UNDERSTANDING PIGMENTATION

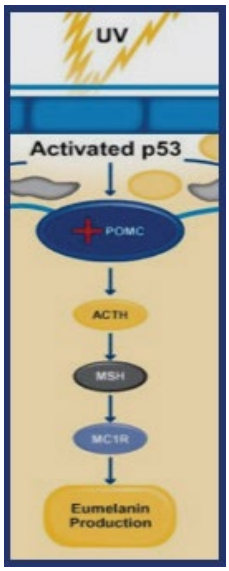
Plexr® PIH & ITS MANAGEMENT

Post-inflammatory hyperpigmentation (PIH) is a frequently encountered problem and can occur as the result of various dermatological disorders as well as therapeutic interventions.

This acquired condition, is characterised by excess pigment formation within the skin, can be attributed to various preceding disease processes that affect the skin. These include infections, allergic reactions, mechanical injuries, reactions to medications, phototoxic eruptions, trauma (eg, burns), and inflammatory diseases (eg, lichen planus, lupus erythematosus, atopic dermatitis).

PIH can also be seen following treatment with a number of electromagnetic devices such as ultrasound, radiofrequency, lasers, light-emitting diodes, and visible light, as well as treatments such as microdermabrasion.

Typically, post-inflammatory hyperpigmentation is most severe in patients whose basal cell layer of the epidermis is disrupted.



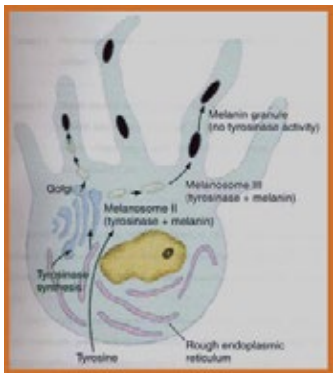
The Process of Pigmentation - Biochemical synthesis of Melanin

Over exposure to UV radiation results in biological damage to the skin.

At the skin level, the processes that take place as a result of this cellular damage include:

1. Increased corneal thickness
2. Increased melanin production

Melanin production is a natural protective reaction to UV radiation which causes photodamage and eventual photoaging. Melanogenesis results from a biochemical synthesis of melanin from amino acids L-phenylalanine and L-tyrosine



At a cellular level:

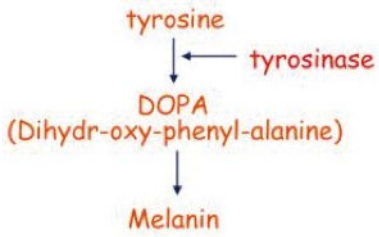
Cellular damage causes the release of pro-opio melanocortin (POMC) from the epidermal cells through the activation of ATR (ataxia telangiectasia and Rad3-related) proteins that are involved in cell cycle regulation.

POMC is then divided into fractions which consist of ATCH, MSH (Melanocyte Stimulating Hormone) and Beta-Endorphin. The latter is responsible for the feel good feeling after sun exposure.

Melanocyte Stimulating Hormone acts on 2 levels:

Centrally:	MSH acts on the hypothalamus - and exerts an appetite suppressant effect.
Peripherally:	MSH stimulates the MC1R (receptor) at the epidermal level and induces the formation of MITF (Melanogenesis Transcriptor Factor) that enables the reading of the genes encoding for the synthesis of enzymes needed to convert Tyrosine into Melanin.

Tyrosinase, a glycoprotein, and one of the most important enzymes involved melanogenesis, is found and synthesized inside melanosomes, which are found inside melanocytes. This enzyme facilitates the conversion of L-Tyrosine to L-DOPA (dihydroxyphenylalanine) via an oxidation process.



Pathophysiology

PIH results from the overproduction of melanin or an irregular dispersion of pigment, secondary to an inflammatory process affecting the skin. It is caused by 1 of 2 mechanisms that result in either epidermal or dermal melanosis.

The epidermal inflammatory response (ie. dermatitis) results in the release and subsequent oxidation of arachidonic acid, a powerful inflammatory mediator, that is converted into prostaglandins, leukotrienes, and other products. These inflammatory products are known to alter the activity of both immune cells and melanocytes.

When PIH is confined to the epidermis, there is a resultant increase in the production and transfer of melanin to surrounding keratinocytes. PIH within the dermis results from inflammation-induced damage to basal keratinocytes or the basal lamina, which release large amounts of melanin into the dermis. The free pigment is then phagocytosed by macrophages, now called melanophages, in the upper dermis and produces a blue-gray appearance to the skin at the site of injury.

With Plexr as evidenced in histology – the basal lamina is not disrupted and therefore the possibility of dermal melanosis would be minimal.

Frequency

Post-inflammatory hyperpigmentation is a universal response of the skin, but it is more common in individuals with darker skin (Fitzpatrick skin types III to VI).

Prognosis

Morbidity associated with post-inflammatory hyperpigmentation is related to the underlying inflammatory process that causes post-inflammatory hyperpigmentation. If the hyperpigmentation is located in cosmetically sensitive regions, a significant amount of emotional distress may result.

Post-inflammatory hyperpigmentation tends to fade with time and therapy, as previously discussed and typically remains for periods of 6-12 months, after the initial inflammatory process resolves. Dermal post-inflammatory hyperpigmentation may even persist for years.

Physical

PIH typically manifests as macules or patches in the same distribution as the initial inflammatory process. The location of the excess pigment within the layers of the skin will determine its coloration. Epidermal hypermelanosis will appear tan, brown, or dark brown and may take months to years to resolve without treatment.

Dermal melanosis has a blue-gray appearance and may either be permanent or resolve over a protracted period of time if left untreated. PIH can worsen with ultraviolet (UV) irradiation or with persistent or recurrent inflammation.

Causes

Post-inflammatory hyperpigmentation can occur with various disease processes that affect the skin. These include:

- Allergic reactions
- infections
- Trauma
- phototoxic eruptions
- Fractional laser photothermolysis occasionally induces post-inflammatory hyperpigmentation.
- Common inflammatory diseases that result in post-inflammatory hyperpigmentation include acne, lichen planus, systemic lupus erythematosus and chronic dermatitis.

Furthermore, lesions of post-inflammatory hyperpigmentation can darken with exposure to UV light and various chemicals and medications such as:

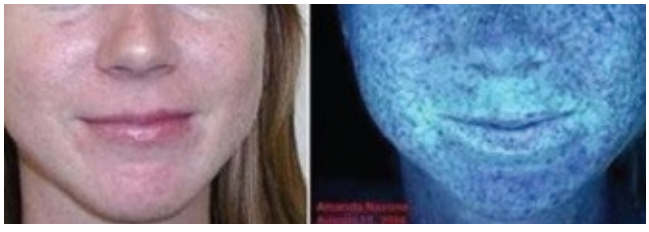
- Tetracycline
- Chemotherapy: bleomycin, busulfan, doxorubicin,
- 5-fluorouracil
- Silver and gold
- Antimalarial drugs
- Estrogen containing oral contraceptive hormones
- TB treatments: clofazimine

Investigation

A Wood lamp examination enables distinction of epidermal post-inflammatory hyperpigmentation (PIH) from dermal post-inflammatory hyperpigmentation.

Epidermal lesions tend to have accentuated borders under a Wood lamp examination.

Dermal lesions appear poorly circumscribed and are not accentuated with a Wood lamp examination.

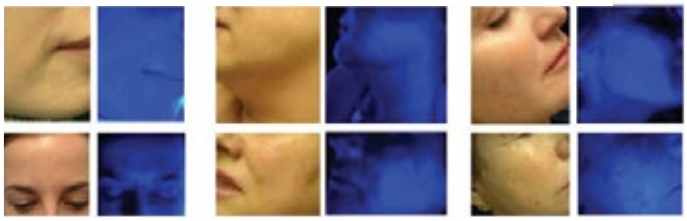


Medical Care

1. Differentiate re: Epidermal vs Dermal PIH – this will give an indication of the prognosis.
2. The treatment of post-inflammatory hyperpigmentation (PIH) tends to be a difficult and prolonged process that often takes 6 - 12 months to achieve the desired results of depigmentation.
3. Each of these treatment options potentially improves epidermal hypermelanosis, but none is proven effective for dermal hypermelanosis. With Plexr Epidermal PIH might be possible.
4. Regardless of treatment option a daily use of a broad-spectrum sunscreen is required. Ideally SPF 50.
5. Early intervention may hasten its resolution, however, remain mindful that treatments may aggravate PIH by causing further irritation and inflammation.

Topical treatments include:

- Epidermal melasma: it stands out with the light (dark fluorescence)
- Dermal melasma: Faint / poor fluorescence
- Mixed melasma: Certain areas are highlighted but not others
- Unapparent melasma: Disappears with the light (V or VI)



Medication Summary

Skin whitening products are used for clinical treatment of post-inflammatory hyperpigmentation.

Topical treatments include:

- Hydroquinone
- Corticosteroids
- Retinol : tretinoin cream
- Ascorbic Acid
- Azelaic acid
- Glycolic Acid
- Trichloroacetic acid

They act at various levels of melanin production in the skin, some being competitive inhibitors of tyrosinase, while others inhibit the maturation of this enzyme or the transport of melanosomes from melanocytes to surrounding keratinocytes. Soy products containing serine protease inhibitors appear to have potential as a therapeutic option for the treatment of hyperpigmentation.

The efficacy and safety retinoids and azelaic acid in individuals with a dark complexion has been demonstrated.

Broad-spectrum sunscreens are an integral part of any treatment regimen.

Prevention

Patients with post-inflammatory hyperpigmentation (PIH) should use sunscreen on a daily basis to prevent any further darkening of lesions.

Plexr®