

## ON THE NATURE OF IDIOPATHIC GUTTATE HYPOMELANOSIS

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**Abstract.** Clinical and morphologic studies were made of 20 cases of guttate hypomelanosis. The sharply demarcated hypopigmented macules were present on both covered and exposed sites, excluding sunlight exposure as a cause. Skin surface replicas and biopsies showed no evidence of post-traumatic or post-inflammatory scarring. The stratum corneum had fewer cell layers, but no abnormalities of keratinization were observed. Light and electron-microscopic and histochemical studies showed only reduced numbers of hypoactive melanocytes. In no case were melanocytes completely absent, excluding vitiligo. Guttate hypomelanosis is a common disorder of unknown origin. The evidence indicates an age-related somatic mutation of melanocytes.

**Key words:** Idiopathic guttate hypomelanosis; Melanocytes; Vitiligo

Idiopathic guttate hypomelanosis (IGH) is a common benign dermatosis which in mild cases may pass unnoticed by the casual observer. Florid examples may be mistaken for vitiligo. These small hypopigmented spots become more common with advancing age and achieve a high prevalence in the elderly. In spite of this, little is known concerning their cause, development, natural history or microscopic anatomy. Etiologic theories have included trauma (1), sunlight exposure (9) and senile degeneration (3) but the evidence for any of these is unconvincing. A recent ultrastructural study of 3 cases (6) advanced our knowledge of the morphology of these lesions but shed no new light on their pathogenesis. We have studied 20 cases by a variety of techniques to better characterize these lesions.

### MATERIALS AND METHODS

Approximately equal numbers of subjects were derived from two sources, either long-term residents in an institution for the elderly, mainly Caucasoid, or clinic outpatients, mainly Negroid. These were 8 females and 12 males with an age range of 50 to 84 years. Informed consent was obtained.

### *Clinical examination*

Clinical examination in good daylight was supplemented by examination with Woods's light in a darkened room, a method known to enhance pigmentary contrasts.

### *Replicas*

Negative impressions were obtained by the application of a quick setting silicone impression material (Cutter Sil silicone elastomer, Cutter Laboratories, USA). Epoxy cement was then applied to the negatives, and the resultant positives examined under the stereomicroscope.

### *Cell layers of the stratum corneum*

Skin blisters were raised over leg lesions by the application of 75% ammonium hydroxide solution to a 1 cm circle of skin. This produced an intra-epidermal blister in about 40 min (modified from 2). Each blister included a centrally placed lesion and surrounding normal skin. The number of horny cell layers was determined by direct coating of cryostat sections swollen in alkali.

### *Histology*

Excision biopsies from various sites on the limbs and trunk were fixed in formalin. 7- $\mu$ m sections were stained with H + E and Fontana's stain for melanin.

### *DOPA whole-mounts*

Shave biopsies were treated with 0.2 M NaBr solution to detach the epidermis. This was then incubated for 6 hours at 37°C in 0.1% DOPA solution buffered at pH 7.4. After fixation and dehydration the epidermis was mounted as a flat sheet for examination of melanocytes.

### *Electron microscopy*

Biopsy specimens were processed as described previously (5).

## RESULTS

### *Clinical appearance*

The lesions were readily visible to the naked eye, consisting of multiple, sharply defined, partly or completely depigmented angular macules between 2 and 8 mm in diameter (Fig. 1). They were most common on the legs, followed by the forearms. They were more numerous on the sun-exposed as-

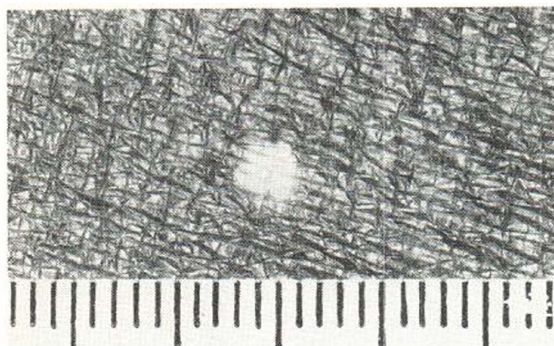


Fig. 1. Isolated hypomelanotic lesion 3 mm in diameter. Normal skin surface markings pass through the lesion.

pects of the extremities. In persons with dense freckling of the back from long exposure to sunlight, guttate hypomelanotic spots contributed to the mottling aspect. Nonetheless, the lesions were by no means confined to exposed sites. In some cases they were even more numerous on protected areas (Fig. 2). Facial spots were rare. No subject gave a history of local trauma; moreover, it is difficult to conceive of an injury that could create discrete angular spots. In contrast, several of the subjects had larger, slightly sunken hypopigmented scars, especially on their shins. Trauma could sometimes be recalled. These lesions have been called 'diabetic dermopathy'. While they may be more extensive in diabetics, they are not a characteristic of that disease, and occur just as frequently in normal persons. Sometimes dermopathic scars and IGH lesions were found in close apposition. The experienced clinician can easily distinguish between the two. Replicas faithfully betrayed scars by showing loss or distortion of the patterning of the surface markings. IGH lesions showed no change in surface topography. Skin markings were as prominent as in normal skin.

#### Autoimmune associations

Anamnesis yielded no suggestion of increased prevalence of autoimmune disease, either in the subjects or in their relatives. Two subjects had maturity onset diabetes and 2 relatives had juvenile onset diabetes. No subject had vitiligo or relatives with vitiligo. Screening for circulating autoantibodies revealed, surprisingly, gastric parietal cell antibodies to a titre of 1:40 in 3 of 9 subjects. The thyroid microsomal titre was normal. Antithyroglobulin and antinuclear antibodies were negative in every case.

Table 1. The number of cell layers in the stratum corneum of lesional and paralesional skin (6 lesions from 3 subjects)

| Case  | Paralesion | Lesion |
|-------|------------|--------|
| O. S. | 19         | 10     |
| H. B. | 43         | 29     |
|       | 28         | 20     |
| E. P. | 25         | 14     |
|       | 44         | 31     |
|       | 41         | 32     |

#### Wood's light

Examination with Wood's light sharpened the contrast between the lesions and normal skin in both black and white subjects; however, in no case did it reveal lesions not already apparent in good daylight.

#### Light microscopy

We observed no major alterations in either epidermis or dermis. The rete ridges were generally well developed. Moderate flattening of the dermo-epidermal junction in a few biopsies could be ascribed to aging. Epidermal cytology was normal, although the horny layer seemed thinner in some cases. In six blister roofs the number of cell layers in the stratum corneum was reduced in relation to surrounding skin. The decrease was considerable, ranging from 8 to 14 cell layers (Table 1). The relative lack of melanin in the intralesional keratinocytes was evident in both H + E and Fontana-stained sections, being more readily apparent in blacks and darkly pigmented subjects (Fig. 3).

#### DOPA whole-mounts

The clinically apparent sharp demarcation of the lesions was confirmed by the marked contrast between the melanin-laden keratinocytes of normal skin and the virtually pigment-free keratinocytes in the lesion itself. Melanocytes were more variable in appearance. In perilesional skin there was a fairly even distribution of moderate sized melanocytes with prominent dendrites. Just inside the depigmented area there were often fewer melanocytes but these were large and well developed with numerous extensive dendritic processes (Fig. 4). At the center of the lesions melanocytes were invariably reduced in number to between 25 and 50% of normal. These melanocytes were of small size with scanty or absent dendritic processes and weak-

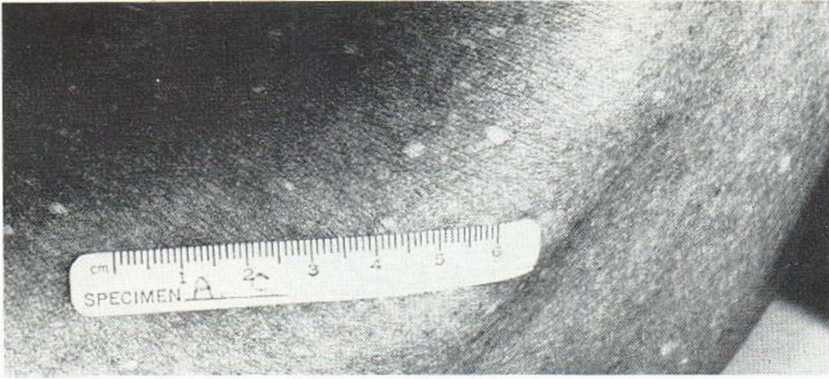


Fig. 2. Multiple hypomelanotic lesions on an area of the hip not exposed to sunlight or trauma.

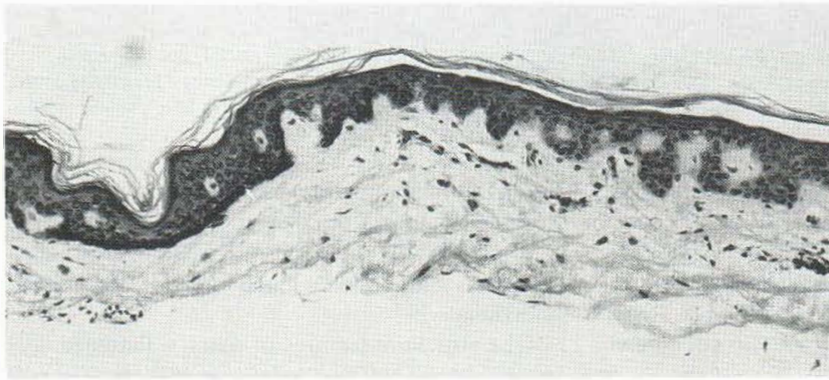


Fig. 3. H & E stained section of the junction between a hypopigmented macule on the right, and normal (Pigmented) skin on the left. The architecture of the epidermis is normal ( $\times 160$ ).

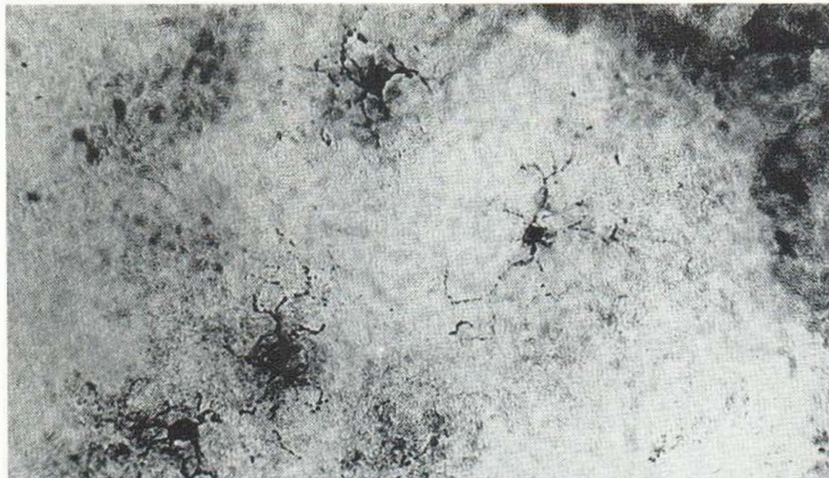


Fig. 4. DOPA-stained epidermal sheet showing active melanocytes at the edge of a lesion ( $\times 400$ ).

ly staining cell bodies (Fig. 5). However, a complete absence of melanocytes was never observed.

*Electron microscopy*

Melanocytes, were infrequently observed, and were quite small, with attenuated dendrites.

Melanosomes were rarely seen and mature forms were not present. Langerhans cells were present in normal numbers. The fine-structural features of the keratinocytes were identical with normal skin, except for the absence of melanosomes (Fig. 6).

The basal cells of the dermo-epidermal junction

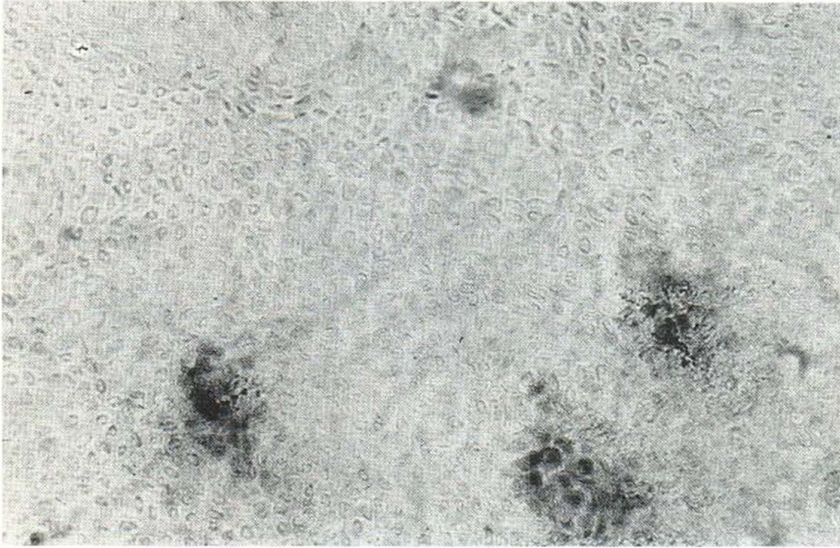


Fig. 5. DOPA-stained epidermal sheet showing reduced, but not absent, melanocytic activity at the centre of a lesion ( $\times 400$ ).

showed somewhat 'blunted' microvillous cytoplasmic projections into the dermis. All of the components of the basal lamina complex (basal cell plasma membrane, lamina lucida, lamina densa, anchoring fibrils, microfibrils) were normal (Fig. 7). Reduplication of the basement membrane was not noteworthy.

The papillary dermis showed thin bundles of col-

lagen without any preferential organization. Interspersed among the collagen were numerous 8-11 nm microfibrils normally associated with elastogenesis and routinely found in the dermis of aged individuals.

The structural features of scars, a flattened dermo-epidermal junction and dense, thin, parallel collagen bundles, were never observed. Although elas-



Fig. 6. Electron micrograph of a portion of the basal cell (BC) population and papillary dermis (PD). Fine structural features of the basal cells appear normal except for the absence of melanosomes. Evidence of scar formation in the papillary dermis was not present ( $\times 6000$ ).

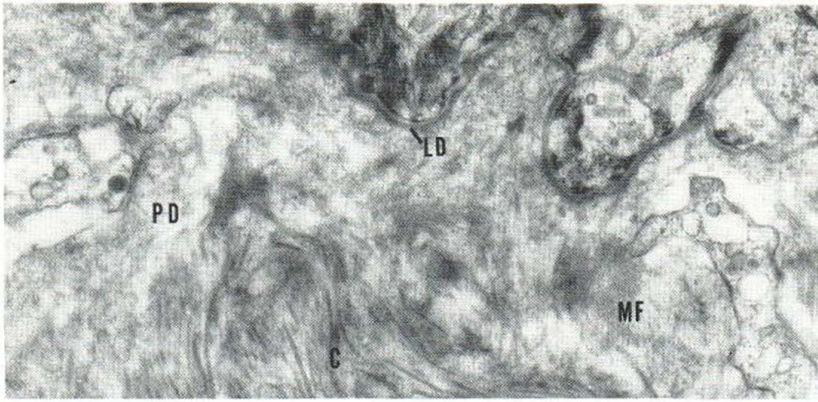


Fig. 7. Higher magnification electron micrograph of a portion of the dermo-epidermal region. Reduplication of the lamina densa (*LD*) portion of the basal lamina complex was not observed. Papillary dermis (*PD*) consisted of thin bundles of collagen (*C*) without any preferential organization. Numerous microfibrils (*MF*) were seen in this region ( $\times 25\,000$ ).

tosis was present in some sections it was appropriate for the age of the subject and in no case approached the severe actinic damage of excessively sun-exposed skin.

#### DISCUSSION

Idiopathic guttate hypomelanosis is the accepted name for a depigmented spot which is especially frequent in the elderly. Although the published work on the subject includes two large surveys (1, 9) and two recent ultrastructural studies (6, 7) our knowledge of this common lesion is still very limited.

These irregularly distributed angular macules occur more commonly, but not exclusively, in the elderly where they may be seen as part of the spectrum of pigmentary changes on sun-exposed extremities. The lesions are more obvious but not more common in those with darker skin coloring. They probably occur in all races. They are entirely asymptomatic and only rarely cause cosmetic disfigurement. Several of our subjects were unaware of their presence.

The cause of the depigmentation is unknown. Various factors may be contributory. Sunlight is probably influential, but variably so. The lesions occur commonly on exposed parts of the body; the forearms and lower legs are typical sites. Whitehead et al. (9) emphasized their frequency on sun-exposed regions. However, we were struck by the occurrence of these hypomelanotic macules on other parts of the body such as the buttocks, thighs and lower abdomen. In some subjects the spots were more numerous on these unexposed sites. Moreover, the high prevalence in blacks argues against a dominant or exclusive role for sunlight.

Local trauma can be excluded as a cause, on morphologic grounds. The lesions do not qualify as scars. The latter show loss of surface markings, flattening of the epidermis and colinear arrangement of fine collagen bundles in the subepidermal region. None of these histological features was present in IGH. Scars, even when very small, show loss or distortion of the geometric patterns of the skin markings. Post-inflammatory hypopigmentation was not seriously considered since we found no evidence of present or past inflammatory lesions.

The prevalence of these lesions increases with age, but our morphological findings do not support the theses of senile degeneration (3) or early aging (7).

Guttate hypomelanosis is not a small lesion variant of vitiligo. Melanocytes were present, but were invariably stunted, atretic and reduced in number. We did not see the normal number of hypoactive melanocytes reported by Savall et al. (7) nor the scattering of normal and active melanocytes observed by Ortonne and Perrot (6) in two of their three cases. Such normal melanocytes were only seen at the edge of the lesions in our cases.

Savall et al. (7) observed atrophy of the epidermis as a constant feature on light microscopy. They also recorded that guttate hyperkeratosis, xerosis and lentiginosis invariably accompanied the hypomelanosis. We found a reduced number of cell layers in the stratum corneum, but were unable to demonstrate any association with other clinical changes.

It is possible that idiopathic guttate hypomelanosis, like vitiligo, is a phenomenon associated with autoimmunity. We did not attempt to detect antibodies to melanocytes, since these have been

demonstrated in patients with vitiligo only with considerable difficulty (4). However, we did find, unexpectedly, that 3 out of 9 male subjects had circulating antibodies to gastric parietal cells. This may be an age-related change not peculiar to this condition.

We think there may be buried treasure in these small lesions, which are anything but uninteresting. In search of speculations, one's mind reverts to the problem of spottiness so brilliantly investigated by Ian Whimster (8). Practically all dermatologic lesions begin as small macular spots. Are we all spotted from the beginning, awaiting only time and its associated impacts to reveal the pattern? Aging increases the likelihood of error in the regulation of cell division. Perhaps these hypopigmented spots are clones of melanocytes derived from somatic mutations.

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