

Volume of Parathyroid Glands in Relation to Dietary Calcium and Phosphorus.

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Enlargement of the parathyroid glands has been observed in the spontaneous rickets of rats¹ and humans^{2,3} and has been experimentally produced in a variety of species by diets low in calcium.⁴⁻⁹ However, typical rickets is produced experimentally by diets low, not in calcium, but in phosphorus. Not low phosphorus diets, but on the contrary, both *high* phosphate diets¹⁰ and parenteral phosphate injections^{11,12} have been found to cause parathyroid enlargement. Recently Ham and co-workers⁹ essayed to determine, by dietary experiments, what alteration in blood calcium or phosphate constituted the essential physiological stimulus to parathyroid enlargement. These authors confirmed the fact that a low calcium diet (Steenbock) with its attendant hypocalcemia caused enlargement of the glands in young

rats. They found no enlargement on a Steenbock low phosphorus diet with hypophosphatemia and marked rickets. Finally by adding a mixture of calcium phosphate and phosphoric acid to a "normal" diet they succeeded in raising the average serum phosphate of 4 rats 2 mg % above that of 3 controls without changing the serum calcium and without increasing parathyroid size. They concluded that "hypocalcemia, instead of hyperphosphatemia, is the primary cause of physiological hypertrophy of the parathyroid glands."

We have attempted to confirm and extend these rather meager data. Albino rats of the Sherman strain have been placed on variations of the Steenbock diet* at weaning (age 3 weeks). After 4 weeks they were killed by bleeding from the heart under ether anesthesia. Pooled specimens of serum were analyzed† for calcium (Clark-Collip) and inorganic phosphate (Fiske-Subbarow). The parathyroids were fixed in Bouin's fluid, embedded in paraffin, serially sectioned at 10 micra and their volumes determined by tracings and planimeter measurements.⁶ Bones were fixed and decalcified in Mueller's fluid and studied histologically. A comparison has been made between the glands of rats on the low phosphorus diet and of

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* Basal low Ca diet: Ground yellow corn 76 parts, gluten flour 20, sodium chloride 1. This diet contained 355 mg Ca per kg by analysis of Dr. Edgar Miller. One drop Lederle's Vitamin B complex was given 6 times weekly to each rat. For low P diet, 3 parts CaCO₃ were added. The rats on Vitamin D supplement received 1 drop Squibb's Viosterol in oil (170 I.R.U.) twice weekly.

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TABLE I.
Effect of Dietary Calcium and Phosphate upon Parathyroid Volume.

Diet	No. rats	Mean body wt (g)	Mean parathyroid vol. (mm ³)	Mean ratio parathyroid/body (mm ³ /100 g)	Serum Ca (mg%)	Serum Inorganic phosphate (mg%)
Stock (aged 30 days)	14	50	.100	.200		
Stock (" 50 ")	10	160	.120	.075		
Stock (" 50 " — restricted intake)	9	63	.091	.144	10.8	6.7
Steenbock Low P	16	50.8	.060	.116	11.8	2.0
Steenbock Low P + 400 mg% K ₂ HPO ₄	10	60	.054	.095	11.9	4.4
Steenbock Low P + 800 mg% K ₂ HPO ₄	9	51.2	.087	.174	10.3	7.1
Steenbock Low P + 1500 mg% K ₂ HPO ₄	16	47.4	.145	.310	10.8	10.2
Steenbock Low P + 3000 mg% K ₂ HPO ₄	8	53	.223	.425	7.3	6.1
Steenbock Low P + Vitamin D	10	49.2	.047	.098	14.1	5.5
Steenbock Low Ca + 800 mg% K ₂ HPO ₄	10	41	.336	.724	5.9	7.8
Steenbock Low Ca + Vitamin D	9	61	.136	.236	10.7	8.3

those on a stock diet.†

Results. Growth was poor on all the modifications of the Steenbock diet. Severe rickets occurred in all the animals on the low P diet. This was completely prevented by the vitamin D supplement. Rickets was mild and inconstant in the animals receiving 400 and 800 mg supplements of K₂HPO₄ and absent in those receiving 1500 mg. Growth was poorest in the animals on the low calcium diet and these animals all had severe low calcium type of rickets.

The chart and table show that the parathyroids were tremendously enlarged in the low calcium group. The glands were very small in the low P group and the addition of vitamin D made them even smaller while raising both the serum calcium and phosphate. The addition of graduated amounts of K₂HPO₄ to the low P diet caused a corresponding increase in parathyroid size and serum phosphate without causing a uniform change in serum calcium. The glands were smaller in rats on the low P diet than in

control rats on the stock diet either (1) of the same age, (2) of the same body weight but younger, or (3) of the same age and weight due to restricted feeding.

Discussion. The difficulty of comparing organ sizes in animals of different age or weight is obvious. In animals of the same age, the *ratio* of organ to body weight is frequently used to advantage where the body weights are widely different. The inadequacy of the Steenbock diet for the production of normal growth even with vitamin B supplements and the marked effect of alterations in dietary calcium and phosphorus on growth have influenced our results. For these reasons the effect of growth retardation through restricted feeding of the stock diet was determined. It is apparent from the table that parathyroid volume and body weight are not proportionately reduced by this expedient. The unpredictable degree of influence of general inanition in the rats on the experimental diet therefore rendered this ratio of limited usefulness in comparing the results.

In spite of this handicap, certain facts are clearly demonstrated by the results. These are: (1) the *increase* in parathyroid volume

† Rockland rat diet: Yellow corn, hulled barley, hulled oats, whole wheat, soy bean meal, meat scraps, powdered whole milk, alfalfa meal, NaCl, CaCO₃. This contains about 2.2% Ca and 1.3% P.

