Nail changes in systemic diseases

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Abstract

Discerning between actual nail conditions and nail changes associated with systemic disease is a very important and interesting part of any clinical examination. This article provides a helpful clinical atlas of nail changes that may be associated with systemic disease and will assist the clinician to identify and verify these clinical signs. The article includes information on common nail changes like koilonychia, longitudinal and transverse grooves, nail pitting, clubbing, pincer nails, pterygia, splinter haemorrhages, nicotine-stained nails, cyanosis, jaundice and brittle nails. It also includes information on the -nychias (micro-, macro-, leuko-, pachy-, melano- and dyschromo-), onycholysis and onychoschizia, red lunulas, yellow nail syndrome, Muehrcke's white bands, Terry's nails and periungual fibromas (Koenen tumours).

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Introduction

Abnormal changes in nails can be due to diseases primarily affecting nails, for example onychomycosis and 20-nail dystrophy, be due to inflammatory dermatoses with nail involvement, for example eczema, psoriasis and lichen planus, or be part of a systemic disease, for example in clubbing, cyanosis, jaundice and splinter haemorrhages. Some of these nail changes can be a presenting feature before other signs of a systemic disease become clinically evident. In diseases such as psoriasis, the nail bed loses its adherent properties, resulting in onycholysis. Disruption of nail matrix epithelium and inflammation result in superficial areas of parakeratosis that clinically appear as nail pitting. Upward growth of thickened nails results in onychogryphosis.

Examination of the nails is part of a full dermatological examination and nail changes may alert one to the diagnosis of a systemic disease. Clinicians must acquaint themselves with these nail changes as they can be a helpful clue in diagnosing systemic diseases: for example, encountering a patient with Koenen tumours on the nails should prompt a clinician to look for signs of tuberous sclerosis complex.

Abnormalities of nail shape

Koilonychia (Greek: Koilos = hollow, Onyx = nail)

This refers to the presence of reverse curvature in the transverse and longitudinal axis, giving a concave dorsal aspect to the nail. These changes result in spooning of the nails. Koilonychia is commonly associated with iron deficiency anaemia and haemochromatosis. The presence of koilonychia should alert a clinician to look for other signs of anaemia and to do a full blood count and serum iron studies. However, the majority of adults with koilonychia demonstrate a familial pattern that may be an autosomal-dominant trait.[1]

Clubbing

Clubbing refers to bullous enlargement of the distal segments of the fingers due to proliferation of connective tissue, particularly on the dorsal surface. Hyperplasia of the fibrovascular tissue at the base of the nail allows the nail to be rocked. Three forms of geometric assessment can be performed in clubbing:[1]

(a) Lovibond's angle is found at the junction between the nail plate and proximal nail fold and it is normally less than 160°. In clubbing, this is increased to over 180° (see Figure 1).

(b) Curth's angle at the distal interphalangeal joint is normally approximately 180°. This is diminished to less than 160° in clubbing (see Figure 2).

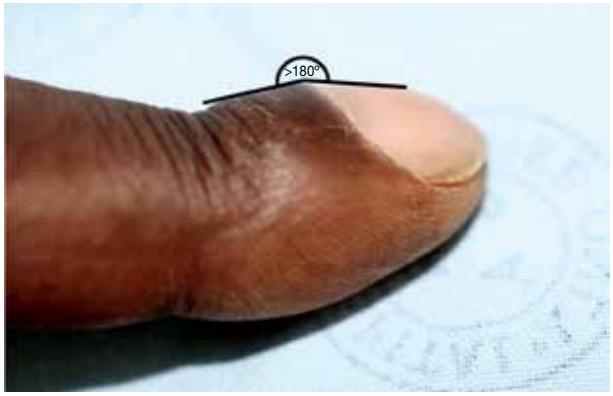


Figure 1: Lovibond's angle

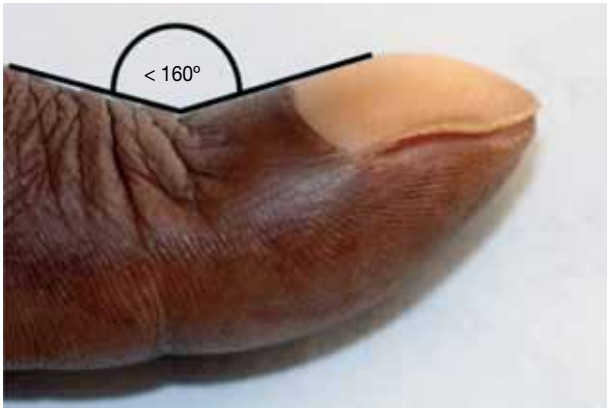


Figure 2: Curth's angle

(c) Schamroth's window is seen when the dorsal aspects of two fingers from opposite hands are apposed, revealing a window of light, bordered laterally by the Lovibond angles. In clubbing, this window closes because the angle is obliterated.

Clubbing may be hereditary, idiopathic or acquired and is associated with a variety of systemic diseases, such as cyanotic congenital heart diseases, infective endocarditis, primary and metastatic lung cancer (see Figure 3), bronchiectasis, lung abscess, cystic fibrosis, mesothelioma, inflammatory bowel disease and hepatic cirrhosis.[2]

Clubbing in patients with primary and metastatic lung cancer, mesothelioma, bronchiectasis and hepatic cirrhosis may be associated with hypertrophic osteoarthropathy, in which subperiosteal new bone formation in the distal diaphyses of the long bones of the extremities causes pain and symmetric arthritis-like changes in the shoulders, knees, ankles, wrists and elbows. The mechanism of clubbing is not well understood, but it appears to be secondary to humoral substance that causes dilation of the vessels of the fingertips.[2]

The most promising proposed pathophysiology of clubbing is that of Dickinson and Martin, which shows that when platelet precursors fail to become fragmented into platelets within the pulmonary circulation, they are easily trapped in the peripheral vasculature, releasing platelet-derived growth factor and vascular endothelial growth factor, promoters of vascularity and, ultimately, clubbing.[3]

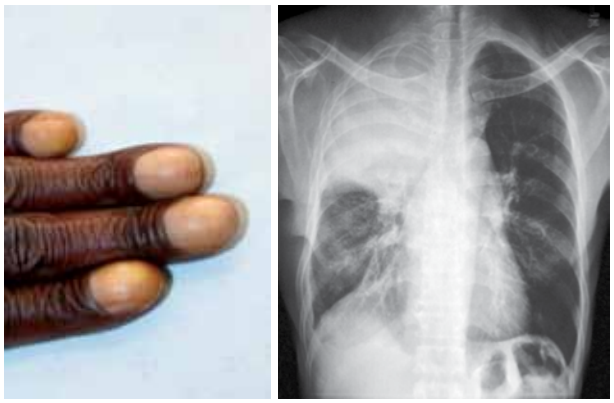


Figure 3: Clubbing in a patient with primary lung carcinoma. His chest X-ray showed homogenous opacity on the right upper and middle zones, a reduced lung volume and tenting of the right hemidiaphragm

Pincer nail

Pincer nail deformity is a curved ingrown nail with bilateral penetration to the nail folds. Pincer nail may be hereditary or acquired. The acquired form is associated with several diseases and medications, but the mechanism of its development remains unknown. Recently Kirkland and Sheth reported a case of acquired pincer nail deformity associated with end-stage renal disease secondary to diabetes mellitus.[4]

Macronychia and micronychia

Macronychia and micronychia nails refer to nails that are too large or too small compared to other nails on nearby digits. Macronychia may be due to local gigantism. Micronychia may occur in association with plexiform neuromas.

Abnormalities of nail attachment

Onycholysis

This is the distal and/or lateral separation of the nail plate from the nail bed. Areas of separation appear white or yellow due to air beneath the nail and sequestered debris. Onycholysis is commonly seen in association with certain skin diseases but may also occur due to general medical conditions, for example hypothyroidism, hyperthyroidism and states of impaired peripheral circulation.

Pterygium

Pterygium occurs when a central fibrotic band divides a nail proximally into two, obstructing normal nail growth. A large pterygium may destroy the whole nail. Pterygium may occur in association with systemic diseases such as graft-versus-host disease and systemic sclerosis.

Abnormalities of nail surface

Longitudinal grooves

These are grooves that run along the longitudinal axis of all or part of the length of the nail. They may be of full or partial thickness. Longitudinal grooves may occur due to the use of oral retinoids or may be familial.

Transverse grooves

These run along the transverse axis of the nail and may be of full or partial thickness. Transverse grooves may be generalised, reflecting a systemic disease such as coronary thrombosis, mumps and pneumonia.

Nail pitting

These are punctuated erosions on the nail surface. They may be shallow or deep with a regular or irregular outline. Nail pitting is common in skin diseases such as psoriasis and alopecia areata. An isolated large pit may produce a localised full-thickness defect in the nail plate termed elkonyxis, which is a feature of Reiter's disease.

Onychoschizia

It is characterised by transverse splitting of the nail plate into layers at or near the free edge in fingers and toes. It is also

called lamellar dystrophy. This can result in discolouration of the nail due to sequestration of debris between the layers. Onychoschizia has been reported in association with polycythaemia.

Brittle nails

Brittle nails are often associated with frequent immersion of hands in water. Other common causes are iron deficiency anaemia and impaired peripheral circulation. A rare cause is disturbance of arginine metabolism.

Abnormalities of nail colour

Leukonychia

This refers to whitish discolouration of nails. Different types of leukonychia occur. In total leukonychia all the nails are porcelain white; this may be due to chronic liver disease, but there are rare inherited forms. In subtotal leukonychia the proximal two-thirds of the nail is white and this is due to delay in keratin maturation. Transverse leukonychia is usually due to systemic problems such as chemotherapy or poisoning affecting nail matrix function. Leukonychia may also be due to nail bed pallor, which may be a nonspecific sign of anaemia (see Figure 4). Other systemic causes of leukonychia are hypoalbuminic states, like in severe malnutrition and chronic liver disease.

Figure 4: Leukonychia in a patient with anaemia due to chronic renal failure

Melanonychia

This refers to longitudinal or transverse brownish to black pigmentation of the nails. It can occur in association with skin diseases such as lichen planus, it can be due to drug therapy with minocycline and zidovudine, it can be due to melanocytic naevi and, most importantly, it can be a sign of malignant melanoma, referred to as Hutchinson's sign.

Cyanosis

Cyanosis refers to a bluish colour of the skin, mucous membranes and nails resulting from an increased quantity of deoxygenated haemoglobin or of haemoglobin derivatives in the small blood vessels of the affected areas (see Figure 5).

Cyanosis may be subdivided into central and peripheral types. In peripheral cyanosis there is slowing of blood flow and abnormally great extraction of oxygen from normally saturated

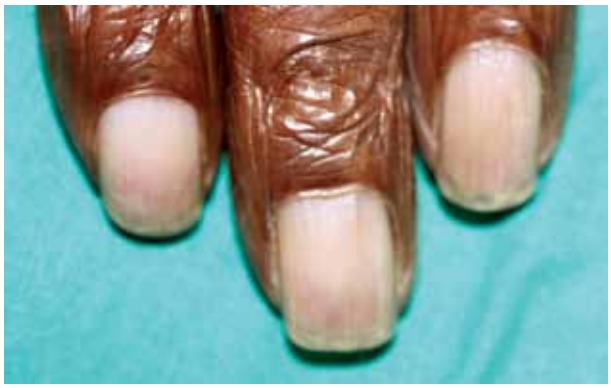


Figure 5: Cyanosis in a patient with congestive cardiac failure due to dilated cardiomyopathy

arterial blood. It results from vasoconstriction and diminished peripheral blood flow, such as occurs in cold exposure, shock, congestive cardiac failure and peripheral vascular disease. Central cyanosis may be due to congenital heart diseases such as tetralogy of Fallot and transposition of great vessels in infants.

Clinical differentiation between central and peripheral cyanosis may not always be simple and in conditions such as cardiogenic shock with pulmonary oedema there may be a mixture of both types.[2]

Jaundice

Jaundice or icterus is a yellowish discolouration of the skin, mucous membranes and nails in severe cases, resulting from deposition of bilirubin in these tissues. Tissue

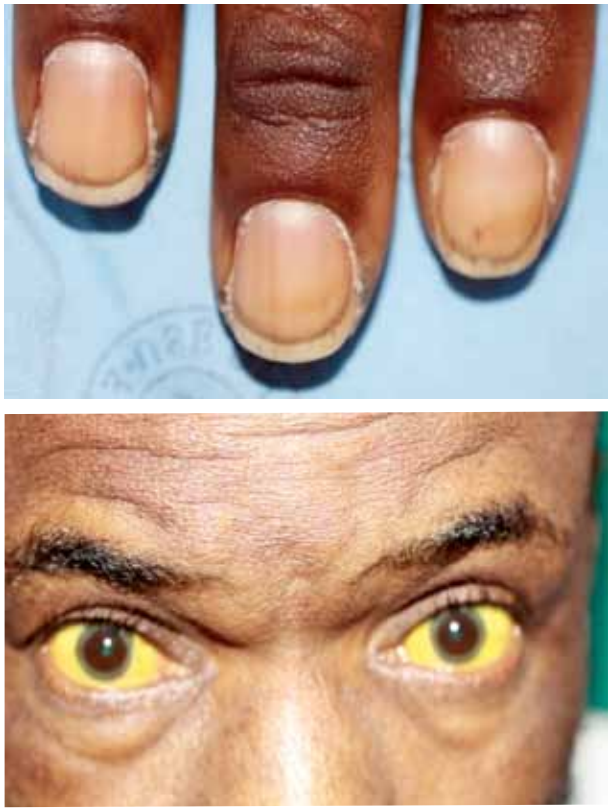


Figure 6: Yellow discolouration of nails and sclerae in a patient with obstructive jaundice

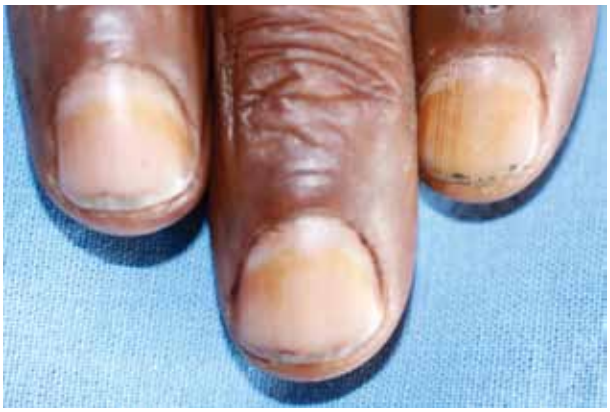


Figure 7: Nicotine-stained nails in a patient with COAD. This patient has 20 pack years.

deposition of bilirubin occurs early in the presence of serum hyperbilirubinaemia and is a sign of either liver disease or, less often, a haemolytic disorder.[5] Slight increases in serum bilirubin are best detected by examining the sclerae, which have a particularly high affinity for bilirubin due to high elastin content. Nails are only affected in severe cases (see Figure 6). Jaundice may be due to prehepatic causes, for example haemolytic anaemia, hepatic causes, for example viral hepatitis, or posthepatic causes, for example in biliary tract obstruction by carcinoma of the head of the pancreas or gallstones.

Nicotine-stained nails

This is a yellow staining of the nails due to nicotine in heavy cigarette smokers (see Figure 7). This is often but not exclusively seen in patients with cigarette-smoking-associated diseases such as carcinoma of the lung, chronic obstructive airway disease and cigarette-smoking-associated cardiovascular diseases.

Splinter haemorrhages

Splinter haemorrhages in nails and petechiae on the skin may occur in the setting of infective endocarditis. Infective endocarditis results from proliferation of microorganisms on the endothelium of the heart valves. The prototypic lesions at the site of infection, referred to as vegetations, are masses of platelets, fibrin, microcolonies of microorganisms and scanty inflammatory cells.[6] This may occur in patients with rheumatic valvular diseases, valvular replacement, intravenous drug abusers and congenital heart diseases.

In evaluating a patient with splinter haemorrhages for infective endocarditis other signs must be sought. These include fever, splenomegaly, changing murmurs, Osler's nodes, Janeway's lesions, Roth's spots and microscopic haematuria. Other rare causes of splinter haemorrhages include vasculitis, as in rheumatoid arthritis, polyarteritis nodosa and anti-phospholipid syndrome.[7] Splinter haemorrhages may be due to nail trauma, especially if located distally.

Muehrcke white bands

These are parallel white bands with a pink band in between that run parallel to the lunula in the nail bed. They are commonly associated with hypoalbuminaemia. Correction by albumin infusion can reverse the sign.

Terry's nails

This refers to nails that are white proximally and normal distally. This is attributed to liver cirrhosis, congestive cardiac failure and adult-onset diabetes mellitus.

HIV-associated dyschromonychia

Dyschromonychia is a change in nail and nail bed colour and is a term generally applied to patients with increased nail pigmentation. Many patients with dyschromonychia in association with advanced human immunodeficiency virus (HIV) infection are seen (see Figure 8). In a study of 75 HIV-positive patients by Leppard at Kilimanjaro Christian Medical Centre, all patients were found to have dyschromonychia, indicating 100% specificity of dyschromonychia as a sign of HIV infection.[8]

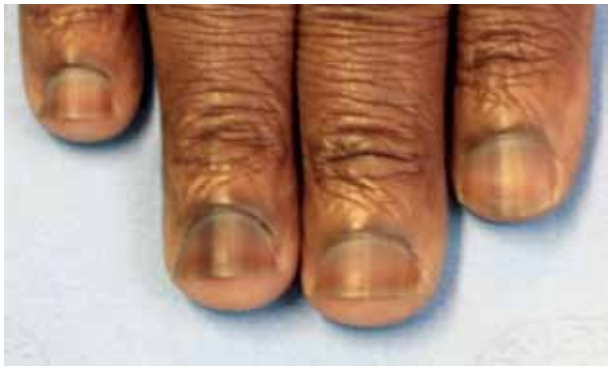


Figure 8: Dyschromonychia in a patient with advanced HIV infection

In a study by Levay et al at Kalafong Hospital in Pretoria the specificity was found to be 66%.[9]. However, we need to mention that dyschromonychia is not unique to HIV infection. It has been reported in an HIV-negative patient with necrotising pneumonia.[9] In some people dyschromonychia may be familial.

Yellow nail syndrome

In yellow nail syndrome the nails are yellow due to thickening, sometimes with a tinge of green, possibly due to secondary infection. The lunular is obscured and there is increased transverse and longitudinal curvature and loss of cuticle. Occasionally there may be chronic paronychia with onycholysis and transverse ridging. The condition usually occurs in adults but may occur in childhood. It may be associated with lymphoedema at one or more sites and respiratory or nasal sinus disease.[1] Yellow nail syndrome is very rare.

Red lunula

This is erythema of all or part of the lunula, which may affect all digits but most prominently the thumb. Erythema is less intense in the distal lunula where it can merge with the nail bed or be demarcated by a pale line and can be obliterated by pressure on the nail plate.

Genodermatoses with nail abnormalities

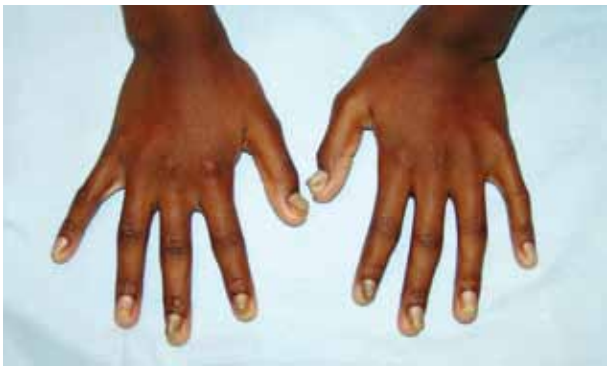
Pachyonychia congenita

This is a rare genodermatosis inherited as an autosomal-dominant trait. Autosomal-recessive patterns of inheritance have also been described. Pachyonychia congenita is characterised by localised areas of hyperkeratosis on the palms and soles with grossly thickened wedge-shaped nails.[10] Three types of pachyonychia congenita occur:

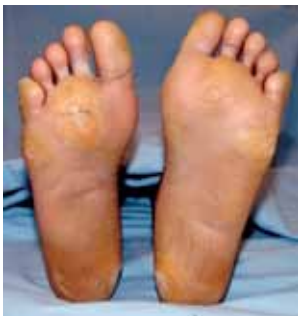
Type I (Jadassohn-Lewandowsky type) is characterised by focal palmo-plantar hyperkeratosis on areas of pressure, localised blistering of the feet, follicular hyperkeratosis and oral leukokeratosis of the tongue and oral mucosa (see Figure 9 a, b, c). Involvement of the larynx may cause hoarseness.[10]

Type II (Jackson-Lawler type) is characterised by the above features plus neonatal teeth, cutaneous cysts and hair abnormalities but no oral lesions.

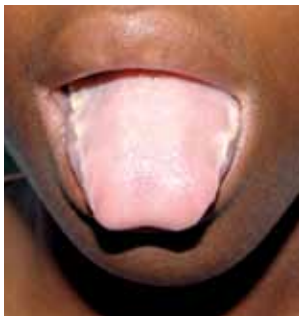
Figure 9: Pachyonychia congenita (Jadassohn-Lewandowsky type)



(a) Wedge-shaped nails with subungual hyperkeratosis



(b) Plantar hyperkeratosis on pressure areas



(c) Oral leukokeratosis

Type III (Schafer-Brunauer type) is characterised by the features of Type II plus leukokeratosis of the cornea.

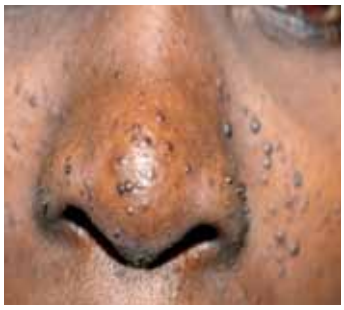
Pachyonychia congenita is a progressive disease with plantar hyperkeratosis producing pain on walking. Treatment with retinoids and keratolytics may reduce the hyperkeratosis.

Koenen tumours (periungual fibromas)

These are periungual fibromas that occur on the nails of the fingers and toes in patients with tuberous sclerosis complex (TSC). It is a rare autosomal-dominant disease with clinical manifestations due to formation of hamartomas in various organ systems.

Cutaneous manifestations include adenoma sebaceum, which is pathognomonic of TSC, ash leaf macules, shagreen patches and Koenen tumours on nails (see Figure 10 a, b). Manifestations of TSC in the central nervous system include mental retardation and epilepsy due to cortical tubers and subependymal giant cell astrocytomas in the brain. In the cardiovascular system, murmurs, ECG changes and heart failure may occur due to intramyocardial rhabdomyomas. Involvement of the respiratory system may result in exertional dyspnoea, cor pulmonale and pneumothorax due to multiple cysts in the lung parenchyma. In the genitourinary system, multiple renal cysts as well as renal angiomyolipomas and infantile polycystic renal disease may occur. Renal cell carcinoma may sometimes occur during infancy or childhood.[11]

Figure 10: (a) Koenen tumour on the nail of a patient with tuberous sclerosis



(b) Adenoma sebaceum in a centrofacial distribution in the same patient

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