HISTOPATHOLOGY OF HYPOTRICHOSIS IN CALVES

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[*Manuscript received September* 28, 1966]

Summary

The histopathology of the skin in hypotrichosis has been studied for a Jersey calf and comparisons made with normal skin. Other abnormalities of the hair follicle have been described in a Hereford mutant.

There is considerable variation in hypotrichosis of the calf, as in mice, all forms involving retardation or arrest of the prenatal and early postnatal skin development.

A feature of the skin in hypotrichosis is a high concentration of abnormally complex arteriovenous anastomoses. It is postulated that this abnormality of cutaneous vascular supply is a predisposing factor in the development of the syndrome. The poor development of the hair follicles and associated sweat glands appears to result from insufficiency of the capillary bed. An analogous situation in humans is cutaneous necrosis of the leg as a result of dilatation of the arteriovenous anastomoses.

While arteriovenous anastomoses do not appear compensatory to lack of sweat glands, they do provide an alternative thermoregulatory mechanism which might be effective at moderate environmental temperature.

I. Introduction

Various types of hypotrichosis, a congenital form of alopecia, have been reported in cattle. The condition of viable hypotrichosis in a Jersey calf has been discussed by McGavin and Alexander (1961) and in Guernseys by Becker, Simpson, and Wilcox (1963). Hutt (1964) pointed out that this syndrome is caused by a recessive autosomal gene. Another form, hypotrichosis anadontia, occurring in three male calves, was described by Drieux *et al.* (1950). This completely hairless condition probably results from the action of a recessive sex-linked gene.

A note on hypotrichosis in a Friesian herd was supplied by Shand and Young (1964). High neonatal mortalities were associated with this condition which was assumed to be caused by a recessive gene.

This paper describes histological abnormalities of the skin in two calves suffering from hypotrichosis, one a Jersey and one a Hereford. Measurements obtained from the Jersey subject are compared with those from a normal Jersey calf. This leads to the conclusion that the pathological condition of the skin is secondary to an abnormal vascular supply.

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II. Materials and Methods

(a) *Pedigree Analysis of Jersey Calf*

Several hypotrichoid calves were born in a pure-bred Jersey herd (herd A) in the North Coast Region of New South Wales, following the introduction of a Jersey sire from Victoria.

In this herd of about 65 cows, 20 hypotrichoid calves were born between 1952 and 1964. They appeared only among calves bred closely to the original sire. In 1962 two of the 13 cows mated to a son of this bull had hypotrichoid calves and in 1963 two cases appeared among 18 progeny.

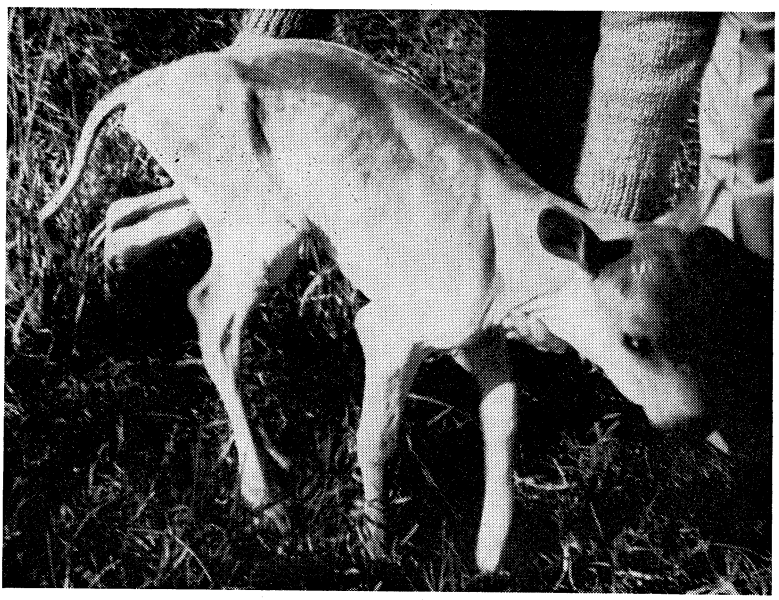


Fig. 1.—Day-old Jersey calf, a case of congenital alopecia, from which skin biopsies were taken for the present study. A tuft of hair can be seen on the tail switch and the ears have fairly normal hair coverage.

Bulls from herd A have been used in herds B and C where hypotrichoid calves have also appeared. In both cases, parents of affected calves can be traced back to herd A. In herd B, four affected calves were born in 1955–56, progeny of a bull introduced from herd A. No further cases occurred until 1964 when a grandson of this sire was used on his female descendants and produced two hypotrichoid calves. In herd C, four cases occurred in 1961–62.

(b) *Gross Description of Calves*

At birth hypotrichoid calves weighed *c.* 10 lb less than the normal weight of 50–55 lb. Because of their weak condition and lack of coat cover they were destroyed at birth. A male calf which survived to 3 months died apparently as a result of sunburn and hyperkeratosis.

While the calves appeared devoid of hair, closer examination revealed a short fine coat with small tufts of hair on the ears, elbows, and tail switch (Fig. 1). The pelage appeared much like that described by Drieux *et al.* (1950).

The Hereford calf likewise had more hair cover on the tail switch, head, and hocks than elsewhere. No normal Hereford calf from the same environment was available for purposes of comparison. This case of hypotrichosis was interesting in that it showed various follicle dysplasias not seen in the Jersey but similar to that reported in mice.

(*c*) *Histology*

Biopsy specimens from the mutant and normal day-old calves were taken for histological examination from the midside with a 1-cm diameter trephine. Samples to be used for the demonstration of capillary supply by the modified azo-dye technique for alkaline phosphatase (Gomori 1952) were wrapped in aluminium foil and held on dry ice. The remaining samples were fixed in 5% formol saline.

All sections were cut on a freezing microtome. Serial transverse sections of 75 μ thickness were cut parallel to the surface to below the apocrine gland level. Vertical sections for demonstrating the piloapocrine profile were cut parallel to the plane of the follicle and its epidermal projection. Sections were of 200 μ thickness for measuring sweat gland size and 100 μ for demonstrating vascular supply. The object of thick sections was to avoid as much as possible the cutting of the glands. Measurements on sweat glands were carried out according to the technique of Nay and Hayman (1956).

Several staining techniques were employed: toluidine blue for transverse sections, haematoxylin–eosin and aldehyde–fuchsin for vertical sections. In each case reagent strengths were adjusted to suit thickness of section. Since the non-specific alkaline phosphatase reaction was shown by the endothelial lining of the larger vessels supplying the papillary layer, this technique was used for demonstrating the arteriovenous anastomoses. Because this method is described as having limited reproducibility, both the normal and mutant skin sections were incubated simultaneously.

III. Results

(*a*) *Quantitative Aspects*

Measurements of nine quantitative characters in skin sections from the mutant and normal Jersey calves are set out in Table 1. The mean values for the mutant skin are significantly less except for follicle density which is significantly greater.

(i) *Follicle Density.*—Apart from small patches of normal coat in certain restricted areas, the pelage in hypotrichosis consists of short fine hairs. The significant difference between the two skin samples in follicle density suggests that the density of these fine hairs is greater than normal. The smaller body weight of the mutant would produce a relatively greater follicle density. As illustrated by a comparison of Figures 1 and 2 of Plate 1, the mutant shows a complete absence of giant hairs.

As only incomplete transverse sections were available the possibility of differential contraction after biopsy affecting follicle density could not be investigated.

(ii) *Hair Diameter.*—The mean hair diameter, calculated from 50 observations, is highly significantly lower in the mutant. The greater variance in the normal population of hairs is largely due to the presence of giant hairs which are absent in the mutant. Independent of these larger hairs the mean hair diameter is still significantly greater in the normal calf ($t = 1 \cdot 99$, $P < 0 \cdot 05$) though the mean diameter and standard error ($11 \cdot 9 \pm 0 \cdot 8\ \mu$) is greatly reduced.

(iii) *Sweat Gland Density.*—The density of inflated glands for the normal and mutant calf is shown in Plate 1, Figures 3 and 4 (transverse sections). An estimation of density where the glands are simple tubular or simple flask-shaped can be obtained from transverse sections. The results in Table 1, which show a much lower density

TABLE 1

COMPARISON OF SKIN THICKNESS AND HAIR FOLLICLE–SWEAT GLAND RELATIONSHIPS BETWEEN A NORMAL AND A HYPOTRICHOID JERSEY CALF

Skin Character	No. of Observations	Mean ± Standard Error		*t* Value
		Normal	Mutant	
Follicle density (No./sq. cm)	5†	5756±204	6362±204	2·45*
Hair diameter (μ)	50	15·5±1·3	10·6±0·3	3·67***
Sweat gland density (No./sq. cm)	4†	4472±429	910±25	9·55***
Sweat gland length (μ)	15	277±18	138±4	7·71***
Sweat gland diameter (μ)	15	73±4	60±2	2·80**
Ratio of sweat gland length to diameter	15	3·95±0·32	2·30±0·09	3·93***
Skin thickness (mm)	5†	1·75±0·04	1·31±0·05	7·88***
Follicle depth (μ)	15	528±29·8	297±17·0	6·94***
Sweat gland depth (μ)	15	721±200	414±20	11·20***

* $P < 0 \cdot 05$. ** $P < 0 \cdot 01$. *** $P < 0 \cdot 001$. † No. of fields.

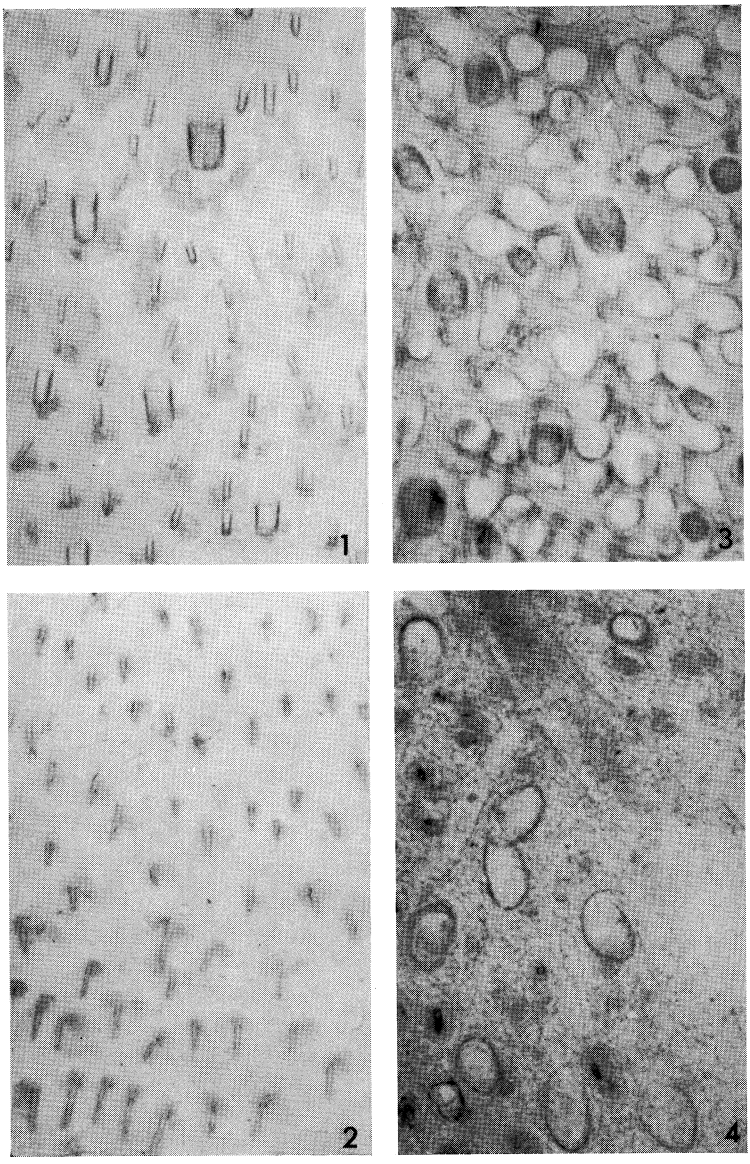
in the mutant, have been obtained in this way. An alternate method is to examine a random selection of follicles for the presence or absence of associated sweat glands. While 78% of the follicles in the normal calf have distended glands, a result consistent with older beef calves (Schleger 1966), the value is as low as 14% in the mutant. There are no apparent differences between the glandular follicles and the remaining follicles in the mutant.

(iv) *Sweat Gland Size.*—The mean length and variance of length of sweat glands are significantly smaller in the mutant calf. The same applies to sweat gland diameter although the effect is not as great. This results in a significantly lower sweat gland length/diameter ratio in the mutant, giving a dilated appearance. This is contrary to the report of Becker, Simpson, and Wilcox which stated that some apocrine sweat glands were dilated, but the majority were normal in appearance.

(v) *Skin Thickness.*—The skin of the mutant calf is significantly thinner than normal.

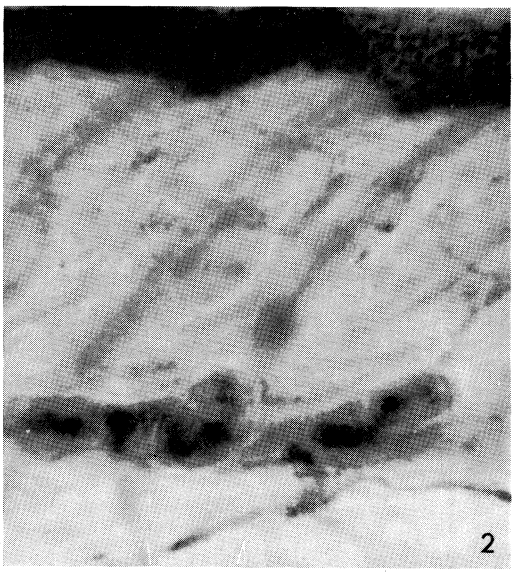
(vi) *Follicle Depth and Sweat Gland Depth.*—The depth of the papillary layer, like the skin thickness, is significantly less in the mutant skin.

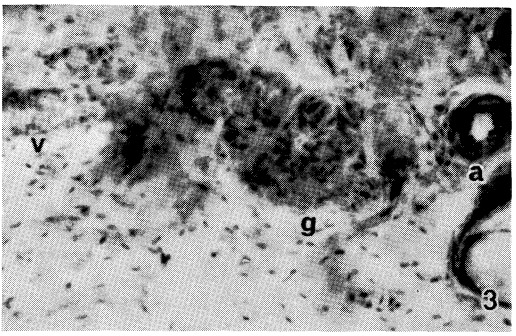
HYPOTRICHOSIS IN CALVES



Photomicrographs of transverse skin sections at subepidermal level for normal (Fig. 1) and hypotrichoid (Fig. 2) Jersey calves, showing the absence of giant hairs in the latter. The corresponding sections through the sweat gland level (Figs. 3 and 4, respectively) illustrate the relative sweat gland density. Toluidine blue. ×80.

HYPOTRICHOSIS IN CALVES



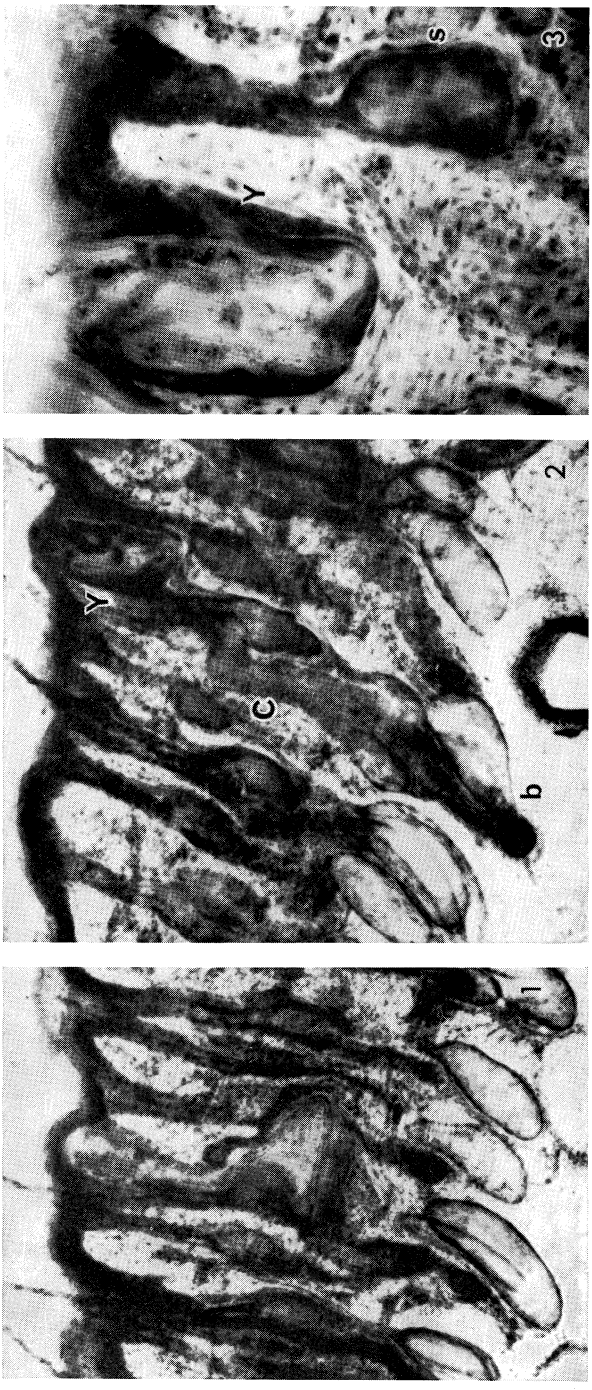


Photomicrographs illustrating the vascular pattern characteristic of the normal and hypotrichoid Jersey calves. There is a rich vascular pattern in the region of the lower follicle in the normal calf (Fig. 1), with a subsidiary supply to the sweat gland. In the mutant calf (Fig. 2) there is no apparent supply to the lower follicle, while the complex arteriovenous anastomoses (demonstrated by alkaline phosphatase reaction) are a prominent feature. The major components of the anastomoses are shown in Figure 3: *a*, artery; *v*, vein; *g*, glomus. ×320 (Figs. 1 and 2); ×200 (Fig. 3).

HYPOTRICHOSIS IN CALVES

Fig. 1.—Photomicrograph of normal Jersey calf showing giant follicle in early anagen with active papilla. Aldehyde–fuschin stain. ×320.
Figs. 2 and 3.—Photomicrographs of the mutant Jersey calf showing follicles in telogen (*T*), middle catagen (C_c), and late catagen (C_d), as described by Schleger (1966). The relatively distended sebaceous glands (*S*) are apparent in the telogen follicles. The follicle in catagen (*C*) phase may be curved (Fig. 3) and tends to be pointed (Figs. 2 and 3). Aldehyde–fuschin stain. ×320.

HYPOTRICHOSIS IN CALVES



Figs. 1–3.—Follicle dysplasias in Hereford hypotrichoid skin. A Z-shaped follicle is illustrated in Figure 1. In Figure 2 is shown a composite follicle consisting of a cyst (*Y*), a non-pigmented shaft in catagen (*C*), and a darkly staining bulb (*b*) of new hair in anagen. Figure 3 shows a follicle cyst (*Y*) and a sebaceous gland (*s*). Haematoxylin and eosin stain. ×80 (Figs. 1 and 2); ×200 (Fig. 3).

(*b*) *Dermal Vascular Supply*

Because of the more complex arteriovenous anastomoses in the mutant sheep without sweat glands (Molyneux and Griffin 1963), this aspect of the cutaneous vascular supply was compared in the normal and mutant Jersey calves. The normal skin shows a high degree of vascularity of the bulb and lower follicle with a subsidiary supply to the apocrine glands (Plate 2, Fig. 1). However, in the mutant (Plate 2, Fig. 2) the capillary supply to the follicles and glands is not at all pronounced but the arteriovenous anastomoses are quite large and complex. Arteriovenous anastomoses are simple and compact in the normal skin and are quite restricted in number. As thin serial sections of normal and mutant skin were not cut, a precise determination of the density of arteriovenous anastomoses could not be made. However, an estimate was made by counting the number of anastomoses and large subpapillary arteries in eight sections of each of the two mounts. Adjusting for slight differences in section length, the total cross-sectional area of normal skin contained 3 anastomoses and 19 arterial sections, while the mutant skin contained 36 anastomoses and no subpapillary arterial sections which were independent of anastomoses.

While there is no differential staining in the alkaline phosphatase technique which might indicate the considerable muscular and adventitial thickening of arteriovenous anastomoses described by Grant in 1930 (quoted from Ham and Leeson 1961), the positive reaction in Plate 2, Figure 2, is obviously that of the arteriovenous bridges. Plate 2, Figure 3, illustrates a coiled anastomosis or glomus (*g*) connecting the artery of origin (*a*) in transverse section, and the wide thin-walled collecting vein (*v*) in longitudinal section. The arteriovenous anastomoses of the Hereford hypotrichosis were characterized by fine complex glomi and were widely distributed throughout the sections.

(*c*) *Miscellaneous Abnormalities*

(i) *Shallow Follicles.*—McGavin and Alexander (1961) reported shallow hair follicles and this was confirmed in the work of Becker, Simpson, and Wilcox (1963). In the former case, skin samples from various parts of the body showed uniformly hairless follicles while follicles in the latter case appeared as an empty core lined with keratinized material or containing a plug of keratin. That is, no emergent shafts were apparent in either case.

All follicles in the Jersey mutant are shallower than in the normal calf (Table 1). While a number of the follicles are in early anagen as in the normal calf (Plate 3, Fig. 1), a disproportionately high percentage of the follicles are in late catagen or telogen phases (Plate 3, Figs. 2 and 3), and in these phases the follicle depth is less than in anagen (Schleger 1966). All follicles appear to have emergent hairs.

(ii) *Distorted Follicles.*—The fine, poorly keratinized shafts, often ending in a slight taper (Plate 3, Figs. 2 and 3), are as reported in alopecia areata by Van Scott (1959).

Some curved follicles (Plate 3, Fig. 3) have been found in the Jersey mutant (cf. pili torti, Rook 1965) and this phenomenon is associated with abnormal orientation of the follicles (cf. ragged mice, Slee 1957).

The follicle structures of the Hereford hypotrichosis case appear similar to that described for mice in transient alopecia or trichomalacia (Pinkus 1965). All emergent hairs appear fine and wavy and they often show broken columns of pigment. In Plate 4, Figure 1, is an abnormal Z-shaped shaft, and some follicular cysts containing coiled hair shafts are found (Plate 4, Figs. 2 and 3). Associated with the cysts are enlarged sebaceous glands, thin non-pigmented hair shafts in catagen, and normal type anagen hairs of the following generation (Plate 4, Fig. 2).

(iii) *Sebaceous Gland Size.*—The sebaceous glands are relatively distended in all follicles especially those in telogen and catagen (Plate 3, Figs. 2 and 3). This is analogous to baldness in humans (Ellis 1958) where the sebaceous glands are abnormally large and have many lobules. In genetically hairless mice, degenerating sebaceous glands whose ducts have been obliterated form cysts in the skin (Crew and Mirskaia 1931). In the Jersey all sebaceous glands appear to be in free communication with the follicle and to be non-cystic. In the Hereford, however, cystic glands are present as shown in Plate 4, Figure 3.

(iv) *Connective Tissue.*—In the hypotrichoid skin the nuclei of the connective tissue fibroblasts are surrounded by abundant basophilic cytoplasm (Plate 3, Figs. 2 and 3), a feature which distinguishes young fibroblast cells in the pre-natal skin (Lyne and Heideman 1959; Ham and Leeson 1961).

(v) *Epidermal Thickness.*—The positively reacting thick epidermis evident in Plate 2, Figure 2, is analogous to the thick epidermis of the 4–6-month cattle foetus (Lyne and Heideman 1959), and the epidermal hyperplasia of ragged mice (Slee 1957). Drieux *et al.* (1950) described the epidermis in his calves as thin with the outer layers keratinized. He obviously referred to the whole skin as epidermis.

IV. Discussion

Although only limited morphological detail is available on the skin of calf mutants reported from time to time under the general description of hypotrichosis, there is apparently considerable variation in the degree and form of follicular abnormality.

Two different types are presented here. Follicle development is more advanced in the Hereford, the follicle dysplasia more complex, sweat gland development less retarded, and arteriovenous anastomoses numerous but fine. Each hypotrichoid variant differs slightly from other reported cases. This is perhaps understandable in view of the wide variation in hair mutants described by Slee (1965) and Chase and Mann (1960) for other mammals. Whatever the controlling mechanism involved, arrest or retardation of the embryonic or neonatal hair-growth cycles is involved, as reported for ragged mice by Slee (1962). Epidermal hyperplasia and a thin adipose layer are regarded by Slee as a consequence of reduced substrate competition and limited follicle downgrowth. Skin thickness in bovine hypotrichosis might be similarly determined. As there is complete absence of guard hairs in the two forms of alopecia reported here the condition is analogous to that of the homozygous mouse mutant.

The effect of nutritional stress on skin structures is well documented (Lorincz 1954; Ryder 1958). One might postulate that the condition of hypotrichosis is

predetermined by the congenital presence of more complex and more extensive arteriovenous anastomoses than is typical of the normal skin. Through their effect on the vascular supply to the subepidermis and dermis they might well affect the nutrition of the papillary layer so that maldevelopment of the piloglandular complex takes place. As Hardy (1951) pointed out, follicles can develop and grow without a blood supply, but they produce smaller hairs. In the case of stasis ulcers of the leg, a permanent dilatation of the arteriovenous anastomoses in the skin leads to a bypass of the capillary bed with resulting tissue necrosis (Welbourn 1964).

Molyneux (1965) considers that the higher density and superficial position of the arteriovenous anastomoses in the skin of the mutant sheep with congenital absence of sweat glands are compensatory to the lack of sweat glands. This view would hardly be tenable if, as is likely, the anastomoses already show their abnormal development at birth. Certainly in the case of the hypotrichoid calf, the anastomoses are highly developed at birth and cannot be regarded as compensatory to lack of sweat glands, as the foetal calf is not subject to any thermal stress and its sweat glands have no thermoregulatory function prenatally. A more likely suggestion is that the sparseness of sweat glands is a reflection of a disturbance in the histogenesis of the piloapocrine complex brought about by the presence of arteriovenous anastomoses.

Dilation of arteriovenous anastomoses in the skin would permit a much greater flow of blood and thereby effect a transfer of heat from the body core to the surface. How effective this would be has not been determined experimentally. Clearly it would not be effective, as sweating is, in dissipating heat against a temperature gradient.

V. Acknowledgments

We are indebted to Mr. D. M. Murray, University of New England, Armidale, N.S.W., for a skin biopsy from a Hereford calf mutant. We wish to commend Mr. K. G. Bean for his capable assistance in all phases of the work. We thank Mr. H. G. Turner for his criticism of the manuscript.

This work was supported in part by the Australian Meat Research Committee.

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