Some Factors Influencing Pigmentation

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Pigmentation according to the Oxford dictionary is the presence of a substance giving colour to animal tissue. In one sense the only human beings who are free from pigment are the ALBINOS, so that every human being should have a certain minimum of pigmentation in his body. This is found where melanin formation is active i.e. in the epidermis (not dermis), the uveal tract, meninges and arachnoid and in the intestinal endothelium.

The origin of the pigment cells was for long a debatable point and only recently has it been established to the satisfaction of most dermatologists that the pigment-forming cells are derived from the neural crest.

The amount of pigment in the skin (epidermis) of individuals from different races varies. At one end we have the platinum blond with practically white hair and very little pigment in the epidermis and at the other end we have the negroes — especially those living in the Ghana, Sierra Leone regions of Africa, which are practically on the Equator.

At this stage it might be worth while reviewing the changes in pigment of races living in the region of the Equator. We have negroes in North America (U.S.A. and Canada.) who by living in regions well away from the equator have gradually lost the "black" pigmentation but have acquired a "Chocolate brown" pigmentation, while the race of negroes known to be their ancestors are of a definitely much darker pigmentation. Here therefore we have the tendency of the negro living in temperate climates gradually, over centuries, to lose his pigmentation at least partially. At the other end we have the Central Americans, most of whom are of Spanish Portuguese or Italian stock and who are now of a much darker pigment than the stock from whom they are derived. A third point of some importance is, that some Ceylonese who live at a distance from the Equator are much darker than the Indians who actually live on the equatorial line. If the theory that the Indians were of European stock originally is believed it enhances the above conclusions that after the passage of centuries the amount of pigment found in a race of people will alter with the amount of sun present in the locality.

Whatever the reason for the difference in the pigment of the epidermis in different races, there is no doubt that its presence is protective. The pigment forming cells of the basal cell layer of the epidermis are not very numerous, but each one of them sends out dendritic processes which enter cells in the vicinity of these cells and when the stimulus to pigment formation occurs (e.g. exposure to the sun) they will inject melanin into these recipient cells. This pigment is deposited above the nucleus in much the same way as a cap.

Mary Rolls has set established the neural origin of these melanocytes; the method in which these cells can be stained, e.g. by methylene blue, is a further suggestion of the neural origin, since other cells of neural origin behave similarly. However, the best way to stain these cells is by 3-4-Dihydroxy-phenylalanine or DOPA used in a 1/1000 solution This substance can be seen to resemble in many ways tyrosine which in its turn is not very different from ascorbic acid. It may be interesting to note en passant that so many diseases of the skin with pigmentation often show a deficiency of suprarenal cortical activity as does for instance Addison's disease. At the same time it is also

known that the largest reservoir of Vitamin C in the human body is the suprarenal cortex. Whatever the relationship, however, the skin pigmentation can be rendered of a paler colour, by the simple process of administering Vitamin C (Ascorbic Acid).

The reaction which produces melanin depends on the action of Dopa on tyrosine, the catalyst being tyrosinase, and if irradiation of the skin is applied beforehand this results in pigmentation. Considerable study has been put into this reaction because as time goes on one sees greater needs for protection against irradiation of all sorts, because this type of melanin does not protect solely against the rays of the sun, but also against other electro-magnetic waves, including X-Ray. Other obvious uses come to mind; the finding of oil in Sahara, for example, requires that the Europeans have more pigmented skins in order to be able to resist the intense sun rays. In Northern Australia the settlers of Northern European stock are finding that they are getting skin cancer much more frequently and at an earlier age than those of Southern European Stock. It seems not impossible that the latter have inherited a more facile way of manufacturing pigment and thus of protecting their cells from the ravages of the sun.

It has already been intimated that there is a strong connection between the Central Nervous System and the skin pigment as well as between this and the suprarenal cortex; however the relationship goes further than that as regards hormones. The anterior pituitary is now known to produce M.S.H., the melanocyte stimulating hormone, formerly known as Intermedin. The production of this pigment is one of the important differences between Primary Suprarenal cortical deficiency or Addison's disease in which disease pigment is a most important feature, and Secondary Suprarenal Cortical deficiency as found in Simmond's disease. In the former disease, moreover, the dependence of the pigment on Suprarenal Cortical deficiency is further demonstrated, because of its disappearance during treatment with nothing else but hormones such as Prednisone. The explanation is, that the hormones formed by the suprarenal cortex inhibit the pituitary; in their absence the pituitary is stimulated into action (with the production among other things of an excess of M.S.H.) in an attempt to activate the atrophic or destroyed suprarenal cortex. As this does not — cannot — respond, the anterior pituitary tries harder and harder but the only thing that comes out of this exertion, is more pigment. As soon as treatment with steroids is started the anterior pituitary. is soothed down and no more (excessive) M.S.H. is produced.

In the Nephrotic Syndrome the same thing happens. The child (or adult for that matter) is both producing (and is often receiving) therapeutically large amounts of Coticosteroids — the result is that the epidermis loses most or all of its pigment and assumes a transparent, marble-like, non-pigmented appearance.

Again there is a group of diabetics in whom the skin seems to take on an angelic appearance with smooth shiny skin and rosy cheeks — these patients too show an almost complete absence of pigment.

Another most important relationship between pigment and hormone activity is to be noticed in the following experiments. If oestrogens are painted on one nipple and subsequently both nipples are exposed to the sun, only the painted nipple will darken in colour. While this experiment prima facie seems to imply that oestrogens aid in the production of pigment, yet it seems more likely that such a painting produces a reactive local concentration of androgens to neutralise the effect of the

oestrogens. Anyway whatever the explanation not much can be concluded from the experiment. On a different footing is the experiment which was carried out on a eunuch. Half his body was exposed to the sun while the other half was shaded. Two months later, a dose of androgens was given; pigmentation was noticed to appear, soon after, on that side of the body which had been exposed to the sun. This shows not only the effect of androgens on pigmentation but also the fact that the stimulus persists for a long time.

Finally, the hormonal influence on pigmentation can also be seen in pregnacy — not only does the skin become more sensitive to the sun rays and hence pigment formation but even in the absence of exposure to the sun, more pigment is deposited in the basal cells of the epidermis — cfr. the pigmentation of the vulva and nipples and the appearance of the linea nigra.

Up to this point an attempt has been made to tabulate the various substances which have an influence on pigment formation. It will, however, soon become apparent to even the casual observer that there must be other non-local causes, as well as local ones. The presence, for instance, of pigment associated with Chronic Heart, Lungs, Kidneys and Liver disease suggest that many influences have still to be found; for leaving apart the bile pigments as a source of pigmentation as well as haemosiderin or other iron pigments there will still be pigmented cases belonging to the above four groups. At the same time the influence of SH- containing amino acids, copper and the heavy metals on local pigment formation, is well recognised, and in fact the presence of anti-oxidants in rubber has resulted in the development of depigmentation in several individuals, a state which is reversible after a suitable period of time has elapsed since the stopping of exposure. On the other hand, many foods as well as local applications may sensitize the skin to the rays of the sun. Most fruits, for instance, as well as many vegetables seem to have this sensitizing effect; while on the other hand many a woman has come up with a tear drop (or larger) area of pigmentation, which was the result of localised increase in pigmentation, produced by the volatile essential oils in the perfume: this is otherwise known as Berloque Dermatitis Tar is another substance well known as a skin sensitizer and with an increasing number of workers being exposed to it for a greater number of years (in road surfacing) we are likely to meet, more often than formerly, with skin cancer.

The administration of arsenic has been stopped by everybody practically, but there are still a few doctors especially those with the "Italian School Influence" who still tend to use it. Arsenic produces pigmentation too, but apart from that it also produces cancer and hence one should be more reluctant to use it medicinally either for internal or external diseases.

Finally the association of pigment on the skin and on the internal mucosa (cfr. the correlation between these two described earlier) together with the appearance of malignant tumours of the small intestine has been described under the Peutz-Jeghers Syndrome and two cases were demonstrated 2 years ago here in Malta.