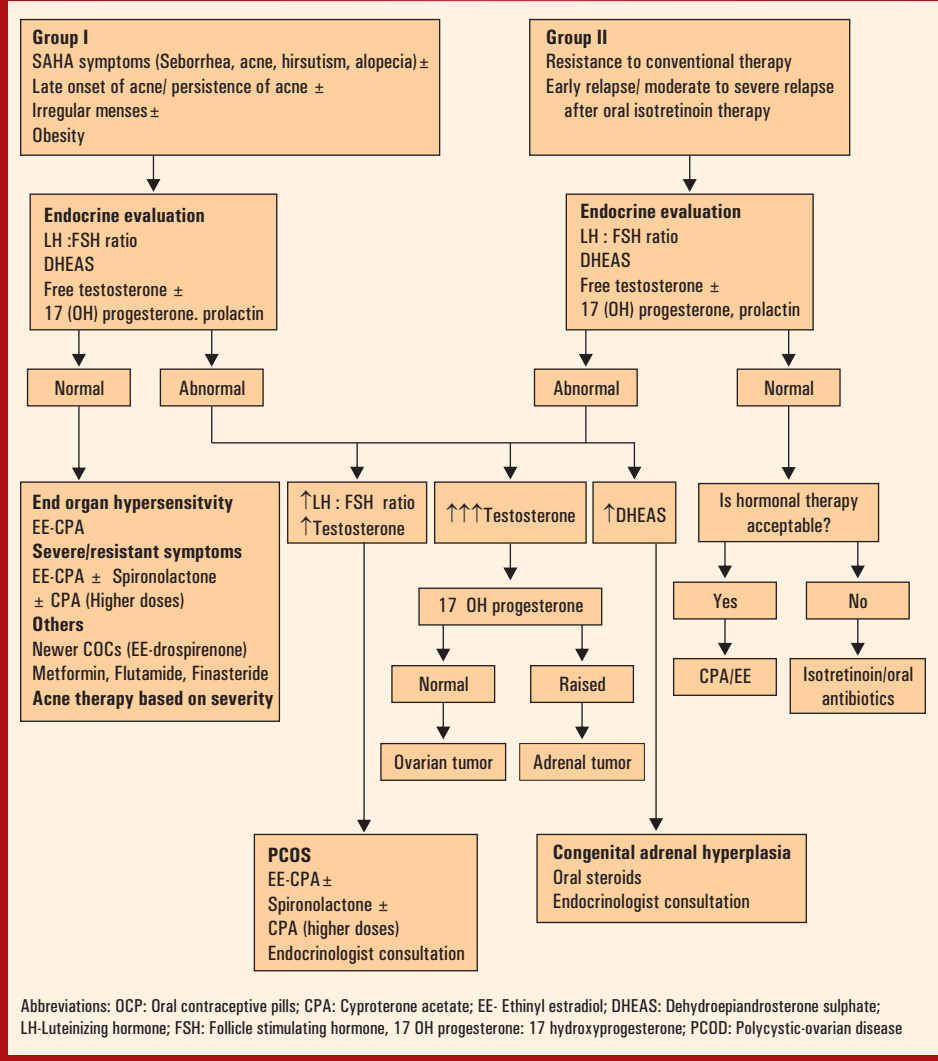
- Treatment of acne depends upon the severity.
- Mild acne responds well to topical retinoid, benzoyl peroxide, glycolic and azelaic preparations.
- Use of sunscreen and moisturiser is beneficial in the treatment of acne.
- For severe acne comprising of multiple pustules, nodules and cysts - oral antibiotics such as doxycycline, lymecycline can be given for 4–6 weeks along with topical treatment.
- In case of scarring tendency, it is advisable to start oral retinoid: isotretinoin, as it helps in preventing development of scars and occurrence of new acne. This is done under the dermatologist's guidance; hence referral to a dermatologist for management is crucial.
- Oral retinoid are vitamin A derivatives and act by reducing the sebaceous gland secretion and altering the keratinocyte activity.
- Procedures such as chemical peels with salicylic and glycolic preparations, light based therapy: intense pulsed light (IPL) can also serve as an adjuvant to oral and topical treatment of acne, overall combining treatments with therapy can significantly reduce the severity and recurrence of acne.

- It is prudent to understand that when acne occurs in PCOS, the recurrence rates are high and sometimes the acne may not respond to conventional therapy. In such a scenario, use of anti androgens such as flutamide, and COC are used in addition to the above mentioned treatment.
- Spironolactone is a potassium sparing diuretic which competitively inhibits androgen receptors and 5- α -reductase and can be used for acne not responding to isotretinoin, spironolactone is also beneficial in female pattern hair loss. The dose can range from 50– 200 mg / day.
- Spironolactone also decreases sebum production and improves acne.
- Flutamide may be used for the treatment of mild to moderate acne.
- Insulin sensitizing agents such as metformin and thiazolidinediones decrease androgen production by lowering hyperinsulinemia.²
- While on the above mentioned medications following monitoring is necessary: liver function test, lipid profile, serum electrolytes, hormonal profile and ultrasonography of pelvis.
- COC pills suppress gonadotropin secretion and ovarian steroid synthesis, leading to decreased androgen production and help in reducing the various features of cutaneous hyperandrogenism.
- The estrogen component has been shown to stimulate SHBG production by the liver whereas the progestin component may lower local androgen effect by inhibiting 5- α -reductase activity in the hair follicle or competitive inhibition for the androgen receptor.

Reference:

1. Malik S, Jain K, Talwar P, et al. Management of Polycystic Ovary Syndrome in India. *Fertil .Sci. Res.* 2014;1:23–43.
2. Sandy S, Chuan R, Chang J. Polycystic Ovary Syndrome and Acne. *Skin Therapy Letter.* 2010;15(10):1–4.

Management of Acne



- The slide depicts the management algorithm for acne.¹

Reference:

- Malik S, Jain K, Talwar P, *et al.* Management of Polycystic Ovary Syndrome in India. *Fertil .Sci. Res.* 2014;1:23–43.

Management of Acne and Alopecia : Recommendations ¹

- In adults and adolescents with PCOS and acne, it is suggested to use topical medication along with pharmacological interventions in consultation with a dermatologist
 - Referral to the dermatologist is crucial for management of acne if the latter is not responding to topical therapy and/ or scarring and post acne pigmentation is noted with the acne
 - In adults with PCOS, it is suggested to use OCPs (cyproterone acetate, drospirenone, or desogestrel as progestin component) as first-line therapy for management of all types of acne lesions
 - In women with PCOS presenting with alopecia, COCs and androgen blockers are recommended as first line therapy¹
-
- Malik S, *et al* recommend for the management of acne and alopecia in Indian patients with PCOS, cyproterone acetate as a more beneficial option than other progestins ¹

Reference:

1. Malik S, Jain K, Talwar P, *et al*. Management of Polycystic Ovary Syndrome in India. *Fertil .Sci. Res.* 2014;1:23–43.

Conclusion

- The pilosebaceous unit is the target of androgen stimulation
- Hirsutism may result from the combined influence of increased androgen production, increased circulating free testosterone, or greater androgen activity within the pilosebaceous unit
- Androgens may worsen acne formation by increasing sebum production within the pilosebaceous unit
- Acanthosis nigricans is an indicator of insulin resistance and may be the presenting complaint in patients with PCOS

Key Points

- Androgenic alopecia is associated with other cutaneous markers of androgen excess, including hirsutism and acne
- Use of minoxidil and various peptide preparations is also done by the dermatologist, this step is key to preventing further hair fall and maintaining the hair growth throughout treatment.
- In situations where oral medication cannot be given for androgenetic alopecia, topical preparations are of importance.
- Physical treatments for stimulating hair growth like platelet rich plasma, mesotherapy and microneedling are also performed by the dermatologist to provide an optimum end result.
- Hence a multi faceted approach is required under a dermatologist guidance to effectively tackle androgenetic alopecia.
- Androgen levels within skin are more important mediators of acne than circulating levels.
- In adult women who do not want to conceive it is recommended to use low combined oral contraceptive with anti-androgen progestin (cyproterone acetate, drospirenone, or desogestrel) for the management of hirsutism.
- In adolescents/children with hyperandrogenism, obesity and signs of insulin resistance, lifestyle modification is first-line therapy.
- In adults with PCOS, it is suggested to use oral contraceptives (cyproterone acetate, drospirenone, or desogestrel as progestin component) as first-line therapy for management of all types of acne lesions.
- In women with PCOS presenting with alopecia, combined oral contraceptive and androgen blockers are recommended as first line therapy.

Suggested Readings

1. Keen MA, Shah IH, and Sheikh G. Cutaneous Manifestations of Polycystic Ovary Syndrome: A Cross-Sectional Clinical Study. *Indian Dermatol. Online J.* 2017;8(2):104–110.
2. Gowri BV, Chandravathi PL, Sindhu PS, *et al.* Correlation of Skin Changes with Hormonal Changes in Polycystic Ovarian Syndrome: A Cross-sectional Study Clinical Study. *Indian J. Dermatol.* 2015;60(4):419.
3. Malik S, Jain K, Talwar P, *et al.* Management of Polycystic Ovary Syndrome in India. *Fertil .Sci. Res.* 2014;1:23–43.
4. Gonçalves de Moura HH, Costa DLM, Bagati E, *et al.* Polycystic ovary syndrome: A dermatologic approach. *An. Bras. Dermatol.* 2011;86(1).

PCOS and Cosmetic Issues

POST-TEST



1. Androgen receptors are located in the:

- a. Dermal papilla
- b. Outer Root sheath
- c. Nerve ends
- d. Both a and b

2. Hirsutism may be caused due to:

- a. Cushing syndrome
- b. Thyroid dysfunction
- c. Ovarian neoplasms
- d. All of the above

3. Causative agent in acne is:

- a. *Propionibacterium acnes*
- b. *Porphyromonas gingivalis*
- c. *Streptococcus pneumoniae*
- d. Both b and c

4. Female pattern hair loss is described as:

- a. Christmas tree pattern
- b. Sunray appearance
- c. Hair raised pattern
- d. None of the above

5. Acanthosis nigricans can be seen in:

- a. Axilla
- b. Neck
- c. Groin
- d. All of the above



6. **Skin tags are common after __ years of age.**
- a. 20
 - b. 40
 - c. 50
 - d. 60
7. **____ hair cover much of the body in men and women.**
- a. Vellus
 - b. Terminal
 - c. Transitional
 - d. Interstitial
8. **Androgen bioactivity is regulated by:**
- a. 5- β -synthase
 - b. 6- γ -phosphate
 - c. 5- α -reductase
 - d. None of the above
9. **Ferriman-Gallwey score of 4–7 indicates:**
- a. Mild hirsutism
 - b. Moderate hirsutism
 - c. Severe hirsutism
 - d. Androgen failure
10. **Which of the following progestins is used in management of hyperandrogenism?**
- a. Cyproterone acetate
 - b. Drospirenone
 - c. Desogestrel
 - d. All of the above

This initiative is supported by an unrestricted educational grant from



B. S. D. Marg, Govandi, Mumbai - 400 088. www.usvindia.com

Developed by: **hansa**
medcell

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.