

Melanomas in Horses¹

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In human beings a striking loss of pigment may occur in the skin and hair surrounding normal nevi, the primary sites of melanomas, cutaneous nodules of metastatic melanoma, and over the surface in the form of vitiligo in those with melanomas. It is generally assumed that vitiliginous changes are associated with the local destruction of normal melanocytes on either an autoimmune or cytotoxic basis because of the presence of a benign nevus or a melanoma. In a report by Millikan *et al.* (1) on pigs with melanocytic nevi that might be melanomas, changes of pigment loss identical to that observed in some human subjects was described. Gray horses ordinarily have a high incidence of melanomas. Dark brown at birth, they probably developed melanomas after turning white and not before. There may be a human counterpart to this phenomenon. Because knowledge of the relationship of changes in hair and skin color during the course of a melanoma is likely to be important in developing a method to control the growth of a melanoma, the animal models should be investigated in detail. The Arabian horse described in this report is one animal with a high predisposition to develop a melanoma.

We examined horses at the 2800-acre Al-Marah Farm in Maryland, the world's largest Arabian horse farm. The horses are descendants of animals that have lived in Asia Minor in Arabia for over 3000 years. The first thing one notices on scanning the fields is that the mares are white and the colts and fillies are dark brown. It is clear that although a few of the Arabian horses remain chestnut in color most of the horses change color with age, being dark brown initially and gradually becoming gray and white. Part of the nose usually has no pigment at birth. The onset of puberty is about 14 months. At 2 years of age the animals begin to gray and by 9 years they are very white. The white patch on the nose remains unchanged. Loss of pigment about the eyes and anus begins after 2 years of age. Not all animals develop vitiligo patches. In those that do partial loss recurs and extends. The life expectancy of the Arabian horse is 12-15 years although some live beyond 20. By 5 or 6 years of age many of the horses have developed melanomas, with tumors beginning about the anus. The animals handle the neoplasm well and go on for many years without apparent difficulty.

¹ This paper was not presented at the Conference on Pigment Cell Biology.

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One gets the impression that hair becomes gray before the melanoma appears. The point, however, is not an obvious one because the melanomas do not metastasize for many years. It is conceivable that small melanotic tumors grew about the rectum and that the pigment loss followed the development of the tumors. The animals have not been studied from that standpoint. Whether the vitiligo about the eyes and anus preceded or followed the melanomas also is not known. Death of a horse from a melanoma usually results from intestinal obstruction or metastases. Metastatic lesions are found in the small bowel, the heart, and in other parts of the body. The larger Lippizaner horses in Austria have the same coloring as the Arabian horses and also develop melanomas. The ordinary work horse that is brown at birth and later becomes gray also is prone to develop a melanoma. Horses that turn gray at about 2 years of age tend to develop melanomas regardless of type.

Most of the Arabian horses seen at Al-Marah Farm had patches of hypopigmentation on the nose present from birth that looked like the lesions of partial albinism. Graying of hair and loss of skin color occurring after 2 years of age probably represents the onset of vitiligo. Eventually the animals develop total vitiligo at least of the hair bulbs. These horses have minimal partial albinism and a progressive vitiligo. Both partial albinism and vitiligo are inherited as dominant traits in man.

Patients with melanomas arising from the skin or eyes are predisposed to vitiligo. Ten to 20% of patients with melanomas have vitiligo whereas only 1% of the general population has vitiligo (2-4). The development of gray hair near a patch of a melanotic tumor in the minipig as described by Millikan *et al.*, followed by total depigmentation of the animal, is similar to the usual human pattern. The course of the Arabian horse seems to be opposite that of man and pig in that the vitiligo appears first and then the melanoma. We know of only two examples in human beings comparable to that of the horse. A man with brown eyes and hair but very light skin began to gray before 30. At 35 he was completely gray. The gray hair plus the light skin and brown eyes gave him a striking appearance. When seen at age 64 he gave a history of having a very black nevus on one leg that was present for approximately 20 years. The nevus slowly enlarged. It was approximately 2 cm in diameter at the time of examination and clearly a melanoma. Surgical removal of the primary was carried out. Later he had regional profusion as well as cross transfer of leukocytes. He died from metastases of the melanoma at age 67. This man had little or no pigment in his skin from birth and resembled an unusual form of extensive partial albinism as opposed to regular albinism. His hair turned gray at an early age as in those with vitiligo. A melanotic tumor had been present for many years, and later metastasized.

The second case was in a girl in her early teens who developed a melanoma and died from metastases 2 or 3 years later. Of interest is the fact that her identical twin sister who is well and without any evidence of melanoma 15 years later has a striking halo nevus on the chest in which the central nevus has disappeared. A brother of the twins has vitiligo.

ACKNOWLEDGMENT

We wish to thank Mr. Connor at the Al-Marah Farm for his guidance when we visited the farm and for providing us with much information on Arabian horses.

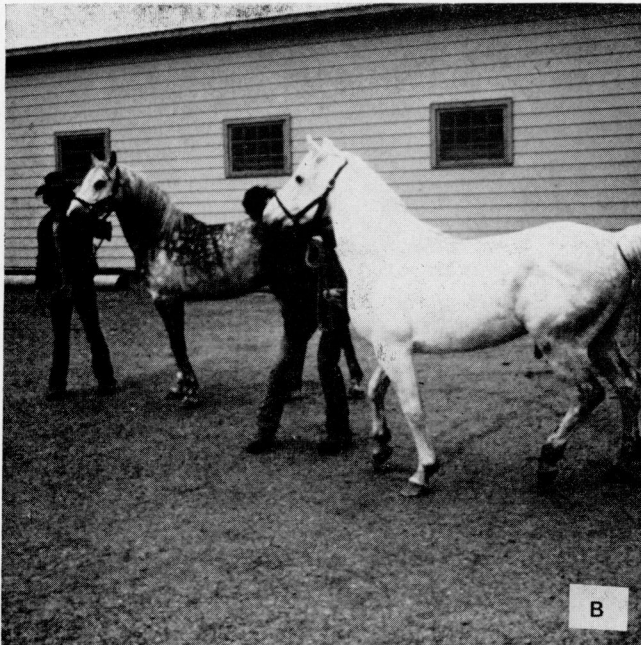
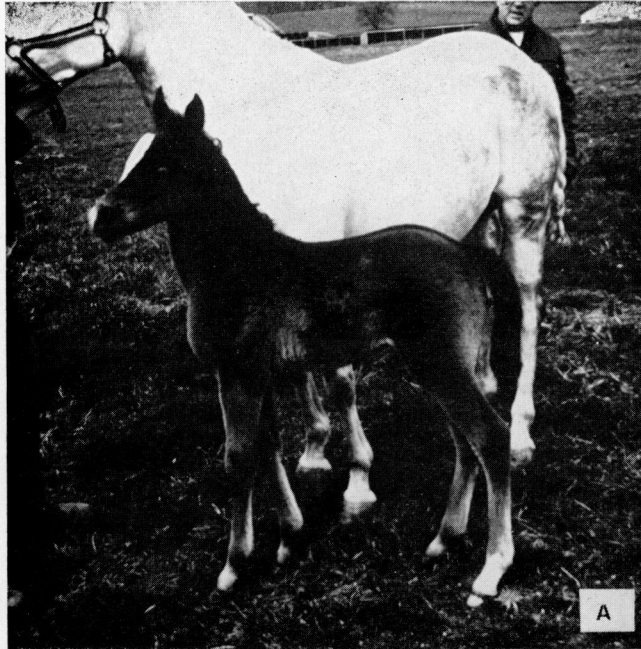
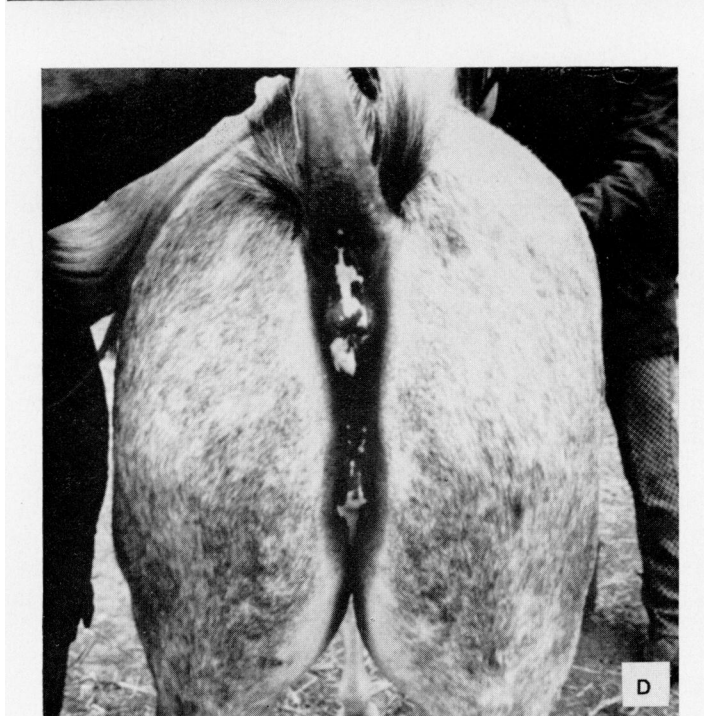
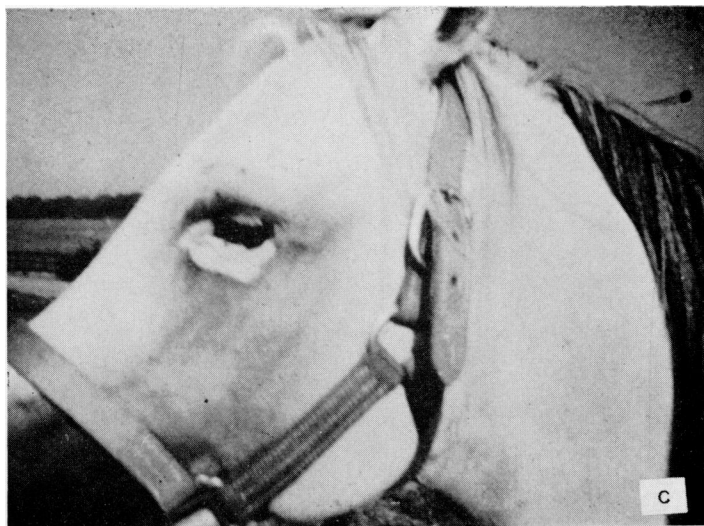


FIG. 1. A. A handsome month-old Arabian foal with his 3- to 4-year-old mother. Originally she had the same coloring as her offspring but began to turn gray at about 2 years of age. This foal will follow a similar course. B. The darker of these two Arabian horses is 2-3 years old and the whiter one 6-8. Pigment loss continues as the animals age. After 9 or 10 years the horses are nearly all white. C and D. Vitiligo about the eye and anus in Arabian horses. This pigment loss occurred after birth. At times, for unknown reasons, some repigmentation may occur. The repigmentation may persist or it may later be lost.



REFERENCES

1. Millikan, L. E., Hook, R. R., and Manning, P. J. Gross and ultrastructural studies in a new melanoma model: The Sinclair swine. *Yale J. Biol. Med.* **46**, 631-645 (1973).
2. Lerner, A. B. On the etiology of vitiligo and gray hair. *Amer. J. Med.* **51**, 141 (1971).
3. Milton, G. W., McCarthy, W. H., and Carlon, A. Malignant melanoma and vitiligo. *Aust. J. Derm.* **12**, 131 (1971).
4. Klaus, S. N., Bluming, A. Z., and Vogel, C. L. Personal communication to the authors.