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Editorial

Pigmentary disorders; an expanding area for research

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Pigmentary disorders are a complex group of dermatoses which may be genetically determined or acquired. Much progress has been made in pigment cell research and molecular biology in the last two decades. Based on this foundation, relatively rapid progress can be expected in the future, especially with the recent developments in the genomics and proteomics. Pigmentary disorders offer an exciting area for further research in basic sciences as well as in the clinical arena. Genetic basis of many hereditary pigmentary disorders may be unraveled in the near future. Effective treatment and controlling the progress of vitiligo and the understanding the mechanisms which determine postinflammatory hyper/hypopigmentation and manipulating these mechanisms to the patients' benefit will probably be the greatest challenges in the near future.

Nomenclature of certain pigmentary disorders; e.g. ashy dermaosois/ erythema dyschromicum pestans/eruptive macular hypermelanosis, progressive macular hypomelanosis etc, is confusing due to lack of understanding of pathophysiology. Another factor is that rare pigmentary disorders in different regions of the world are described by different names, due to lack of consensus on nomenclature.

The interest in this area has increased tremendously; partly because, the people of coloured skin outnumber the skin types I and II in the world now, and partly because more and more 'coloured people' in Asia and elsewhere have become concerned about even minor pigmentary abnormalities. Even the pharmaceutical companies invest heavily on research into treatment of acquired hypermelanoses. Where sophisticated laboratory facilities are not available, inter-laboratary and inter-country collaborative research become useful options.

Classifying pigmentary disorders

There are several ways that pigmentary disorders can be classified. Clinical basis aetiological basis and pathological basis are some of the methods of classifying pigmentary disorders. However pathological features of many pigmentary disorders are not specific for a particular condition. Where exact aetiology is not known, and the pathology is non specific, a clinical classification based on clinical features with secondary divisions on a pathologic basis where possible, would be useful to the clinician

In a clinical classification, an attempt should be made to include most known hyperpigmented, depigmented, hypopigmented and mixed pigmentary conditions[1-18]. Not only pigmentation due to melanin, but also other agents causing a 'hyperpigmented appearance' should be included for a clear understanding of numerous anomalies that afflict the human skin, leading to the discolouration of skin, apparent or real.

Visible (perceived) pigmentation may be due to 'visible colours' due to pathology at different levels; epicutaneous (external) e.g. silver, epidermal e.g. sun tanned skin, dermal e.g. postinflammatory hyperpigmentation, or subcutaneous e.g. haematoma.

Visible colour may be affected by factors other than true pigmentation; e.g. air trapping effect of scales of a psoriatic plaque, ambient light and relative colour contast. Melanin, and haemoglobin (to a lesser extent) are the main pigments that give the colour to a person's skin. In darkly pigmented skin, slight variations of perfusion are not clearly visible as 'erythema', as in the lightly pigmented skin. Bilirubin and beta carotene also play minor roles in physiological and pathological pigmentation.

Clinically, pigmentary disorders can be classified along the lines whether the lesions are hyper pigmented, depigmented, hypopigmented or with both features of hypo and hyper pigmentation (on the basis of visible colour). Then they may be subdivided whether the lesions are present at birth or manifesting later. Some of the conditions which are genetically determined, manifest many years after birth. Then may then be subclassified according to the nature of distribution; whether localized, or generalized. Later, the well known conditions may again be grouped under various patterns, such as linear, whorled, reticulated, guttate, patchy (large macules) or diffuse. Some diseases in various stages of evolution and resolution may fall into more than one category, going by the clinical features.

Generally, increased melanin content in the epidermal prickle cell layer gives the distinct colour of an individual. The number of melanocytes do not vary in different races, but it is the amount of melanin in the melanosomes and the distribution of the pigment and the melanosomes that make the difference among the Caucasians and the Blacks. In most of the Caucasians, the Indians and the Africans, the predominant pigment is eumelanin. In the Mongoloids and the Red headed Caucasians, the predominant pigment is pheomelanin. In different diseases, the pigment synthesis, transfer or destruction may be defective[5,10, 19-21]. The melanocytes are influenced by many factors including cytokines produced by the keratinocytes, lymphocytes and fibroblasts, hormones, and UV light. Infact, proper understanding of pigmentary disorders requires understanding of the 'multicelluar epidermal melanin unit'. In this, the melanocyte is the key player. The inherent genetic encoding expressed by the melanocyte is the most important determinant in a given person's general pigmentation. Tyrosinase is the most important enzyme in melanogenesis. A classic example is that absence of the gene that encodes for tyrosine causes oculocutaneous albinism.

Histopathologically, absence of melanocytes suggests vitiligo, melanophages in the dermis suggests post inflammatory hyperpigmentation (which could be due to numerous causes), melanocytes in the dermis suggests conditions such as Mongolian blue spot and Hori's naevus, deeper naevoid cells suggest a lesion such as a blue naevus. On the other hand, a 'clinically bluish lesion' may be due to a underlying vascular lesion such as a vascular malformation. Many other features have to be taken into consideration before making a final histopathological diagnosis. Electron microscopy reveals changes in the size, shape and numbers of melanosomes. Molecular biological assays reveal the chemical mediators involved in melamnogenesis. However these facilities are too costly for routine clinical use.

Some pigmented lesions are peculiar to a specific area e.g. melasma on the face, naevus of Ota around an eye, Peutz-Jeghers syndrome around the mouth. Some lesions are particularly common in certain age groups e.g. solar lentigo in the elderly, pustular melanosis in the neonates.

Some lesions are more common in certain skin types (races) e.g. ashy dermatoses, progressive macular confluent hypomelanosis in dark skinned races. Some conditions are transient e.g. post inflammatory hyperpigmentation. These features help narrow down the diagnosis in a given condition. Some conditions affect the skin and mucous membranes, some characteristically affect the skin only.

A comprehensive classification based on structural and ultrastructural details is not possible due to non-availability of comparable histopathological, immunohistochemical and electron microscopic data of many conditions. Basic light microscopic histopathological features alone are not diagnostic of many pigmentary disorders.

A strictly compartmentalized clinical classification is difficult in pigmentary disorders as one condition may present in many ways, some conditions overlap, very little is known about some conditions due to their rarity or pathology is not specific. Most accurate nomenclature will be on a gene basis (e.g. piebaldism is due to a genetic defect in c-kit gene, Griscelli syndrome is due to RAB & MYO5A defect). However, it is unlikely that all inherited pigmentary disorders will be genomically identified in the near future. More than one gene is involved in many diseases. In the OMIM (online Mendelian inheritance in man; a catalogue of human genes and genetic disorders, edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins), specific numbers have been allocated to known genodermatoses including pigmentary anomalies, making it easier to collate data for research. In this 6 digit numbering system the first digit indicates the mode of inheritance (e.g. AD,AR,XL,YL, Mitochondrial etc) of the gene involved. For clinical work this type of numbers are less practical.

Skin types[8,10, 22,23]

Fitzpatrick's classification of skin types is the most widely accepted classification still. This is based on visually perceived colour of skin and the dynamic ability of the skin to respond to UV light. This assessment is based on the individual's claim of burning or tanning capacity, and this classification is more suited for the light skinned Caucasians rather than tan coloured Asians or Black Africans.

Another limitation of this categorization is that individuals with coloured skin, have only a weak relationship between skin colour and minimal erythema dose(MED). Youn et al, in a study done in Korea has found that Korean skin has skin prototypes II to V and there was a range of MED from 50-90 mJ/cm^2. Leenuphong has recorded that Thai skin types included Type II to V, and that the constitutive skin colour did not correspond well with the Fitzpatrick classification. Furthermore, the MED also had varied greatly, and there was a significant amount of overlap between skin types.

Some Japanese workers have classified skin types into 3 types depending on sensitivity to UV and the propensity to sunburn or tan.

In general, the UVB MED of Fitzpatrick Type I skin would be around 15-30 mJ/cm^2, and that of dark brown or black skin could go upto 150 mJ/cm.

Another way of classifying skin types is based on the propensity of the skin to produce excessive amounts of pigmentation following an inflammatory stimulus. This type of classification helps predict post inflammatory hyperpigmentation following chemical peeling and laser resurfacing.

Objective measurement of pigmentation[24-30]

Objective measurement of skin colour has become popular in the recent past because of the limitations in the clinical assessments and classifications based on response to UV light. They too have some limitations depending on the mechanism of each instrument. These instruments are often used to assess the degree of erythema or increase or decrease of pigmentation in the same patient rather than compare the pigmentation of different individuals. Even in the same person different areas of the body have different intensities of pigmentation.

Light reflection from the skin depends on the air/stratum corneum interface (illumination angle, scales etc.) and scattering in and back scattering from deep structures particularly the dermis. High wavelengths (red) penetrate skin more deeply and undergo relatively greater absorption in the tissue, which is why the deeper tissue such as arteries and veins may be dominated by the contrast colour and look blue.

Measurement of skin colour can be made by using 2 different principles;

1. Spectrophotometric (e.g. Mexameter^R) – using broad band or selected wave lengths in visible light range, measuring absorbance and reflectance. Spectrophotometers can measure haemoglobin (Erythema Index) or melanin (Melanin Index) according to the colour characteristics.

2. Tristimulus colorimetry (e.g. Chromameter^R) – analysis of light reflected from skin structures using three colours; blue, red and green. Most commonly used system is the CIE (Commission International d'Eclairage) L*a*b* system established in 1976[24,25]. According to this system L* indicates lightness-darkness axis, a* indicates red-green axis and b* indicates blue-yellow axis.

Erythema index usually correlates well with a* values of the colorimeter. Melanin index is generally a better marker of pigmentation than L*. In general constitutively dark skin type have lower L* values, higher a* values and higher b* values than constitutively light skin types .

In most situations both types of instruments measure erythema and melanin well. Spectrophotometric measurements are superior in some situations. However, accurate independent measurement of colour and erythema are more difficult in darkly pigmented individuals.

The Asian perspective

In the Asian region, Japanese dermatologists and basic science researchers have done a yeoman service in research into pigmentary disorders. It is timely that the rest of the Asian countries also take an interest in pigment cell research rather than wait for the new knowledge to come from outside sources, describing the conditions prevalent in the Asian region. In the developing counties where most of the pigmented races live in, an effort should be made to collect data on the prevalence of various pigmentary disorders, psychosocial impact on the patients, comparative data on various treatment modalities, record clinical features, natural history, and inheritance pattern of rare pigmentary disorders. This will be a good foundation to do advanced collaborative pigment cell research. Advances in the standard of medical research in the Asian giants India and China are an encouraging trend in this respect. Currently, the only official Asian Pigment Cell Research Society in the International Federation of Pigment Cell Societies is the Japanese Society for Pigment Cell Research. Perhaps it is time to establish a vibrant pigment cell research group in Asia to complement the regional research groups in other parts of the world, such as the Pan American Society for Pigment Cell Research and the European Society for Pigment Cell Research.

Abnormalities of pigmentation cause severe psychosocial impact among the dark skinned patients, in addition to a diverse array of possibly associated anomalies of central nervous system, cardiovascular system, ocular and endocrine systems. More research in pigmentary disorders, originating in Asian countries, would be a necessity rather than a luxury, as Asia is the home for billions of people of 'coloured skin' who are relatively more visibly affected, by disorders of congenital and acquired pigmentary anomalies, compared to the Western World.

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