prices for pharmaceutical products, especially patented ones, are so severely controlled that production is scarcely profitable, there will be little incentive to engage in research and development and little money to finance it. This then reverts to the point made earlier: the extent to which prices for patented products will be allowed to rise above those that would prevail in a non-patent situation is essentially related to the incentives that the government wishes to provide for research aimed at the development of new drugs.

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Aetiopathogenesis and Treatment of Vitiligo

Vitiligo, also known as leukoderma, is an acquired disorder characterized by patchy progressive depigmentation of the skin. It affects 1% of the world's population with the incidence in India ranging from 6% in Calcutta to 1.25% in Delhi. As there have been good reviews on this subject recently\(^1\)\(^4\) where the neural, autoimmune and free radical hypotheses were discussed, I will only deal with areas which have been left largely uncovered, i.e. its aetiopathogenesis and treatment.

It is generally agreed that there are no functional melanocytes in the vitiligo macule\(^1\)\(^4\) but none of the many theories put forward explain the causes for their loss.\(^1\)\(^4\) After methods for getting pure cultures of melanocytes from baby foreskin and other sites became established,\(^5\) attempts to study the abnormality responsible for the premature loss or destruction of the melanocytes were made by Puri et al.\(^6\) To do this they examined the epidermis from three different regions of untreated vitiligo subjects, namely uninvolved skin, perilesional skin and the vitiligo patch.

Melanocytes from uninvolved skin of untreated vitiligo subjects in culture manifest a lag period in the onset of their growth of about 6 to 11 days while the melanocytes from normal adult humans do not show any such lag. Also the number of melanocytes observed 48 hours after plating 10\(^6\) epidermal
cells from the uninvolved area was only half the number observed after plating the same number of cells from normal adults. This was in spite of the fact that the melanocyte cell number in uninvolved, untreated vitiligo epidermis was the same as that in normal humans. The melanocytes from an uninvolved area of untreated vitiligo subjects can also not be passaged, i.e. they do not survive detachment by trypsinization, while melanocytes from normal humans survive many such detachments from culture dishes.6

The melanocytes from perilesional areas of untreated vitiligo patients do not grow at all in culture and show an abnormal morphology compared to cells from an uninvolved area.6

If these abnormal growth characteristics were related to the disease, one would expect that they would be corrected once the individual was treated successfully. In fact they were corrected using psoralens, ultraviolet A (PUVA) therapy.7 That repigmentation by PUVA therapy might have been a result of increased growth factors for melanocytes in the circulation is indicated by the fact that serum from repigmenting vitiligo subjects increases the proliferation rate of melanocytes from normal human beings and that the serum from normal adults is more stimulatory to the growth of melanocytes from normal or treated vitiligo subjects than the serum from untreated vitiligo subjects. 7

A new hypothesis for the aetiology of vitiligo was thus postulated, that a deficiency of growth factor for melanocytes, locally or in the circulation could result in their premature loss.7

It is also commonly believed that vitiligo is transmitted as an autosomal dominant trait with incomplete penetrance. For example, in a border area of Gujarat and Maharashtra there is a community known as Somavamsha Sahasajuna Kshatriya (SSK), some of them migrated to Bangalore many centuries ago. This community has a number of parallel relationships with the Khatri community of South Gujarat which has a high incidence (3.6%) of vitiligo in this country.8 Both these communities belong to the Kshatriya caste and work in the silk industry. The small number of SSKs in Bangalore have been marrying within their community for centuries. At the request of their leaders who felt that the high incidence of vitiligo should be investigated, we took detailed histories and examined 52 cases. The onset of vitiligo in this community was earlier than in the general population9 and 47 (90%) of the patients had close relatives with the condition.9 This suggests a genetic predisposition.10 Others too, in this country11 and in the USA,12 have found that there is a familial basis for vitiligo.

These observations are further strengthened by a report that 7 twins out of 10 genetically identical pairs were affected by vitiligo while only 1 was affected in 11 fraternal pairs.13 The age of onset and in some cases the areas of skin involved were remarkably similar in the genetically identical pairs.13

Further evidence on the genetic predisposition for vitiligo comes from studies on the depigmenting mouse labelled the vit/vit mouse by Lerner.14 This is one of the most promising animal models for human vitiligo, and it has been found that the vit gene of the vit/vit mouse maps to the mi locus of the laboratory mouse.15 The human homologue of the mi gene of the mouse has now been cloned.16 It now remains to be seen whether mutations in the human homologue of this gene are related to the pathology of vitiligo.

The standard treatment of vitiligo is PUVA which is the most effective therapy available for repigmentation of vitiliginous patches. This has its roots in the original description of the disease in the Atharva Veda where the oral intake of an oily extract of the seeds of the psoralen containing Psoralia corylifolia (Bouchi, Bavachi and Vasuchika) was advocated followed by exposure to sun. PUVA helps about 50% of patients.

Other treatments include melagenina, an alcoholic extract of human placenta, which has been advocated by Cuban dermatologists. Unfortunately there is not much scientific evidence to support this treatment because
experimentally melagenina, with or without exposure to ultraviolet light for periods up to 6–8 weeks, produces no effects on melanocytes. The addition of melagenina to cultures of human or murine melanocytes also does not affect growth rates or tyrosinase activity. Finally, double-blind placebo-controlled studies done in Venezuela, Mexico and India do not confirm the claims of Cuban investigators.

Recently, mini pulse therapy with betamethasone was tried on vitiligo patients who have extensive or fast spreading disease with a 40% success rate.

Surgical methods have been developed in the last few years in cases where vitiligo is stable, limited to a few patches and unresponsive to other treatments. The techniques range from autologous epidermal punch grafts, epidermal grafts obtained from suction blisters and autologous melanocyte transplants. The transplants are performed after culturing melanocytes alone or with keratinocytes from the uninvolved epidermis of patients, expanding the cell numbers in culture and when their growth reaches confluency, adding calcium chloride to the culture medium resulting in differentiation of the keratinocytes. The multi-layered cell sheet thus obtained is detached from the culture dishes by sterile petrolatum gauze and transplanted on to dermabraded vitiligo macules under local anaesthesia.

I have little doubt that the genes responsible for vitiligo and the triggering factors are likely to be identified soon and more efficient methods of treatment will be available within the next 4 to 5 years.

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