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Effects of breed and family on rate of copper accretion in the liver of purebred Charollais, Suffolk and Texel lambs

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Abstract

The feeding of housed lambs on conserved forages and pelleted rations is accompanied by a high risk of chronic copper (Cu) poisoning (CCP) which might be reduced by selecting sires for low liver Cu status. Livers were therefore retrieved from Suffolk, Texel and Charollais lambs, slaughtered during the course of a performance trial, to ascertain sire and possibly breed effects on the rate of Cu accretion in the liver. In total, 160 livers were obtained, 100 from Suffolk, 40 from Texel and 20 from Charollais lambs, the progeny of 14, eight and eight sires, respectively. Lambs came from three separately managed flocks but were brought together at 8 weeks of age, weaned onto a common complete diet containing 6.1 mg Cu per kg dry matter (DM) and offered *ad libitum*. One-fifth of each breed group was slaughtered at 14, 18 or 22 weeks and the remaining 40% at 26 weeks of age. Mean (s.e.) liver Cu concentrations at those ages were 3220 (450), 4639 (464), 6426 (468), and 6513 (370) $\mu\text{mol/kg DM}$ for Suffolk, and 5843 (811), 6579 (857), 8017 (811) and 10406 (589) $\mu\text{mol/kg DM}$ for Texel, respectively. The pattern of liver Cu accretion differed, the Suffolk starting at a low value yet reaching a plateau at about 22 weeks of age (significant quadratic regression coefficient), the Texel, continually increasing from a high initial value at an average rate of 53.7 (s.e. 10.6) $\mu\text{mol/kg DM per day}$. There was a significant effect of sire on liver Cu in the Suffolk ($P < 0.05$) with a heritability of 0.85 (s.e. 0.44); in the Suffolk and Texel combined, the heritability was 0.60 (s.e. 0.33). The data available on the Charollais were too limited to test for sire effects but at 26 weeks of age, where most information was available, the mean liver Cu concentration was 7285 (s.e. 826) $\mu\text{mol/kg DM}$. At a given age, food intake, liver weight and live weight were each lowest in the Texel but when expressed as a proportion of live weight (LW), both food intake (43 g/kg LW) and liver weight (5.15 g DM per kg LW) were similar among breeds ($P > 0.05$). Thus, differences in liver Cu accretion are unlikely to reflect differences in Cu intake per unit liver weight. There was a tendency for liver size per kg LW to decrease as liver Cu rose in the Texel but not in the Suffolk. Continued hepatic Cu accretion in the Texel may reflect a breed-specific inability to cope with Cu overload. Increases in liver Cu to marginally toxic levels in some Suffolk, some Charollais and most Texel lambs, and to a level commonly associated with toxicity in one Texel lamb, on a ration of moderate Cu concentration highlights the difficulty of controlling risk of CCP by manipulating dietary composition. The current EC limit for Cu in ovine diets, 17 mg Cu per kg DM, is clearly too high for the breeds and dietary conditions used in this study. However a safe limit would be hard to achieve and hence the need to exploit sire variation in propensity to accumulate liver Cu to reduce disease risk.

Keywords: breed differences, copper, sheep, toxicity.

Introduction

Genetic variation in copper (Cu) metabolism is more marked in sheep than in any other species and is associated with breed differences in susceptibility to deficiency (Wiener, 1966) and excess (Wiener and Macleod, 1970). Crosses between breeds have susceptibilities intermediate between those of the parent breeds and the Cu status of blood, brain and liver is also intermediate (Wiener, 1987). It should, therefore, be possible to improve the resistance of sheep to Cu deficiency and excess by appropriate cross breeding or selection programmes.

This possibility was demonstrated in an experimental flock created as the cross between breeds that were relatively more (Scottish Blackface) and less (Welsh Mountain) susceptible to Cu deficiency. Selection for low or high plasma Cu concentration in ram lambs produced two lines with Cu status matching those of the respective parent breeds after one generation. Furthermore, susceptibility to hypocuprosis on 'improved' hill pastures was reduced in the fourth and fifth generations of the 'high' line (C. Woolliams *et al.*, 1986; J. Woolliams *et al.*, 1986).

The Texel accumulates Cu at a relatively high rate (Luke and Marquering, 1972; Visscher *et al.*, 1980; van der Berg *et al.*, 1983; Littledike and Young, 1993) and is thus more susceptible to Cu poisoning than most other breeds. Woolliams *et al.* (1982) compared Texel sires with five other breeds when crossed with Scottish Blackface ewes, offspring being reared on common basal diets containing 12 or 20 mg Cu per kg dry matter (DM). Plasma aspartate amino transferase activities indicated liver damage to be worst in the Texel cross, followed by the Suffolk cross at the higher Cu intake. Variation between sires was not significant maybe because on average, only four sire families per breed were considered with five or fewer progeny assessed within a family. Studies with much larger sire and progeny groups of Merino at pasture produced a high heritability estimate of 0.60 (s.e. 0.32) for liver Cu (Judson *et al.*, 1994) but there appear to have been no comparisons between breeds suited to intensive lamb production.

Until such information is available, it is impossible to gauge how much progress might be made by within-breed selection to enhance resistance to chronic Cu poisoning (CCP). Progress is needed because losses from CCP are common in intensively reared lambs and now far outnumber those from swayback in the UK. A study involving the serial slaughter of lambs from different sires of three breeds, Charollais, Suffolk and Texel, afforded an opportunity to begin to fill this gap in knowledge.

Material and methods

Animals

This experiment was auxiliary to a larger study conducted in 1997 at the Scottish Agricultural College (SAC), Edinburgh that involved 100 Suffolk lambs, half male and half female, 40 male Texel lambs and 20 male Charollais lambs (Young *et al.*, 1999). The Suffolk lambs were obtained from the SAC Suffolk flock, and were the progeny of 14 sires. The Texel lambs were purchased from the ANTUR flock at the Institute of Rural Studies (IRS), Aberystwyth, and the Charollais lambs were purchased from two pedigree breeders. Texel and Charollais lambs were each the progeny of eight sires.

The Suffolk lambs were weaned at 8 weeks of age. From two weeks prior to weaning, they were offered free access to a performance test diet consisting of (g/kg) barley (582.5), dried grass (200.0), Hipro soya-bean meal (70.0), fish meal (60.0), molasses (50.0) and a mineral and vitamin mix (37.5) which did not contain added Cu antagonists. The chemical composition of the diet is given in Table 1. The Texel and Charollais lambs were obtained shortly after weaning at approximately 8 weeks of age and gradually introduced to this same ration, with *ad libitum* access to hay, over several weeks. All lambs were housed together in a single shed, group penned (one lamb per 2 m²) according to breed and sex, with *ad libitum* access to the ration for at least 6 weeks prior to the first sampling event.

Table 1 Chemical composition of the diet

Measure	Amount
Dry matter (DM; g/kg)	881
Crude protein (g/kg DM)	188
NDF (g/kg DM)†	260
AHEE (g/kg DM)†	30
Ash (g/kg DM)	86
NCGD (g/kg)†	781
Metabolizable energy (MJ/kg DM)‡	11.7
Calcium (g/kg DM)	16.5
Phosphorus (g/kg DM)	4.5
Magnesium (g/kg DM)	1.7
Potassium (g/kg DM)	12.8
Sodium (g/kg DM)	7.4
Sulphur (g/kg DM)	2.7
Copper (mg/kg DM)	6.1
Iron (mg/kg DM)	110.0
Manganese (mg/kg DM)	46.1
Zinc (mg/kg DM)	53.9

† NDF = neutral-detergent fibre; AHEE = acid hydrolysed ether extract; NCGD = neutral cellulase gammanase digestibility.

‡ Predicted from $0.014\text{NCGD} + 0.025\text{AHEE}$ (Thomas *et al.*, 1988).

Measurements

The lambs were weighed weekly. The food intake of a pen was recorded over a fortnight period on three occasions at 3-week intervals for four pens of Suffolk lambs, two male and two female. Corresponding data for Texel lambs was obtained from four pens of males but for two pens, one sampling point was missed and for one pen, two points were missed.

The design of the experiment involved one-fifth of lambs within a breed and sex being slaughtered at 14, 18 and 22 weeks of age and the remainder slaughtered at 26 weeks of age. Lambs were assigned at random to a slaughter age within sire families. Lambs were weighed prior to slaughter. At slaughter, the liver was collected and frozen. Among other carcass measures, the cold carcass weight was also recorded.

Once thawed, the liver was trimmed of any adhering tissue and weighed. This was considered as the fresh liver weight. A sample of approximately 50 g liver was then freeze-dried, milled and duplicate 0.5-g subsamples taken for Cu determination by atomic absorption spectrophotometry (AAS), using a Pye Unicam 9200X. Liver samples were digested and prepared for AAS by the method of Thompson and Blanchflower (1971). Quality control was achieved by interspersing samples of a certified standard (NIST Bovine Liver Reference Material 1577b) at regular intervals amongst the unknowns. There was no consistent drift during these analyses with only trivial adjustments made to the unknowns based on deviations in standard performance. The mean for the 19 certified standards was 2528 (s.d. 16), compared with the certified value of 2523 (s.d. 126) $\mu\text{mol/kg DM}$.

Statistical analyses

Copper accretion. Our assessment of the accretion of Cu in the liver focused on the 94 Suffolk and 39 Texel lambs on which liver samples had been collected. Due to the limited number of Charollais lambs slaughtered at the three younger ages, they were excluded from this analysis. The data on one Texel ram slaughtered at 26 weeks of age was discarded because its liver Cu concentration was in excess of three standardized residuals above the mean.

A description of the liver Cu concentrations across slaughter categories was obtained by fitting a linear-mixed model using the residual maximum likelihood (REML) procedure (Genstat 5 Committee, 1998). This was done separately for the Suffolk and Texel breeds. The distribution of Cu concentrations was upwardly skewed ($P < 0.05$) and analyses were therefore

conducted with both measured and natural log-transformed values. In initial analyses, slaughter age (14, 18, 22 or 26 weeks), the lamb's sex and birth type (singleton or multiple), and all relevant two-way interactions, were fitted as fixed effects. Sire and residual error were fitted as random effects. The effect of sex was found to be unimportant and the two-way interactions did not define appreciable variation in Cu concentration ($P > 0.10$) and were excluded from the final analyses. Sire could not be fitted in the Texel analyses (negative variance estimates were obtained) probably reflecting the small number of rams used and observations available. As an alternative to fitting slaughter age, the linear and quadratic regression of age (in days) at slaughter on Cu concentration was included in the model in separate analyses.

The data on the Suffolk and Texel lambs was also combined for an analysis fitting breed and birth type, and the linear and quadratic regression of Cu concentration on age (in days) at slaughter as fixed effects. The interaction of breed with the linear and quadratic age covariate was also fitted. Sires nested with breed and residual error were included in the model as random effects. This analysis was done to allow comparison of Cu concentrations in the two breeds.

Liver size. The largest number of observations on every breed was available at the final slaughter (26 weeks). At this slaughter point, liver weights were available on eight Charollais, 37 Suffolk and 15 Texel lambs. These data were used to assess differences in the fresh and dry liver weight as a proportion of slaughter and cold carcass weight across breeds, and to examine the relationship between liver Cu concentration and liver size. At this final slaughter point, fresh and dry liver weights were assessed across breeds (Charollais, Suffolk and Texel) along with the amount of Cu in the liver. Absolute and proportional liver weights (relative to live and carcass weight at slaughter) were considered. Breed alone was fitted in the statistical model as no other fixed effects were significant ($P > 0.05$). Residual error was fitted as the random effect.

Results

The mean live weight in the Suffolk and Texel, respectively, was 38.9 (s.e. 1.8) and 30.3 (2.4) kg at 14 weeks of age and increased to 70.8 (s.e. 1.4) and 52.9 (1.8) kg by 26 weeks of age. Food intake was proportional to live weight but similar among breeds ($P > 0.10$) and averaged 43 (s.e. 3) g/kg live weight (LW) per day.

Table 2 Summary statistics for liver copper concentration on the measured (Cu, $\mu\text{mol/kg}$ dry matter (DM)) and natural log-transformed (LnCu) scale in Suffolk (no. = 94) and Texel (no. = 38) lambs across slaughter categories

Measure	Breed	Mean	s. d.	CV	Skewness†	Kurtosis‡
Cu	Suffolk	5719	2285	0.40	0.78	0.33
	Texel	8355	2842	0.34	0.95	-0.28
LnCu	Suffolk	8.574	0.401		-0.07	-0.63
	Texel	8.980	0.316		0.47	-0.64

† A skewness coefficient of 0.25 or larger in Suffolk, or 0.42 or larger in Texel, indicates the distribution was asymmetric (positively skewed) around the sample mean ($P < 0.05$).

‡ A kurtosis coefficient of absolute value 0.51 in Suffolk or 0.84 in Texel is significant at $P < 0.05$. A positive coefficient implies a higher proportion of observations in the tails than in a normal distribution and *vice versa*.

Liver Cu concentration

In Table 2 the mean and distribution of liver Cu concentration (DM basis) on both the measured and log-transformed scale is shown. Transformation to a log scale produced a normal distribution, with substantial reduction in the variation (relative to the mean) within breeds.

The least-squares means for Cu concentration is shown for each slaughter age in Table 3 for Suffolk and Texel lambs. The Cu concentration was always higher in the Texel ($P < 0.01$). The pattern of accumulation of Cu in the liver also differed between breeds (Figure 1). In the Texel, liver Cu concentrations (log transformed) increased linearly over time whereas in the Suffolk the accumulation of Cu reached a plateau at 22 weeks. In the Suffolk, there was less than a 2% increase in Cu concentration (as measured) in the last 4 weeks, whilst in the Texel the increase was nearly 30% ($P < 0.01$). Thus, both the linear and quadratic covariates were necessary ($P < 0.05$) to describe the change in liver Cu concentration with age in the Suffolk, whilst only the

Figure 1 The fitted regression showing the trend in liver copper concentration with age in Suffolk (—) and Texel (---) lambs, and the least-squares means at 14, 18, 22 and 26 weeks.

Table 3 Least-squares mean and standard error (s.e.) of liver copper concentration on the measured (Cu, $\mu\text{mol/kg}$ dry matter (DM)) and natural log-transformed (LnCu) scale by slaughter age from the within-breed analyses†

Measure (weeks)	Slaughter age	Suffolk		Texel	
		Mean	s.e.	Mean	s.e.
Cu	14	3220 (19)‡	450	5843 (8)	811
	18	4639 (19)	464	6579 (7)	857
	22	6426 (18)	468	8017 (8)	811
	26	6513 (38)	370	10406 (15)	589
LnCu	14	8.071	0.073	8.665	0.087
	18	8.405	0.076	8.779	0.092
	22	8.716	0.076	8.959	0.087
	26	8.723	0.061	9.206	0.063

† Within a Cu concentration measure (Cu, LnCu) and breed, means varied significantly with slaughter age ($P < 0.01$).

‡ Number of values shown in parentheses.

linear covariate was important in the Texel ($P < 0.01$; Table 4). Combined analysis of the Suffolk and Texel data revealed interactions between breed and the linear and quadratic age covariates ($P < 0.05$).

The mean Cu (s.e.) concentrations of sire families ranged from 4242 (514) to 6639 (514) $\mu\text{mol/kg}$ DM in the Suffolk and from 6668 (1010) to 8564 (1017) in the Texel. It was possible to fit sire as a random effect in the Suffolk alone, and in the combined Suffolk and Texel data. Although the sample was too small to accurately estimate genetic effects, differences in Cu concentrations (both on the measured and log-transformed scale) between sire families explained proportionately over 0.15 of the overall (phenotypic) variation. This corresponded with a heritability of 0.85 (s.e. 0.44) in the Suffolk, and a heritability of 0.60 (s.e. 0.33) in the Suffolk and Texel combined.

Liver size and Cu accretion

At 26 weeks of age, the liver Cu concentration in the Texel was at least 1.44 times more ($P < 0.05$) than that

Table 4 Coefficients, standard errors and significance levels for the linear regression of copper concentration ($\mu\text{mol/kg}$ dry matter) as measured (Cu) and after natural log-transformation (LnCu) on age at slaughter (days) from the within-breed analyses

Measure	Term	Suffolk (no. = 94)			Texel (no. = 38)		
		Coefficient	s.e.	Significance	Coefficient	s.e.	Significance
Cu	Linear	199.9	66.5	***	53.7	10.6	***
	Quadratic	-0.5563	0.2258	*			
LnCu	Linear	0.04326	0.01051	***	0.00630	0.00112	***
	Quadratic	-0.000123	0.000036	***

Figure 2 The relationship between liver weight (g dry matter (DM)) and live weight (kg) in Charollais (●), Suffolk (▲) and Texel (■) lambs at 26 weeks of age.

in the Charollais and Suffolk (Table 5). However, the absolute amount of Cu found in the liver did not differ between these breeds ($P > 0.20$), largely because the liver weighed less in the Texel ($P < 0.05$). When liver weight was expressed relative to the slaughter weight (Figure 2), the proportional liver weight did not differ among breeds (overall means 17.52 g fresh weight and 5.15 g DM per kg LW; $P > 0.10$). In short, Cu levels in Texel were higher as a proportion of their body and liver weight rather than absolutely. The DM fraction of the liver was 0.294 (s.e. 0.002) of liver fresh weight and was slightly

higher (1.02 times; $P < 0.05$) in the Texel than in the Suffolk. In the Texel, there was also a reduction in the proportional liver weight with an increase in liver Cu concentration of -0.12 (s.e. 0.04) g DM per kg LW for each mmol liver Cu per kg DM.

Efficiency of hepatic Cu retention

The proportions of the daily intakes of Cu being retained in the liver at the end of the trial by Suffolk and Texel lambs were approximated. This approximation was based on food intakes of 3.04 and 2.28 kg/day, respectively, at 26 weeks of age (0.043 times final LW), rates of increase in liver Cu of 1.53 and 77.8 $\mu\text{mol/kg}$ DM (the difference between antilogs of the 22- to 26-week period in Table 3), and the final liver sizes of 351 and 268 g (Table 5). Texel lambs were retaining 9.5% of ingested Cu in their livers while Suffolk lambs were retaining only 1.3%.

Discussion

Variation between breeds

The consistently higher liver Cu concentrations found in Texel than in Suffolk lambs (Figure 1) confirms previous rankings for these breeds within their crossbred offspring (Woolliams *et al.*, 1982). In the past, it has been argued (Weiner *et al.*, 1978) or assumed (Woolliams *et al.*, 1982 and 1985) that breed differences in Cu status are due principally to differences in the proportion of Cu intake that is absorbed. The contrasting patterns of liver Cu accretion shown by Texel and Suffolk lambs over

Table 5 Least-squares mean and standard error (s.e.) of liver weight, and the copper weight and concentration in the liver in groups slaughtered at 26 weeks of age

Liver	Charollais (no. = 8)		Suffolk (no. = 38)		Texel (no. = 15)	
	Mean	s.e.	Mean	s.e.	Mean	s.e.
Weight (kg dry matter)	0.363 ^a	0.023	0.351 ^a	0.011	0.268 ^b	0.017
Cu weight (μmol)	2653	281	2381	231	2781	205
Cu concentration ($\mu\text{mol/kg}$ DM)	7285 ^a	826	6870 ^a	384	10498 ^b	603

^{a, b} Means within a row with different superscripts differ ($P < 0.05$).

time in this study appear to be more readily explained by differences in the hepatic retention of absorbed Cu.

The significant differences in initial Cu concentrations between the Texel and Suffolk (Figure 1) may in part have been caused by differences in the management and nutrition of the source flocks and may have influenced the early responses to the common experimental diet. Thus the uncharacteristically slower early accretion of Cu in the Texel than in the Suffolk may have been caused by the earlier induction of enhanced biliary Cu secretion in Texel lambs, given their almost two-fold higher mean initial value at 14 weeks of age. By 22 weeks of age, the Suffolk lambs attained Cu concentrations similar to those of the Texel at the start of the experiment. Thus the contrast in accretion rates over the last 4 weeks is probably indicative of breed differences in the ability of the liver to adapt to a high Cu burden. The plateau shown by the Suffolk has been a common finding and explained by increases in the biliary secretion of Cu as liver Cu stores rise (Woolliams *et al.*, 1983).

The opposite tendency in the Texel (Table 3), confirmed by the seven-fold differences in estimated final hepatic retention efficiencies, has not been described before and may indicate a partial breakdown in homeostatic mechanisms that limit hepatic Cu retention. It is known that increasing numbers of hepatocytes are lost by apoptosis as liver Cu concentrations rise to the top of the marginally toxic range (King and Bremner, 1979). A negative relationship between liver size (on LW basis) and liver Cu concentration was first found across breeds with the Texel cross at one extreme (high liver Cu yet low liver weight) and the pure Scottish Blackface at the other (Woolliams *et al.*, 1982). Decreases in liver size of 0.12 g liver DM per kg LW per mmol increase in liver Cu can be derived from their data as was observed in the Texel in the current study. This may reflect hepatotoxicity and would represent a loss of about one-sixth in liver mass across the range of concentrations found in the Texel. However, there remains the possibility that the underlying problem in the Texel is inadequate feedback control of Cu absorption when liver Cu concentrations reach potentially dangerous levels.

It could be argued that cause and effect should be reversed; that is those breeds, and those individuals within a breed, that have high liver Cu concentrations do so because they have small livers. However, the Texel did not have smaller livers in proportion to LW than the Suffolk. A slowing of the

rate of increase in liver size with the approach to mature body weight in the face of a constant supply of absorbed Cu could contribute to positive curvature in liver Cu concentrations but such a phenomenon should not be confined to the Texel. The influence of a second factor on liver Cu accretion, under independent or lesser genetic control than Cu absorption, would complicate assessing genetic effects on liver Cu status.

In our study, breed comparisons involving the Charollais are risky because of the small representation of the breed at the earlier samplings. However, the fact that the final mean liver Cu concentration for Charollais was similar to that of the Suffolk and reached with a diet containing a moderate level of Cu suggests that the susceptibility of the Charollais to CCP might also benefit from selection against high liver Cu accretion rates. An additional incentive to reduce liver Cu levels in all breeds is the increasingly stringent limits to the maximum acceptable concentrations of potentially toxic elements in foods meant for human consumption.

Variation between sires

While our estimates for the heritability of liver Cu concentrations were imprecise (s.e. 0.33 and 0.44), their high value (0.60 and 0.85) was consistent with that found for another breed in a different dietary context (0.60, s.e. 0.32; Judson *et al.*, 1994). Genetic progress should be attainable within breeds by selecting against high accretion rates for hepatic Cu where the supply of dietary Cu has been relatively uniform and above requirements.

Selection decisions to reduce Cu retention could be based on *in vivo* measurement of Cu concentration through liver biopsy but this poses ethical concerns. An alternative may be to use Cu in the plasma as a selection criterion. J. Woolliams *et al.* (1985 and 1986) found that selection against (and for) Cu in the plasma decreased (and increased) Cu in the liver in an interbred population of Scottish Blackface X Welsh Mountain sheep under grazing conditions. Unfortunately, the difference in plasma Cu levels between housed lines that was evident when they were given a diet containing 5 mg Cu per kg DM was indistinguishable once dietary Cu was raised above 10 mg Cu per kg DM, although liver Cu levels were still markedly different (Woolliams *et al.*, 1985). Liver Cu is more closely correlated with plasma indices of liver cell damage than with plasma Cu when Cu status is high and glutamate dehydrogenase may provide the best substitute for a direct measure of liver Cu overload.

High rates of liver Cu accretion

Substantial increases in liver Cu concentrations occurred in both Texel and Suffolk lambs on a ration containing only 6.1 mg Cu per kg DM. That is only 35% of the maximum permissible Cu level in European foodstuffs (equivalent to 17 mg/kg DM; directive 70/524/EC) and emphasizes the need to reduce the uptake of Cu by all possible means. In the Texel, which started the experiment with mean liver Cu values close to the threshold between 'normal' and 'marginally toxic' levels (6400 µmol/kg DM; Underwood and Suttle, 1999), average Cu values rose to levels associated with subclinical liver damage (King and Bremner, 1979; Woolliams *et al.*, 1982). In fact, one individual reached a level commonly associated with clinical toxicity (> 16 000 µmol/kg DM). Littledike and Young (1993) found concentrations of 6300 µmol Cu per kg DM in Texel lambs on diets containing only 3.6 to 5.1 mg Cu per kg DM. In the case of the Suffolk, mean values rose to the upper limit of normality, with a maximum value likely to cause mild liver injury.

The high rates of liver Cu accretion are probably due in part to a lack of Cu antagonists in the diet. Proprietary compound diets often contain Cu antagonists (added Fe, Mo, S and Zn in various combinations and at various levels) to reduce the risk of CCP. The low levels of Fe and Zn reported in Table 1 indicate that they were not deployed in this way in this study. The moderate level of S found and the decision not to add Mo indicate that there was little or no constraint upon Cu accretion from these two elements. With such 'low antagonist', concentrate-based diets, the clear implication is that the current EC limit on dietary Cu concentrations is far too high for Texel and Suffolk ram lambs. However, a sufficiently low legal limit, say < 6 mg Cu per kg DM, is not suited to breeds susceptible to Cu deficiency, such as the Scottish Blackface, or compatible with the naturally high Cu concentrations found in diets containing a protein-rich supplement (usually > 10 mg Cu per kg DM). Antagonists cannot be relied upon to induce a three-fold reduction in Cu retention when other EC regulations limit concentrations of the most potent antagonist, Mo, to a mere 2.5 mg/kg DM. Thus, there remains a strong case for lowering liver Cu accretion rates by genetic selection.

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