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Experimental Osteodystrophic Diseases in Goats.

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THE late Sir Arnold Theiler started an elaborate programme of work with the object of studying bone diseases in various species of common farm animals. These experiments have contributed markedly to the elucidation of the complicated problem of osteodystrophic diseases, their aetiology and histological differentiation. Phases of this project dealing with cattle, pigs and horses have been published by Theiler A., du Toit, P. J., and Malan, A., I., in two studies (1937) and by Groenewald (1937). As these publications deal fully with the relevant literature, their review here is considered superfluous. Although the histological bone pictures show distinct differences between rickets on the one hand and osteofibrosis or osteodystrophia fibrosa on the other, clinical symptoms vary in the different species.

Marek (1931) gives illustrations of ostitis fibrosa in the goat, from which it may be seen that the facial swellings are higher than in the horse, stretching up to the lachrymal, and malar bones. Wester (1935) writes that spontaneous rickets occurs in goats in Holland and that such goats are stiff, stunted in growth and frequently walk on their knees. It is conceivable that the domesticated milk-goat type of Europe would be more likely to suffer from some bone disease or other, if adequate rations are not given, than the unproductive goats which are accustomed to fend for themselves on the veld in this country.

Experimental work recently carried out by Glock *et al* (1939) showed that osteofibrosis was produced in goats fed for a relatively short period on a ration consisting of flaked maize and bran, with a minimum amount of hay. Not only was the blood serum calcium low, but actual swellings of the jaws, lameness, and paresis occurred. These authors are of the opinion that the higher vitamin D present under South African conditions may have contributed to the fact that the investigators in the latter country were unable to show that the blood calcium could be affected by a low intake of calcium. An abundance of vitamin D was present in the case of all the work done in South Africa.

Experimental.

Eight six-months old goats were selected for this work. Unfortunately the available animals varied considerably in regard to type, but this objection is less serious in view of the fact that the main criterion was to be the clinical symptoms and bone pathology, instead of body weight and size.

Four groups of two animals each were treated as follows:—

Basal Ration.	*Composition* (gm.).		
	P_2O_5	CaO	Protein.
50 gm. Hay	0·10	0·20	3·0
300 gm. Samp	0·27	0·05	30·0
50 gm. Blood meal	0·20	0·08	35·0
100 gm. Green feed	0·10	0·10	2·0
Total (gm.)	0·67	0·43	70·0

In addition to the basal ration which was fed in boxes placed in individual pens, the mineral supplements were administered orally to each animal, once daily. The total calcium and phosphorous intake per animal, as well as the $CaO:P_2O_5$ ratio was:

Group.	CaO Intake.	P_2O_5 Intake.	$CaO:P_2O_5$.
4	3·95 gms.	3·73 gms.	1·06:1·0
1	0·43 gms.	4·73 gms.	1:11
2	9·92 gms.	0·67 gms.	14·8:1
3	0·43 gms.	0·67 gms.	1:1·6

The supplements were given in the form of calcium carbonate ($CaCO_3$), and di-sodium phosphate (Na_2HPO_4). It will, therefore, be seen that the object was to create extreme conditions of: low calcium—high phosphorus; high calcium—low phosphorus; low calcium—low phosphorus, but in a normal ratio; and sufficient calcium—sufficient phosphorus in a normal $CaO : P_2O_5$ ratio.

The kids were run in a small cement-floored paddock during the day. In spite of this floor the animals had to be muzzled, as they made attempts at every opportunity to get hold of manure or to lick the floor. During the night they stayed in their individual pens, also on cement floors, but provided with sleeping boards. Food consumption was poor and unsatisfactory in all cases. At every opportunity the animals persisted in lying in the feed boxes with the result that these, as well as the feed, were fouled with faces and urine. On this account weighing back of the unconsumed feed, although done regularly, was unreliable from the point of view of exact calculation. However, it may definitely be stated that food consumption was far more satisfactory in the case of group 4 (control) than in the other groups.

All the animals were bled monthly for the determination of blood calcium and inorganic phosphorus. Monthly live weights were recorded and rib-resections were made periodically for histo-pathological studies. Internal parasites were carefully controlled, as well as the general health of the animals attended to.

Results.

The clinical progress very briefly given for each group is as follows:—

GROUP 1.— : $\frac{CaO}{0{\cdot}43 \text{ gms.}}$: $\frac{P_2O_5}{4{\cdot}73 \text{ gms.}}$ = 1 : 11.

Date.	Goat 41661.	Goat 40922.
20/ 5/35	Experimental ration started.....	Experimental ration started.
6/ 7/35	Diarrhoea, which occurred at frequent intervals throughout the experiment	Diarrhoea, which occurred at frequent intervals throughout the experiment
18/12/35	—	Developed peculiar gurgle in its throat.
3/ 4/36	—	Rib section taken—bone normal.
7/ 8/36	—	Slight swelling on right side of face.
20/ 8/36	—	Rib section, very slight red seams, slight fibrosis.
20/10/36	—	Rib section—slight fibrosis.
2/ 6/37	Rib section—slight fibrosis.....	—
28/ 4/37	—	Very weak and stunted appearance.
4/ 5/37	—	Died—Marked atrophy or osteoporosis. No osteofibrosis.
15/ 2/38	Died—Marked atrophy or osteoporosis. No osteofibrosis	—

GROUP 2.— : $\frac{CaO}{9{\cdot}92 \text{ gms.}}$: $\frac{P_2O_5}{0{\cdot}67 \text{ gms.}}$ = 14·8 : 1.

Date.	Goat 41594.	Goat 41906.
20/ 5/35	Experimental ration started.....	Experimental ration started.
11/ 7/35	Constipated.....	—
3/4/36	Rib resected—rickets.....	Weak and lies down a lot.
23/ 4/36	—	Too weak to walk far.
11/ 6/36	—	Accidentally killed by an ox.—Slight rickets.
26/ 6/36	Developed bad "cowhocks".....	—
20/ 7/36	Hind legs badly bent.....	—
27/ 8/36	Given mineral supplement.....	—
23/ 9/36	Improved considerably.....	—
23/11/36	Died—Abscess in lung; bone atrophy	—

GROUP 3.— : $\frac{CaO}{0{\cdot}43 \text{ gms.}}$: $\frac{P_2O_5}{0{\cdot}67 \text{ gms.}}$ = 1 : 1·6.

Date.	Goat 41459.	Goat 41902.
20/ 5/35	Experimental rations started.....	Experimental rations started.
1/ 9/35	Lame in front leg.....	—
24/ 2/36	—	Weak on its legs.
9/ 4/36	—	Rib resection—Marked rickets.....
20/ 8/36	Rib resected—Slight rickets.....	—
25/ 8/36	Lame in right hind leg, joints, painful	—
20/10/36	Rib resected—Slight rickets.....	—
3/ 6/37	Rib resected—Normal, but slight osteoid seams	—
7/ 2/38	Died—Slight atrophy.....	—

GROUP 4.— : $\frac{CaO}{3{\cdot}95 \text{ gms.}}$: $\frac{P_2O_5}{3{\cdot}73 \text{ gms.}}$ = 1·06 : 1.

Date.	Goat 41915.	Goat 44323.
20/ 5/35	Experimental ration started.....	Experimental ration started.
16/ 9/35	—	Gave birth to a kid which was very weak and small.
27/ 1/36	—	Kid destroyed in order to give the mother a better chance.
2/11/36	—	Died sequel to pulmonary haemorrhage; bone normal.
3/ 6/37	Rib resected—Normal.....	—
16/ 3/38	Destroyed—Bone normal.....	—

The clinical record of the goats indicates that marked symptoms of osteofibrosis were not seen. Rickets made its appearance and was especially marked in No. 41594, Group 2. Both goats in Group 3, Nos. 41459 and 41902 became weak and were inclined to show lameness which became aggravated at times.

Interesting facts were revealed from the rib section and autopsy studies.

Group 1. *Low Calcium: High Phosphorus.*—About 15 months after the commencement of the experiment a diagnosis of slight osteofibrosis was made. However, a year later marked atrophy or osteoporosis was recorded in the case of both animals in this group. This fact is consistent with the relatively poor food consumption of these goats, and the occurrence of intermittent diarrhoea.

Group 2. *High Calcium: Low Phosphorus.*—The histological diagnosis of advanced rickets was made on No. 41594, eleven months after this goat had been placed on the experimental ration. An autopsy on this animal's group mate No. 41906, two months later showed that rickets, although present, was less marked. When No. 41594 was considered to be practically *in extremis*, the mineral

supplements of Group 4 (control) was administered. Although the animal improved clinically, feed consumption remained poor and death eventually occurred as a sequel to lung abscesses. At this stage, 6 months after a diagnosis of rickets had been established histologically, the bone picture left no doubt as to the presence of atrophy.

Group 3. *Low Calcium: Low Phosphorus.*—Histological examination of the rib, in the case of No. 41902, showed that marked rickets was present eleven months after the commencement of the experiment. Four months later the group mate No. 41459 showed only slight rickets. When the latter animal was autopsied, ten months later, osteoporosis was diagnosed.

Group 4. *Sufficient Calcium: Sufficient Phosphorus.*—Notwithstanding the fact that one of these young animals accidentally became pregnant and gave birth to a normal kid, histological examination of the bone showed that it remained normal. The group mate of this animal outlived all the other animals in the experiment and was found to have a normal healthy bone at the conclusion of the work.

The general appearance and condition of the animals was recorded in a photograph taken after they had been on the experimental ration for 15 months. Unfortunately three goats had already been lost by this time.

Fig. 1.

The animals numbering from left to right are: Group 1, Nos. 41661 and 40922; Group 2, No. 41494; Group 3, No. 41459; and Group 4, No. 41915.

From the appearance of the animals shown in Fig. 1 it is apparent that they were of mixed origin. As shown No. 41661 (Group 1) is a much bigger and stronger animal than its group mate No. 40922. The control animal No. 41915 is shown to be in good condition and to have a good glossy coat.

The average group weights in pounds are given in Fig. 2.

It will be seen from the monthly weights that very satisfactory gains were recorded in the case of Group 4 (control). Although the average weight gains for the other groups were poor, Group 1 (calcium low) appeared to be the best, but this may be attributed largely to the fact that No. 41661, as already shown was a stronger animal. The poorest group, in so far as a depression of average monthly weights was concerned, was undoubtedly Group 2 (phosphorus low). The sudden upward trend of the curve was due to the death of the weakest kid.

The monthly average group blood calcium figures are given in Fig. 3.

From these curves it will be seen that there were no marked group differences in the average blood calcium figures. However, Group 2 (high calcium: low phosphorus), did show a high blood calcium figure which gradually declined and was normal by the eighth month of the experiment.

The curves illustrating the average monthly inorganic blood phosphorus are given in Fig. 4.

This figure shows that the inorganic blood phosphorus was definitely high in the case of Group 1 (low calcium—high phosphorus). The average blood phosphorus, although relatively low during the first half of the experimental period in Group 3 (low calcium—low phosphorus), showed an improvement during the latter half of the period.

Discussion.

A survey of the results obtained once again demonstrates the advantage of bone biopsy as an aid to the study and diagnosis of deficiency diseases. For instance, an unfavourable factor such as poor and irregular food consumption would have rendered the work practically useless if weight gains and clinical symptoms alone had been the criterion of changes produced. However, since histological studies were carried out periodically on the bone sections, the progressive development of the osteodystrophic conditions could be followed and a better understanding of bone ossification obtained. For instance, a careful perusal of the results in the case of the two animals which received an intake of 0·43 grams CaO and 4·73 grams P_2O_5 daily, and where the $CaO:P_2O_5$, ratio was 1:11, shows that both these animals had developed slight osteofibrosis in about 18 months to two years after the commencement of the experiment. However, it would seem that these animals adapted themselves to a new low level of metabolism and mineral conservation, since the autopsy done approximately a year later showed that instead of the osteofibrosis progressing as could be expected, a marked atrophy of the bone became evident. A tendency to calcium conservation may thus explain why the development of osteofibrosis may be retarded or even prevented. In this case an over-abundance of phosphorus did not prevent bone atrophy when once a total deficiency of nutrients occurred. As direct sunlight and green feed were

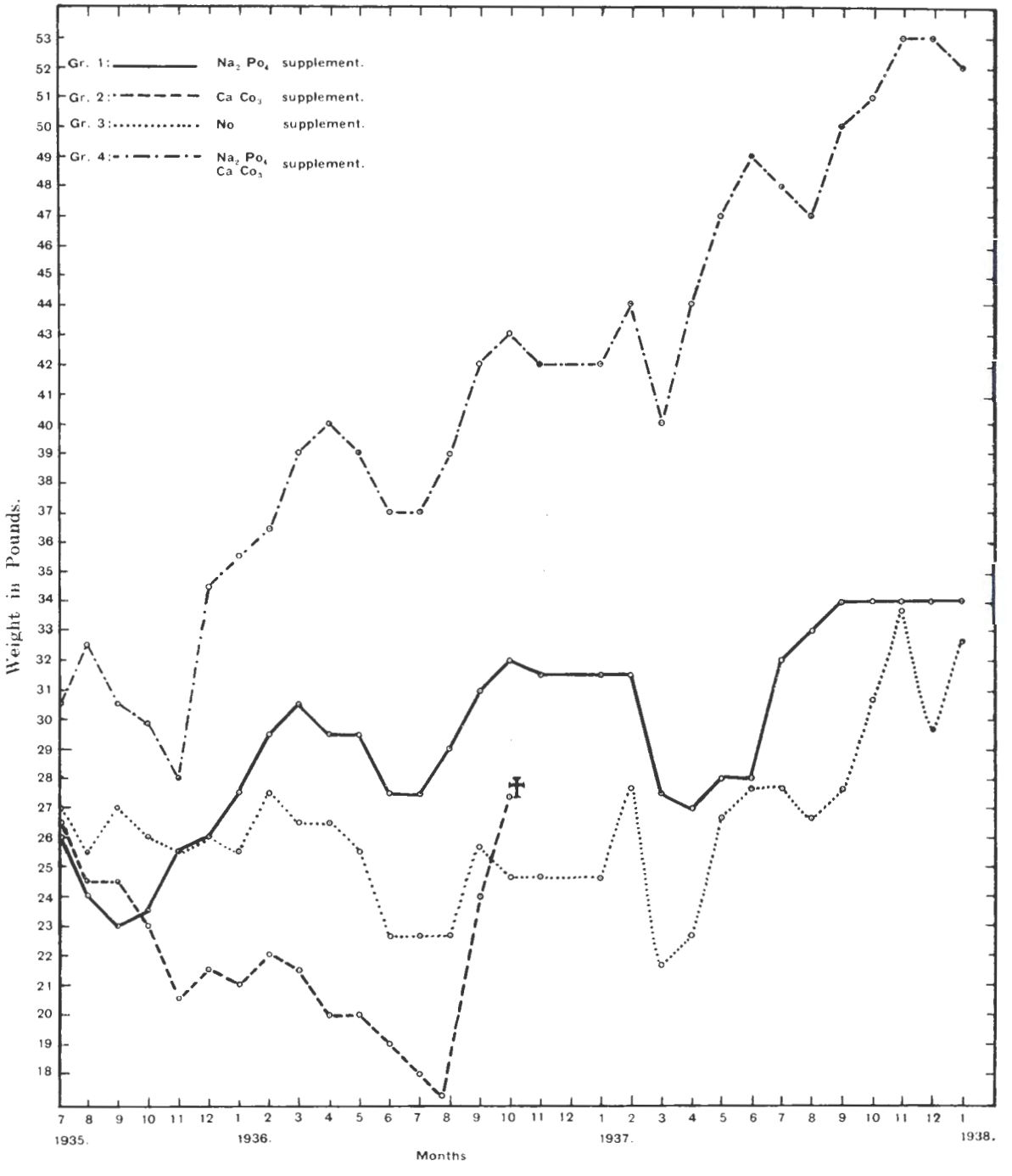

Fig. 2.– Monthly Group Weights.

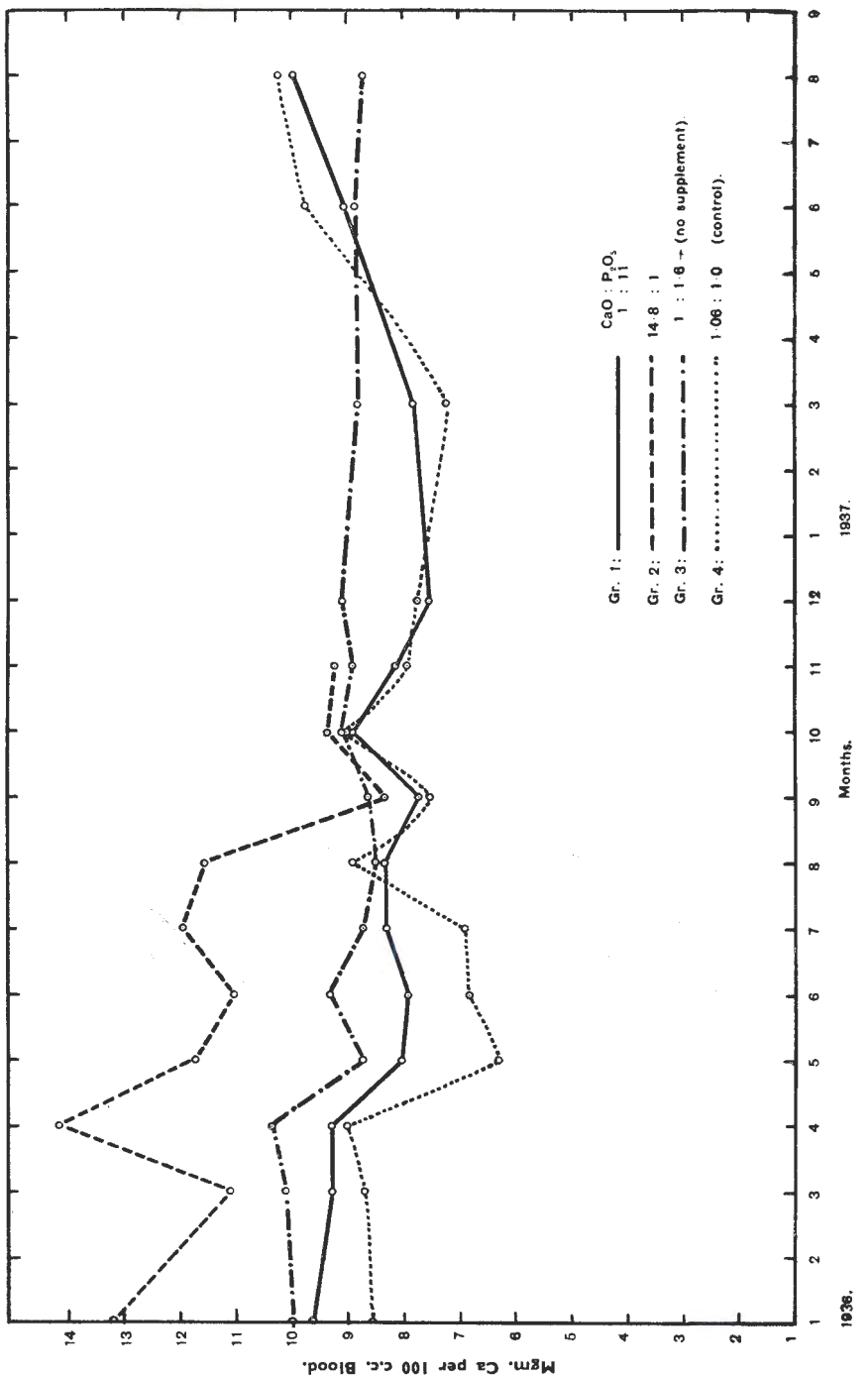

Fig. 3. Blood Calcium.

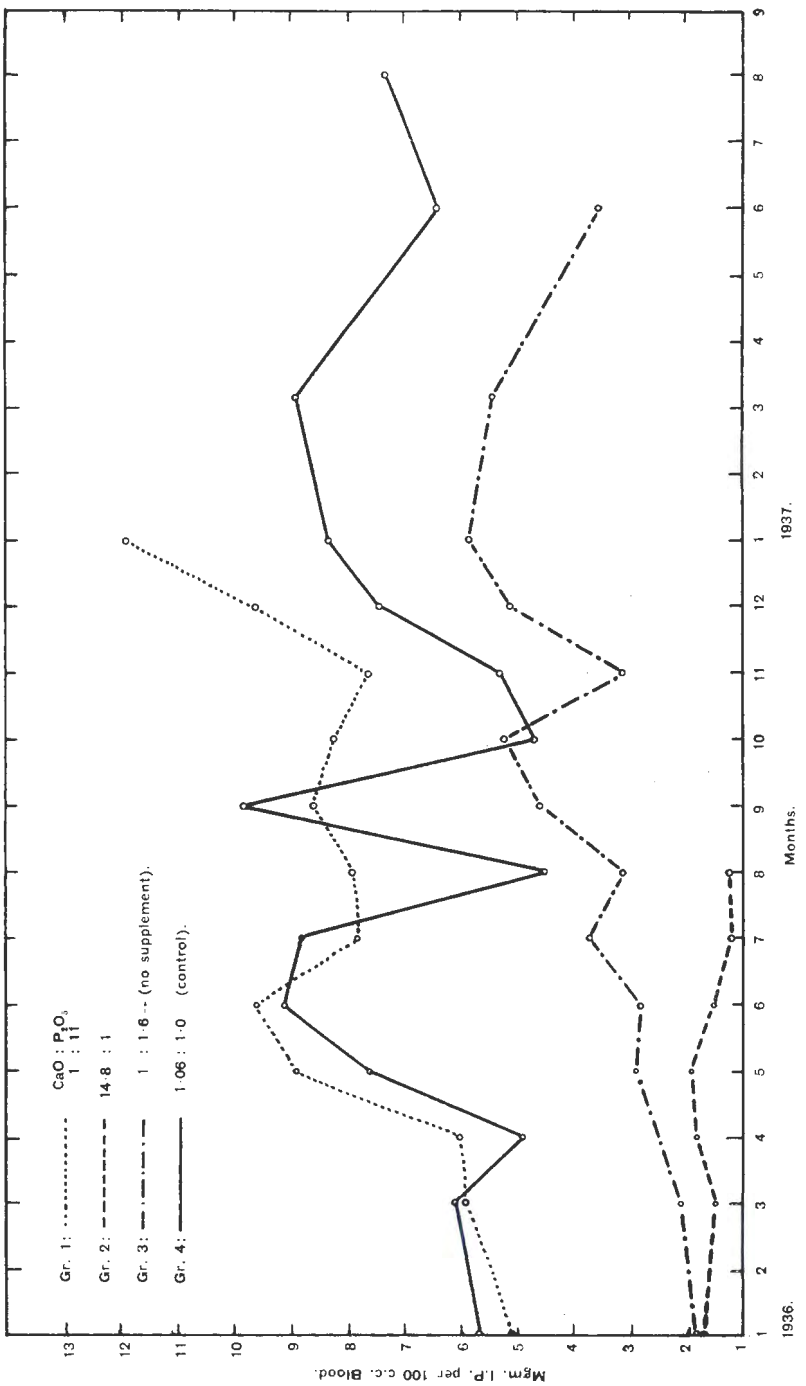

Fig. 1.—Inorganic Blood Phosphorus.

available at all times, it may be accepted that there was no lack of vitamins A and D. The inorganic blood phosphorus (Fig. 4), shows that this element was present in an abnormally high blood concentration and supports the contention that other factors, e.g. a protein deficiency must have prevented its proper utilization.

The low food intake was accompanied by a disinclination of the goats to walk and a general inactivity. The stunted appearance of these animals (Fig. 1) indicates that growth was severely retarded. Some or all these factors possibly exercised an inhibitory influence on the development of osteofibrosis.

A consideration of the results obtained in Group 2, where the calcium intake was 9·92 gms. and the phosphorus 0·67 gms. daily, with a calcium : phosphorus ratio of 14·8:1, shows that eleven months after the commencement of the experiment advanced rickets was recorded in one animal. The group mate had slight rickets when accidentally killed a month later. Eight months after diagnosing rickets in the former case, this animal actually showed severe clinical rickets. At this stage the mineral supplement was changed to that of the control group. The animal showed a considerable degree of clinical improvement, but upon death three months later, a diagnosis of bone atrophy was made.

The weight curve (Fig. 2) shows that the low phosphorus intake resulted in a marked weight depression. Similarly the inorganic blood phosphorus never reached the level of 2 mgm. per 100 c.c. blood. The calcium appeared to be relatively high, but gradually sank until it reached the normal level of approximately 9 mgm. per 100 c.c. blood in eight months' time.

Although the food consumption of these animals was as poor as that of the kids on the low calcium intake, marked rickets became manifest in the former in a shorter period than did osteofibrosis in the latter Substantiating evidence of the early development of conditions favourable to rickets may be seen in the body weights of this group.

When the calcium intake was 0·43 grams and the phosphorus 0·67 grams daily, with a $CaO:P_2O_5$ ratio of 1:1·6, as shown in Group 3, very marked rickets was established in one kid at the end of the first year. The group mate of this animal only showed slight rickets six months later. At the conclusion of the experiment a diagnosis of slight atrophy was made in the latter case. With the exception of a comparatively low inorganic blood phosphorus figure, shown in Fig. 3, no definite conclusion can be drawn from the other observations in this group.

Theoretically, when the calcium and phosphorus intakes are so low that no growth takes place, through voluntary starvation or inadequacy of these elements in the diet, one would expect nothing worse than bone atrophy to develop. In practice, however, such low intakes of calcium and phosphorus are not easily affected, and as in the present experiment rickets, which is relatively easily produced on a phosphorus deficient diet, develops. Although bone biopsy established florid rickets in one of the animals that received

both calcium and phosphorus low intakes in conjunction with a favourable ratio, definite clinical rickets was recognized only in one case where the calcium intake was high and the $CaO:P_2O_5$ ratio consequently wide.

The control group, the animals in which received 3·95 grams of CaO and 3·73 grams of P_2O_5 each daily, and where the $CaO:P_2O_5$ ratio was 1·06:1·0, remained in good condition as shown by the steady increase in weight (Fig. 2). Examinations of all bone sections showed that both animals in this group remained normal.

Conclusions.

(1) Starvation proved to be an important factor in the development of bone atrophy in the case of two kids which received a ration low in calcium and high in phosphorus, where the $CaO:P_2O_5$ ratio was wide.

(2) Clinical symptoms of rickets were observed only in a case where the phosphorus intake was low and that of calcium high, with a wide ratio.

(3) When the calcium and phosphorus intakes were both low, their ratio being normal, the histological examination of the bone showed the presence of rickets.

(4) The inhibition of normal growth, due to semi-starvation, resulted in the eventual development of bone atrophy and not osteofibrosis. Even rickets, which is more easily produced than osteofibrosis, in time gives way to atrophy in the presence of cessation of bone growth.

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REFERENCES.

GLOCK, G. E. AND MURRAY, M. M. (1936). Preliminary observations on the effects of a low calcium diet on goats and kids. *Jour. of Com. Path. and Ther.*, Vol. 52, pt. 3, pp. 229-248.

GROENEWALD, J. W. (1927). Osteofibrosis in equines. *Onderstepoort Jour. of Vet. Sc. and An. Ind.*, Vol. 9, No. 2, pp. 601-620.

MAREK, J. AND WELLMAN, O. (1931). Die Rhachitis. *Pathologischen Teil. Jena, Gustav Fischer*, pp. 51-64.

THEILER, A., DU TOIT, P. J. AND MALAN, A. I. (1937). Studies in the mineral metabolism XXXVIII. The influence of variations in the dietary phosphorus and in the Ca : P ratio on the production of rickets in cattle. *Onderstepoort Jour. of Vet. Sc. and An. Ind.* Vol. 8, No. 2 pp. 375-414.

THEILER, A., DU TOIT, P. J. AND MALAN, A. I. (1937). Studies in mineral metabolism XXXVIII. Calcium and phosphorus in the nutrition of growing pigs. *Onderstepoort Jour. of Vet. Sc. and An. Ind.* Vol. 9, No. 1, pp. 127-164.

WESTER, J. (1935). Orgaanziekten by de groot huisdieren. Drukkery J. van Boekhoven, Utrecht en Amsterdam, bl. 630.