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Effects of Abomasal Supplements of Methionine on the Wool Follicles and Skin of Wheat-fed Sheep

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Abstract

In wheat-fed sheep, supplemented abomasally with 1·5–6·0 g methionine per day, poor formation and improper keratinization of the wool fibres were evident 4 days after the start of the methionine supplementation. This led to kinking of the fibres. Subsequently severe distortion of the fibres, accompanied by gross thickening of the outer root sheaths, occurred in the distal (upper) halves of most follicles. Within this thickened region partial degradation of the distorted fibres occurred before emergence from the skin surface, causing a marked reduction in the tensile strength of the wool.

It is postulated that kinking of the fibres stimulated the accumulation of outer root sheath cells, which led to hyperactivity of the process that normally degrades the inner root sheath, so that the poorly keratinized fibres were also partly degraded.

Thickening of the epidermis and cellular infiltration of the upper dermis sometimes occurred during the infusions of methionine, whereas there were negligible effects on the sebaceous and sweat glands.

Disappearance of the excess accumulation of outer root sheath cells after cessation of the methionine supplementation occurred gradually following improvement in keratinization and elimination of kinking of the fibres.

Introduction

Supplements of cyst(e)ine or methionine given so as to avoid degradation in the rumen, e.g. by abomasal infusion, increase the wool growth rate of sheep consuming moderate amounts of roughage diets in pens or at pasture (Reis and Schinckel 1963; Reis 1967; Langlands 1970; Robards 1971; Williams *et al.* 1972; Reis *et al.* 1973; Dove and Robards 1974). Above-optimal supplements of methionine usually depress wool growth (Reis 1967; Reis *et al.* 1973). Likewise, even small amounts of methionine, infused abomasally into sheep on a diet consisting solely of wheaten grain, depress wool growth and in addition markedly reduce the tensile strength of the fibres (Reis and Tunks 1974).

This paper describes unusual changes in the wool follicles and features of the skin associated with the deleterious effects of methionine on wool growth observed in two of the experiments reported by Reis and Tunks (1974). Histological observations commenced in the first experiment only after the deleterious effects on wool became obvious. In the second experiment, earlier times of sampling were undertaken to obtain information concerning the onset of the effects.

Table 1. The nutritional regimes and the state of the wool, follicles and epidermis of the sheep in experiments 1 and 2

Abbreviations are as follows. For *wool*: S = sound; W = weak; VW = very weak; L = some wool lost; I = improved strength. For *follicles*: upper case letters refer to a majority of follicles and lower case letters to a minority. Lower case letters in parentheses refer to less than 10% of follicles. K = normal keratinization of fibres in the proximal halves of follicles; P,p = poor formation and impaired keratinization of fibres in the proximal halves of follicles; F = normal fibres in the distal halves of follicles; D,d = distorted and partly degraded fibres in the distal halves of follicles; R = normal outer root sheaths in the distal halves of follicles; H,h = hyperplasia and thickening of the distal outer root sheaths of follicles. For *epidermis*: E = normal epidermis; T_o,t_o = thickening of the epidermis around follicle orifices; T = general thickening of the interfollicular epidermis as well as around follicle orifices

Expt No.	Sheep	Period 1				Period 2			Period 3		
		Week 1	Week 5								
		Wool	Wool	Follicles	Epidermis	Wool	Follicles	Epidermis	Wool	Follicles	Epidermis
			Wheat+1·5 g Met/day			Wheat+1·5 g Met/day			Roughage+0		
1	1	W	W	Pdh	T_o	W	—	—[A]	S	K(d)(h)	T_o
	2	W	L	PDH	E	L	PDH	T	S	K(d)(h)	T_o
	3	S	S	pFR	E	S	pFR	t_o	S	KFR	E
			Wheat+3·0 g Met/day			Wheat+1·5 g Met/day+ 2·0 g Lys/day+1·0 g Trp/day			Roughage+0		
	4	W	W	Pdh	T_o	W	Pdh	T_o	S	KFR	E
	5	W	L	PDH	t_o	L	PDH	t_o	S	KFR	E
	6	W	L	PDH	E	L	PDH	E	I	Kdh	E
			Wheat+6·0 g Met/day			Wheat+0			Roughage+0		
	7	W	L	PDH	T_o	I	KF(h)	T_o	S	KF(h)	t_o
	8	W	L	PDH	E	S	KFR	T_o	S	KFR	E
	9	W	L	PDH	T_o	I	KFR	T_o	S	KFR	T_o

Expt No.	Sheep	Pre-treatment			Period 1 Day 4			Day 7	Days 16–18			Period 2 Day 18		
		Wool	Follicles	Epidermis	Wool	Follicles	Epidermis	Wool	Wool	Follicles	Epidermis	Wool	Follicles	Epidermis
			Wheat					Wheat+0					Wheat+0	
2	10	S	KFR	E	S	KFR	E	S	S	KFR	E	S	KFR	E
	11	S	KFR	T_o	S	KFR	T_o	S	S	KFR	T_o	S	KFR	T_o
			Wheat					Wheat+2·0 g Met/day					Wheat+0	
	12	S	KFR	E	S	PFR	T_o	VW	VW	PDH	T_o	I	Kdh	T_o
	13	S	KFR	T_o	S	Pdh	T_o	VW	VW	PDH	T_o	I	Kdh	T_o
			Wheat					Wheat+6·0 g Met/day					Wheat+0	
	14	S	KFR	T_o	S	Pdh	T_o	VW	VW	PDH	T	I	pdh	T_o
	15	S	KFR	E	S	Pdh	T_o	VW	VW	PDH	T	I	pdh	T_o

[A] No skin sample taken because this sheep refused to eat wheat.

Materials and Methods

Experimental Details

The sheep studied were the 15 adult castrated male sheep used by Reis and Tunks (1974) in their experiments 1 and 2. The daily ration of each sheep consisted of 500 g whole wheaten grain and 5 g each of sodium chloride and calcium carbonate.

In experiment 1, nine sheep (five Merinos, one Corriedale, one English Leicester × Merino and two Border Leicester × Merinos) were maintained on the wheaten diet for *c.* 2 months and divided into three groups of three sheep. As listed in Table 1, these groups received respectively 1·5, 3·0 and 6·0 g DL-methionine per head per day infused slowly as an aqueous solution into the abomasum throughout each 24 h for a period of 5 weeks. During a further period of 5 weeks each sheep in the first group continued to receive 1·5 g DL-methionine per day abomasally, those which had received 3·0 g DL-methionine per day were changed to a supplement of 1·5 g DL-methionine, 2·0 g L-lysine and 1·0 g L-tryptophan per day, and those which had been given 6·0 g DL-methionine per day received no supplement. One sheep in the first group refused to eat wheat during this period and was changed to a daily ration of 600 g of a 1 : 1 mixture of chaffed lucerne and oaten grain. At the end of the second 5-week period all the sheep were transferred to this ration.

In experiment 2, six Merino sheep were maintained on the wheaten diet for *c.* 6 weeks, and divided into three groups of two sheep (Table 1). These groups received respectively no methionine (control group), 2·0 and 6·0 g DL-methionine per day infused abomasally for 18 days. After this period the sheep were maintained on the wheaten diet, except for one of the control sheep which had been eating only about half of its ration of wheat; this sheep was changed to a roughage diet.

Skin Sampling and Histological Processing

Duplicate skin samples, 1 cm in diameter, were taken from the midside region of the trunk of each sheep near the end of each 5-week infusion period in experiment 1, and 2 weeks after supplementation ceased. Similar skin samples were taken in duplicate from each sheep in experiment 2 before the infusions began, on days 4 and 16 of the infusion period and 18 days after the infusions ceased.

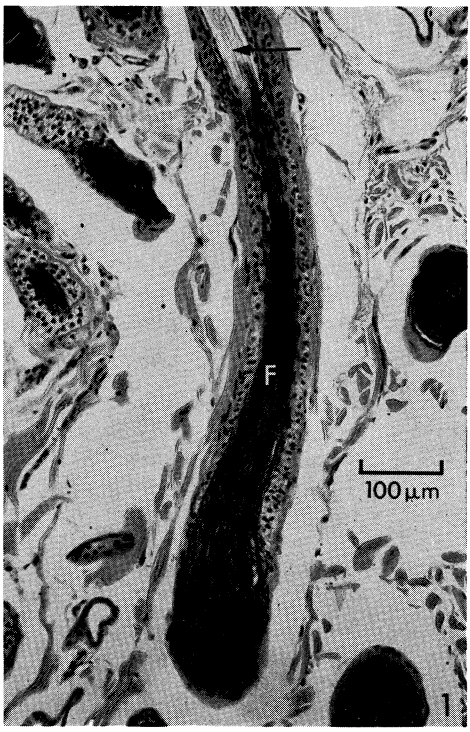
The skin samples were fixed in 10% buffered formalin, dehydrated in alcohol and embedded in paraffin. Serial sections, 8 μm thick, were cut longitudinal to the follicles from one sample of each pair, and transverse to the follicles at sebaceous gland level from the other sample. Half of the sections from each sample were stained with haematoxylin, eosin and picric acid, and the remainder with methylene blue after performic acid oxidation (Clarke and Maddocks 1965).

Results

Information on the strength of the wool and on features of fibre formation, the follicles and epidermis during the various periods of experiments 1 and 2 are listed in Table 1. None of the effects described below was related to the breed of the animals studied.

Wool

All the sheep that received supplements of methionine, except for one on 1·5 g methionine per day in experiment 1, had weakness in the wool about 1 week after the infusions began. By the end of the 18-day infusion period in experiment 2 all four sheep that received methionine had a band in the wool just above skin level, in which the fibres were severely weakened. At the end of the first 5-week infusion period in experiment 1 one of the two sheep, which showed signs of weakness in the wool after 1 week on 1·5 g methionine per day, had lost a considerable amount of wool; the fleece of the third sheep in this group was still sound. Two of the sheep that received 3·0 g methionine per day and the three on 6·0 g per day lost part of their fleeces, and the wool of the third sheep on 3·0 g per day was weak.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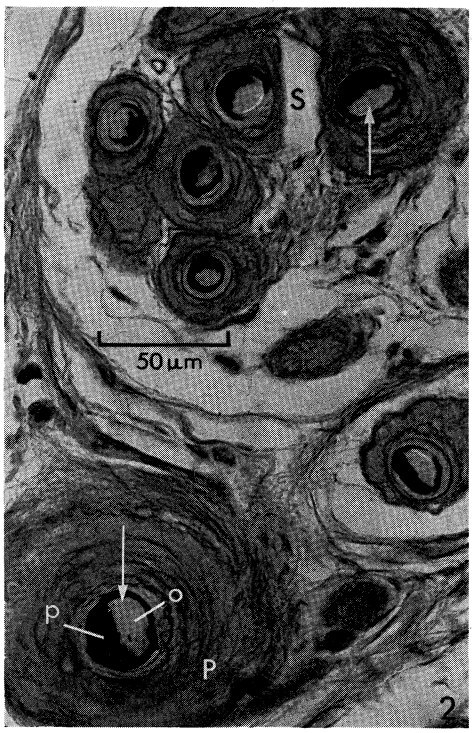
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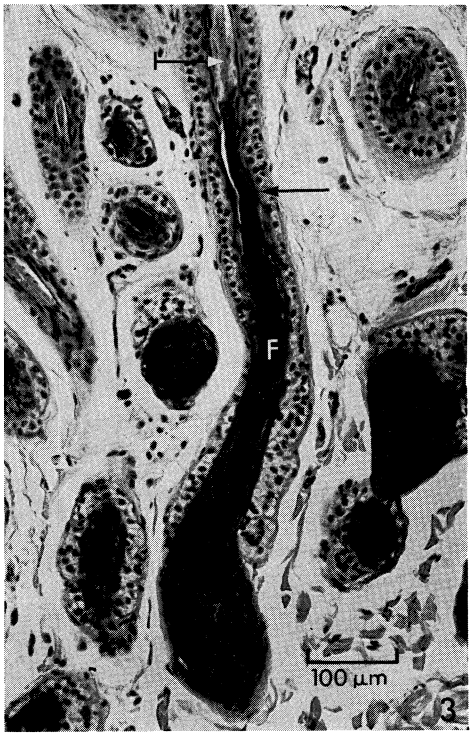
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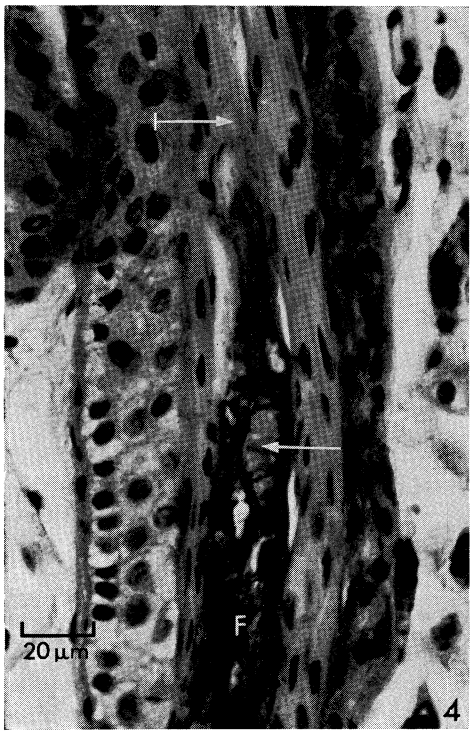
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The effects persisted in the sheep which received methionine during the second 5-week period of experiment 1, and were not alleviated by the simultaneous infusion of lysine and tryptophan. Following cessation of the methionine infusions in both experiments there was gradual improvement in the strength of the wool.

Follicles

The follicles and fibre formation appeared to be generally normal on the wheat diet, prior to administration of methionine (Fig. 1; Table 1). Cortical segmentation in the fibres was mostly bilateral (Fig. 2), except in a small percentage of primary follicles, in which the fibres stained as virtually all orthocortex.

Four days after the start of the infusion of both 2·0 and 6·0 g methionine per day in experiment 2 there was poor fibre formation in the lower halves of many follicles (Fig. 3); the fibres were irregular and poorly keratinized, as judged by an eosinophilous staining reaction instead of the normal picrophilous reaction. Some fibres contained vacuoles in the keratogenous zone (Fig. 4), suggesting impaired protein synthesis.

After 16 days on daily supplements of 2·0 and 6·0 g methionine in experiment 2, and after 5 weeks on 1·5, 3·0 and 6·0 g methionine per day in experiment 1, poor fibre formation was still detectable in the proximal halves of follicles. In addition, severe distortion and degradation of fibres were occurring in the distal parts of many follicles (Fig. 5). The degraded fibres were very irregular in cross section, and bilateral segmentation was not detectable (Fig. 6). Associated with the distortion and degradation of the fibres was gross hyperplasia and thickening of the surrounding follicle outer root sheaths (Figs 5 and 6).

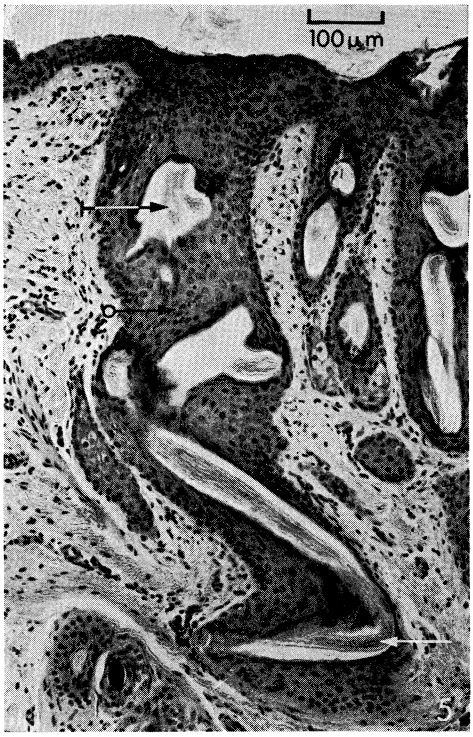
In the second 5-week period of experiment 1, the continued administration of 1·5 g methionine per day caused little further change in the wool and follicles of the two sheep that continued to eat wheat in this group. No skin sample was taken near the end of this period from the third sheep that refused to eat wheat. The reduction in the amount of methionine from 3·0 to 1·5 g per day and the addition of lysine and tryptophan to the supplement of the second group produced a slight decrease in the proportion of distorted follicles in one sheep, but further increase in the other two.

Fig. 1. A longitudinal section of the proximal half of a wool follicle in the skin of a Merino sheep after being fed a wheat diet for *c.* 6 weeks, and before the commencement of abomasal infusion of methionine. Formation of the fibre (*F*) appears to be normal, as does keratinization, judged by the picrophilous nature of the fibre at the level indicated by the arrow (←). (Haematoxylin, eosin and picric acid.)

Fig. 2. Cross-sections of fibres (←) in a primary follicle (*P*) and associated secondary follicles (*S*) in the skin of a Merino sheep after being fed a wheat diet for *c.* 6 weeks, and before the commencement of abomasal infusion of methionine. The fibres all exhibit clear bilateral distribution of the ortho- (*o*) and para-cortical (*p*) segments. (Methylene blue and eosin after performic acid oxidation.)

Fig. 3. Longitudinal section of the proximal half of a wool follicle 4 days after the start of an abomasal infusion of 6·0 g methionine per day in a Merino sheep on a wheat diet. The fibre (*F*) is kinked (←) and is eosinophilic (↦), indicating poor keratinization. (Haematoxylin, eosin and picric acid.)

Fig. 4. Longitudinal section of portion of a wool follicle at a level similar to that depicted by the arrows in Fig. 3, 4 days after the start of an abomasal infusion of 2·0 g methionine per day in a Merino sheep on a wheat diet. The fibre (*F*) contains vacuoles (←) and, as indicated by eosinophilic staining (↦), appears to be poorly keratinized. (Haematoxylin, eosin and picric acid.)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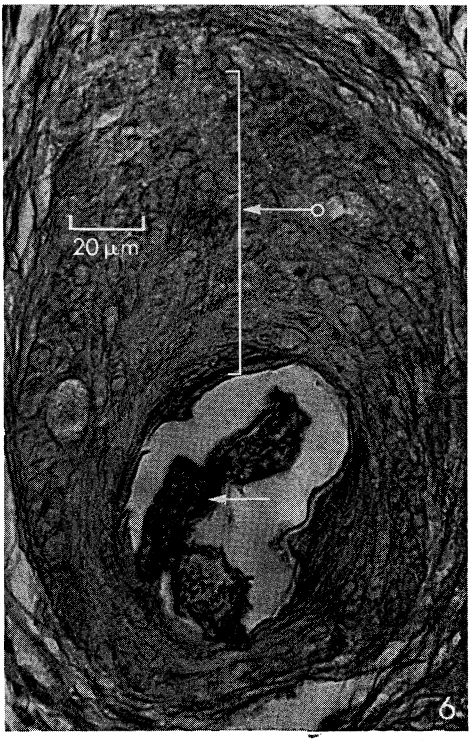
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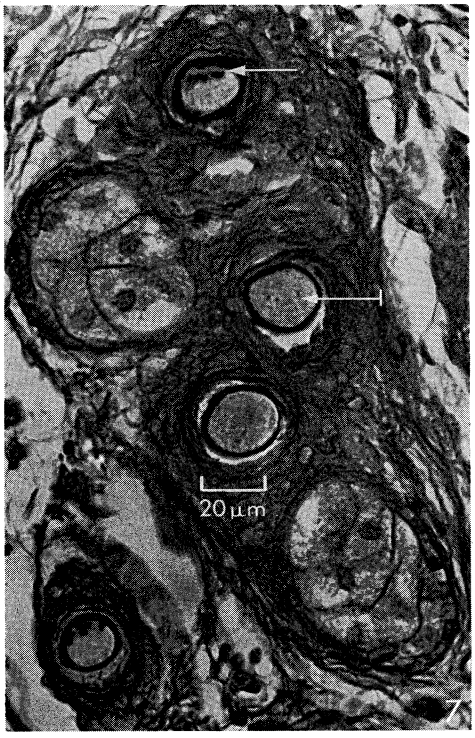
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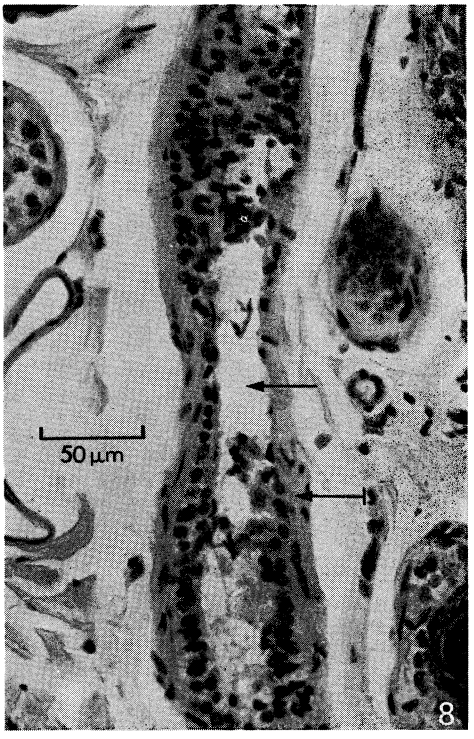
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Following cessation of the methionine infusion in the group previously on 6·0 g methionine per day, the gross thickening of the outer root sheaths and distortion of the fibres subsided appreciably, but not entirely, while still on the wheat diet. In one sheep of this group many of the fibres stained as if virtually all orthocortex (Fig. 7).

The extent to which poor keratinization, distortion and degradation of fibres and gross thickening of distal outer root sheaths were observed in follicles was related to the degree of fibre weakness and loss of wool. The one sheep on 1·5 g methionine per day, whose wool was unaffected in experiment 1, and the two control sheep, which received no methionine in experiment 2, had respectively very few and no follicles with impaired keratinization of the fibres. They also had no follicles with both gross thickening of the distal outer root sheaths and severe degradation of the fibres (Table 1). In the two sheep that had weak fibres, but did not lose wool in experiment 1 (one each on 1·5 and 3·0 g methionine per day), most fibres appeared improperly keratinized, but relatively few follicles had thickened distal outer root sheaths and degraded fibres. In contrast, in all the sheep that lost wool in experiment 1, or had bands of severely weakened fibres in experiment 2, the distal outer root sheaths of most follicles were grossly enlarged and the fibres were severely distorted and degraded.

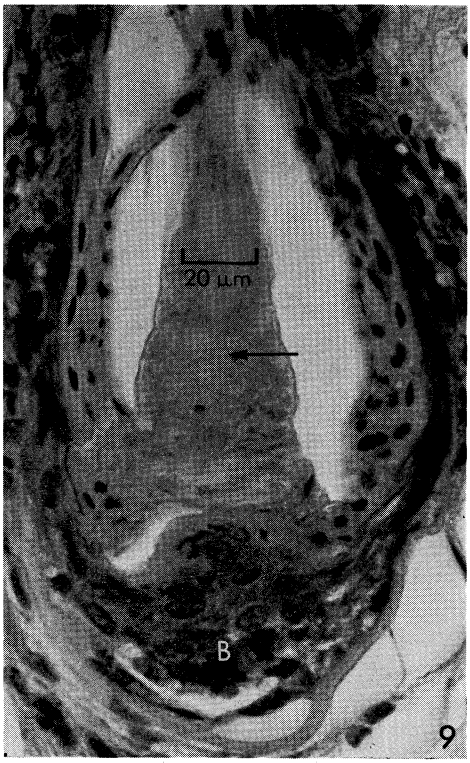
After two weeks on a roughage diet, following cessation of the administration of methionine in experiment 1, the sheep in the groups that had been on 1·5 g methionine per day with or without lysine and tryptophan had considerably fewer follicles with gross enlargement of the outer root sheaths and fibre degradation. In the proximal half of a small number of follicles in one sheep in each of these groups lysis of the cells in the fibre and inner and outer root sheaths had occurred (Fig. 8). In one other sheep in the second group there was clumping of the fibre in the bulb region of *c.* 1% of the follicles (Fig. 9). The third group, which initially was on 6·0 g methionine per head per day, had by this time been on the wheat diet without methionine supplementation for 5 weeks and on the roughage diet for a further 2 weeks. The follicles in two of these sheep had returned to normal, while in the third sheep gross thickening of the distal outer root sheath persisted in some primary follicles (Fig. 10). Many of the fibres in this last sheep still appeared to be virtually all orthocortex, as in the previous sample (Fig. 7).

Fig. 5. A longitudinal section of the distal half of a wool follicle with gross enlargement of the outer root sheath (○→), containing a severely distorted (←) and partly degraded fibre (↦), produced by a 5-week abomasal infusion of 6·0 g methionine per day in a Border Leicester × Merino sheep on a diet of wheat. (Haematoxylin, eosin and picric acid.)

Fig. 6. Cross-section of the distal part of a follicle, similar to that in Fig. 5, containing sections of convolutions in a degraded fibre (←) within the grossly thickened outer root sheath (←○) in a Border Leicester × Merino sheep. Cortical segmentation is not evident in the fibre. (Methylene blue and eosin after performic acid oxidation.)

Fig. 7. In a Border Leicester × Merino sheep, maintained on a wheat diet for 5 weeks after cessation of an infusion of 6·0 g methionine per day, the fibres stained as if virtually all orthocortex, with little (←) or no (↤) paracortex. (Methylene blue and eosin after performic acid oxidation.)

Fig. 8. Longitudinal section of a proximal part of a wool follicle in which lysis of cells of the fibre, inner root sheath and part of the outer root sheath has occurred (←) within the connective tissue sheath (↤) 2 weeks after an infusion of 1·5 g methionine per day ceased in a Merino sheep. (Haematoxylin, eosin and picric acid.)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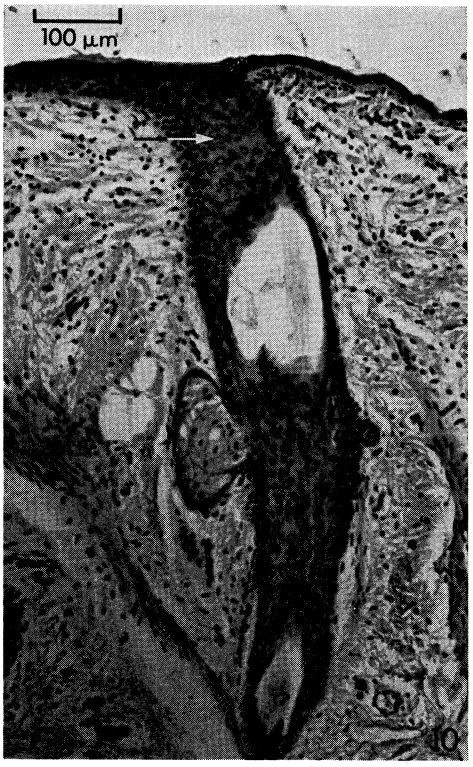
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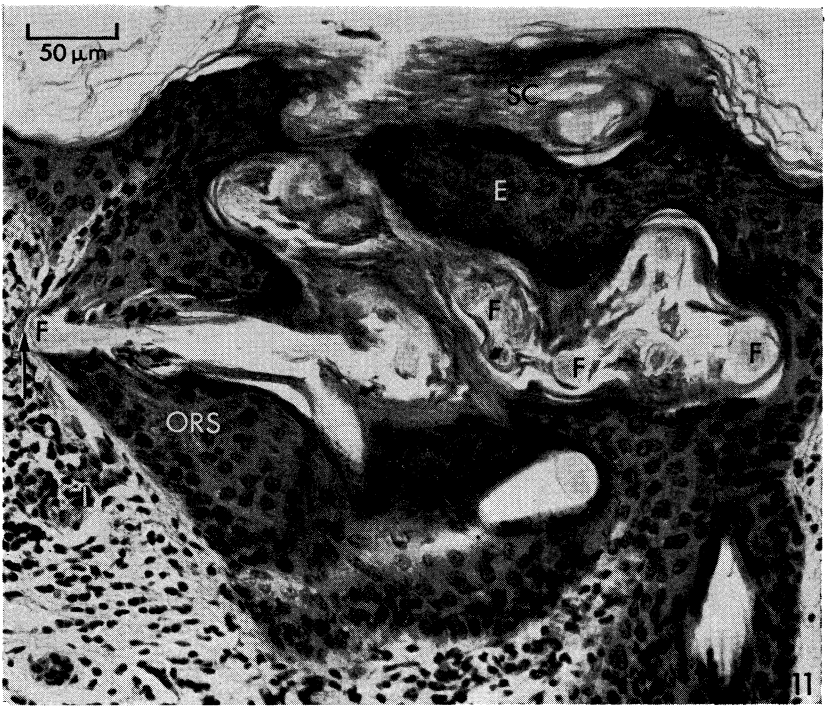
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Eighteen days after the infusions of methionine ceased in experiment 2, distortion of the upper parts of some follicles and the contained fibres was still present in the four infused sheep which were kept on the wheat diet (Fig. 11). There were also still signs of poor fibre formation in the lower halves of some follicles in the two sheep that had received 6·0 g methionine per day in this experiment.

Epidermis

After being on the wheat diet for *c.* 6 weeks and before the methionine infusions began, one of the two sheep in each of the groups in experiment 2 had thickening of the epidermis around the follicle orifices (Table 1). Associated with this thickening was accumulation of considerable amounts of stratum corneum in the orifices. During the infusions of methionine thickening of the epidermis around the follicle orifices was present in one sheep on 1·5 g per day, in two sheep in each of the groups on 3·0 and 6·0 g per day in the first period of experiment 1, and in both sheep in the groups on 2·0 and 6·0 g per day in experiment 2 (Table 1). In addition, a doubling of the thickness of the interfollicular epidermis occurred in the two sheep on 6·0 g per day in experiment 2, but not in the sheep infused the same amount in experiment 1. A general thickening of the epidermis also occurred during the second period of experiment 1 in one sheep on 1·5 g per day, in which the epidermis had been relatively unaffected by the same dose rate during the first 5 weeks. There was little change in the other sheep on 1·5 g methionine per day either with or without lysine and tryptophan during the second period of experiment 1.

Thickening of the epidermis around follicle orifices and excessive production of stratum corneum were still present in some of the sheep 2 weeks after cessation of the second period of methionine supplementation in experiment 1. All the sheep that received methionine in experiment 2 likewise exhibited residual thickening of the epidermis around some follicle orifices 18 days after the infusions ceased (Fig. 11).

Sebaceous Glands

The sizes of the sebaceous glands did not change during any of the infusion periods. However, gland sizes of the three sheep that received 1·5 g methionine per day plus lysine and tryptophan increased during the 2 weeks after cessation of the supplementation.

Fig. 9. Longitudinal section of a wool follicle with a degenerated bulb (*B*) and a thickened suprabulbar region in which clumping of the fibre (←) has occurred 2 weeks after the cessation of an infusion of 1·5 g methionine, 2·0 g lysine and 1·0 g tryptophan per day in a Merino sheep. (Haematoxylin, eosin and picric acid.)

Fig. 10. Longitudinal section of a primary follicle with thickening of the distal outer root sheath (→) still present 7 weeks after the cessation of an infusion of 6·0 g methionine per day in a Border Leicester × Merino sheep. (Haematoxylin, eosin and picric acid.)

Fig. 11. Longitudinal section of wool follicles 18 days after the cessation of an infusion of 2·0 g methionine per day in a Merino sheep kept on a diet of wheat. Features still present include thickening of the outer root sheaths (*ORS*) around distorted fibres (*F*), excess stratum corneum (*SC*) over a somewhat thickened epidermis (*E*), and cellular infiltration (*I*) of the dermis, particularly where a distorted fibre has penetrated the outer root sheath (↑). (Haematoxylin, eosin and picric acid.)

Sweat Glands

These glands appeared to be unaffected by any of the infusions or dietary changes.

Dermis

Areas of slight cellular infiltration, predominantly perivascular, were present in the upper dermis of all the sheep in experiment 2 while on the wheat diet prior to the infusion of methionine. The infiltration became more extensive and intense in one sheep on 2·0 g methionine per day and in one on 6·0 g per day, particularly near follicles with grossly enlarged outer root sheaths. Likewise during the infusion periods in experiment 1, cellular infiltration of the upper dermis was present in four of the sheep in which there was gross enlargement of the follicle outer root sheaths. Of these four, one received 1·5 g methionine per day, one 3·0 g per day and two 6·0 g per day.

After the methionine supplementation ceased, the cellular infiltration subsided to some extent during the following 14 or 18 days. However, areas of fairly intense infiltration remained near some follicles in which portions of the distorted fibres had penetrated the follicle walls (Fig. 11).

Discussion

It appears that in sheep which receive an infusion of methionine, while on a wheat diet, there is a sequence of events commencing with improper formation, poor keratinization and kinking of the fibres in the proximal halves of the follicles, that leads eventually to severe distortion and partial degradation of the fibres in the distal halves of the follicles. Included in this sequence is gross enlargement of the distal outer root sheaths which appears to be a necessary condition for fibre degradation to occur; all the sheep that lost wool had many follicles with grossly enlarged outer root sheaths, whereas, conversely, the sheep that lost no wool had few or no affected follicles. No explanation can be offered for the variation between sheep in their response to the same level of methionine supplementation; breed differences did not appear to be involved.

The reason for the gross thickening of the distal outer root sheaths is conjectural. It could have resulted from excessive proliferation or impaired migration and reduced sloughing of outer root sheath cells, or a combination of these processes. However, from the extent of the increase in outer root sheath tissue it would seem that there was indeed stimulation of cell proliferation. This stimulation, in turn, may have been triggered by the kinking and distortion of the fibres, since it was only in those sheep in which fibres exhibited impaired keratinization and kinking that there was thickening of the distal outer root sheaths.

The means by which the fibre degradation occurred in the distal parts of the follicles is also a matter for speculation. Possibly the process which normally degrades the inner root sheaths became overactive because of the accumulation of outer root sheath cells, and attacked not only the inner root sheaths but also the fibres. The fibres themselves may have been more prone to attack by being incompletely keratinized, and because of the severe distortion of the fibres the residence time of successive portions of the fibres in the distal parts of the follicles may have been longer than normal, in spite of a recorded slight increase in length growth rate (Reis and Tunks 1974).

In contrast to the increased proliferation of outer root sheath cells, there was no concomitant stimulation of the follicle bulb cells, because wool growth and fibre diameter were depressed by the methionine infusions (Reis and Tunks 1974). The reductions recorded in both wool growth and fibre diameter may, in fact, have been greater than the actual reduction in output by the follicle bulbs, because of the partial degradation of the fibres before they emerged from the skin.

The above features associated with enlargement of the *distal* outer root sheaths contrast markedly with those associated with enlargement of the *proximal* outer root sheaths, which occurs in sheep that grow 'doggy' wool (Chapman *et al.* 1960). Associated with the latter are increases in fibre weight, diameter and strength, but loss of staple and fibre crimp (Chapman and Short 1964; Chapman 1965), in contrast to the degradation and loss of strength of the fibres associated with the former.

The sebaceous and sweat glands were relatively unaffected by infusion of methionine. This is in contrast to the atrophy of sebaceous glands recorded in rats receiving excess methionine, which occurred along with atrophy of the hair follicles and various histopathological changes in other organs, particularly the pancreas, gastrointestinal tract and salivary glands (Klavins *et al.* 1963; Klavins and Johansen 1965). It has not been ascertained whether or not other organs in sheep are adversely affected by supplementation of a wheat diet with methionine.

The reasons why a small percentage of follicles did not resume normal fibre formation after cessation of the methionine infusions (Figs 8 and 9) are unknown. However, subsidence of the enlargement of the distal outer root sheaths was presumably accomplished by the progressive exfoliation of the excess outer root sheath cells through migration and sloughing, and required in excess of 2 weeks. Resolution of the condition appeared to rely upon the resumption of normal keratinization of the fibres.

Acknowledgments

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