Clinics in Dermatology (2019) **37**, 580–590

Clinics in Dermatology

The color of skin: yellow diseases of the skin, nails, and mucosa

Ian T. Logan, MRCP[a,*], Richard A. Logan, FRCP[b]

[a]*Department of Dermatology, Addenbrooke's Hospital, Cambridge, England, United Kingdom*
[b]*Department of Dermatology, Princess of Wales Hospital, Bridgend, Wales, United Kingdom*

Abstract The colors reflected from the skin are important indicators of dermatologic and systemic disorders. Incident light is subject to absorption by chromophores in the skin and scattering. Chromophores associated with yellow light reflection include the carotenoids and bilirubin. Various pathophysiologic mechanisms associated with these and other chromophores manifest with a yellow hue on examination. This review describes these mechanisms and the clinical features of yellow skin disorders by morphology. A brief summary of the differential diagnosis, laboratory investigations, and treatments are presented. Yellow skin disorders are a heterogenous group composed of abnormalities in keratin, elastic and connective tissue, lipid metabolism, and other states of metabolic, inflammatory, or organ dysfunction. Patients will present through different routes, and skin disease may precede or follow systemic disease. Dermatologists have an essential role in identifying those with malignant or systemic associations to ensure early diagnosis and treatment.

Overview

The interpretation of color has been an essential part of human advancement and is evolutionarily integrated with various physiologic and behavioral responses.[1] The three qualities of visible light include chroma (purity), value (lightness or darkness), and hue (color).[2] Hue is the most obvious visible characteristic of use in clinical assessments. A yellow hue may develop through a range of pathophysiologic mechanisms which will be explored in this review to help clinicians answer the question of why the skin may turn yellow. Yellow is the color the human eye sees when it receives light with a dominant wavelength between 570 to 590 nm. It is a primary color between orange and green on the visible light spectrum with a complementary color of purple.[3] To create a list of yellow skin conditions and to categorize their clinicopathologic features, we reviewed the classic clinical dermatology textbooks, dermatoscopic atlases, and the literature. On the basis of correlation with their published descriptions, we have included diseases accepting that there will be a spectrum of clinical appearances for each disorder. Brief descriptions of relevant systemic diseases have been made with a focus on skin complaints that present directly to dermatologists. This review is relevant primarily in the assessment of patients with Fitzpatrick skin types I-III due to the dominant light absorption effect of melanin pigment in Fitzpatrick skin types IV-VI.[4]

* Corresponding author.
E-mail address: i.logan@nhs.net (I.T. Logan).

https://doi.org/10.1016/j.clindermatol.2019.07.019

Synonyms

Historically, skin diseases have been named according to their clinical appearance with terms usually originating in Greek or Latin, or eponymously after their first describer in the literature. Familiar terms used to describe a yellow appearance of the skin include jaundice, uremic pallor, carotenoderma, hypercarotenemia, and diseases including a prefix derived from the Greek word *xanthos* meaning yellow.[5] The xanthodermatoses are a heterogenous group of disorders with yellow as a typical or predominant feature. *Jaundice* is derived from the old French word *jaune* and *jaunice* meaning yellow or yellowness. These patients may also be described as *icteric*, a word derived from the ancient Greek word *ikteros* which denoted jaundice.[5,6] Carotenoderma refers to a yellow or orange discoloration of the skin, as a consequence of hypercarotenemia.[7]

Definition

Yellow light is reflected by a variety of natural sources and is dependent on the chemical and structural composition of the reflecting surface.[8] Yellowness of skin in Caucasian subjects has been shown to be perceived as associated with health and attractiveness.[9] The color of human healthy and diseased skin is determined primarily by pigments and is a dynamic process responding within hours to illness.[4,10] In science, the word pigment is used to refer to any coloring of animal or plant matter and is derived from the Latin word *pingere* meaning to paint.[5] To establish a consistent lexicon for describing color in the skin, it has been proposed that all chemicals and structural items that impart color to the skin be called *chromophores*, and that chromophores are divided into melanotic and nonmelanotic groups.[4] Chromophore is the word used to describe the moiety within the pigment molecule responsible for its color.[4,8]

There are both endogenous and exogenous yellow chromophores that color the skin. Endogenous yellow chromophores include the hemoglobin breakdown products bilirubin, biliverdin, and urobilin.[11] Urobilin, also known as urochrome, is the molecule responsible for the yellow color of urine. Exogenous chromophores include those directly applied or inserted into the skin, such as cadmium sulfide in tattoos and those obtained through dietary ingestion including the carotenoids.[7,12] In normal human physiology, adipose tissue, plasma, and skin have a yellow hue (excluding the skin of Fitzpatrick skin types IV-VI). Plasma is yellow due to the presence of bilirubin, carotenoids, hemoglobin, and iron transferrin.[13]

Yellow in human skin, fat, and in dermatologic disorders associated with lipids is predominantly generated by carotenoid chromophores. The word *carotene* originates from the Latin word *carota* from which we derive carrot.[14] Carotenoids are photosynthetic pigments that are exclusively synthesized by plants.[15] Carotenoids are metabolized from the precursor geranylgeranyl pyrophosphate, from which vitamins E and K, and chlorophyll are also synthesized.[16] They function as accessory pigments to absorb energy from light that is not absorbed by chlorophyll with an additional function as photoprotection against photooxidative stress.[16] Carotenes include phytoene, lycopene, α-carotene and β-carotene (metabolized in sequence), and together with xanthophylls make up the carotenoids.[16] The carotenes absorb light in the blue wavelengths (400-500 nm), leading to reflection of orange and yellow light.[17] β-Carotene (provitamin A) is the most abundant carotenoid in human diets, and is also used as a nutritional supplement (6-15 mg/d) or as an oral photoprotectant in photosensitivity disorders (60-180 mg/d).[15,18]

Carotenoids are fat soluble due to their lipophilic hydrocarbon molecular structure and are predominantly transported after absorption with low-density lipoproteins.[19] Herbivores and omnivores ingest carotenoid pigments during consumption of carotenoid containing plants and foods. Grass-fed cattle have a yellower adipose than grain-fed counterparts, associated with tissue concentrations of β-carotene 5 to 7 times higher, and a healthier profile for human consumption.[20,21] In contrast to the distinctive yellow of human adipose, the color of adipose in certain herbivora, such as sheep, goats, and rabbits, appears colorless or white due to metabolic differences, resulting in only small traces of carotenoids present in the systemic plasma.[22] Vitamin A functions to maintain vision, epithelial integrity, cell differentiation, and with carotenoids has an important role in innate and acquired immunity.[18,23]

Etiology and pathogenesis

The etiology of yellow skin disorders is diverse reflecting the heterogeneity of skin disorders grouped by color. Inherited disorders which present with yellow features include the palmoplantar keratodermas, familial hyperlipidemia-related xanthomatoses, some elastic disorders, such as pseudoxanthoma elasticum (PXE), and some disorders with a genetic predisposition to tumors.[24–26] Acquired disorders with exogenous causes include those associated with behavioral factors, such as cumulative sun exposure, iatrogenic intervention with medications, nutritional intake, or direct contact of substances with the skin, such as topical ascorbic acid application, tobacco smoking, or sunless tanning products.[11,15,25,27,28] Acquired disorders with endogenous causes include those associated with biliary or hepatic disease, renal failure, endocrine disorders, inflammatory and autoimmune disease, depositional disorders, and malignancy among others.[25] For some yellow skin disorders, such as those within the histiocytoses, the etiology has yet to be fully confirmed.[29]

The pathophysiologic mechanisms by which the skin may appear yellow during clinical examination are illustrated in Figure 1 and described here by four different pathways: (1) skin surface changes, (2) lipid accumulation, (3) structural changes, and (4) circulatory hyperpigmentation. Some

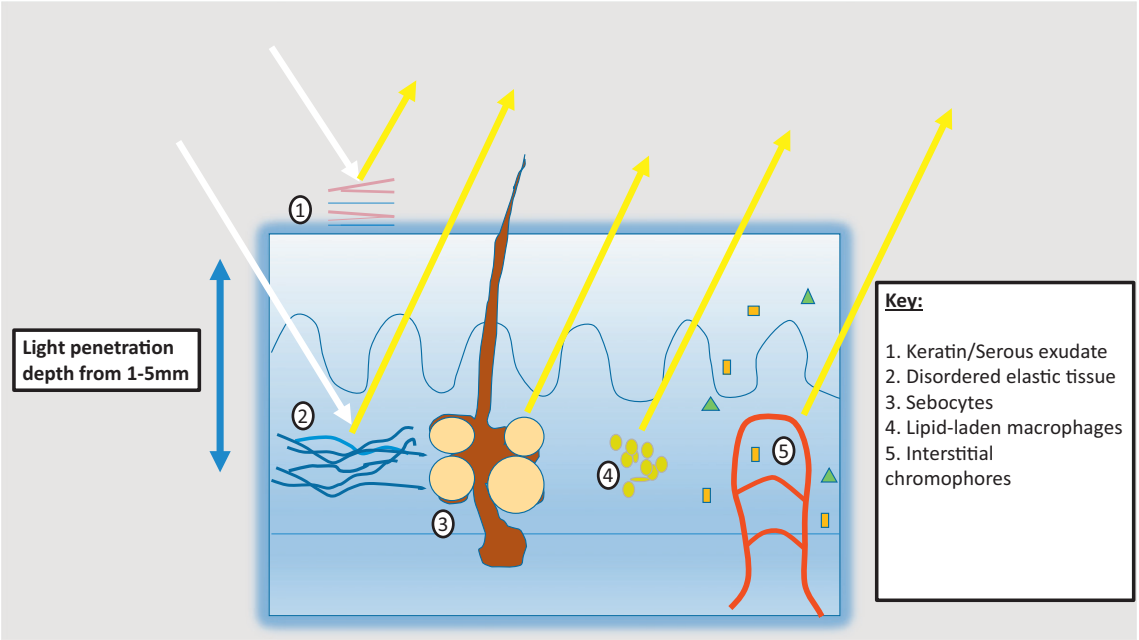

Fig. 1 Pathophysiologic mechanisms creating a yellow light reflection from the skin.

disorders appear yellow through a combination of two or more of these pathways. The color of light reflected by the skin is subject to a number of variables including chromophore concentration and depth, tissue water content, and tissue structure which affects the absorption spectra and scattering of visible light in the skin.[8] The depth of visible light penetration is to between 1 and 5 mm depending on the wavelength.[30]

Disorders, inducing hyperkeratosis on the skin surface, may be observed locally or regionally to impart a yellow hue to the affected area.[31] This is seen, for example, in the keratotic crust of actinic keratoses or in calluses, corns, or the ichthyoses.[32] Keratin mutations or mutations in other molecules that affect the keratin cytoskeleton, such as desmoplakin and desmoglein-1, also cause hyperkeratosis (Figure 2).[31] The phenotypic distribution is determined by the mutation, as a reflection of the variety in keratin expression in different tissues. Serous exudate having accumulated and dried onto the skin surface appears yellow due to plasma chromophores. Seropurulent exudate and slough appear opaque to a yellow or brown color due to devitalized tissue, microorganisms and the inflammatory cytokine response. The inflammatory phase of wound healing is associated with black and yellow colors, shifting to red during the proliferative phase due to oxyhemoglobin.[33]

The appearance of yellow within macules, papules, and nodules is due to the accumulation of yellow chromophore-rich substances within the visible skin layers. This is most commonly in the form of lipids and due to the chromophore β-carotene. Lipids are found in high concentration in adipocytes for storage and sebocytes for sebum production.[34] Disorders in the control of the populations of these cell types may cause yellow papules and nodules to form.[26,35,36]

Xanthomatous infiltrates are usually associated with disorders of lipoprotein metabolism, with high plasma concentrations of lipids (primarily free and esterified cholesterol) and permeation of lipoproteins through the dermal capillary walls.[37] Macrophages phagocytose the lipid component of lipoproteins becoming "foam cells" and are the histopathologic explanation for the yellow color of cutaneous xanthomata. The color seen is dependent on the amount of lipid present and its depth below the surface.[37,38] The migration of monocyte-derived macrophages to skin sites of xanthoma has been associated with the adhesion molecule expression characteristics of vascular endothelial cells.[37,39] A ratio of 10:1 macrophages to endothelial cells has been found in xanthomas, compared with 5:1 in normal skin.[39] Xanthomatization refers to the lipid accumulation which is a feature of histiocytic, dendrocytic, and Langerhans cell proliferations which may be a secondary phenomenon.[37,40] In the case of myeloma and monoclonal gammopathy, the paraprotein complexes with low-density lipoprotein and these complexes are subsequently phagocytosed. Apart from xanthelasmata, it is unusual for xanthomata to form in normolipemic states. When they do, it may be due to lipoprotein alterations or lymphoproliferative disease.[40,41]

The perceived color of light reflected from the skin is partly determined by skin structure including epidermal thickness and dermal collagen quality and thickness.[4,8,42] The skin thickness varies by anatomic region of the body being thinnest over the face and genital skin and thickest over the back and acral surfaces. Skin thickness starts to reduce from 45 years of age.[43,44] In normal circumstances, subcutaneous adipose does not contribute to the color of the skin. If there is skin thinning or fat herniation, then the proximity of subcutaneous fat to the skin surface may contribute to a yellow appearance of

the skin in affected areas.[45] This may be evident in patients' faces due to aging and photodamage-related skin changes referred to as "citrine skin," and evident in the sun-exposed sites in the dermatohelioses.[35,46] PXE is a multisystem disorder of ectopic mineralization of elastic fibers due to a gene-related reduction of the anticalcifying circulating factor, inorganic pyrophosphate.[47,48]

Yellow chromophores that circulate in the blood include bilirubin and carotenoids.[13,49] An increase in the concentration of these chromophores will cause a dynamic change in the yellow hue of the skin.[10] The degree of color change also depends on the rate of diffusion into tissue, and the absorption and binding of the chromophore to tissue. Hyperbilirubinemia imparts a yellow hue to the skin and sclera due to bilirubin deposition in the tissues with an affinity for elastic tissue, becoming noticeable at serum concentrations >2.5 mg/dL.[11,27] Jaundice develops through prehepatic, intrahepatic, and posthepatic mechanisms.[11] Hypercarotenemia may be genetic (familial carotenemia) with normal dietary intake but failure in metabolism to vitamin A, or due to systemic disease, or excessive carotenoid ingestion from eating large quantities of green, yellow, and orange vegetables.[7,11,50]

Absorption and bioavailability of β-carotene is augmented by micellarization with dietary fat and through rupturing of plant cell membranes that occurs during food processing.[51]

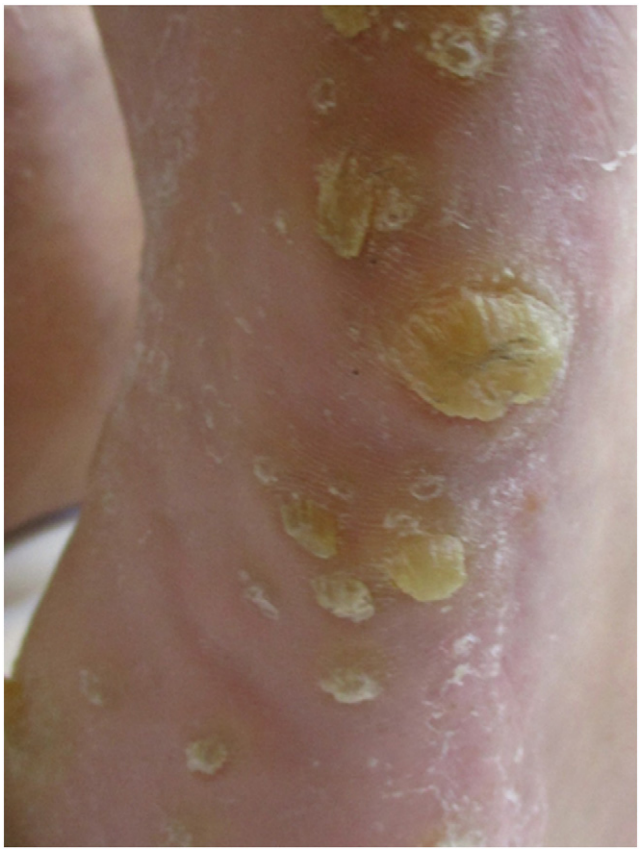

Fig. 2 Punctate keratoderma of the sole of a 44-year-old woman demonstrating the yellow hue of hyperkeratosis.

Thyroxine accelerates the conversion of β-carotene into two molecules of retinol (vitamin A). In hypothyroid states, there is an increase in the serum β-carotene concentration causing the characteristic yellow skin change.[52] The yellow tinge and occasionally xanthomatosis of the skin in patients with chronic renal failure has been attributed to compensatory hyperlipoproteinemia, and the retention of fat-soluble pigments of carotenoids, nitrogenous pigments (urochromes), and lipochromes in the skin or subcutaneous tissue.[53,54]

Clinical and histologic manifestations

Generalized yellow skin changes suggest systemic causes. Carotenoderma presents with a yellow hue predominant on the acral surfaces and the nasolabial folds, sparing the sclera and mucous membranes. Carotenes are excreted by the colon and epidermis, with accumulation in the stratum corneum in states of excess. It may persist clinically for up to 5 months after normalization of dietary intake when due to diet.[7,27,49] A yellowish discoloration of the seborrheic areas of the face may be due to lycopenemia which is associated with an excessive ingestion of lycopene found in high concentrations in tomatoes.[55] Lycopene is excreted by sebaceous and eccrine glands and partly reabsorbed by the horny layer of the skin.[55]

In contrast, jaundiced patients will develop yellow changes of the sclera and mucous membranes, and darkening of the urine color in obstructive jaundice.[11] Scleral icterus is an important differentiating feature in xanthoderma.[27] Patients with hypothyroidism occasionally exhibit a jaundicelike appearance without urinary changes.[52,56] Topical application of the fake tanning product dihydroxyacetone reacts with lipids in the epidermis to form melanoidin, creating a yellow-brown color which is more pronounced on palms due to skin thickness and basal layer penetration.[57]

Surface skin changes that create a yellow color include hyperkeratosis and serous or seropurulent exudate. Hyperkeratosis due to palmoplantar keratodermas presents with thickened yellow plaques on acral sites.[31] Friction-related hyperkeratoses can be found in the form of corns or calluses on the hands and feet. Hyperkeratosis is also found on friction prone areas as a side effect of sorafenib or sunitinib multikinase inhibitors.[58]

Actinic keratoses present as localized hyperkeratotic patches on sun-exposed sites in fair-skinned individuals.[59] Yellow chromonychia may be due to thickening or dystrophy of the nail plate as found in onychomycoses, yellow-nail syndrome, lichen planus, or due to jaundice, smoking, or topical product application (eg, ascorbic acid).[25,28] Serous exudate may leave a yellow crust on the surface of the skin in response to trauma, infection, or inflammation. Impetigo presents with a characteristic golden skin surface crusting, most commonly in children and due to *Staphylococcus aureus.*[60] Impetiginization may also complicate dermatitis, eczema herpeticum, and herpes simplex virus infection.[60] Trichomycosis

(trichobacteriosis) axillaris or pubis (flava variant) demonstrates yellow concretions in moist flexural areas surrounding hair shafts due to overgrowth of *Corynebacterium tenuis*.[61]

Regional flat yellow skin changes are described here. Palmar crease xanthomas are yellow plaques in the palmar creases associated with familial dysbetalipoproteinemia.[40] Diffuse plane xanthomas are yellow plaques that can be widely distributed and are divided into two groups according to lipid status (hyperlidemic versus normolipemic). Normolipemic diffuse plane xanthomatosis may be associated with a lymphoproliferative disorder or biliary cirrhosis.[40,62] In ecchymoses, hemoglobin breakdown within the skin will turn yellow after 7 to 14 days after conversion to bilirubin.[63] Necrobiosis lipoidica is a form of granulomatous inflammation which leads to necrosis of the dermal connective tissue, most commonly on the lower legs of diabetics.[64,65] Dermal destruction allows the underlying fatty tissue to show through, giving the plaques a yellow hue. Lichen aureus is a type of pigmented, purpuric eruption in which focal lichenoid inflammation leads to extravasation of red blood cells in the dermis. The red cells are broken down in the skin to create a yellow-gold color.[66]

Yellow papules may be caused by sebocyte, tumoral, depositional, inflammatory, or elastic tissue disorders.[25] Sebocytes are distributed around the body in sebaceous tissue which secrete lipid-rich sebum.[67] Fordyce spots are small yellow papules found on the genitalia and oral mucosa as modified sebaceous glands. Sebacous gland hyperplasia is seen commonly on the face of older patients, particularly men. The lesions are small, umbilicated, cream or yellow papules usually less than 5 mm in diameter. They have a characteristic dermatoscopic appearance and are more numerous in patients with photodamage and on long-term cyclosporine.[68]

Sebaceous nevus is a congenital disorder presenting in infants as a yellow plaque on the head and neck, especially the scalp.[69] Steatocystoma multiplex is a rare nevoid condition in which multiple epidermal and sebaceous gland-lined cysts present as numerous yellow papules on the chest.[36] Depositional disorders, such as gout due to hyperuricemia or calcinosis cutis, present with yellow- or cream-colored papules and nodules usually on the extremities.[70,71]

The cutaneous Langerhans and non-Langerhans cell histiocytoses are diverse, encompassing such disorders as juvenile xanthogranuloma, xanthoma disseminatum, and necrobiotic xanthogranuloma. They are characterized by a proliferation of histiocytes of unknown etiopathogenesis, presenting with yellowish papules, plaques, or nodules due to lipid-laden histiocytes.[72] Disorders of elastic tissue, such as PXE and papillary dermal elastolysis, present with regional yellow textural skin change and clusters of yellow papules around the neck, axillae, and groin due to an inherited disorder of elastic tissue metabolism and photodegeneration of dermal connective tissue respectively.[47,73] Connective tissue nevi may present with yellow patches or clustered papules due to excess collagen (collagenoma) or elastic tissue (elastoma).[74] Buschke-Ollendorff syndrome is a rare hereditary disorder presenting usually in the first year of life with yellow papules coalescing into plaques with systemic associations including sclerotic bony lesions.[75]

Yellow nodules may develop due to keratinizing tumors, cysts, depositional disorders, or lipid-laden tumoral lesions.[24,25] Squamous cell carcinoma and keratoacanthoma often contain a yellow hue within the tumor mass with associated keratin accumulation and crusting.[76] Sebaceous carcinomas are usually yellow-tan nodules 1 to 4 cm wide, which arise in the ocular adnexa (eyelids), and less commonly at extraocular sites.[77] A high-risk human papillomavirus–associated variant has been identified in younger patients.[77] Xanthomatized dermatofibromas have a homogenous yellow area, corresponding to foamy histiocytes.[78] Eruptive xanthomata present abruptly with widespread, multiple yellow nodules as a marker of raised plasma triglycerides, usually in association with poorly controlled diabetes.[79] Tuberous xanthomata present more slowly over joint extensor surfaces and are associated with a variety of dyslipidemias.[39,79,80] Cutaneous histiocytic disorders may present with yellow nodules as with the solitary nodule or papule of the benign condition juvenile xanthogranuloma (Figure 3).[29] Soft yellow-pink cutaneous nodules may be due to fat herniations, either as a solitary nevoid abnormality (nevus lipomatosis superficialis) or as a manifestation of focal dermal hypoplasia (Gorlin-Goltz) syndrome.[32,45,81]

Pustules, vesicles, and bullae often contain yellow fluid due to the chromophores within them which originate in the plasma.[13] A yellow-green color may be apparent in the presence of the antibacterial enzyme myeloperoxidase released by neutrophils.[33,82]

- Pustules are small raised yellow fluid-filled papules which may be either sterile or nonsterile, although in some cases "sterility" may just be a reflection of the limitations of routine microbiological culture methods.[83] Pustular disorders are diverse and may be generalized as in pustular psoriasis or localized as in acneiform drug eruptions.[32,35,84] The age of the patient and distribution are helpful indicators of etiology.[84]
- Vesicles may become yellow when secondarily infected, for example, in crusted herpes simplex infection, or contain serosanguinous fluid as in cutaneous lymphangioma circumscriptum.[60,85]
- Bullous disorders that retain the epidermis by virtue of a split at the level of the basement membrane seal in an exudate of plasma, inflammatory cells, and microorganisms and, therefore, develop yellow bullae. Bullous disorders with intact bullae include bullous pemphigoid, linear immunoglobulin A disease, pemphigoid gestationis, and fixed drug eruptions.[32,86]

Dermatoscopy permits the visual assessment of shapes and structures not visible to the naked eye, through magnification and modification of the optic characteristics of the skin. In addition to pattern analysis, color assessment is an integral part of the dermatoscopic diagnosis. The colors seen macroscopically are different to those seen dermatoscopically, for example, in

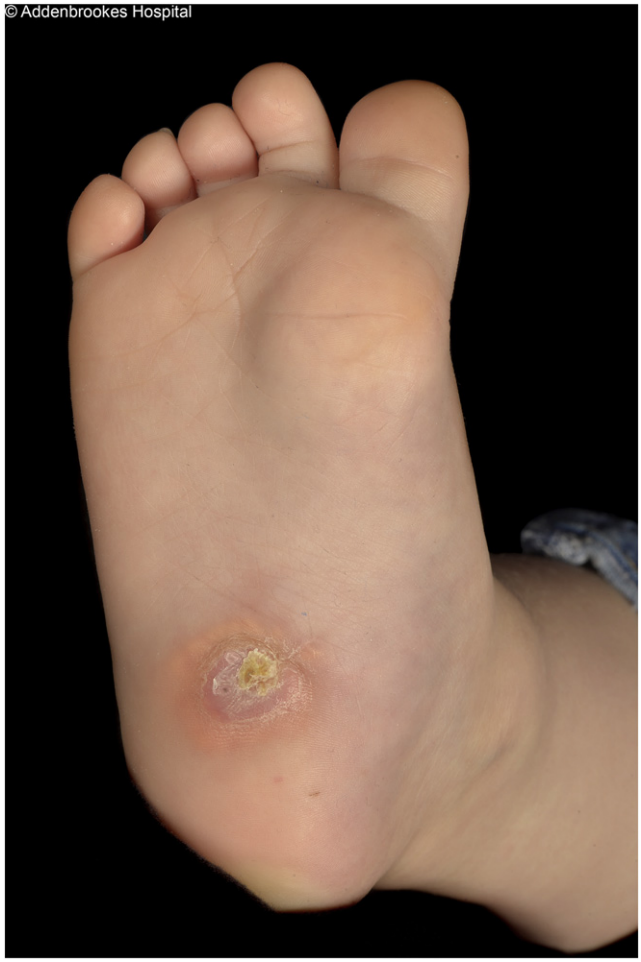

Fig. 3 Diffuse plane xanthomatosis. This patient was normolipemic and the xanthomas were secondary to multiple myeloma. (permission requested from Elsevier to re-use photograph) Credit line to be added when permission received: "Reproduced with permission from the Atlas of Clinical Dermatology 3rd edition by A. du Vivier."

cutaneous mastocytoma which may appear clinically as a red nodule but dermatoscopically yellow.[87] Dermatoscopically, yellow corresponds to keratin and, therefore, the normal epidermis appears yellow.[24,88] An acanthotic epidermis ranges from opaque yellow-brown to gray-brown, as the number of stacked pigmented epidermal keratinocytes increases.[89] Regions of increased hyperkeratosis and horn pseudocysts are white-yellow.[89] As nonpolarized light is better for observing superficial skin layers, yellow color (keratin), such as in milia-like cysts and orthokeratosis or hyperkeratosis, may be better visualized using nonpolarized light.[88] Lipids present in sufficient volume will also be visible dermatoscopically as a yellow color.[24]

If the diagnosis is not obvious clinically, histologic assessment of yellow skin disorders is performed using standard staining techniques, and supplementary tests including stains for lipids (eg, Oil Red O stain), immunohistochemistry, and immunophenotyping when indicated.[90] The common histologic findings associated with a yellow color include: (1) hyperkeratosis; (2) intracellular or dermal deposition of lipids; and (3) sebaceous and elastic tissue disorders.

Hyperkeratosis is identified by a thickening of keratin within the stratum corneum. Keratin cysts demonstrate circular collections of eosinophilic keratin with an epithelial lining.[90] Steatocystoma features cysts with yellowish oily lipid material and keratin with adjacent sebaceous glands and is the only true sebaceous cyst.[91]

Xanthomas contain foam cells in the dermis (Figure 4), with small numbers of inflammatory cells in younger lesions, and fibrosis or cholesterol clefts in older lesions. Foam cells are lipid-rich macrophages which are highlighted by lipid stains.

Xanthogranulomas are granulomas composed of numerous histiocytes with foamy, pale cytoplasm and other inflammatory cells including Touton giant cells.[90,91] In juvenile xanthogranuloma, the predominant lipid is cholesterol, and the histopathologic features vary depending on the time-course of the lesion at biopsy.[29,90]

Comedones, as found in acne and Favre-Racouchot syndrome, are cystically dilated hair follicles containing abundant keratinous material with severe solar elastosis accompanying the latter.[90] Sebaceous hyperplasia demonstrates large, mature sebaceous lobules grouped around a central dilated duct, usually filled with debris.[91] Sebaceous carcinomas show infiltrative lobules or sheets of cells with variable sebaceous differentiation separated by fibrovascular stroma.[37,92]

Degenerative conditions of elastic tissue, such as solar elastosis and PXE, histologically demonstrate clumped basophilic fibrillary material in the dermis. In solar elastosis, these changes are present in the papillary and middermis, but confined to the middermis in PXE, where calcification of the irregular fibers may be seen.[47]

Differential diagnosis

The differential diagnosis of yellow skin disorders categorized according to macroscopic morphology is detailed in Table 1. Separating these disorders clinically requires further

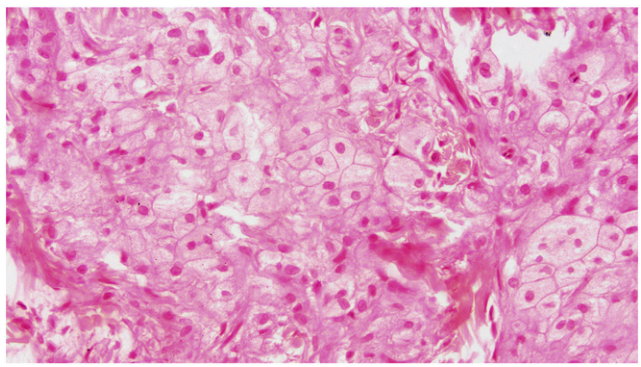

Fig. 4 Histology of xanthelasma showing foamy lipid-laden macrophages. (Hematoxylin and eosin x 20).

Table 1 Differential diagnosis by morphology of yellow skin

Morphology	Differential diagnosis
Macular/patches	**Xanthodermatoses:** palmar crease xanthoma,*,† diffuse plane xanthomatosis*,†
	Infectious: slough
	Inflammatory: lichen aureus
	Photoinduced: solar elastosis
	Traumatic: ecchymoses
Plaques/crusted	**Infectious:** impetigo, onychomycosis, trichomycosis axillaris and pubis
	Keratin-related: palmoplantar keratodermas,* hystrix epidermolytic hyperkeratosis,* ichthyosis hystrix,* keratoderma blenorrhagicum, actinic keratosis, viral keratosis, sorafenib/sunitinib-induced hyperkeratosis, yellow-nail syndrome, seborrhoeic keratosis, pachyonychia congenita,* dystrophic nail disorders (lichen planus)
	Congenital: connective tissue nevus
	Metabolic: xanthelasma,* plane xanthoma,† diffuse plane xanthomatosis.*,† Primary hyperlipoproteinemia,* secondary hyperlipoproteinemia (diabetes mellitus, obstructive liver disease, cerebrotendinous xanthomatosis,* phytosterolemia,* pancreatitis, estrogen)
	Immunologic: verruciform xanthoma, necrobiosis lipoidica diabeticorum
Papular/nodular	**Histiocytic:** Langerhans cell histiocytosis, benign cephalic histiocytosis, juvenile xanthogranuloma,*,† Erdheim-Chester disease, progressive nodular histiocytosis, xanthoma disseminatum,† xanthomatous dermatofibroma, reticulohistiocytosis (solitary or multiple†)
	Sebaceous: sebaceoma, sebaceous adenoma,* sebaceous carcinoma,* sebaceous gland hyperplasia, nevus sebaceous, nevus sebaceous syndrome,* Fordyce spots
	Adipose: piezogenic pedal papules, fat herniation, nevus lipomatosus superficialis, Goltz syndrome*
	Photoinduced: colloid milium, papillary dermal elastolysis, Favre-Racouchot syndrome, keratoelastoidosis marginalis
	Cystic: steatocystoma multiplex,* epidermal cyst, pilomatricoma
	Elastic: pseudoxanthoma elasticum,* Buschke-Ollendorf syndrome,* middermal elastolysis (type II), elastomas, elastosis perforans serpiginosum*
	Metabolic: tendon xanthoma,* tuberous xanthoma,* tuberoeruptive xanthoma,* eruptive xanthomata,* gouty tophi, calcinosis cutis, lipoid proteinosis*
	Immunologic: cutaneous mastocytoma, necrobiotic xanthogranuloma†
	Tumoral: keratoacanthoma, squamous cell carcinoma
Vesicular/bullous	**Autoimmune:** bullous pemphigoid, bullous lupus erythematosus, linear immunoglobulin A disease, pemphigoid gestationis, epidermolysis bullosa acquisita
	Infectious: bullous impetigo, eczema herpeticum, crusted herpes simplex, varicella zoster virus (shingles)
	Iatrogenic: fixed drug eruption
Pustular	**Generalized:** acute generalized exanthematous pustulosis, subcorneal pustular dermatosis, pustular psoriasis, folliculitis, erythema toxicum neonatorum, transient neonatal pustular melanosis, Ofuji disease
	Localized: folliculitis, comedonal acne, acneiform drug eruption, acrodermatitis continua, rosacea, perioral dermatitis, palmoplantar pustulosis, eosinophilic folliculitis, cutaneous candidiasis, erosive pustular dermatosis of the scalp
Generalized/regional	**Iatrogenic:** quinacrine (mepacrine)
	Behavioral: nicotine staining, fake-tan (dihydroxyacetone), cadmium tattoo, henna, anorexia nervosa, turmeric
	Dietary: carotenemia (Familial carotenemia*), lycopenemia
	Organ dysfunction: jaundice (hepatic, hemolytic), renal failure, hypothyroidism, diabetes mellitus, biliary disease

* Indicates a genetic association.
† Indicates a paraneoplastic association.

examination of the distribution, morphology, and chronicity of the skin features, in conjunction with a systems review and consideration of the demographics and family history. Yellow disorders more commonly found in children include juvenile xanthogranuloma, carotenoderma, sebaceous nevus, and pilomatricoma.[7,29] Yellow disorders more commonly found in elderly patients include dermatohelioses and xanthomatoses.[79]

Laboratory studies

Considering yellow skin is found in diverse disorders of keratinization, elastic tissue, lipid accumulation, or chromophores in the circulation, systemic disease associations are often present.[11,27,40,56] Investigations are used to further characterize the skin disease and help to establish systemic associations which may have important prognostic value.[11,25,40,56]

Hyperkeratosis in actinic keratoses or due to friction does not require investigation.[59] Palmoplantar keratodermas may be stratified by genetic testing to define the keratin mutation.[31] Acral scaling suggestive of keratoderma blenorrhagicum in Reiter's syndrome requires screening for gastroenterologic and genitourinary infections including HIV.[93] Skin swabs for bacterial culture or viral polymerase chain reaction may be used in indeterminate cases of impetigo, or herpes simplex virus.[60] Onychomycotic nail changes should be investigated with nail clippings for fungal culture or polymerase chain reaction before systemic therapy.[94] Abnormal nail keratinization suggestive of pachyonychia congenita requires genetic screening, and in yellow-nail syndrome, chest imaging may elucidate respiratory disease.[31]

In select cases, acne may require investigation to exclude a systemic association such as an adrenal tumor, or polycystic ovarian syndrome.[95] Identification of sebaceous tumors (adenoma, epitheliomas, carcinomas) should prompt genetic screening for Muir-Torre syndrome (*MSH2* or MLH1 gene mutations).[26] In steatocytoma multiplex, keratin 17 gene mutations have been found, but their identification is currently not altering the clinical management.[96] The xanthomatoses are associated with primary or secondary hyperlidpidemias, and investigations should include fasting blood samples to establish the lipid profile and categorization to Fredrickson type.[79,97] Abnormal values should prompt referral to the patient's primary physician due to the associated cardiovascular risks.[79,80] Within the cutaneous histiocytoses, those which have an association with systemic involvement may require radiologic screening, endocrine profiling (eg, diabetes insipidus), and screening for a primary malignancy (eg, hematologic malignancy in diffuse plane xanthomatosis).[29,32,40]

The photoinduced elastic tissue disorders solar elastosis, Favre-Racouchot syndrome, colloid milium, and papillary dermal elastolysis, do not require laboratory investigation.[73,98] Elastomas, in the context of the Buschke-Ollendorff syndrome, require radiologic screening for osteopoikilosis, and ophthalmologic assessment.[75] As PXE is associated with cardiomyopathy, mitral valve prolapse, and peripheral vascular disease, cardiovascular imaging is required in addition to ophthalmologic assessment for angioid streaks which untreated may lead to blindness.[47,48]

Hypercarotenemia may be confirmed with serum carotene levels > 250 μg/dL.[27,99] For patients with lycopenemia, ultrasound scanning of the liver may reveal depositional fatty cysts.[55] Jaundice is optimally investigated by specialist physicians, with screening for hemolysis, intrahepatic disease, or biliary tree obstruction.[11] Serum uric acid levels may be tested to confirm gout and repeated to monitor treatment response.[71]

Treatment

Crusting or hyperkeratosis is treated depending on the cause. Hyperkeratosis may be treated topically with emollients and keratolytic agents and often resolves after removal of etiologic factors (eg, friction).[100] Surgical treatment of problematic hyperkeratotic areas may be achieved with curettage, shave excisions, or laser ablation.[101] Actinic keratoses may be treated topically or with cryotherapy, curettage, or photodynamic therapy.[59] Palmoplantar keratodermas may be treated systemically with retinoid therapy, and benefits have been reported with laser treatments, 5-fluorouracil chemotherapy, and surgical treatment in select cases but no cure exists.[31,101,102] When of sufficient severity to the patient, nail plate changes due to onychomycosis may be treated with systemic antifungal agents.[94] Oral antimicrobials for impetigo are reserved for cases with numerous or extensive lesions, outbreaks affecting multiple people, or ecthyma.[60,103]

Early treatment with surgical excision or Mohs micrographic surgery is recommended for sebaceous carcinoma, with no systemic treatment identified as effective for this aggressive tumor.[77,90,92] Steatocystoma multiplex has been treated with oral isotretinoin, cryotherapy, surgery (punch-extrusion), and lasers with variable success.[96] Treatment of hyperlipidemias is complex and includes dietary and cardiovascular risk modification, pharmacotherapy, and in specialist cases lipoprotein apheresis and liver transplant.[79,80,104] If desired, xanthelasmata and xanthomata may be treated for their cosmetic effect, with interventions based on mechanical removal such as chemabrasion, surgical excision, chemical peel, or laser ablation.[62]

Some of the conditions in the diverse range of histiocytic disorders, for example, juvenile xanthogranuloma and benign cephalic histiocytosis, are benign or self-limiting, and may be left untreated.[25,29] Others, such as diffuse plane xanthomatosis and necrobiotic xanthogranuloma, are associated with underlying hematological malignancies, and the management is of the underlying disorder.[41,62] Identification of somatic mutations has led to

the recognition of Langerhans cell histiocytosis as a true malignancy of dendritic Langerhans cells, and targeted drug therapy (eg, BRAF protein inhibitors) has subsequently been introduced as a treatment option.[105]

There is no specific and preventive treatment available for patients with PXE. Etidronate is an inorganic pyrophosphate analog that has been identified as a potential therapeutic agent to inhibit ectopic mineralization.[48]

In hypercarotenemia and lycopenemia, nutritional advice and dietary modification is used to reduce carotenoid intake to the normal range.[7,27,55] Jaundice treatment may be with surgical or medical intervention, or behavioral modification dependent on the cause.[11] Uremic pallor due to chronic renal failure is treated by restoring or replacing renal function, and hypothyroidism usually by medical correction of thyroid hormone levels.[53,56] Gout may be treated by systemic uric acid lowering therapy and avoiding triggers.[71]

Conclusions

Appreciation of the physical and pathophysiologic mechanisms producing a yellow color in the skin is helpful in the clinician's comprehension of skin disease. Carotenoids, being fat soluble, color lipid-rich substances and cells yellow, including sebum, sebocytes, and adipose tissue and any accumulation of lipids within the visible depth of the skin. Bilirubin colors plasma and serum yellow and contributes to the characteristic appearance of many vesiculobullous and pustular disorders. In addition, keratin disorders and some disorders of elastic tissue appear yellow due to their photoreflective properties and lipid content.

Skin disorders with a yellow appearance are a heterogenous group clinicopathologically, and color features are best interpreted through experience and with an understanding of electromagnetic phenomena and chromophore handling in health and disease. Combining color features as an integral part of the extended clinical examination permits the dermatologist to generate the differential diagnosis by which all subsequent treatments and clinical outcomes are determined.

Disclosures

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors have no conflicts of interest to declare.

References

1. Elliot AJ, Maier MA. Color psychology: effects of perceiving color on psychological functioning in humans. *Annu Rev Psychol* 2014;65:95-120.
2. Elliot AJ. Color and psychological functioning: a review of theoretical and empirical work. *Front Psychol* 2015;6:368.
3. Alfenas ER, da Silva J, Silveira MES, et al. A painting technique using ceramic pigments for the artificial iris of an ocular prosthesis guided by applying Newton's color wheel. *J Prosthodont* 2019;28:e822-e825.
4. Nordlund JJ, Cestari T, Grimes P, et al. A more precise lexicon for pigmentation, pigmentary disorders, and "chromatic" abnormalities. In: Nordlund JJ, Boissy RE, Hearing VJ, King RA, Oetting WS, Ortonne JP, eds. The Pigmentary System. 2nd ed. Malden, Massachusetts: Blackwell Pub; 2006. p. 499-503.
5. Shah VV, Mlacker S, Aldahan AS, et al. Dermatologic etymology: descriptive terms of color. *JAMA Dermatol* 2016;152:428.
6. Macpherson G. *Black's Medical Dictionary.* London: A. & C. Black. 2002.
7. Chattopadhyay M, Pramanik R, McGrath JA, et al. Familial carotenaemia and carotenoderma. *Clin Exp Dermatol* 2014;39:771-772.
8. Tseng SH, Bargo P, Durkin A, et al. Chromophore concentrations, absorption and scattering properties of human skin in-vivo. *Opt Express* 2009;17:14599-14617.
9. Rowland HM, Burriss RP. Human colour in mate choice and competition. *Philos Trans R Soc Lond Ser B Biol Sci* 2017;372.
10. Henderson AJ, Lasselin J, Lekander M, et al. Skin colour changes during experimentally-induced sickness. *Brain Behav Immun* 2017;60:312-318.
11. Stillman AE. Jaundice. In: Walker HK, Hall WD, Hurst JW, eds. Clinical Methods: The History, Physical, and Laboratory Examinations. Boston: Butterworths Publishers; 1990.
12. Nguyen LQ, Allen HB. Reactions to manganese and cadmium in tattoos. *Cutis* 1979;23:71-72.
13. Elkassabany NM, Meny GM, Doria RR, et al. Green plasma-revisited. *Anesthesiology* 2008;108:764-765.
14. Barnhart RK, Steinmetz S. *Chambers Dictionary of Etymology.* Edinburgh: Chambers. 1999.
15. Parrado C, Philips N, Gilaberte Y, et al. Oral photoprotection: effective agents and potential candidates. *Front Med (Lausanne)* 2018;5:188.
16. Llorente B. Regulation of carotenoid biosynthesis in photosynthetic organs. *Subcell Biochem* 2016;79:141-160.
17. Lichtenhaler HK, Buschmann C. Chlorophylls and carotenoids: measurement and characterization by UV-VIS spectroscopy. *Curr Protocols Food Analytical Chem* 2001:F4.3.1-F4.3.8.
18. Borel P, Desmarchelier C. Genetic variations associated with vitamin A status and vitamin A bioavailability. *Nutrients* 2017;9.
19. Green AS, Fascetti AJ. Meeting the vitamin A requirement: the efficacy and importance of β-carotene in animal species. *ScientificWorldJournal* 2016;2016, 7393620.
20. Darwish WS, Ikenaka Y, Morshdy AE, et al. β-carotene and retinol contents in the meat of herbivorous ungulates with a special reference to their public health importance. *J Vet Med Sci* 2016;78:351-354.
21. Dunne PG, Monahan FJ, O'Mara FP, et al. Colour of bovine subcutaneous adipose tissue: a review of contributory factors, associations with carcass and meat quality and its potential utility in authentication of dietary history. *Meat Sci* 2009;81:28-45.
22. Goodwin TW, Gregory RA. Studies in vitamin A. 7. Carotene metabolism in herbivores. *Biochem J* 1948;43:505-512.
23. Rubin LP, Ross AC, Stephensen CB, et al. Metabolic effects of inflammation on vitamin A and carotenoids in humans and animal models. *Adv Nutr* 2017;8:197-212.
24. Banuls J, Arribas P, Berbegal L, et al. Yellow and orange in cutaneous lesions: clinical and dermoscopic data. *J Eur Acad Dermatol Venereol* 2015;29:2317-2325.

25. Frew JW, Murrell DF, Haber RM. Fifty shades of yellow: a review of the xanthodermatoses. *Int J Dermatol* 2015;54:1109-1123.
26. John AM, Schwartz RA. Muir-Torre syndrome (MTS): an update and approach to diagnosis and management. *J Am Acad Dermatol* 2016;74:558-566.
27. Stack KM, Churchwell MA, Skinner Jr RB. Xanthoderma: case report and differential diagnosis. *Cutis* 1988;41:100-102.
28. Dong H, Wang Y. A case of yellow chromonychia and yellow skin induced by topical ascorbic acid. *Australas J Dermatol* 2019;60:145-147.
29. Haroche J, Abla O. Uncommon histiocytic disorders: Rosai-Dorfman, juvenile xanthogranuloma, and Erdheim-Chester disease. *Hematology Am Soc Hematol Educ Program* 2015;2015:571-578.
30. Barun V. Absorption spectra and light penetration depth of normal and pathologically altered human skin. *Appl Spectrosc* 2007;74:430-439.
31. McLean WH. Genetic disorders of palm skin and nail. *J Anat* 2003;202:133-141.
32. Richard G, Ringpfeil F. Ichthyoses, erythrokeratodermas and related disorders. In: Bolognia J, Jorizzo JL, Rapini RP, eds. Dermatology. Spain: Mosby; 2003. p. 775-808.
33. Iizaka S, Kaitani T, Sugama J, et al. Predictive validity of granulation tissue color measured by digital image analysis for deep pressure ulcer healing: a multicenter prospective cohort study. *Wound Repair Regen* 2013;21:25-34.
34. Schneider MR, Paus R. Sebocytes, multifaceted epithelial cells: lipid production and holocrine secretion. *Int J Biochem Cell Biol* 2010;42:181-185.
35. Elston DM, Berger TG, Andrews GC, et al. Errors in metabolism. In: Elston DM, Berger TG, Andrews GC, eds. Andrews' Diseases of the Skin: Clinical Dermatology. London: Saunders Elsevier; 2011. p. 506-538.
36. Apaydin R, Bilen N, Bayramgurler D, et al. Steatocystoma multiplex suppurativum: oral isotretinoin treatment combined with cryotherapy. *Australas J Dermatol* 2000;41:98-100.
37. Weedon D. Cutaneous infiltrates - non-lymphoid. In: Weedon D, ed. Weedon's Skin Pathology. 3rd ed. London: Churchill Livingstone Elsevier; 2010. p. 961-965.
38. Brinster E, Calonje E. Degenerative and metabolic diseases. In: Calonje E, Brenn T, Lazar A, McKee PH, eds. McKee's Pathology of the Skin. 4th ed. Philadelphia: Elsevier/Saunders; 2012. p. 520-590.
39. Matsumoto M, Kunimitsu S, Wada K, et al. Vascular endothelial cell distribution and adhesion molecule expression in xanthoma. *J Cutan Pathol* 2007;34:754-761.
40. Oka M, Okamura A, Kawano S, et al. Diffuse plane normolipemic xanthoma associated with chronic myelomonocytic leukemia-1. *Eur J Dermatol* 2014;24:112-113. France.
41. Szalat R, Arnulf B, Karlin L, et al. Pathogenesis and treatment of xanthomatosis associated with monoclonal gammopathy. *Blood* 2011;118:3777-3784.
42. Masuda Y, Ogura Y, Inagaki Y, et al. Analysis of the influence of collagen fibres in the dermis on skin optical reflectance by Monte Carlo simulation in a nine-layered skin model. *Skin Res Technol* 2018;24:248-255.
43. Leveque JL, Corcuff P, de Rigal J, et al. In vivo studies of the evolution of physical properties of the human skin with age. *Int J Dermatol* 1984;23:322-329.
44. McGrath JA, Eady RAJ, Pope FM. Anatomy and organisation of human skin. In: Burns T, Breathnach S, Cox N, eds. Rook's Textbook of Dermatology. Oxford: Blackwell Publishing; 2004. p. 3.1-3.84.
45. Ghosh SK, Bandyopadhyay D, Jamadar NS. Nevus lipomatosus cutaneous superficialis: an unusual presentation. *Dermatol Online J* 2010;16:12.
46. Durai PC, Thappa DM, Kumari R, et al. Aging in elderly: chronological versus photoaging. *Indian J Dermatol* 2012;57:343-352.
47. Li Q, van de Wetering K, Uitto J. Pseudoxanthoma elasticum as a paradigm of heritable ectopic mineralization disorders: pathomechanisms and treatment development. *Am J Pathol* 2019;189:216-225.
48. Kranenburg G, de Jong PA, Bartstra JW, et al. Etidronate for prevention of ectopic mineralization in patients with pseudoxanthoma elasticum. *J Am Coll Cardiol* 2018;71:1117-1126.
49. Priyadarshani AMB. Insights of hypercarotenaemia: a brief review. *Clin Nutr ESPEN* 2018;23:19-24.
50. Maharshak N, Shapiro J, Trau H. Carotenoderma—a review of the current literature. *Int J Dermatol* 2003;42:178-181.
51. Bengtsson A, Larsson Alminger M, Svanberg U. In vitro bioaccessibility of beta-carotene from heat-processed orange-fleshed sweet potato. *J Agric Food Chem* 2009;57:9693-9698.
52. Aktuna D, Buchinger W, Langsteger W, et al. Beta-carotene, vitamin A and carrier proteins in thyroid diseases. *Acta Med Austriaca* 1993;20:17-20.
53. Comaish JS, Ashcroft T, Kerr DN. The pigmentation of chronic renal failure. *J Am Acad Dermatol* 1975;55:215-217.
54. Lupi O, Rezende L, Zangrando M, et al. Cutaneous manifestations in end-stage renal disease. *An Bras Dermatol* 2011;86:319-326.
55. La Placa M, Pazzaglia M, Tosti A. Lycopenaemia. *J Eur Acad Dermatol Venereol* 2000;14:311-312.
56. Lause M, Kamboj A, Fernandez Faith E. Dermatologic manifestations of endocrine disorders. *Transl Pediatr* 2017;6:300-312.
57. Draelos ZD. Cosmetic therapy. In: Wolverton S, ed. Comprehensive Dermatological Drug Therapy. New York, NY: Elsevier; 2013. p. 604-605.
58. Reyes-Habito CM, Roh EK. Cutaneous reactions to chemotherapeutic drugs and targeted therapy for cancer: Part II Targeted therapy. *J Am Acad Dermatol* 2014;71:211-217.
59. de Berker D, McGregor JM, Mohd Mustapa MF, et al. British Association of Dermatologists' guidelines for the care of patients with actinic keratosis 2017. *Br J Dermatol* 2017;176:20-43.
60. Hartman-Adams H, Banvard C, Juckett G. Impetigo: diagnosis and treatment. *Am Fam Physician* 2014;90:229-235.
61. Bonifaz A, Váquez-González D, Fierro L, et al. Trichomycosis (trichobacteriosis): clinical and microbiological experience with 56 cases. *Int J Trichology* 2013;5:12-16.
62. Lorenz S, Hohenleutner S, Hohenleutner U, et al. Treatment of diffuse plane xanthoma of the face with the Erbium:YAG laser. *Arch Dermatol* 2001;137:1413-1415.
63. Maguire S, Mann M. Systematic reviews of bruising in relation to child abuse-what have we learnt: an overview of review updates. *Evid Based Child Health* 2013;8:255-263.
64. Feily A, Mehraban S. Treatment modalities of necrobiosis lipoidica: a concise systematic review. *Dermatol Reports* 2015;7:5749.
65. Erfurt-Berge C, Seitz AT, Rehse C, et al. Update on clinical and laboratory features in necrobiosis lipoidica: a retrospective multicentre study of 52 patients. *Eur J Dermatol* 2012;22:770-775.
66. Fink-Puches R, Wolf P, Kerl H, et al. Lichen aureus: clinicopathologic features, natural history, and relationship to mycosis fungoides. *Arch Dermatol* 2008;144:1169-1173.
67. Lovaszi M, Mattii M, Eyerich K, et al. Sebum lipids influence macrophage polarization and activation. *Br J Dermatol* 2017;177:1671-1682.
68. McDonald SK, Goh MS, Chong AH. Successful treatment of cyclosporine-induced sebaceous hyperplasia with oral isotretinoin in two renal transplant recipients. *Australas J Dermatol* 2011;52:227-230.
69. Moody MN, Landau JM, Goldberg LH. Nevus sebaceous revisited. *Pediatr Dermatol* 2012;29:15-23.
70. Valenzuela A, Chung L. Calcinosis: pathophysiology and management. *Curr Opin Rheumatol* 2015;27:542-548.
71. Solomon DH, Avorn J, Levin R, et al. Uric acid lowering therapy: prescribing patterns in a large cohort of older adults. *Ann Rheum Dis* 2008;67:609-613.
72. Emile JF, Abla O, Fraitag S, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. *Blood* 2016;127:2672-2681.
73. Foering K, Torbeck RL, Frank MP, et al. Treatment of pseudoxanthoma elasticum-like papillary dermal elastolysis with nonablative fractional

resurfacing laser resulting in clinical and histologic improvement in elastin and collagen. *J Cosmet Laser Ther* 2017:1-3.
74. Arora H, Falto-Aizpurua L, Cortes-Fernandez A, et al. Connective tissue nevi: a review of the literature. *Am J Dermatopathol* 2017;39:325-341.
75. Pope V, Dupuis L, Kannu P, et al. Buschke-Ollendorff syndrome: a novel case series and systematic review. *Br J Dermatol* 2016;174:723-729.
76. Zalaudek I, Giacomel J, Schmid K, et al. Dermatoscopy of facial actinic keratosis, intraepidermal carcinoma, and invasive squamous cell carcinoma: a progression model. *J Am Acad Dermatol* 2012;66:589-597.
77. Tetzlaff MT, Curry JL, Ning J, et al. Distinct biological types of ocular adnexal sebaceous carcinoma: HPV-driven and virus-negative tumors arise through nonoverlapping molecular-genetic alterations. *Clin Cancer Res* 2019;25:1280-1290.
78. Iwata J, Fletcher CD. Lipidized fibrous histiocytoma: clinicopathologic analysis of 22 cases. *Am J Dermatopathol* 2000;22:126-134.
79. Zak A, Zeman M, Slaby A, et al. Xanthomas: clinical and pathophysiological relations. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2014;158:181-188.
80. France M, Rees A, Datta D, et al. HEART UK statement on the management of homozygous familial hypercholesterolaemia in the United Kingdom. *Atherosclerosis* 2016;255:128-139.
81. Uzuncakmak TK, Akdeniz N, Karadag AS, et al. Multiple yellow nodules in a 13-year-old girl. *Clin Exp Dermatol* 2019;44:307-309.
82. Grigorieva DV, Gorudko IV, Sokolov AV, et al. Myeloperoxidase stimulates neutrophil degranulation. *Bull Exp Biol Med* 2016;161:495-500.
83. Masuda-Kuroki K, Murakami M, Tokunaga N, et al. The microbiome of the "sterile" pustules in palmoplantar pustulosis. *Exp Dermatol* 2018;27:1372-1377.
84. Mengesha YM, Bennett ML. Pustular skin disorders: diagnosis and treatment. *Am J Clin Dermatol* 2002;3:389-400.
85. Jha AK, Lallas A, Sonthalia S. Dermoscopy of cutaneous lymphangioma circumscriptum. *Dermatol Pract Concept* 2017;7:37-38.
86. Wick MR. Bullous, pseudobullous, & pustular dermatoses. *Semin Diagn Pathol* 2017;34:250-260.
87. Adya KA, Inamadar AC, Palit A. Dermoscopy of cutaneous mastocytoma. *Indian Dermatol Online J* 2018;9:218-219.
88. Cabo H. *Color Atlas of Dermoscopy.* New Delhi, Jaypee: The Health Sciences Publisher. 2017:13-21.
89. Stolz W, Braun-Falco O, Bilek P, et al. *Color Atlas of Dermatoscopy. 2nd ed.* Berlin: Blackwell Publishing. 2002:11-17.
90. Weedon D. *Weedon's Skin Pathology. 3rd ed.* London: Churchill Livingstone Elsevier. 2010.
91. Rapini RP. *Practical Dermatopathology. 2nd ed.* Elsevier Saunders: Edinburgh. 2012.
92. Knackstedt T, Samie FH. Sebaceous carcinoma: a review of the scientific literature. *Curr Treat Options in Oncol* 2017;18:47.
93. Kanwar AJ, Mahajan R. Reactive arthritis in India: a dermatologists' perspective. *J Cutan Med Surg* 2013;17:180-188.
94. Gupta AK, Mays RR, Versteeg SG, et al. Update on current approaches to diagnosis and treatment of onychomycosis. *Expert Rev Anti-Infect Ther* 2018;16:929-938.
95. Vieira H, Brain C. Cushing syndrome associated with an adrenal tumour. *BMJ Case Rep* 2012;2012.
96. Gordon Spratt EA, Kaplan J, Patel RR, et al. Steatocystoma. *Dermatol Online J* 2013;19, 20721.
97. Gotoda T, Shirai K, Ohta T, et al. Diagnosis and management of type I and type V hyperlipoproteinemia. *J Atheroscler Thromb* 2012;19:1-12.
98. Tierney EP, Hanke CW, Petersen J, et al. Clinical and echographic analysis of ablative fractionated carbon dioxide laser in the treatment of photodamaged facial skin. *Dermatol Surg* 2010;36:2009-2021.
99. Wageesha ND, Ekanayake S, Jansz ER, et al. Studies on hypercarotenemia due to excessive ingestion of carrot, pumpkin and papaw. *Int J Food Sci Nutr* 2011;62:20-25.
100. Jacobi A, Mayer A, Augustin M. Keratolytics and emollients and their role in the therapy of psoriasis: a systematic review. *Dermatol Ther (Heidelb)* 2015;5:1-18.
101. O'Connor EA, Dzwierzynski WW. Palmoplantar keratoderma: treatment with CO2 laser case report and review of the literature. *Ann Plast Surg* 2011;67:439-441.
102. Lienemann AO, Colucci VJ, Jones MS, et al. Treatment of palmoplantar keratoderma with continuous infusion 5-fluorouracil. *Cutis* 2004;73:303-308.
103. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2014;59:e10-e52.
104. Wollina U, Koch A, Hansel G, et al. Eruptive xanthomas–two case reports with distinct features. *Open Access Maced J Med Sci* 2018;6:2152-2154.
105. Wollina U, Langner D, Hansel G, et al. Cutaneous Langerhans cell histiocytosis: the spectrum of a rare cutaneous neoplasia. *Wien Med Wochenschr* 2018;168:243-247.