88. BLOOD COPPER OF EWES DURING PREGNANCY

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IN a previous communication [Eden, 1941] comparison was made in connexion with an experiment on 'border pine' between the blood Cu levels in two different years of a group of sheep grazing on a Northumbrian hillside. The first samples were taken at a stage of late pregnancy in February and March 1939 and the corresponding animals were again bled in June 1940, about two months after lambing. No significant differences in the average Cu values at the two bleedings were found, but the further observation was made that the wide variations found between different individual sheep [Eden, 1939] also occurred within the same sheep at different times. Considering the group as a whole no evidence could be found of a difference of blood Cu level associated with pregnancy. Shearer *et al.* [1940], in studies on ewes in Derbyshire where prophylactic use of Cu during pregnancy has such a marked effect on the incidence of 'swayback' in lambs, observed that the blood Cu values of the ewes just after lambing were higher than in November and January bleedings, dates which corresponded to early and middle pregnancy. The average initial Cu level in their records, however, was considerably lower than the average of other ewes reported in the literature, and the authors, without giving actual protocols, state that subsequent work on sheep in Cambridge did not confirm the suggested rise during pregnancy. Beck [1940], in a private communication from Australia, also stated that he had not observed any significant rise during pregnancy in the sheep.

Several groups of workers have reported a gradual elevation in blood Cu levels of women during pregnancy. Tompsett & Anderson [1935] in a random selection of bloods of women in various stages of pregnancy reported a definite rise associated with the later stages, but unfortunately the available data on normal variations in the human subject are not sufficient to reveal the range to be expected irrespective of pregnancy. The much larger number of data accumulated for sheep over the last few years shows that extremely wide variations are encountered in apparently normal sheep and no physiological explanation for this variability has yet been offered. Equally wide normal variations may exist in other mammals, and if so they would tend to make the interpretation of considerable fluctuations of blood Cu very difficult in particular cases. It is thus probable that the securing of more data on women and increased knowledge of the normal distribution of such data might cause a revision of the idea of elevated blood Cu levels associated with pregnancy in the human subject.

The writer carried out a limited number of observations on rabbits some years ago in connexion with studies on foetal Cu and observed no rise in blood values of the does during pregnancy, but at the time it was felt that the data were insufficient to warrant a definite conclusion. More recently the increasing recognition of the importance of Cu in relation to certain diseases of sheep has stimulated further interest in the possible importance of variations in blood Cu

under different conditions, and occasion was therefore taken to reinvestigate the gestation factor on an available group of 21 ewes at this Institute by blood sampling at monthly intervals throughout the whole course of pregnancy.

Experimental

The ewes were part of the Institute flock of Cheviot-Border Leicester sheep of varying ages and were crossed by a Suffolk ram about September and October. They were wintered out of doors in a sheltered paddock and received the usual ration of hay, roots and a small allowance of concentrates. They were bled each month until after they had lambed. Blood obtained by jugular puncture was collected into Cu-free potassium oxalate and the Cu was determined by the photometric diethyldithiocarbamate method [Eden & Green, 1940]. Haemoglobin was estimated by the acid haematin method using a standardized disk. The analytical data are given in Table 1 together with the overall range of Cu values for each ewe throughout pregnancy and the average value at each bleeding.

Table 1. *Blood Cu and haemoglobin of Weybridge sheep during pregnancy*

Sheep no.	Blood Cu mg./100 ml.								Hb g./100 ml.							
	Sept. and Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	Over-all range	Sept. and Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	
2	0.135	0.130	0.144	0.176	0.148	0.130	0.144	0.046	12.8	13.0	11.4	12.3	12.6	13.6	13.4	
3	0.158	0.135	0.236	0.190	0.153	0.094	0.176	0.142	12.7	10.9	10.7	12.2	12.2	12.5	10.8	
5	0.116	0.112	0.138	0.197	0.116	—	—	0.075	12.7	12.3	12.6	12.3	13.2	—	—	
17	0.116	0.180	0.130	0.188	0.122	0.112	0.122	0.066	13.9	12.4	11.5	12.6	12.5	13.6	12.2	
30	0.122	0.155	0.247	0.141	0.153	—	—	0.125	12.1	10.8	10.2	12.9	11.9	—	—	
36	0.132	0.108	0.154	0.141	0.158	0.116	0.178	0.070	12.6	12.3	10.7	12.7	12.2	12.8	12.2	
38	0.168	—	0.108	0.135	0.130	0.102	0.120	0.066	12.3	10.9	10.6	13.0	11.2	12.0	11.1	
39	0.104	0.116	0.122	0.122	0.116	0.122	0.120	0.018	10.2	10.5	10.1	11.0	9.6	10.9	10.5	
296	0.209	0.100	0.074	0.109	0.088	0.070	0.140	0.139	11.7	12.0	10.8	13.3	12.1	13.4	12.9	
297	0.106	0.064	0.045	0.076	0.094	0.082	0.128	0.083	10.4	11.2	10.9	13.0	11.8	12.1	12.0	
298	0.239	0.140	0.118	0.132	0.100	0.116	0.135	0.139	10.9	—	11.1	13.9	12.0	13.0	11.5	
299	0.126	0.180	0.094	0.144	0.135	0.220	0.144	0.094	10.5	11.8	10.9	13.2	—	12.0	11.6	
300	0.085	0.124	0.110	0.132	0.112	0.144	0.120	0.059	12.0	12.8	10.9	14.3	12.4	12.7	13.4	
301	0.106	—	0.076	0.106	0.173	—	—	0.097	11.8	—	10.8	13.9	12.8	—	—	
302	0.148	0.084	0.050	0.064	0.074	0.097	0.082	0.098	10.2	10.9	10.0	11.9	11.5	9.4	12.8	
303	0.102	0.080	0.088	0.088	0.110	0.120	0.108	0.040	10.7	10.7	9.4	12.6	11.6	12.4	8.9	
304	0.112	0.100	0.118	0.120	0.156	0.150	—	0.056	10.3	11.1	10.9	12.4	16.1	13.9	—	
305	0.108	0.126	0.108	0.091	0.114	0.144	0.124	0.053	10.9	12.7	10.5	13.7	12.3	12.2	13.2	
961	0.122	0.122	0.171	0.148	0.148	0.144	0.160	0.049	11.8	10.7	8.9	11.3	12.0	11.7	10.7	
998	0.120	0.110	0.124	0.135	0.158	0.188	0.130	0.078	12.6	11.1	11.1	13.0	12.6	12.8	12.8	
1000	0.130	0.155	0.158	0.135	0.135	0.198	0.138	0.068	12.6	10.9	10.6	13.2	12.1	13.9	13.0	
General mean	0.132	0.122	0.124	0.132	0.128	0.137	0.132	—	11.7	11.5	10.7	12.8	12.2	12.5	11.9	
Group mean	0.136	0.122	0.107	0.116	0.123	0.136	0.132	—	11.7	11.5	10.6	12.8	11.9	12.4	11.9	

Four sheep either aborted or gave birth to dead lambs and, being required for other work in the Institute, were not bled again. Of the original 21 animals, 17 were bled all through the period of pregnancy but no samples are recorded for Nos. 5, 30, 301 and 304 after the date of abnormal parturition. In determining the average Cu values at each bleeding two means are given corresponding to (a) the 17 animals that went to full term and (b) all the animals at each bleeding. With the exception of the December and January figures these means are practically identical, but the slight differences at these bleedings are accounted for by omission of the high values of two animals, Nos. 5 and 30, from the averages. Considering the values as a whole the averages are for all practical purposes constant throughout the period of pregnancy.

Discussion

The general run of the blood Cu figures shows that the Institute sheep have higher levels (0.13 mg./100 ml.) than those reported from the Northumbrian area (0.08 mg./100 ml.) or from the Derbyshire 'swayback' area. The haemoglobin data give no indication of anaemia, all values being within the normal range for sheep, and there is no apparent correlation between Hb and Cu levels. The general mean of all the blood Cu figures in the present investigation is 0.130 mg./100 ml., a figure of the same order as the 0.117 reported in 1939 as the mean of 18 laboratory sheep selected at random irrespective of age, sex or condition. 69% of the values lie within ± 0.03 mg./100 ml. of the mean, an order of variation similar to that already reported for Northumbrian sheep in 1939 and 1940.

The data once again emphasize the wide variations existing between different sheep and in the same sheep at different bleedings. Of the 21 sheep only one, No. 39, had a range of variation over all the bleedings of less than 0.02 mg./100 ml., while 4 animals had an overall variation greater than 0.12 mg./100 ml. The extreme range of all values is from 0.045 to 0.239, which may be compared with that of 0.016 to 0.164 obtained in Northumbrian sheep in 1939 and 0.007 to 0.210 obtained in 1940. The extreme values bore no relation to the state of health of the animals.

The present data indicate that any changes in blood Cu level during pregnancy of sheep are within the normal range of variation for non-pregnant sheep and also that such changes as are observed are not related to the particular stage of pregnancy. A fall is as frequent as a rise and increase and decrease may alternate in successive months. As Shearer *et al.* [1940] suggest, it may be that a physiological rise in blood Cu during pregnancy may only occur when the initial level is too low to satisfy the demands of the foetus, but the evidence for this idea is meagre. It is apparent that the normal range of variation is such as to swamp possible physiological changes specifically associated with pregnancy.

SUMMARY

Blood Cu determinations were made on 21 breeding ewes at monthly intervals throughout the period of pregnancy. Although individual fluctuations were considerable the average values at each bleeding were very constant and there is no support for the view that pregnancy in sheep is accompanied by a physiological rise in blood Cu. Such changes as were observed fell within the normal range of variation previously found for non-pregnant sheep, and increase and decrease of individual values bore no relationship to the stage of pregnancy.

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