Hyperpigmentation

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Facial Hyperpigmentation

- Riehl melanosis (Pigmented cosmetic dermatitis)
- Poikiloderma of Civatte (Erythromelanosis interfollicularis)
- Erythromelanosis follicularis faciei et colli
- Peribuccal pigmentation of Brocq
- Berloque dermatitis
- Erythema dyschromicum perstans (Ashy dermatosis)
- Lichen planus pigmentosus
- Drug-induced hyperpigmentation
- Post inflammatory Hyperpigmentation
- Melasma

Riehl melanosis
(Pigmented cosmetic dermatitis)

- A distinctive pattern of grey-brown facial pigmentation was first described by Riehl in Vienna between 1916 and 1920.
- Riehl attributed this pigmentation to contact with noxious substances or to wartime living conditions.
- It was subsequently reported from other parts of the world.
- Pigmented cosmetic dermatitis-like (Riehl's melanosis-like) pigmentation has been reported in patients with primary Sjogren's syndrome.

Riehl melanosis (Pigmented cosmetic dermatitis)

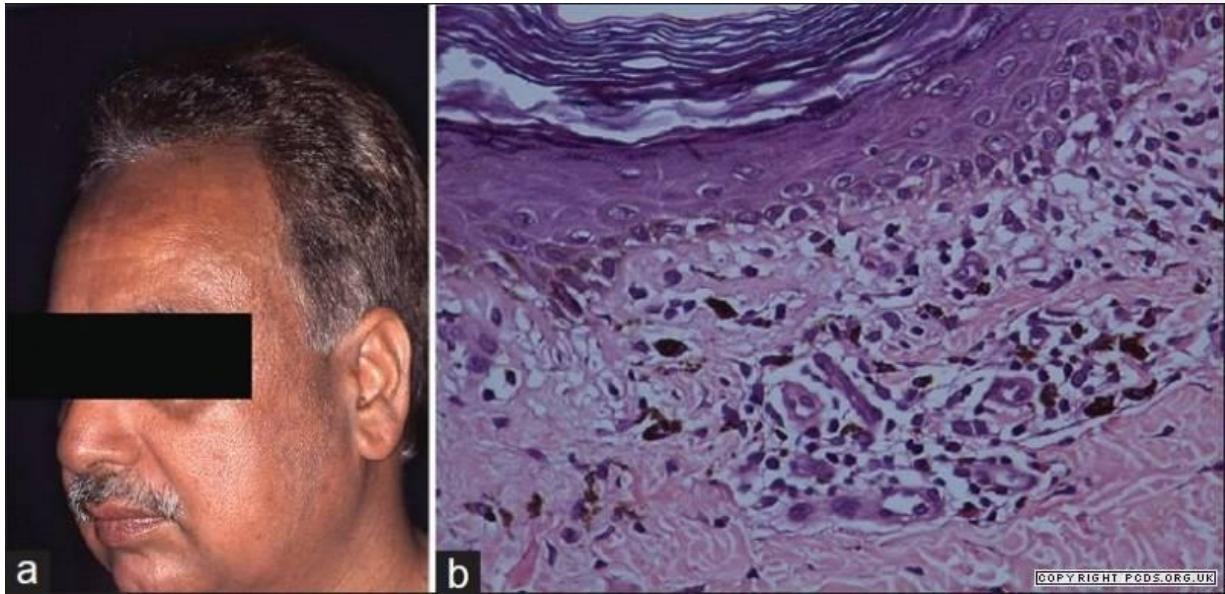
- Middle age women
- Predisposing factors:
  - Tar derivatives
  - Fragrances
  - Cosmetic ingredients

Riehl melanosis (Pigmented cosmetic dermatitis)

- Clinical features:
  - Brownish-grey pigmentation more intense on the forehead and temples.
  - The pigmentation may extend to the other parts of body.
  - Horny plugs fill the follicles and there may be some scaling.

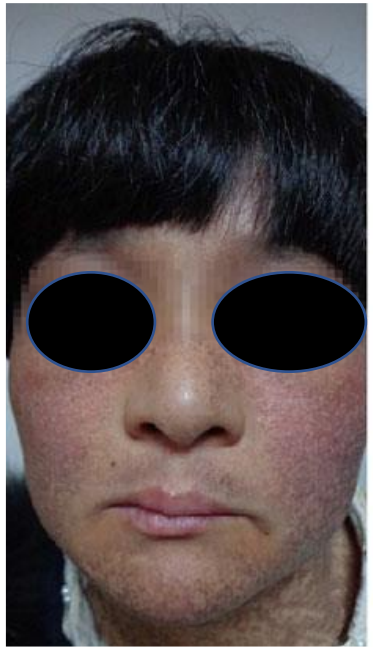
Riehl melanosis (Pigmented cosmetic dermatitis)

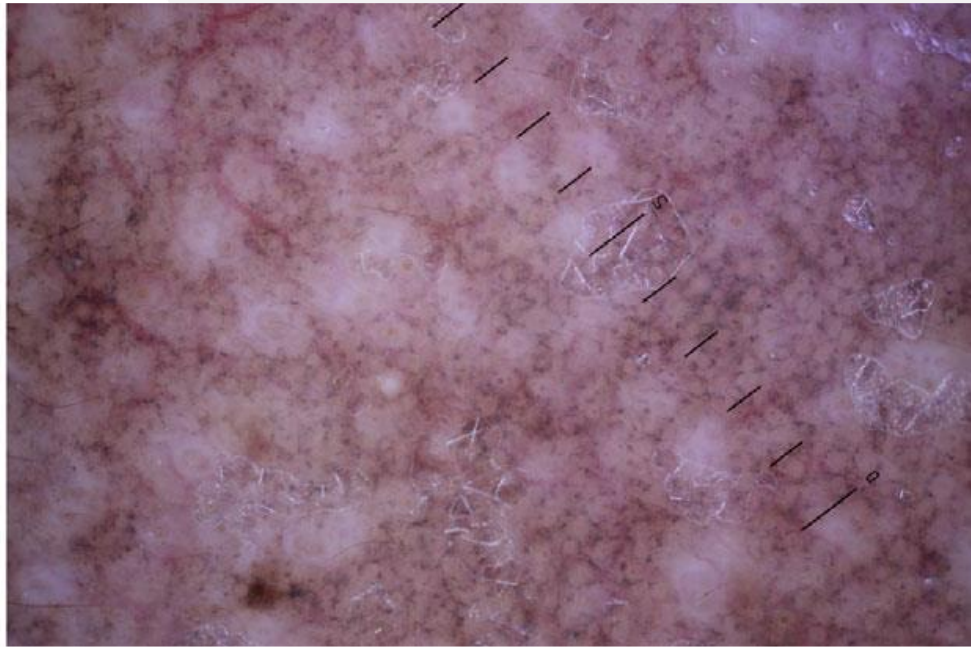
- Pathology:
  - Liquefaction degeneration of the basal layer
  - Perivascular or band-like dermal infiltrate
  - Pigmentary incontinence (in the early stages)
  - Many melanophages in the upper dermis (in late stages)



Riehl melanosis (Pigmented cosmetic dermatitis)

- Dermoscopy:
  - slight scales
  - pseudonetwork
  - grey dots/granules
  - follicular keratotic plugs
  - perifollicular whitish halo
  - telangiectatic vessels





Riehl melanosis (Pigmented cosmetic dermatitis)

- Diagnosis:
  - Patch testing

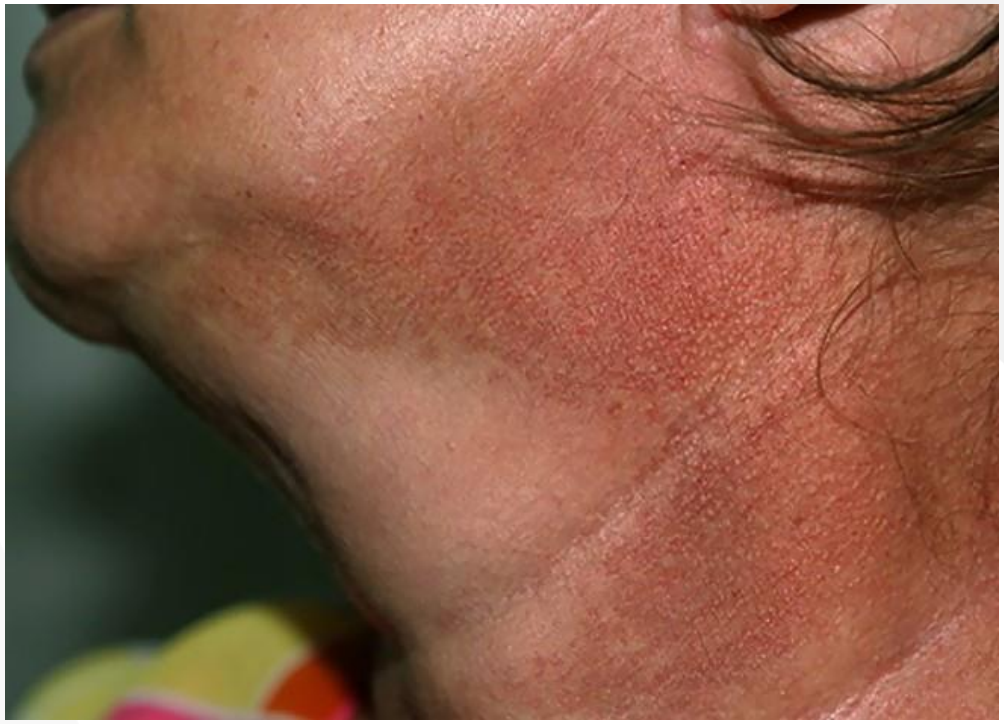
- Treatment:
  - Where a contact cause can be identified, it should be avoided.
  - Sun protection
  - Hydroquinone 2–5% plus tretinoin or glycolic acid
  - Intense pulse light (IPL) and Q-switch Nd:YAG laser

Poikiloderma of Civatte (Erythromelanosis interfollicularis)

- This characteristic pattern of reticulate hyperpigmentation of the face and neck was first reported in 1923 by Civatte.
- It usually presents as a triad of atrophy, telangiectasia, hyper- and hypopigmentation, which typically appears on the sides of the face and neck and on the upper anterior chest after years of repeated UV exposure.

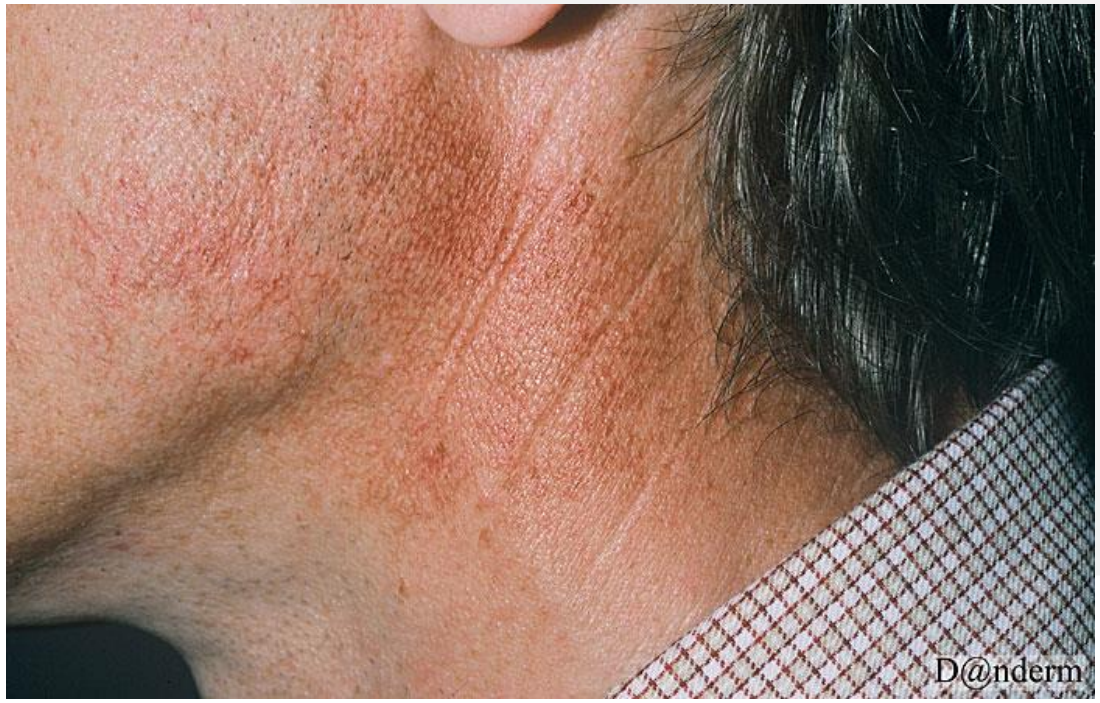
Poikiloderma of Civatte (Erythromelanosis interfollicularis)

- More common in fair skin, middle age, women
- **Predisposing factors**
  - Exposure to light
  - Phototoxic or photoallergic substances in cosmetics



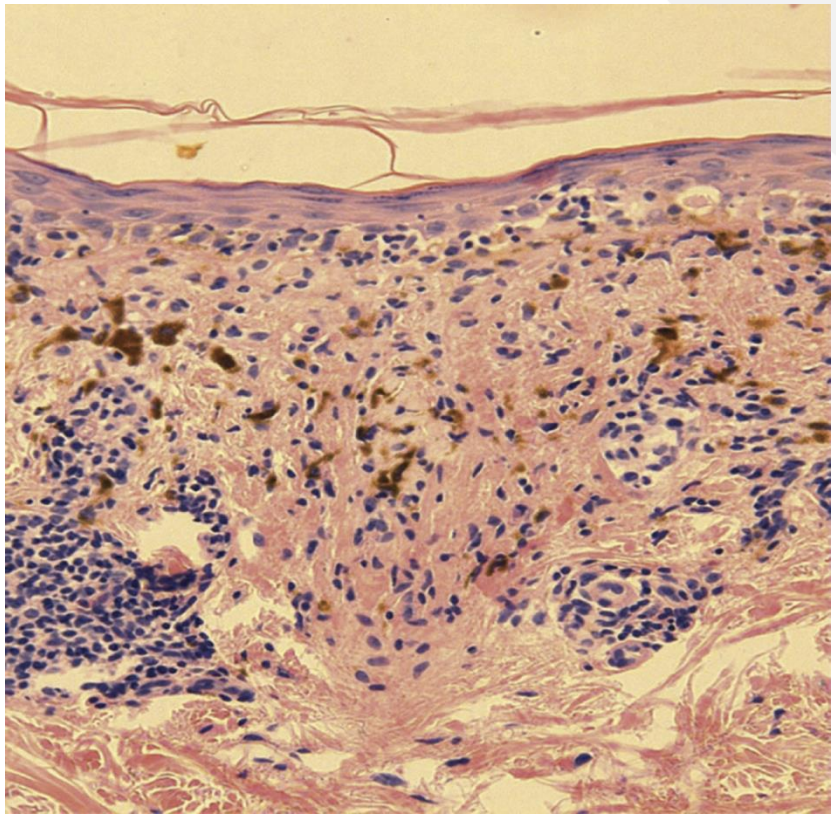
Poikiloderma of Civatte (Erythromelanosis interfollicularis)

- Clinical features:
  - It develops symmetrically on the sides of the face, neck and upper aspect of the chest
  - The submandibular and submental areas are spared thus implicating sunlight in the pathogenesis of this condition.
  - It is mostly asymptomatic, although some patients experience itching, burning and flushing.



Poikiloderma of Civatte (Erythromelanosis interfollicularis)

- Pathology:
  - Thinning of epidermis
  - Hydropic degeneration of the basal cell layer
  - Melanophages in the papillary dermis
  - Dilatation of the papillary dermal capillaries



Poikiloderma of Civatte (Erythromelanosis interfollicularis)

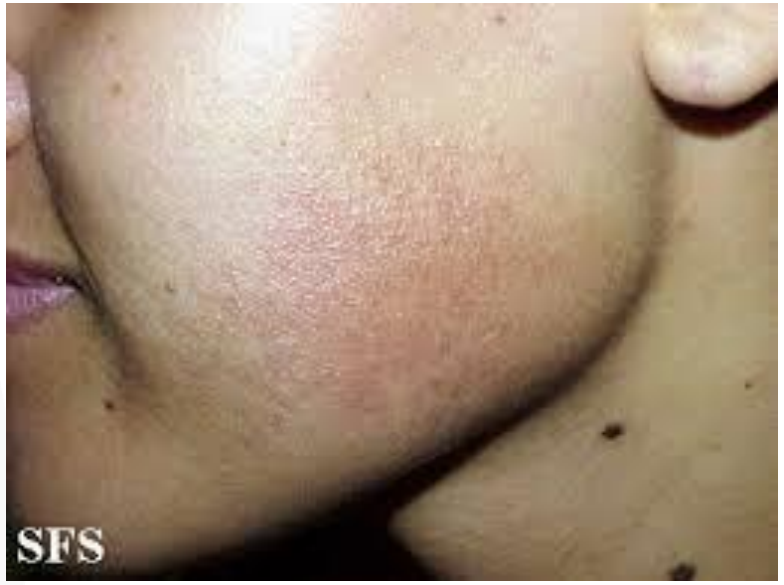
- Diagnosis:
  - Patch testing can be useful if induction by allergen is suspected.
- **Treatment:**
  - Photoprotection with a high SPF sunscreen
  - Avoiding perfumes
  - Intense pulsed light
  - Tunable dye laser
- It is slowly progressive and irreversible.

Erythromelanosis follicularis faciei et colli

- This syndrome, of unknown origin, was originally described in Japan by Kitamura *et al*. in 1960.
- **Age**
  - Peak age of onset in the second decade of life.
- **Sex**
  - Affects both sexes.
- **Ethnicity**
  - Affects all races, but more frequent in Asians.
- **Associated diseases**
  - May be associated with keratosis pilaris
- **Genetics**
  - Few familial cases have been reported.

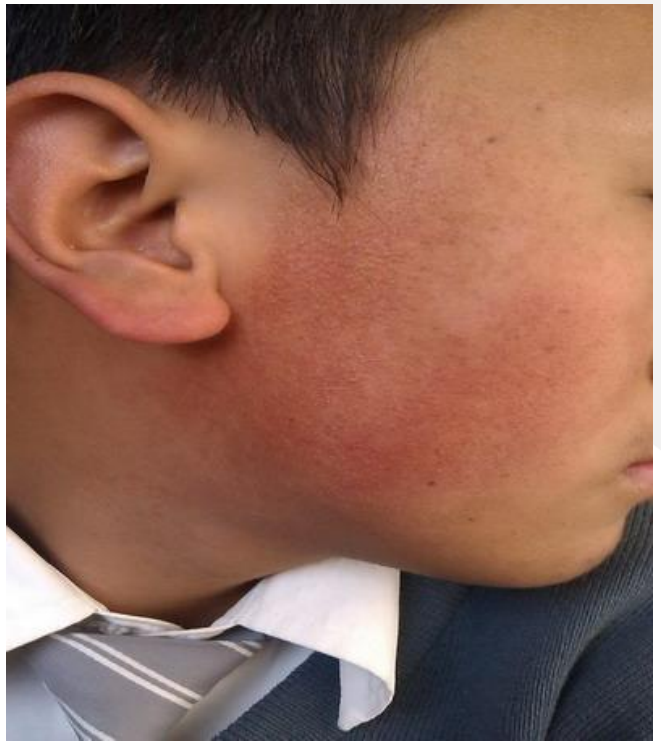
Erythromelanosis follicularis faciei et colli

- Clinical features:
  - It is characterized by a triad of hyperpigmentation, follicular plugging and erythema, with or without telangiectasia, affecting the lateral aspects of the cheeks and in some cases the neck.



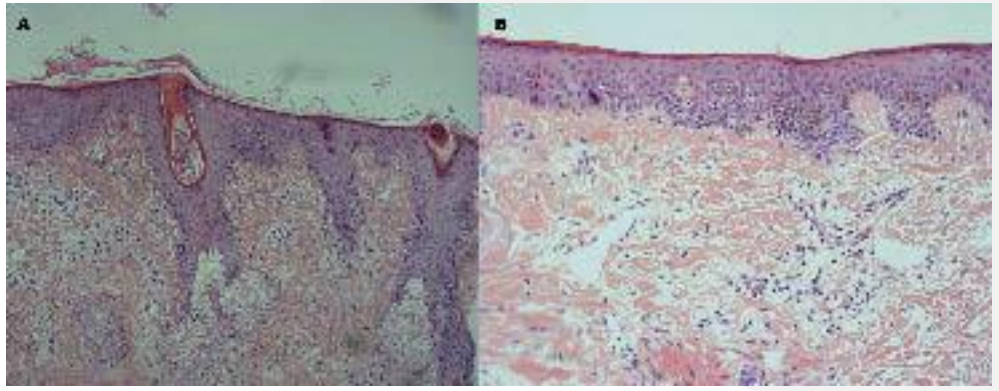
Erythromelanosis follicularis faciei et colli

- Clinical features:
  - The majority of affected vellus hairs are lost, but terminal hair follicles of the scalp and beard are usually not affected.
  - The distribution, and lack of clinical follicular keratosis, or scarring readily distinguish it from other forms of keratosis pilaris and from other facial melanoses.



Erythromelanosis follicularis faciei et colli

- **Pathology**
  - Slight hyperkeratosis and hyperpigmentation of the basal layer.
  - The hair follicles are enlarged and contain lamellar horny masses (follicular plug).
  - The epidermis overlying the affected follicle is flattened and contains excess melanin.
  - In the dermis, lymphocytic infiltrate surrounds dilated vessels.



Erythromelanosis follicularis faciei et colli

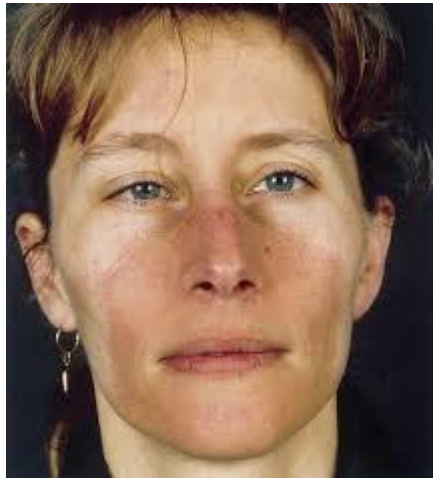
- Treatment:
  - It spreads slowly, is persistent and response to therapy is generally poor and prone to relapse.
  - Avoidance of solar exposure and use of sunscreen is recommended.
  - Topical keratolytic: urea cream (10–20%), ammonium lactate lotion (12%), tretinoin cream (0.05–0.1%)
  - Metronidazole cream, tacalcitol cream
  - Salicylic acid peels and glycolic acid peels
  - Oral Isotretinoin (0.1–1 mg/kg/day)
  - Laser treatment (PDL) of the background erythema

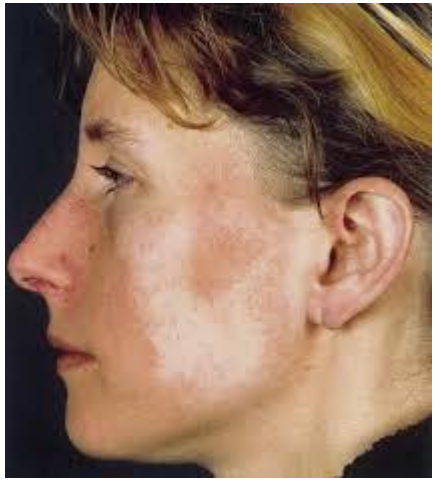
Peribuccal pigmentation of Brocq

- It was Brocq in 1923 who first reported a case of perioral hyperpigmentation in a unique clinical pattern.
- Predominantly in middle-aged women and has only rarely been reported in men.
- A photodynamic substance in cosmetics is probably responsible.

Peribuccal pigmentation of Brocq

- Clinical features:
  - Diffuse brownish-red pigmentation develops symmetrically around the mouth but spares a narrow perioral ring.
  - It may extend up the center of the face to the forehead and in some cases there are well-defined patches of pigmentation over the angles of the jaw and the temples.





Peribuccal pigmentation of Brocq

- Treatment:
  - The erythematous component, and the intensity of the pigmentation, may fluctuate over short periods.
  - The pigmentation is usually persistent but tends to fade gradually if the cause is eliminated.

Berloque dermatitis

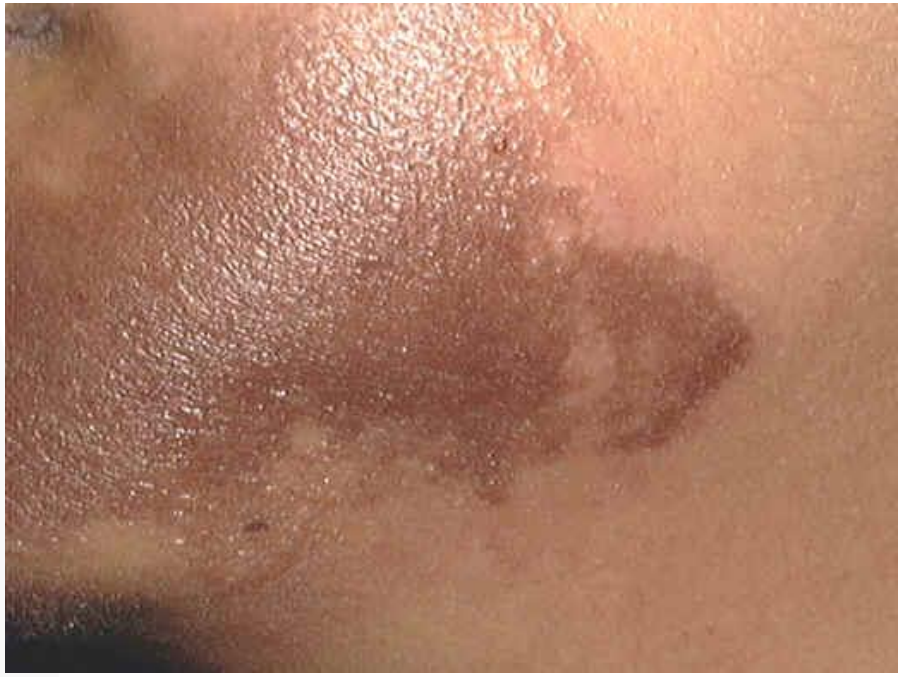
- Skin pigmentation due to phototoxic reaction to perfumes applied to the skin.
- It can be seen in any age, any sex, and any racial group.
- It results from the UV-stimulated melanogenesis by 5-methoxypsoralen (bergapten) in perfumes containing bergamot oil.

Berloque dermatitis

- The reaction occurs in only a small proportion of those exposed and depends on:
  - The readiness with which the bergapten is absorbed,
  - The quantity applied,
  - The intensity and duration of exposure to UV light.

Berloque dermatitis

- **Clinical features:**
  - Deep-brown pigmentation follows the pattern formed by droplets of perfume over the skin from their points of application and then fades after weeks or months.



Erythema dyschromicum perstans (Ashy dermatosis)

- This clinical syndrome of unknown origin was first reported by Ramirez of El Salvador in 1957 under the term ‘los cenicientos’ (the ashy ones) due to the ashy discoloration of the skin.
- A further case series was reported by Convit, Kerdel-Vegas and Rodriguez from Venezuela in 1961 who commented on the presence of raised erythematous borders in the early stages and proposed the term ‘erythema dyschromicum perstans’ .
- It has been proposed that ashy dermatosis be used for all such cases but that erythema chronicum perstans be limited to those cases in which an inflammatory phase with erythema has been observed.

Erythema dyschromicum perstans (Ashy dermatosis)

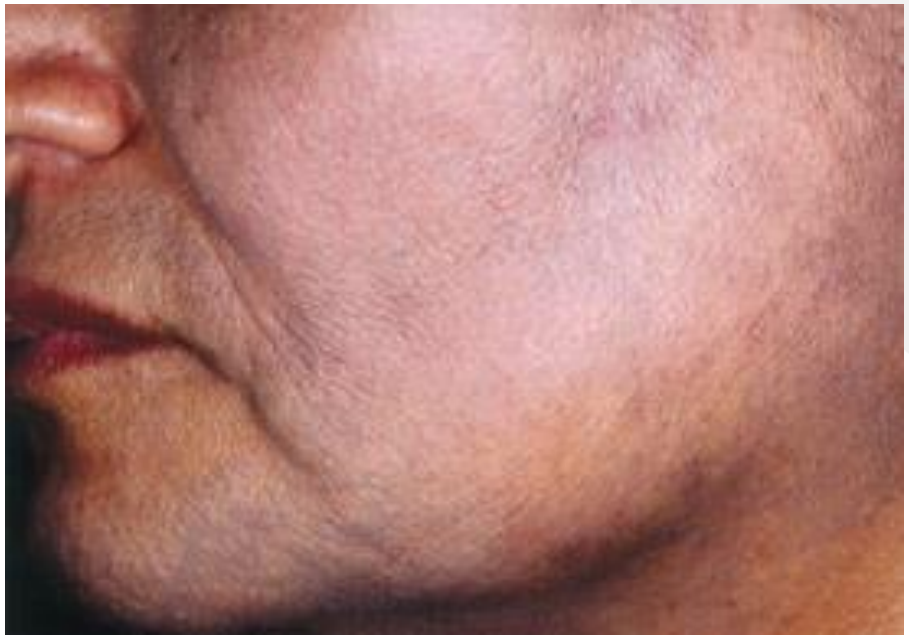
- **Age**
  - From childhood to old age, most frequently in young adults.
- **Sex**
  - It occurs in both sexes, but females more than males.
- **Ethnicity**
  - Mainly observed in intermediate skin types. Most published cases have been from Central and South America or East Asia.

Erythema dyschromicum perstans (Ashy dermatosis)

- Pathomechanism:
  - Still unknown.
  - Parasite infection
  - Chemicals such as ammonium nitrate and barium sulfate
  - Environmental allergens
- An immunological response to any of these factors might define the extent of lesional inflammation of the skin based on the genetic profile, i.e., a strong inflammatory reaction against these factors might lead to EDP, where-as a mild reaction might lead to AD.

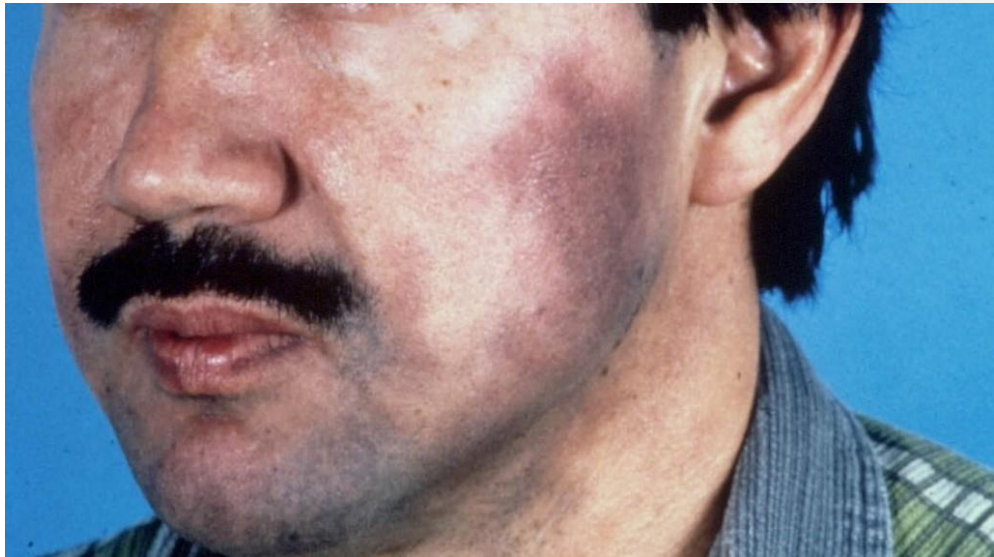
Erythema dyschromicum perstans (Ashy dermatosis)

- **Clinical features**
  - It is characterized by numerous macules of varying shades of grey.
  - There may initially be signs of inflammation with a red, slightly raised and palpably infiltrated margin (erythema dyschromicum perstans).



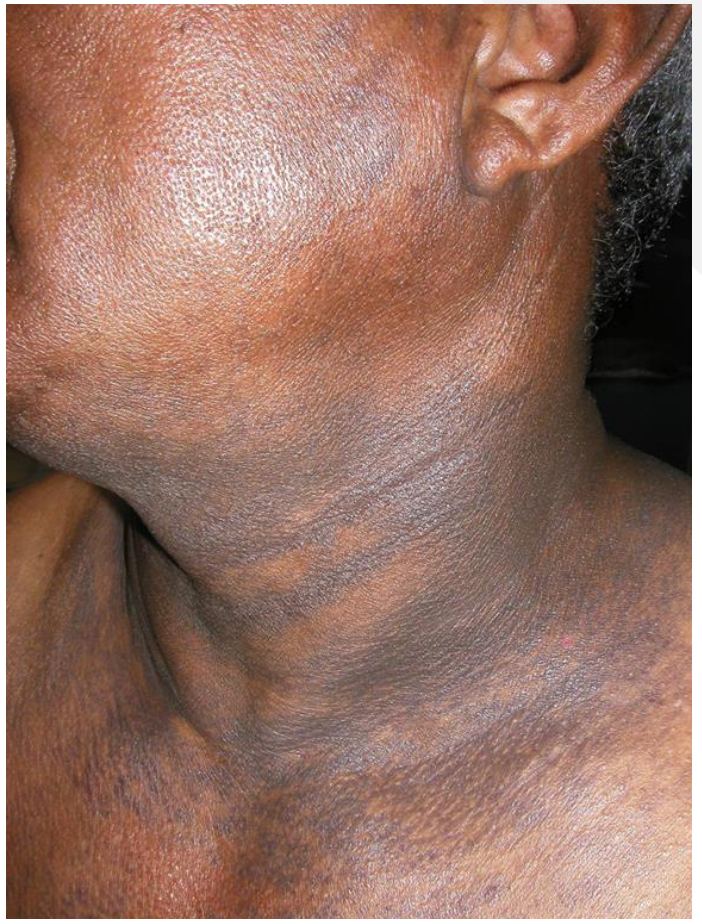
Erythema dyschromicum perstans (Ashy dermatosis)

- In a recent review of 68 patients from Korea, less than a fifth were observed to have peripheral erythematous borders to their lesions.
- In this study, the trunk was affected in two-thirds and the face in one-third of patients.
- The erythematous halo was associated with only 17.3% of patients.



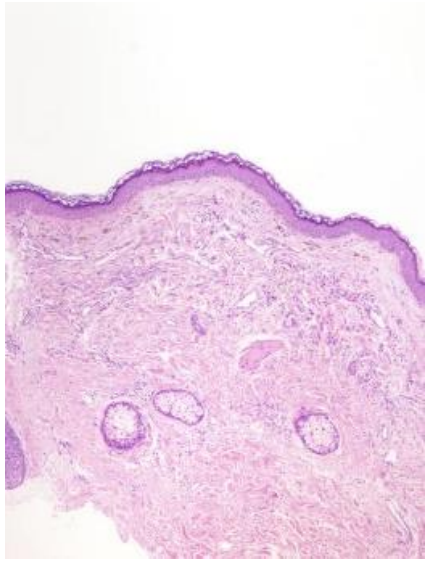
Erythema dyschromicum perstans (Ashy dermatosis)

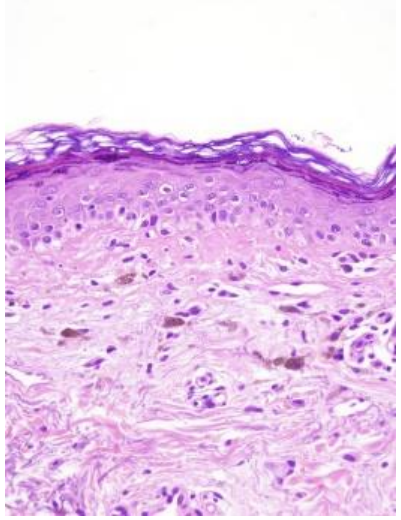
- **Clinical features**
  - The macules vary in size and tend to coalesce over extensive areas of the trunk, limbs and face.
  - Against the general greyish background are macules of hypomelanosis or hypermelanosis.
  - The lesions are mostly asymptomatic, although some patients may experience mild pruritus.
  - Mucous membranes are spared.



Erythema dyschromicum perstans (Ashy dermatosis)

- **Pathology**
  - The active border shows vacuolar degeneration of the basal cells and epidermis contains much pigment and there is pigmentary incontinence.
  - The dermal vessels are sleeved with an infiltrate of lymphocytes and histiocytes, and there are many melanophages.





Erythema dyschromicum perstans (Ashy dermatosis)

- **Treatment:**
  - There is no consistently effective treatment and the initial erythematous phase tends to settle after several months and the pigmentation is persistent with a tendency to extend gradually over years.
  - Camouflage creams and make-up
  - Clofazimine 100 mg/day for 3 months in inflammatory cases (response rate of 66–87%)
  - Dapsone 100 mg/day for 3 months
  - Oral corticosteroid therapy
  - UV therapy
  - Fractionated non-ablative treatment sessions utilizing the 1,550 nm erbium-doped fiber laser in combination with topical tacrolimus ointment
  - Rarely spontaneous resolution over several years after has been reported.

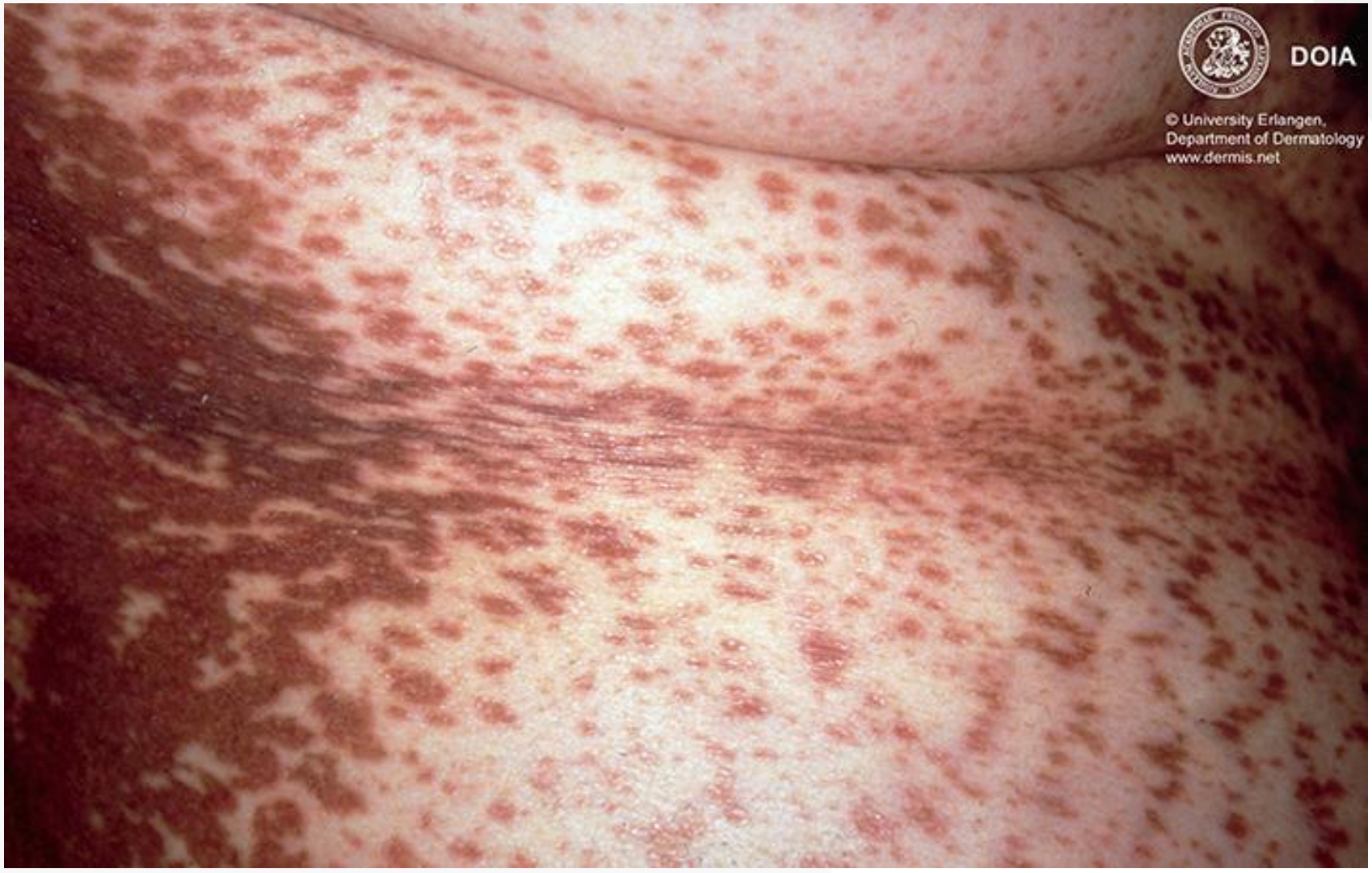
Lichen planus pigmentosus

- A rare variant of lichen planus that occurs predominantly in individuals with darker skin phototypes (III to V)
- It generally affects young to middle-aged adults, especially those from India, Latin America, and the Middle East.
- Photodistribution suggests that ultraviolet (UV) light may play a role in the pathogenesis of LPP.
- Mustard oil (which contains allyl isothiocyanate, a potential photosensitizer) and amla oil have been suggested as possible inciting agents
- . There are multiple reports of the coexistence of LPP and frontal fibrosing alopecia, illustrating that LPP may be the herald sign of this scarring type of hair loss and that both entities may have a pathogenic link

Clinical features

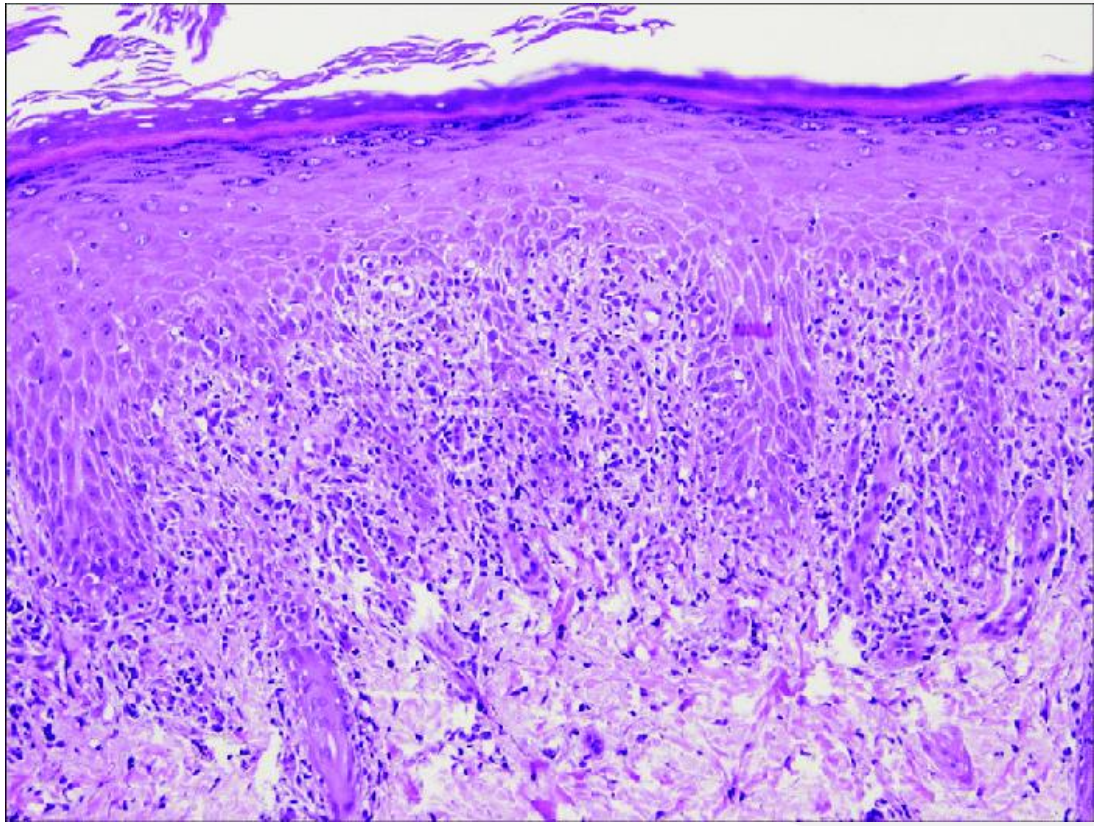
- LPP typically presents with oval or irregularly shaped, brown to gray-brown macules and patches in sun-exposed areas, including the forehead, temples, and neck .
- It may also occur on the trunk and in intertriginous areas (lichen planus pigmentosus inversus).
- Lesions are usually symmetric but can present in a unilateral, linear fashion.
- In contrast with erythema dyschromicum perstans, early LPP lesions lack an erythematous border.

Lichen planus pigmentosus



Histology

- Hyperkeratosis
- Vacuolar cell degeneration in the basal layer with apoptotic keratinocytes
- A band-like dermal lymphocytic infiltrate with pigment incontinence, and melanophages.



differential diagnosis

- Lichen planus
- Erythema dyschromicum perstans
- Melasma
- Lichenoid drug eruptions
- Postinflammatory hyperpigmentation

treatment

- LPP is a chronic, relapsing disorder with exacerbations and remissions.
- First-line treatment involves the use of sun-protective measures to prevent further darkening.
- Other treatment options include
- Topical corticosteroids
- Topical calcineurin inhibitors
- Skin-lightening agents
- Oral retinoids
- UV light therapy
- Antimalarials
- Laser therapy

Drug-induced hyperpigmentation

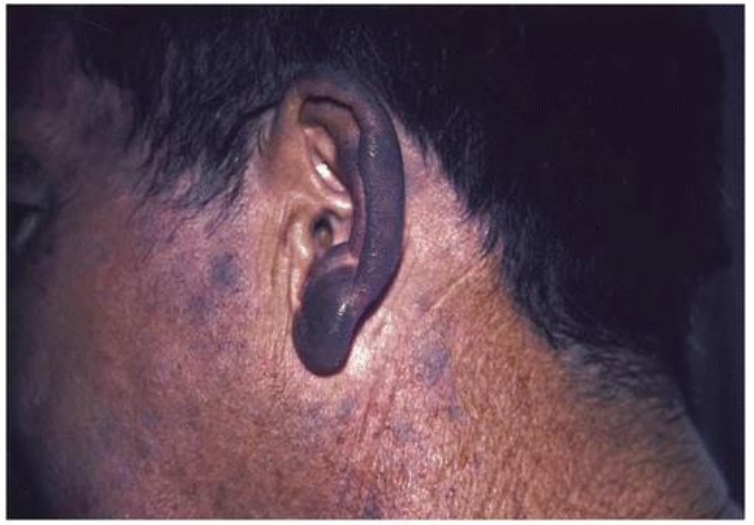
- Drug-induced hyperpigmentation accounts for 10–20% of all cases of acquired hyperpigmentation.
- Several mechanisms are involved in drug-induced changes of pigmentation of the skin:
  - Increased melanin synthesis
  - Increased lipofuscin synthesis
  - Deposition of drug-related material
  - Post-inflammatory hyperpigmentation

Drug-induced hyperpigmentation

- Amiodarone
- Antimalarials
- Clofazimine
- Minocycline
- Fixed drug eruption
- Ochronosis

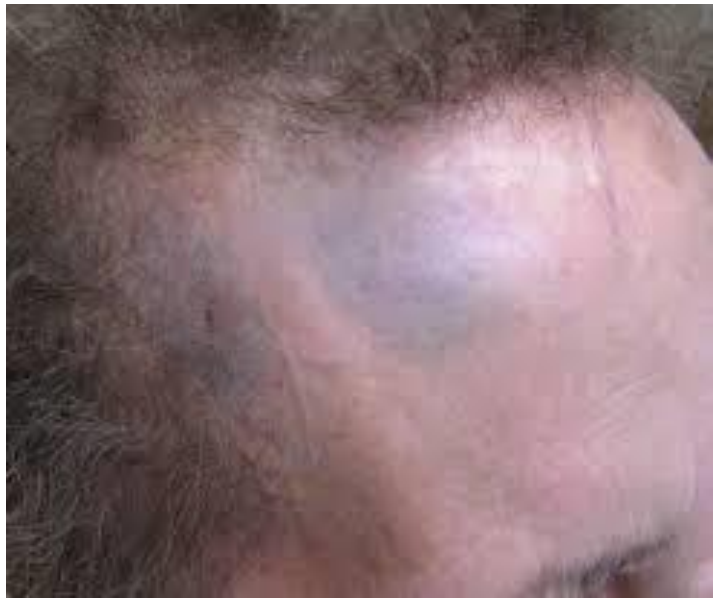
Amiodarone

- Fewer than 5% of patients develop drug-induced discoloration of the skin, characterized by a slate-gray or purple discoloration of mainly the sun-exposed skin,



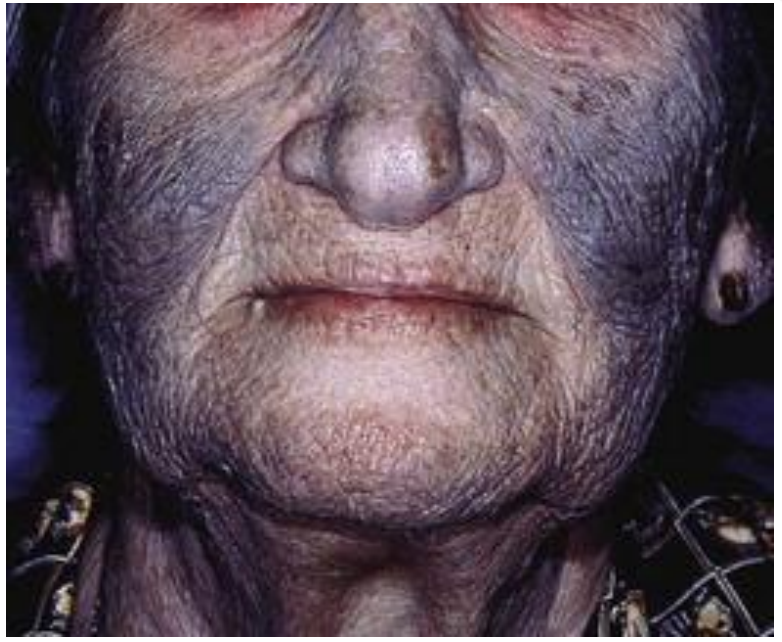
Antimalarial drugs

- Bluish-grey pigmentation appears mainly on sun-exposed areas.
- Bleaching of the colour of the hair occurs.



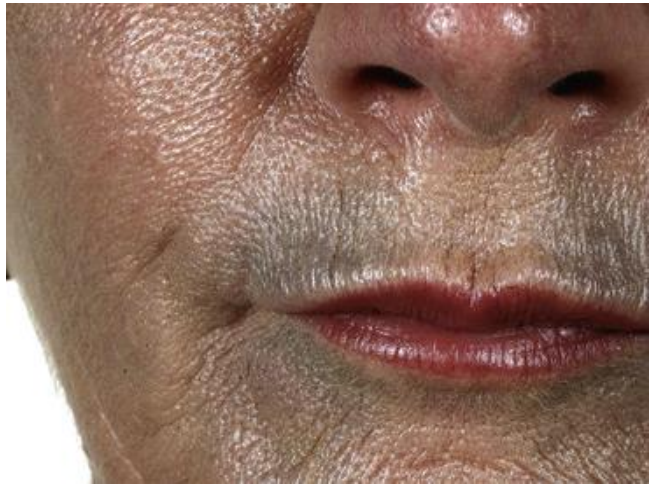
Clofazimin

- It produces an initial redness of the skin due to an accumulation of the drug.
- Later, with prolonged treatment, a violaceous brown colour develops that is most noticeable in face and lesional skin.



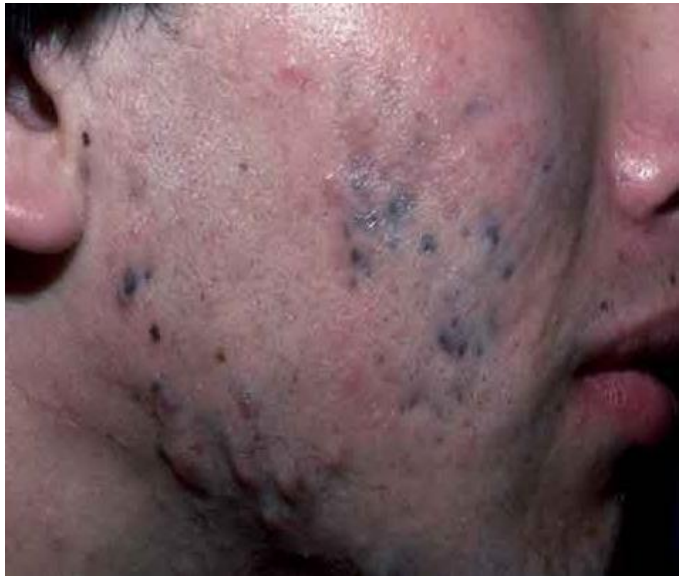
Minocyclin

- Minocycline-induced hyperpigmentation may affect up to 15% of patients receiving minocycline, particularly in long-duration treatments.



Minocyclin

- Four unique patterns with well-circumscribed blue-grey macules located:
  - In areas of acne scars (type I)
  - At sites of previous inflammation and mostly affecting sun-exposed areas (type II)
  - 'Muddy skin syndrome' characterized by diffuse symmetrical brown-grey discoloration with a tendency to photo-aggravation (type III)
  - The vermilion of the lower lip (type IV)

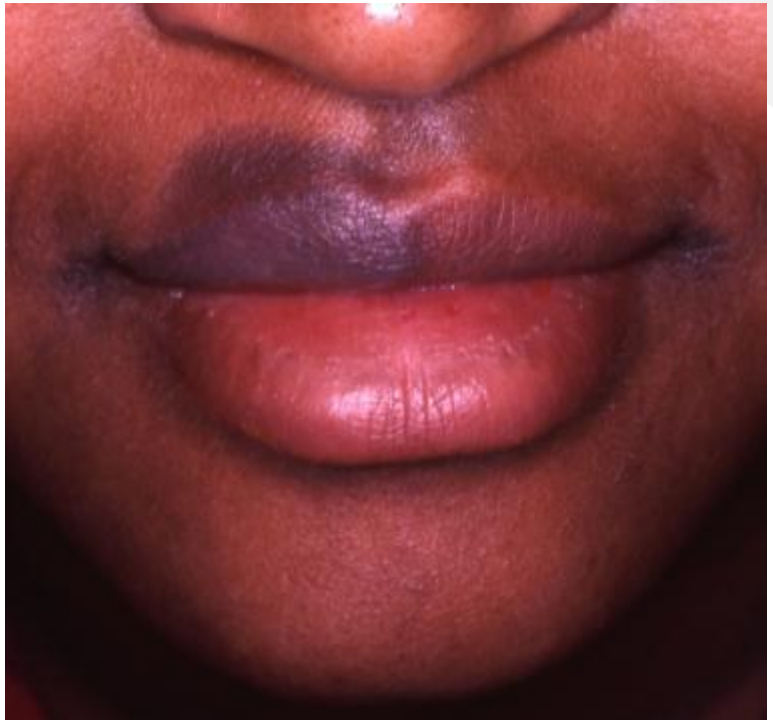


Fixed drug eruption

- Fixed drug eruption is one of the most common forms of drug-induced exanthems.
- The acute eruption characteristically settles leaving residual hyperpigmentation, especially in those with darker skin types so they are particularly frequent in black people.
- Most frequently reported drugs include tetracyclines, non-steroidal anti-inflammatory drugs, sulfonamides and sedatives.

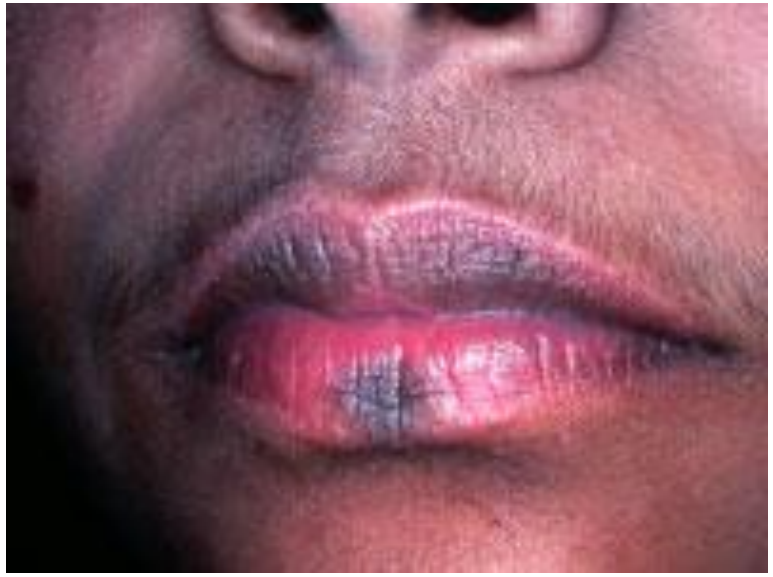
Fixed drug eruption

- Clinical features:
  - Well-circumscribed areas of slate-brown pigmentation commonly follow the erythematous and bullous stages of fixed eruptions .
  - The genitalia and perianal area are often affected, although the eruption can appear anywhere on the skin surface.



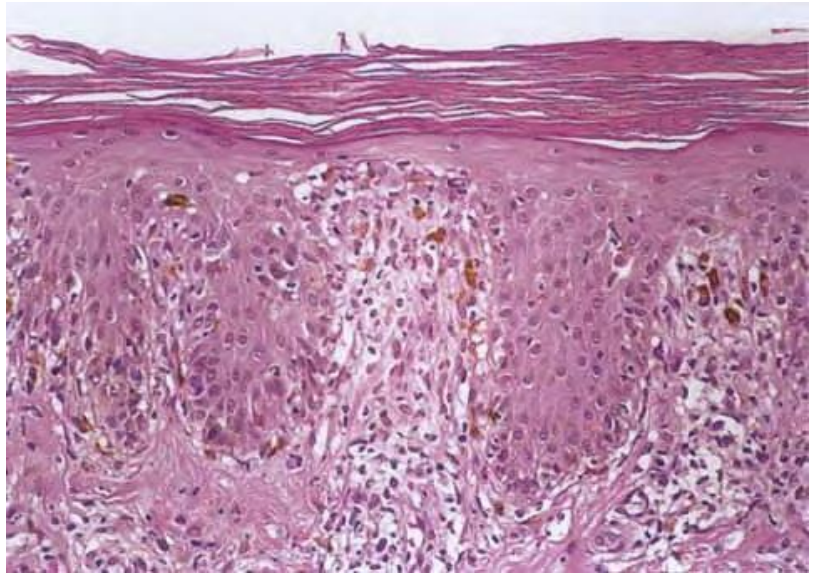
Fixed drug eruption

- Clinical features:
  - The characteristic course is recurrence of lesions at the same sites with development of new areas of involvement with repeated exposure to the causative agent.



Fixed drug eruption

- The slate-brown colour in fixed drug eruption is due to pigmentary incontinence with melanophages in the upper dermis .
- It is suggested that the eruption may be mediated by a type IV hypersensitivity.
- Immunohistological findings suggest that the characteristic same-site recurrence may be induced by prolonged ICAM-1 expression in the lesional keratinocytes.

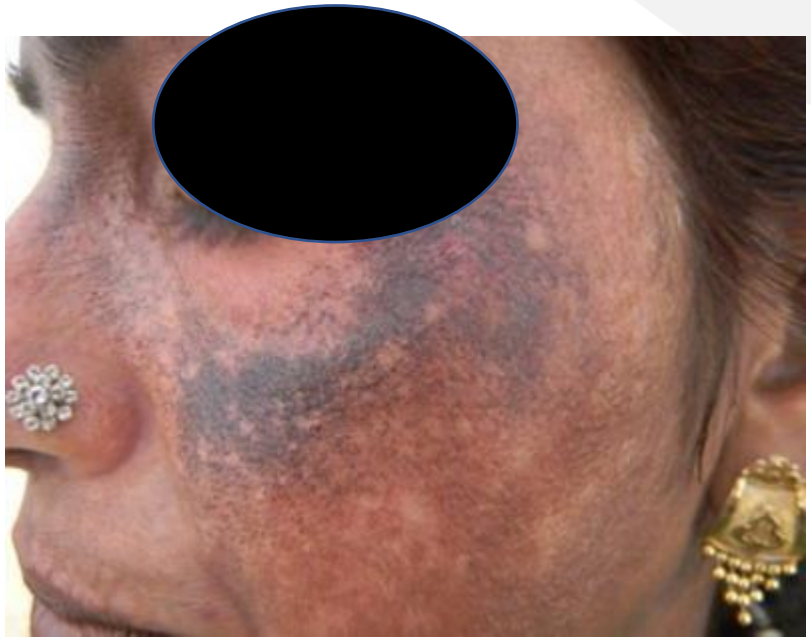


Ochronosis

- Ochronosis is the bluish black discoloration of certain tissues, such as the ear cartilage and the ocular tissue, seen with alkaptonuria, a metabolic disorder.
- Additionally, exogenous ochronosis can occasionally occur from exposure to various substances such as phenol, trinitrophenol, resorcinol, mercury, picric acid, benzene, hydroquinone, and antimalarials.

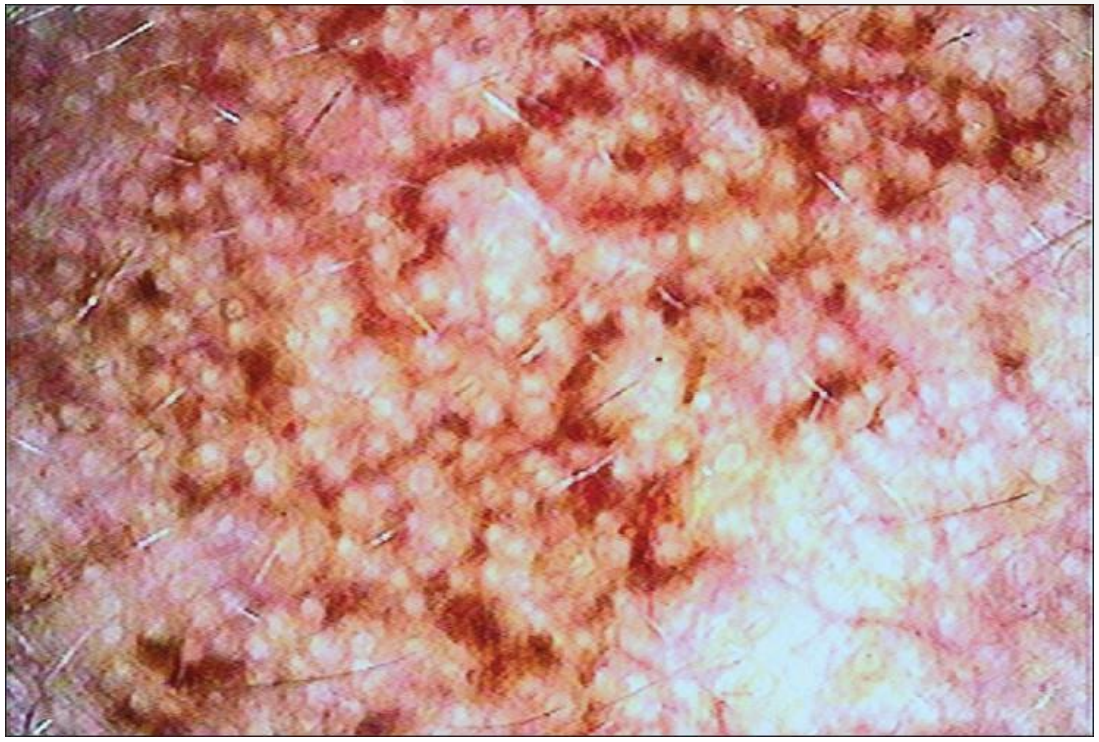
Ochronosis

- It is reported that 35% of African blacks exhibit ochronotic skin changes when using a 6-8% hydroquinone preparation over a prolonged period.
- This figure was 69% in a South African study.
- In African Americans, this cutaneous adverse effect of hydroquinones has been reported, even when using 2% hydroquinone products.
- With exogenous ochronosis, the arthropathy seen with alkaptonuria does not occur.



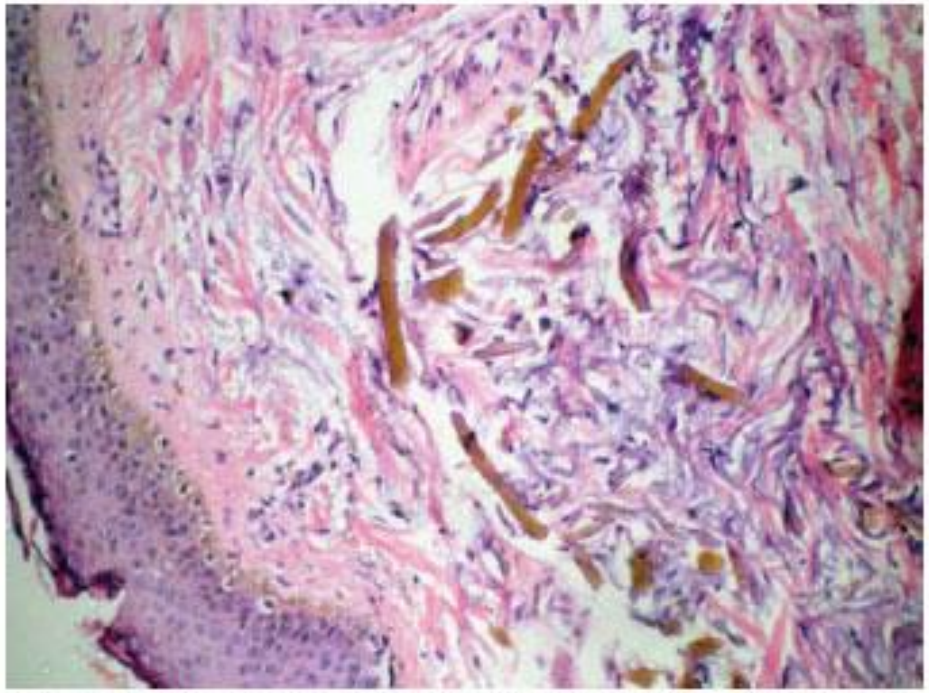
Ochronosis

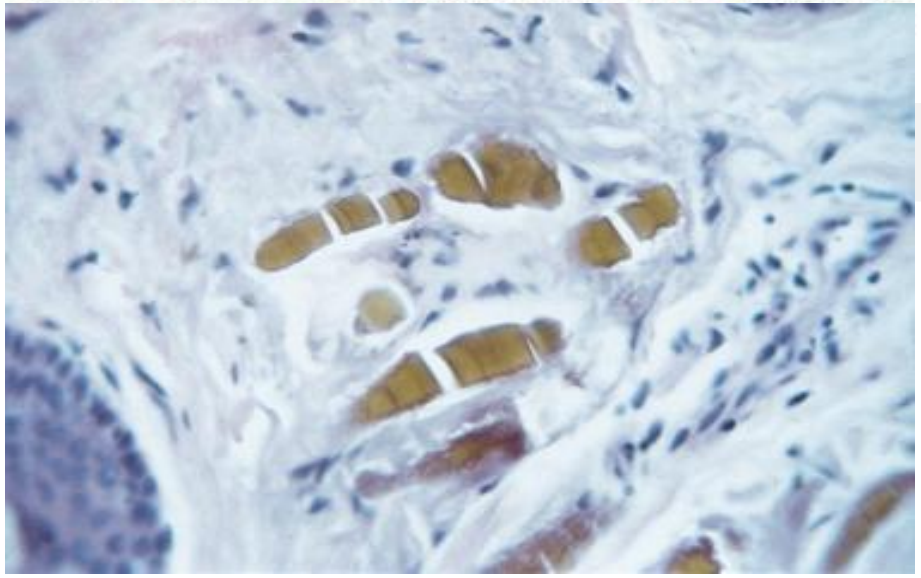
- Dermoscopy:
  - Amorphous, densely pigmented structures obliterating some follicular openings and multiple thin, short, arciform structures.



Ochronosis

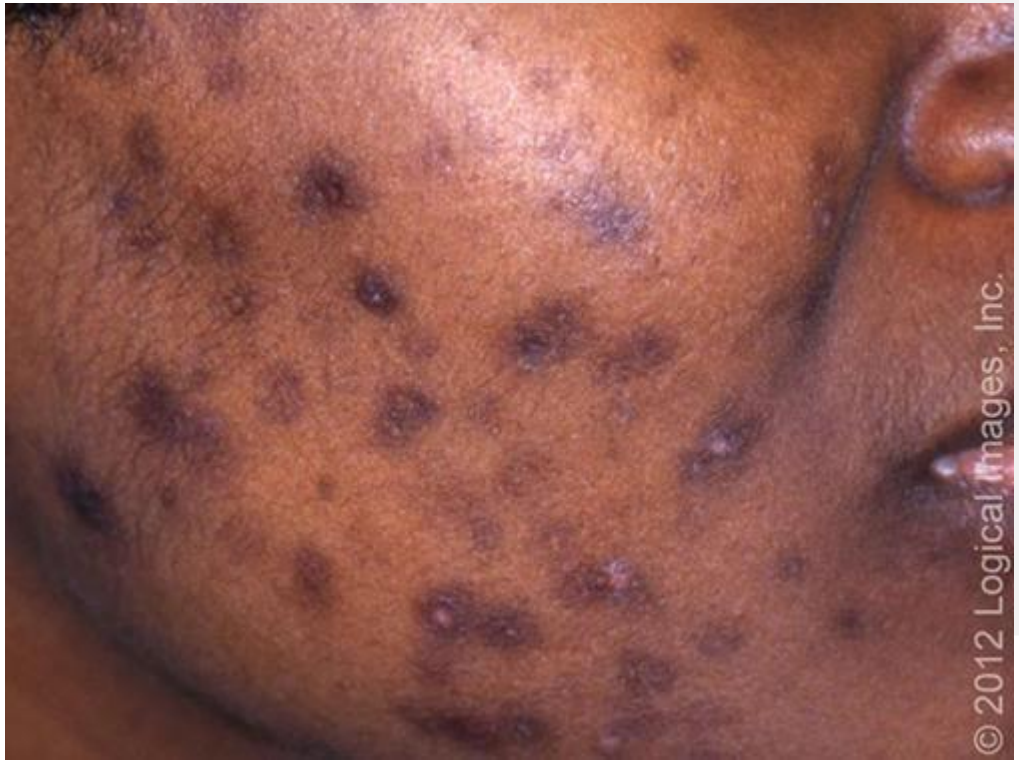
- Pathology:
  - Ochronotic collagen fibers leading to the formation of ochronotic colloid milium
  - Dermal cell infiltrate is variable but often granulomatous.
  - Transfollicular elimination of these ochronotic fibers has been reported.





Postinflammatory hyperpigmentation (PIH)

- A reactive hypermelanosis of the skin that occurs as a sequela of cutaneous inflammation
- Common causes of PIH include acne vulgaris, eczematous dermatoses, and burn injury
- PIH is a frustrating problem that can have a strong psychologic toll on affected patients.



ETIOLOGY

Endogenous :

- Acne vulgaris, atopic dermatitis, irritant contact dermatitis, allergic contact dermatitis, psoriasis, and lichen planus

Exogenous:

- Accidental burns, nonionizing radiation therapy, phototoxicity, chemical peels, and laser procedures

PATHOGENESIS & HISTOPATHOLOGY

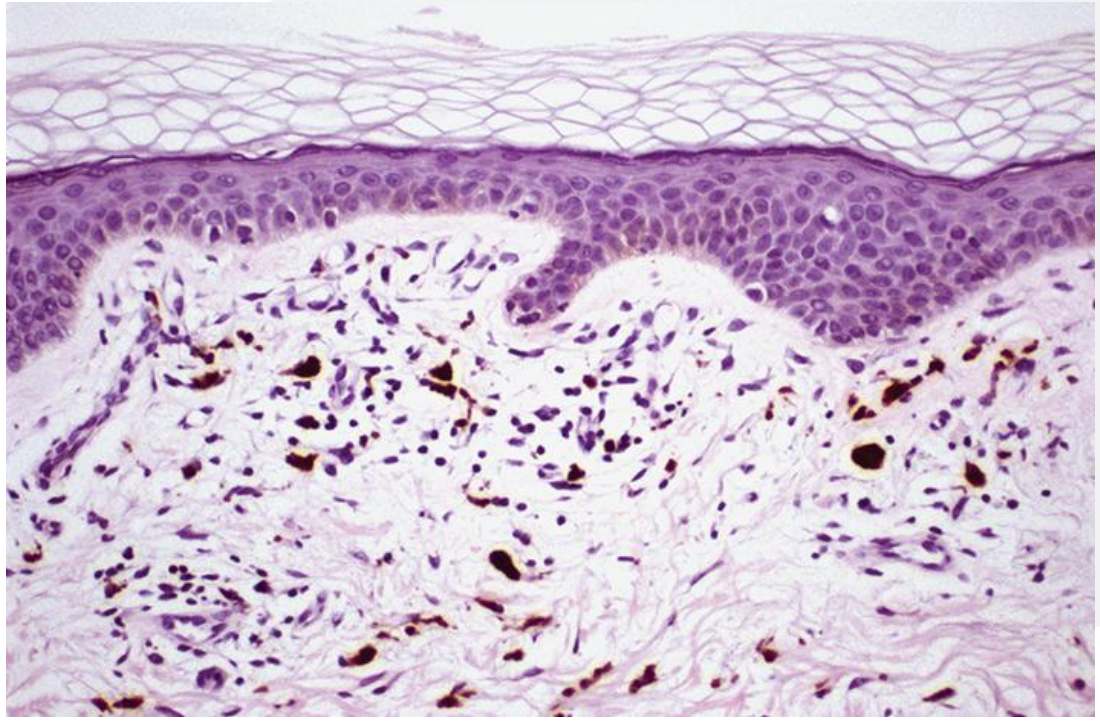
Epidermal Melanosis:

- Result from effects of the release and oxidation of arachidonic acid to prostaglandins and leukotrienes or the effects of other inflammatory mediators in inflamed skin
- Inflammatory mediators may stimulate melanocytes to increase production of melanin and transfer melanin to surrounding keratinocytes

PATHOGENESIS & HISTOPATHOLOGY

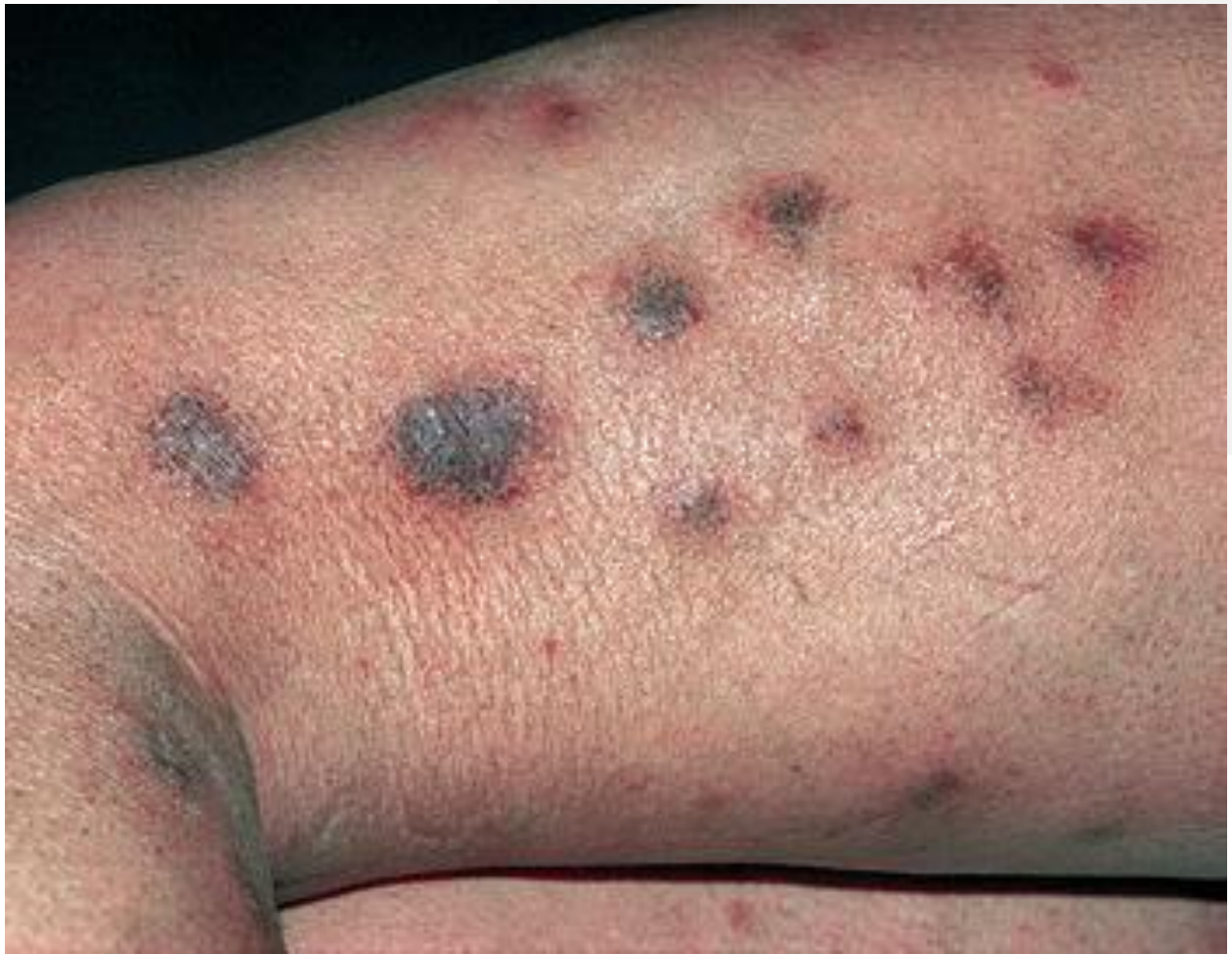
Dermal Melanosis:

- Pigmentary incontinence, may occur when inflammation leads to a disruption of the basal layer of the epidermis, causing the release of melanin into the papillary dermis
- Macrophages in the papillary dermis then phagocytize the released melanin
- Alternatively, macrophages may enter the epidermis, phagocytize epidermal melanosomes, and return to the dermis
- Macrophages that have phagocytized melanin are often called "melanophages



CLINICAL MANIFESTATIONS

- The color of PIH depends on the position of excess pigment within the skin.
- PIH tends to appear as tan to dark brown when excess pigment is within the epidermis.
- In contrast, excess pigment in the dermis tends to manifest with a dark gray or blue-gray appearance



TREATMENT

- A broad-spectrum sunscreen with SPF of at least 30
- Sun-protective clothing
- Elimination of exacerbating factors (acne, drug…)

First-line therapy:

- Topical hydroquinone

Second-line therapy:

- Topical retinoids
- Hydroquinone-retinoid-corticosteroid triple-agent therapy
- Azelaic acid
- Chemical peels
- Laser

Melasma

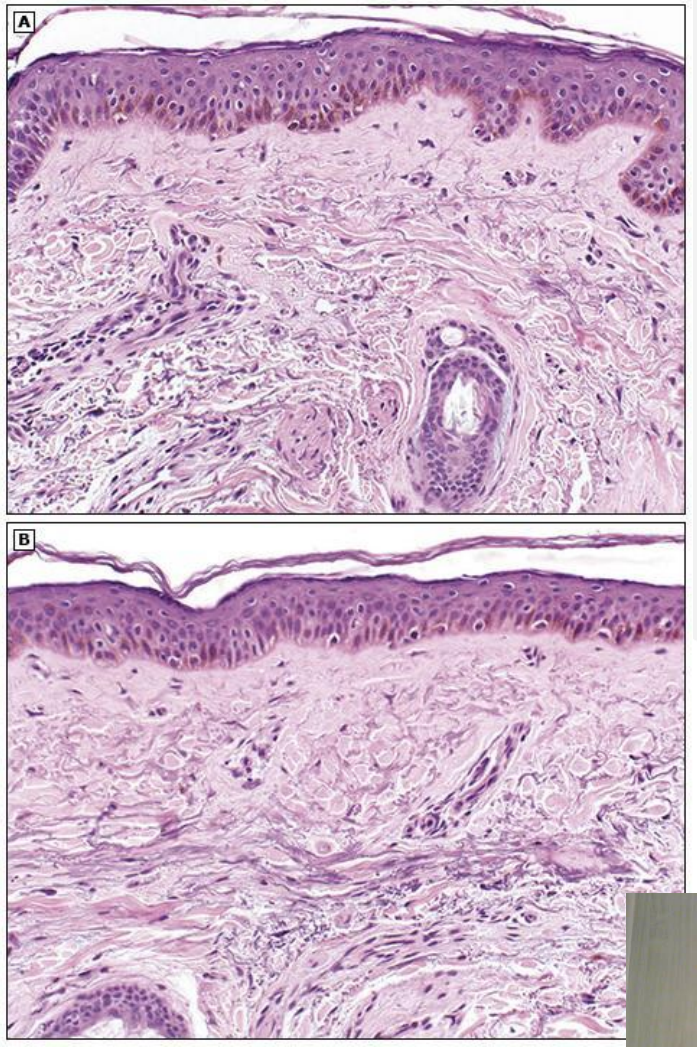
- Melasma is a common, chronic, and recurring disorder of hyperpigmentation arising from hyperfunctional melanocytes that deposit excessive amounts of melanin in the epidermis and dermis
- Melasma is particularly common in women, especially those of reproductive age, and in body areas with high amounts of sun exposure, notably the face

RISK AND TRIGGER FACTORS:

- Genetic predisposition
- Exposure to sunlight (including ultraviolet [UV] and, possibly, visible light)
- Skin phototype
- Hormonal factors (including pregnancy, hormonal therapies, and use of oral contraceptives)
- Cosmetics
- Medicines (eg, photosensitizing drugs and anticonvulsants)
- Zinc deficiency

PATHOLOGY

- Hyperactive melanocytes without hyperplasia
- Similar melanocyte number in lesional and perilesional skin
- Larger melanocytes, more melanosomes and prominent dendrites
- Keratinocytes with increased number of melanosomes
- Disruption to the basement membrane
- Lymphohistiocytic infiltrates
- Dermal elastosis
- Increased vascularization

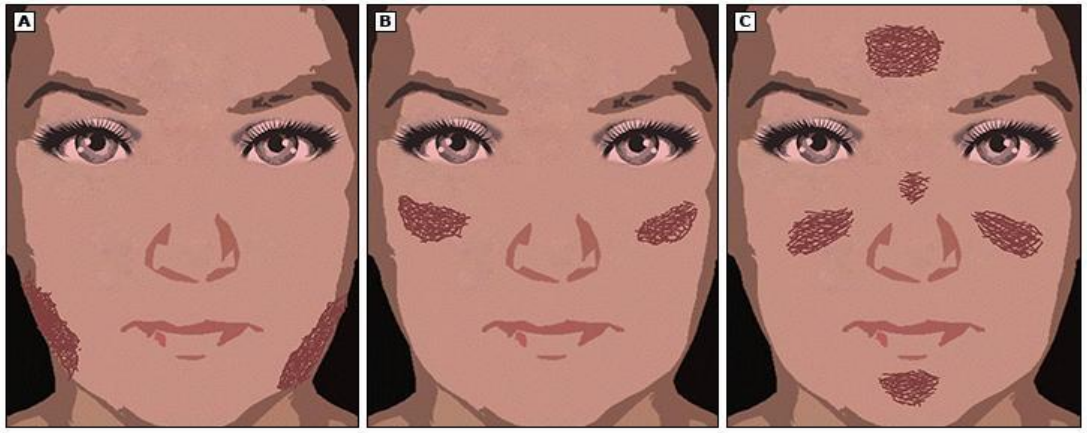


PATHOGENESIS

- **Genetics:** polygenic inheritance
- **Hormones**: oral contraceptive, pregnancy, menopause (for extrafacial involvement) and hormonal replacement therapy
- **Barrier function and oxidative stress:** Chronic UV exposure reduces synthesis of epidermal free fatty acids and triglycerides, which are important in maintaining the skin's barrier function.
- **Neural involvement:** Melasma lesions often follow the path of the trigeminal nerves, which implies a neural component to the pathogenesis

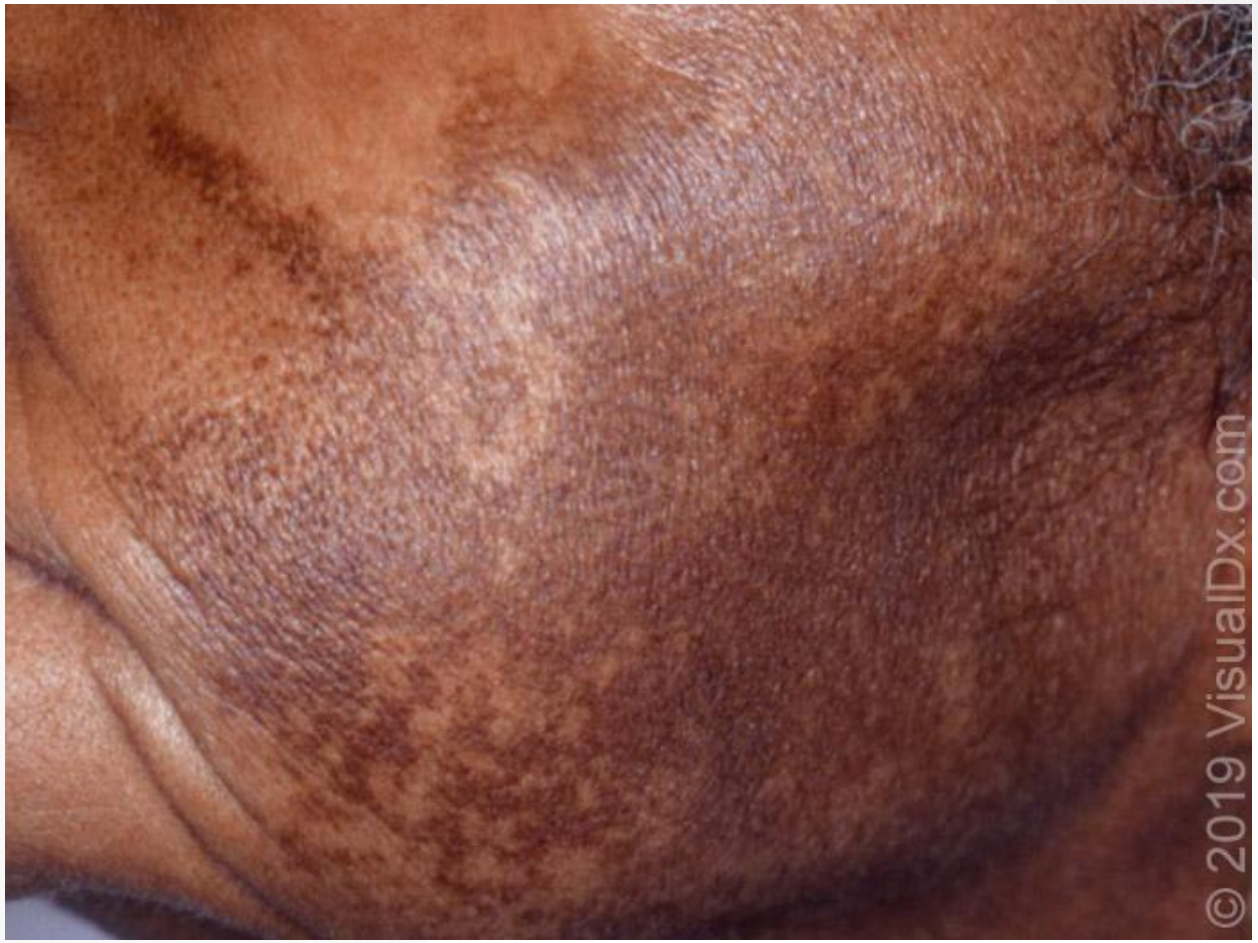
CLINICAL PRESENTATION

- A: Mandibular
- B: Malar
- C: Centrofacial



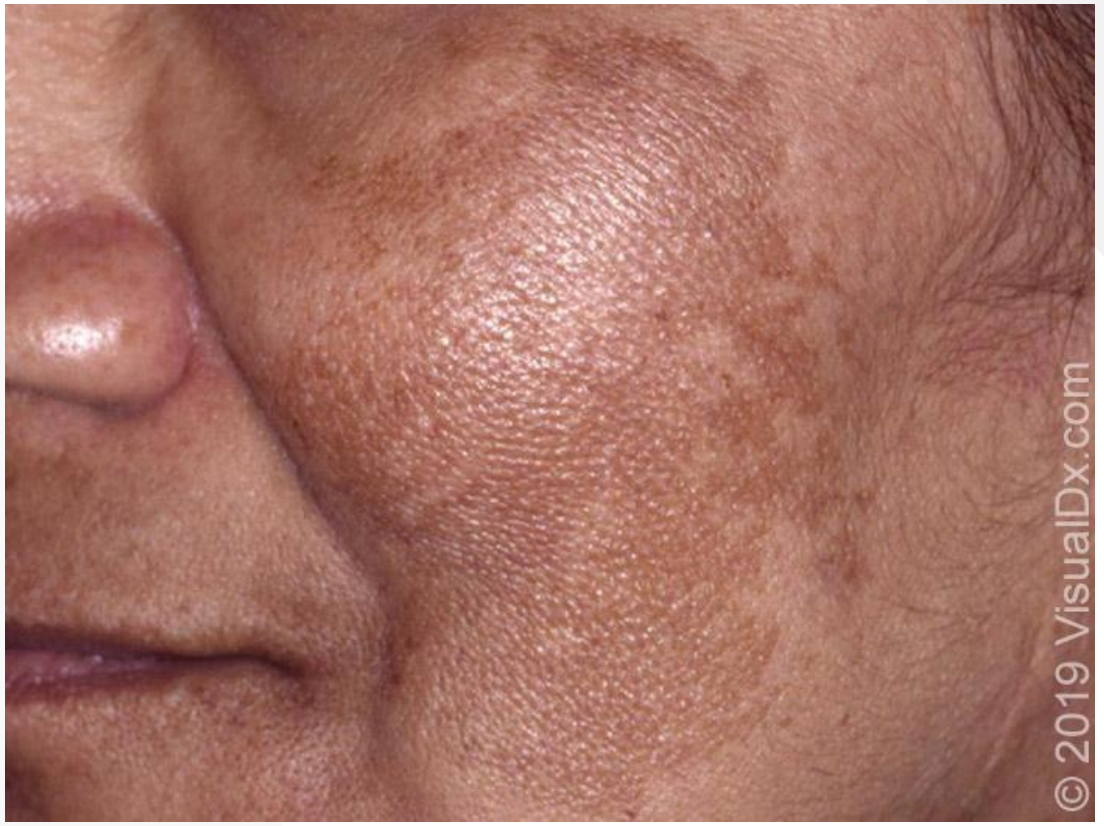
Mandibular

- Lower jawline



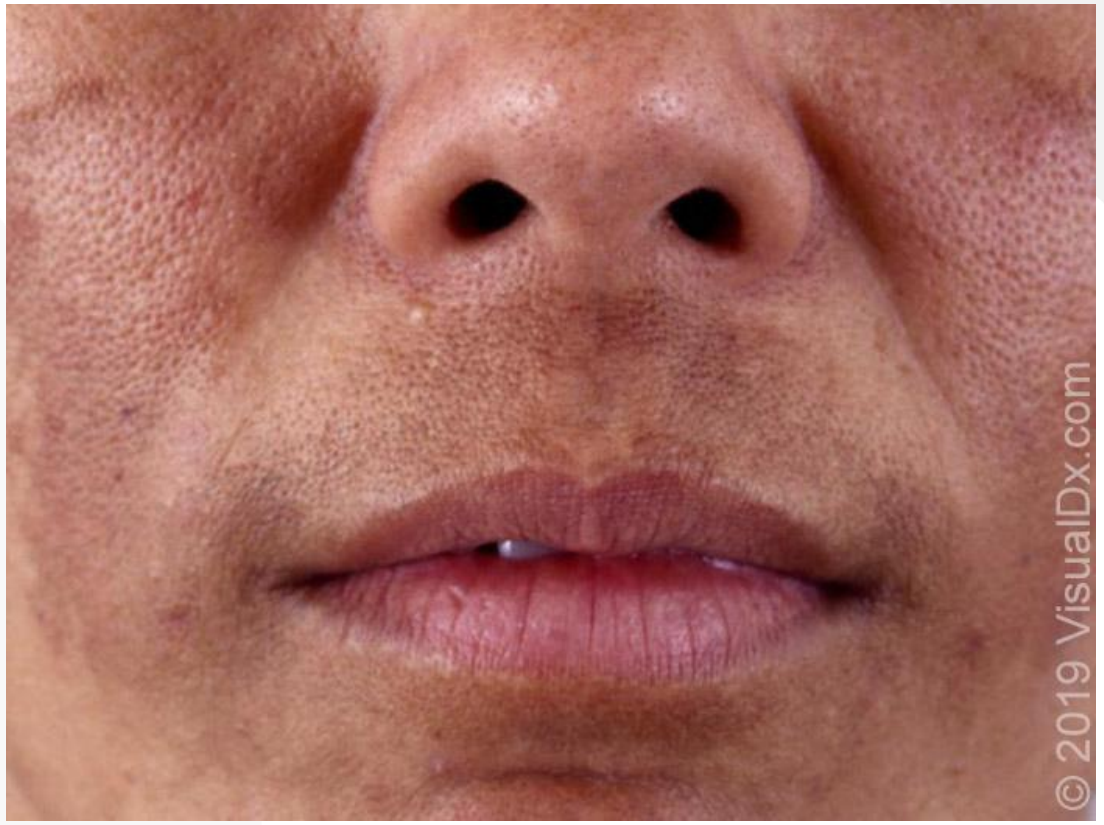
Malar

- lateral cheek



Centrofacial

- Forehead
- Cheeks
- Nose
- Upper lip
- Chin

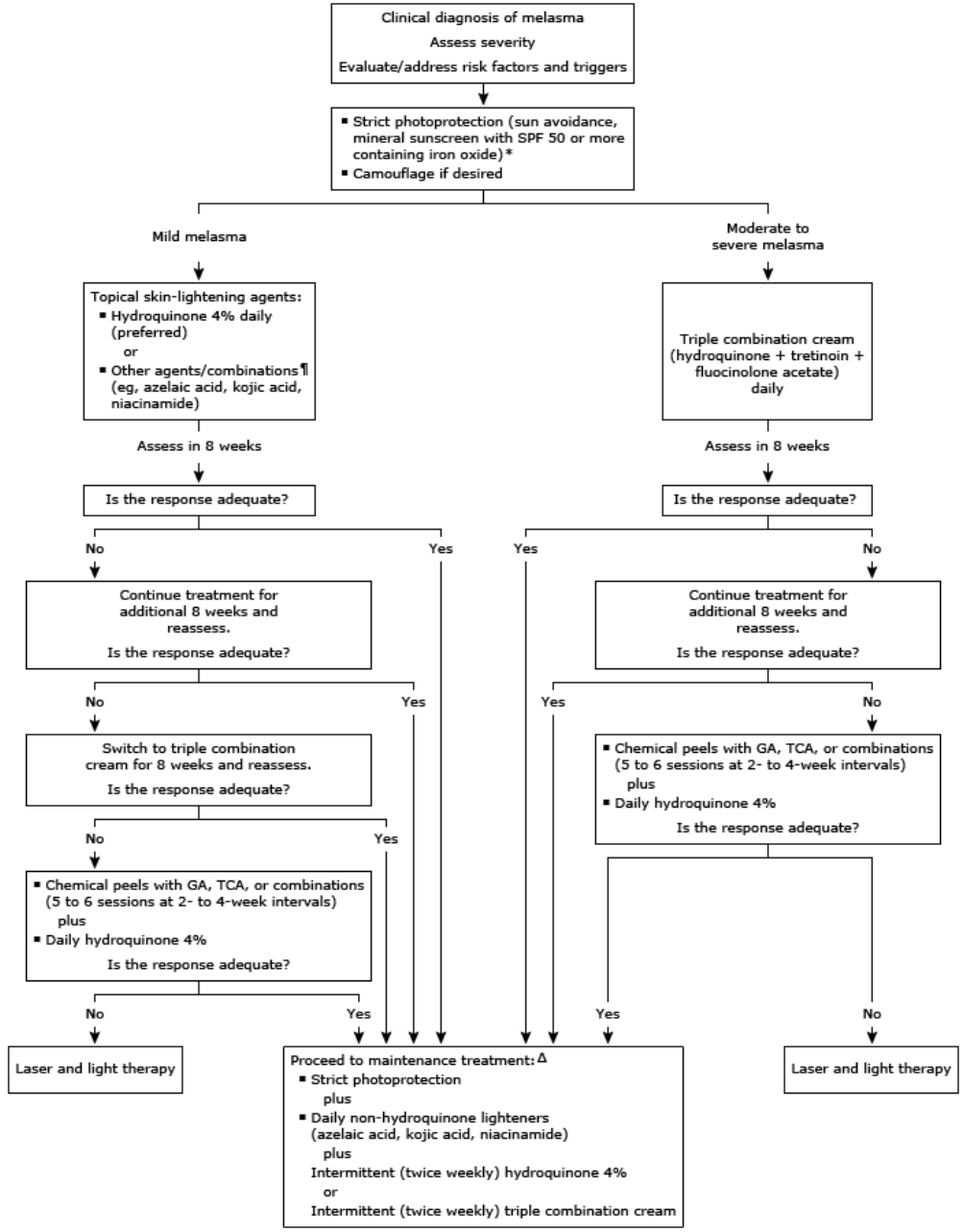


Extrafacial Melasma

- Arms (95 percent)
- Forearms (80 percent)
- Chest (47 percent)
- Back (11 percent)

APPROACH TO TREATMENT

- **Pretreatment evaluation**
- **Patient education**
- **Photoprotection**
- **Cosmetic camouflage**
- **First-line therapies:** Topical skin-lightening agents
- **Second-line therapies**: Chemical peels and oral tranexamic acid
- **Third-line therapies:** Lasers and light therapies


Clinical diagnosis of melasma
Assess severity
Evaluate/address risk factors and triggers
▪ Strict photoprotection (sun avoidance, mineral sunscreen with SPF 50 or more containing iron oxide)*
▪ Camouflage if desired
Mild melasma
Moderate to severe melasma
Topical skin-lightening agents:
▪ Hydroquinone 4% daily (preferred)
or
▪ Other agents/combinations¶ (eg, azelaic acid, kojic acid, niacinamide)
Triple combination cream (hydroquinone + tretinoin + fluocinolone acetate) daily
Assess in 8 weeks
Assess in 8 weeks
Is the response adequate?
Is the response adequate?
No
Yes
Yes
No
Continue treatment for additional 8 weeks and reassess.
Is the response adequate?
Continue treatment for additional 8 weeks and reassess.
Is the response adequate?
No
Yes
Yes
No
Switch to triple combination cream for 8 weeks and reassess.
Is the response adequate?
▪ Chemical peels with GA, TCA, or combinations (5 to 6 sessions at 2- to 4-week intervals)
plus
▪ Daily hydroquinone 4%
Is the response adequate?
No
Yes
▪ Chemical peels with GA, TCA, or combinations (5 to 6 sessions at 2- to 4-week intervals)
plus
▪ Daily hydroquinone 4%
Is the response adequate?
No
Yes
Yes
No
Laser and light therapy
Proceed to maintenance treatment:Δ
▪ Strict photoprotection
plus
▪ Daily non-hydroquinone lighteners (azelaic acid, kojic acid, niacinamide)
plus
Intermittent (twice weekly) hydroquinone 4%
or
Intermittent (twice weekly) triple combination cream
Laser and light therapy

Emerging topical therapies to treat pigmentary disorders: an evidence-based approach 2021

- A comprehensive search on PubMed was conducted to identify patientbased evidence on the most common ingredients used as topical lightening agents: arbutin, ascorbic acid, cysteamine, hydroquinone, kojic acid, niacinamide, retinoids, and triple-combination therapy

Arbutin

- Arbutin is a naturally occurring b-d-glucopyranoside derivative of hydroquinone originating from the bearberry plant
- Its depigmenting actions result from its hydrolysis into hydroquinone and subsequent dose-dependent inhibition of tyrosinase activity

Ascorbic acid (vitamin C)

- Ascorbic acid, also known as vitamin C, is a water-soluble antioxidant commonly found in citrus fruits
- It reduces melanogenesis by blocking copper at the active site of tyrosinase

Niacinamide (vitamin B3)

- Niacinamide is a water-soluble, biologically active form of niacin (vitamin B3) found in many vegetables
- The agent reduces skin pigmentation by reversibly inhibiting the transfer of melanosomes from melanocytes to keratinocytes

Kojic acid

- Kojic acid is a metabolic product of the fungal species Acetobacter, Aspergillus, and Penicillium
- It functions as an antioxidant, a reactive oxygen species scavenger, and inhibits tyrosinase through chelation of copper at the enzyme's active site

Azelaic acid

- Azelaic acid (AA) is a dicarboxylic acid isolated from Pityrosporum ovale, the organism responsible for pityriasis versicolor
- This agent inhibits tyrosinase and selectively targets highly active melanocytes with minimal effect on uninvolved skin

Cysteamine

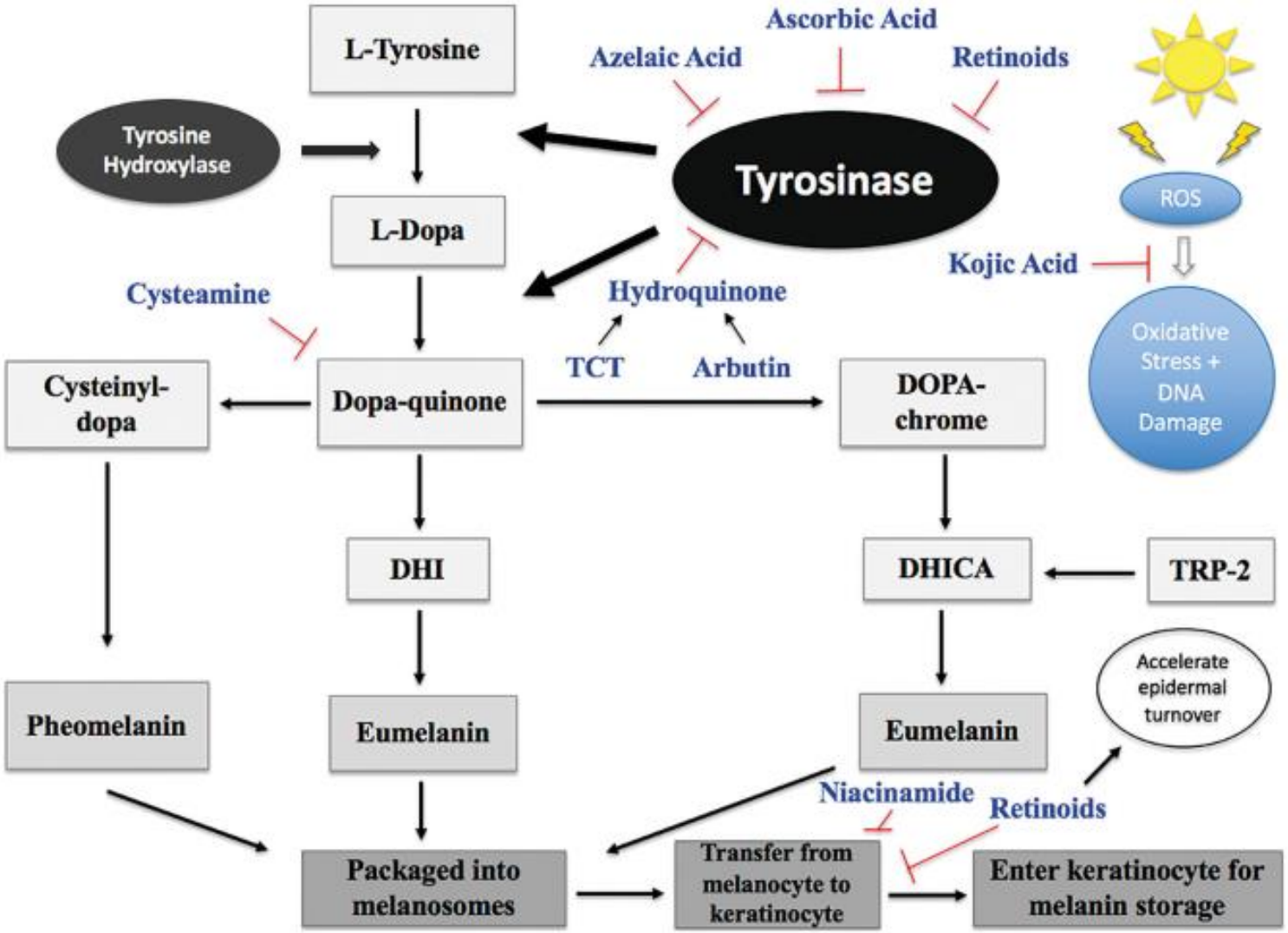
- Cysteamine (ß-mercaptoethylanine hydrochloride) is a biological antioxidant that is naturally present in the human body as a degradation product of the amino acid, L-cysteine
- Two clinical trials demonstrated the efficacy of cysteamine in the treatment of melasma

Retinoids

- Retinoids are vitamin A derivatives that interfere with pigment transfer, accelerate epidermal turnover, and directly inhibit tyrosinase

Triple combination therapy

- Triple combination therapy (TCT) treats hyperpigmentation with a combination of hydroquinone, retinoic acid, and a corticosteroid
- The concept behind the effectiveness of TCT is that tretinoin prevents the oxidation of hydroquinone and enhances epidermal penetration while the topical steroid reduces irritation from the other two ingredients


L-Tyrosine
Ascorbic Acid
Azelaic Acid
Retinoids
Tyrosine Hydroxylase
Tyrosinase
ROS
L-Dopa
Kojic Acid
Cysteamine
Hydroquinone
Oxidative Stress + DNA Damage
TCT
Arbutin
Cysteinyl-dopa
Dopa-quinone
DOPA-chrome
DHI
DHICA
TRP-2
Accelerate epidermal turnover
Pheomelanin
Eumelanin
Eumelanin
Niacinamide
Retinoids
Packaged into melanosomes
Transfer from melanocyte to keratinocyte
Enter keratinocyte for melanin storage

A Case Report on The Use of Topical Cysteamine 5% Cream in the Management of Refractory Post-Inflammatory Hyperpigmentation (PIH) Resistant to Triple Combination Cream (hydroquinone, topical corticosteroids and retinoids)

- A 20-year-old woman with Fitzpatrick skin type (FST) V presented with facial hyperpigmented patches since childhood following an intermittent erythematous, pruritic facial rash. Skin biopsy confirmed PIH secondary to possible burnt-out morphea.
- Treatment with topical adapalene 0.1% gel and triple combination cream (containing hydroquinone,topical corticosteroids and retinoids) proved unsuccessful. Treatment with cysteamine 5% cream over 4 months resulted in significant improvement with a reduction in the melanin index

A comparative study of topical 5% cysteamine versus 4% hydroquinone in the treatment of facial melasma in women

- A quasi-randomized, multicenter, evaluator-blinded clinical trial was conducted on 40 women with facial melasma who were submitted to the nightly application of 5% cysteamine (CYS) or 4% hydroquinone (HQ) on hyperpigmented areas for 120 days.
- Both groups were required to use tinted sunscreen (SPF 50; PPD 19).
- Subjects were assessed at the inclusion and after 60 and 120 days of treatment for mMASI, MELASQoL, and the difference in colorimetric luminosity between melasma and the adjacent unaffected skin.
- The Global Aesthetic Improvement Scale was used to assess the difference in the appearance of the skin through standardized photographs
- Cysteamine proved to be safe, well-tolerated, and effective, despite its inferior performance to hydroquinone in decreasing mMASI and MELASQoL in the treatment of melasma.

An emerging technology in lipid research for targeting hydrophilic drugs to the skin in the treatment of hyperpigmentation disorders: kojic acid-solid lipid nanoparticles

- Kojic acid (KA) as tyrosinase inhibitor shows insufficient skin penetration and several adverse events
  due topical administration.
- KA solid lipid nanoparticles (KA-SLNs) were prepared using high speed homogenisation followed by ultra-probe sonication method for improve its effectiveness.
  KA-SLNs was optimised by Glyceryl mono-stearate (GMS) and Cholesterol (Chol) as lipid excipients and span 60 (SP 60) and Tween 20 (Tw 20) as co-emulsifiers (particle size 156.97 ± 7.15 nm, encapsulation efficiency 59.02 ± 0.74%, drug loading 14.755 ± 1.63%, polydispersity index (PDI) of 0.388 ± 0.004 and zeta potential (ZP) of -27.67 ± 1.89 mV).
- Optimum formulation (KA-SLN3 dispersion) was stable at 4 and 25 C for 3 months. Also, TEM image confirmed these results. The results of XRD, DSC and ATR-FTIR .
- KA-SLN3 dispersion have more tyrosinase inhibition potency in comparison with pure KA.
- Also, the results of the ex vivo and in vitro percutaneous absorption show that KA-SLN3 dispersion improved percutaneous delivery of KA as a promising and potential novel topical preparation and might open new avenues for treatment of hyperpigmentation disorders

Spherical Nucleic Acids for Topical Treatment of Hyperpigmentation

- Oligonucleotide-based materials such as spherical nucleic acid (SNA) have been reported to exhibit improved penetration through the epidermis and the dermis of the skin upon topical application.
- Herein, we report a self-assembled, skin depigmenting SNA structure, which is based upon a bifunctional oligonucleotide amphiphile containing an antisense oligonucleotide and a tyrosinase inhibitor prodrug.
- The two components work synergistically to increase oligonucleotide cellular uptake, enhance drug solubility, and promote skin penetration.
- The particles were shown to reduce melanin content in B16F10 melanoma cells and exhibited a potent antimelanogenic effect in an ultraviolet B-induced hyperpigmentation mouse model

Comparison of the Use of 5% Methimazole Cream with 4% Kojic Acid in Melasma Treatment

- A single-blind study of 45 patients with melasma, right-and left-sided treatment
  was performed by comparing with 5% methimazole cream and night time 4% kojic
  acid in random order.
- Sun protection factor 30 sunscreen was used in the morning and afternoon.
- The evaluation was carried out every 2 weeks by assessing the Melasma Area and Severity Index (MASI), mexameter score, patient satisfaction and adverse
  effects.
- 5% thiamazole (methimazole, 1-methyl-2-mercaptoimidazole), a thionamide-class antithyroid
  drug that works by inhibiting peroxidase in the process ofmelanogenesis

Comparison of the Use of 5% Methimazole Cream with 4% Kojic Acid in Melasma Treatment

- Decreases in MASI score and pigment amount were higher by using 5%
  methimazole cream than 4% kojic acid.
- Patient satisfaction, concerning the use of 5% methimazole cream was higher than with 4% kojic acid.
- Adverse effects were mostly found with the use of 5% methimazole cream

Comparison of the Use of 5% Methimazole Cream with 4% Kojic Acid in Melasma Treatment

- A comparison of the MASI score, pigment amount and patient satisfaction
  scales showed that 5% methimazole cream was superior to 4% kojic acid.
- Five percent methimazole cream can be used as an alternative therapy in the treatment of melasma

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