VITILIGO

A REVIEW AND REPORT OF TREATMENT OF 60 CASES IN THE GENERAL HOSPITAL, SINGAPORE FROM 1954 - 1958

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As recently as 10 years ago, the problem of vitiligo was largely unsolved. In one sense, it was because many doctors were not sure what this condition was and whether what they called vitiligo was a mixed bag of conditions variously labelled leucoderma. The problem is world-wide and at least in our part of the world and I refer not only to Malaya but to South-East-Asia, it can be a very importment disease. Some years ago, when Prime Minister Pandit Nehru spoke before a group of drug manufacturers, he expressed the hope that patients with the three most important diseases in India — tuberculosis, leprosy and vitiligo should be helped with the advances in therapy. One could spend a lot of time on this fascinating subject, but perhaps with the time at our disposal it is best to proceed to the pathological physiology of the condition and then to discuss the clinical aspect and, lastly, to round it up with the therapy that is at present available to the medical profession.

It was Laennec himself who made the historical report on melanoma in 1826 in his treatise on auscultation. The discovery of the microscope made it possible for the closest study of the black pigment that had been previously described in the skin. In 1917, Bloch and Ryhiner reported that when frozen sections of fresh human skins were placed in 1 :1,000 aqueous solution of L-3, 4 dihydroxyphenylalanine called "DOPA" for short, at pH 7.4 developed a blackening of dendritic cells at the epidermo-dermal junction. Bloch called such cells "Melanoblasts". Blackening also occurred in leucocytes and in active cytochrome systems. The origin of melanoblasts from the neural crest has been demonstrated by Dushane in 1943. This experimental method for amphibians cannot be used in the case of man in whom the similarity of melanoblast and melanocytes to nervous cells by staining methods with methylene blue, gold and silver, resistance to x'ray therapy on the part of melanoma as are most malignant nervous tumours and for other reasons, have convinced most workers that these cells are of nervous origin. Thus the melanocyte is a specialised cell which is distinct from other cells and is characterised by one, two or more dendritic processes. It contains in its pigmented form large numbers of light or dark brown cytoplasmic granules. The melanocyte is derived from the melanoblast which as mentioned before arises in the neural crest and the outer layer of the optic cup and migrates during the neonatal life to three principal sites, namely (1) the skin, chiefly the epidermal-dermal junction of the skin. (2) the mucous membrane and the hair bulb, (3) the central nervous system, mainly the leptomeninges and the eye including the uveal tract and the retina. (Fig. 1). In the skin, melanocytes form a horizontal network at the plane of the dermo-epidermal zone and are closely integrated with the epidermal cells which it establishes contact by means of its numerous cytoplasmic processes, giving rise to the appearance of a fish net when viewed as a whole section. In its close proximity to the epidermal cells, the melanocytes are able to transfer melanin granules into the adjacent epidermal cells. This function of melanocytes has been termed cytocrine by Masson in 1948. As the epidermal cells moved outwards to become the stratum corneum, the melanin granules contained within them are carried along and appear in the latter area not as granules but as fine pigmented particles which are irregular in size. In Negroid peoples, the stratum corneum is regularly flecked with fine melanic particles. In contrast the stratum corneum of caucasians is not ordinarily pigmented except after exposure of ionizing and ultra-violet radiation. It has been shown by Thomson (1955) that the greater tolerance of negroid skin to ultra-violet exposure was relacted to the degree of melanisation of the stratum corneum. It was formerly believed that this was caused by a greater thickness of the stratum corneum in negroid skins. Thomson therefore has shown conclusively that it was due to melanisation rather than thickness which in fact is the same as caucasians. In 1954, Szabo showed melanocytes are symmetrically distributed and do not differ significantly in shape, size and population density in various races. Therefore variations in skin colour between racial groups and also between different individuals of the same race are related not to the number of melanocytes but to the rate and amount of melanin production by the melanocytes. Hyperpigmentation of the skin is the result generally of an increase rate of melanin formation in pre-existing melanocytes and not due to increase in the melanocyte population. It has been known for some time that tyrosine was probably the mother substance of melanin. It seems DOPA could

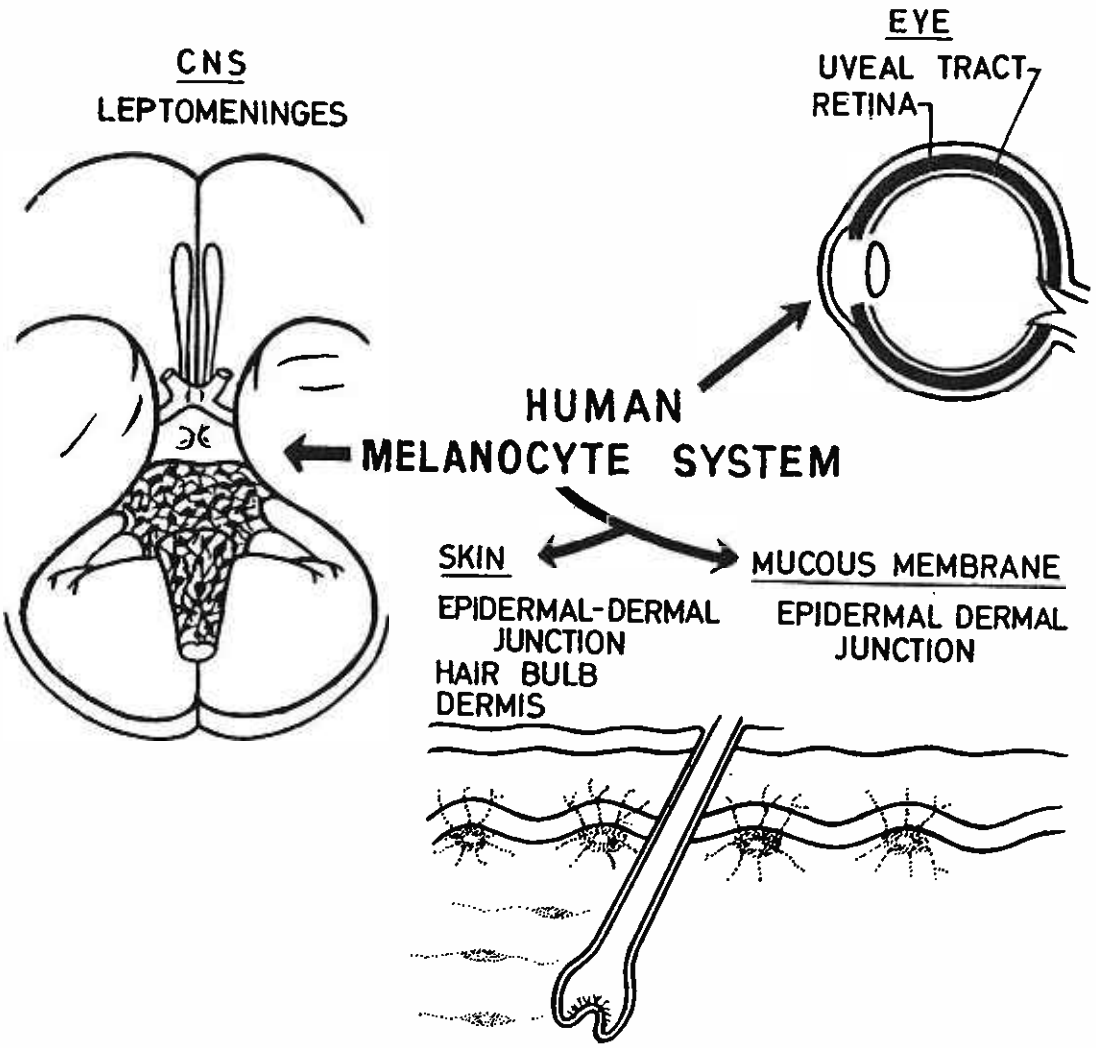

Fig. 1. Human Melanocyte System. (After Fitzpatrick and Szabo (1959).

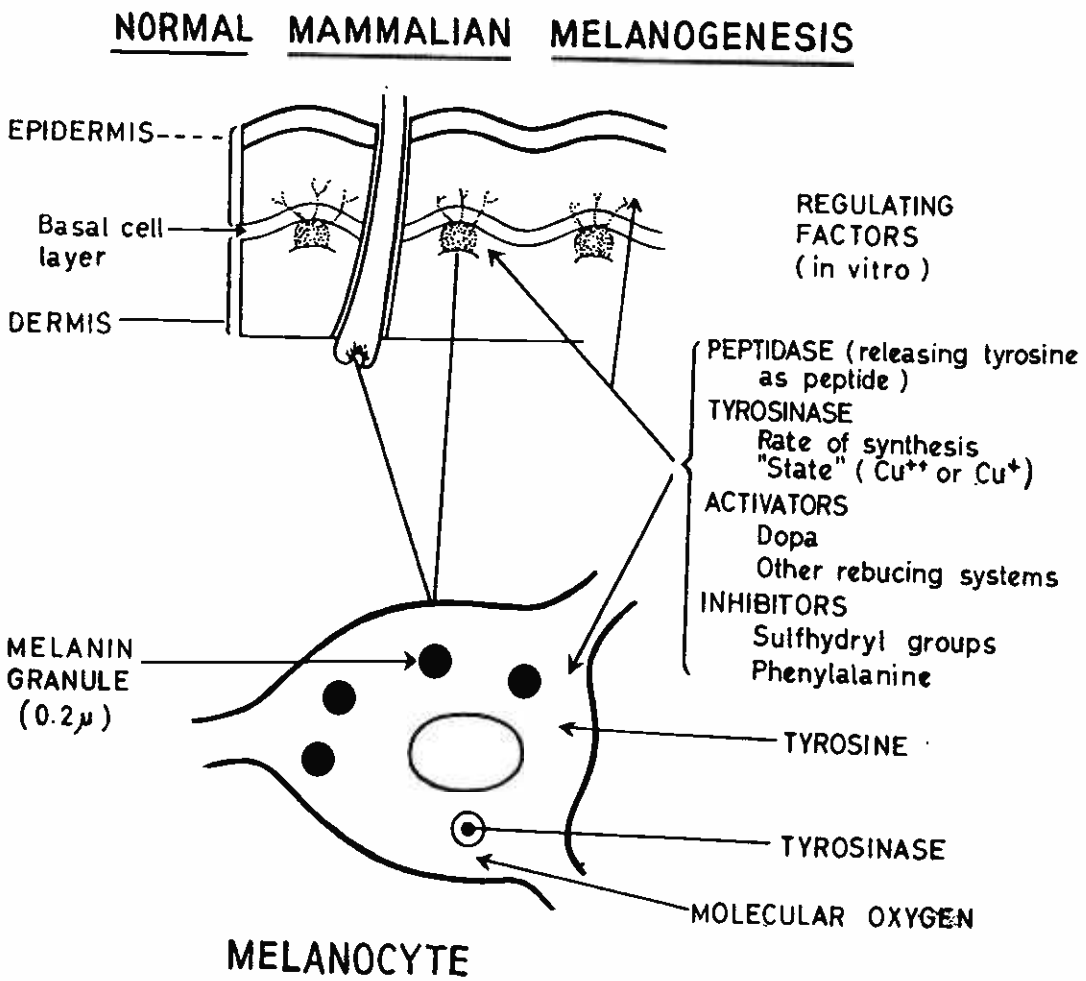

Fig. 2. (After Fitzpatrick and Szabo). Showing factors regulating mammalian melanogensis.

not be shown in the human skin. Fitzpatrick et al in 1950 demonstrated the tyrosine reaction which corresponds closely with the DOPA reaction but the former is specific while the DOPA reaction is not. Melanin is a protein conjugate formed by the coupling of a quininoid polymer, indole-6-quinone with protein. This polymerization and coupling occur on the surface of a subcellular cytoplasmic particle, the melanin granule. The quininoid polymer is derived from the amino acid, tyrosine, by a chemical reaction catalysed by an aerobic oxidase, tyrosinase which is attached to the melanin granule.

Various factors determine the rate and amount of melanin information: (1) The availability of tyrosine, the melanin procursor, (2) the rate of tyrosine synthesis, (3) the presence of factors that activate tyrosinase *e.g.* DOPA, (4) the presence of naturally occuring inhibitors of the tyrosine-melanin pathway, *e.g.* Phenylalanine and Sulfhydryl groups. (Fig. 2) There is also an inverse relationship of tyrosinase activity to melanisation of the melanin granule. With exposure to sunlight three types of reaction taken place — (1) melanin darkening, (2) melanin migration and (3) melanin formation. (Blum 1945).

(1) Melanin darkening appears within minutes after exposure to relatively long wavelength (3,000 - 4,200 A) with a maximally effective action spectrum of 3,400 A. The rapidity of the response makes it hightly unlikely that melanin synthesis could occur. (2) Several days after exposure to sunlight or ultra-violet light, melanocytes become "dendritic" and this has been interpreted as due to melanin migration. These dendritic melanocytes are also seen in Addison's disease and post-inflammatory states. The dendritic appearance is due to packing of the melanocytes with newly-formed melanin granules. (3) Lastly, melanin formation which follows exposure to ultra-violet light is the result of an increased melanogenesis in the pre-existing melanocytes and not due to melanocyte proliferation. The effective wavelengths for melanin formation is 2,800 to 3,100A.

In 1956, Lee and Lerner announced the isolation of two melanocyte stimulating hormones, alpha and beta MSH which are polypeptides from the hog pituitary gland. Injection of MSH in man causes rapid darkening of the skin and is alleged to cause formation of pigmented naevi. There is much evidence that in man, MSH from the intermediate lobe of the pituitary gland is a potent darkening agent in conditions such as Addision's disease, tumours of the pituitary gland, hyperthyroidism and chronic illnesses such as malnutrition and tuberculosis. In 1958, Lerner and his co-workers described the isolation of a lightening agent from the pineal glands of cows. This hormone, designated Melatonin, is a 5-hydroxyindole compound which is probably produced from the metabolism of the amino-acid, tryptophane. Other hormones, such as adrenaline, nor-adrenaline, acetylcholine, serotonin and tri-iodothyronine are known to lighten frog melanocytes. However, melatonin is 10^5 times as effective as nor-adrenaline in its action on the frog's skin. Melatonin has been demonstrated in human pineal glands and bovine hypothalamus and peripheral nerves by Lerner and his co-workers (1959). The lightening action of nor-adrenaline, adrenaline and serotonin can be reversed by ergotamine and related substances, but the effect of tri-iodothyronine and melatonin is not reversed by these adrenergic blocking agents. When MSH is added to pigment cells, melanin granules clumped about the nucleus escape out towards the periphery and become uniformly distributed, so that the melanocyte becomes opaque. Addition of Melatonin reverses this process, the granules stream back towards the centre and most of the cells appear transparent (Fig. 3)

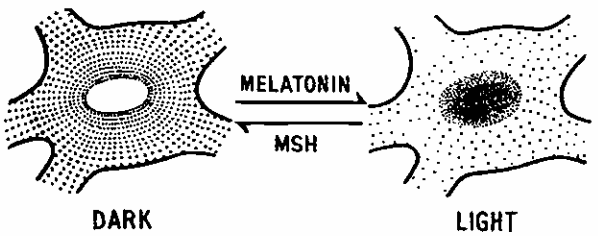

Fig. 3. (After Lerner and Case (1959). Showing dispersion and aggregation of pigment granules in frog melanocytes is a reversible reaction.

With the progress in knowledge of vitiligo, it is not easy to give a clear-cut definition. The textbook of Ormsby-Montgomery, (1954) defines it thus: "Vitiligo is an acquired cutaneous achromia characterised by variously-sized and shaped single or multiple patches of milk white colour, usually presenting hyperpigmented borders and tendency to enlarge peripherally". Becker, Jr. et al in 1952 demonstrated the presence of junction cells corresponding to melanocytes, but lacking the ability to form pigment, in sections of vitiligo. These "clear cells" or "White melanocytes" can be seen at the dermal-epidermal junction in haemotoxyline-eosin stained section. There is absence of enzyme activity when the sections are treated with DOPA or tyrosine and therefore there are no melanin granules in the melanocytes or epidermal cells. On the other hand, at the border of the vitiliginious area there are unusually large, highly dendritic, and highly melanized cells. In this border, one can also find melanin-carrying

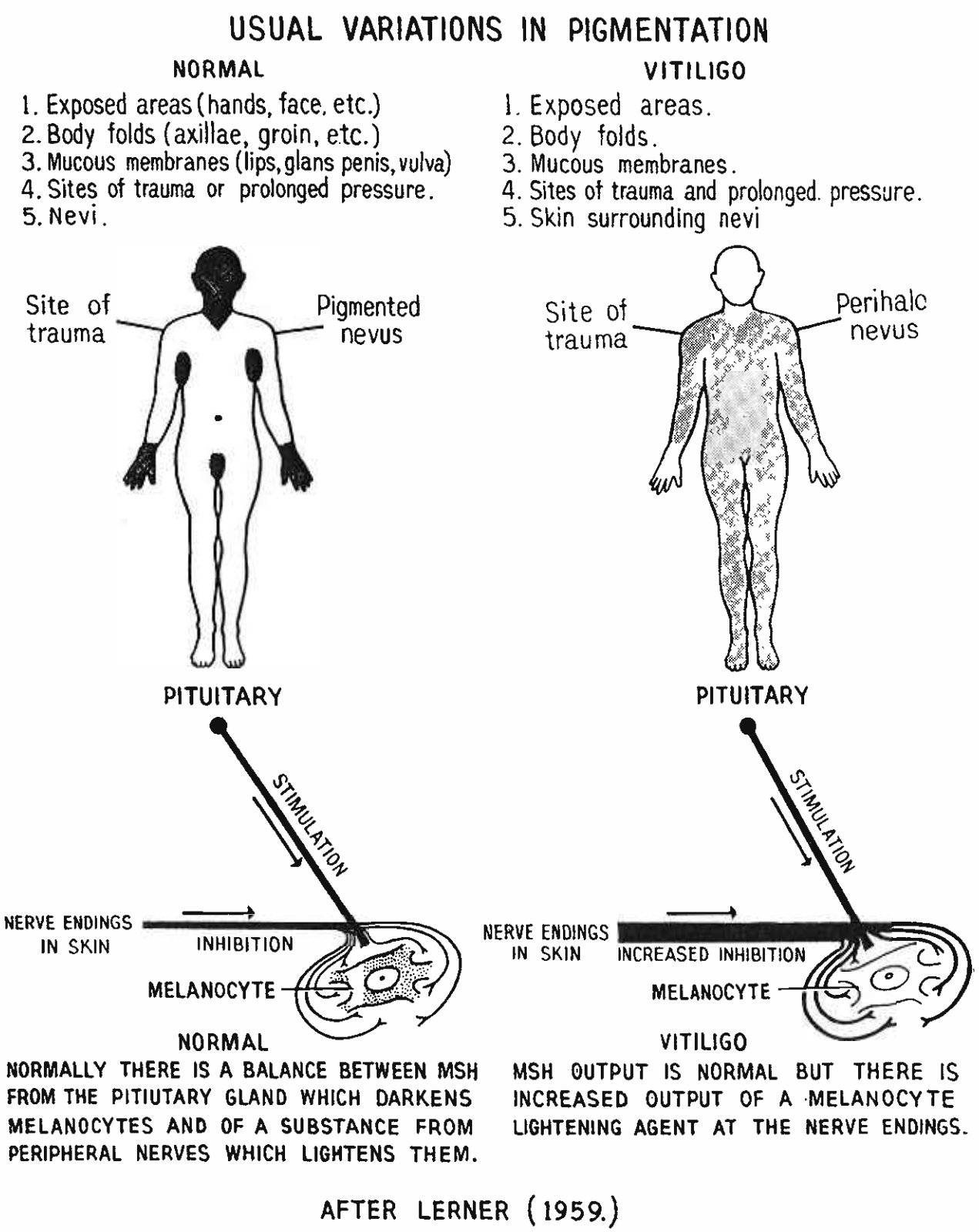

Fig. 4. Comparison of sites of pigmentation in normal and in Vitiligo.

macrophages in the cutis and ofter there is some inflammatory infiltration around the blood cells in the epidermis. Exchange transplantation between normal and vitiliginious area have given somewhat contradictory results. Haxthausen (1947) found that split skin grafts change colour quickly. Spencer (1951) and later Spencer and Tolmach (1952) found that full thickness grafts preserve their original characteristics for as long as sixteen months. From Japan, Kato (1955) confirmed this difference in the reaction of thin and thick grafts. On the whole, results seem to indicate that there is no marked anatomical change but purely a functional disability of the melanocytes. In the cases where re-pigmentation occur, the vitiliginious area does not gradually darken but the pigmentation takes place either spontaneously or under treatment with psoralens by creeping extension of the pigment from the margins or from perifollicular foci, which presumes a transfer of new pigment from the melanocytes in the hair bulb. Pinkus in 1959 postulates one of two mechanisms: (i) either in a hereditary change of melanocytes in certain foci and these abnormal achromatic melanocytes multiply and push back the normal ones. When re-pigmentation occurs, the abnormal cells are crowded out by the normal melanocytes. (ii) The other hypothesis is that there is an inhibition of pigment formation which seems to "infect" the neighbouring cells. Inhibition may result from enzyme blockage or from actual loss of the enzyme-forming mechanism. In this case, repigmentation either takes place by infectious spread of either the enzymatic mechanism or an unblocking agent. Lerner (1959) believes that vitiligo results from increased output at the peripheral nerve endings of a substance that lightens melanocytes. (Fig. 4).

Metabolic investigation Lerner carried out a very comprehensive metabolic study in his series in 1959. The patients were examined for urine nor-adrenaline, 17-ketosteroids, and melanocyte stimulating hormone excretion, gastric analysis before and after histamine, serum protein bound-iodine, I^{131} uptake by the thyroid glands, basal metabolic rate, serum copper, thymol turbidity, cephalin cholesterol flocculation, skin temperature and sweat measurements. Lerner found no difference in the excretion pattern of nor-adrenaline. He concluded that the average female patient with vitiligo secretes less than the normal amount of free HCl after histamine challenge. The capacity of the sweat glands to react is the same in vitiliginous and pigmented areas. However, it would appear that there may be greater activity of the sweat glands in the areas of vitiligo than in non-vitiliginious site. With regard to skin temperature, thermocouple readings showed little changes in temperature. Although vitiligo had been reported in early hyperthyroidism and Grave's disease, it is known that hyperpigmentation is often the case with the latter condition. Robert had observed elevated B.M.R. in 10 out of 50 patients with vitiligo. However, Lerner using the serum protein bound-iodine (PBI) found that the PBI test in 24 patients was within normal limits. With regard to I^{131} uptake, in 20 patients the results were elevated in 2 and the lower limits of normal in 1. He concludes that most patients with vitiligo have normal thyroid function. With regard to 17-ketosteroid excretion, 4 out of 5 males and 4 out of 15 females had low 17-ketosteroids values. A most interesting result is the measurement of the excretion of MSH in 22 cases. In 20 the values were within normal limits. Lerner concludes therefore that adrenal-cortical function was normal because if it were decreased there would have been a corresponding increase in the release of MSH. The results are in conflict with the previous values of 17-ketosteroids, the low values suggesting hypoadrenalism. Serum copper estimations in 12 cases were normal. Liver function tests were carried out in 25 patients. With one single exception, the tests were normal. Lerner concludes that vitiligo occurs in people whose general state of health is good. The relationship between vitiligo and central nervous system lesions was very well demonstrated in a case which Lerner described. This female patient had transverse myelitis with paralysis below the waist. She developed vitiligo on the face and the upper portion of the body, the neck, axillae, arms and hands. Below the leval of cord damage, there was no vitiligo, unlike the classical case. She underwent a hysterectomy and there was no depigmentation at or near the surgical scar. This patient had a family history of vitiligo. The finding of increased sweating in the vitiliginious area by Lerner (1954) together with the report of vasoconstriction by Miramarosi and Nogy in 1950 suggest that there is some type of increased adrenergic nerve ending activity in areas of vitiligo. Lerner also cited ample evidence that in animals, such as frogs and fish, neurogenic control of the melanocytes can be demonstrated. Cutting sympathetic fibres to the fish fin results in hyperpigmentation of the fin distal to the ligation. This hyperpigmentation persists until the nerves regenerate. Faradic stimulation of the nerve supplying the fin results in a marked lightening of the fin. And of course, the lightening agent melatonin, which is present in peripheral nerves and is more potent than nor-adrenaline and serotonin can decrease the melanin content of normal frog skin and of melanomas in hamsters. One could therefore conclude that vitiligo is a result

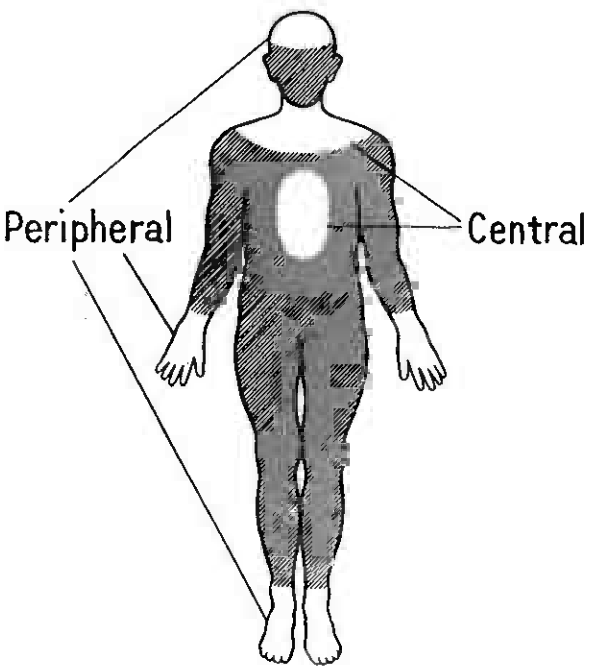

Fig. 5. Central and Peripheral Vitiligo.

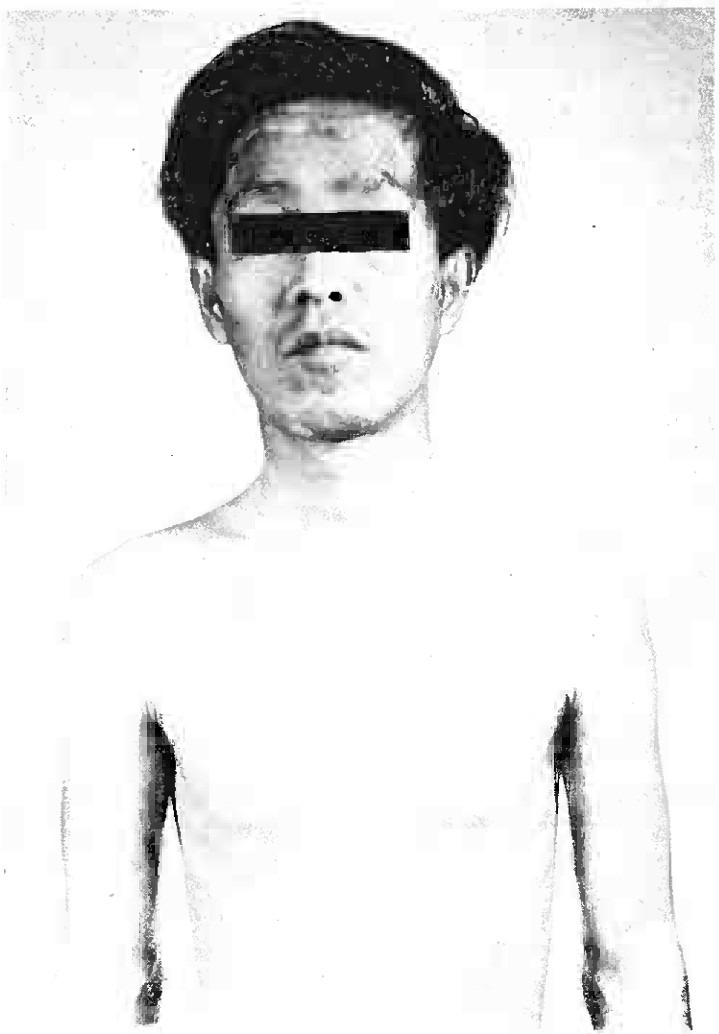

Fig. 6. Vitiligo in a Japanese. Front view — Central Punctate lesions.

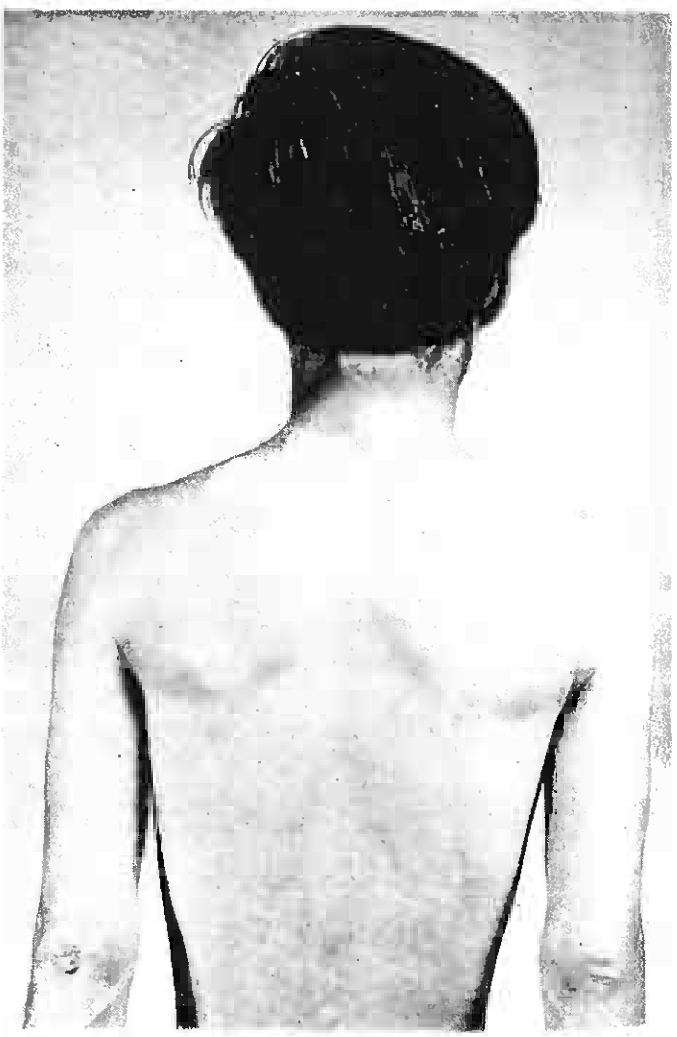

Fig. 7. Vitiligo in a Japanese. Back veiw — Central Blotchy lesions.

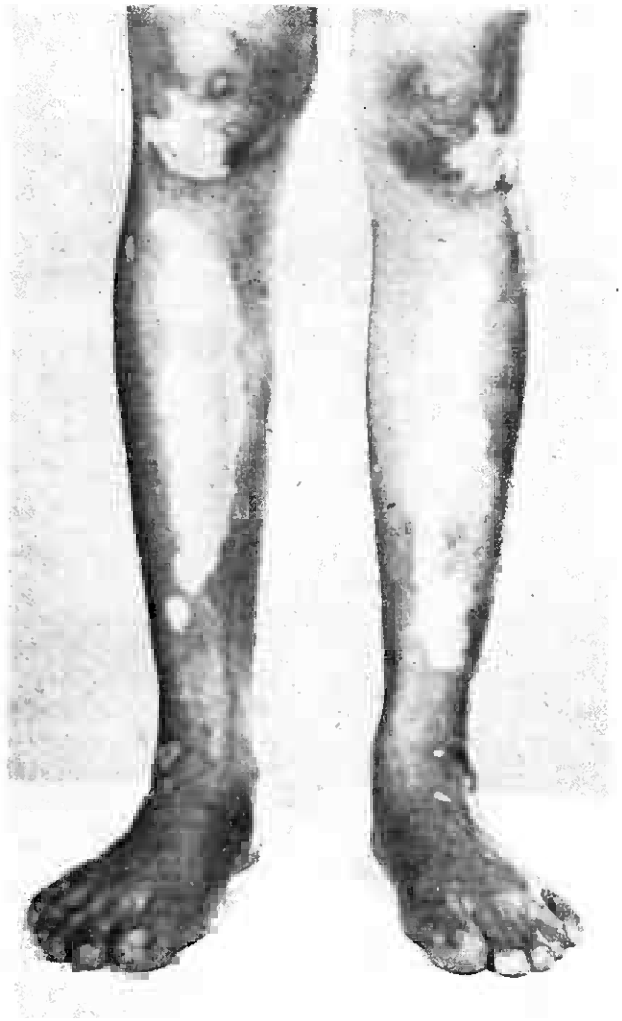

Fig. 8. Peripheral blotchy lesion (Segmental type) Vitiligo.

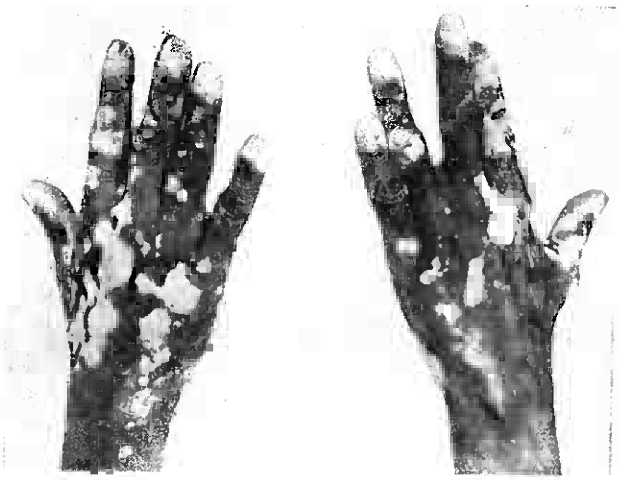

Fig. 9. Peripheral (Punctate type) Vitiligo

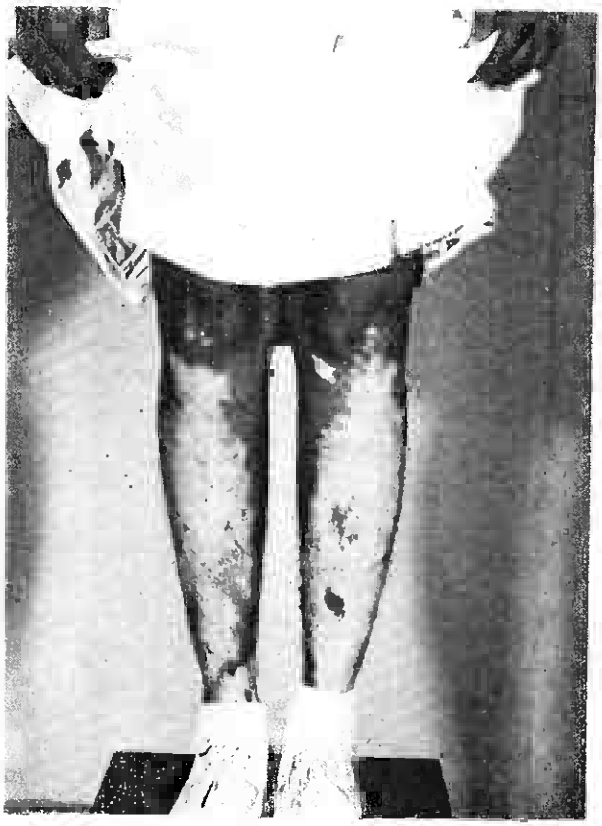

Fig. 10. Before treatment.

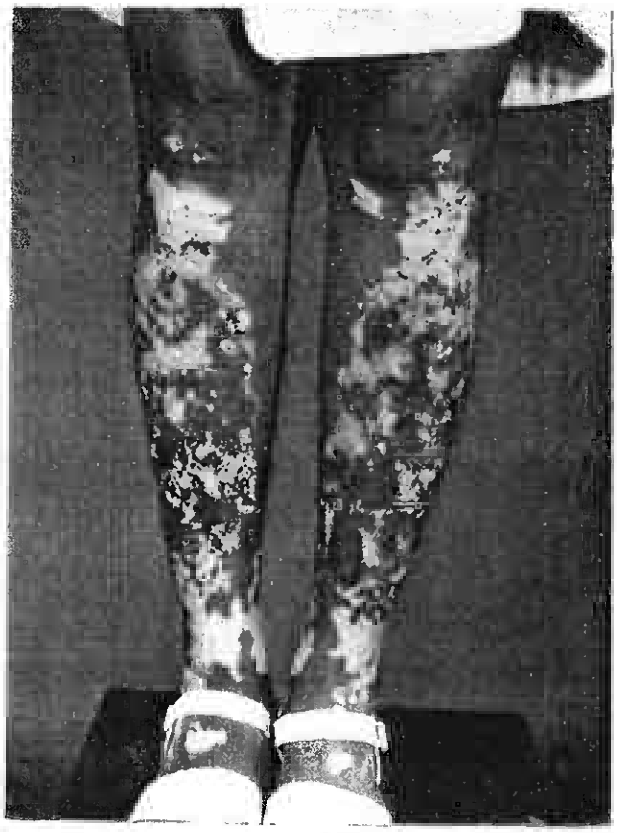

Fig. 11. Repigmentation during treatment with Meladinin paint and tablets. Note perifolli-cular grouping of pigmentation.

of increased activity of the peripheral nerve endings in the skin relasing an agent like melatonin which lightens the colour of pigment cells and decreases melanin formation.

In 1954, when we had a skin clinic in the General Hospital, we began the study of some 200 cases of vitiligo of all ages. We were not able to study them in detail and therefore mention will be made of them only in so far as treatment is concerned. A very complete study was made by Lerner in 1959 and his article should be studied in full if any one wishes to know more of the condition. I have had cases from the Chinese population, Malays and Indians and other races *e.g.* Negros, Arabs, Japanese, from all classes of people, and it does not seem to spare any special group. We have seen it in young children as well as in old people. However, we would not agree with Lerner that the onset is most common before the age of 25.

In my series more than one-half the cases were in the 20-50 age range and less than one-third were 20 years of age and under (Table 4). We divided our cases into central and peripheral with a sub classification into punctate (or discrete) or massive (or blotchy). (Figs. 5, 6, 7, 8, 9) However, Lerner's classification would appear to be more complete, namely, (1) Vitiligo vulgaris, the common form, (2) Vitiligo Totalis or total vitiligo where the whole body is involved, (3) segmental vitiligo or partial or focal vitiligo. Depigmentation occurs in segmental areas corresponding to nerve distribution. (4) Perihalo neavus which is also known as leukoderma acquisitum centrifugum or Sutton's disease. In this lesion is a central naevus surrounded by a circle of depigmentation.

Perhaps, it is wise at this juncture to differentiate leucoderma from vitiligo. Leucoderma is a more general term which includes vitiligo, albinism, depigmentation due to burns, trauma, leprosy, syphilis and pinta. In my experience the onset of vitiligo is often associated with some specific event and this is borne out by other workers including Lerner who had the same impression that it followed a severe stress reaction usually emotional in character. In one remarkable case, the onset of vitiligo in distal segments of limbs and head coincided with the change to white hair almost overnight in a man who lost his business in the same period of time. However, business worries, marital quarrels, the loss of loved ones, tension in the office and other places of work and chronic anxiety with exacerbation are precipating factors. The presence of vitiligo aggravates and perpetuates anxiety further. In most cases, the patients usually report that there is an extension of the process since the onset. In some cases, the rash spreads maximally at the onset and then recedes. In married women there is an association of vitiligo with pregency. There is also an association with other conditions, such as eczema, migraine, hyperthyroidism, pernicious anaemia in western countries, syphilis. Vitiligo is world-wide, the incidence varying from country to country. In Switzerland, the incidence as as reported by Robert in 1941 is 0.39% of patients in one clinic. Robert reviewed the literature and found the incidence was 1.64% in Japan as compared to 0.42% in London. In India, the incidence is said to be 3%. In Singapore in a survey of 1,000 consecutive cases of skin disease in the skin clinic at the General Hospital, the incidence of vitiligo was found to be 0.7%. (Khoo, 1954).

CLINICAL DESCRIPTION

The clinical description of patients with vitiligo is best described under the following headings: (1) Site, (2) Size, (3) Shape, (4) Shade, (5) Severity,

1) *Site* (Distribution)

In classical vitiligo, external orifices of the body including not only the mouth but the junction of the extensions of the trunk, such as the head, the limbs, the ears, nose, are more liable to be affected by vitiligo. Thus not uncommonly one sees cases with depigmentation around the mouth, around the base of the neck, around the wrists including the hands as well, around the umbilicus, both feet as high up as the knees, around the forehead often involving the hair. (Figs. 6 & 7).

2) *Size*

As mentioned before, the individual area involved could be pin-point or larger than a ten cent coin or it could be massive involving the entire trunk or limited to the exposed area of the body. (Fig. 8 and 9)

3) *Shape*

The shape of the lesion is usually dependent on the type. If it is peripheral and distal it tends to be sharply delineated or demarcated from the normal skin. If it is segmental, there is correspondence to nervous segmental distribution. However, incomplete vitiligo leaves dark areas of normal skin as islands in the depigmented area, thus giving a very irregular pattern. It is usual for vitiligo to be bilateral and symmetrical if it involves the terminal portion of the body. It tends to be equally affected on both sides of the body at the same time. However this is not invariable and one can see areas developing on

one side to be followed by a similar development on the other side at some interval of time.

4) *Shade*

Depigmentation may be complete in that there is absence of pigment giving rise to a milk white colour or the pigment loss may be minimal which might require more sensitive means of assessment such as by the spectrocolorimeter as was described by Dr. Thambipillai and myself recently (1961). We used this method not only for detection of the grade of vitiligo but also for the follow-up of cases after therapy.

5) *Severity*

Vitiligo could be minimal involving perhaps the chest the hands or the neck or it could be total vitiligo involving complete whole areas of the body such as face and the arms. However, I do not think I have seen a case of total vitiligo approaching that of albinism. The difference of course is very easily detected not only by the colour but also the involvement of the eyes in the Albino. When the vitiliginous area involves the scalp or the hairline, there is also a tendency which is not invariable to greying of the hair or to total loss of hair pigment giving rise to white hair. This, of course, is very noticeable in black hair in dark-skinned people.

THE TREATMENT OF VITILIGO

As this is not a new disease, various treatment have been prescribed in the past and there is no treatment that has not enjoyed success for some time. Thus, dermo-abrasion has been used by various workers such as Sidy and Bourgeois-Ganandis in 1953 and by Taylor in 1949. Mehta in 1956 described a series of cases treated by abrasion with an electric drill and then tattooing the area with an oscillating needle at the rate of 120 times a minute. A melanin-like powder is compounded to the exact shade required and used in the form of a paste. Recently, a very ancient method was revived in the use of the psoralens in the treatment of vitiligo. In ancient Indian medical literature, such as the *Astanga Hridaza Samhita* by Vagbhata, a plant known to cure the condition of leucoderma was *Bavachee*, a species containing psoralin. Perhaps the still more ancient "Vasuchika" possessed the same property and is probably the old name of Bavachee. In Chinese literature Laufer has found a plant known as Bwa-ku-ci or Pu-ku-c (Bu-kut-tsi) is mentioned in the treatment of leucoderma. (quoted by Fitzpatrick and Parthak, 1959). Laufer claims that the name is of Indian origin, and resembles the Sanskrit Va-ku-ci (Vasuchika) or Psoralea corylifolia which has been used by the Hindus in the Ayurvedic system of medicine. In the Nile valley, a weed, the Ammi Majus, had been used for centuries in the treatment of vitiligo. In 1947, Fahmy and Abu-Shady isolated three crystalline compounds from the Ammi Majus plant and named them Ammoidin, Ammidin and Majudin. Ammoidin or 8-methoxpsoralen had been isolated in 1911 from a different plant and Majudin or 5-methoxypsoralen was a well-known constitutent of Oil of Bergamot well-known in the perfume industry. In 1948, El-Mofty carried out a trial of the three compounds in vitiligo with some success. Since then, the psoralens have been used extensively in various continents.

CLINICAL TRIAL IN SINGAPORE

In the period 1954-1958 we were treating a series of cases of vitiligo of out-patients attending the Skin Clinic of the General Hospital. Over this period 200 cases were seen but a large number defaulted or attended irregularly so that only about 60 cases in all were followed up.

METHOD

All cases that were treated in the series were cases of primary vitiligo. Secondary vitiligo such as due to abrasions or dermatitis were excluded in the treatment. The method of treatment followed consisted of oral therapy and topical therapy. Oral therapy for adults consisted of 2 tablets of Meladinin every morning after breakfast. Meladinin contains 10 mgm. of Ammoidin, (8-methoxypsoralen) and 5 mgm. of Ammidin (8-Isoamyleneoxy-psoralen) in each tablet. For a child of under 12 years old, a quarter to half a tablet was given.

Topical therapy: Initially, the patient paints on the vitiliginous skin a solution of 20% Meladinin paint made up in 60% alcohol. 20% Meladinin solution is made up of 120 grams of Ammoidin and 50 grams of Ammidin in 1 litre of 60% alcohol. The strength is gradually increased up to 60% - 80%. Six hours later, the vitiliginous patch is exposed to ultra-violet irradiation from an Alpine sun lamp. The light source in this lamp comes from a high pressure mercury vapour arc tube of quartz emitting a wavelength from 1,850A to 4,000A. For small patches, the Kromayer lamp, using the same actinic source was used. Exposure was gradually increased with time and graded by individual reaction. Usually the patients were treated by ultra-violet light, three times a week. When blistering occurred treatment was stopped and later resumed with shorter exposure. Patients were warned not to be exposed initially to our tropical sunlight. Certain precautions were emphasised. In the presence of hepatic and renal damage in the history, the drug was not given by mouth. Secondly, patients were warned of severe blistering if they exposed the painted areas to direct sunlight. Where such a reaction has

taken place, the treatment was stopped temporarily. The blisters were then treated as for severe burns and it was often possible to resume treatment again in the matter of 2-3 weeks.

RESULTS

Our 60 cases comprised 47 Chinese, 8 Indians, 3 Malays and 2 Eurasians. Their ages ranged from 2 years to 57 years. The sex incidence showed a definite predominance of females, there being 43 females compared to 17 males in the series (see Table 1). They were classified according to our previous method which were two categories: 1) central and 1) peripheral types. Eash type was then subdivided into (a) blotchy and (b) punctate types. 50 cases had the peripheral type of distribution of which one was punctate and the rest were blotchy. Only 3 cases showed pure central types of lesions of which all were blotchy in distribution and none were punctate. There were 7 cases which had a mixed character, that is, features of central and peripheral type (Table 2). The results are briefly reported as follows. Out of 60 cases, 4 cases were cured, 19 showed distinct improvement, 13 showed some improvement, 23 cases were unchanged and one case was worse after treatment (see table 3). This last case which was worsened showed punctate lesions. Thus 60% of our cases were improved by treatment. According to the ethnic groups, the results among the Chinese patients reflected the general picture of improvement, that is, 27 cases out of 47 or 57.5% showed improvement. Of the 8 Indians in the series, 3 improved after treatment and 3 showed no improvement. There were 3 cases among the Malays of whom 2 cases improved and 1 showed no improvement. The 2 Eurasians showed improvement. During the course of the follow-up which varied from six months to 3 years, it was evident that the cases which showed the most improvement did so fairly early on so that visible improvement was noticed at each visit in contrast to the slowly progressive types. (Fig. 10 & 11). Increasing the strength of the paint did not materially help those cases that were slow to improve. There was also no relationship between the site of the irradiation and the rate of improvement. Where improvement was rapid, the treatment was continued in some cases without irradiation. After a period of irradiation with ultra-violet light, patients were then allowed exposure to sunlight. In our series, 19 cases were under 20 years of age. Of these, 8 showed improvement, 6 showed slight improvement and 5 were unchanged. Therefore 73.6% were improved. Five cases were over 50 years old. Of these 2 improved and 3 cases were unchanged. Then we have a third category, whose ages are between 20-50 years. Of these 13 cases improved markedly, 7 cases were slightly improved and 15 cases were the same; one became worse. Therefore 55% were improved. Of the 57 cases with (including 7 cases of mixed type) peripheral type lesions, 34 cases showed improvement (22 were markedly improved, 12 were improved moderately) and 22 showed no improvement and I was worse (Table 4). Of the central type (including 7 from mixed type) lesions, 7 showed improvement of which 6 were markedly improved; 3 remained the same. It is clear therefore that improvement varied inversely with age. Over 70% of patients under 20 years improved, 55% of those between 20-50 years improved and 40% of those above 50 years of age showed improvement after treatment. It would also appear that central lesions respond better to treatment than do peripheral lesions (70% in former compared to 59% improvement in latter). By means of the spectrophotometer assessment of the degree of skin pigmentation during treatment could be ascertained by means of the spectral deflection curve. With this instrument, it was possible to grade the state of melanisation and it was often found that the eventual state of the skin may became even darker than the adjoining area. Early this year in March, I began to use a new psoralen, trimethylpsoralen. This synthetic psoralen derivative is said to exhibit roughly 2 times the photosensitising property of 8-methoxypsoralen. It is given in smaller dosage than meladin, that is, one or two tablets, 5 mgm ingested 2 hours before the exposure to ultra-violet light. According to the manufacturers, this drug has a low toxicity and although it is too early to assess its effects, a preliminary communication might not be out of place at this stage.

In the first place, patients who have become resistant to meladinin paint soon found that they had a fresh response with trimethylpsoralen. Secondly in the dosage given, no toxic effects have been seen so far.

I shall conclude by commenting that we know much more about vitiligo today than we did 10 years ago, that its treatment is promising though not specific and that basic research has brought us important gains in our knowledge of the nature of the peripatetic melanocyte and the forces which influence its fate. In a divided world where skin colour plays such an important part, such knowledge is humbling and yet exciting in its implication that medical science has partly unlocked the secret.

TABLE I

Showing Incidence of Vitiligo

Race		Sex		Age	
				Years	No. of Cases
Chinese	47	Males	17	< 20	19
Indians	8	Females	43	20-50	36
Malays	3			> 50	5
Eurasians	2				
	60				

TABLE 2

Classification of Vitiligo		No. of Cases
Peripheral	Punctate	1
	Blotchy	49
Central	Blotchy	3
Mixed		7
	Total	60

TABLE 3

Results	No. of cases	Percentage
Marked Improvement (including 4 'cured')	23	60%
Some Improvement	13	
Unchanged	23	38.3%
Worse	1	1.7%
Total	60	100%

TABLE 4

Correlation between Age and results after treatment

Age in years	Improved ++	Improved +	Unchanged	Worse	Total
< 20	8	6	5	—	19
20 - 50	13	7	15	1	36
> 50	3	—	3	—	5
Total	24	13	23	1	60

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