Pigment and Hair Disorders

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Objectives

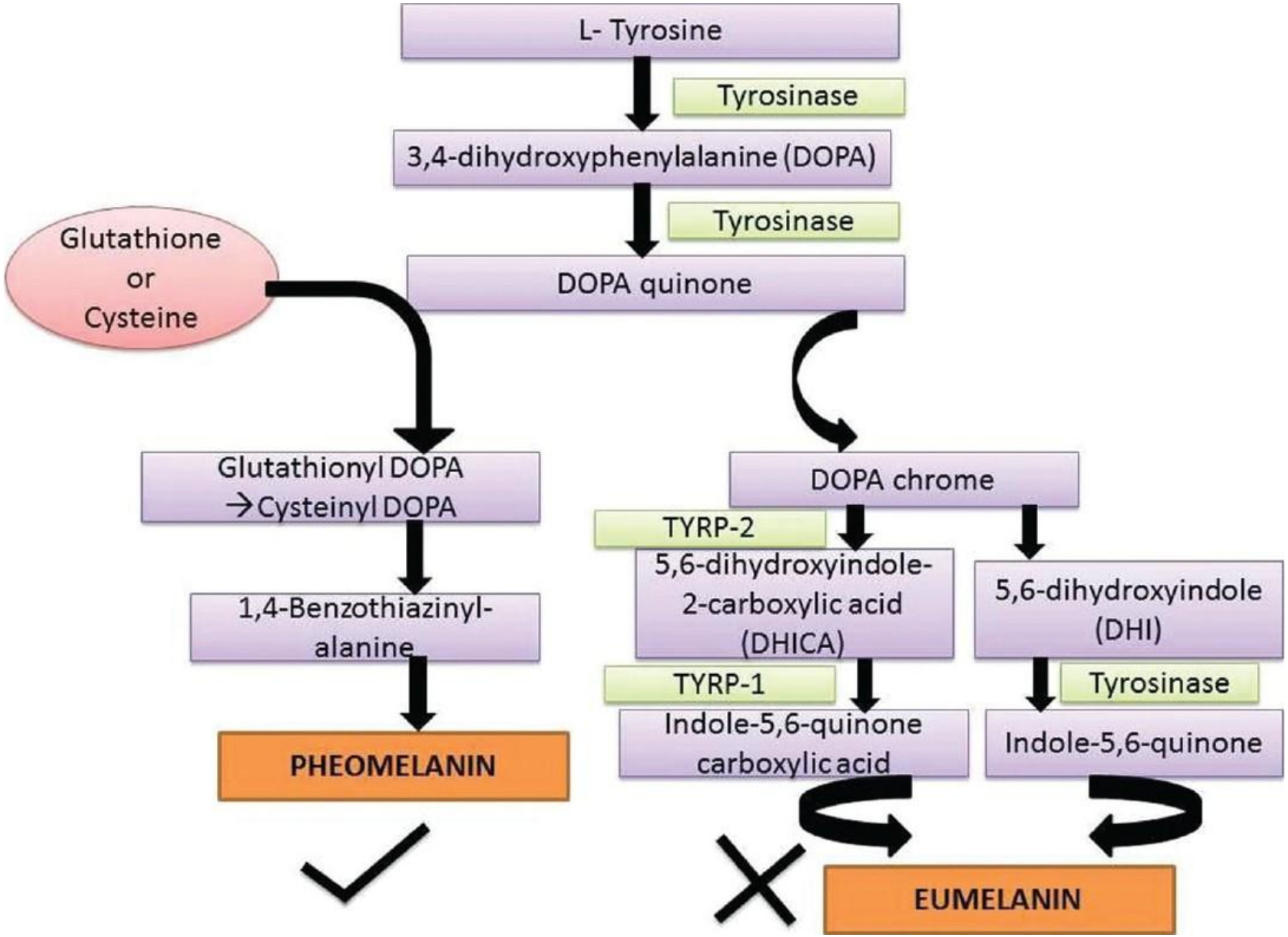
- To be familiar with physiology of melanocytes and skin color.
- To be familiar with common cutaneous pigment disorders, pathophysiology, clinical presentation and treatment
- To be familiar with physiology of hair follicle
- To be familiar with common hair disorders, both acquired and congenital, their presentation, investigation and management
- Reference is the both the lecture and the TEXTBOOK

Skin Pigment

- Reduced hemoglobin: blue
- Oxyhemoglobin: red
- Carotenoids : yellow
- Melanin : brown
- Human skin color is classified according to Fitzpatrick skin phototype.

THERE ARE 6 DIFFERENT SKIN TYPES

PHOTOTYPE	HAIR	SKIN	TENDENCY TO BURN	TANNED
I	Red Hair	Milky	Constant high	Null
II	Blonde Hair	Light	Constant medium	Mild
III	Brown	Light	Frequent	Clear
IV	Dark Brown	Matt	Infrequent	Dark
V	Very Dark Brown	Matt	Exceptional	Very dark
VI	Black	Black	No	Black


L- Tyrosine
Tyrosinase
3,4-dihydroxyphenylalanine (DOPA)
Tyrosinase
DOPA quinone
Glutathione
or
Cysteine
Glutathionyl DOPA
→Cysteinyl DOPA
1,4-Benzothiazinyl-
alanine
PHEOMELANIN
DOPA chrome
TYRP-2
5,6-dihydroxyindole-
2-carboxylic acid
(DHICA)
5,6-dihydroxyindole
(DHI)
TYRP-1
Tyrosinase
Indole-5,6-quinone
carboxylic acid
Indole-5,6-quinone
EUMELANIN

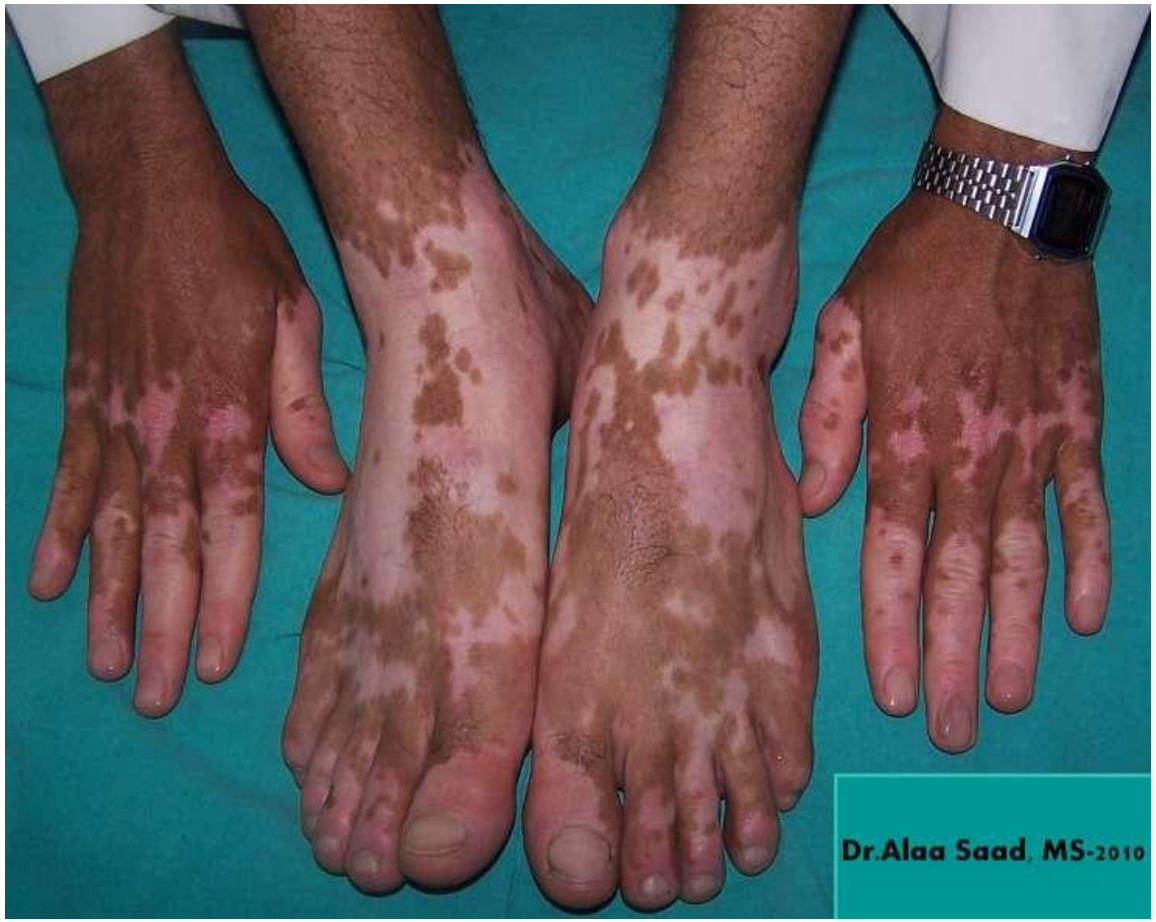
Vitiligo

- Incidence 1%
- Early onset
- A chronic autoimmune disease with genetic predisposition
- Complete absence of melanocytes
- Could affect skin, hair, retina, but Iris color no change
- Rarely could be associated with: alopecia areata, thyroid disease, pernicious anemia, diabetes mellitus
- Koebner phenomenon

Vitiligo

- Ivory white macules and patches with sharp convex margins
- Slowly progressive or present abruptly then stabilize with time
- Focal
- Segmental
- Generalized (commonest)
- Trichrome
- Acral
- Poliosis

www.metro.co.uk



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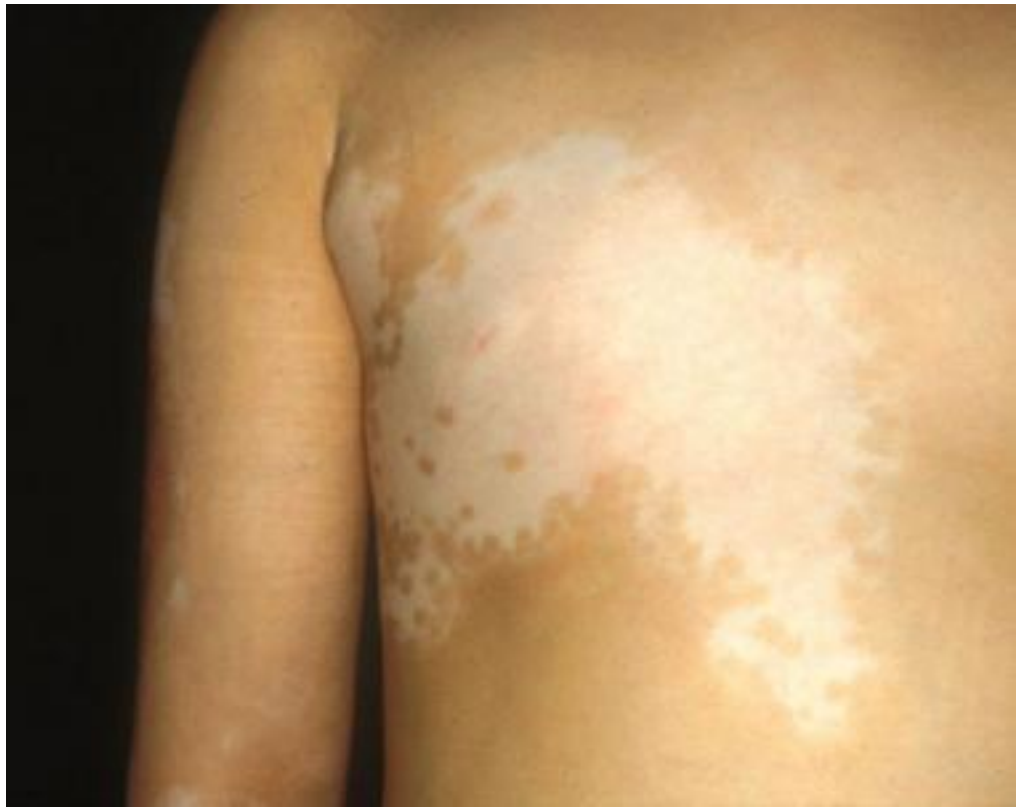
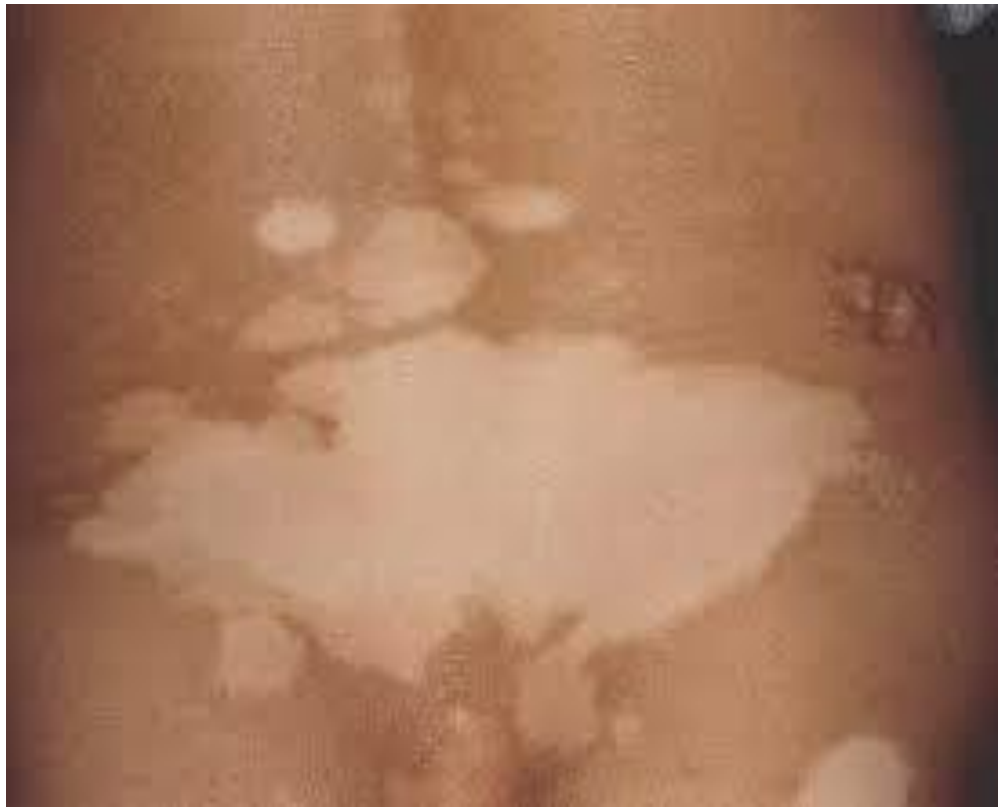


www.medscape.com



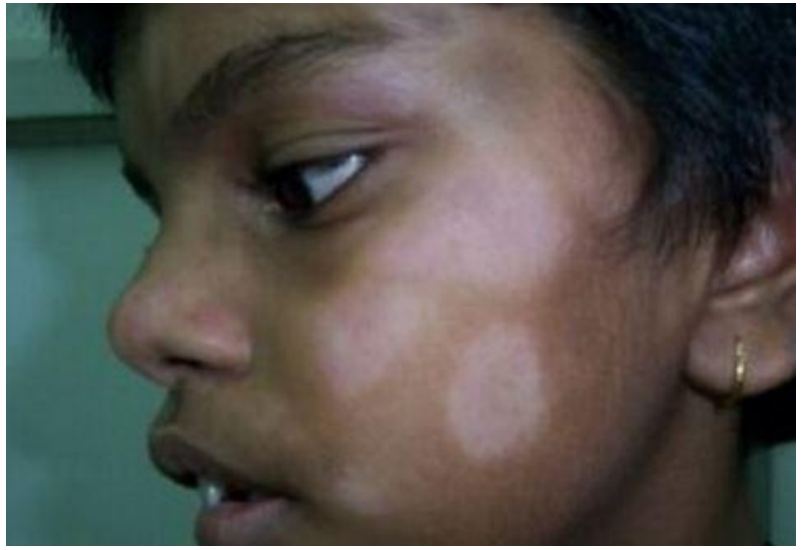
www.jaad.org

Vitiligo

- Diagnosis usually clinically
- Wood’s lamp for early vitiligo, white person
- Pathology shows normal skin with no melanocytes

Differential Diagnosis of Vitiligo

- Pityriasis alba
- leprosy
- Hypopigmented pityriasis Versicolor
- Discoid lupus erythematosus
- Post inflammatory hypopigmentation
- Mycosis fungoides
- Chemical leukoderma
- Nevus anemicus
- Nevus depigmentosus
- Hypomelanosis of Ito
- Piebaldism



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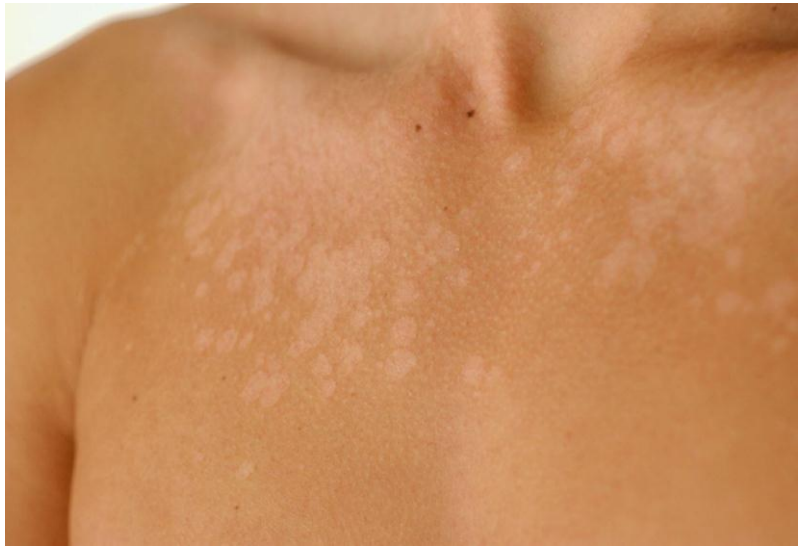

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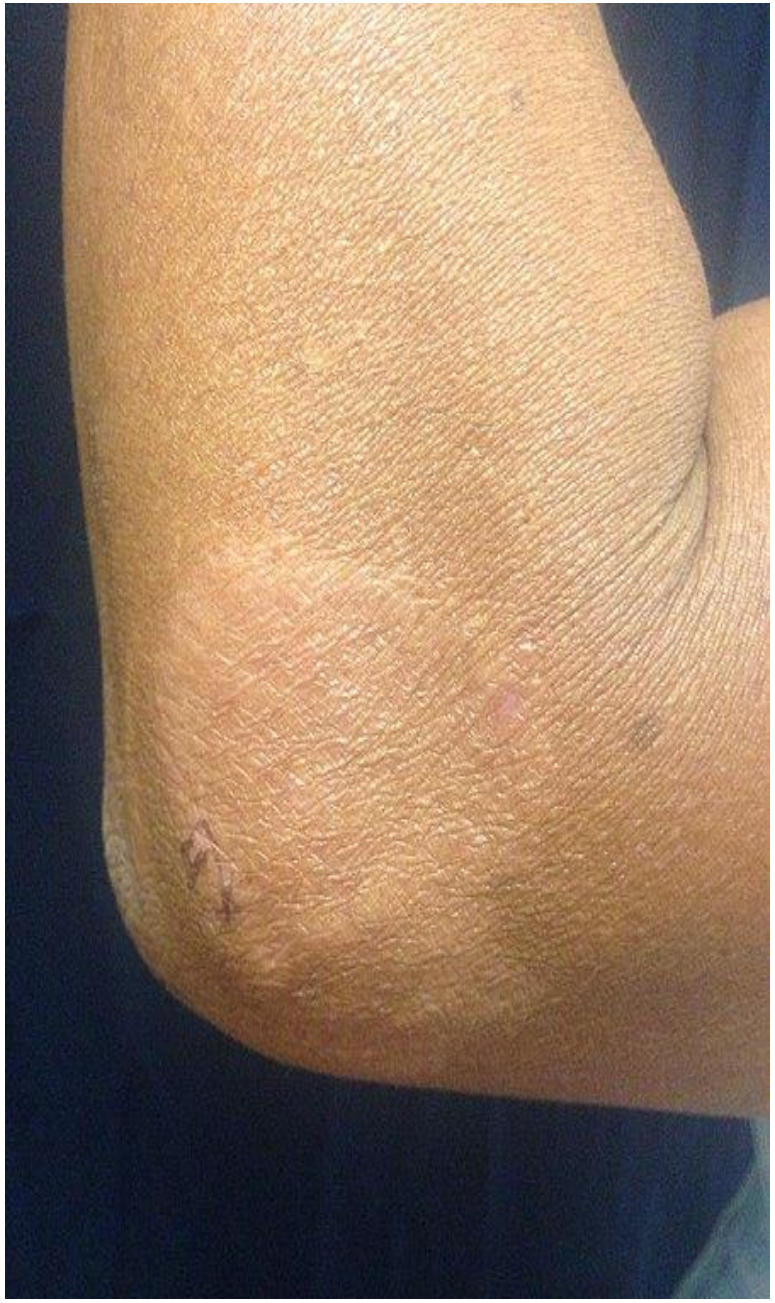

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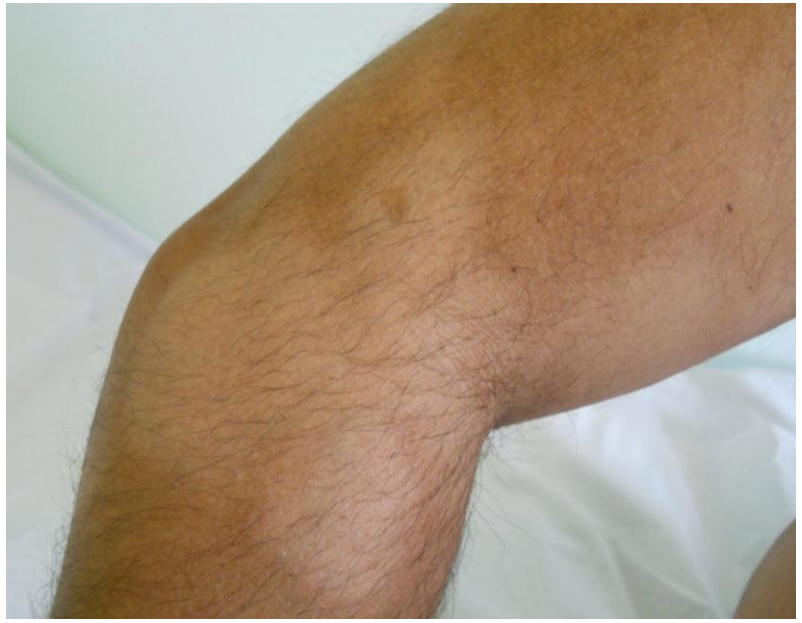
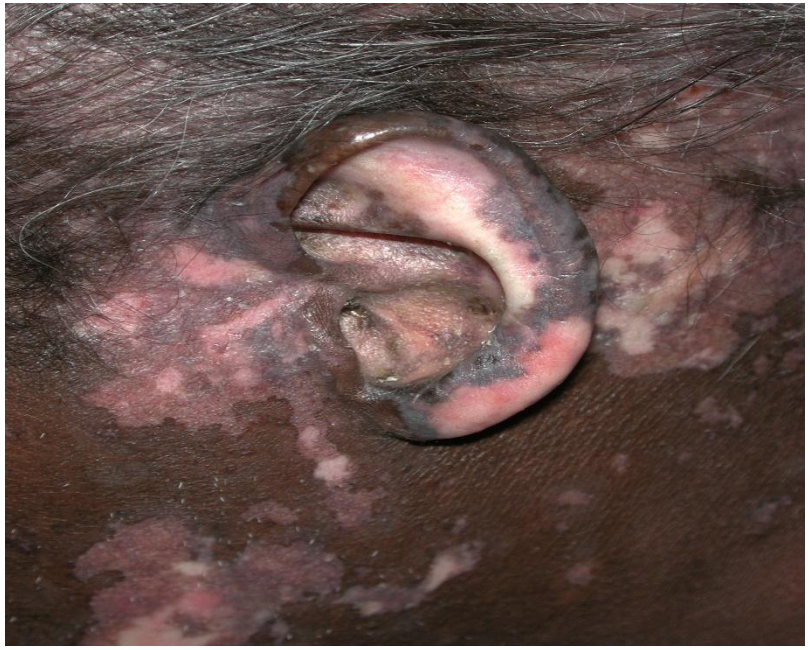


casereports.bmj.com



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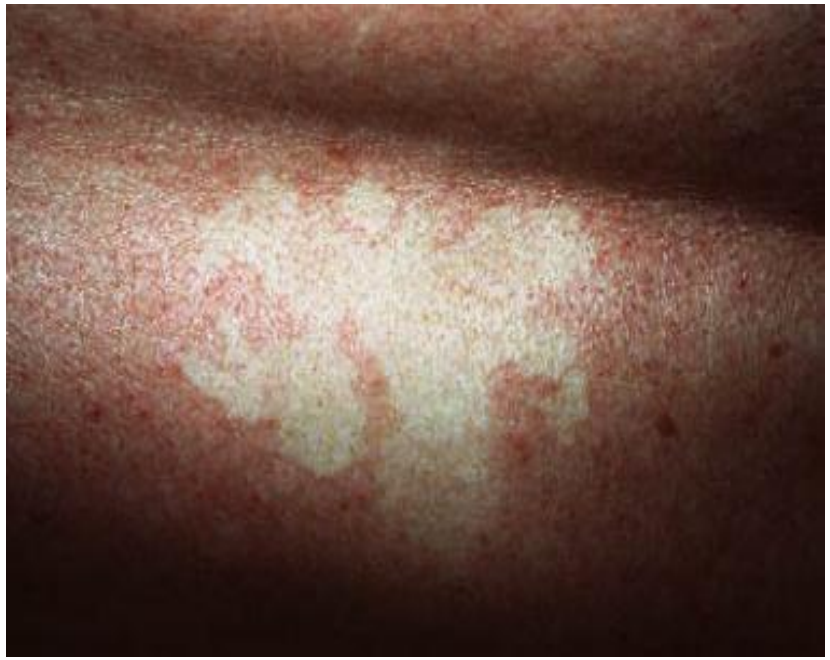

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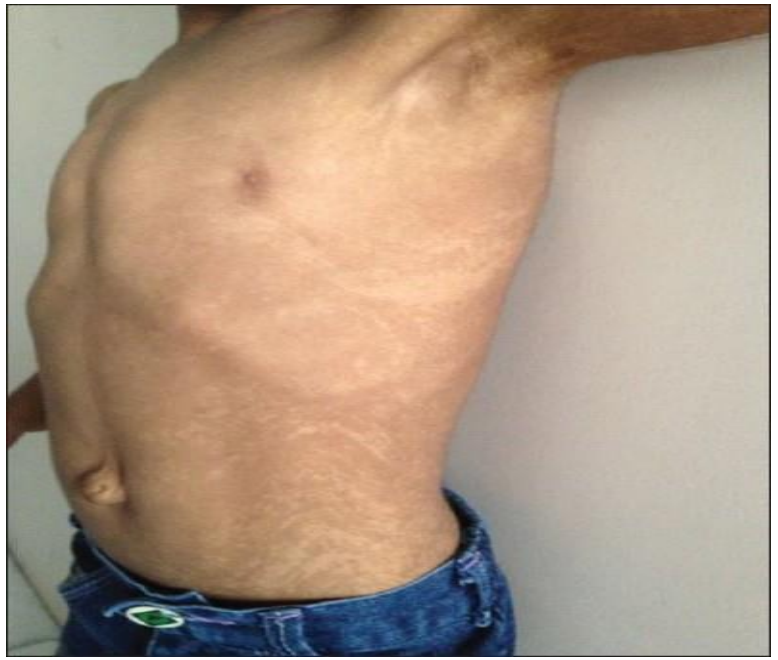

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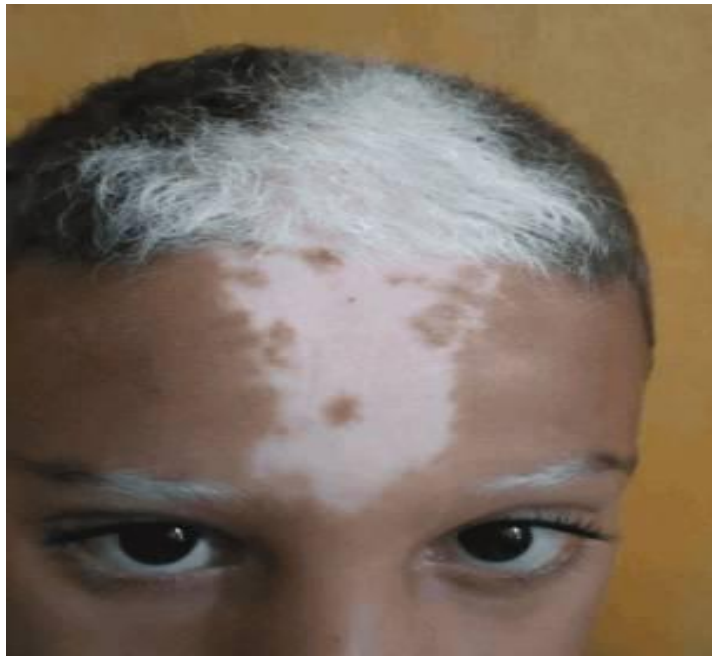

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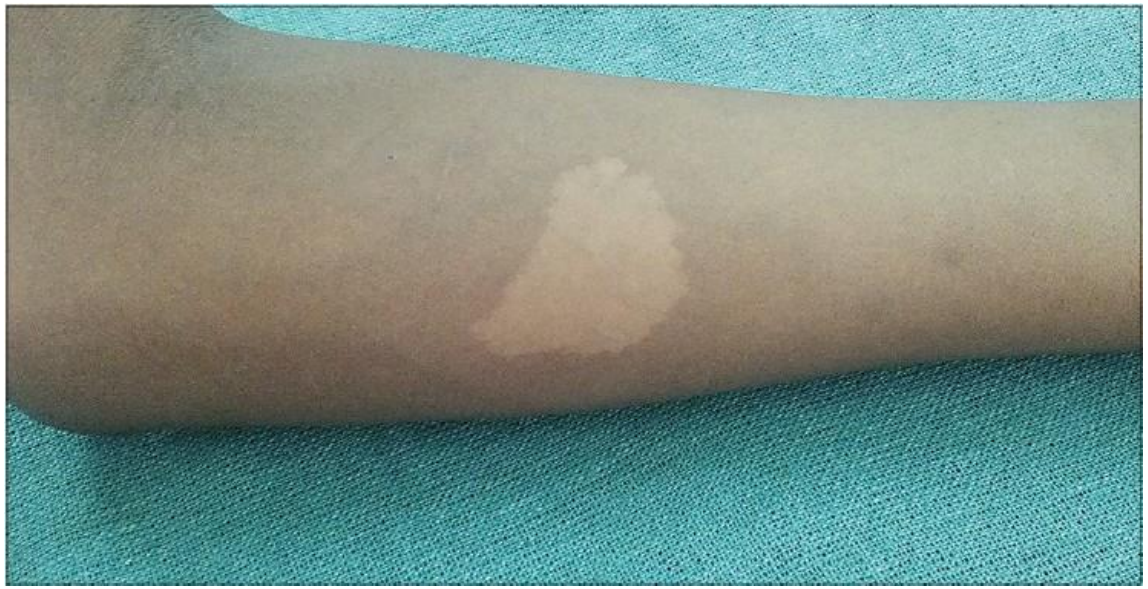
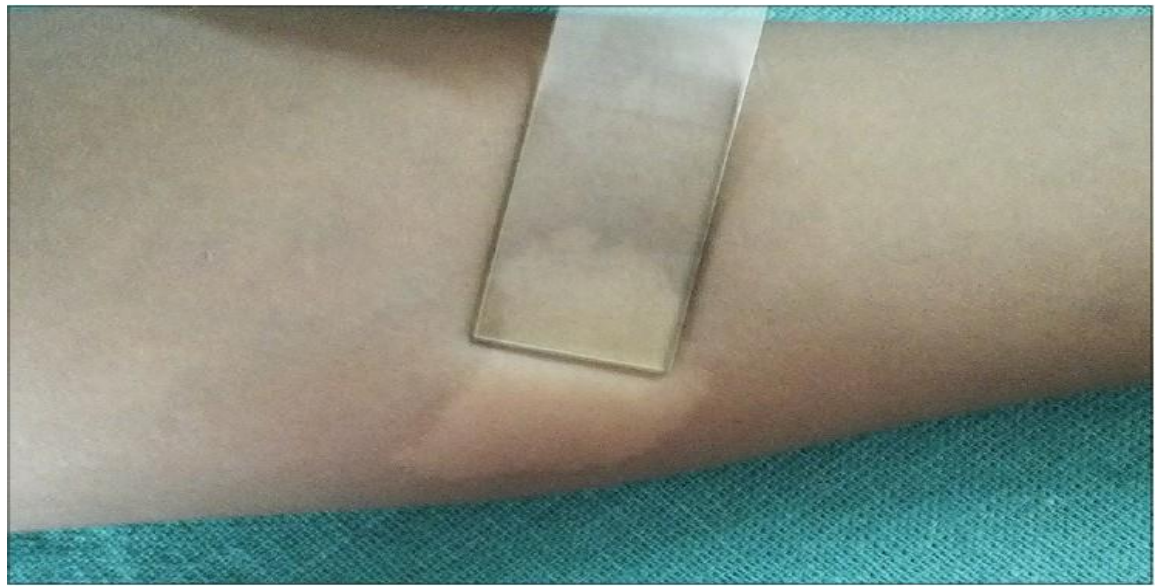




www.pigmentinternational.com

Disease entity	Clinical features
Nevus anemicus	Borders merge with normal skin on diascopy
Ash leaf macule	Usually multiple, associated features of tuberous sclerosis, accentuated on Wood's lamp examination, lance-ovate shape, confetti macules
Vitiligo	Absence of melanocytes, negative 3,4-dihydroxyphenylalanine reaction, chalky white appearance on Wood's lamp examination, koebnerization seen
Hypomelanosis of Ito	Whorled hypopigmented macules and patches, unilateral or bilateral, involve two or more body surfaces, follow lines of Blaschko, associated abnormalities of the brain, eyes and bones
Hansen's disease	Loss of sensation, presence of acid fast bacilli, characteristic histopathology
Incontinentia pigmenti	History of evolution of lesion from vesicles, plaque and pigmentation
Piebaldism	White forelock with depigmented polygonal patch

Post Inflammatory Hypopigmentation

- Could happen after any inflammatory dermatosis
- Pityriasis versicolor hypopigmentation secondary to dicarboxylic acid
- Post chemical peel or laser
- Post intralesional corticosteroid injection
- Treatment: make up, tattoo, Excimer laser, NB-UVB

Pityriasis Alba

- Macular scaly hypopigmented macules and patches in children
- Prevalence 5%
- Affects mostly face and neck
- Associated with atopic dermatitis and dry skin
- Ill defined margins, not itchy, fine scales
- Self limited
- Might be treated by topical corticosteroids, tacrolimus

Nevus Anemicus

- Congenital, at birth pale whitish macule or patch <10 cm
- No enhancement with Wood's lamp
- After rubbing: no erythema while surrounding skin is red
- Blood vessels in the patch are more sensitive to catecholamines
- Pathology: normal skin
- No need for treatment

Nevus Depigmentosus

- Congenital, solitary depigmented patch
- Cutaneous mosaicisim with altered clones of melanocytes with decreased ability to produce melanin
- Stable
- Mostly in trunk and extremities
- Treatment: make up, tattoo, melanocyte transfer

Vitiligo Management

- Face and trunk with good response
- Acral location or poliosis with poor response
- Sun protection: sun-avoidance, clothes, hats, sunscreens
- Make up
- Tattoo
- **Psychological Support**

Vitiligo Management

Focal disease:

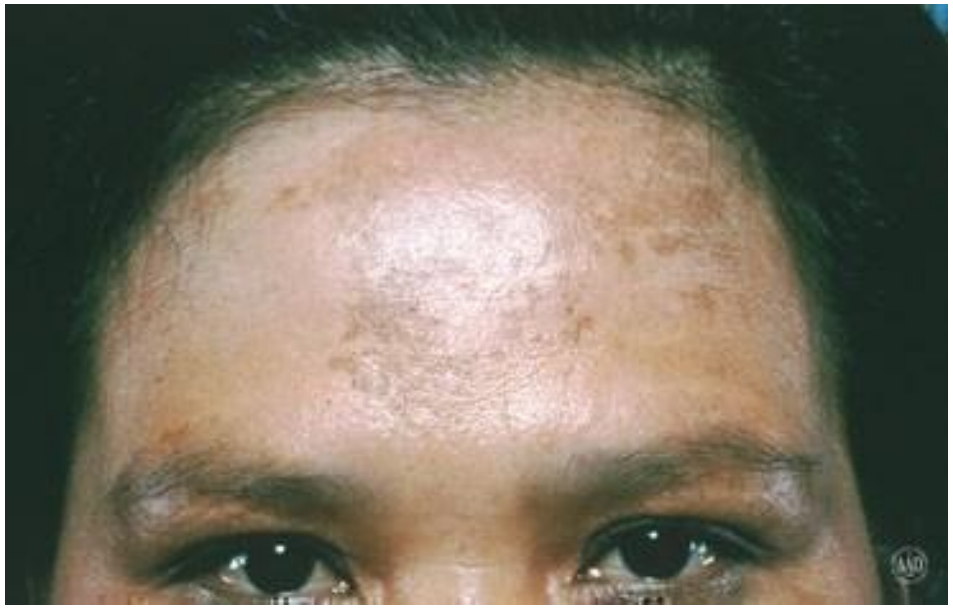
- Corticosteroids
- Tacrolimus
- 8-MOP topical phototherapy
- Excimer laser
- NB-UVB
- Surgical: melanocytes transfer, blister graft, punch graft
- Experimental: topical JAK inhibitors (topical Ruxolitinib)

Vitiligo Management

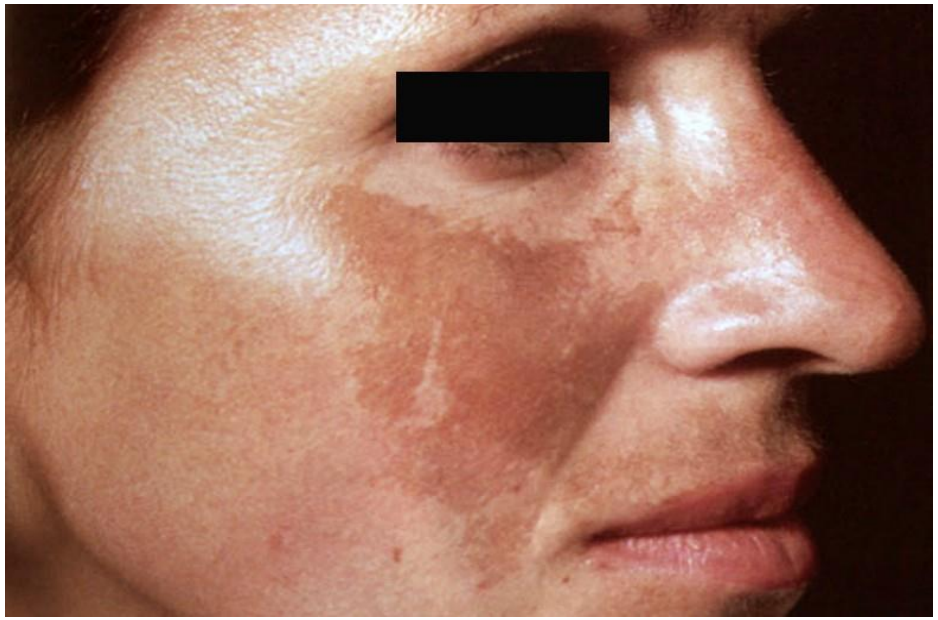
- Generalized:
- NB-UVB
- Oral PUVA
- Depigmentation with 20% monobenzylether of hydroquinone cream
- Depigmentation with Q-switched laser and cryotherapy
- Systemic therapy: oral corticosteroids, methotrexate, cyclosporine, mycophenolate mofetil, azathioprine
- JAK inhibitors orally with very high relapse rate

Melasma

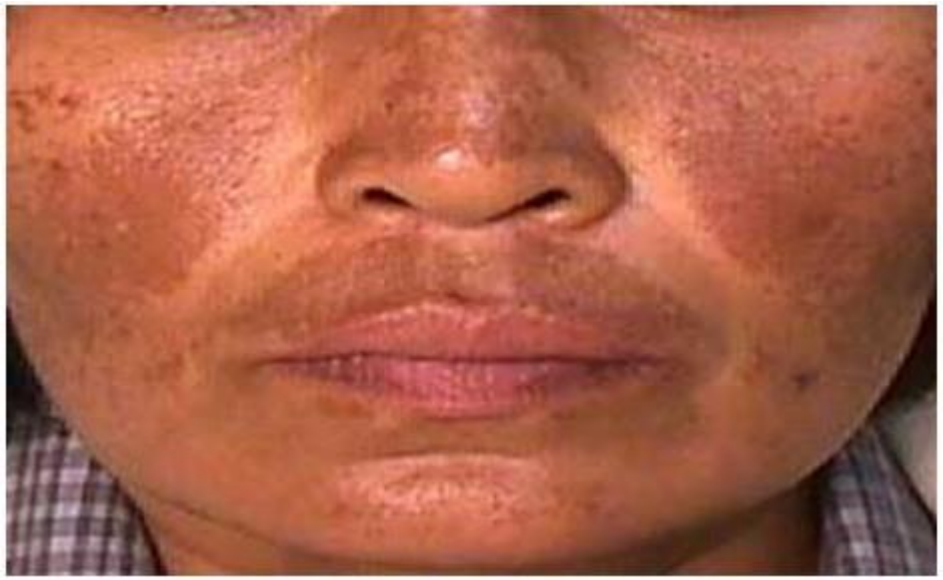
- Acquired symmetrical blotchy hyperpigmentation mostly on face
- Epidermal, dermal, mixed (most common)
- Mostly in young females(20-40), only 10% males
- Genetic predisposition, excessive sun exposure, pregnancy, oral contraceptives, hypothyroidism can trigger the disease
- Present as sharply marginated macules and patches with irregular borders on cheeks and forehead



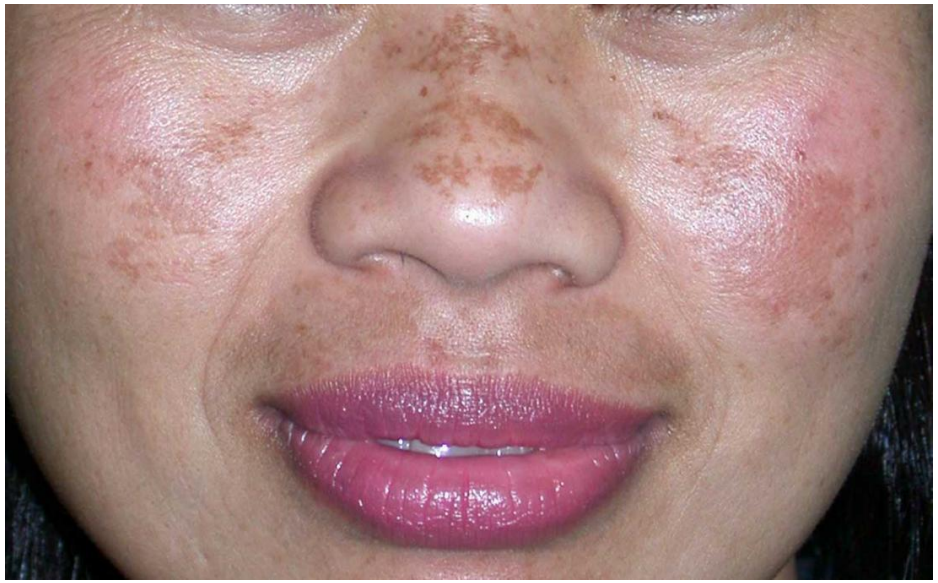
www.aad.org



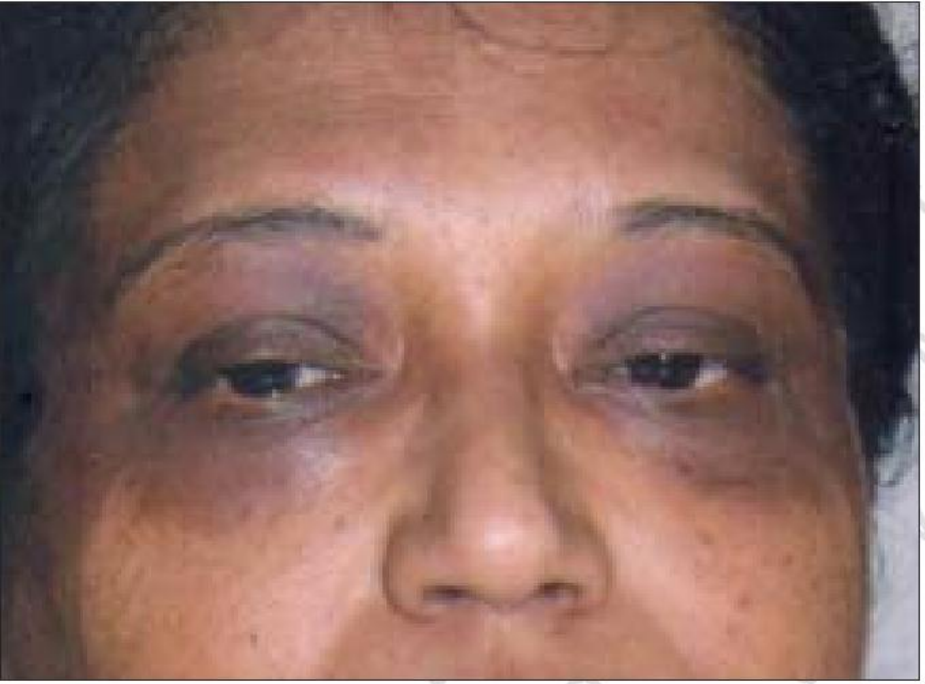
www.skinofcolorsociety.org

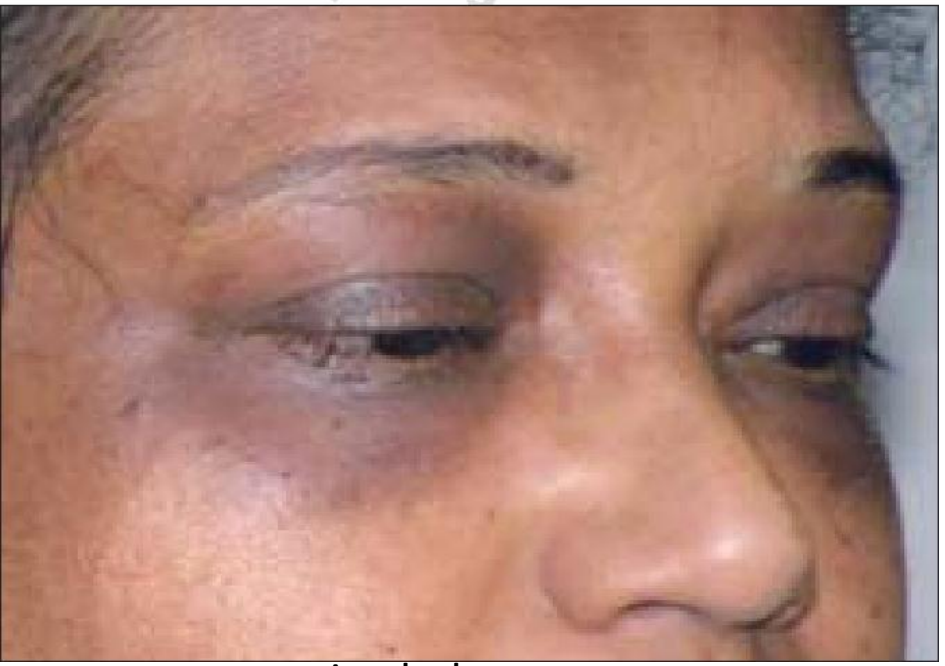


www.aesthetics.venkatcenter.com



www.medicalnewstoday.com





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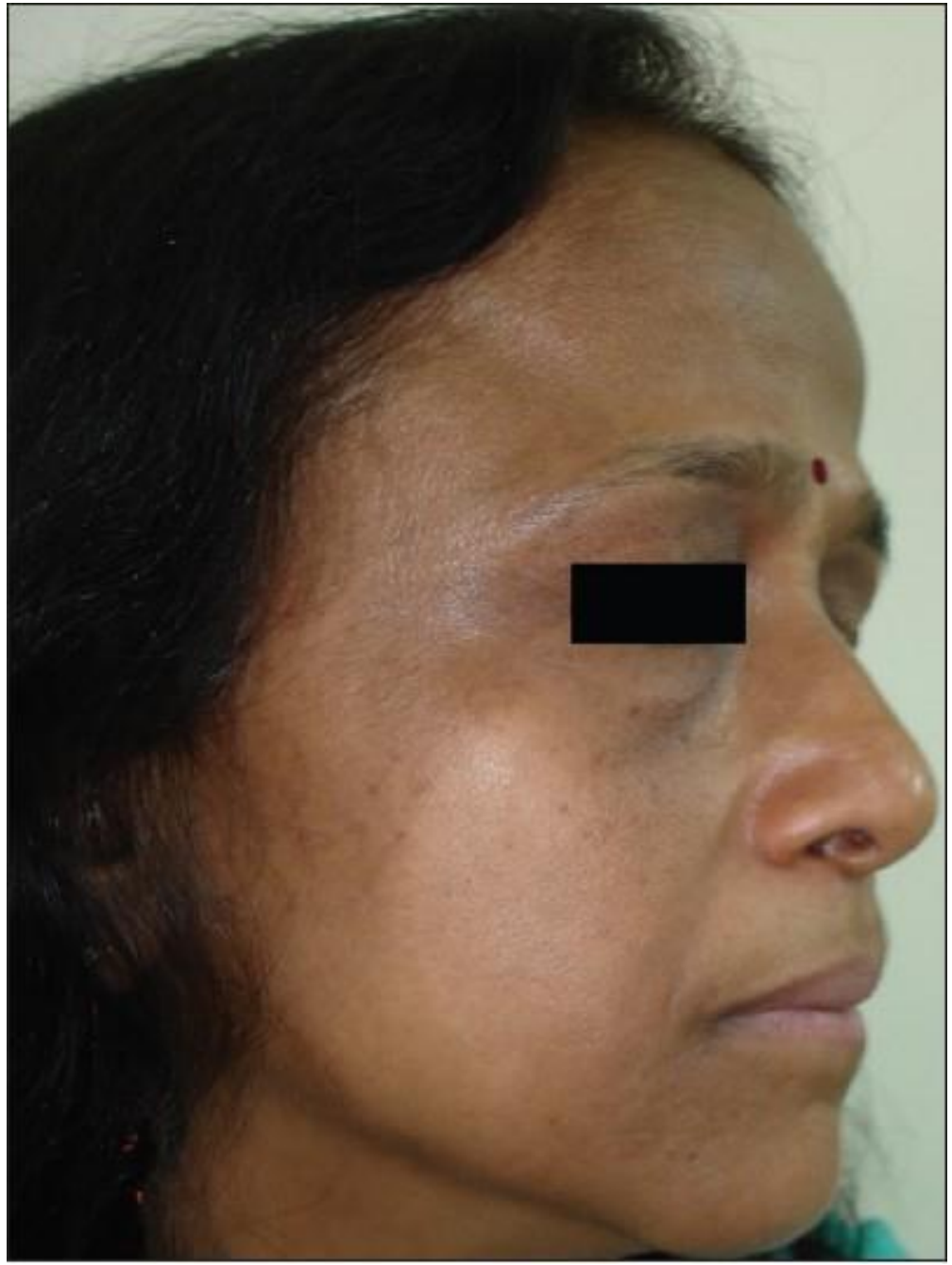


www.ijdvl.com

Melasma Management

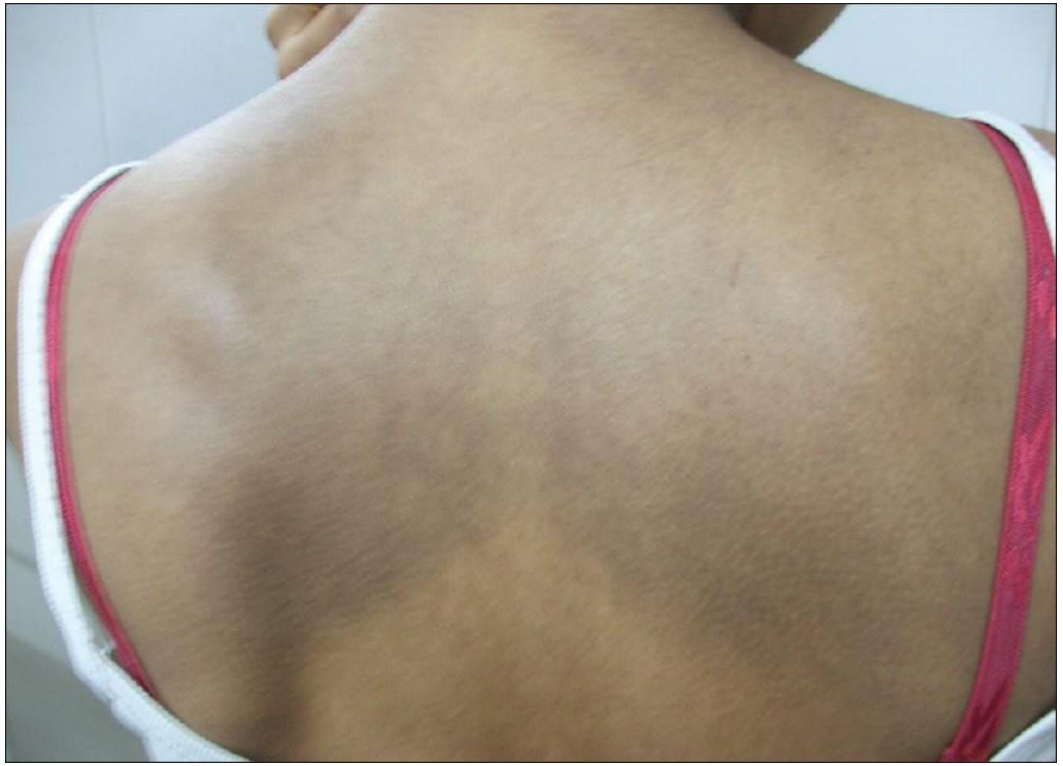
- Sun protection
- Kligman’s formula: Hydroquinone+Tretinoin+corticosteroid
- Hydroquinone 4% cream
- Glycolic acid, azelaic acid, kojic acid
- Arbutin, mulberry extract, licorice
- Chemical peels: glycolic acid, TCA, phenol, resorcinol
- Fractional laser
- Oral tranexamic acid

Post Inflammatory Hyperpigmentation

- Any inflammatory disease can cause it
- Acne, eczema, psoriasis, trauma, laser hair removal, burns, etc.
- More severe with lichen planus
- Improve with time but may persist for years
- Treatment as melasma

Macular Amyloidosis

- Reticulated brown patches mostly from excessive scratching and rubbing
- Affect young women
- Upper back, shins, arms
- Deposition of amyloid protein in papillary dermis
- Amyloid is derived from keratinocytes
- Not associated with systemic disease
- Treatment: control pruritus, topical corticosteroids, oral sedative antihistamines, bleaching agents, peels, laser



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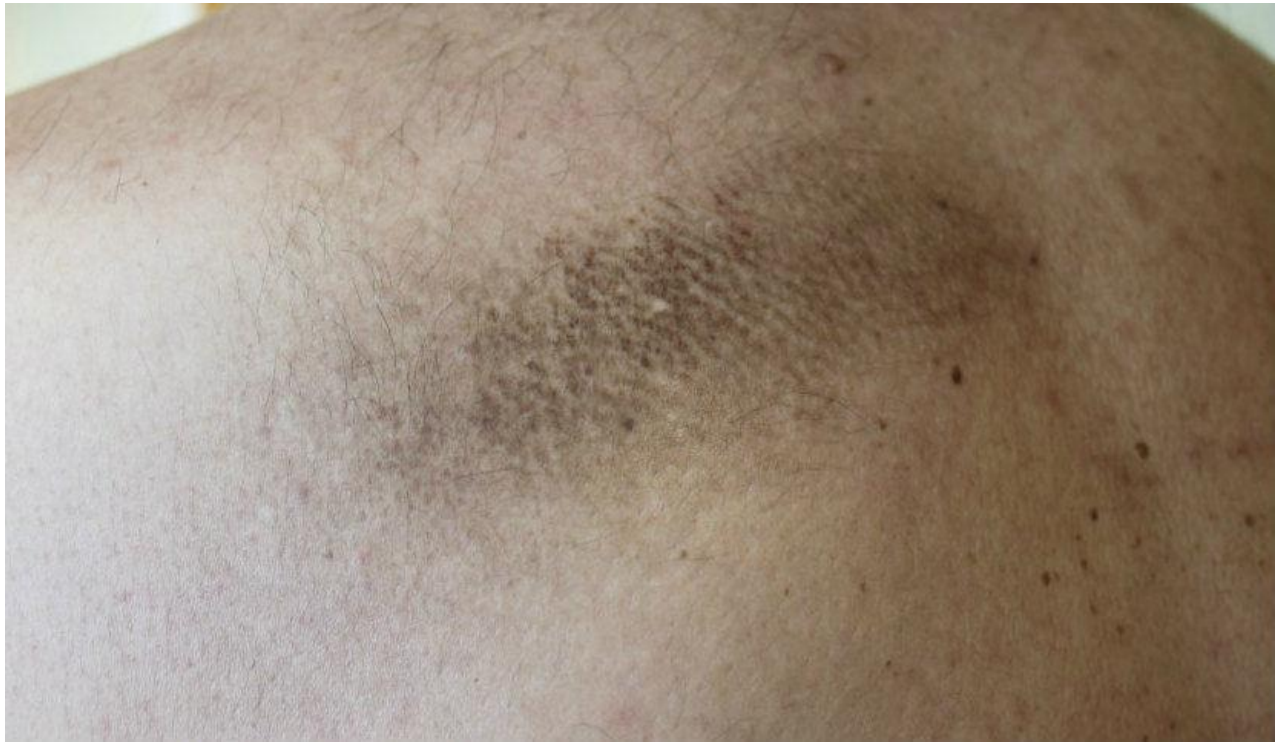

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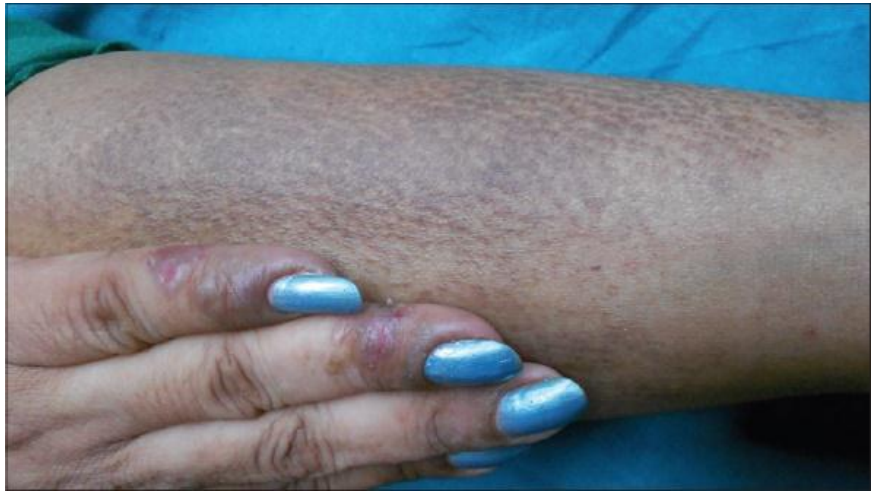

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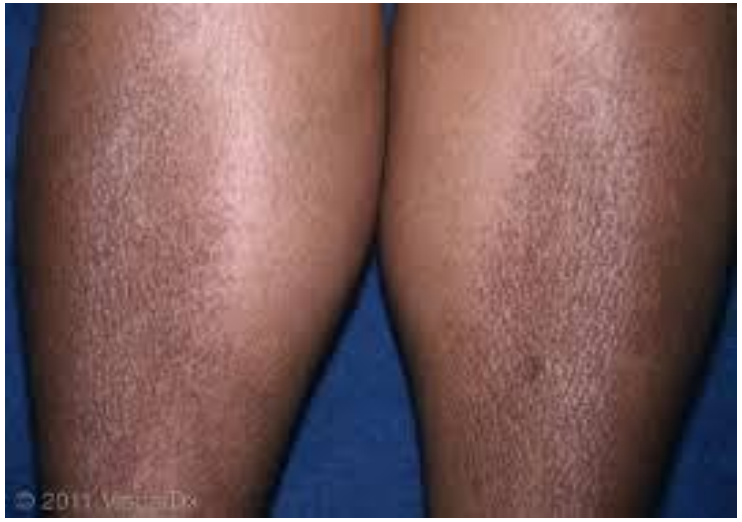

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Disorders of Hair Follicle

Hair Cycle

Anagen

- Growth phase
- Determines the ultimate length of the hair
- 80-85% of hair
- 3-6 years

Telogen

- Resting phase
- 5-15%
- 3-4 months

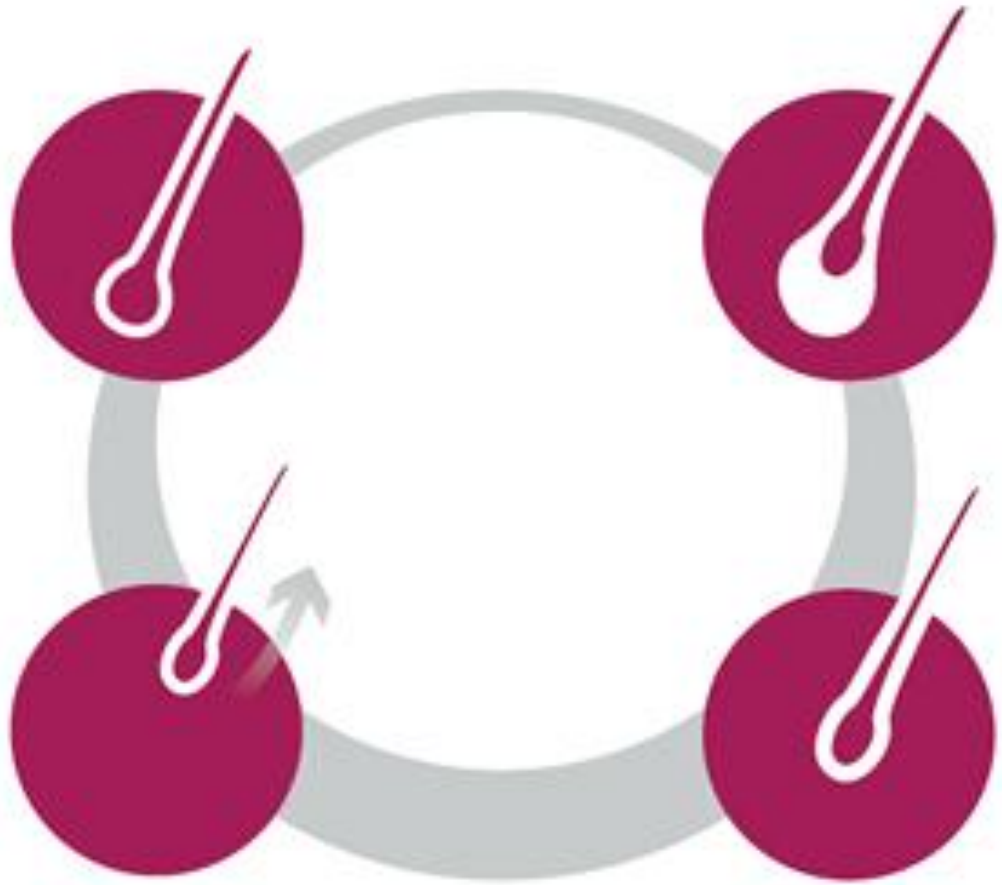
Catagen

- Transitional phase between anagen and telogen (apoptosis driven)
- 1% of hair
- 1-2 weeks

Exogen

1. Anagen
(Growing Phase)

The growing phase lasts two to seven years and determines the length of our hair.



2. Catagen
(Regression Phase)

This stage lasts about ten days. The hair follicle shrinks and detaches from the dermal papilla.

3. Telogen
(Resting Phase)

The resting phase lasts around three months. Around 10-15% of hairs are in this phase. Whilst the old hair is resting, a new hair begins the growth phase.

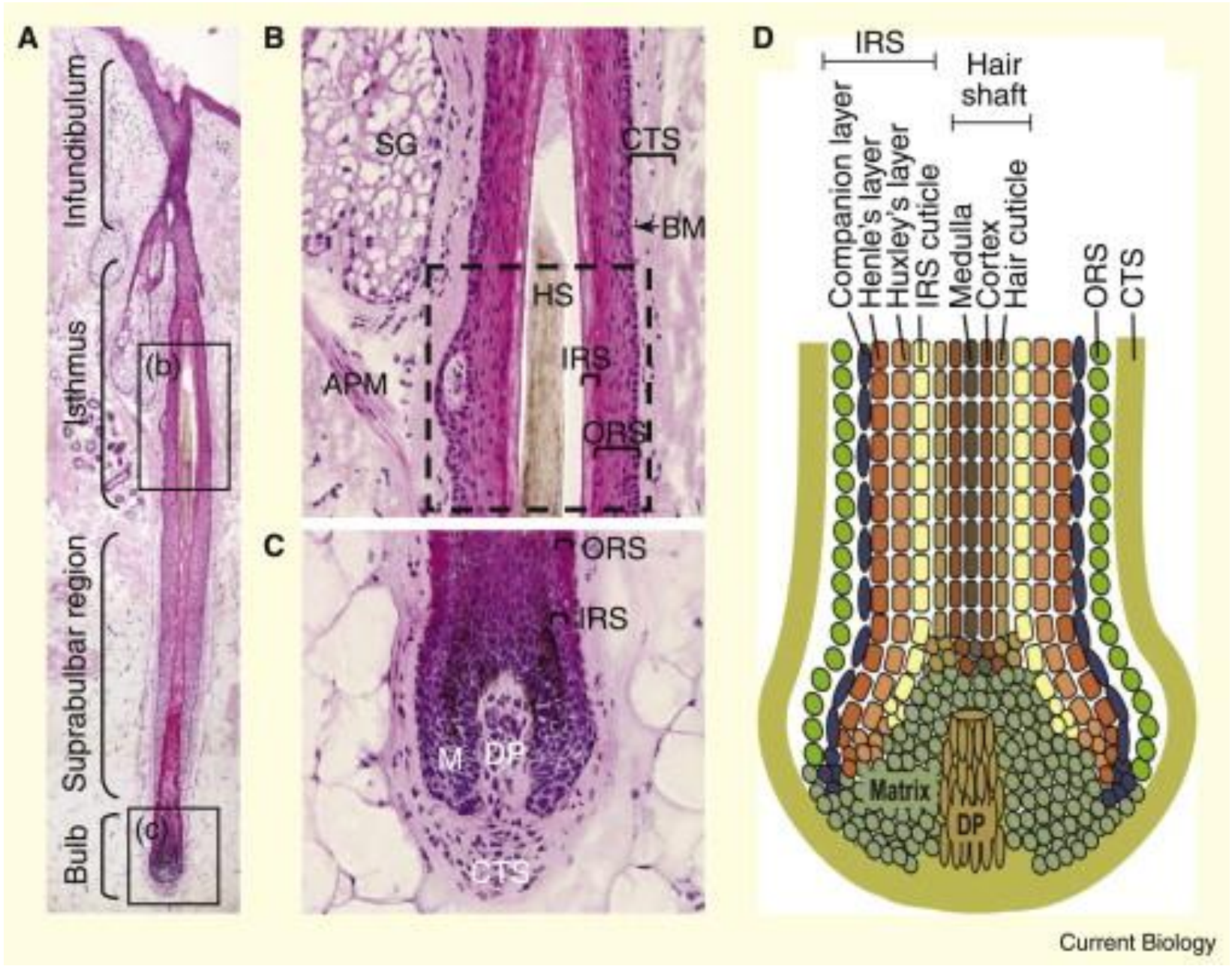
4. Exogen
(Shedding Phase)

The Exogen represents the period from when a resting hair reaches its terminal position in the follicle to when it finally detaches. The resting hair is gradually loosened resulting in shedding of the hair.

www.viviscal.com.au

Anagen

- Duration of anagen determines the final length of the hair
- Length varies according to body site
  - Scalp hair 02-08 Y
  - Legs 05-07 M
  - Arms 02-03 M
  - Eyelashes 01-06 M
  - Fingers 01-03 M



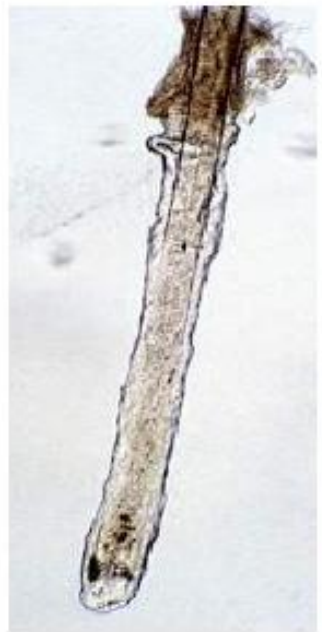
www.sciencedirect.com

Types of Hair

- Lanugo hair: fetus, shed before birth
- Vellus hair: fine, non-pigmented hair
- Terminal hair: thick pigmented hair

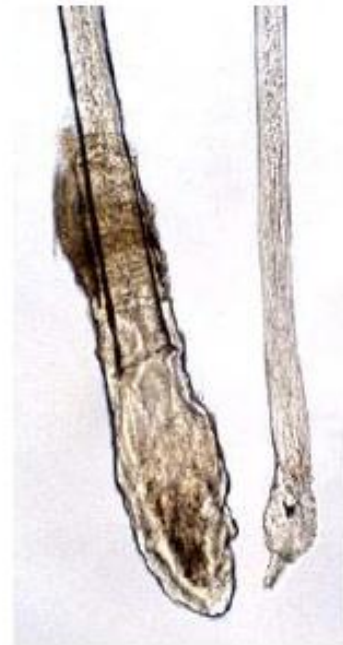
Diagnosis

- Hair pull test: 6+ is positive
- Trichogram: 50 hair pull for anagen/telogen hair ratio
- Trichoscopy: dermatoscope
- Scalp biopsy
- Scanning Electron Microscopy



Anagen

Catagen



Telogen

Male Pattern Hair Loss

- Most common type in adult men
- Genetic predisposition and androgen hormones
- Susceptibility genes inherited from both mother and father
- Chinese and Japanese are less affected
- Genetic sensitivity of hair follicle receptors to Dihydrotestosterone(DHT)
- DHT decrease anagen phase from years to months or weeks
- DHT is regulated by 5 alpha reductase

Male Pattern Hair Loss

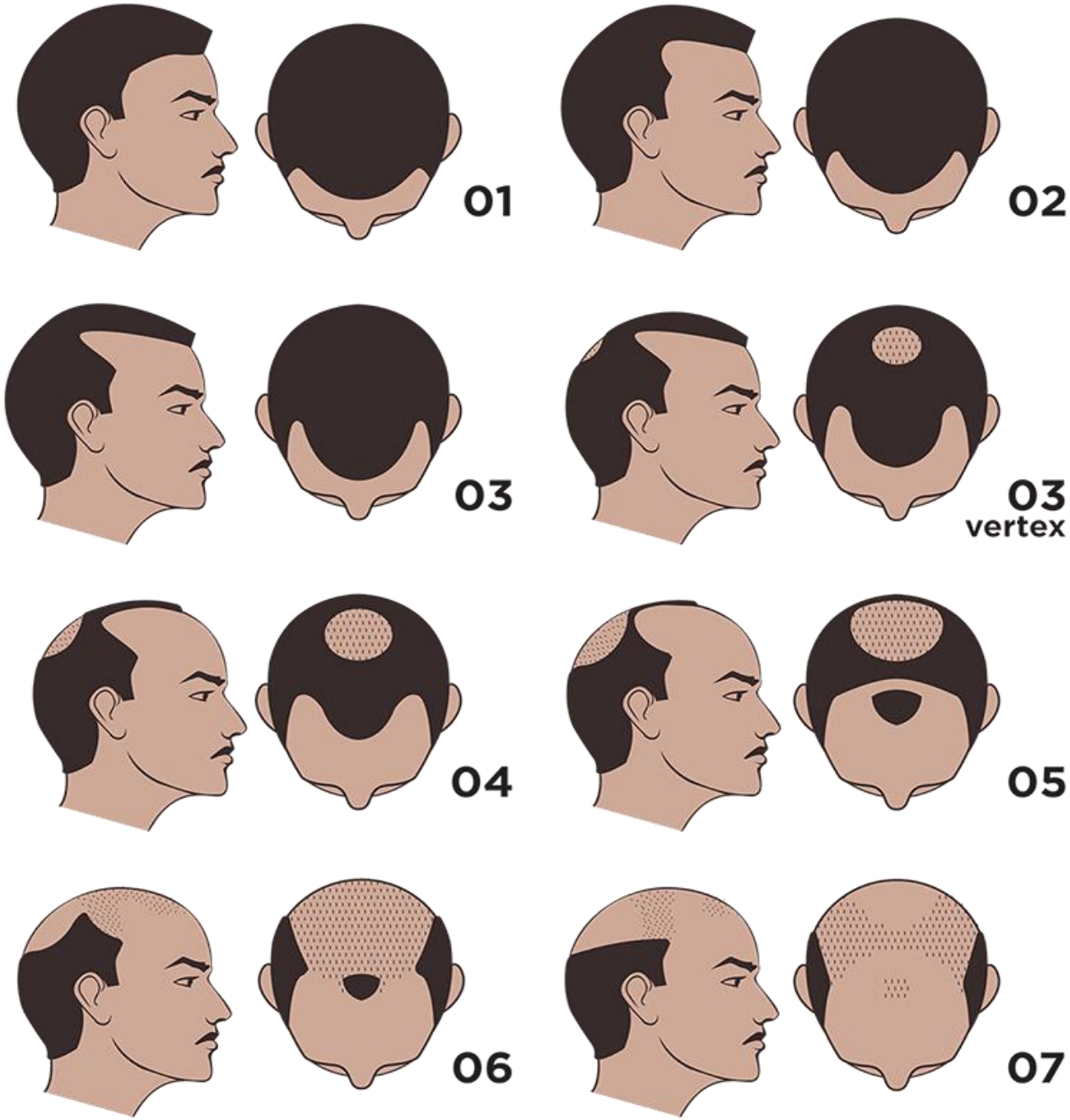
- Testosterone: growth of axillary & pubic hair, sex drive, penis and scrotum growth, spermatogenesis
- DHT in prostate and skin: growth of hair, prostate, androgenic alopecia and acne
- Testosterone → 5alpha reductase I&II→ DHT
- Type I 5 alpha reductase: sebaceous &adrenal glands, kidney, liver
- Type II alpha reductase: scalp&beard hair, seminal vesicle, prostate, epididymis, scrotum
- Finasteride 5 alpha reductase II inhibitor, has no affinity for androgen receptors (2% of patients might have reversible erectile dysfunction and decrease libido)

Male Pattern Hair Loss

- Hair miniaturization:

scalp hair grow in tufts of 3-4 hairs, in MPHL the tufts progressively lose hair, hair become finer with decrease length and diameter

- Present as receding hair line and hair loss on frontal area and vertex



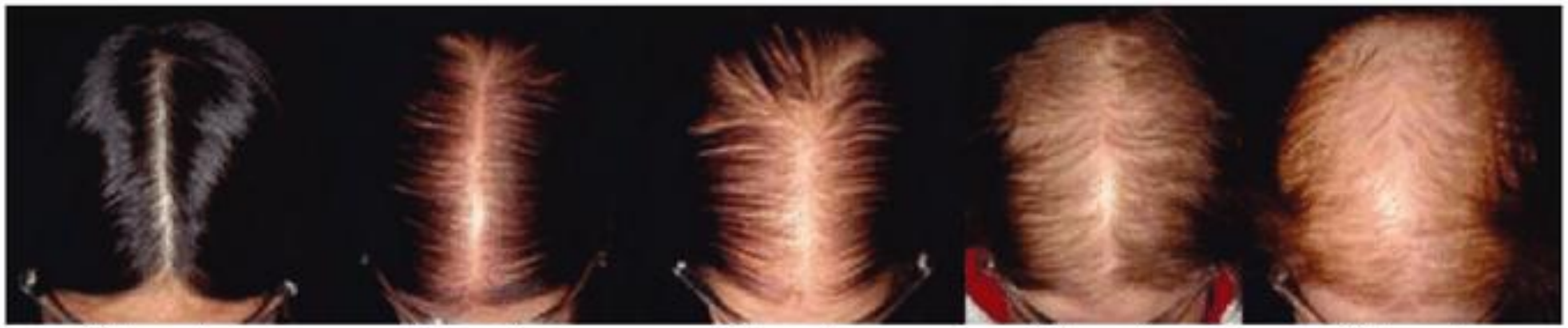
www.naturaltransplants.com

Management

- Minoxidil solution 2% and 5%
- Finasteride 1mg/d (type II 5 alpha reductase inhibitor)
- Dutasteride 2.5mg/d (type I & II)
- Platelet rich plasma
- Hair transplant
- Hair piece
- Tattoo
- powder

Female Pattern Hair Loss

- 40% of women ages 50 has some hair loss
- Diffuse thinning of hair due to shedding and decrease volume
- Genetic predisposition, polygenic, either parent
- Normal androgen level
- More common after menopause, ? Estrogen stimulate hair growth
- Comes in waves of severe hair shedding then normal shedding, but progress over time
- Psychological stress in women than men
- Polycystic Ovarian Syndrome(PCOS), Congenital Adrenal Hyperplasia(CAH)



www.researchgate.net

Differential Diagnosis

- Diffuse pattern alopecia areata
- Telogen effluvium
- Hair loss secondary to:

Systemic lupus erythematosus, thyroid disease, severe iron deficiency anemia, or drugs

Investigation

- Trichogram
- CBC, Iron, Ferritin, TIBC
- LH/FSH
- DHEAS
- Prolactin
- Free testosterone
- Thyroid function test
- ANA
- Scalp biopsy

Management

- Minoxidil 2%, 5%(may cause hypertrichosis on face and neck)
- Finasteride and dutasteride
- Spironolactone and flutamide
- Cyproterone acetate
- Oral minoxidil 0.25mg/d + spironolactone 25mg/d in one study
- Hair spray, powder, hair piece
- Hair transplant
- ?Platelet Rich Plasma PRP

Alopecia Areata

- Autoimmune with T-cells around hair follicles
- 50% in childhood, 80% before age of 40
- Genetic predisposition, 10-20% positive family history
- Association with vitiligo, thyroid disease, atopic dermatitis and Down syndrome
- Triggers: viral infection, trauma, hormonal changes, severe emotional stress

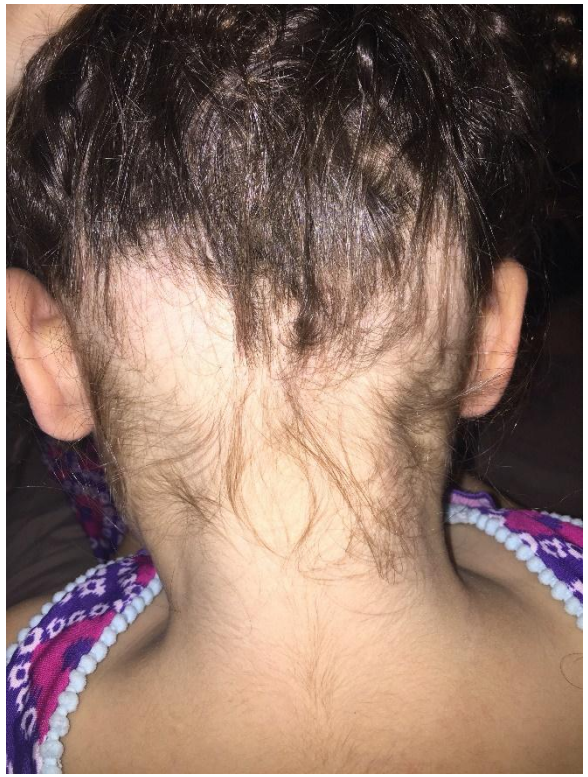
Alopecia Areata

- Patchy AA (the most common)
- Patchy hair loss of scalp, beard, eyebrow, eyelash hair
- Sudden onset
- Progressively increase the size of the patch then stabilize
- Regrowth of hair spontaneously after months in many cases but my persist for years
- Regrowth of white hair then pigment comes back
- Exclamation marks are 2-3 mm broken hair with distal end broader than proximal ! at the margin of the hairless patch
- Nail pitting and ridging in 10-50% of patients

Alopecia Areata

- Alopecia totalis: all scalp hair, 5%
- Alopecia universalis: whole body, 1%
- Ophiasis: occipital and lateral scalp
- Diffuse alopecia areata:

- Sudden diffuse thinning of hair
- Persisting hair turn grey
- Positive hair pull test



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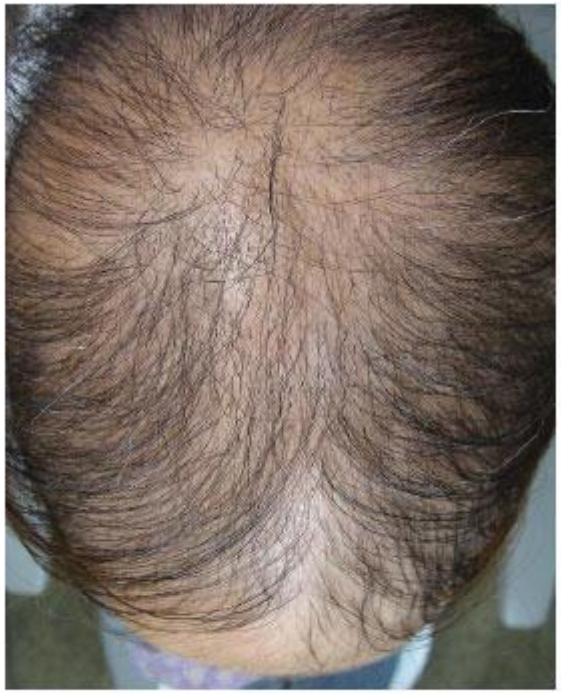
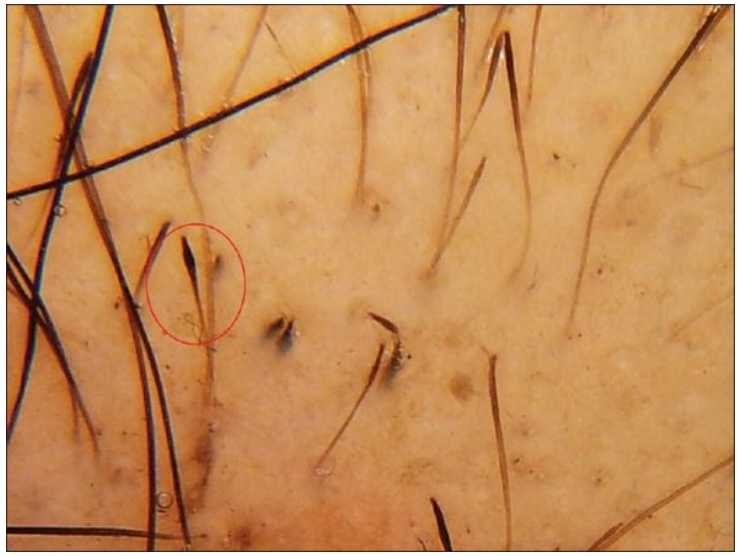


Figure 1 - Clinical picture at 2 weeks from the onset of hair shedding.

www.scielo.br

www.newhorizonsatlanta.com



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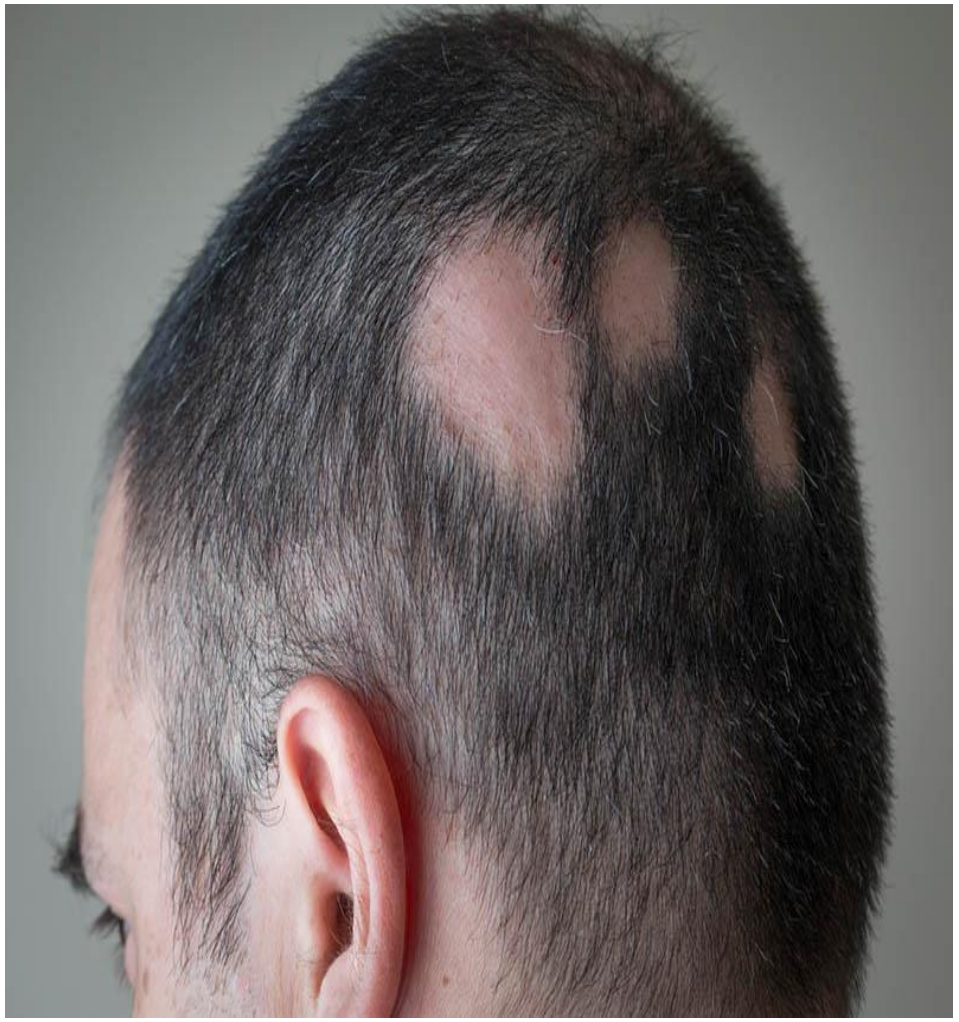


www.embellishmentshairrestorationstudio.com

Management

- Intralesional corticosteroids
- Minoxidil solution
- Dithranol
- Diphencyprone (DPCP)
- phototherapy
- Systemic corticosteroids, pulse therapy
- Methotrexate, azathioprine
- JAK inhibitors (Tofacetinib, Ruxolitinib)
- IL-15 may be a future target
- Artificial eyelashes, eyebrow tattoo, hair piece

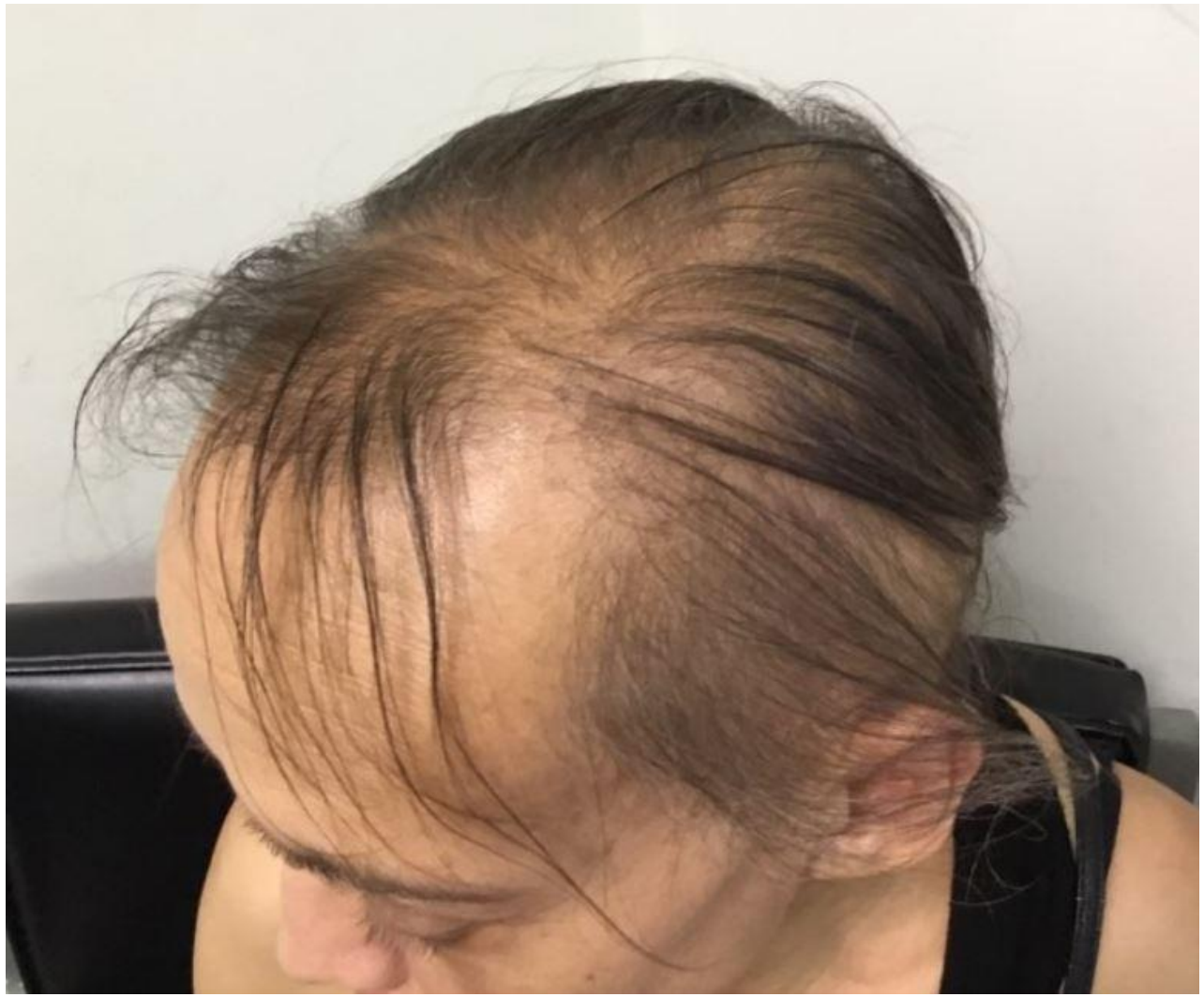
Prognosis

- Single patch: 80% resolution in 1 year

- **Poor prognostic factors:**
- Extensive disease
- Duration >1 year
- Ophiasis pattern
- Nail involvement
- Childhood onset
- Positive family history
- Other concomitant autoimmune diseases
- Atopy
- Down syndrome

Telogen Effluvium

- Temporary hair loss of telogen hair
- System shock: change anagen hair to telogen
- Up to 70% of anagen hair could be affected leading to severe hair loss
- Fever, surgery with general anesthesia, childbirth, severe emotional trauma, severe weight loss
- Drugs: heparin, warfarin, B-blockers, Ace-inhibitors, lithium, anticonvulsants(especially valproic acid)
- Might take 2 months after shock to start losing hair
- Usually last for 6-9 months with incomplete recovery
- Could be chronic, but doesn’t cause complete baldness

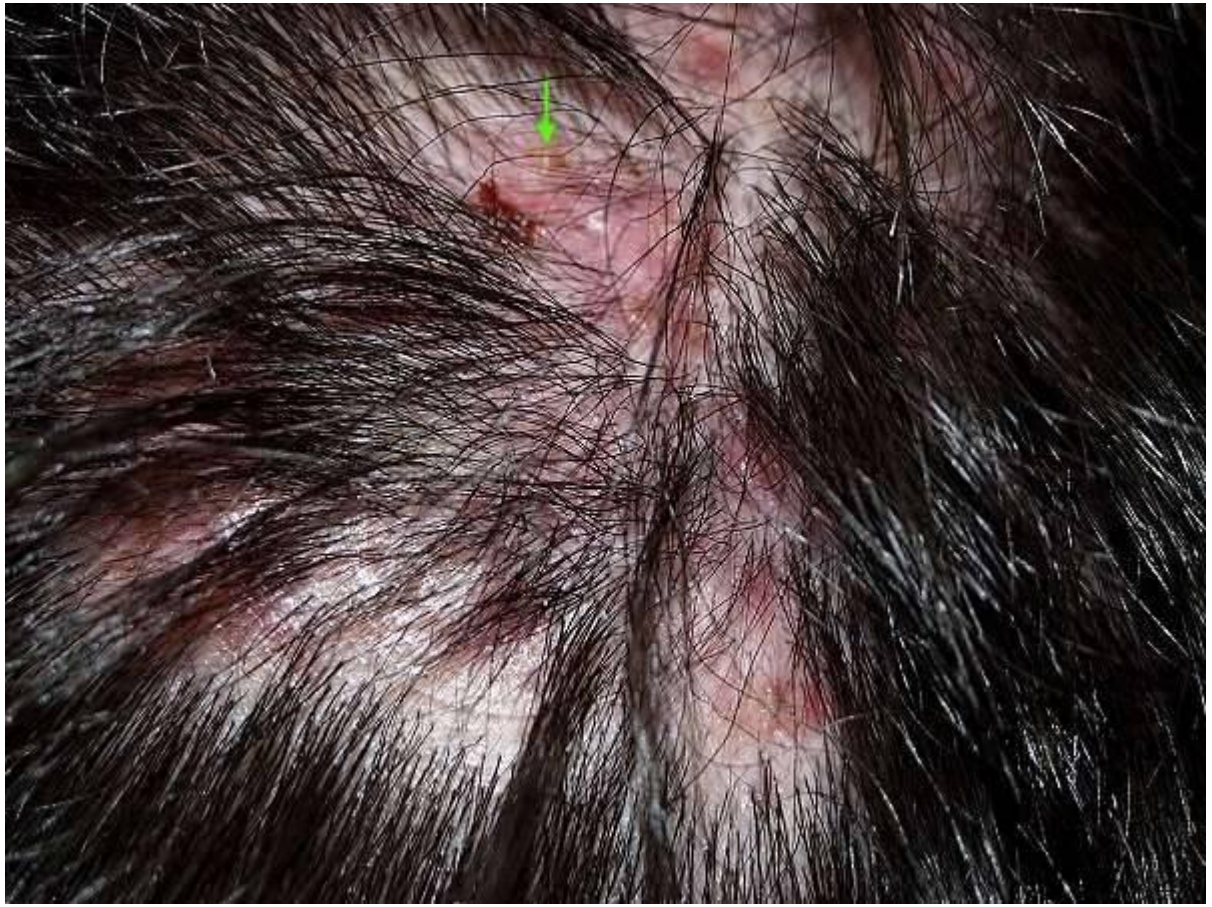


www.clinicaladvisor.com

www.embellishmentshairrestorationstudio.com

Tufted Hair Folliculitis

- Folliculitis decalvans
- Rare progressive, chronic scarring alopecia in adults
- Presence of 10-15 hairs emerging from single follicle opening
- Cause unknown, not contagious
- Positive culture of staphylococcus aureus, ? Role
- Could be associated with drugs: cyclosporine, lapatinib
- Scarring hairless patches with hair tufts, tender, with swelling, crusts, and pus could be expressed form lesion
- Culture and biopsy
- Hyperkeratosis, parakeratosis, hyperplastic epidermis, with follicular plugging and perifollicular mixed inflammatory infiltrate
- Antibiotics (clindamycine,rifampicin), I/L steroids, isotretinoin, surgery



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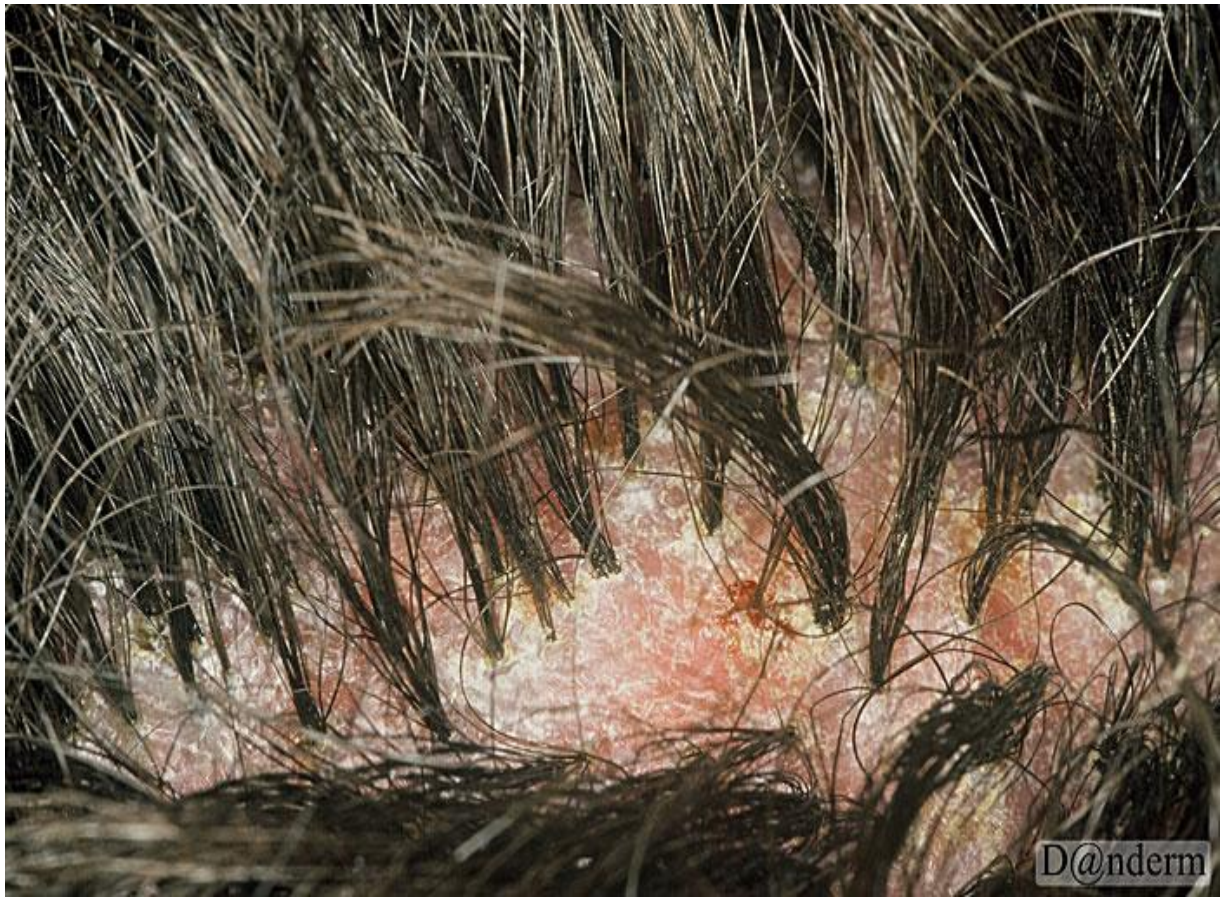
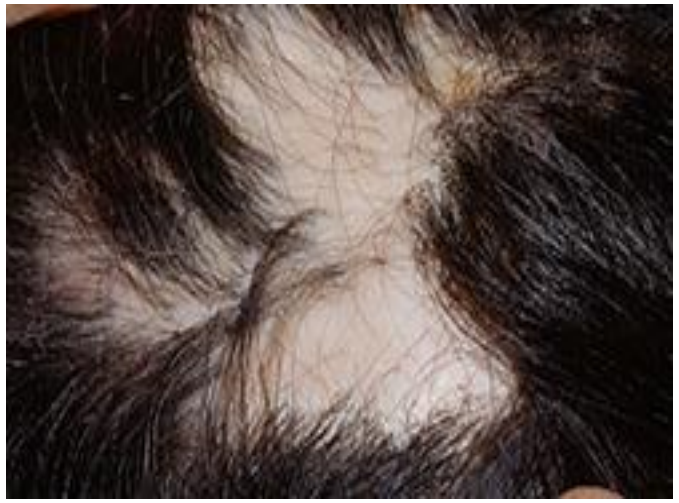


www.danderm.dk

Scarring Alopecia

- Lichen planopilaris LPP
- Frontal fibrosing alopecia: post menopausal women
- Central centrifugal cicatricial alopecia
- Pseudopelade: non inflammatory
- Discoid lupus erythematosus of scalp
- Traction alopecia
- Trichotillomania: non-scarring psychiatric alopecia, might lead to scarring alopecia, different length of hairs, RBCs around hair bulb
- Acne keloidalis nuchae



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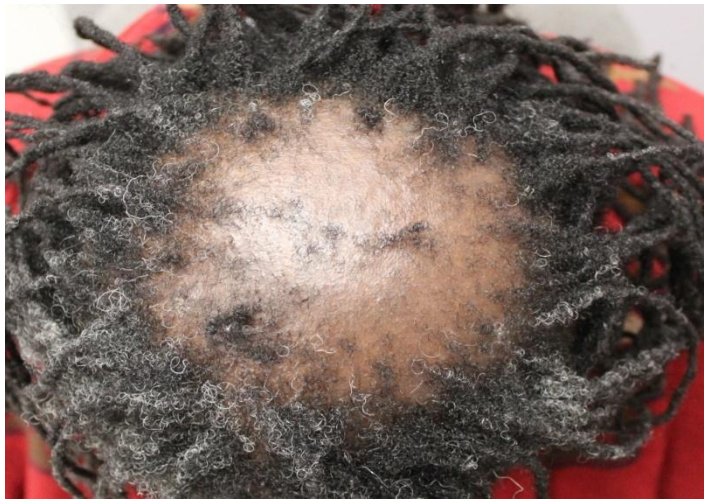
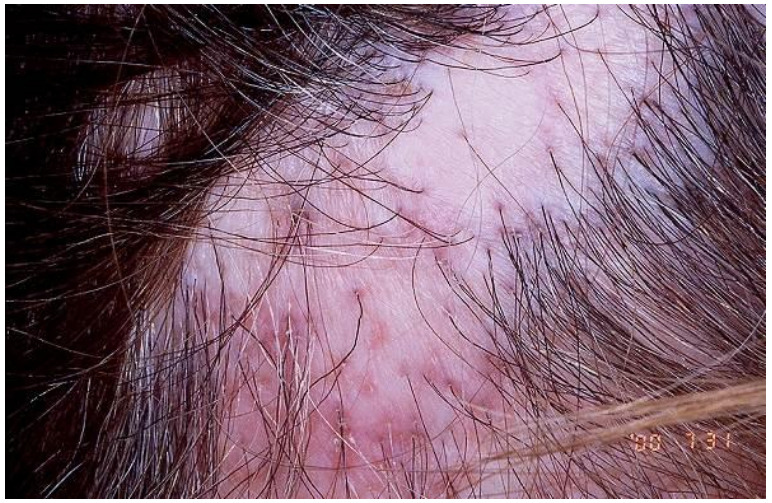


www.canadianhairlossfoundation.org



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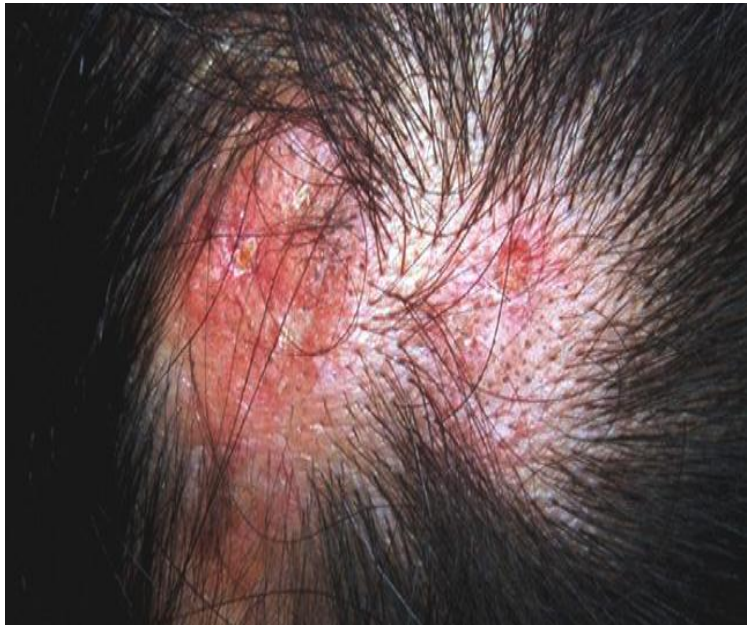

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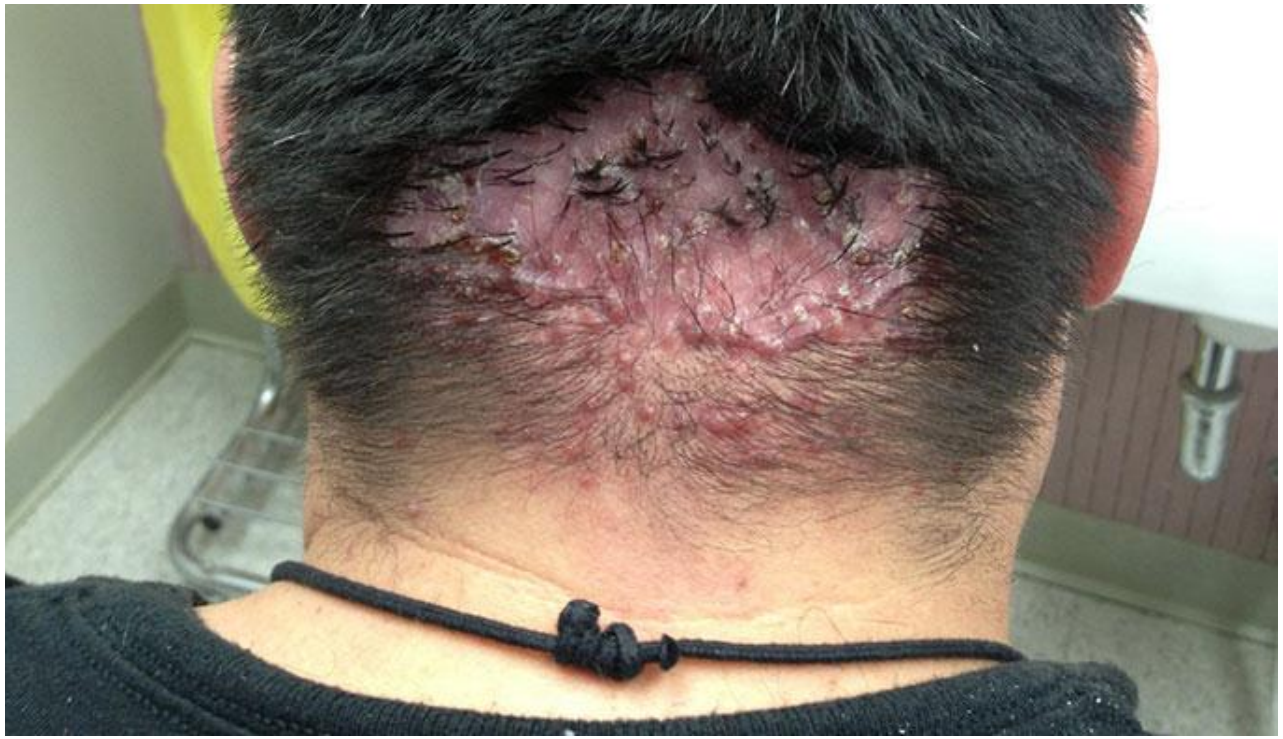

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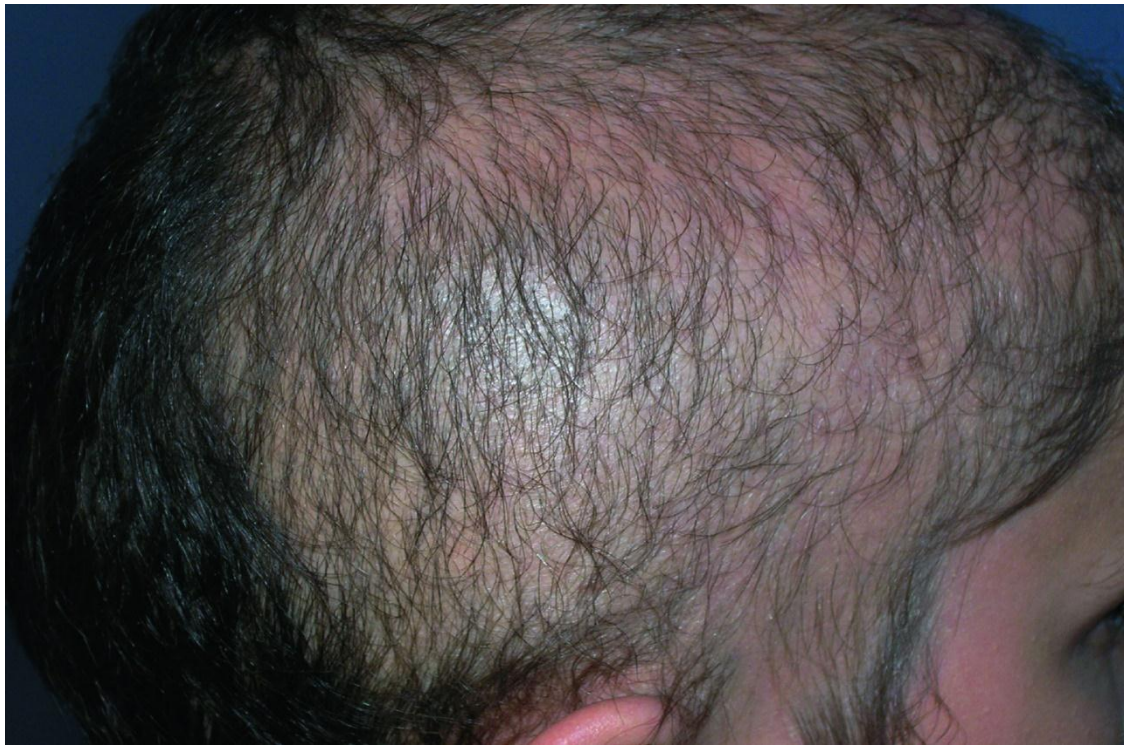


www.msdmanuals.com

Hirsutism

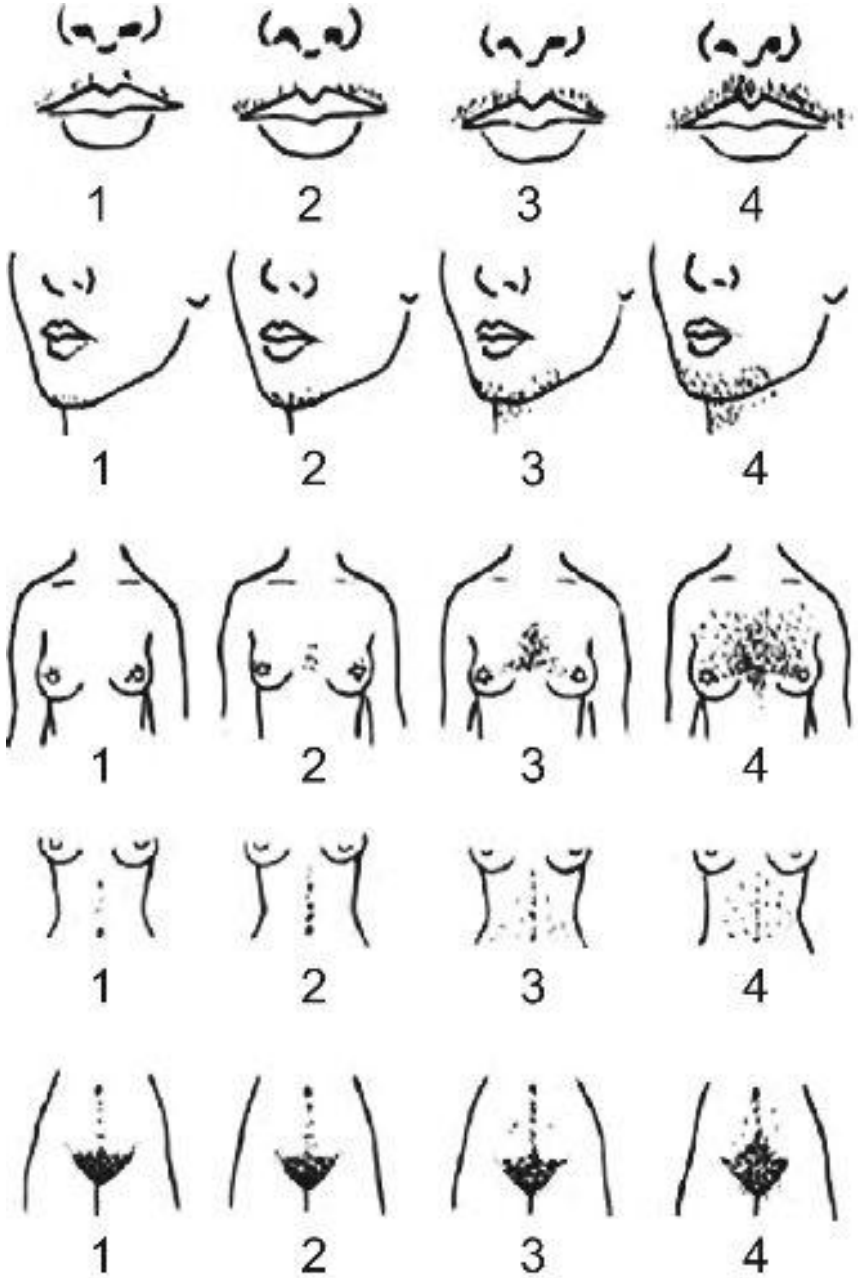
- Male pattern hair growth in women
- Genetically determined, 10% of women affected
- Increase androgen and testosterone
- PCOS
- Weight gain
- Stopping oral contraceptives
- Cushing syndrome
- CAH (21 hydroxylase deficiency)
- Tumors of adrenal glands (almost always malignant)
- Ovarian tumors (arrhenoblastoma)
- Pituitary gland (ACTH dependent)

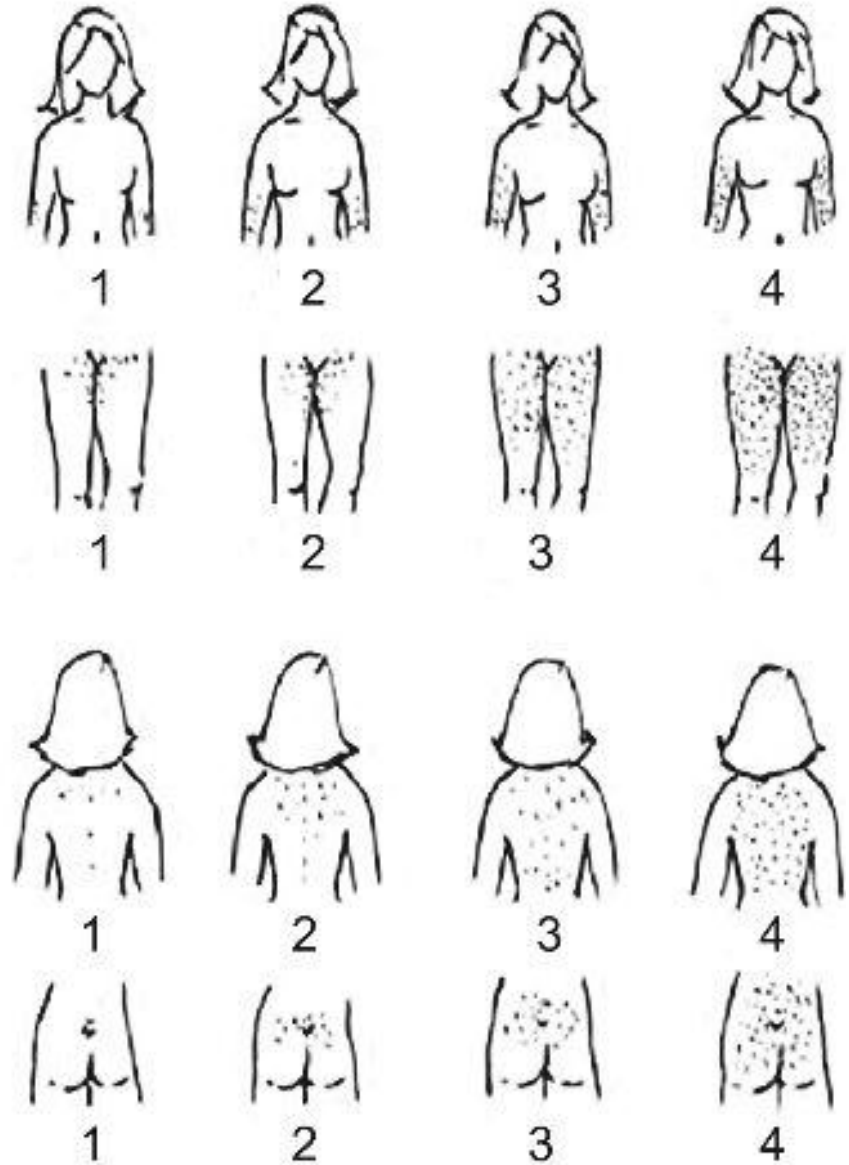
Hirsutism

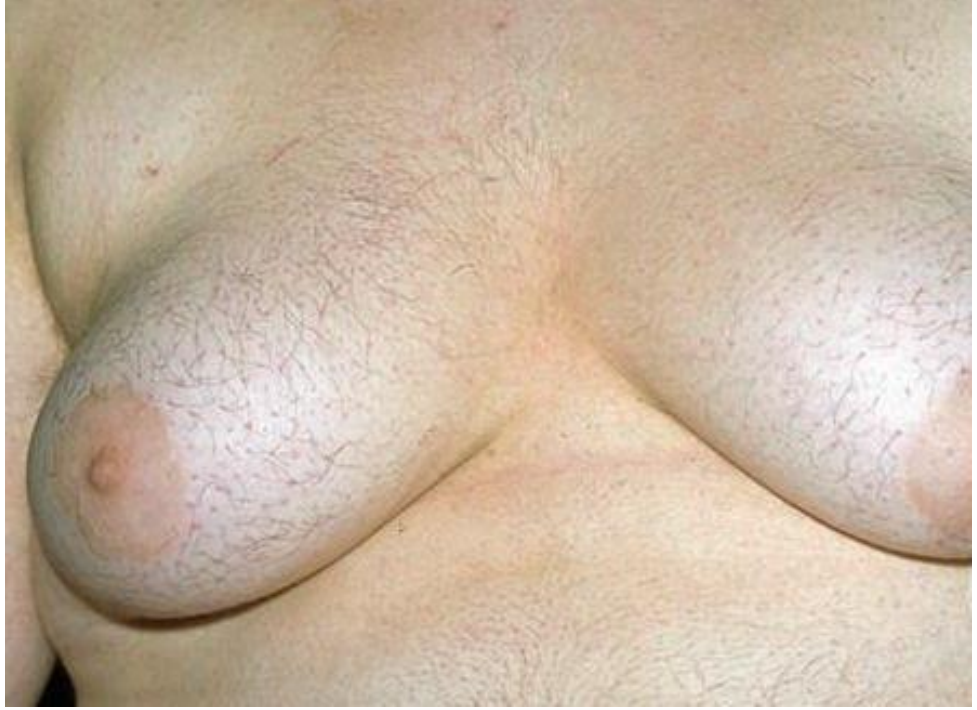
- Androgen change anagen phase, dermal papilla size and dermal papilla cells activity (both keratinocytes &melanocytes)
- Facial hair, below umbilicus, around nipple, upper back, inner thighs
- Associated findings: acanthosis nigricans, galactorrhea, striae, acne, virilization(increase muscle bulk& size of clitoris, deep voice, baldness, menstrual irregularities

- Oral corticosteroids are pure with no androgenic activity so it cause hypertrichosis but not hirsutism

- Ferriman-Gallaway scale: 9 area, from 1-4, hirsutism if score >8







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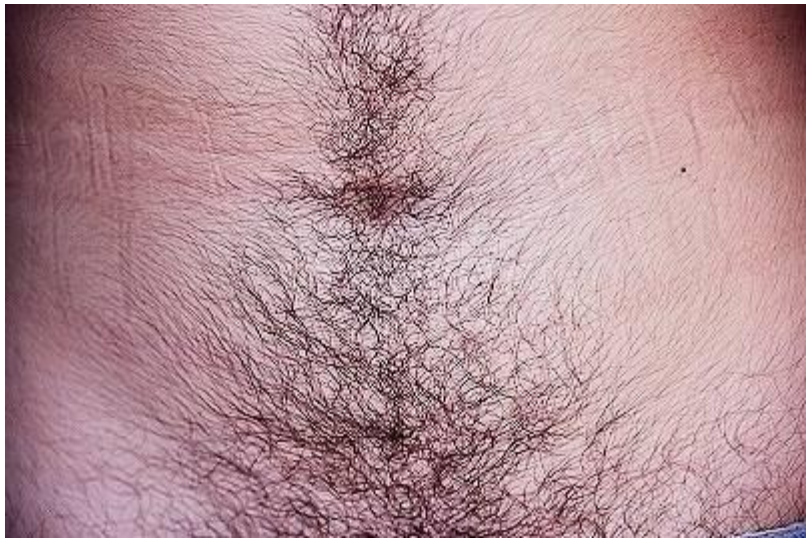


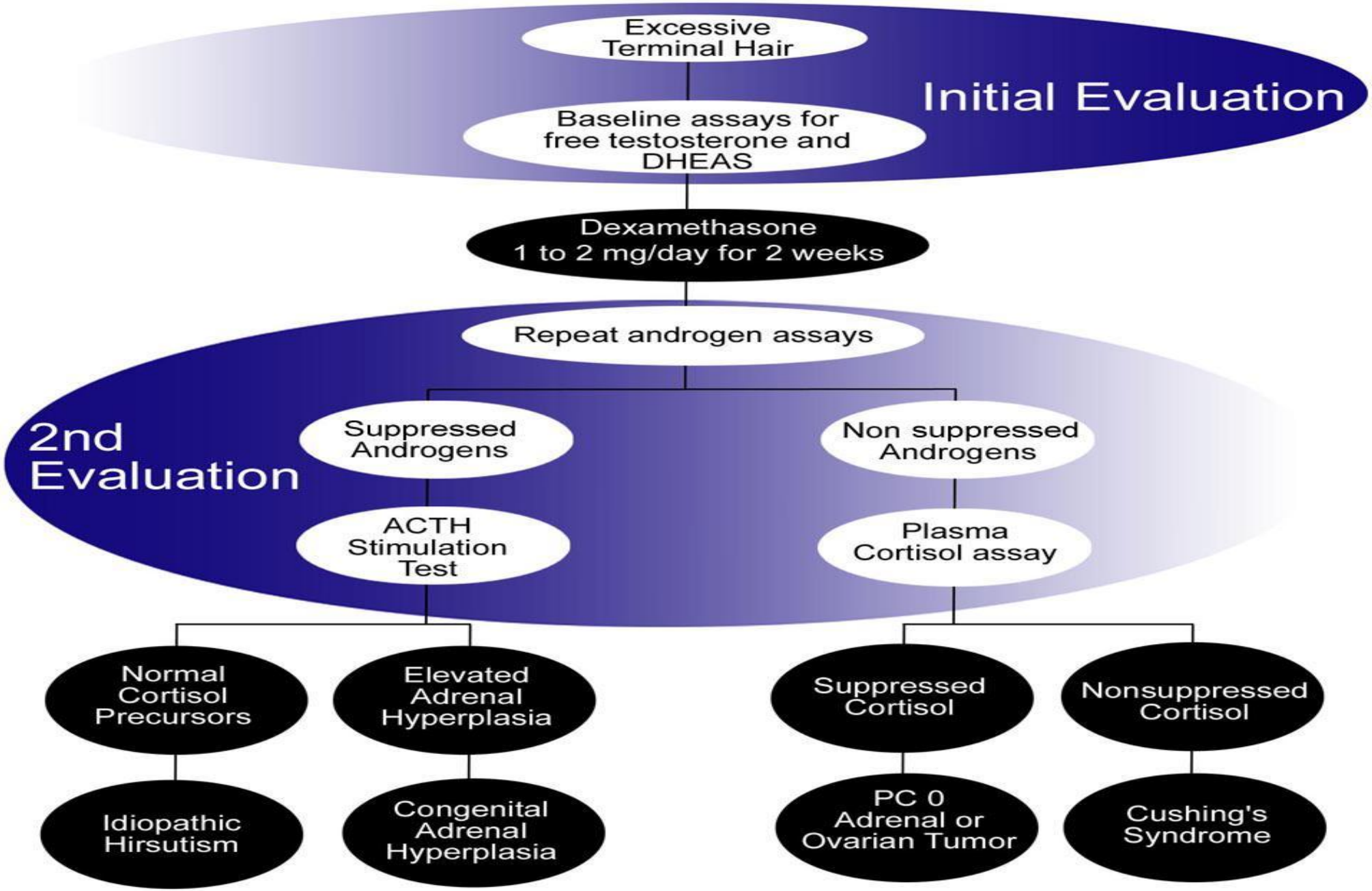
www.pcds.org.uk

www.gponline.com

Investigation

- Free testosterone, prolactin, thyroid function
- LH/FSH ratio: PCOS
- Dihydroepiandrosterone sulfate (DHEAS): Adrenal (↑testo+↑DHEAS)
- Androstenedione: Ovary (↑testo + normal DHEAS)
- 17-hyroxyprogesterone: CAH
- Urinary and serum cortisol
- Dexamethasone suppression test: to exclude ACTH dependent hirsutism
- Prostate specific antigen(PSA): a marker for increase androgens
- U/S pelvis, CT-Scan, MRI

Etiologic Diagnosis of Hirsutism



Management

- No drug is FDA approved for hirsutism

- Treat the underlying cause
- Drugs are either decrease androgen production or inhibit androgens in the skin
- Spironolactone 50-200 mg/d (blocks androgen receptors)
- Flutamide 125mg/d (hepatitis)
- Oral contraceptives
- Cyproterone 50-200 mg x10 days per cycle
- Metformin
- Finasteride
- Corticosteroids (ACTH dependent hirsutism)

Table 3. Treatment of hirsutism

Medications	Cosmetic treatments
Birth control pills	Shaving
Androgen receptor blockers	Eflornithine cream
Spironolactone	Waxing
Flutamide	Bleaching
Glucocorticosteroids	Plucking
Dexamethasone	Depilatory agents
Prednisone	Electrolysis
Methylprednisolone	Laser
Enzyme inhibitors	
Finasteride	
GnRH analogs	

Hypertrichosis

- Excessive growth of lanugo, vellus, or terminal hair
- Congenital or acquired
- Generalized hypertrichosis: porphyria cutanea tarda, malnutrition, malignancy, hypothyroidism, drugs(minoxidil, cyclosporine, phenytoin, androgenic steroids)

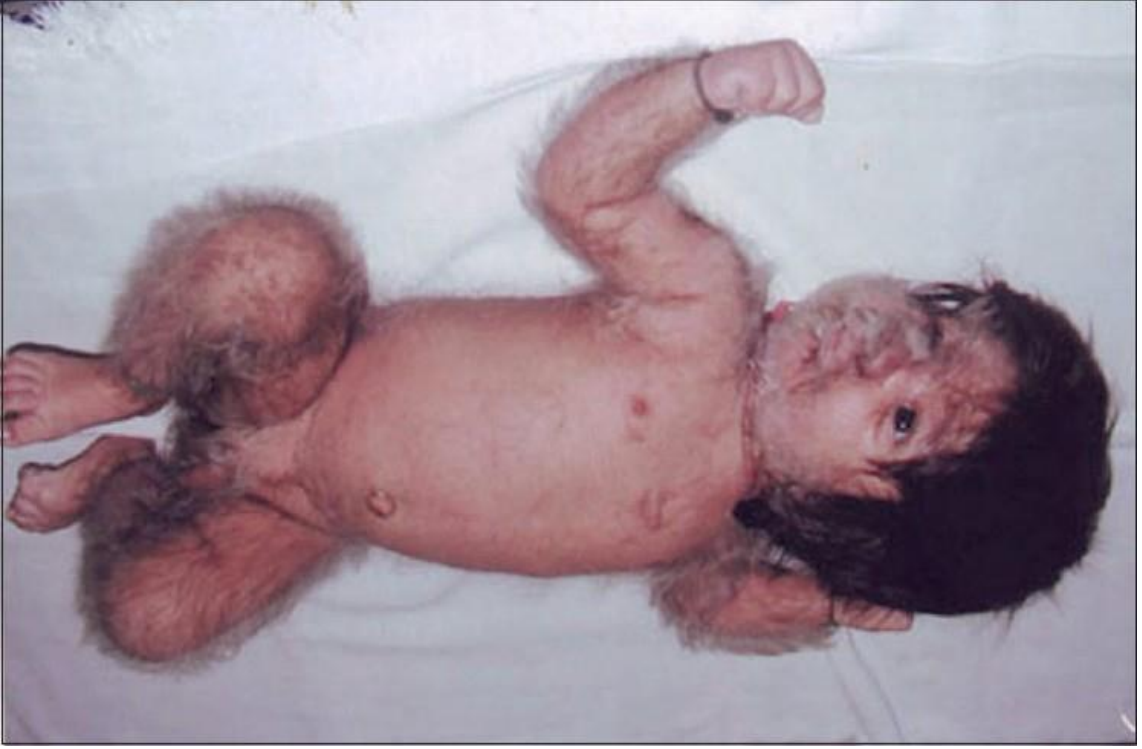
- Localized: increased vascularity, chronic itching and rubbing, topical minoxidil, topical corticosteroids, PUVA
- Nevoid hypertrichosis: spina bifida
- Hypertrichosis associated with nevi: congenital melanocytic nevus, Becker's nevus, vascular malformation
- Trichomegaly (Bimatoprost, Erlotinib)

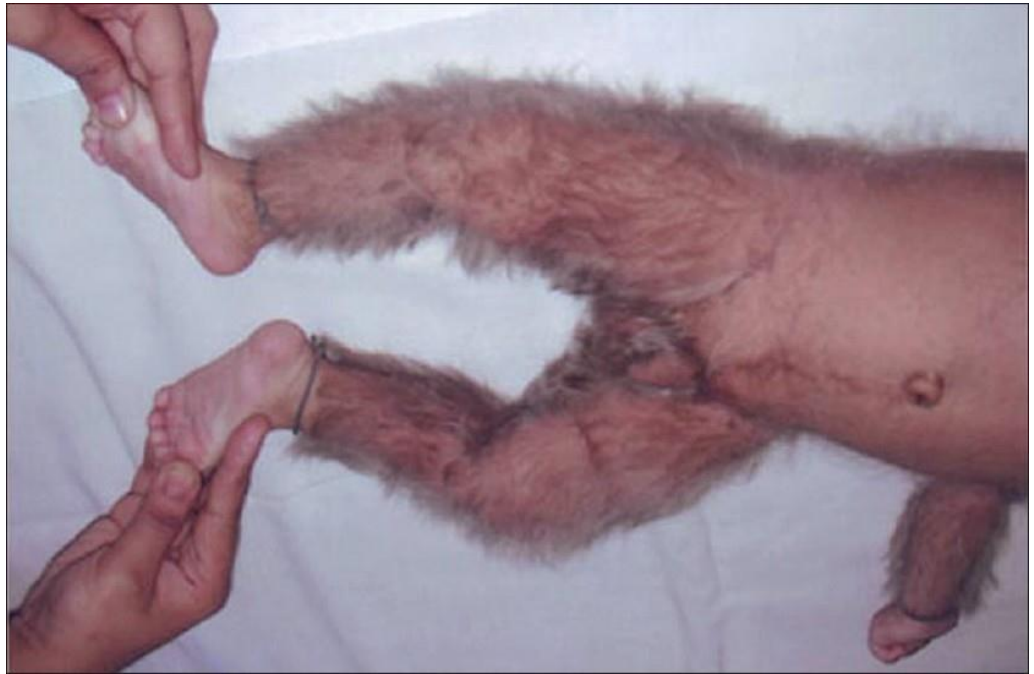
Hypertrichosis

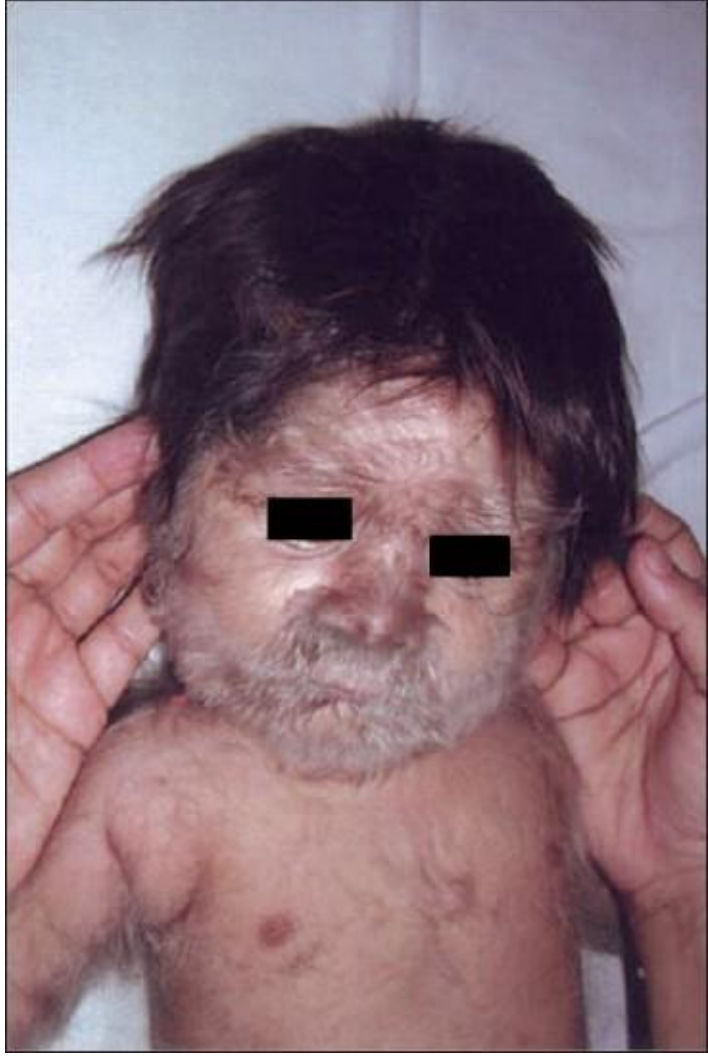
Congenital hypertrichosis lanuginosa

- Only 50 cases reported
- Hair grow up to 2 year of age
- Most will lose the hair with time
- No associated abnormalities
- Palms, soles, glans penis, mucous membrane, labia minor are spared

Ambras syndrome (werewolf syndrome)







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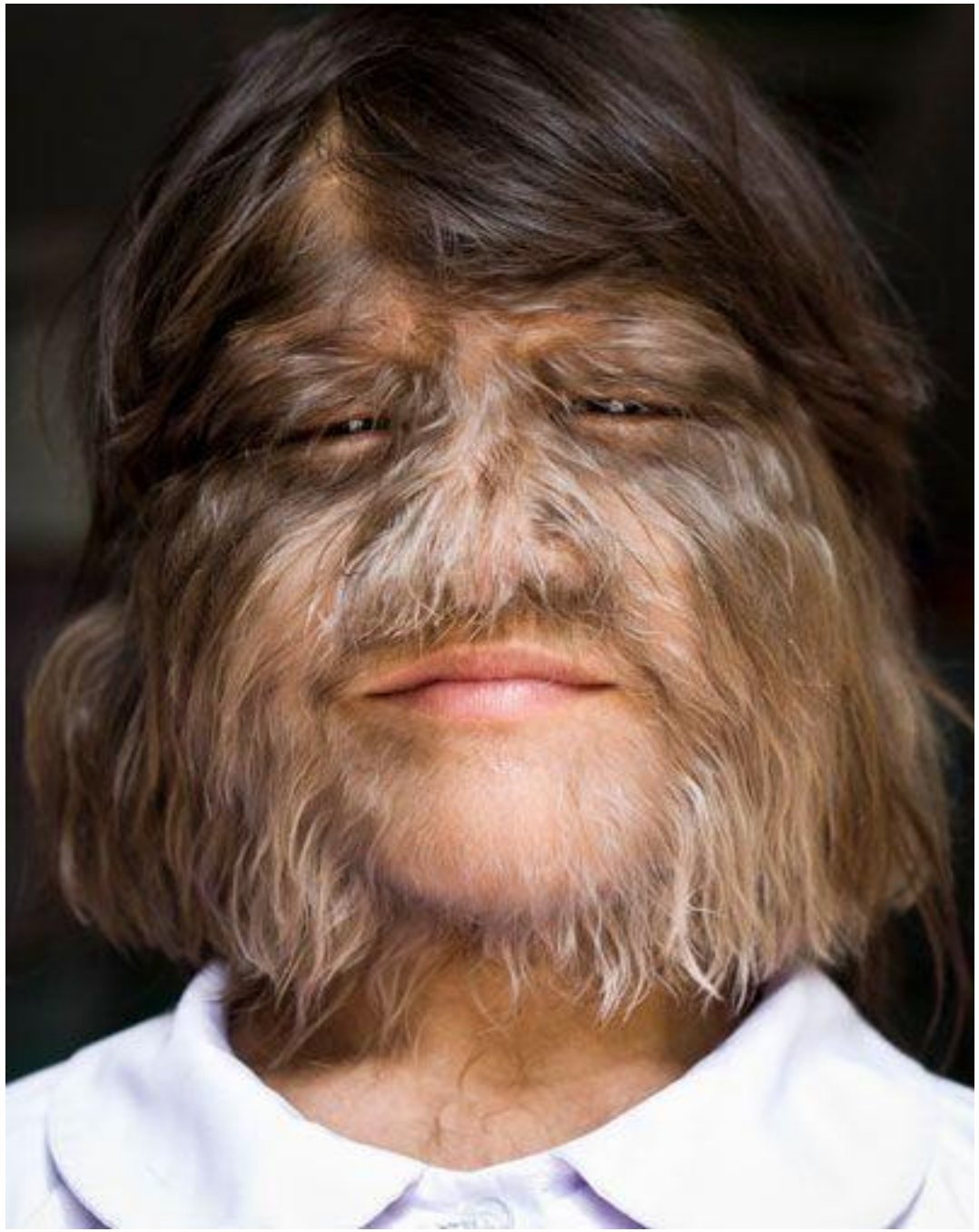

www.pinterest.com

Questions ????