2. (a) Low calcium diet with 5% viosterol. Callus formation fair, somewhat better than with low calcium diet alone.

(b) When 500% viosterol was added to the above diet the calcifying effect in the callus was very apparent.

(c) When 1% $CaCO_3$ and 500% viosterol were added to a high phosphorus and low calcium diet, the calcium deposition in the callus was definitely increased, but the degree of deposition did not approach that of a normal callus or a callus in the experiments in which less phosphorus and the same amounts of calcium and viosterol were used.

Unoperated animals kept on a stock diet showed nearly complete healing of fractures in 18 days.

The results seem to indicate again the importance of diet in parathyroidectomy experiments. They prove clearly that in the presence of a parathyroid deficiency calcification does not occur regularly, if calcium is also lacking in the diet. They also show that the property of viosterol in elevating the serum calcium level after parathyroidectomy is evident in its ability to promote callus calcification. In comparison with the normal animal, however, callus calcification is somewhat delayed.

## 5283

## Role of the Parathyroids in Calcification, and Susceptibility of Parathyroidectomized Rats to Viosterol.

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The long continued administration of parathyroid extract to animals results in an increased excretion of calcium and phosphorus from the body.[1, 2, 3] Similarly, the presence of hyperfunctioning parathyroid glands results in a negative calcium and phosphorus balance and bone decalcification termed clinically, *osteitis fibrosa cystica.* Several observers noticed marked improvement when one or more of these glands was removed. Hence, in hypofunction a marked retention of calcium and phosphorus should result. Greenwald,[4] contrary to previous assumptions, demonstrated retention of

[1] Greenwald, I., Gross, J., *J. Biol. Chem.*, 1926, **68**, 325.

[2] Bodansky, A., Blair, J. E., Jaffe, H. L., *J. Biol. Chem.*, 1930, **88**, 629.

[3] Albright, F., Bauer, W., Ropes, M., and Aub, J., *J. Clin. Invest.*, 1929, **7**, 139.

[4] Greenwald, I., Gross, J. J., *J. Biol. Chem.*, 1925, **66**, 185.

these elements after thyroparathyroidectomy in dogs. The validity of Greenwald's conclusions may be questioned because the thyroid extirpation may have contributed to this retention. However, in metabolism experiments on rats, in which the parathyroids alone were removed, retention of calcium and phosphorus was observed, provided the diet contained a certain amount of these elements,[5] thus substantiating, in part, Greenwald's hypothesis. However, no attempts have as yet been made to determine the depots of retention of calcium and phosphorus. That their deposition is not always in the osseus tissue is evidenced by the observations of Erdheim,[6] Iselin,[7] and Toyofuku.[8] Leopold and Von Reuss[9] found that the combined soft tissues of parathyroidectomized rats contained more calcium than those of control rats.

In the course of study on the effect of calcium, phosphorus and viosterol intake on parathyroidectomized rats it was noted that they were much more susceptible to viosterol hypercalcification than normal animals. A dose of viosterol, which ordinarily would not produce calcification in a normal rat in a given length of time, may cause calcification in the organs of the parathyroidectomized animals, provided certain amounts of calcium and phosphorus be present in the diet. The effect was absent when the calcium intake was very low, and more pronounced when the intake of phosphorus was high and that of calcium at optimal levels.

It was also observed that parathyroidectomized animals receiving no viosterol, but which were on diets containing calcium with normal or high phosphorus concentrations, developed calcification of their vascular system, especially the aorta and the vessels of the kidney. One animal developed extensive calcification of both lungs.

It was shown[10] that normal animals are more susceptible to viosterol overdosage when their diet contained minimal calcium and high phosphorus concentrations. The increased intake of phosphorus apparently caused a transitory or permanent increase of this element in the body and, in the presence of calcium and calcifying agent, such as vitamin D, these ions in excess of the solubility product constants are deposited in the tissue as the insoluble salt. A similar mechanism may operate in the parathyroidectomized organism. It was also shown[4, 5] that the immediate effects of depri-

[5] Shelling, D. H., to be published.

[6] Erdheim, J., *Frankfurt Z. f. Path.*, 1911, **7**, 175.

[7] Iselin, H., *Deutsche Z. f. Chir.*, 1908, **93**, 494.

[8] Toyofuku, T., *Frankfurt Z. f. Path.*, 1911, **7**, 249.

[9] Leopold, J. S., and Von Reuss, A., *Wien. klin. Wchnschr.*, 1908, **21**, 1243.

[10] Shelling, D. H., PROC. SOC. EXP. BIOL. AND MED., 1930, **28**, 298.

vation of the parathyroids is the retention of phosphorus and decrease or an absence of this element in the urine. The decreased excretion of calcium, which follows, may be the result of the parathyroid extirpation primarily or it may be due to the increased phosphorus retention and the retained calcium is thus deposited in the tissues as the insoluble salt.

The relation of hypoparathyroidism to abnormal calcification such as in Paget's disease, juvenile sclerosis, renal sclerosis, otosclerosis, and general arteriosclerosis is worthy of consideration. The association of a low serum calcium and low calcium excretion in otosclerosis has been frequently observed by otologists; and the occurrence of cataracts in parathyroid tetany in human beings and experimental animals has been noted by many observers. The association of extreme calcification of the vascular system and renal disease has been noted clinically and pathologically and it is possible that the parathyroid plays a rôle in this syndrome.

The rôle of the parathyroids and high phosphorus diets, such as meat, in general arteriosclerosis of the middle aged can only be speculated upon at present.

## 5284

## Note on Individual Differences in Human Blood.

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1. Previously an agglutinable property of human blood designated as P was described, which could be demonstrated by the use of immune agglutinins from rabbits,[1] and it was mentioned[2] that reactions of a more or less similar specificity occur with a certain type of irregular human isoagglutinins. Inasmuch as these 2 reagents are not always easily available it seems worth mentioning that similar results can readily be obtained with various absorbed normal animal sera, *e. g.*, those of horses, pigs and rabbits. In horse serum the agglutinins were found rather frequently.

2. An anti-dysentery immune serum from a goat was shown by Eisler[3] to contain agglutinins for human blood which can be ab-

[1] Landsteiner, K., and Levine, Philip, *J. Exp. Med.*, 1928, **47**, 757.

[2] Landsteiner, K., and Levine, Philip, *J. Immunol.*, 1930, **18**, 91.

[3] Eisler, M., *Z. f. Immunitätsf.*, 1930, **67**, 38.