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ALBINISM, PARTIAL ALBINISM, AND VITILIGO

Albinism, partial albinism, and vitiligo are three clinically distinct conditions having in common a deficiency of melanin pigment. As such they present the physician with the same basic problems—cosmetically disfiguring lesions and extreme sensitivity to sunlight of the involved areas. None of the diseases is itself an immediate threat to life, but the social disabilities, especially among dark-skinned individuals, are of great magnitude. Each disorder has been well known for over a century, and many detailed case reports are on record. Vitiligo, being by far the most common of the three, has received the greatest amount of attention. Albinism and partial albinism, because of their obvious characteristics, have received their share of study, especially from geneticists. To our knowledge, however, there has not been an attempt to correlate the available information on the three conditions. This is the purpose of the present report.

Albinism and vitiligo were dealt with extensively elsewhere,[9,11] and new material will be confined to the first published example of a nevus from a human albino. Partial albinism is less well known and will be described in more detail. A new family pedigree—only the seventh to be reported in the United States—will be presented, and for the first time a histological study will be reported. Finally, the pertinent information will be summarized in table form for convenient reference.

ALBINISM

Clinical manifestations. Albinism is the best known and most adequately studied of the various disorders of pigmentation. In its classical form it is unmistakable, because from birth the individual is completely devoid of melanin in all tissues where this pigment is normally present—skin, hair, and eyes. However, many albinos are capable of a very limited degree of pigment formation, particularly as they grow older. From the standpoint of

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color they may appear indistinguishable from a very blond Caucasian. These lightly pigmented persons often are referred to as incomplete albinos by geneticists and as partial albinos by ophthalmologists, the latter being consulted because of the patients' visual difficulties. The term 'partial albino' is not a good one since it is used by dermatologists and geneticists to refer to an entirely separate disorder which will be discussed below.

The most characteristic findings in albinism, aside from the obvious absence of skin and hair pigment, are in the eyes. The non-pigmented iris and retina give the pupil and iris a reddish appearance and, as might be expected, result in severe photophobia. The vessels of the choroid and retina are very prominent on fundoscopic examination. There may or may not be an associated hypoplasia of the macula.[9] A searching nystagmus is usually present associated with severely impaired visual acuity. Often it is this amblyopia which is the patient's major source of difficulty. "Ocular albinism" may occur as an isolated finding with otherwise normal pigmentation.

Other congenital anomalies may be associated with the pigment defect in albinism. They probably are an expression of multiple recessive traits resulting from a consanguinous mating rather than a product of the same genetic defect that caused the hypopigmentation.[9] Mental deficiency and short stature often have been described as associated findings.[8]

Rarely will any difficulty be encountered in identifying a true albino. The characteristics differentiating him from a person with hypopigmentation of another etiology are the following: (i) generalized lack of pigment; (ii) congenital onset with minimal change in pigmentation occurring throughout life; and (iii) ocular nystagmus with amblyopia and other congenital anomalies.

Incidence. On a world-wide basis the incidence of albinism is about one in 20,000 population.[9] In some areas, because of consanguinity, the incidence is much greater. There is no known difference in incidence between the sexes except that only males have the form of the disease confined to the eye.

Etiology. The etiology of albinism is generally assumed to be a genetically determined absence of the enzyme tyrosinase which is essential for the oxidation of tyrosine to dihydroxyphenylalanine and other intermediates in the pathway of melanin synthesis. This assumption is based upon the repeated failure to demonstrate tyrosinase activity upon *in vitro* incubation of albino skin and hair in suitable substrates. Unanimity of opinion is still lacking since it is known that under various circumstances a limited amount of pigment formation can be stimulated.[7, 10] The nystagmus and other ocular changes have not been satisfactorily explained.

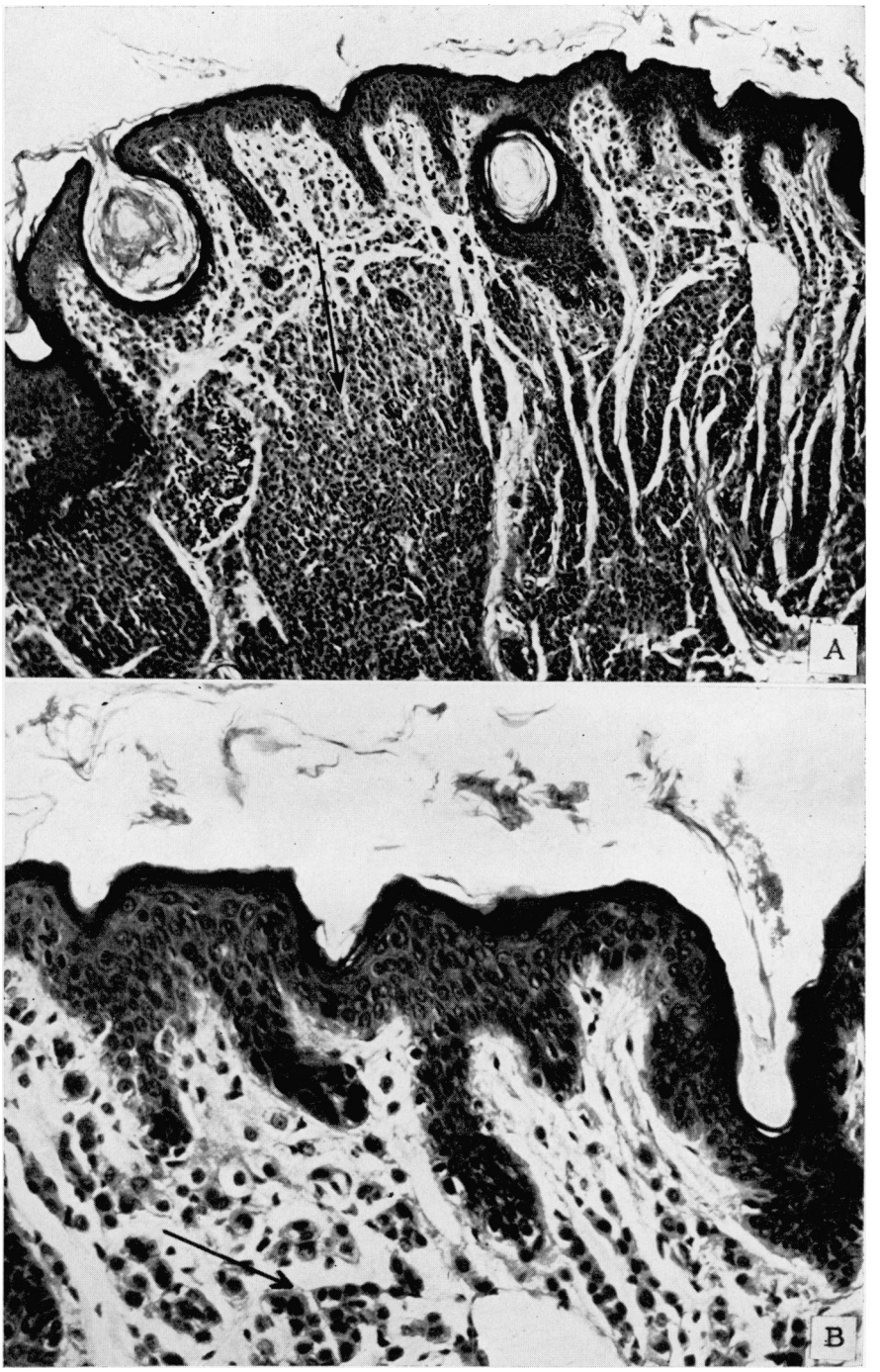


FIG. 1. Intradermal nevus from a total albino showing an accumulation of clear cells or melanocytes in the dermis. Melanin granules are not present. Stained with hematoxylin and eosin. (A) mag. x100. (B) mag. x265.

Histopathology. It has been shown beyond any reasonable doubt that the pigment forming cells, or melanocytes, are present in normal numbers in human albinism.[1, 2, 10] Nevi composed of non-pigmented melanocytes have been found to occur, although the example presented here (Fig. 1) is apparently the first to be published. A few instances of melanomas, made up of non-pigmented, anaplastic melanocytes have also been reported in albinos.[17] The histochemical techniques used to demonstrate melanin and melanocytes are of no use in histological studies of albinism. That is to say, darkening of the cytoplasm of the melanocyte by dopa or tyrosine, which requires the presence of active tyrosinase, does not occur; and the reduction of silver salts, which is performed by the melanin granules, also cannot take place.[6] Since this phenomenon is characteristic of all the disorders in the group it cannot be used as a diagnostic criterion.

Genetics. The mode of inheritance of total albanism has been studied carefully by numerous investigators. Almost invariably the defect has been inherited as an autosomal recessive.[3] By contrast, inheritance of ocular albinism is well documented as a sex-linked recessive. Female carriers of the trait for ocular albinism show characteristic pigmentation changes in the retina.[5]

Therapy. For practical purposes there is no therapy. Tinted eyeglasses and protection of the skin from excessive sunlight are the only convenient symptomatic measures.

Prognosis. The prognosis in patients with albinism depends essentially upon the nature of the associated defects. The absence of melanin *per se* is not incompatible with a normal life span, but survival is difficult in afflicted persons exposed to intense and prolonged sunlight, as in the tropics, because there is an increased incidence of skin cancer[15] in such individuals. With aging, some patients develop increased pigmentation, accompanied by improvement in visual acuity. This, plus the fact that they learn to accommodate to their handicap at an early age, means that often a satisfactory adjustment to environmental conditions can be made.

PARTIAL ALBINISM

Clinical manifestations. Partial albinism is entirely distinct from total albinism and is not to be confused with incomplete albinism. It also is known by many other names including piebaldism, white-spotting, white forelock, congenital vitiligo, albinoidism, congenital achromia, etc. Perhaps the term partial albinism should not be used because of possible ambiguity, but since it is the most familiar it will be adopted here.

This disorder is characterized by localized patches of hypopigmentation which are present from birth and do not change in size throughout life. The remainder of the body is of normal color. The most familiar form of the disease is that manifested by the white forelock. Usually the skin lesions are distributed over the ventral thorax, abdomen, extremities, brow, and scalp under the white forelock.[4] The lesions are bilateral and asymmetrical, vary greatly in size, and may contain islands of normally pigmented skin. There is no hyperpigmented border as seen in some patients with vitiligo, but there may be varying shades of melanin pigmentation in a single subject (Fig. 2). The eyes are not involved. Characteristically, other members of the patient's family have similar depigmented areas since the disorder is inherited as a dominant trait. The patients presented in this report showed remarkably similar lesions, but this is not always the case. In contrast with total albinism, there are no associated anomalies. The patients are asymptomatic unless there is much involvement of skin in the exposed areas with no protection against sunlight.

In summary, partial albinism can be differentiated from total albinism by the circumscribed nature of the lesions and by the absence of nystagmus or other constitutional abnormalities. Unlike vitiligo, the lesions of partial albinism are present at birth and do not change. The hyperpigmented border which is often seen in vitiligo is not present in partial albinism. Examination of other members of a patient's family may be helpful, but since vitiligo may appear as a dominant trait in a family, this may prove misleading.

Incidence. The true incidence of partial albinism has not been determined, but it is certainly more common than the approximately 25 cases recorded in the literature would indicate. One author believes the incidence to be about equal to that of total albinism.[12] Many individuals probably never seek medical attention because they are asymptomatic, and their lesions are insignificant.

Etiology. No satisfactory theory has been proposed to explain this disease. Many feel that it is analogous to white-spotting in the coats of lower mammals.

Histopathology. Although the disorder is clinically and genetically similar to white-spotting in lower mammals, the histological findings are notably different. In the white areas of spotted mice, rats, and guinea pigs, pigment cells identified as "clear cells" are totally lacking.[14, 16] Skin biopsies taken from a lesion of the patient presented below by contrast showed clear cells or melanocytes, normal in number and morphology[10] (Fig. 3). Hence the lesions of partial and total albinism are histologically indistinguishable.

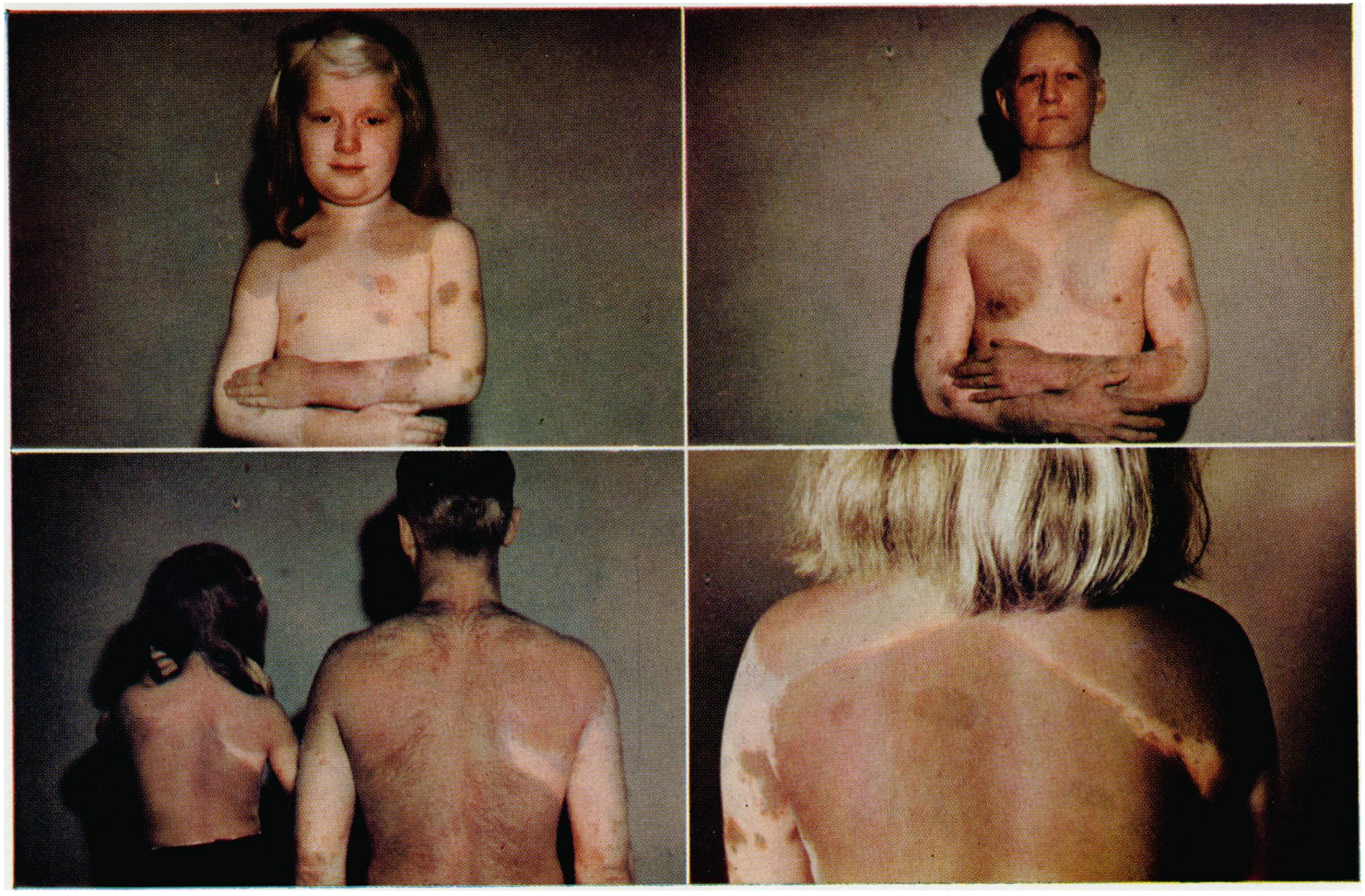


FIGURE II

Father and daughter with partial albinism. Note distribution of lesions and their similarity on the backs of the two patients. Note also the hyperpigmented areas on the back.

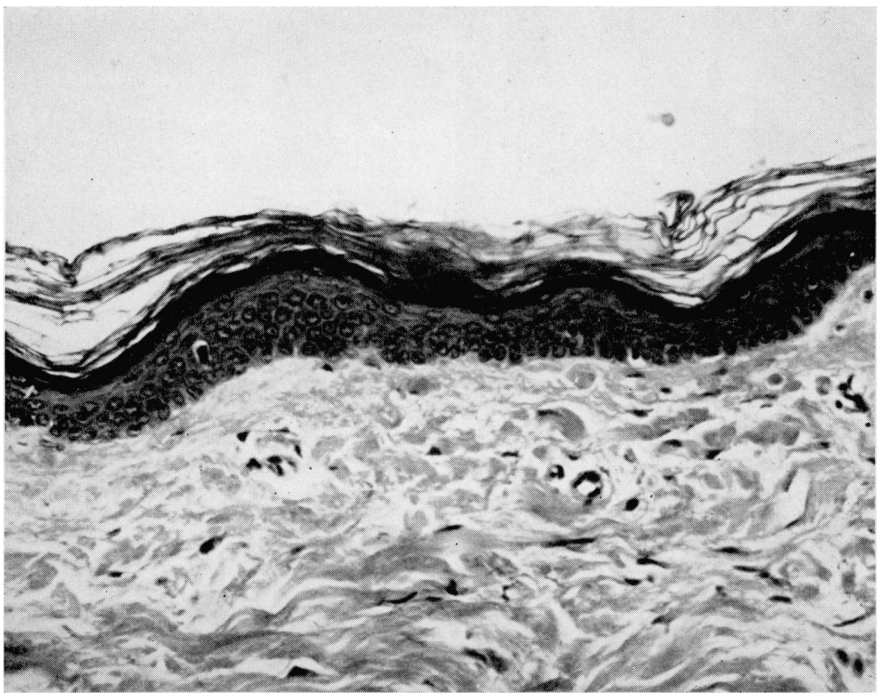
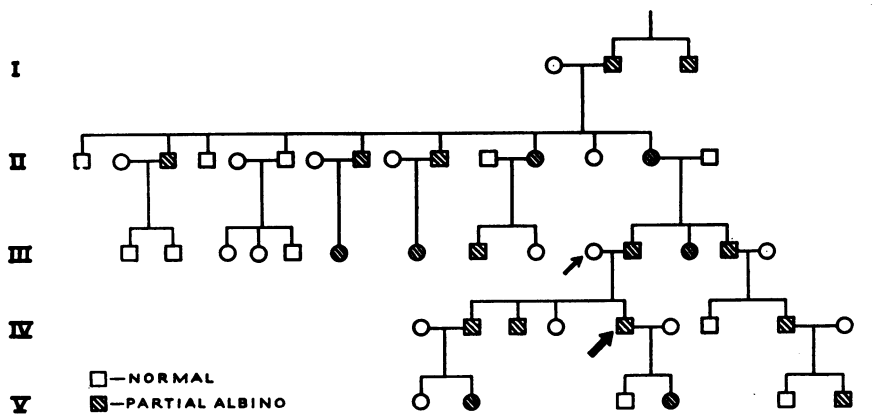


FIG. 3. Biopsy section of a lesion in partial albinism showing the presence of melanocytes, identified as clear cells, in the basal layer of the epidermis; mag. x265.

Genetics. Virtually the entire existing literature on this disorder is concerned with its mode of inheritance, which has been well worked out as an autosomal dominant. Thus it is to be expected that 50 per cent of individuals in an affected family will show the defect in some manner.

Prognosis. The lesions themselves are permanent and never change. There are no constitutional effects from the disease so that health and life expectancy are usually normal.

Case Report. R. A., a 38-year-old Caucasian male, was first seen together with his 5-year-old daughter, G. A., in the Dermatology Clinic of the Yale-



PEDIGREE OF "PARTIAL ALBINISM" IN A NEW ENGLAND FAMILY
(BIRTH ORDERS ARE NOT INDICATED)

FIG. 4. Pedigree of partial albinism demonstrating dominant pattern of inheritance. Arrows refer to informants, the heavy arrow denoting the father described in the report.

New Haven Medical Center in 1956. Both showed extensive areas of depigmented skin which had been present since birth without change in size or color. In addition, the girl had a triangular white blaze of hair. Both patients were asymptomatic and were concerned mainly with the cosmetic appearance of the defect. The skin in the affected areas burned on exposure to sunlight and had no capacity for tanning. The remainder of the body tanned normally. Further questioning of the father and his mother revealed other members of his family with the same disorder as indicated in the accompanying pedigree (Fig. 4).

Upon examination both patients were physically normal in every respect except for the characteristic skin lesions of similar distribution over the scalp, face, thorax, back, and extremities (Fig. 2). Some parts of the skin were hyperpigmented and contained macules that looked like *café au lait* spots.

VITILIGO

Clinical manifestations. Vitiligo is a common disease of considerable importance in the practice of medicine. It is highly variable in its manifestations and has aroused much curiosity among pigment researchers. The lesions may range in size from a single, small circumscribed area of depigmentation to "complete" vitiligo in which virtually the entire body is involved. Commonly there are multiple patches which may or may not be symmetrical or segmental in distribution. The exposed areas are usually involved, but the lesions may appear anywhere on the body surface. Depigmentation may be partial or complete. Hair may be gray (white) or uninvolved. Lesions often have a hyperpigmented border with rings of gradually increased pigmentation extending peripherally. Another characteristic is the perihalo nevus which is a pigmented nevus surrounded by an area of depigmentation. Vitiligo may begin at any age. It tends to come on early, with 50 per cent of the cases occurring before the age of 20 years in one study.[11] Onset of the disease may be associated with physical or emotional trauma. Some patients have co-existent organic or emotional illness. An increased incidence of vitiligo in patients with pernicious anemia, hyperthyroidism, and Addison's disease has been reported.[11] The disease has periods of quiescence or progression which are usually unpredictable. Lesions spread peripherally, and new ones may appear, too. The psychological implications, particularly in the darker races, are enormous.

Vitiligo may be distinguished clinically from albinism and partial albinism by the following points: (i) Vitiligo usually begins after birth; (ii) the lesions change in extent and severity; and (iii) hyperpigmented borders of depigmented areas and perihalo nevi are common in vitiligo. In the differential diagnosis, vitiligo must be distinguished from acquired hypopigmentation due to other causes such as trauma, syphilis, atopic dermatitis, etc.

Incidence. A number of studies have been undertaken to determine the incidence of vitiligo in various parts of the world, with estimates ranging from 0.14 to 3.2 per cent. It is possible that the disease is more prevalent among dark-skinned races, but this higher incidence may be more apparent than real. It is probably safe to state that the incidence of vitiligo on a world-wide basis is about one per cent.

Etiology. There is much evidence to suggest that vitiligo results from the presence in the skin of a yet unknown neurohormone that can lighten melanocytes.[11]

Histopathology. As in the previously discussed disorders of pigmentation, melanocytes are present in normal numbers in the lesions of vitiligo. In the hyperpigmented border which is often present they appear to occur

TABLE 1. FEATURES OF ALBINISM, PARTIAL ALBINISM, AND VITILIGO

	Albinism	*Partial albinism*	*Vitiligo*
Incidence	1:20,000	Unknown (rare)	1:100
Etiology	Deficiency of tyrosinase	Deficiency of tyrosinase	Excess amounts of neurohormone in skin
Extent of lesion	All tissues containing melanin	Discrete, circumscribed areas of skin and hair	Variable — usually discrete lesions of skin and hair
Sites commonly involved	Entire body, but eyes alone may be involved	Any area, particularly scalp	Exposed areas, esp. dorsum of hands, about body orifices and in body folds
Characteristic findings	Amblyopia and searching nystagmus	White forelock	Hyperpigmented border of lesion, perihalo nevus
Associated illnesses	Other congenital defects	None	Hyperthyroidism, pernicious anemia
Age of onset	Congenital	Congenital	Any age but usually by early adulthood
Clinical course	A minimal degree of pigment formation may occur with increasing age	Lesions do not change in relative size throughout life	Exacerbations and remissions characteristic; repigmentation may occur
Histopathology	Dopa-negative melanocytes present	Melanocytes present	Melanocytes present with little or no dopa activity
Heredity	Autosomal recessive; ocular form sex-linked	Autosomal dominant	Inconsistent — may show dominant pattern

with an increased population density and are strongly reactive upon incubation in solutions of dopa or tyrosine.[10] The melanocytes in the areas of depigmentation show reduced or absent tyrosinase activity.[8] The findings otherwise are non-specific. Inflammatory cells may be evident sub-epidermally but their significance is unknown.

Genetics. Vitiligo tends to occur in families and may show a pattern consistent with a dominant mode of inheritance. There obviously must be

modifying factors affecting the expression of the trait since the majority of patients have no relatives with the disease.[11] More detailed statistical study is necessary to clarify this point.

Prognosis. Vitiligo, like partial albinism, has no direct effect upon health or life expectancy. However, patients with this disease may be disabled for cosmetic reasons, and they may burn excessively when exposed to sunlight. So far as the lesions themselves are concerned, the course is variable with periods of progression and quiescence being common. Physical or emotional trauma may initiate an exacerbation. Repigmentation of some degree occurs in about 50 per cent of patients. This begins from the periphery of the lesion or from perifollicular foci in areas where the hairs are still pigmented.[18] Complete cure may result, but this is uncommon.

The accompanying table summarizes the important and distinguishing features of albinism, partial albinism, and vitiligo.

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