The Nails – A Review

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Abstract:

In this part of "The Nails – A Review", the anatomy of the nail is demonstrated. Some nails affection is discussed. To start with we covered in short, some main topics as abnormal nail discoloration which included most leukonychial nail affections and some causes of melanonychia, subungual melanoma, yellow nail syndrome and nail discoloration from drugs as well as some rare congenital causes of nail discoloration.

Hereditary diseases involving the nails especially those associated with atrophic changes, total and partial absence of nails, hypertrophic congenital nail changes and periungual involvement were briefly discussed. We tried to illustrate these conditions by available photographs.

This could help as a quick short reference to these nails changes. To start with, it is important to know clearly the anatomy of the nail unit in order to understand the nail affection in disease.

The anatomy of the nail is illustrated [1] in (Fig.-1a) As shown in figure (1) the anatomy of the nail unit shows the following parts:

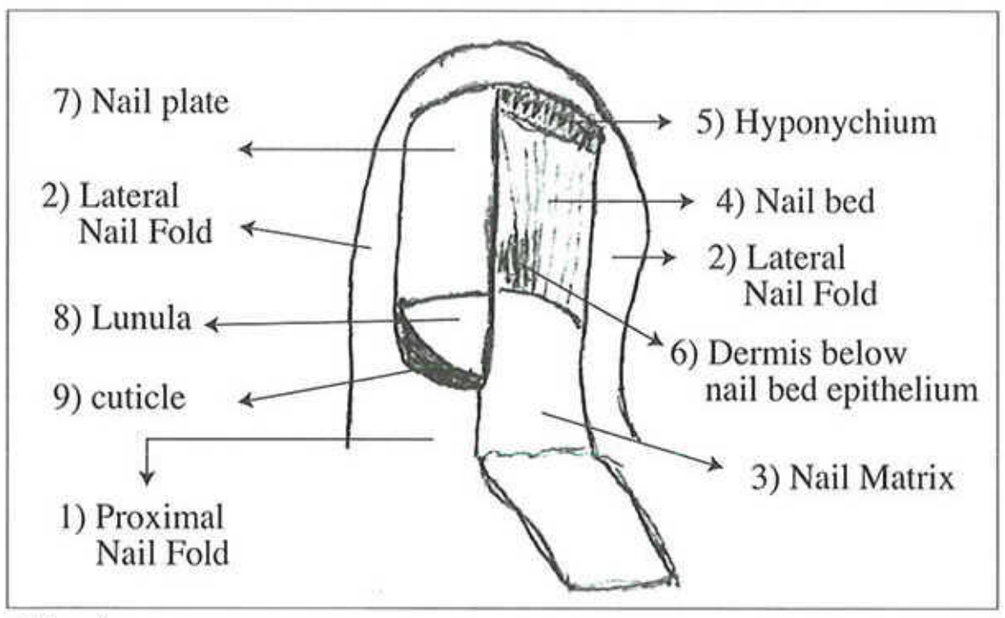

Fig.1a

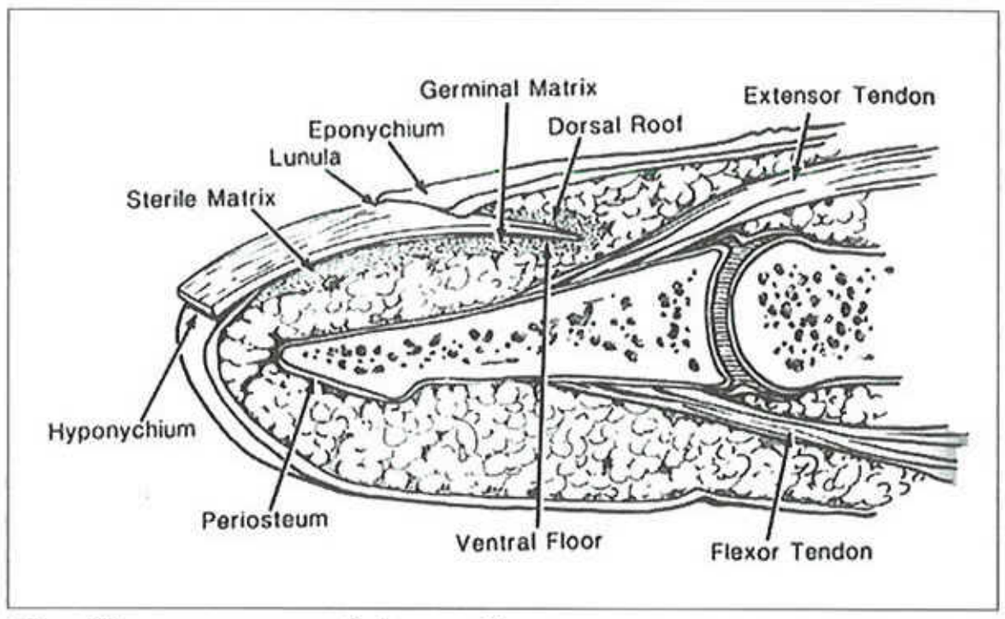

Fig.1b: anatomy of the nail

1- Proximal nail fold which is a skin fold that lies over the proximal portion of the matrix and the proximal portion of the plate which is the nail root
2- Lateral nail folds which are on either side of the nail plate
3- The matrix, which lies beneath the proximal nail, fold and is responsible for development of the nail plate. The matrix may be divided into 3 parts.
   a) a proximal part which produces the superficial portion of the nail plate
   b) an intermediate part which produces the central part of the nail plate
   c) a distal part at the level of the lunula and produces the under surface of the plate which lies next to nail bed. The lunula is visible on most digits as half moon[2]. Adult thumbs and index fingers. The lunula is the germinative nail matrix. The growth rate of the nail is altered by disease state
4- The nail bed
5- The hyponychuim
6- The dermis below the nail bed epithelium
7- The nail plate which is the horny end product produced by the nail matrix
8- The lunula represents the distal part of the nail matrix
9- The cuticle at the proximal part of the lunula
10- Melanocytes are present in the nail bed and matrix.

The melanocytes are more numerous and more strongly dopa positive in the distal part of the nail matrix [3]. The number of melanocytes in the nail matrix is less than anywhere in the skin and they produce small quantities of melanosomes and melanin. They reside in the lower 2-4 germinative cell layers of the matrix rather than within the basal cell layer [4]. Melanosomes are transferred by dendrites to matrix cells, which migrate distally as they transform to nail plate

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corneocytes [5].

The transparent nail overlies a highly vascular nail bed and nail matrix (namely the distal part marked as the Lunula in Figure (1).

Through the nail unit the physician can see the effect of systemic diseases, medications, trauma, nutritional deficiencies and infections.

First discussion is of abnormal discoloration of Nails:

Abnormal pigmentation of the nail may be seen in many systemic diseases [6]

A) **one of these pigmentary changes is Leukonychia (or white nails):** (Fig 2, 3, 4) Leukonychia may be striate, punctuate, total or partial [7]. Subtotal leukonychia may progress to total leukonychia[8]. The color can be milky, chalky or porcelain white. Congenital leukonychia (Fig. 5) is uncommon and could be inherited, as autosomal dominant with subtotal white discoloration of nails and tend to affect several nails each with a 2-3 mm transverse white line and the distal nail is pink (Fig 6). Congenital leukonychia patients often have multiple sebaceous cysts and renal calculi [9]. Congenital and hereditary leukonychia may be an association with Acrokeratosis Verriciformis of Hopf, Darier's diseases, LEOPARD syndrome, psoriasis and deafness. Acquired white striate leukonychia may be caused by exogenous and endogenous agents. These acquired striate leukonychia are temporary and are reported in association with many conditions such as stress, menstruation, acute myocardial infarction, shock, starvation and some drugs as cyclophosphamide [10] and Sulfonamides [11]. Occupational contactants such as salt solutions may produce punctuate leukonychia [7].

White lines of the nail are believed to be caused by parakeratosis in the nail bed [12]. The presence of air in the nail plate has been suggested as a mechanism of leukonychia [13,14].

- Leukonychia in transverse lines affecting multiple nails at the same site is called Mees lines and are classically described with arsenic poisoning. These Mees lines have the contour of the lunula and move with the growing nail. Mees lines were also reported with trauma and serious illness.
- Terry's Nails most commonly affect the index and thumb and is characterized by white discoloration that obscures the lunula [15] in patients with hepatic cirrhosis. In persistent hypo-albuminemia (usually less than 2.2 g/dl) transverse white lines in pairs appear on nails and these lines are vascular and do not move distally with nail growth. These lines are known as Muehrcke's lines [16]. The hypoalbuminemia may be caused by chronic renal insufficiency, nephrotic syndrome, renal transplant or severe hepatic disease [17]. Zinc deficiency may present with Muehrcke's lines [18]. Low serum zinc may be secondary to hypoalbuminemia since 85% of the zinc is bound to albumin [19].
- 10% of patients with renal failure and azotemia show Half and Half Nails. The nail show 4-6 mm proximal white and may occupy 60% of the nail and obscure the lunula and a distal dark brown or reddish area [20]. The brown color is due to stimulation of matrix melanocytes. Successful renal transplant causes regression of these pigmentary changes [21].

B) **Another pigmentary disorder is hyper pigmentation of the nail (Melanonychia) (Fig. 7):** Banded pigmentary and longitudinal melanotic striations are more common than diffuse type of pigmentation (Fig 8). Longitudinal melanonychia (Fig. 9) has been associated with Addison's disease[22], after adrenalectomy for Cushing's syndrome [23], vitamin B12 deficiency [24, 25], Peutz-Jeghers Syndrome [26]. It is also seen in irradiation[27], with the use of cytotoxic drugs (Fig. 10) as 5-fluorouracil [28], nitrogen mustard and cyclophosphamide [29], in Langier-Hunziker syndrome [30], Basex syndrome [31], intestinal leiomyosarcoma [32], systemic lupus erythematosis [33], Junctional nevocellular nevus [34], subungual basal cell epithelioma [35] and acrolentigenous melanoma [36]. Striate pigmentation is a normal finding in dark skinned persons [37]. The pigmentation is produced by matrix melanocytes [38] and is more frequent on thumbs and index fingers.

C) **A third cause of pigmentary disorder of nails:** Subungual Melanoma and Melanonychia striate longitudinalis (Fig. 11). Subungual melanoma may present with longitudinal striated bands and hyperpigmentation was reported in 25-75% of subungual melanomas and when the pigmentation spreads periungually into the proximal and lateral folds is called Hutchinson sign, whose presence mandates histopathologic examination.

Subungual melanomas are often diagnosed late at an advanced stage of tumor. Several benign conditions may mimic the clinical features of subungual melanoma including the presence of Hutchinson's sign but certain guide lines have been proposed and may help in diagnosing subungual melanoma[17,37,40,41,42,43] and these guide lines include:

1- The appearance of melanonychia striate longitudinalis after middle age.
2- Pigmented bands that are larger than 6mm in width at time of diagnosis.

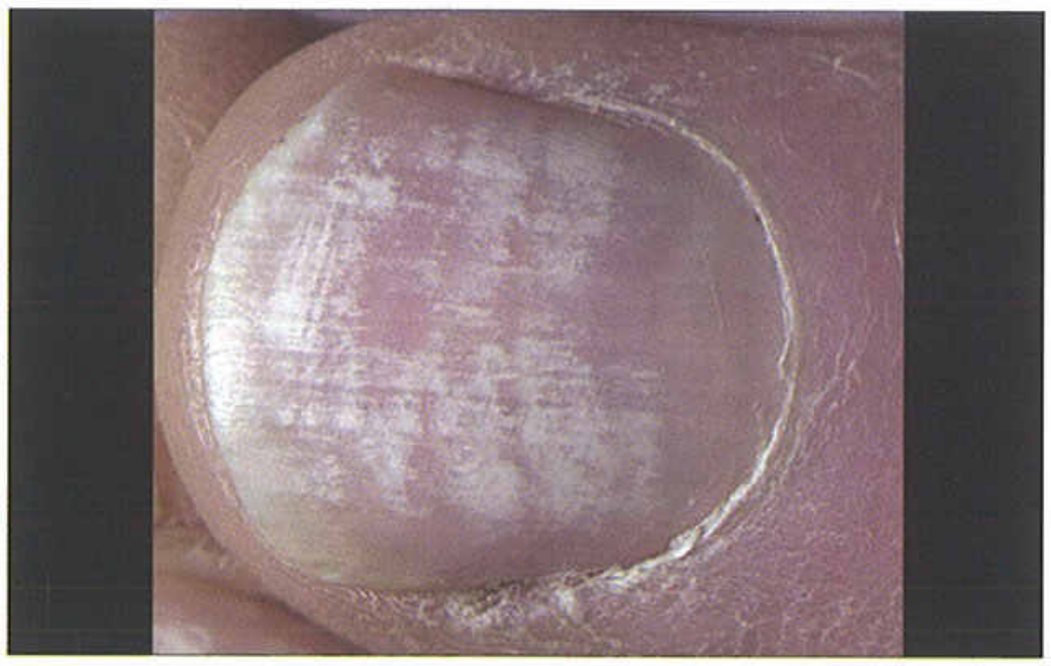

Fig. 2: leukonychia

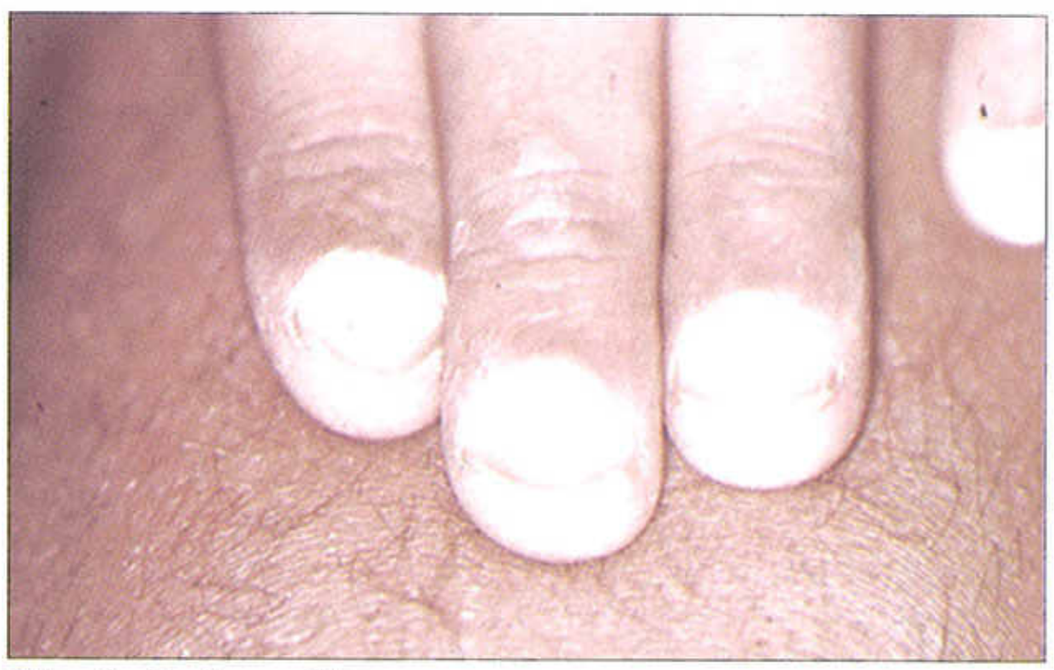

Fig. 3: leukonychia

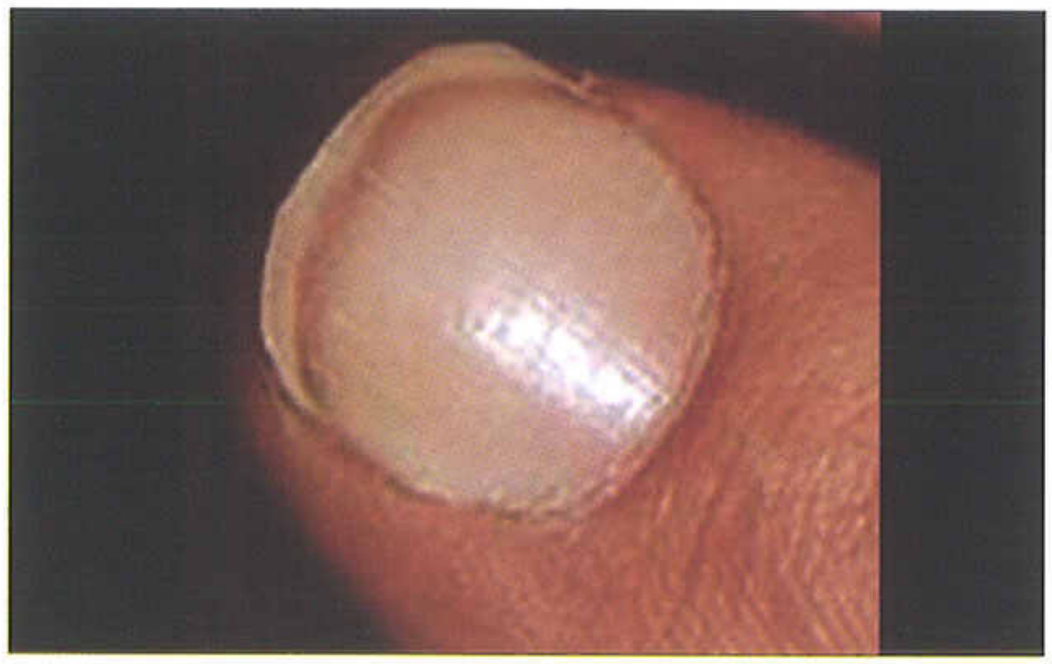

Fig. 4: leukonychia

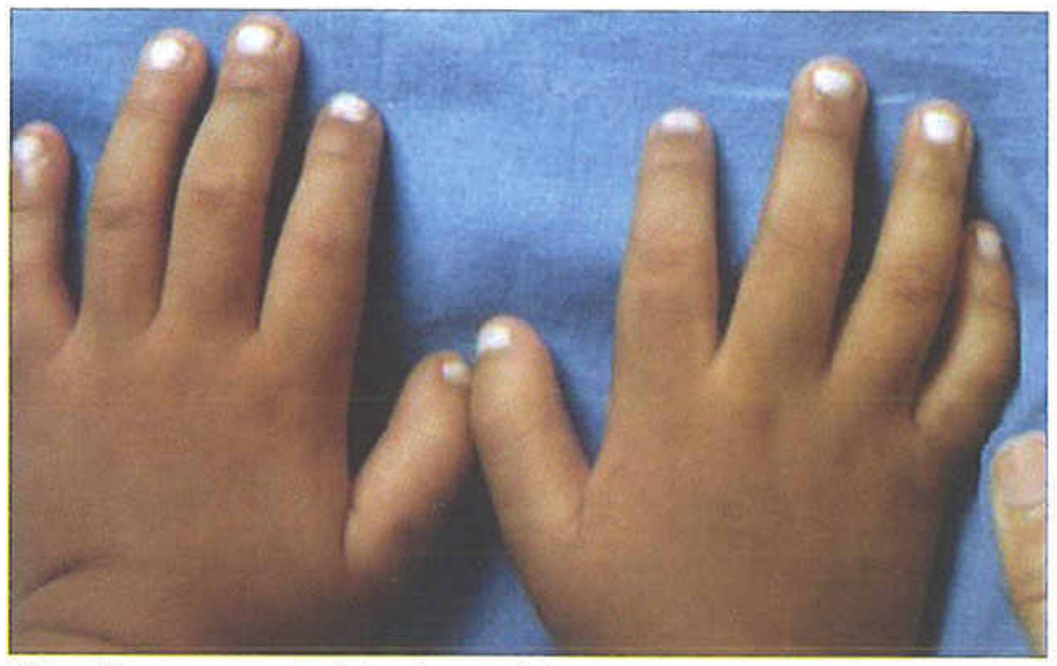

Fig. 5: congenital leukonychia

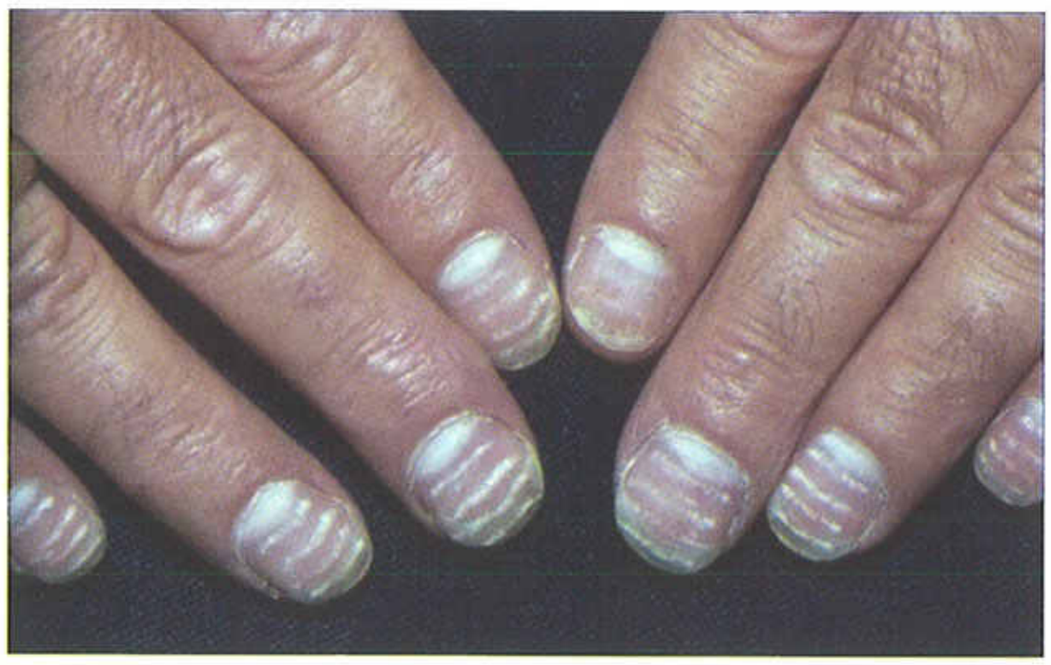

Fig. 6: transverse leukonychia

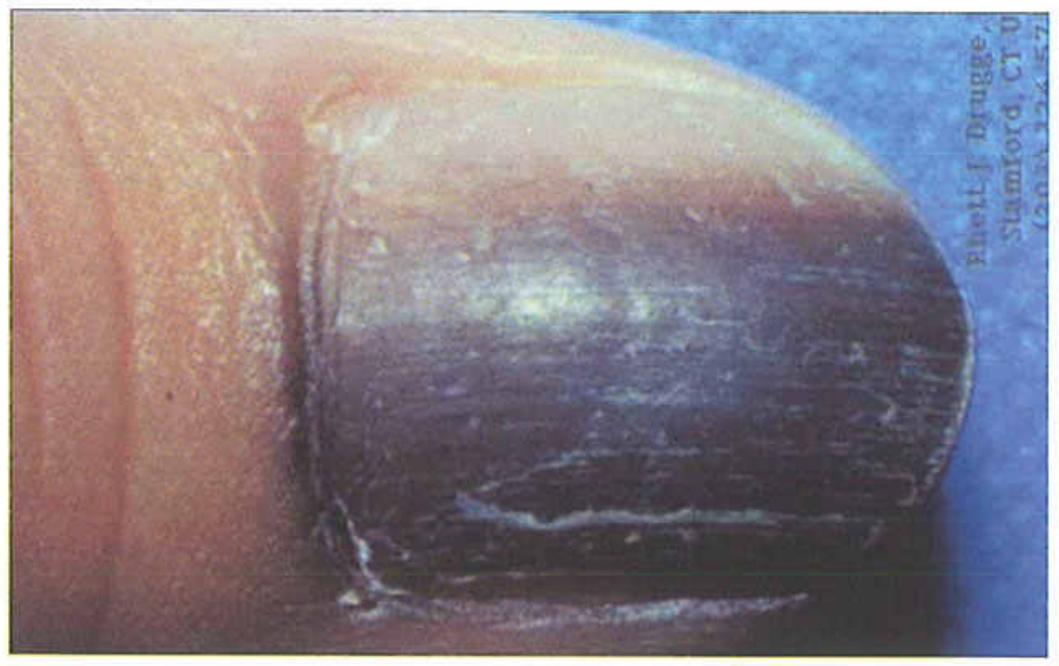

Fig. 7: melanonychia

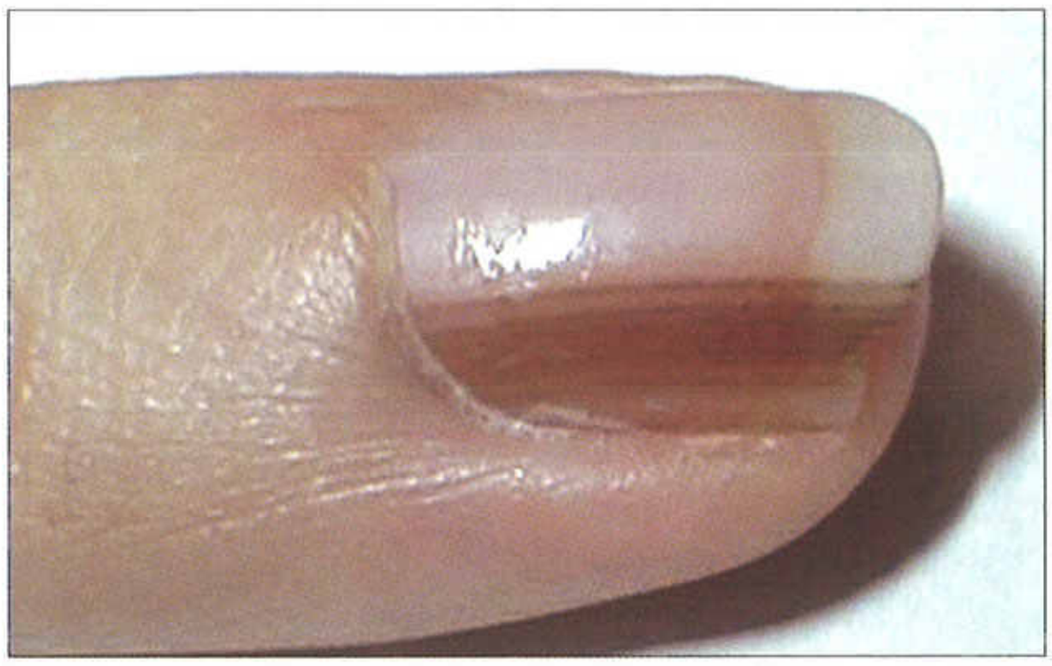

Fig. 8: Banded melanongchia

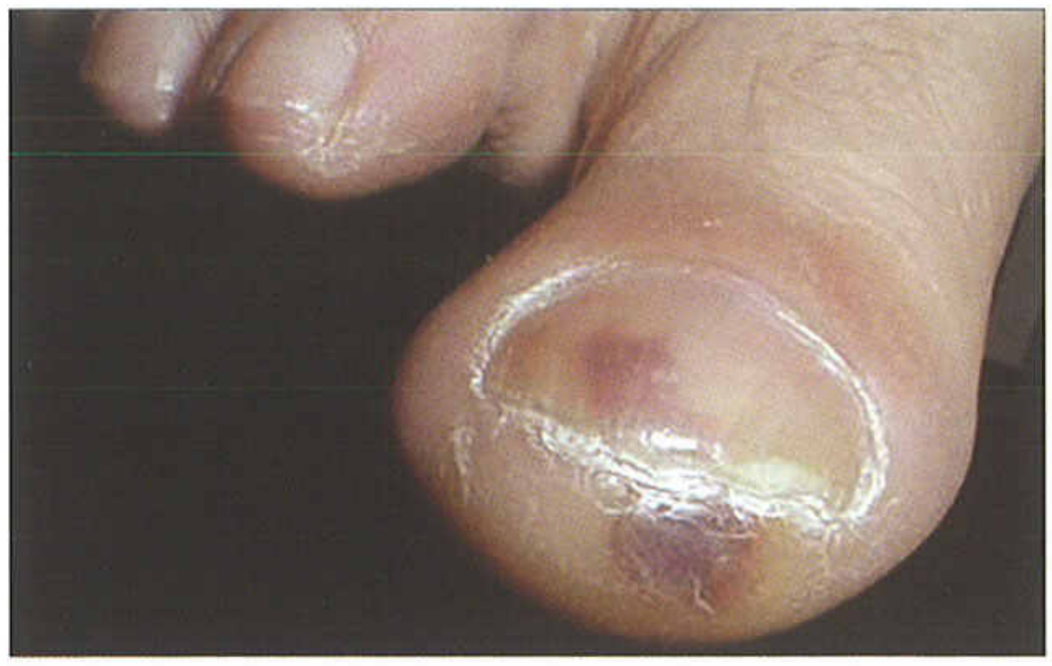

Fig. 9: longitudinal melanonychia

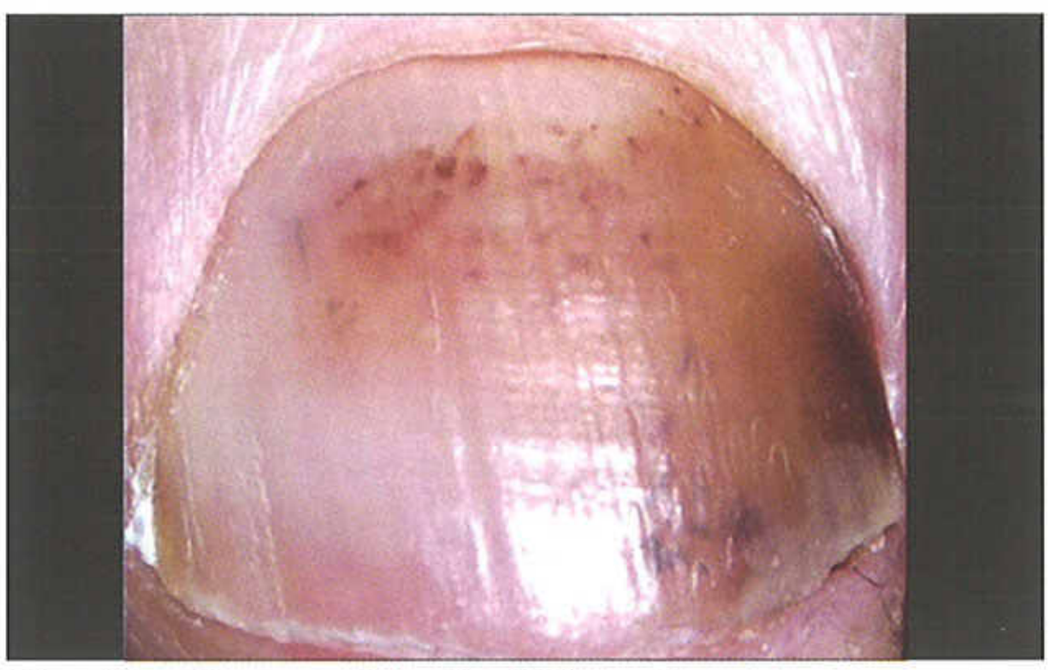

Fig. 10: pigmentation of nail from drug

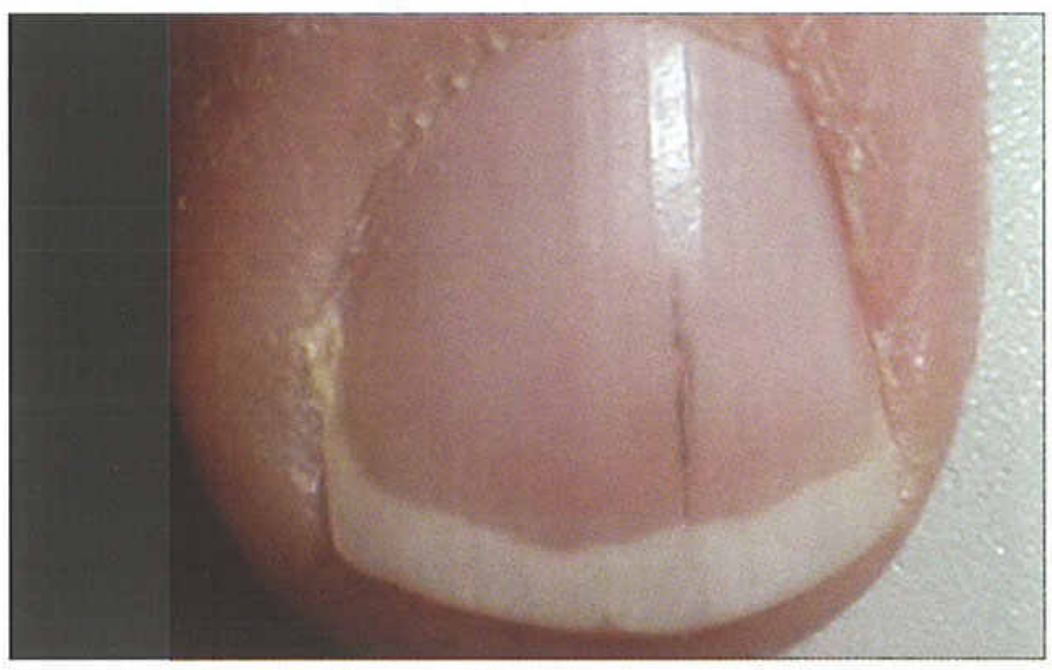

Fig. 11: striate melanonychia

3- Presence of Hutchinson's sign.
4- Variegate discoloration with brown as the prominent feature with varying coloration ranging from tan to black.
5- Nail dystrophy
6- Abrupt onset and blurred edges
7- History of dysplastic nevus syndrome or a previous diagnosis of melanoma
8- Presence in the thumb, great toe or index finger
9- Melanonychia striate longitudinalis with sudden widening.

It is a known fact that up to 20% of periungual and subungual melanomas are amelanotic [44].

In order to make a sure diagnosis of pigmented lesions of the nail a biopsy is mandatory despite that it may lead to a deformed nail but we should not miss the diagnosis of malignant melanoma which could be fatal to the patient if the diagnosis is missed.

D) A fourth discoloration of the nail is Yellow Nail Syndrome (Fig. [illegible])12·13·14

It is a rare syndrome characterized by yellow discoloration of nails, pleural effusion and lymphedema[45]. The syndrome may be associated with bronchiectasis, sinusitis, bronchitis and chronic respiratory infection [46]. The yellow color of the nail may precede or follow the appearance of lymphedema. The growth rate of the nail is reduced and its cuticle is missing [47] and some ridging may occur due to variation in growth [17].

The yellow nail syndrome was reported in association with thryoiditis [48], Raynaud's disease [49], rheumatoid arthrites [48], nephrotic syndrome [51], hypogammaglobulinemia [52], a single yellow nail may be associated with drugs, acquired immune deficiency disease or diabetes mellitus [6].

E) A fifth discoloration of the nail is due to Drugs, Toxins and injestants.

Drugs may produce changes in color, in growth or may cause deformity or shedding.

The nail color may be the only clue to exposure to drugs, chemicals, poisons or topical contactant. Tetracycline's may be associated with nails discoloration and photo induced onycholysis [53, 11] and produces yellow fluorescence under wood's light [54]. Minocycline rarely produces blue grey discoloration of proximal nail and is usually associated with pigmentation of other sites of skin [55]. Zidovudine (Retrovir) as antiviral used to treat HIV patients is associated with transverse pigmented bands of all fingers [56] and longitudinal melanonychia [57] and may produce finger and toe nail discoloration [58]. Antimalarial agents cause blue brown or slate grey pigmentation of nail bed or plate and topical hydroquinone may cause brown pigmentation of nails[59].

Chemotherapeutic agents may produce leukonychia or hyperpigmentation which may be diffuse or band like as seen in cyclophosphamide alone or in combination with doxorubicin [60], Blue nails are seen in Wilson's disease with deposition of copper through out the body and ochronosis [61]. Argyria as well as phenolphthalein used as laxative was associated with azure discoloration of lunula and phenothiazines impart a slate blue color to nails [62, 63].

F) Rare Congenital Syndrome causing nail discoloration:

1- Bluish color of nails is part of hereditary acrolabial telanjiectasia, which is also characterized by bluish color of nipple, areola and vermilion ridge of lips[64].
2- Tricho-odonto-onychial ectodermal dysplasia – The nails show punctuate leukonychia, longitudinal ridges and dystrophic nails [65].
3- Tricho-dento-osseus syndrome characterized by peeling brittle nails [66].
4- KID syndrome – autosomal recessive with keratitis, icthyosis, deafness and white finger nails [66].
5- Pachyonychia congenita (autosomal dominant) characterized by thickened dystrophic wedge shaped nails that become yellow or brown [66].
6- Progeria (autosomal recessive) the patient shows thin yellow atrophic brittle nails [66].

Second discussion is to cover in short some congenital and hereditary diseases involving the nails

Diseases and syndromes associated with atrophic nails changes:

1) The atrophic changes may be manifested by complete atrophy and absence of the nails where the matrix is absent and the proximal nail fold adheres to the nails bed known clinically as nail pterygium.
2) The atrophic changes may be manifested by poorly developed nail or partially developed nail due to varying degrees of matrix abnormalities that may result in thin narrow ridged longitudinally irregular grooved nail plate with isolated adhesions of skin of proximal nail fold to the nail plate.
3) Total or partial absence of nails may be seen with:
   (A) Blistering diseases as commonly seen in epidermolysis bullosa (Table 1).
   (B) Focal dermal hypoplasia with congenital localized absence of the skin with associated anomalies resembling epidermolysis bullosa [81,82,83]
   (C) Hidrotic ectodermal dysplasia with mildly dry skin, sebaceous hypoplasia, palmar keratosis, normal to slight alopecia, minimal dental anomalies, slight pigmentation around skin folds and nails which show atrophy and dystrophy [81, 84].
   (D) Anhidrotic ectodermal dysplasia, the nails show atrophy, no sweating, the skin is dry and hot, partial or complete atrichosis, various degrees of dental aplasia, cataract, saddle nose, prominent lips and characteristic features [81, 85].
   (E) Nail-patella-elbow syndrome (Fig. 15) with hypoplasia of matrix mainly affecting medial and lateral aspects of index, forefinger and thumb nails. Fingernails are involved more than toe nails. It is an autosomal dominant associated with a variety of bone anomalies including absence or hypoplasia of patellas, sublaxation of elbow joints, iliac horns and thickening of scapulas [87, 88]. Condition is often associated with proteinurea in 40% of patient with specific renal abnormality [89, 90, 91, 92]. Lester iris with an irregularly hyperpigmented papillary border [93].
   (F) Dyskeratosis Congenita (Fig. 16, 17, 18) atrophic nail, aplastic anemia, hypersplenism, heart block, bone anomalies, dysphagia, leukoplapkia oris, reticulated pigmentation.

(G) Familial pigmentation with nail atrophy with slight skin and mucosa atrophy with hyperpigmentation of trunk, palms and oral mucosa [97,,98].

Lester iris with an irregularly hyperpigmented papillary border [93]. In a typical case the nails are grossly defective being smaller and never reaching the free nail edge. Triangular lunulae when present are considered pathognomonic of the disorder [94], collagen fibrils are detected by electron microscopy in thickened basement membranes of renal glomeruli and is a specific renal abnormality [95]. The genetics of the disease have been recently elucidated with the identification of the causative gene on the long arm of chromosome 9 [97, 98].

(H) Chondroectodermal dysplasia with atrophy or absence of nails with teeth erupted already at birth with bone anomalies [102].

(I) Progeria (Hutchinson-Gilford syndrome) [103]

(J) Incontinentia pigmenti [104, 105]

(K) Acrocephalosyndactylia [81]

(L) Palatoglossus ankylosis, microglossia, hypodontia, anomalies of extremities [81].

4) Hypertrophic congenital nail change is seen in Pachyonychia congenita (P.C.) (Fig. [redacted] 19·20·21·22·23

PC consists of a group of inherited ectodermal disorders characterized by hypertrophic nail dystrophy. It is an autosomal dominant inherited disease. The most common two forms of PC are:

(a) PC-1 (Jadassohn-Lewandowsky type). The nails are normal at birth, and within several months the nails become thickened and discolored with increased transverse curvature and subungual hyperkeratosis [106]. It is associated with focal symmetric palmoplanter keratoderma with or without hyperhidrosis, angular cheilitis, follicular hyperkeratosis hoarseness and oral leukokeratosis.

(b) PC-2 (Jackson-Lawler type) has less severe nail thickening, minimal oral involvement and milder keratoderma [107]. It is readily distinguished by the presence of multiple steatocystomas that manifest mainly during puberty, pili torti and some cases may show erupted teeth at birth.

It is now known that the genetic cause of PC are mutations in 4 differentiation specific keratin genes that are expressed by the affected epithelia. PC-1 is due to mutations of keratin 16 (K16) gene located on chromosome 12 or its expression pattern, the K6a isoform of K6 located on chromosome 17 [108]. PC-2 is due to mutation in keratin 17 (K 17) gene or the K6b isoform, which are located on chromosome 17 and 12 respectively [109].

5) Periungual involvement in acrodermatitis enteropathica. There is paronychia but no nail hypertrophy. There is oral and nasal candida albicans infection. There is conjunctivitis. The skin shows periorificial dermatitis and dermatitis of groin and buttock. Patients suffer from diarrhoea and may have fibrocystic disease of pancreas or lung [110]. The disease is due to zinc deficiency. Candida albicans infection may involve the nails and may progress to nail shedding. The nail plate and nail bed may be dystrophic and may be thickenend and eventually may fall off.

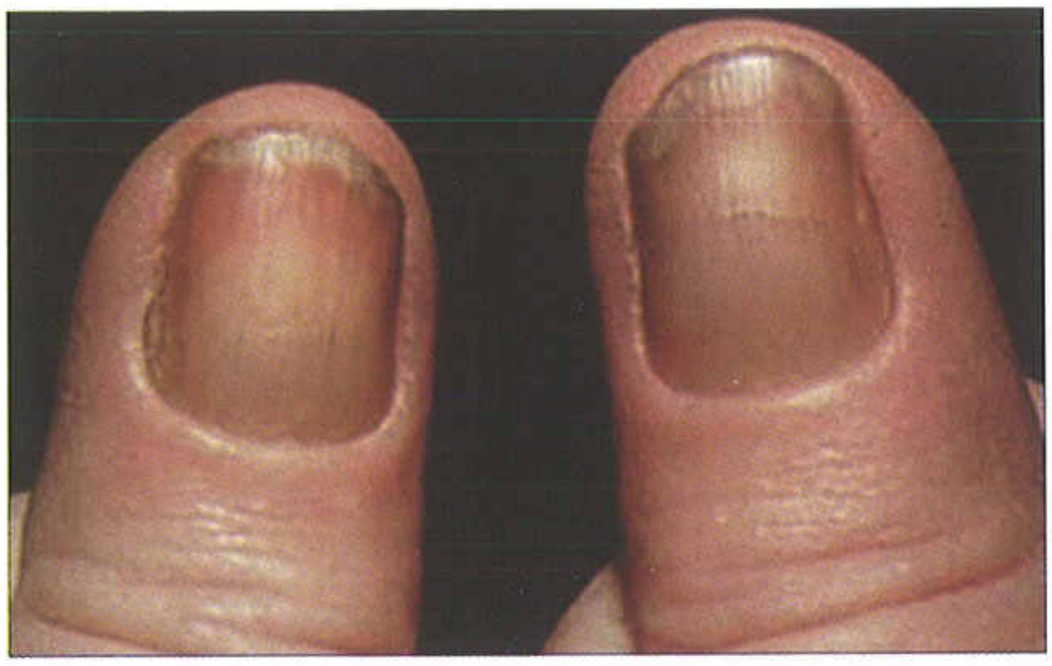

Fig. 12: yellow nail

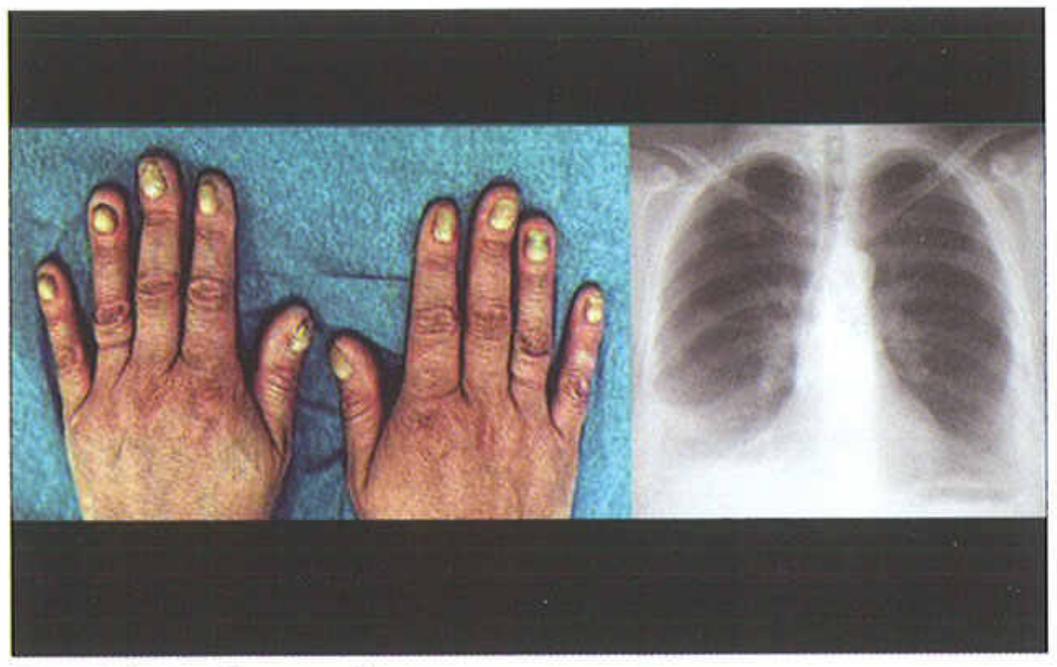

Fig. 13: yellow nail