Skin pigmentation

Rhonda Meys

Abstract

Pigmentation in humans varies widely and depends on ethnic, genetic and physiological factors. Many skin conditions causing dyspigmentation affect the physical appearance, and hence have a huge psychological and social impact on patients. Pigmentary conditions can be divided into disorders manifesting as hyperpigmentation, in which excess pigment is apparent, and hypopigmentation, where pigment is reduced; these can be localized or generalized. Characteristic pigmented lesions or pigmentation patterns may be associated with genetic disorders such as multiple lentigines (xeroderma pigmentosa, Peutz–Jeghers syndrome), café-au-lait macules (tuberous sclerosis, neurofibromatosis) or pigmentation in a Blaschkoid pattern (pigment demarcation lines, incontinentia pigmenti). The most commonly encountered pigmentation problems in clinical practice are melasma and the secondary phenomenon of post-inflammatory hyperpigmentation – which can result from virtually any inflammatory skin condition including connective tissue disease, eczema, acne and drug reactions. Generalized pigmentary disorders can indicate underlying genetic conditions (albinism), autoimmune conditions (vitiligo) or general medical conditions such as haemochromatosis and endocrine disorders (Addison's disease, Cushing's disease, hypo- and hyperthyroidism). Treatment is possible in some cases and should involve a discussion of camouflage options, including addressing psychological aspects of the condition and the management of the patient's expectations.

Keywords Drugs; endocrine; Fitzpatrick; generalized; genetic; hyperpigmentation; hypopigmentation; localized; medications; treatment

Key points

- Pigmentation varies widely depending on ethnicity
- Dyspigmentation can manifest as hyper- or hypopigmentation, and many skin conditions can present with both
- A basic understanding of pigmentary disorders is imperative to exclude recognizable genetic and general medical conditions
- Many common dermatological conditions are easy to recognize by the pattern of pigmentary change; these include melasma, pityriasis alba, pityriasis versicolor and vitiligo
- Post-inflammatory hypo- and hyperpigmentation are exceedingly common and can occur secondary to virtually any primary dermatological condition

Introduction

The natural colour of human skin is a balance between three different chromophores: carotenoids (orange/yellow pigments in keratinocytes, ingested in root vegetables), haemoglobin (in blood vessels) and the most important, melanin. The wide variation in constitutive skin pigmentation of different ethnic groups is linked to the production and modification of melanin by melanocytes.

Melanocytes are highly branched dendritic cells located in the basal epidermis that are in contact with around 35 keratinocytes in the upper layers of the epidermis – the 'melanocytic unit'. The melanocytes 'inject' pigment as melanosome packages into the keratinocytes. This melanin pigment exists in two forms: dark brown to black eumelanin (which is photoprotective) and reddish-brown phaeomelanin (poorly protective against ultraviolet (UV) radiation). The light-coloured phaeomelanin together with the pigment derivatives trichochromes accounts for the distinctive colouring of individuals with red hair.[1]

Fitzpatrick first developed the concept of 'skin types' I–VI in 1998 to characterize the inter-racial variations in UV-related burning and tanning responses[2] (See also Table 1 of How to examine a patient with skin cancer). A detailed history of genetic heritage in addition to determining Fitzpatrick type can help to better predict the tanning response and the likelihood of iatrogenic pigmentation in darker skin types (III and above). A Wood's lamp that emits UV light is a useful diagnostic tool to help identify vitiligo (where complete depigmentation is strongly accentuated in UV light) and also help in differentiating epidermal pigment (accentuated) from dermal pigment (unchanged).

Generalized pigmentary disorders

Generalized hyperpigmentation

Generalized hyperpigmentation can arise from a number of systemic conditions such as morphea, systemic sclerosis, paraneoplastic pigmentation and acanthosis nigricans (Table 1). Endocrine abnormalities, such as Addison's disease, can also cause pigmentary change (Table 2). Pigments other than melanin can also produce generalized skin darkening, for example in haemochromatosis, renal failure and argyria (cutaneous silver deposition); Table 1. However, the most common cause of generalized hyperpigmentation (in sun-exposed sites) is a suntan.

Generalized hypopigmentation

Generalized hypopigmentation is usually the result of genetic factors and can be racial or reflect a congenital defect of skin melanization. Oculocutaneous albinism is the most important genetic cause of hypopigmentation of the skin, hair and eyes. There are several other rarer that are beyond the scope of this article. Other systemic causes of an acquired generalized reduction of skin colour include anaemic pallor, hypothyroidism and primary or secondary pituitary failure with decreased concentrations of melanocyte-stimulating hormone (Table 2).

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Systemic diseases causing generalized hyperpigmentation[1]

Disease	Clinical features of hyperpigmentation	Mechanism
Paraneoplastic	Diffuse hyperpigmentation	Uncertain mechanism, possibly an MSH-like compound
Acanthosis nigricans: • Malignant (rare), usually with adenocarcinoma	• Severe skin hyperkeratosis, thickened warty plaques, axillary skin tags, and in groin and neck ± oral and palmar-plantar involvement	• Tumour production of pituitary peptide, IGF or other epidermal growth factors
• Benign/pseudo-acanthosis nigricans	• Less marked, develops in adolescence, associated with diabetes mellitus, insulin resistance, acromegaly, Cushing's syndrome, polycystic ovary syndrome, obesity, drugs	• Increased insulin, IGF and other epidermal growth factors stimulate epidermal growth
Connective tissue disease	Systemic sclerosis, scleroderma, morphea, dermatomyositis, systemic lupus erythematosus	Pigmentation can be diffuse and Addisonian; can also present as post-inflammatory hyperpigmentary changes in lesional skin
Renal failure	Diffuse brown skin discolouration — worst on hands and face; macules on palms and soles	Accumulation of MSH, carotenoids, lipochromes or middle-molecular-weight substances
Vitamin deficiencies and malabsorption	B_{12} — mottled hyperpigmentation of hands, feet, face Folate deficiency — diffuse Vitamin A — desquamation, generalized Vitamin B_6/niacin — pellagra: darkly pigmented, dry, cracked and scaly skin on sun-exposed sites	Various mechanisms
POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, Skin changes)	Skin manifestations include hyperpigmentation, haemangiomas, skin thickening, acrocyanosis, hypertrichosis, acquired facial lipoatrophy, livedo and white nails	Non-specific pigmentation, mechanism unknown
Haemochromatosis	Generalized bronzed or slate grey pigmentation, initially on sun-exposed sites. Associated with diabetes mellitus, endocrinopathy, cirrhosis	Increased melanin production and cutaneous iron deposition
Primary biliary cirrhosis	Sun-exposed sites	Hypermelanosis
Amyloidosis	Hyperpigmentation can be associated with macular or lichen types	Melanophages containing melanin in papillary dermis — derived from degenerate keratinocytes and melanocytes
Other: rheumatoid arthritis, Still's disease, cutaneous T cell lymphoma	Non-specific	Can be disease-related or secondary to drugs

IGF, insulin-like growth factor; MSH, melanocyte-stimulating hormone.

Table 1

Localized pigmentary disorders

Localized hyperpigmentation

Localized patches of hyperpigmentation can occur for many reasons and can be congenital or acquired. The colour of cutaneous melanin is variable, depending on its depth in the skin and the extent of scatter and reflection of visible light. Scattered light is bluish because of the Tyndall effect, so deeper pigment appears blue.[1] Therefore, superficial junctional naevi are black or dark brown, compound naevi with components at variable depths are shades of brown, and deeper naevi are blue (blue naevi); dermal naevi, in which melanocytes are too deep to reflect any light, appear skin-coloured. Mongolian spots (usually manifesting as well-defined bluish patches over the lower back) are a common dermatological finding in individuals with darker skin types and comprise extensive sheets of dermal melanocytes. The related naevi of Ito (on the shoulder or arm), Ota (on the face, periocularly and sometimes involving the conjunctivae and eyes) and Hori (facial, bilateral) present with a similar appearance but are less common.

Café-au-lait macules (CALMs) are congenital, well-demarcated, bland uniform brown patches measuring greater than 0.5 cm. They usually represent an isolated increase in

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