

100 cc. urine were not considered significant. This method is open to criticism in that substances such as uric acid and urates may be precipitated in the presence of acid. This would sometimes give a false positive test. The clinical results do not indicate that this interference was encountered very frequently.

A series of tests were made on a number of cases of liver disease and also on cases in which there was no evidence of liver pathology. The results of these experiments may be summarized as follows: Bile salts can be demonstrated in urine where a frank clinical jaundice exists. The results are negative in most cases of liver pathology without jaundice. This robs the method of any advantage over the various tests of liver function now in use. The conditions where physical examination might leave hepatic pathology in doubt, for example cases of early cirrhosis, gall bladder disease and metastatic carcinoma, do not show any well marked increases in the concentration of bile salts in the urine. The threshold of elimination of bile salts by the kidneys seems to approximate closely that bilirubin. The clinical significance of the occurrence of both substances would therefore seem identical. The quantitation of urinary bilirubin is not difficult, so that it would be preferable as a clinical test. These facts relegate the determination of bile salts in urine to a secondary place among the tests of hepatic function.

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### Tetany and Blood Calcium After Thyro-Parathyroidectomy in the Goat.

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Though it is a well-known fact that tetany does not often follow parathyroidectomy in herbivorous animals, no adequate explanation has been offered. Of the 2 interpretations offered, the more common is that the decomposition products of the food of herbivorous animals are less toxic than those of the food of carnivorous animals. The other is that aberrant parathyroids are sometimes found in the thymus gland of herbivorous animals. Parathyroid tetany in the goat following the removal of the thyroid and the parathyroids has not occurred as frequently as in the dog. MacCallum *et al*<sup>1</sup> who oper-

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<sup>1</sup> MacCallum, W. G., Thomson, H. S., and Murphy, J. B., *Johns Hop. Hosp. Bull.*, 1907, xviii, 333.

ated on 8 goats, noted violent tetany in only 2 cases. Christens<sup>2</sup> observed tetany in 3 goats following thyro-parathyroidectomy.

A series of 12 goats were thyro-parathyroidectomized by removing the entire thyroid capsule with the contained thyroid and parathyroids. The blood vessels were ligated at least one inch from the thyroid capsule so that any parathyroids which might be close to the

TABLE I. *Length of life and blood serum calcium.*  
Calcium determinations are expressed as mg. per 100 cc. of blood serum.

Goat number	Approx. Age Months	Blood Calcium			Survival Period Days	Cause of Death	Addenda
		Before Operation	Minimal after Operation	At Death			
1	12	9.89	9.2	8.12	9	Died during attempted thymectomy	Tremors of front and hind legs
2	12	9.23	8.93		91	Sacrificed	Bread diet for over 1 month
3	8	9.76	8.96	10.23	219	Sacrificed	Muscle tremors. Bread diet for over 1 month.
4	12	9.8	8.33	6.53	20	Pneumonia of left lung	
5	4	10.1	8.89	10.1	193	Sacrificed	Symptoms of thyroid deficiency
6	4	9.7	9.3	10.1	102	Sacrificed	Bread diet for over 1 month
7	16	9.28	7.28	7.93	84	Pneumonia	Was lactating at time of operation. Muscle tremors and chorea-like movements of the head.
8	4	10.1	8.55	7.22	18	Unknown	
9	4	10.1	9.42	10.05	83	Sacrificed	
10	6	10.5	9.54	9.5	82	Sacrificed	
11	2	10.1	8.38	9.65	74	Sacrificed	
12	2	9.9	8.35	10.05	74	Sacrificed	Evidence of cretinism. Evidence of cretinism.

<sup>2</sup> Christens, M. S., *Compt. Rend. Soc. de Biol.*, 1905, lvii, 335.

superior pole would be removed. The part of the thymus lying outside of the thoracic cavity was also removed in all but 2 of the animals. Half of the animals were young; the other half, young adults. Two of the former were less than 2 months old when the operation was performed.

The animals were kept on a diet of corn, oats, hay and water. All were autopsied and a careful search was made for any accessory parathyroid tissue. Blood for the blood calcium determinations was drawn from the external jugular vein. The determinations were made according to the method of Clark and Collip.<sup>3</sup>

The blood calcium in some of the goats fell slightly after thyro-parathyroidectomy. The fall was not to as low a level as sometimes seen in the dog. Only in one case was a blood calcium found to be below the tetany level for the dog. Two of the other animals had blood calciums which were near the tetany level. From the results as judged by the blood calciums, it seems as though we were unable to effect a complete thyro-parathyroidectomy even if we did remove a part of the thymus gland. The maintenance of the normal level of the blood calcium in the dog is certainly influenced by the parathyroids. Three of these animals were on a diet of filter paper and white bread for one month. This diet has a very low calcium content. Neither the behavior nor the blood calcium of these animals was altered appreciably by this diet.

Our results are somewhat similar to those of the other investigators who have worked on this problem. We did not see violent tetany in any of our animals, though we did observe decided muscle tremors in 3 of them.

Since various authors<sup>4, 5, 6, 7, 8</sup> have stated that parathyroid glands are frequently found in the thymus, we removed the part of thymus gland outside of the thoracic cavity. This, however, did not rule out the possibility of parathyroids in that part of the thymus gland inside of the thoracic cavity. Though we made an effort to remove all suspicious looking tissue at the time of operation and found no parathyroid tissue at autopsy, we feel that there must have been accessory parathyroid tissue.

*Summary.* In the goat the usual operation for the removal of

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<sup>3</sup> Clark, E. P., and Collip, J. B., *J. Biol. Chem.*, 1925, lxxiii, 461.

<sup>4</sup> Baggio, G., *Arch. Scienc. Med.*, xxxvii, 354. Quoted from Dragstedt, L. R., *Physiol. Rev.*, 1927, vii, 502.

<sup>5</sup> Shapiro, S., and Jaffee, H. L., *Endocrinol.*, 1923, vii, 720.

<sup>6</sup> Nicholas, J. S., and Swingle, W. W., *Am. J. Anat.*, 1925, xxxiv, 469.

<sup>7</sup> Paton, D. N., and Findlay, L., *Quart. J. Exp. Physiol.*, 1917, x, 203.

<sup>8</sup> Meyer, A. W., *Anat. Rec.*, 1909, iii, 272.

the thyroids and parathyroids does not result in tetany. Tetany does not supervene because the goat can maintain a normal or nearly normal blood calcium.

## 4224

**Use of Paramecia for Studying Toxins and Antitoxins (Measles, Scarlet Fever and Diphtheria).**

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At the suggestion of Dr. Hektoen the effect of bacterial toxins and antitoxins on paramecia has been studied. Others have used paramecia for testing toxic action. Hamilton<sup>1</sup> observed that normal human serum, at a dilution of 1:5, usually was not toxic to paramecia, while serum from scarlet fever patients was nearly always toxic (85%) and serum from pneumonia patients was toxic in 66%. Takenouchi<sup>2</sup> found that strong diphtheria and tetanus toxins and hemolytic staphylococcus and streptococcus culture filtrates had no effect on paramecia. Cultures of *B. pyocyaneus* caused death of paramecia, but this seemed due to alkalinity of the filtrate and not to any specific pyocyanolysin, because, neutralization of the filtrate caused the effect to be entirely lost. Philpott<sup>3</sup> found that virulent *B. pyocyaneus* and *B. enteritidis* were toxic to paramecia. Diphtheria toxin had no appreciable effect on the division or death rate of 3 species of paramecia tested.

In testing the action of filtrates of bacterial cultures on paramecia it is necessary to grow the bacteria in a medium that is itself not toxic for the paramecia. The solutions must be isotonic with the paramecia, which according to Balbiani<sup>1</sup> corresponds to 0.3% solution of common salt. Crane<sup>4</sup> states that paramecia can live 24 hours in any hydrogen ion concentration between pH 5 to 7.6.

One percent dextrose broth, pH 7.6, made with Liebig's beef extract and Witte's peptone and containing 1% sheep blood, was found suitable for the production of streptococcus toxins and was in itself not toxic to paramecia. No sheep blood was added to the dextrose broth for the production of diphtheria toxin. The bacteria were grown 5 days at 36° C. and the cultures filtered through

<sup>1</sup> Hamilton, A., *J. Infect. Dis.*, 1904, i, 211.

<sup>2</sup> Takenouchi, M., *J. Infect. Dis.*, 1918, xxiii, 396.

<sup>3</sup> Philpott, C. H., *J. Morph. and Physiol.*, 1928, xlii, 85.

<sup>4</sup> Crane, J. *Phar. and Exp. Therap.*, 1921, xviii, 319.