CCLV. THE RECIPROCAL RELATIONSHIP OF CALCIUM AND INORGANIC PHOSPHORUS OF THE BLOOD OF SHEEP.

By ALLAN HENRY HECTOR FRASER.

From the Rowett Research Institute, Aberdeen.

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HOWLAND AND KRAMER [1923] showed that in rickets the concentration product of calcium and inorganic phosphorus falls below a certain critical level. Their work suggested a fundamental relationship between the levels of Ca and inorganic P of the blood.

Bourne and Campbell [1932] by simultaneous determinations of calcium and inorganic P of the blood in rabbits have shown that the concentrations of these two substances bear a reciprocal relation to each other. Their work is fully supported by the work of Dupré and Semeonoff [1931]. On the other hand Theiler, Green and du Toit [1927] found in their extensive work on cattle that the blood-Ca remained normal even with an inorganic P of one quarter the normal figure. This contradiction might suggest that in this respect ruminants differed fundamentally from rabbits.

Recent work by Auchinachie and Fraser [1932], however, on the blood of sheep fed a Ca-deficient ration has shown that an abnormally low serum-Ca may be accompanied by an abnormally high inorganic P, and that there is evidence of a reciprocal relationship between the Ca and inorganic P of the blood of sheep.

METHODS.

In November 1930 five sheep were put on a Ca-deficient diet. Five other sheep were put on the same diet *plus* 5 cc. of cod-liver oil per sheep per day. Simultaneous estimations of blood-Ca and inorganic P were made at intervals in each individual of both groups. Both groups were kept out of doors.

RESULTS.

The average figures for serum-Ca are given in Table I. In Group I the serum-Ca fell to the low level of 7.06 mg./100 cc. in March rising to 8.15 in June. During the same period (November-June) the addition of cod-liver oil maintained the serum-Ca at a normal level.

Table I. *Ca in mg./100 cc.*

	January	March	June
Group I (Ca-deficient)	10.65	7.06	8.15
Group II (Ca-deficient + cod-liver oil)	11.10	10.25	10.00

The average figures for inorganic P are given in Table II. It is apparent that while the P in both groups shows a seasonal increase, the blood-P in the Ca-deficient group was very much higher than when cod-liver oil was fed, particularly in March.

Table II. *P in mg./100 cc.*

	January	March	June
Group I	5.63	10.53	9.15
Group II	6.11	7.29	7.66

It is evident that there is a significant difference between the two groups both in blood-Ca and blood-P.

There is, however, a remarkably close correspondence between the Ca and P concentration products of the two groups, as is shown by Table III.

Table III. *Ca $\times$ P concentration product.*

	January	March	June
Group I	67.1	72.3	77.3
Group II	67.8	74.7	76.3

In each group there is evidence of a seasonal rise in the product, but at any one period there is a close correspondence between the products of both groups. This is important in view of the divergent values obtained for Ca alone and for P alone. It suggests that the Ca and P levels of the blood in sheep are reciprocally related, the P level rising proportionately to the fall in Ca and *vice versa*, a result in keeping with the results of Bourne and Campbell and of Dupré and Semeonoff on rabbits.

DISCUSSION.

These results on sheep were obtained on small groups and have not yet been repeated. They must therefore be regarded as of a preliminary nature. At the same time the evidence of a reciprocal relationship in this particular case is perfectly clear and is in agreement with similar results on rabbits. In discussing the possible interpretation of this relationship, there are several main possibilities to consider. In the first place the basal diet whilst deficient in Ca was adequate in P. It is conceivable that the blood-P might rise owing to the Ca-deficiency leading to a reduced rate of formation of insoluble compounds of Ca and P in the intestine. This interpretation is ruled out by the effect of cod-liver oil, where no extra lime entered the intestines, and yet the blood-P fell markedly below that of the Ca-deficient group.

It seems more probable that the phenomena of reciprocal relationship of

the Ca and P of the blood are bound up with the metabolism of bone in the manner suggested in the following hypothesis.

As a result of deficiency in the food, the amount of Ca absorbed from the gastro-intestinal tract is insufficient to maintain the normal level of serum-Ca, and the calcium reserves of the bones are utilised to supply the needs of more essential tissues. But since Ca is present in bone mainly as calcium phosphate the transference of calcium from bone to blood will be accompanied by a simultaneous transference of phosphorus. This view is supported by the work of Evans [1930] on swine, and of Bekker and Rousseau [1930] on sheep, which shows that neither a Ca nor a P deficiency in the diet alters the percentage composition of the bones. Provided that P is being assimilated in normal amount, the liberation of bone phosphate will lead to a rise in the blood-P level, and the extent of this rise will be proportionate to the rapidity of mobilisation of the calcium reserves in the bones. Cod-liver oil by raising the serum-Ca level, reduces the demand on the Ca bone reserves, decreases the liberation of bone phosphate, and hence lowers the blood-P level. On this hypothesis the blood-P will rise in response to a fall in serum-Ca, and fall in response to a serum-Ca rise, thus leading to a reciprocal relationship of Ca and P in the blood, and to a relative constancy of the $\text{Ca} \times \text{P}$ concentration product.

In cases where both calcium and phosphorus are deficient in the diet, or where conditions favouring assimilation are sub-normal, it is obvious that this reciprocal relationship will not be clearly shown.

SUMMARY.

1. In sheep under outdoor conditions, fed a basal ration deficient in calcium, or such a ration supplemented with cod-liver oil, the $\text{Ca} \times \text{P}$ product of Howland and Kramer tends to approach a constant, in spite of wide variations in serum-calcium and blood-inorganic phosphorus produced by differences in diet.

2. The relative constancy of the $\text{Ca} \times \text{P}$ product is shown to depend upon the reciprocal relationship of the calcium and phosphorus of the blood, the level of phosphorus rising as that of calcium falls, and *vice versa*.

3. It is suggested that this reciprocal relationship is due to factors involved in utilisation of the mineral reserves of the bones.

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