Pigment Anomalies Encountered in the Transkei

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SUMMARY

The function and production of pigmentation are discussed in relation to pigment anomalies encountered in the Transkei.

S. Afr. Med. J., **48**, 2345 (1974).

Pigmentation is generally believed to be a genetically determined, irreversible condition, yet it is well known that some birds, reptiles and mammals alter their pigmentation in conditions of changing climate, temperature and emotion. Certain diseases, e.g. Addison's, hyperthyroidism, cachexia and even schizophrenia, cause hyperpigmentation. Some chemicals can reduce pigmentation, and others increase it.

MELANOGENESIS

The embryonic neural crest is the site of origin of melanoblasts which, during development, migrate laterally and ventrally and eventually cover the whole integument or skin (every 4th - 5th cell in the epidermis is a secretory cell, the function of which is to manufacture melanin and supply it to the epithelial cells). These cells are also found in other parts of the body, e.g. the uveal tract of the eye, the hair bulbs and meninges of the brain. In mammals the melanocytes are derived from these melanoblasts, and in reptiles the melanophores are responsible for their rapid change in colour. Once the melanocytes have reached their destination, a chemical process takes place. Phenylalanine is converted into an amino acid, tyrosine, and in the presence of phenylalanase combines with peroxidase in the premelanocyte to form dopa. Eventually, through enzymatic activity in the presence of copper and zinc, dopa forms melanin, which is deposited on a protein to form the substance which gives colour to the skin, be it red, yellow or black.

The number of melanocytes in all humans, including albinos, is the same; the colour of the skin depends on the activity of the melanin cells, and not on the numbers. Melanin is by no means an inert substance. It is a biological electron exchange polymer, able, by means of its capacity for oxidation and reduction, and its stable free radical state, to protect melanin-containing tissue and its surroundings against reducing or oxidising conditions, which might otherwise set free those radicals capable of disrupting metabolism.

FACTORS WHICH INFLUENCE PIGMENTATION OF NORMAL SKIN

It is considered by Wassermann[1] and others that the darkly pigmented skin of persons living in the tropics is

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part of a general effective adaptation to the total tropical environment, and not only to sunlight. Tropical peoples, be they negroid, Indian or Malaysian, all have lowered adrenocortical activity and increased function of the reticulo-endothelial system, with increased phagocytic ability and gamma-globulin production. In other words, an increased defence mechanism has developed phylogenetically and individually to cope with the tropical milieu of malaria, parasites, bilharziasis, etc.

In lower vertebrates, the darkening or lightening of normal, functioning skin is caused by a dispersion or clumping, respectively, of melanin granules in the melanocytes. In mammals the change in skin colour depends on the transfer of melanin granules to epidermal cells in the 'epidermal melanin unit'. There are many factors which influence this action:

1. The pineal body is a light receptor in lower vertebrates and amphibians, and is thought to be one in mammals, through impulses received by the superior cervical ganglia from the optic nerve, hormones and stimulation of the preganglionic sympathetic fibres. It manufactures serotonin and melatonin from the amino acid tryptophan, an activity which is increased 15-fold in the dark. These substances in turn stimulate production of norepinephrine in the posterior ganglions, which in turn act on the melanocytes, causing clumping of granules and lightening of skin.[2]

2. Sex hormones influence activity of the melanocytes; oestrogen causes lightening, and progesterone darkening, of the skin, and so we have eunuchs with pale skins, and darkening of the skin in pregnant women and in non-pregnant women on the contraceptive pill.

3. Melanin production and transfer to epidermal cells are decreased, with consequent lightening of the skin, in adrenocortical activity, in anxiety, and in traumatic and emotional shock. This is due to the action of the adrenal cortex on the pituitary (α and β cells) and a suppression of melanocyte-stimulating hormone (MSH). Conversely, where there is suppression of the adrenal cortex, as in Addison's disease, there is darkening of the skin.

4. Psoralens increase the thickness of the epidermal layer of the skin with an accumulation of pigment cells which do not desquamate, and so the skin darkens.

5. Ultraviolet light suppresses the inhibitors of melanin formation, with resultant darkening of the skin.

6. Hydroquinones, originally found in the rubber industry, and now used cosmetically (in place of mercury) to lighten skin, act by inhibiting the action of tyrosinase and so prevent pigment formation.

7. Anything which combines with copper, e.g. mercury, gold, BAL and sulphahydrole groups, will cause lightening of the skin, since copper is the necessary metallo-enzyme for the tyrosine-to-melanin reaction. In the same way arsenic, which combines with the sulphahydrole group, releases copper and so increases pigmentation.

8. Severe inflammation of the basal layer of the skin causes a leucocyte phagocytosis of the melanin granules and transfer through the lymphocytes to the macrophages, and eventually to the lymph nodes.

UNUSUAL ANOMALIES OF PIGMENTATION

Abnormalities of pigmentation are more striking in the dark-skinned races, and in the Transkei many interesting anomalies have been encountered in disease and in health.

In tuberculosis of the skin we found hyperpigmentation and desquamation of the superficial layers of the skin. In erythematosus there were areas of hypopigmentation, with surrounding areas of hyperpigmentation, and this was found even on the feet. Lupus erythematosus presented in one case as depigmentation of the lower lip. This particular symptom of hypopigmentation of the lip, not as yet fully understood, is frequently found even among our oesophageal cancer patients.

Vitiligo

Vitiligo is quite commonly encountered. In this condition the epidermis is deficient in melanin and lacks tyrosinase-positive epidermal melanoblasts. It has been said to be caused by anxiety, migraine and dermatosis, and after tri-iodothyronine therapy for myxoedena. In congenital vitiligo there is a great deal of fibrous tissue in the vitiliginous skin, and the changing pH and abnormalities in gaseous exchange may account for lack of pigment. In none of the children examined was there any previous history to account for the gradual onset of loss of pigment in patches on the body, a condition which is actually aggravated by sunlight.

Albinism

Albinism is an autosomal recessive oculocutaneous deficiency of pigment. There are two types in Man. Melanocytes are present in both, as well as melanocyte-stimulating hormone and tyrosine. In the first type the enzyme tyrosinase is thought to be absent, and the fault lies with the conversion of tyrosine to melanin, so there is a total lack of pigment. In the second type the tyrosine-melanin conversion is intact, but there appears to be a fault in the transfer of melanoprotein across the cell membrane. The second type is more common in negroid races and, as the individuals age, there is some deposition of pigment in the form of freckles and increased colour of the eyes, with actual improvement in sight. The tyrosinase-negative type is more common in caucasoids, and these people never pigment.

The frequency of the genes for albinism is estimated at 1 in 40 000. However, in 1960 Dr Burrell kept a register of albinos in the Transkei, and found 500 cases. This gives a figure of 1 in every 3 000 cases, which confirms Dr Keen's figures for Soweto township in Johannesburg.

Of the 71 albinos in the Transkei examined by me, all appeared to be of the first type. Most of them had 'splotchy' freckles, and eyes varying in colour from blue to a yellowish khaki colour.

While examining the albinos, people with red skins were brought to me. These people usually have brown eyes, yellow hair and a red skin which, when young, is sensitive to the sun.

The 'red' people in New Guinea have been described by Walsh[3] and Harvey,[4] who claim that they are not related to albinos, although nystagmus and photophobia (albino characteristics) were present in some. However, on investigating the family histories of albino families, it was found that most had a member who was 'red', and all the 'red' people investigated had some albino relative; thus the only conclusion one can come to is that these 'red' people have a form of partial albinism, since the gene of albinism is not a single one.

Piebaldism

Piebaldism can be distinguished from albinism by the fact that, in the latter, the melanocytes are normal in number, whereas in the former, melanocytes are replaced by Langerhans clear cells in the depigmented areas, as in vitiligo. In piebaldism, however, the lack of pigment may be the result of defective melanocytes derived from genetically abnormal melanocyte clones.[5]

On examining a piebald boy, found in the Transkei, and comparing him with pictures of other piebald persons described in the literature, the most striking features in the ventral depigmentation were the white forelock and lower lip. This leads one to suppose that the fault is a developmental anomaly closely related to Waardenburg's syndrome.

Waardenburg's Syndrome

It is really rather amazing that Waardenburg's syndrome was first described in Europe as late as 1951.[6] Not long after, it was recognised in other countries, and in South Africa it was first described in 1962 by Scott and Van Beukering.[7] And yet I cannot believe that the condition can be so rare, for in a school for the deaf in Umtata (consisting of 165 deaf pupils) I found 3 cases in one day. Two of the children came from Natal and one from the Transkei. All 3 were totally deaf, 2 had beautiful, transparent blue eyes, all had heterochromia of the eyes, 1 had the characteristic white forelock, and the other 2 had grey hairs scattered over their heads, and patches of white hairs on their arms. The widening of the inner canthus of the eyes was marked in two of the children. Blepharophimosis was evident in one. It was impossible to get a familial history in any of the cases.

This syndrome is genetically determined and is basically a developmental fault in the neural crest, the site of origin for pigment cells and the auditory nerve. What is interesting about the condition is that these two seemingly unrelated factors, hearing and pigmentation, are in fact so closely related, and are both connected with survival. In fact, they always appear simultaneously in nesting animals some time after birth and in running animals at birth. A similar condition to Waardenburg's syndrome is found in the animal world, where completely albino cats with blue eyes are invariably deaf.

DISCUSSION

Pigmentation, apart from social implications, has received relatively little attention, considering how intimately it is related to survival factors, and thus to health, and protection from and susceptibility to cancer, and one wonders why so few observations on its function have been undertaken.

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