

SHORT REPORTS

Progressive Depigmentation of the Coat of C3H Mice after Neonatal Thymectomy

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Abstract. Progressive depigmentation of the coat has been observed in C3H mice thymectomized at birth and reared in a germ-free environment. The origin of the pigmentary anomalies is discussed. It is probable that a causative relationship exists between thymectomy and the acquired depigmentation observed.

Key words: Thymectomy; Depigmentation; C3H Mice

Various factors may be responsible for depigmentation of the coat in animals. Deficiency of trace elements or vitamins can cause a change in hair colour in different species of mammals (7). Application of various chemical compounds (1), X-irradiation (2), and certain types of physical trauma, particularly ischaemia (9), can produce localized pelt depigmentation in the treated areas. The development of progressive depigmentation of the coat after neonatal thymectomy of a pure species of pigmented mice does not seem to have been reported previously in the literature.

MATERIALS AND METHODS

C3H mice. C3H mice were obtained from the National Selection Centre and from the Animal Breeding Centre of the Laboratories of CNRS. They were bred in a continuous line for 7 years in the laboratory where the experiments were carried out. For 5 years, breeding was carried out in isolation.

Neonatal thymectomy. Hypoaesthesia was effected by cooling. Thymectomy was performed by substernal suction during the first 24 hours of life. The thymectomized animals were subsequently reared in germ-free conditions. They were fed with Purina Duquesne sterilizable diet. The maximum duration of observation of these animals was 18 months, at which time they were sacrificed.

RESULTS

Nineteen animals survived the first week and there were no deaths in the ensuing 14 months. Depigmentation of hair was observed in 8 of the 19 mice. It appeared initially in circumscribed patches of 3 mm diameter as tufts of white hair. In individual animals, the period before development of white patches varied from 8 months in the earliest case, to 1 year in the most delayed. From the initial moment of appearance, hair depigmentation extended continuously.

The mode of propagation of the depigmentation was essentially the same in all 9 animals, beginning as circumscribed plaques with well-defined outlines around the eyes, on the head and thorax and on the tips of the paws. Other plaques eventually appeared on the back, flanks and sacral region. The depigmented skin was of a greyish white colour. Eighteen months after thymectomy, some mice were uniformly totally depigmented, while others retained the appearance of localized depigmentation.

Colour change was not accompanied by hair fall nor alopecia. No other pathological manifestations were observed in the mice.

DISCUSSION

Hair depigmentation observed in C3H mice thymectomized at birth cannot be ascribed to genetic causes.

The dark brown colour of the coat of these mice is due to the presence of hairs of two different colours—hair which is entirely black, and hair of which the proximal part and tip are black separated by a thin yellow band (8). The characteristic colour resulting from this mixture of hairs of different shades is called "agouti".

Histological, ultrastructural and biochemical studies of the coat of these animals suggest that during the anagen phase of the hair cycle, the melanocytes synthesize eumelanosomes and pheomelanosomes during a very short period of this stage. Eventually, return to eumelanogenesis occurs. These cyclic changes of hair colour which are under genetic control, cannot explain the

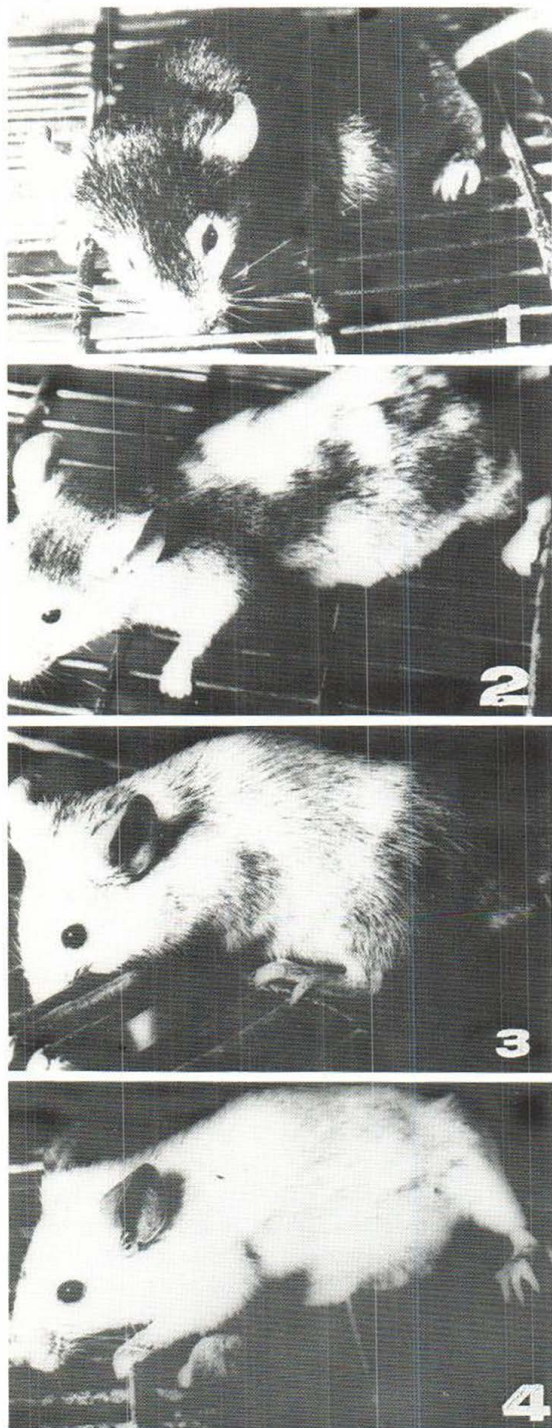


Fig. 1. Coat depigmentation begins as circumscribed plaques around the eyes and on the flanks.

Fig. 2. Plaque size increases and individual areas become confluent.

Fig. 3. Depigmentation becomes diffuse.

observed depigmentation of the coat in the thymectomized mice. Furthermore, they are not manifested macroscopically and the colour of the C3H mice does not change with age.

Premature greying of hair has recently been described in one species of mouse (6). This premature greying is transmitted as an autosomal dominant trait. However, a genetic cause does not apply to the animals subjected to thymectomy, as they were the progeny of a species maintained in the laboratory for more than 5 years without any change of pelt colour being observed.

An acquired depigmentation must therefore be envisaged. No irradiation nor chemical depigmenting products were applied to the thymectomized mice: the possibility of physical or chemical agents as a cause can therefore be discounted. The possibility of a deficiency state remains. Coat depigmentation may be observed in rats (5), cats (4), rabbits (11), cattle (10) and sheep deficient in copper. The delay after thymectomy in appearance of the pigmentary anomaly in the coat of the mice would be compatible with such a hypothesis. It is unlikely to be due to deficiency in nutrient knowledge been associated with the development of pigmentary problems. It is possible that thymectomy may have induced in the mice supplementary requirements of certain nutrient elements. Thus the nutrient supply of the diet sufficient for non-thymectomized mice may no longer be adequate in the face of extra need in treated animals.

However, copper deficiency in animals not only causes pigmentation problems. It is also characterized by stunted growth and neurological anomalies, particularly ataxia, which is evident immediately on clinical examination. In copper-deficient sheep, abnormalities of the wool arise.

In man, Menkes syndrome, due to hereditary malabsorption of copper, comprises cerebral vascular anomalies and appendageal abnormalities, particularly of the hair (3). In the thymectomized mice, no disturbances other than change of colour of the coat were observed. Although no biochemical investigation was carried out, the possibility of copper deficiency seems unlikely.

Not only can copper deficiency produce pig-

Fig. 4. In the final phase of evolution the entire coat is of greyish white colour, contrasting with the original *agouti*.

mentary change in the coat of animals or the skin of man. Such anomalies have been observed in zinc, protein, and various vitamin deficiencies (7, 12). However, in most of these, generalized symptomatology develops; we have not observed such in the thymectomized mice.

The histological basis of the coat depigmentation described above, could unfortunately not be studied. It is impossible to conclude with certainty that depigmentation of the coat is related directly to thymectomy. Although the hypothesis of a deficiency origin of coat depigmentation may be correct, the exact mechanism remains obscure.

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Phylogenetic Studies with Pemphigus and Pemphigoid Antibodies¹

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Abstract. Indirect immunofluorescence (IF) studies were performed on skin from a variety of vertebrate specimens and IgG fractions from pemphigoid and pemphigus sera. Pemphigoid antigen was present in fish, amphibian, reptilian, avian and mammalian skin, whereas pemphigus antigen was observed in avian and mammalian skin only.

Key words: Epidermal antigens; Phylogenesis; Immunofluorescence; Pemphigus; Pemphigoid

Pemphigus and pemphigoid are two human diseases showing an abnormal epidermal cell adhesion (cell-to-cell in pemphigus and cell-to-basement membrane in pemphigoid) and an autoimmune antigen/antibody reaction, taking place on the surfaces of epidermal cells (differentiating keratinocytes in pemphigus and basal cells in pemphigoid). The defect in cell adhesion and the autoimmune phenomenon seem to be pathogenetically related (5, 7, 10). Pemphigoid antibodies react with an antigen located in the lamina lucida of the dermo-epidermal junction of mammalian skin, producing a linear pattern of staining by IF techniques (1, 4). Pemphigus antibodies, on the other hand, react with an antigenic moiety closely related to the outer leaflet of the cell membrane of differentiating keratinocytes (11). They produce a honeycomb staining of the epidermis by immunofluorescence (1). Pemphigus antibodies react only with stratified squamous epithelia, while pemphigoid antibodies react not only with these epithelia, but also with certain other epithelia, e.g. bladder and gall bladder (1). The

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Abbreviations: PBS=phosphate-buffered saline, IF=immunofluorescence, CF II=Cohn's Fraction II, FITC=Fluorescein Isothiocyanate, BMZ=Basement Membrane Zone.