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Influence of Thyro-parathyroidectomy and of Parathyroid Hormone upon State of Calcium in Serum of the Cat.†

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Trendelenburg and Goebel¹ demonstrated that serum from thyro-parathyroidectomized cats, when used as a nutrient fluid for the isolated heart of the frog, diminished the amplitude of contraction of the heart, as compared with serum from normal cats. They attributed this effect to a reduction in the total calcium of the serum, with a corresponding decrease in ionized calcium, but were unable to rule out the possibility of the formation of an un-ionized compound of calcium, presumably by combination with an organic acid.

Two of the authors have shown that the sensitivity of the frog's heart to changes in the concentration of calcium is specific for ionized calcium, bound calcium being inert with respect to the preparation, and have utilized this property of the heart for direct quan-

* P represents a preliminary, C a complete manuscript.

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¹ Trendelenburg, P., and Goebel, W., *Arch. f. exp. Path. u. Pharm.*, 1921, **89**, 171.

titative estimations of Ca^{++} concentrations in biological fluids.² They have also shown³ that the ionization of calcium in the protein-containing fluids of the human body follows, as a first approximation, a simple mass-law relationship, expressed by the equation

$$(1) \quad \frac{[\text{Ca}^{++}] \times [\text{Prot}^{\pm}]}{[\text{Ca Prot}]} = K = 10^{-2.22}$$

from which it is possible to calculate Ca^{++} concentrations, from analysis for total calcium and total protein, with a degree of accuracy at least as great as that of direct observation by the frog heart method.

Using the methods of direct observation and of calculation of Ca^{++} concentrations, the authors have studied the influence of thyro-parathyroidectomy and of the administration of the parathyroid hormone upon the ionization of calcium in the serum of the cat. The cat was chosen as the experimental animal because its serum was found to be especially favorable for observations by the frog heart method, which is not the case with the dog, and because the state of calcium in its serum was found to be accurately described by the mass-law relationship above referred to, which is not the case with the rabbit. The cat was found, in every instance, to respond to administration of the parathyroid hormone with a typical rise in the serum calcium level, resulting, in some cases, in death following the symptoms of hyperparathyroidism. A wide variation, however, was found in the rapidity of the response of cats to uniform daily doses of parathyroid extract. This variability, which may account for the conflicting statements in the literature⁴ as to the response of the cat to the parathyroid hormone, is being further investigated.

In more than 50 observations upon 9 cats the mass-law relationship previously described for normal human serum has been found to hold for the cat over the entire range from hypo-calcemia with tetany to the maximum hypercalcemia induced by administration of the parathyroid hormone. The values for the constant in the mass-law equation were, within the limits of experimental error, the same as those found for normal human serum, and there was good agreement between observed and calculated values for Ca^{++} concentrations over the entire range. Since on account of the limitations of the frog heart method, it was not possible to make direct observa-

² McLean, F. C., and Hastings, A. B., *J. Biol. Chem.*, 1934, **107**, 337.

³ McLean, F. C., and Hastings, A. B., *Proc. Soc. Exp. Biol. and Med.*, 1934, **31**, 529.

⁴ Thomson, D. L., and Collip, J. B., *Physiol. Rev.*, 1932, **12**, 309.

tions of Ca^{++} in undiluted hypercalcemic serum, observations upon these sera were made upon diluted serum only. Diluted hypercalcemic serum from the cat was found to conform to the mass-law Equation 1, as is also the case with diluted normal serum from the cat and from man.

In summary, the hypo-calcemia following thyro-parathyroidectomy results in a correspondingly diminished concentration of Ca^{++} and the hyper-calcemia following administration of the parathyroid hormone results in a correspondingly increased concentration of Ca^{++} . No evidence of any effect of removal of the parathyroid glands, or of administration of the parathyroid hormone, upon the qualitative state of calcium in the serum has been found, the changes observed being simply the quantitative changes predicted by the mass-law Equation 1.

Symptoms of tetany have usually appeared at a Ca^{++} concentration of approximately 0.6 mM per kg. H_2O , have increased in severity at still lower levels, and have disappeared as the Ca^{++} concentration rose again above the 0.6 mM level. Of 7 cats operated upon, 6 have developed tetany, the lowest Ca^{++} concentration observed being 0.40 mM per kg. H_2O (0.43 calculated), accompanying severe tetany, with a total calcium concentration of 1.04 mM per liter. The normal Ca^{++} range in the serum of the cat may be put tentatively at from 1.05 to 1.25 mM per kg. H_2O , and the level at which death from hyper-parathyroidism may occur at from 1.7 to 2.0 mM per kg. H_2O .

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Peristaltic Effect of Stimulation of the Chorda Tympani.*

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Dixon,¹ Dale² and Loewi³ originally established acetylcholine as the humoral agent that produces motility of the gastro-intestinal tract. Later research, recently summarised by Cannon⁴ and Dale⁵

* Aided by the Louis L. Cohn Fund.

¹ Dixon, W. E., *Brit. Med. J.*, 1906, **2**, 1807.

² Dale, H. H., *J. Pharm.*, 1914, **6**, 147.

³ Loewi, O., *Pflüger's Arch.*, 1921, **193**, 201.

⁴ Cannon, W. B., *Am. J. Med. Sciences*, 1934, **188**, II:145.

⁵ Dale, H. H., *Brit. Med. J.*, 1934, **1**, 835.