HIRSUTISM

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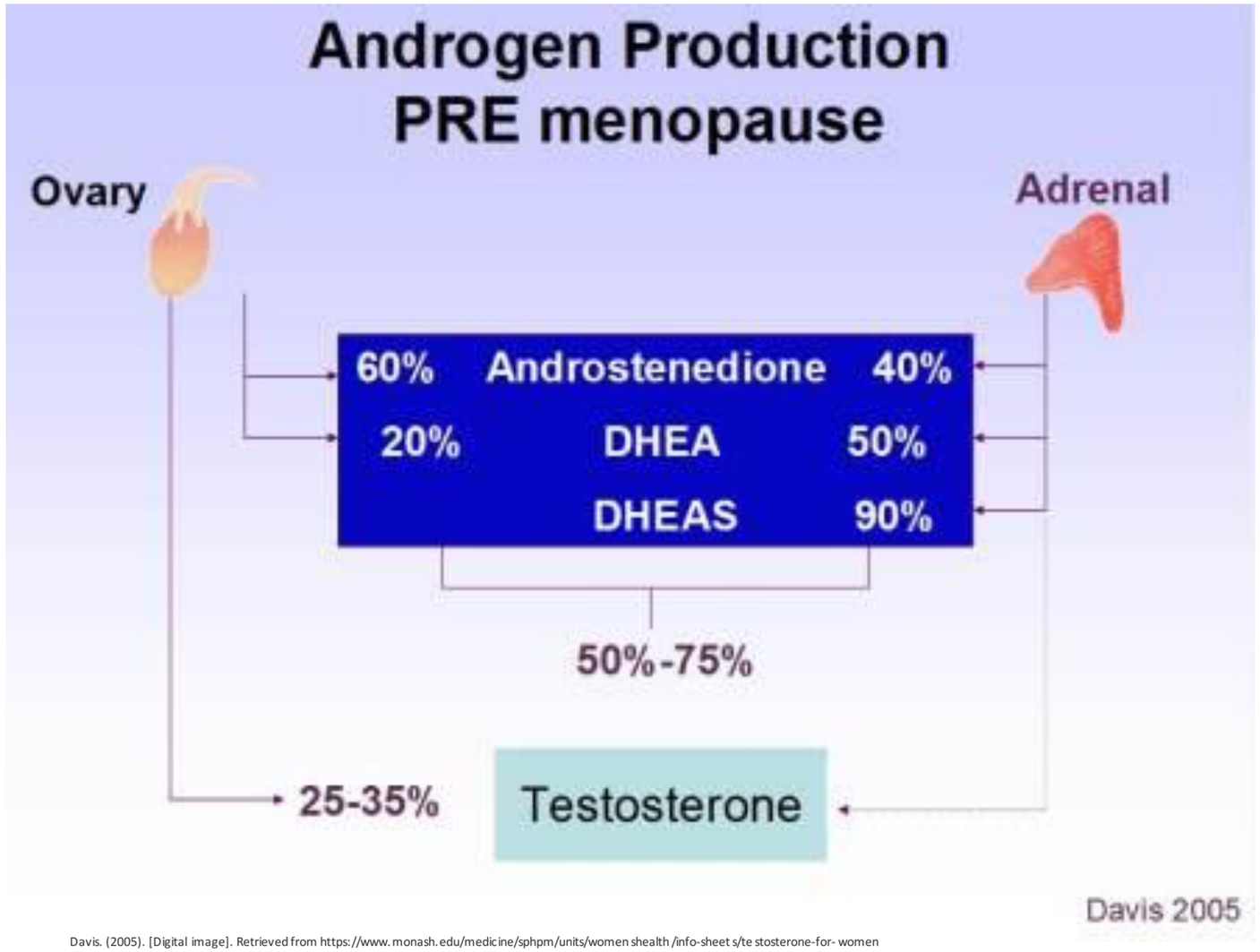
Hirsutism

- **Hirsutism-** excessive terminal hair growth in androgen-dependent areas
  - Face, chest, abdomen, lower back, upper arms, thighs
- 5-10% of reproductive aged women

Androgen Production

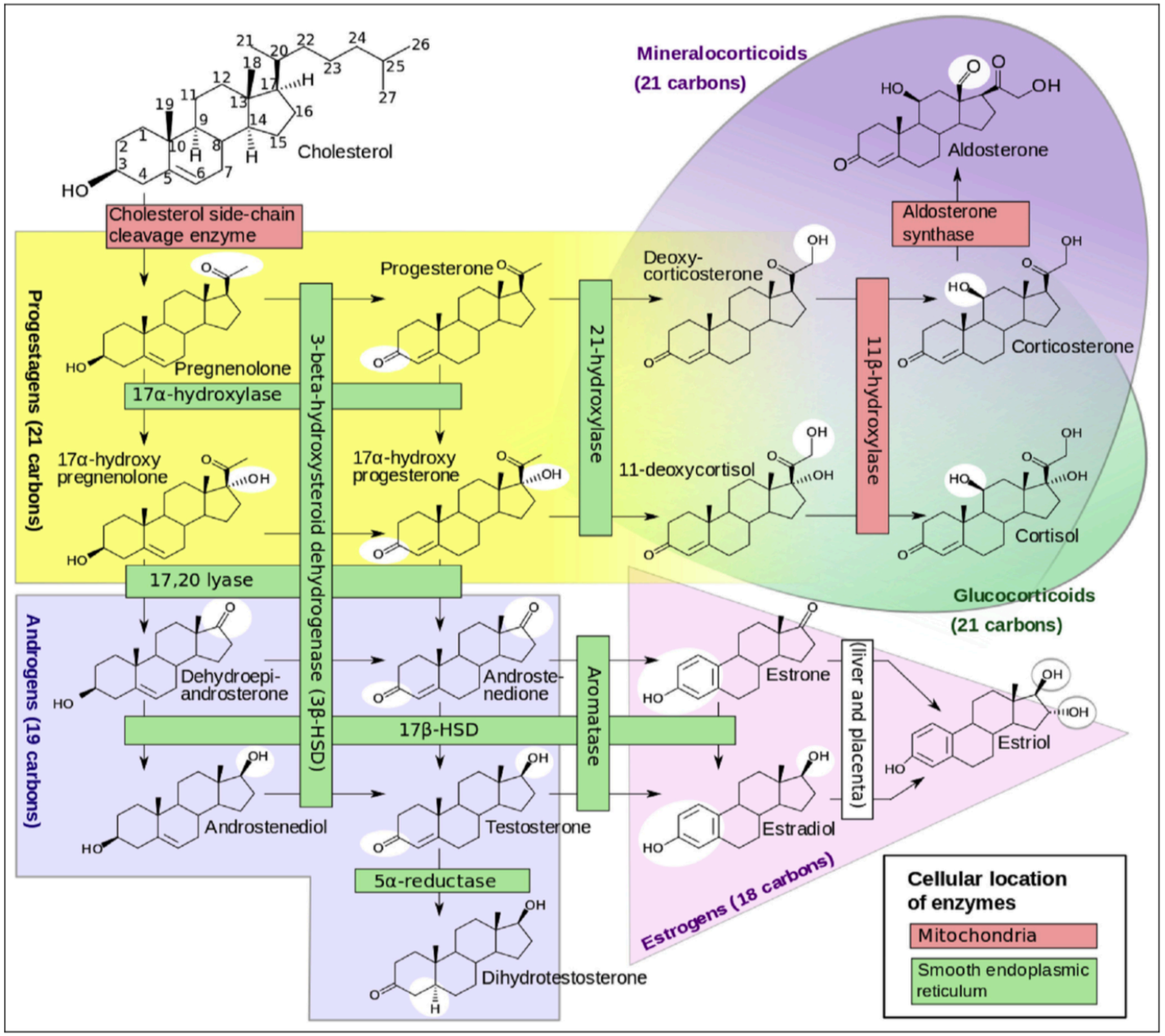
- Androgens are produced by ovary and adrenal gland



Davis. (2005). [Digital image]. Retrieved from https://www.monash.edu/medicine/sphpm/units/women shealth /info-sheet s/te stosterone-for- women

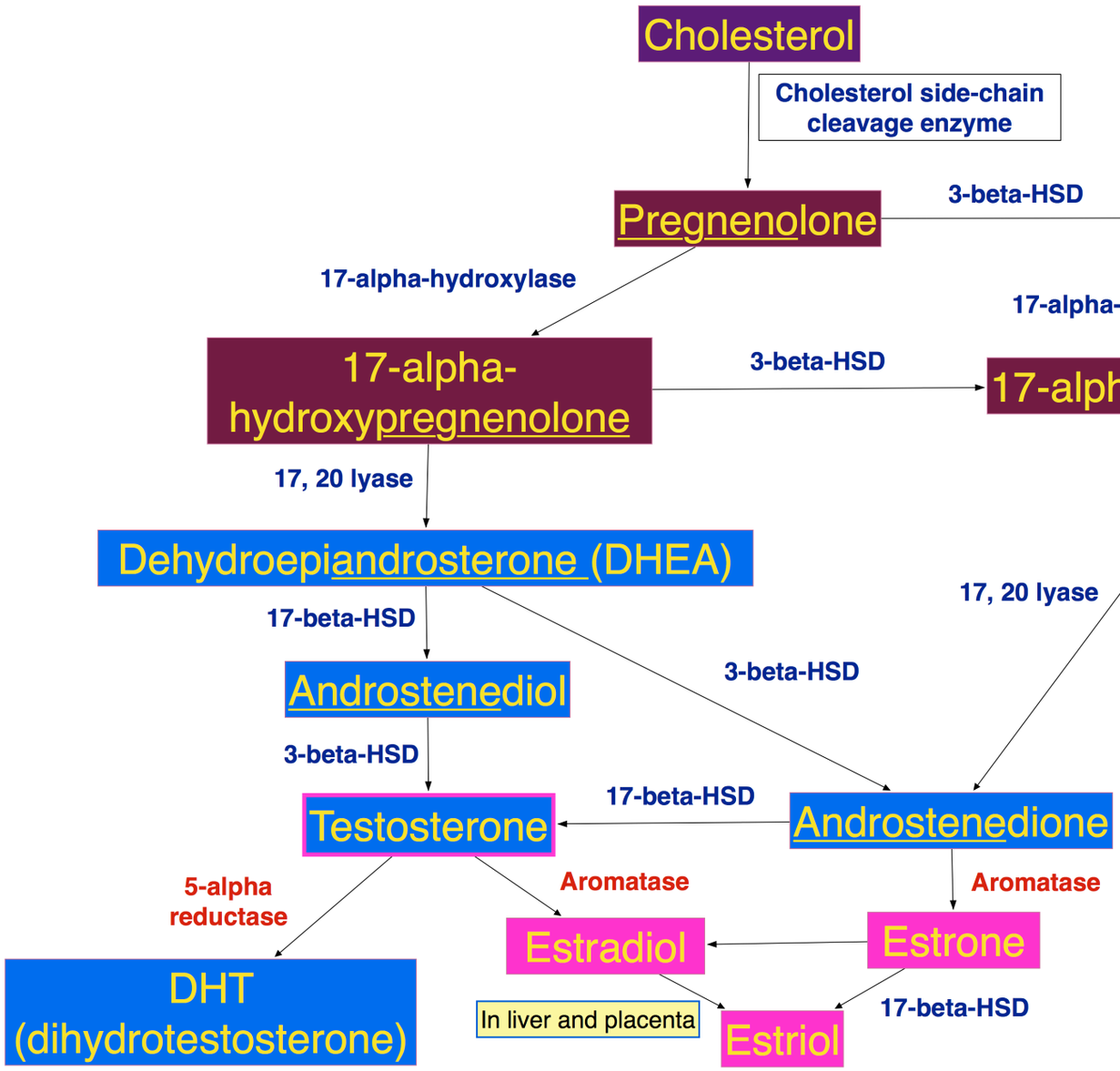
Steroidogenesis Pathway

Figure 2. Steroidogenesis pathway.



From Häggström M, Richfield D. Diagram of the pathways of human steroidogenesis. WikiJournal Med 2014;1(1):4.

Steroidogenesis Pathway



Dr. Maria Giroux
Last modified January 2019

Reference:
Liu, K., Motan, T., & Claman, P. (2017). No. 350- Hirsutism: Evaluation and Treatment. *J Obstet Gynaecol Can, 39*(11), 1054-1068.

Enzymes located in mitochondria (3):
Cholesterol side-chain cleavage enzyme
11-beta-hydroxylase
Aldosterone synthase

Enzymes located in smooth endoplasmic reticulum (SER) (7):
3-beta-HSD (hydroxysteroid dehydrogenase)
17-alpha-hydroxylase
17, 20 lyase
21-hydroxylase
17-beta-HSD
5-alpha reductase
Aromatase

Androgens: 19 carbons
Dehydroepiandrosterone (DHEA)
Androstenediol
Androstenedione
Testosterone
DHT (dihydrotestosterone)

Estrogens: 18 carbons
Estrone
Estradiol
Estriol

Progestogens: 21 carbons
Pregnenolone
17-alpha-hydroxypregnenolone
17-alpha-hydroxyprogesterone
Progesterone

Mineralocorticoids: 21 carbons
Aldosterone
Deoxycorticosterone

Glucocorticoids: 21 carbons
Cortisol
Corticosterone
11-deoxycortisol

Hyperandrogenism

- ↑ androgen production
- Level of ↑ androgen does not correlate with severity of hirsutism

Clinical presentation:

- Oligomenorrhea, anovulation
- Infertility
- Acne, oily skin
- Hair thinning
- Seborrhea (dandruff)
- Acanthosis nigricans
- Loss of female body contour

Masculinization

- **Masculinization-** development of male secondary sex characteristics

Male secondary sex characteristics

- Facial hair
- Deep voice
- Body fat distribution
- Increased pectoral musculature

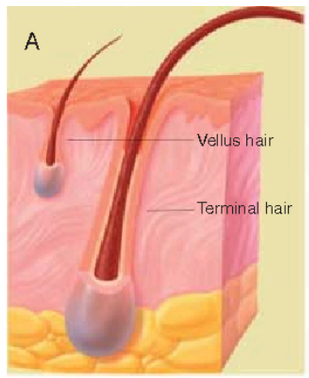
Fowler, L., & Cohen, P. (2014). Treatment options for women with facial hair [Digital image]. Retrieved from https://www.clinicaladvisor.com/consultations/treatment-options-for-women-with-facial-hair/article/332876/

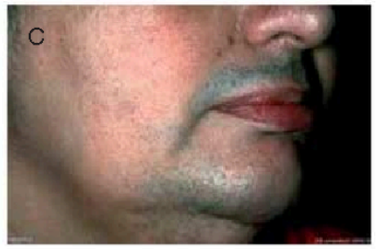
Virilization

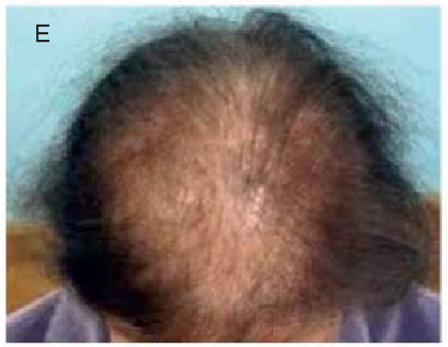
- **Virilization-** extreme degree of hirsutism and masculinization due to high and rapid androgen production
  - Can be due to androgen-secreting tumour

Clinical presentation

- Deep voice
- Male pattern balding (alopecia)
  - Fronto-temporal, vertex thinning of scalp hair
- Loss of female body contour
- Increased muscle bulk
- Changes in libido
- **Clitoromegaly**- clitoral diameter **>4mm**







Markopoulos„ M., & Kassi, E. (2015). Figure 1 Signs of physiological relative hyperandrogenism [Digital image]. Retrieved from https://www.semanticscholar.org/paper/Hyperandrogenism-after-menopause.-Markopoulos-Kassi/33f6d0c16d1264ab7b66bb21a2300eebb555ec9c/figure/0

Hypertrichosis

- **Hypertrichosis-** excessive hair growth
  - Abnormal hair length or density
  - Due to meds, rarely due to hormonal abnormalities
  - No pattern- affects limbs, trunk, back, face
- Once stop meds, hair growth usually returns to normal

Meds that can cause hypertrichosis:

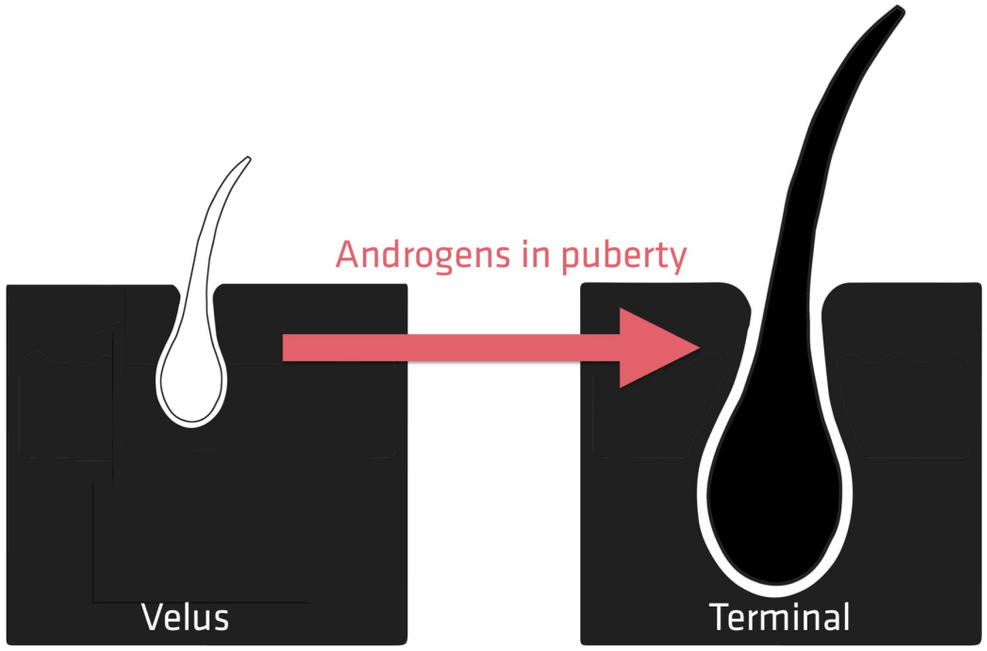
- **Phenytoin**
- **Streptomycin**
- **Cyclosporine**
- Acetazolamide
- Latanoprost
- Psoralen
- Diazoxide
- Minoxidil

Hypertrichosis - the excessive hair growth above the normal for the age,sex and race of an individual. (n.d.). Retrieved 2018, from https://www.reddit.com/r/Damnthatsinteresting/comments/7yzmgv/hypertrichosis_the_excessive_hair_growth_above/.

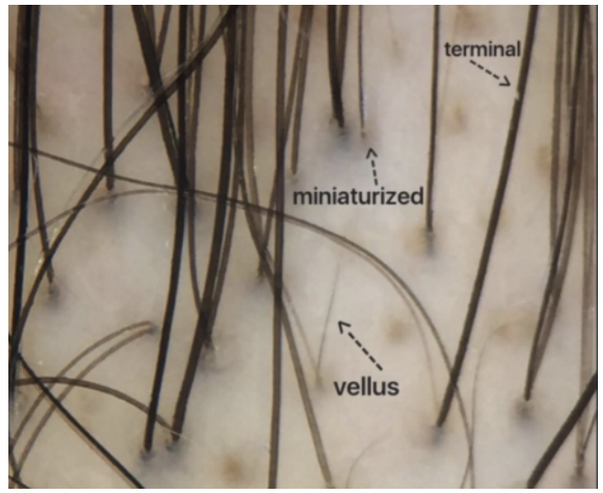
Types of Hair Follicles

Vellus hair	Terminal hair
• Prepubertal • Non-medullated • Short, soft • Lightly pigmented	• Fully matured • Medullated • Long, stiff • Pigmented

Villines, Z. (2017, October 30). Vellus hair develops in infancy and finer than terminal hair [Digital image]. Retrieved from https://www.medicalnewstoday.com/articles/319881.php



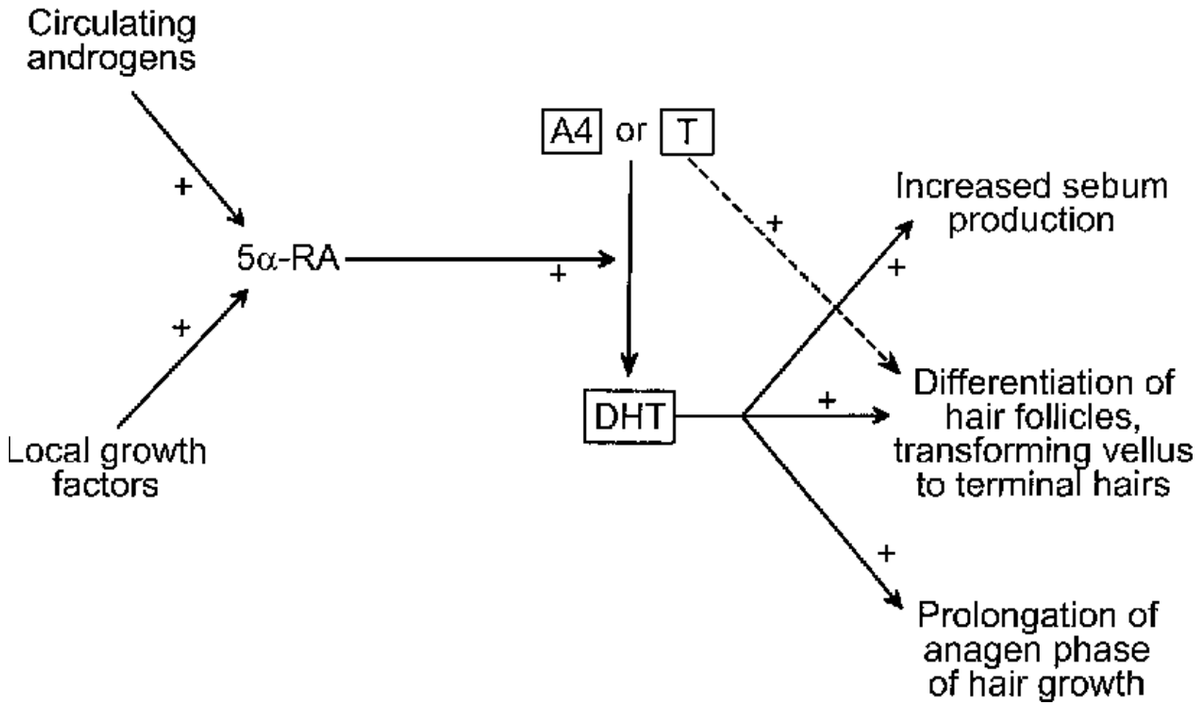
[Digital image]. (n.d.). Retrieved from https://www.2passclinic.com/permanent-hair-removal/electrolysis-hair-removal/



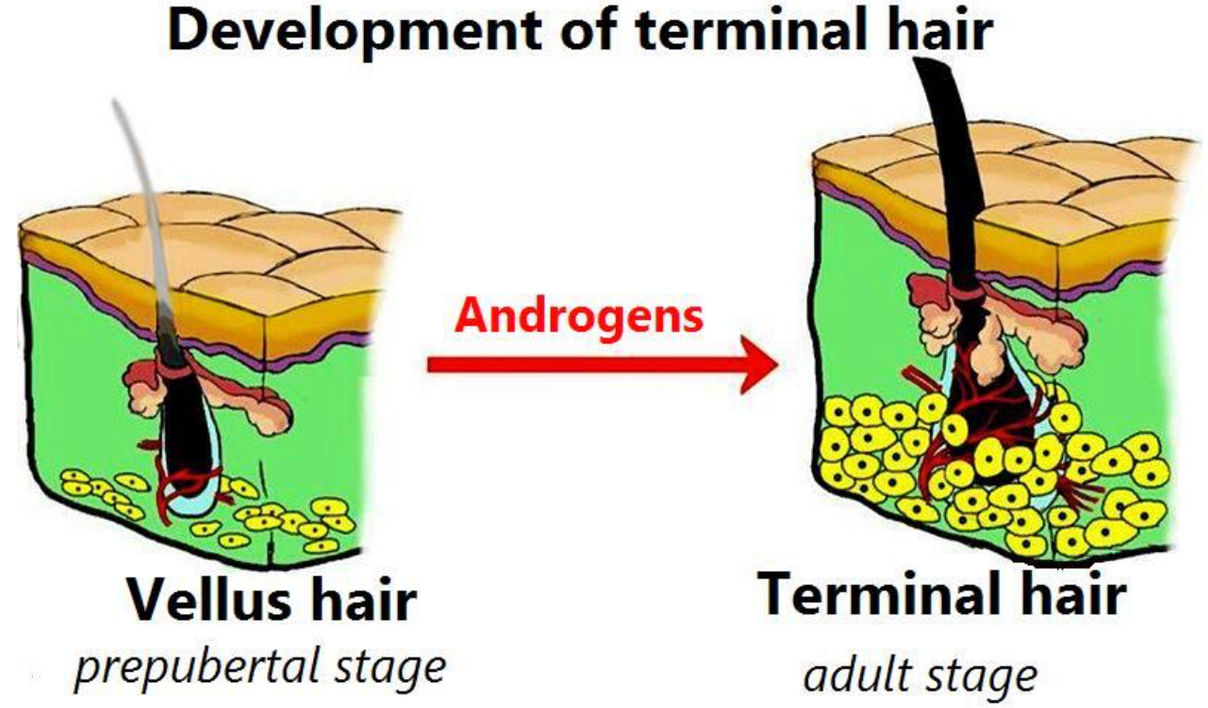
Donovan, J. (2017, June 12). [Digital image]. Retrieved from https://donovanmedical.com/hair-blog/2017/6/12/different-hairs-in-aga

Pathophysiology of Hirsutism

- Androgens act on the pilosebaceous unit → stimulate vellus hair to develop into terminal hair
- Due to
  - ↑ sensitivity of pilosebaceous unit to androgens
  - ↑ peripheral metabolism of androgens



Azziz, R., Carmina, E., & Sawaya, M. (2000). Proposed regulation of the activity of 5a-RA and the production of DHT in body hair [Digital image]. Retrieved from https://www.google.com/url?sa=i&rct=j&q=&esrc=s&source=images&cd=&cad=rja&uact=8&ved=2ahUKEwi9yJmPtcDfAhVl4oMKHaCFDMgQjhx6BAgBEAM&url=https://www.semanticscholar.org/paper/Idiopathic-hirsutism.-Azziz-Carmina/6bf6d09caf77bcad2873bf5b91d26b202ed5023c/figure/2&psig=AOvVaw0dw9reHxeT9SNya2p2neuv&ust=1546013973637519



Comparison of the vellus hair (left) to the terminal hair (right) in humans [Digital image]. (n.d.). Retrieved from https://en.wikipedia.org/wiki/Terminal_hair

Risk Factors

RF:

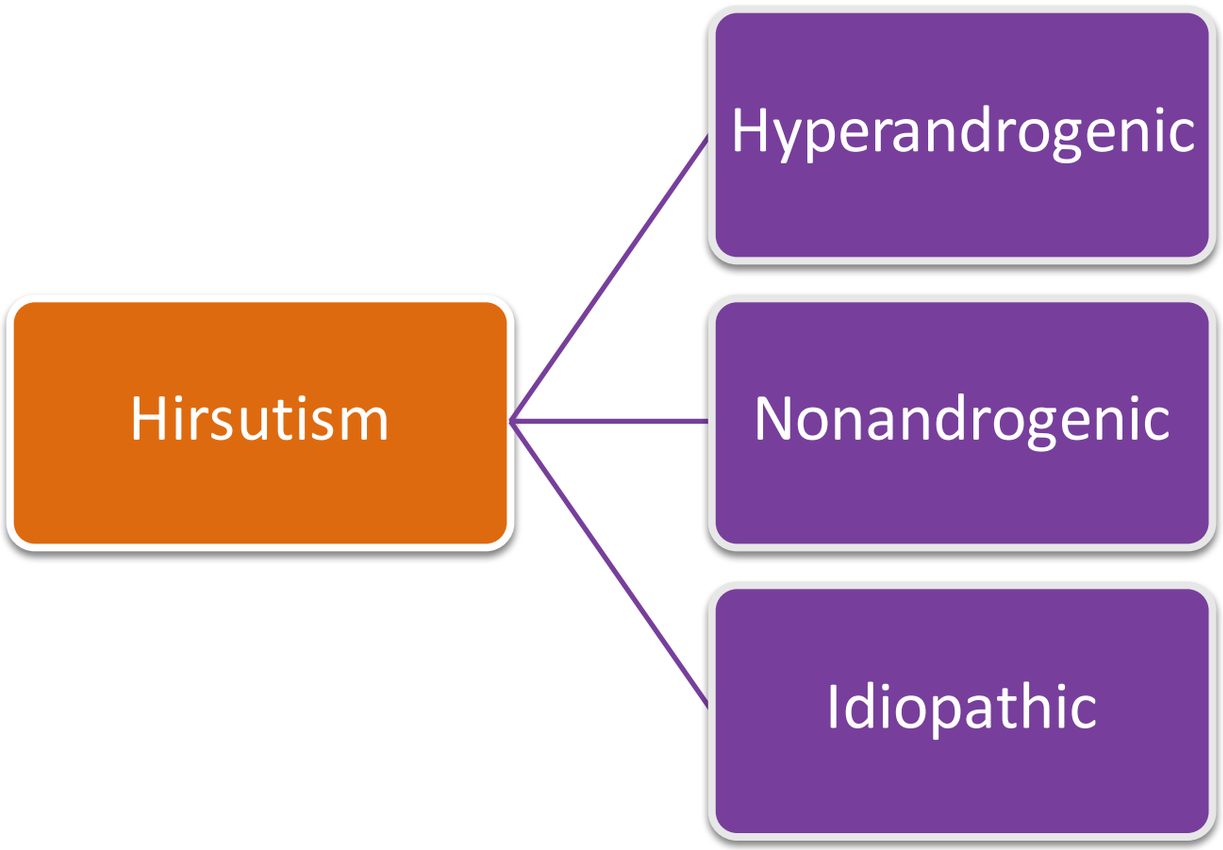
- Race
  - Caucasian > Black > Asian
  - Caucasians have the highest density of hair follicles on scalp biopsy

CAUSES OF HIRSUTISM

Causes of Hirsutism

Most commonly benign

Most common: PCOS, idiopathic



Due to excessive androgen production by ovaries or adrenal glands

- **PCOS (most common- 70-80% of hirsutism)**
- Androgen-secreting tumours (ovarian or adrenal)
  - ½ are malignant
  - Adrenal tumours are rare- 0.2% of hirsutism
- Non-classical congenital adrenal hyperplasia (NCAH) (2-4%)
- Classical adrenal hyperaplasia with poor medication compliance or inadequate replacement steroid dose

- Meds
- Thyroid disease: hypo or hyperthyroidism
- Hyperprolactinemia
- Cushing's syndrome
- Acromegaly (rarely causes hirsutism)

2nd most common (5-15% all hirsutism, 50% mild hirsutism)

Meds

Meds that can cause hirsutism:

- **Danazol**
- **Glucocorticoids**
- **Performance-enhancing anabolic steroids**
- **Progestins**
- Estrogen antagonists- **clomiphene, tamoxifen**
- **Phenytoin**
- **Cyclosporine**
- Minoxidil (anti-hypertensive)
- Diazoxide (anti-hypertensive, treats hypoglycemia)
- Penicillamine
- Interferon
- Cetuximab
- Androgen creams or patches

Idiopathic Hirsutism

- Diagnosis of exclusion
- Normal ovulatory cycles, androgen levels, ovarian morphology
- Possible causes
  - ↑ sensitivity of pilosebaceous unit to androgens
  - Or ↑ peripheral conversion of testosterone to DHT
  - Or change in androgen receptor function

Clinical presentation:
- Regular menses
- Fx hirsutism
- Normal androgens

Familial hirsutism:
- Mediterranean
- East Indian

Clinical Presentation

- Hirsutism (excessive hair growth)
  - Onset
  - Location: upper lip, chin, chest, back, abdomen, upper arms, thighs
  - Sudden onset, rapid progression, severe virilization (androgen-secreting tumour)
- **Hyperandrogenism**
  - Acne, oily skin, acanthosis nigricans
  - Deep voice, male pattern balding (alopecia), dandruff (seborrhea), changes in libido, weight gain
- Galactorrhea (hyperprolactinemia)
- Signs/symptoms of Cushing's, thyroid disease, ovarian CA
- Irregular menses, infertility
- Fx hirsutism, hyperandrogenism (Fx virilization is rare, hyperandrogenism is common)
- Meds
- Effect on QOL- social embarrassment, depression (pt's rating of hirsutism is often more severe than physician's rating)

O/E:

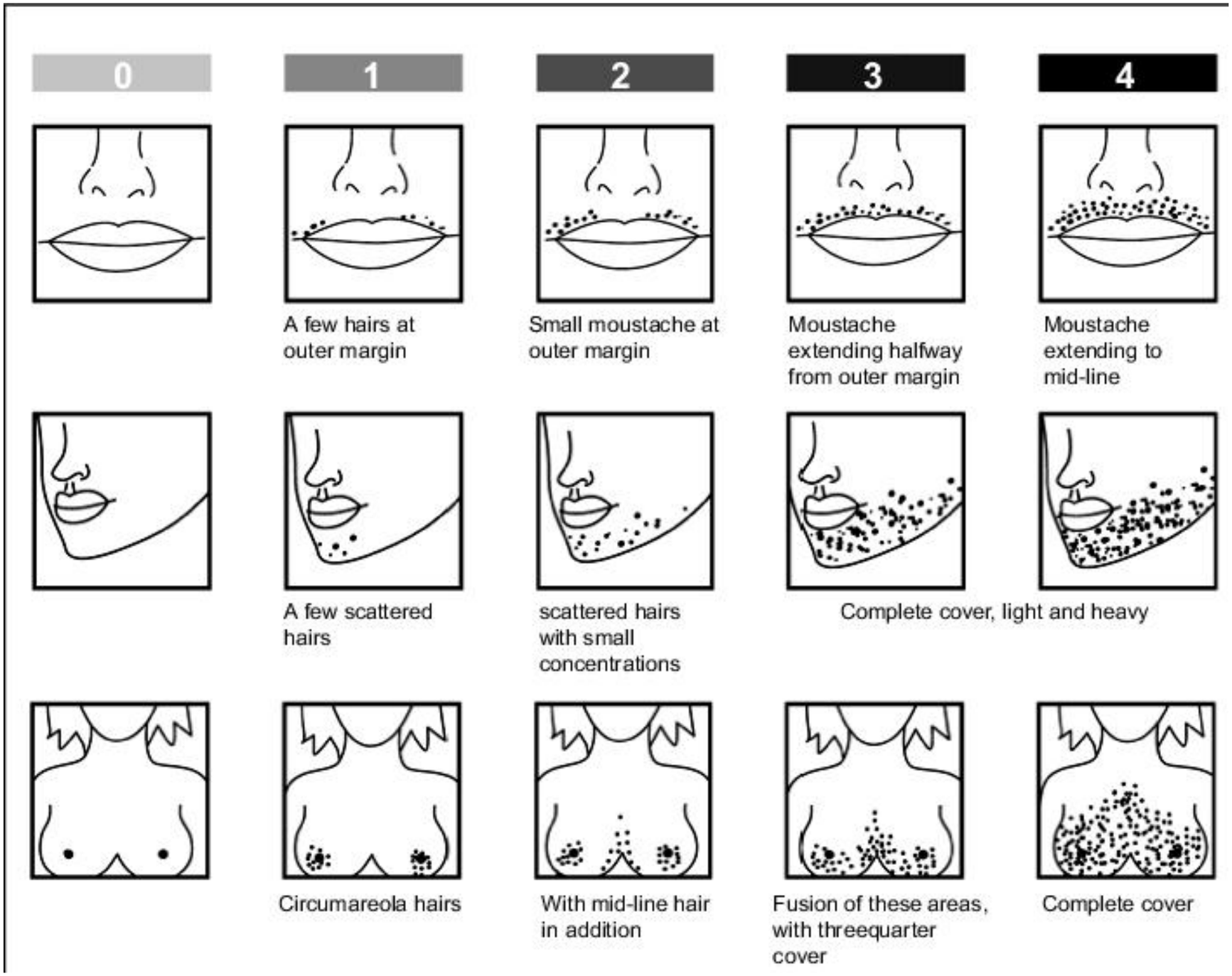
- BMI (obesity)
- **General inspection:**
  - Severity of hirsutism (modified Ferriman-Gallwey score)
  - **Signs of hyperandrogenism:** acne, oily skin, hair thinning, dandruff (seborrhea), acanthosis nigricans, loss of female body contour
  - **Signs of virilization:** deep voice, male pattern balding (fronto-temporal and vertex alopecia), increased muscle bulk
  - Signs of Cushing's syndrome, thyroid disease, acromegaly
- **Thyroid:** goiter
- **Breast:** galactorrhea
- **Abdo:** abdominal/pelvic mass (androgen-secreting tumour)
- **External genitalia:** clitoromegaly (diameter >4mm)

Modified Ferriman-Gallwey Score

Upper lip

Chin

Chest



Blume-Peytavi, U., Atkin, S., Shapiro, J., Lavery, S., Grimalt, R., Hoffmann, R., Gieler, U., Messenger, A. (2009, November/December). [Digital image]. Retrieved from http://www.jle.com/en/revues/ejd/e-docs/european_consensus_on_the_evaluation_of_women_presenting_with_excessive_hair_growth_282783/article.phtml

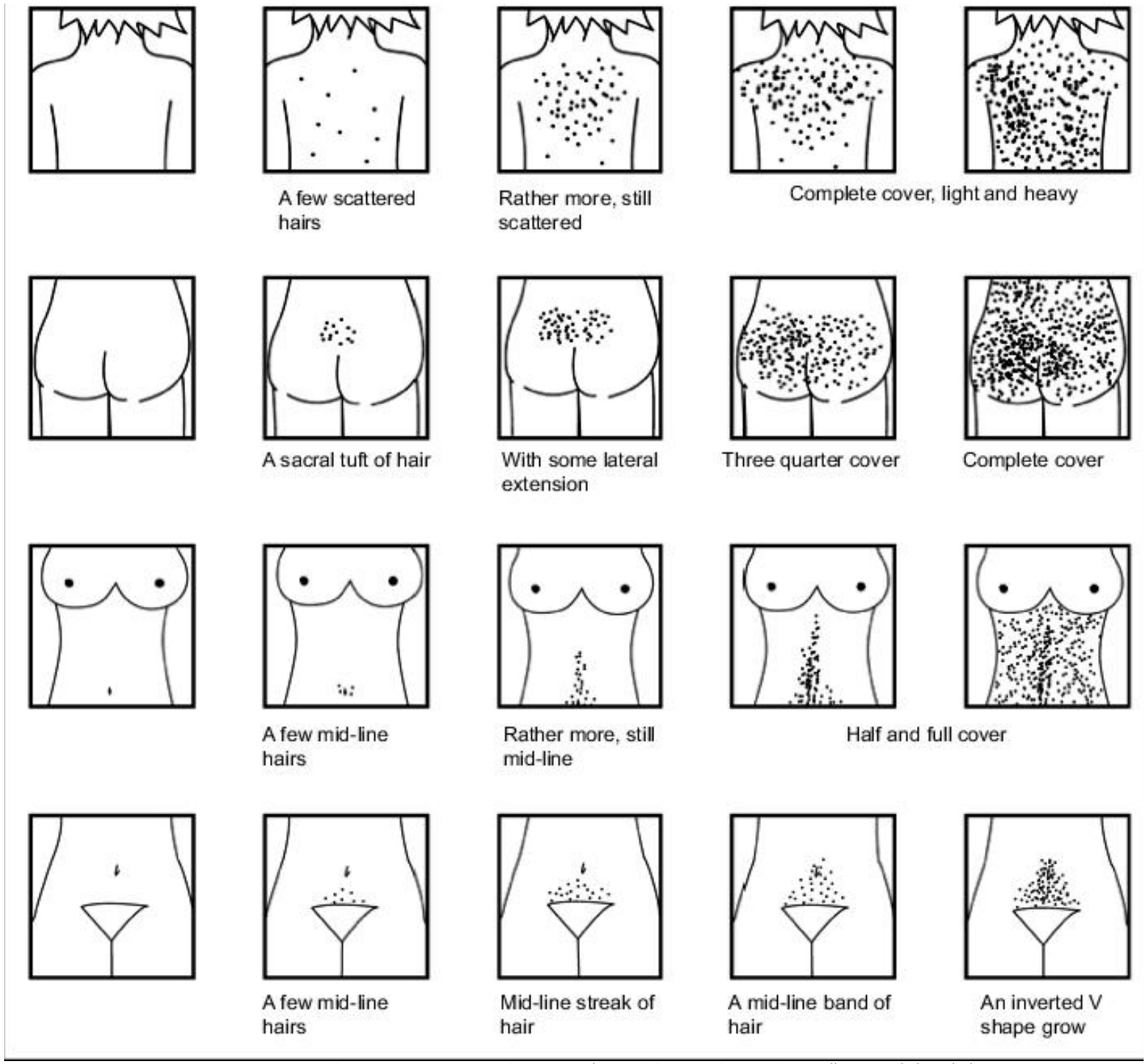
Modified Ferriman-Gallwey Score

Upper back

Lower back

Upper abdomen

Lower abdomen



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Modified Ferriman-Gallwey Score

Upper Arms

Thighs

Rosenfield, R. (2015). Ferriman-Gallwey hirsutism scoring system [Digital image]. Retrieved from http://pediatrics.aappublications.org/content/pediatrics/136/6/1154.full.pdf

- Range: 0-36
  - 0= complete absence of terminal hair growth
- **≥8- excessive hair growth (hirsutism)**
  - 8-15- mild hirsutism
  - 16-25- moderate hirsutism
  - >26- severe hirsutism

INVESTIGATIONS

When To Investigate

- Endocrine Society guidelines:
  - **Mild** hirsutism and normal menses can be **treated without investigations**
  - Investigate if moderate/severe hirsutism

Investigations

- **Androgens:** total testosterone
  - ↑ androgens in hyperandrogenic hirsutism (ovarian or adrenal)
  - Free testosterone not recommended
    - Less reliable, often not available, does not provide additional info
- **SHBG (sex-hormone binding globulin)**
  - ↓ SHCG associated with insulin resistance, ↑ risk T2DM
- if ↑ androgens (hyperandrogenic hirsutism)
  - **DHEAS**
    - ↑ DHEAS- almost always adrenal source
  - **17-hydroxyprogesterone (≤6 pmol/L rules out CAH)**
    - ↑ in congenital adrenal hyperplasia
    - Draw 7-9AM during follicular phase; at any time if anovulatory

PCOS:
- ↑ total testosterone
- ↑ androstenedione
- ↓ SHBG

NCAH:
- ↑ androgens
- ↑ 17-hydroxyprogesterone

Androgen-secreting tumour:
- ↑ total testosterone 2 times normal

Investigations

- **TSH**
  - Hypo or hyperthyroidism
- **Prolactin** (if galactorrhea or irregular menses)
  - Hyperprolactinemia
- **Screen for Cushing's disease only if signs/symptoms**
  - ↑ 24-hour urinary free cortisol
  - ↑ Late night salivary cortisol
  - Dexamethasone suppression test

Investigations

Imaging

- **Pelvic US** (if suspect ovarian CA)
  - For androgen-secreting ovarian tumour, PCOS
  - To evaluate endometrium if oligomenorrhea or amenorrhea
- **MRI or CT** (if suspect adrenal neoplasm)

Other

- Endometrial biopsy if thickened endometrium to rule out endometrial hyperplasia

Investigations

- **LH, FSH**
  - PCOS: ↑ LH/FSH ratio (>2:1) (may also be normal)
  - Normal or ↓ in androgen-secreting and adrenal tumours

MANAGEMENT

Management Overview

- Combination therapy is most effective
- Multi-disciplinary approach
- Refer to endocrinology/REI if meets criteria
- Permanent hair reduction only with laser hair removal and electrolysis, the rest of treatments are temporary

When to refer to endocrinology/REI

- Virilization
- Serum testosterone or DHEAS >2 times normal (androgen-secreting tumour)
- Signs/symptoms of Cushing's disease
- 17-hydroxyprogesterone >6nmol/L (CAH)

Effect on QOL

- Treatment results in both cosmetic and psychologic benefit
- Predictors of QOL
  - Obesity (most important)
  - Hirsutism

Management Overview

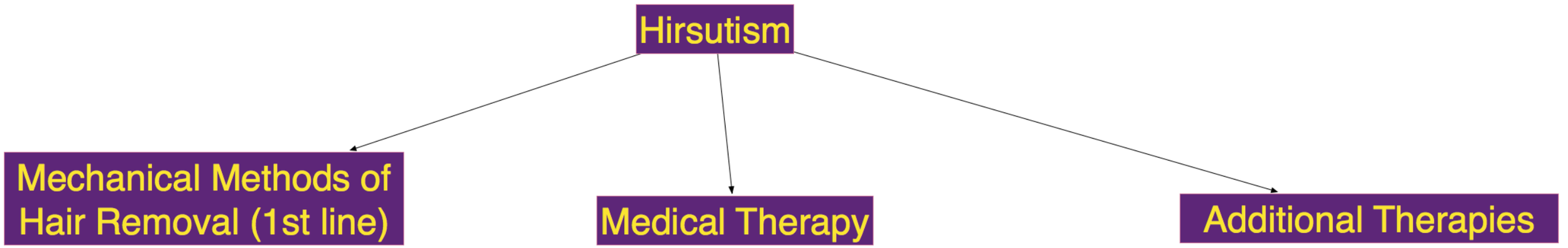
Combination therapy:

1. Mechanical removal of excess hair
2. Medical therapy
    - Suppress ovarian androgen production
    - Anti-androgen meds

1st line:

- Mechanical removal of excess hair and/or topical therapy
- CHC

Management



Temporary:
Shaving
Bleaching
Chemical depilation
Plucking, waxing, threading

Permanent hair reduction, may need periodic retreatment:
Electrolysis
Laser (Nd:Yag)

Topical therapy (1st line):
Eflornithine hydrochloride cream (Vaniqa) BID at least 8hrs apart

Combined hormonal contraceptives (CHC) (1st line):
Oral, vaginal ring, transdermal patch

Anti-androgens (for moderate/severe hirsutism):
Spironolactone 100-200mg PO daily (can be combined with CHC). Monitor lytes 3m after starting and q1yr.
Diane 35 (cyproterone acetate (CPA) 2mg combined with ethinyl estradiol 0.035mg)
Finasteride 5mg PO daily (can be combined with CHC)
Flutamide 250-500mg PO daily (can be combined with CHC). Monitor serum transaminase levels before starting, q1m x4, then q1yr (can cause hepatotoxicity)

Glucocorticoids (for NCAH)
GnRH agonists (for ovarian hyperandrogenism, refractory to therapy)
Short-term MPA (for PCOS)

Other Considerations

- Consider long-term consequences of hyperandrogenism and PCOS
  - AUB, anovulation
  - Infertility
  - Metabolic syndrome
  - Obesity
  - HTN, HTN and pre-eclampsia in pregnancy
  - Diabetes, dyslipidemia, CVD

AUB

- Need regular withdrawal bleeds to decrease risk of endometrial hyperplasia and CA (due to unopposed estrogen)
- Treatment: CHC, regular progesterone, progestogen-induced withdrawal bleeding

Infertility

- May need ovulation-induction therapy

MECHANICAL THERAPY

Mechanical Removal

- Treatment option depends on pt's preference (cost, tolerance) rather than efficacy

Table 4. Mechanical methods of hair removal

Method	Advantages	Disadvantages	Costs	Effect
Shaving	• Easily available • Can be done at home	• Less acceptable to women • Early "stubble" during initial days following shaving	$	Temporary
Bleaching	• Easily available • Can be done at home • Good for moustache and sideburn areas	• Can cause severe skin irritation	$	Temporary
Chemical depilation	• Easily available • Can be done at home • Pain-free	• Can cause skin irritation	$	Temporary, lasts about 10 days
Plucking	• Easily available • Can be done at home • Good for individual long hairs	• Can cause ingrown hairs, folliculitis, and scarring	$	Temporary
Waxing	• Easily available • Can be done at home • Can be used for larger areas	• May cause skin irritation, especially on the face	$	Temporary, lasts 3 to 6 weeks
Threading	• Can be done at home • Mainly used for face	• Requires skill	$	Temporary, lasts 3 to 6 weeks
Electrolysis	• All hair and skin types	• Requires qualified operator • Painful • Time-consuming, targets one hair follicle at a time, impractical for large areas	$$ to $$$	Permanent hair reduction
Laser	• Can be used for larger areas	• Requires qualified operator • Painful • Time-consuming, usually 6 treatments and possible maintenance therapy • Best for darker hair	$$ to $$$	Permanent hair reduction

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Mechanical Hair Removal

- Bleaching, shaving, chemical depilators do not change underlying hair or follicle

Torres, N. (2017, September). [Digital image]. Retrieved from https://www.liveabout.com/bleaching-facial-and-body-hair-101-1716732

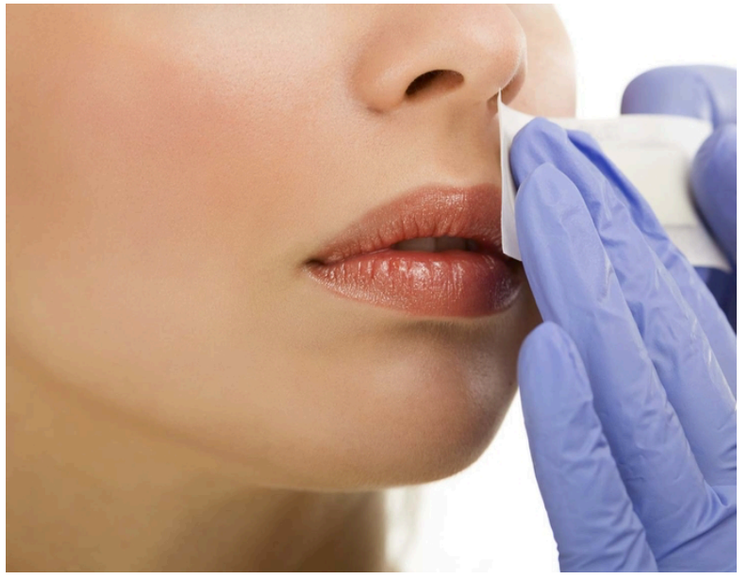
[Digital image]. (2016, August). Retrieved from http://hudabeauty.com/2017/11/02/why-shaving-my-face-is-the-best-thing-i-ever-did/

[Digital image]. (n.d.). Retrieved from https://hairfreelife.com/best-hair-removal-creams-sensitive-skin/

Mechanical Hair Removal

- Plucking, waxing, threading, laser can reduce regrowth of hair, especially if combined with medical therapy

[Digital image]. (2018, April 13). Retrieved from https://rayanworld.com/20180413073635001/Causes-of-Excess-Facial-Hair-in-Women?subarticle=12



Faragalli, S. (2015, September 7). [Digital image]. Retrieved from https://www.instyle.com/news/your-guide-to-waxing-your-upper-lip

[Digital image]. (n.d.). Retrieved from https://www.pinterest.com/refinedDaySpa/threading-eyebrow-facial-hair-removal/

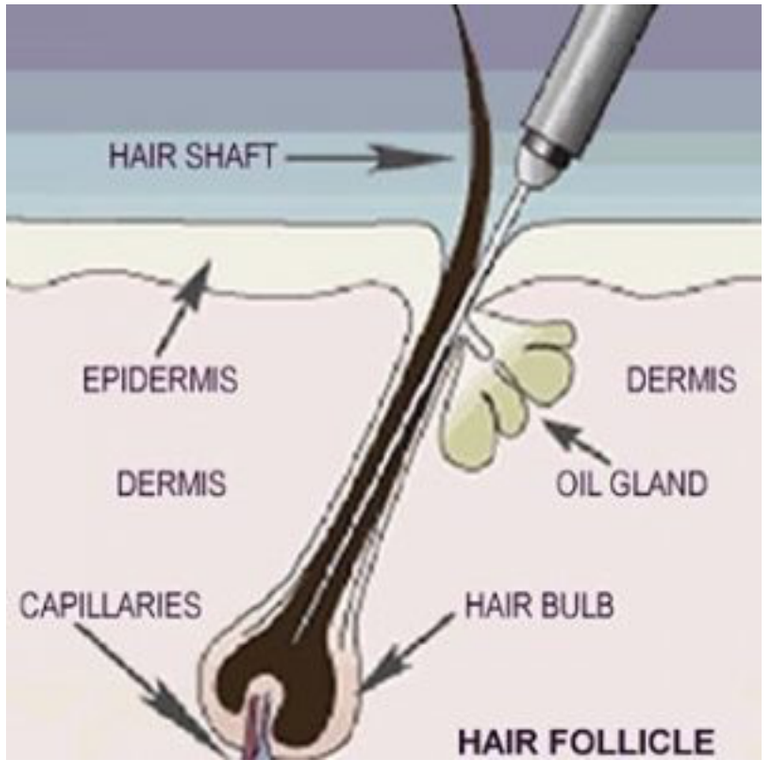
Mechanical Hair Removal

- Laser and electrolysis reduce hair growth long-term

Lasers
- Nd:Yag and diode-based laser best for pts with dark skin
- Laser is more practical than electrolysis for large SA

Electrolysis
- Hair root is destroyed with microprobe, then hair is removed with tweezers

George, S. (2017, October). [Digital image]. Retrieved from https://medium.com/@AstraHealth/must-do-tips-after-laser-hair-removal-treatment-d94c43984645



[Digital image]. (n.d.). Retrieved from https://beautyworksspa.com/electrolysis-permanent-hair-removal/

Vertonghen, E. (2016). [Digital image]. Retrieved from https://www.youtube.com/watch?v=cB8KXdLxRiE

MEDICAL THERAPY

Medical Therapy

- May be used in both hyperandrogenic and idiopathic hirsutism
- Chronic use
- **Need at least 4-6m to see initial response to treatment and significant improvement in hirsutism**
    - Since the lifespan of terminal hair is at least 6m
    - Terminal hair then become replaced by finer hair
    - May use mechanical hair removal techniques in the mean time → may speed up effects of medical therapy
- Hair growth recurs once stop medical therapy

Medical Therapy

Table 5. Medical therapy for hirsutism

Treatment	Usage	Side effects/adverse effects
Topical therapy		
Eflornithine hydrochloride	• For facial hirsutism • Thin layer applied twice daily at least 8 hours apart	• Local irritation, pruritus, and stinging
OC		
CHC	• Oral, vaginal ring, and transdermal patch formulations	• Breakthrough bleeding, amenorrhea • Nausea, bloating • Headache • Breast tenderness • Venous thromboembolism (rare)
Anti-androgens		
Spironolactone	• 100 to 200 mg once daily • Can be combined with CHC • Monitor electrolytes 3 months after starting and annually	• Irregular menses • Transient diuresis • Fatigue • Headache • Gastric upset • Breast tenderness • Feminization of a male fetus if taken during pregnancy
CPA	• 2 mg combined with ethinyl estradiol 0.035 mg (Diane 35)	• Irregular menses, breakthrough bleeding, amenorrhea • Nausea, bloating • Headache • Breast tenderness • Venous thromboembolism (rare) • Decreased libido • Liver toxicity • Feminization of a male fetus if taken during pregnancy
Finasteride	• 5 mg once daily • Can be combined with CHC	• Minimal • Feminization of a male fetus if taken during pregnancy
Flutamide	• 250 to 500 mg once daily • Can be combined with CHC • Monitor serum transaminase levels before treatment, monthly ×4 months then annually	• Hepatotoxicity • Hot flashes • Decreased libido • Diarrhea • Feminization of a male fetus if taken during pregnancy

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Eflornithine Hydrochloride (Vaniqa)

- Ornithine decarboxylase inhibitor
  - Ornithine decarboxylase is an enzyme involved in hair growth
- For facial hirsutism
  - In Canada, only licensed and indicated for management of unwanted **facial** hirsutism
  - Has been shown to decrease facial hirsutism after using for 8w
- Can be used as adjuvant to laser
- Hirsutism recurs once stop using

Side/adverse effects
- Local irritation
- Pruritis
- Stinging

Elfornithine hydrochloride apply BID at least 8hrs apart

Combined Hormonal Contraceptives (CHC)

- 1st line therapy
  - PO, vaginal ring, or transdermal patch
  - Evidence shows effectiveness
- Suppressed androgens → decreases free testosterone levels
  - Suppresses gonadotropins (LH, FSH)
  - Decreases ovarian androgen production
  - Increases hepatic production of SHBG

Side/adverse effects

- Breakthrough bleeding
- Amenorrhea
- Nausea, bloating
- Headache
- Breast tenderness
- VTE (rare)
  - Pts with PCOS may have increased risk of VTE
  - Concern for VTE from retrospective and case control studies, risk not demonstrated in prospective studies

Anti-Androgens

- Prevent androgens from acting on target tissues
- Used for idiopathic hirsutism and as an adjunct to androgen suppressive therapies
- Used for moderate/severe hirsutism or for mild hirsutism to ensure optimal response
- **Can combine with CHC**
  - For moderate and severe hirsutism, can improve effect of CHC
  - **CHC also has contraception effect (some anti-androgens have potential teratogenic adverse effects)**

Anti-androgens
- Spironolactone
- Diane 35
- Finasteride
- Flutamide

If pt wants to conceive
- Stop anti-androgens before discontinuing CHC

Spironolactone

- Can be used alone or together with CHC
- Mechanism of action
  - Competes with androgen receptor in skin fibroblasts
  - Limited suppression of androgen production by ovary and adrenal gland
- Monitor lytes 3m after starting, then q1yr to for electrolyte imbalances

Spironolactone 100-200mg PO daily

Side/adverse effects

Side effects decreased with increasing dose

- Transient diuresis
- Fatigue
- **Irregular menses**
  - Dose-dependent, managed with CHC
- Headache
- GI upset
- Breast tenderness
- **If taken during pregnancy: feminization of male fetus!**

Diane 35

- Diane 35= Cyproterone acetate (CPA) 2mg+ ethinyl estradiol 0.035mg
- Mechanism of action of CPA
  - Inhibits gonadotropin (LH, FSH) release → decreases androgen production
  - Competitively binds to androgen receptors
- May be used alone or together with spironolactone 100mg daily
  - Combination with spironolactone has been shown to be effective
  - No studies for CPA monotherapy
  - 1 study for combination with CHC showed no difference in effectiveness

Side/adverse effects

- Irregular menses, amenorrhea, breakthrough bleeding
- Nausea, bloating
- Headache
- Breast tenderness
- VTE (rare)
- Decreased libido
- Liver toxicity
- Depression
- **If taken during pregnancy: feminization of male fetus!**

Finasteride

- Can be combined with CHC

Side/adverse effects

Minimal side effects

- **If taken during pregnancy: feminization of male fetus!**

Finasteride 5mg PO daily

Flutamide

- NSAID, no hormonal activity
- May be used alone or together with CHC
- Equally or more effective than other anti-androgens, but issues with hepatotoxicity and cost!
- Monitor serum transaminase levels before starting, then q1m x4, then q1yr
  - Contraindicated if transaminases ≥2 times the normal limit

Side/adverse effects

- **Hepatotoxicity**
- Hot flashes
- Decreased libido
- Diarrhea
- **If taken during pregnancy: feminization of male fetus!**

Flutamide 250-500mg PO daily

ADDITIONAL THERAPIES

Additional Therapies

- Not enough evidence for
  - Insulin sensitizers (metformin, thiazolidinediones) in PCOS
  - Long-term use of MPA for hyperandrogenism

Additional therapies

- Glucocorticoids
- GnRH agonists
- Short-term MPA

Glucocorticoids

- Suppress androgen production by adrenal glands
- May be used in NCAH
    - No evidence available for other causes of hirsutism, has side effects

GnRH Agonists

- Induces medical oophorectomy
- For ovarian hyperandrogenism refractory to therapy
    - Most studies show no benefit to add GnRH agonist over CHC to medical therapy
- Need add-back therapy or CHC due to hypoestrogenic side effects

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MPA

- SOGC: **insufficient evidence** to recommend for treatment of hyperandrogenism
- Has been suggested for pts with contraindications to estrogen-containing therapy (CHC)
- PO MPA
    - Short-course can cause withdrawal bleeding in pts with PCOS → decreases androgen levels
- SQ MPA
    - Decreases SHBG
    - No difference in total testosterone and free testosterone levels
    - Significant weight gain
- No evidence for long-term therapy

References

Liu, K., Motan, T., & Claman, P. (2017). No. 350- Hirsutism: Evaluation and Treatment. *J Obstet Gynaecol Can, 39*(11), 1054-1068.