only when stimulated with mammotropic hormones. 4. Grafted fibroadenoma cells remained latent in many rats until administered mammotropic hormones brought about their rapid growth. Administration of this hormone could be delayed as long as 7½ months. 5. It is concluded that radiations bring about an irreversible modification of some cells, depending on severity of the dose; mammotropic hormones are not carcinogens but, as promoters of mammary epithelium, promote carcinogenesis and growth of some tumors.

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Erythrocyte Survival Studies in Experimental Molybdenosis of Sheep.* (26797)

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The toxicity of a high molybdenum intake in the diet has been extensively studied. In cattle, the effects of toxicity include severe diarrhea, emaciation, loss of coat color and anemia. In sheep on similar intakes of molybdenum, the clinical picture appears to be principally associated with signs of a copper deficiency. The relationship between molybdenum and copper metabolism together with the influence of inorganic sulfate has been recently reported by Dick(1). It was shown that the symptoms of copper deficiency in sheep develop only in presence of increased molybdenum and sulfate in the diet. Similar molybdenum sulfate-copper relationships in cattle have been reported(2). Experimental molybdenosis has not been shown to influence hematology in sheep(3) or cattle(2) even though an anemia is associated with the natural condition in cattle.

This report presents data concerning the life span of erythrocytes in experimental molybdenosis of sheep using the direct glycine-2-C^{14} method. Erythrocyte life span for normal sheep using this method has been previously reported(4).

Materials and methods. Two female lambs (6161, 6170), one year of age and weighing 28 and 32 kg, respectively, were used. Each lamb was initially placed on a daily oral intake by capsule of 45.4 mg of molybdenum as sodium molybdate for 54 days. Since no clinical symptoms of toxicity appeared, daily intake was doubled for the next 35 days, during which time severe diarrhea developed. Daily intake was then returned to the original amount for 10 days. At this time, 100 μc and 150 μc of glycine-2-C^{14} were injected intravenously into lambs 6161 and 6170, respectively. Molybdenum administration was continued throughout the trial.

The procedures employed for determination of median survival time for erythrocytes in sheep have been reported(4,5). Median survival times ($t_{½}$), of the erythrocytes of the sheep in this study were estimated from their survival probability function, $p(t)$, the probability that an erythrocyte will have a survival time greater than t.

Plasma and liver copper levels were determined in the sheep at termination of the trial

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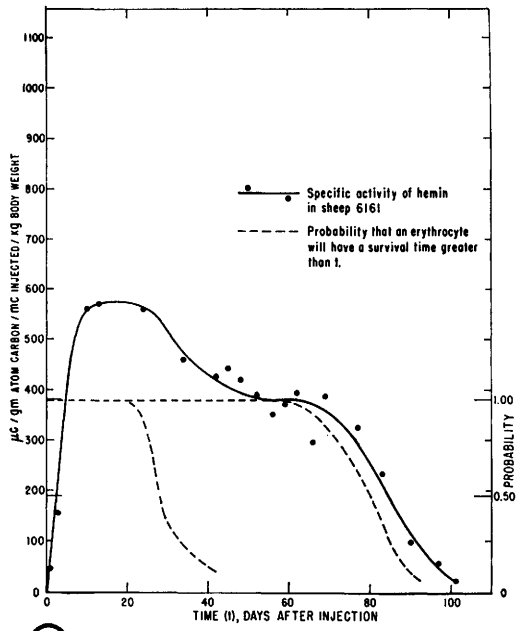
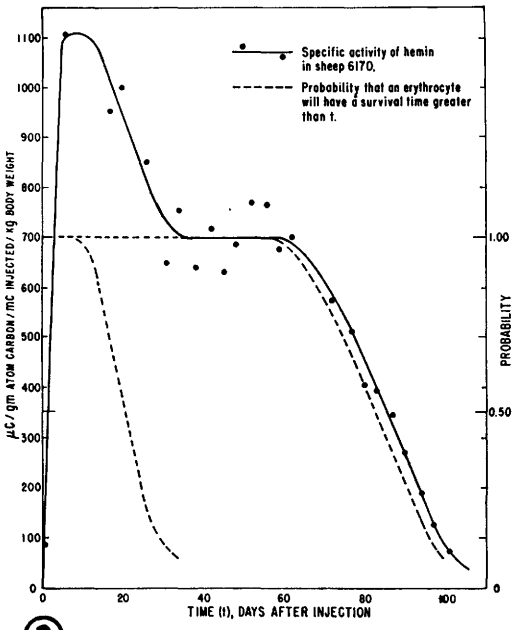


(1)



(2)

FIG. 1. Specific activity of hemin and survival probability function in a sheep with molybdenosis.
FIG. 2. Specific activity of hemin and survival probability function in a sheep with molybdenosis.

by methods previously reported(6). Hematological determinations were performed by standard methods.

Results and discussion. The specific activities of hemin and their respective survival probability functions are presented in Fig. 1 and 2. The 2 distinct plateaus of the specific activity curves are not in accord with the single plateaus observed in the curves of normal sheep(4). A similar finding of 2 plateaus in the life span curve has been reported for the normal aoudad sheep(5). This was interpreted as the existence of 2 separate populations of erythrocytes with different survival times. Similar calculations for the curves obtained in the present study resulted in median erythrocyte survival times of 28 and 80 days for sheep 6161, and 20 and 84 days for sheep 6170. The second population of red cells with longer survival times in each sheep was comparable to that found in normal sheep(4).

We attribute the first decrease in specific activity of hemin to death of one population of erythrocytes and the second decrease to death of a second population. It can be estimated(5) that in these sheep, 30-40% of the total populations exhibited the shorter survival times. In rabbits recovering from experimentally produced anemia, it has been reported(7) that some of the cells had a shortened life span. This finding was also observed in the rat(8) under similar conditions. It was suggested that new red cells produced rapidly in response to the anemia were functionally inadequate and thus were short lived. This would imply that the daily turnover of erythrocytes in these sheep should be greater than normal. However, erythrocyte and leukocyte counts performed on the sheep were within normal limits during the entire course of the experimental trials. Some polychromasia was observed in the peripheral blood smears but myeloid-erythroid ratios of bone marrow samples were also within normal limits.

The levels of plasma copper obtained in these sheep were 22 and 43 μg % for 6161 and 6170, respectively. These values are below normal values of 58-160 μg % reported for sheep(6). Liver copper levels were 4.3 and 5.7 mg/100 g wet weight for sheep 6161 and 6170, respectively, and are near the lower limit of the 4-25 mg/100 g wet weight reported for normal sheep(6). Dick(1) has

postulated that plasma copper levels in sheep fall due to depletion of copper stores as a result of prolonged molybdenum and sulfate administration. Sulfate intake was not measured in the trials reported here. It would appear, however, that sulfate intake in these sheep was sufficient, together with the added molybdenum to lead to a copper depletion. The requirement for copper in synthesis of heme is known and Anderson and Tove(9) have recently demonstrated a direct role for copper in this synthesis. Copper deficiency in sheep characteristically exhibits a demyelinating lesion in the central nervous system of lambs while only under extreme conditions will anemia occur in the ewe. Anemia is also a characteristic of molybdenosis in non-ruminant animals and has been attributed to inability of these animals to utilize stored copper(10). Bush, *et al.*(11), found a shortened red cell survival using Fe^{59} in copper deficiency of swine and attributed this to subnormal levels of copper within the red cell. If the phenomenon were similar in these sheep, one might expect to find a shortening of survival time of the entire red cell population rather than 30-40% as found in the present study, unless only a marginal deficiency had occurred.

Summary. Median survival times of the erythrocytes of sheep in experimental molybdenosis were determined using glycine-2-C^{14}. The existence of 2 distinct populations of erythrocytes was observed in each sheep. Median survival times for the first erythrocyte populations in 2 sheep were 20 and 28 days, with 80 and 85 days for the second populations.

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Quantitative and Temporal Studies on Effect of Dexamethasone on Corticosterone Secretion in the Rat.* (26798)

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Depression of plasma or adrenal corticosterone concentration by exogenous steroid administration is well known. Pfeiffer and co-workers suggested the substitution of dexamethasone-blocked animals for hypophysectomized animals in assays of ACTH using peripheral plasma corticosterone concentration as the index of adrenocortical response (1). Peron and Dorfman found that measurement of adrenal corticosterone content provided a useful method of assaying the ACTH-suppressing potency of certain corticoids(2). This report describes the suppressive influence of dexamethasone on adrenal corticosterone secretion rate in the rat.

Methods. Adult male Sprague-Dawley rats weighing 200-250 g were used following a 4 to 10 day acclimatization period in the laboratory. Dexamethasone-21-phosphate†

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