A luer syringe, graduated in hundredths of a c.c., with a blunt needle corresponding to the lumen of the capillary tube, serves very well for filling the tubes, which are held nearly perpendicular while filling, thus avoiding the entrance of air.

Successive readings did not vary more than 0.03 degree and were often not more than 0.01 degree apart. The further technic and the calculations are carried out in the usual way.

The availability of the method is shown by the following results of a determination in which this method was employed:

Saccharose solution percentage.	Sp. Gr.	Rotation read in:		Spec. rotation in:	
		50 mm. tube	100 mm.	50 mm.	100 mm.
4.839	1.021	1.66°	3.32°	67.18	67.18
4.860	1.022	1.78	3.36	66.84	67.20
5.360	1.026	1.95	3.68	66.61	66.90
9.140	1.036	3.18	6.34	67.24	67.10
10.120	1.038	3.52	7.01	67.00	66.70

The table gives an average of +66.98 instead of +66.73, the theoretical value, for a 5 per cent. solution, and +67.00 instead of +66.65, the theoretical value for a 10 per cent. solution.

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Studies on the physiology of the parathyroids.

By HARALD A. SALVESEN (by invitation).

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We possess at the present time no exact knowledge concerning the function of the parathyroids. There are many theories, but only three have gained some importance, namely that the parathyroids control (1) the guanidine metabolism and by doing so regulate the tonus of the muscles; (2) the calcium metabolism; (3) the acid-base equilibrium and their removal cause alkalosis. The parathyroids also are supposed to control the sugar metabolism to some extent.

In the present work the changes in certain constituents of the blood have been studied following partial and complete parathyroidectomy in dogs, care being taken to leave enough thyroid tissue to prevent cachexia. Partial extirpation was done in 7 dogs, complete removal in 10 dogs.

I. Partial Parathyroidectomy. Three glands were removed. In no case did the animals show any symptoms of tetany, and apart from a little depression and loss of appetite the first few days showed no symptoms at all. In 6 of these dogs the fourth gland was removed later.

The blood sugar was absolutely unchanged. The alkali reserve usually was lowered the first few days after the operation; corresponding to this lowered alkali reserve there was an increase of acid elimination. The serum calcium decreased from a normal value of 10.0 mg. to a minimum of 7 mg. per 100 c.c.

In 2 of the 7 dogs there was no decrease in calcium; microscopic examination showed that only two parathyroids were taken out; in one of these dogs the third parathyroid was removed some time afterwards and the calcium dropped down to about 8 mg. Within two weeks the calcium was restored again to the normal. As a control a normal dog was given the same anesthetics used in the operations (chloroform and ether, equal parts); the alkali reserve dropped considerably, but the calcium remained unchanged. Another normal dog was given large doses of N/10 hydrochloric acid for three weeks; there was a heavy drop of the alkali reserve, but the calcium was unchanged. The calcium decrease found in partial parathyroidectomized dogs therefore cannot be due to anesthetics or acidosis.

II. Complete Parathyroidectomy. In 10 dogs complete parathyroidectomy was performed; in 6 of these partial parathyroidectomy was done previously, while in 4 all the parathyroids were removed at once. All of these 10 dogs developed acute tetany. Five of them died untreated within 3½ days; 1 died 22 days after; the condition was complicated by extensive necrosis of 3 legs following unsuccessful intravenous injections of calcium chloride. Four of these dogs were preserved by treatment and passed into a state of latent tetany.

A. Acute Tetany.

1. Blood analysis during development of the symptoms in this acute stage showed: Blood sugar unchanged; there was no

hypoglycemia even during the most acute symptoms shortly before death. The alkali reserve almost invariably decreased after the operation; it might be normal even during tetany. Corresponding to this drop of the alkali reserve there was an increase in the excretion of acids and there was no evidence of alkalosis, even close before the very onset of tetany. Calcium dropped from the normal value of 10 mg. per 100 c.c. serum and was, when tetany occurred, always below 7 mg. usually much lower. There seemed in this acute stage to be a certain relation between the degree of the lowering of calcium and the violence of the symptoms. The inorganic phosphorus of the blood serum increased considerably. After the initial rise the phosphorus might drop again, but still seemed to be decidedly above the normal value.

2. The Fate of Intravenously Injected Calcium Chloride in Parathyroidectomized Dogs.

One of the reasons why the decrease in calcium found in tetany is not regarded as the essential cause of the symptoms of parathyroidectomized dogs is, that they die in spite of calcium injections. This may be due to rapid elimination or carrying away of the injected calcium in some manner. The doses used by MacCallum and Voegtlin and others have been relatively small. In the present experiments 3 dogs were treated intravenously with a 10 per cent. solution of calcium chloride. A total of 2 grams a day was injected. This checked the symptoms, but almost invariably there was violent tetany again the next day, which was checked by a new injection. Such doeses of calcium *must* raise the calcium content of the body fluids considerably, and it is easy to calculate *how much* it will be raised knowing the value of blood calcium before injection, the weight of the dog and assuming an even distribution. Now, whenever convulsions reappeared after injection, the serum calcium always was found to be down to the same low level again, which shows that the injected calcium is disposed of in some manner.

To clear up this question 3 of the tetanic dogs were given a fixed dose of calcium chloride intravenously and the urine and feces for 24 hours were analyzed for calcium. The curves for the serum calcium and phosphorus were determined during this period.

TABLE I.

Dog II. Calcium and Phosphorus in Serum Following Injection of 1.6 gm. Calcium Chloride Intravenously. Weight 14.5 kg.

Time.	Ca | P (inorg.). in 100 c.c. of serum.		Remarks.
	mg.	*mg.*	
June 20			11:15 a.m., injection of 16 c.c. 10 per cent. sol. of $CaCl_2$.
before	5.2	7.9	
11:30 a.m.	15.8	7.9	
2:00 p.m.	10.0	7.8	
3:30 p.m.	7.2	7.9	
8:00 p.m.	6.6	8.3	
12:00 a.m.	5.8	5.4	
June 21			
11:15 a.m.	5.3	6.7	

Table I shows that 15 minutes after the injection the calcium was 15.8 mg. and decreased rapidly; 24 hours after, the calcium had the same value as before injection; that is, there had disappeared from the blood an amount of calcium exactly corresponding to the amount injected. Assuming an even distribution, the injected calcium would increase the serum calcium to 10.9 mg.; it will be seen that this level is not reached until about 2½ hours later; which means that calcium chloride diffuses slowly from the blood. There was also a rise in the phosphates.

TABLE II.

Dog II. Calcium Excretion in Urine and Feces, June 20-21, 1922.

Urine calcium.	Feces calcium.	Total.
g.	*g.*	*g.*
0.042	0.505	0.546
Injected		0.578

As Table II shows there was excreted an amount of calcium corresponding to the amount injected, but more than 9/10 was excreted in the feces and less than 1/10 in the urine (the colon was rinsed out at the beginning and close of the period). This is remarkable, as the calcium in the blood for some time must have been decidedly above the threshold and still only small amounts passed through the kidneys. This rapid disappearance of calcium may explain why calcium treatment reported by previous workers failed to keep the animals alive.

B. The Preservation of Completely Parathyroidectomized Dogs. Latent Tetany.

Four of the completely parathyroidectomized dogs survived; 2 of them recovered spontaneously during milk feeding; the other 2 recovered following vigorous calcium treatment combined with milk feeding. In these latter dogs after a week or two the doses employed (usually 1 or 2 grams of calcium chloride a day intravenously) could be lowered and at last omitted; the dogs lived without any symptoms and were to all appearance normal on a milk diet. These 4 dogs could be kept alive indefinitely on this diet; one lived for 21 months and was then killed; the others were either killed or at will brought into tetany from which they died. These dogs which appeared absolutely normal could, whenever it was wanted, be brought into tetany, usually within 24 hours, by changing the diet to meat. This condition formed an excellent opportunity for studying the various factors involved in the production of tetany. Though to all appearances normal these dogs showed one characteristic finding in the blood: *The calcium was still low.* It varied to some extent, but was usually between 5 and 6 mg. The inorganic phosphorus was usually at the upper border of the normal level or above. Numerous experiments have been performed on these dogs.

1. *The Diet in latent Tetany.* On a milk diet (minimum 500 c.c. a day with bread or porridge) these dogs after the first critical period was passed could be kept without symptoms for as long a time as wanted. Meat always produced tetany, loss of appetite, and depression. Prolonged meat feeding killed two of the dogs. Experiments with various forms of diet showed that it was the withdrawal of milk which produced tetany, not meat diet in itself, and the conclusion is, that milk contains substances which prevent tetany. This substance proved to be calcium of which milk contains 1.2 grams per liter, corresponding to about 10 grams of calcium lactate. Ninety per cent. of this calcium was precipitated by sodium oxalate, care being taken not to get any excess of oxalate in the milk, and this milk was now useless in preventing tetany; usually within 24 hours the dogs got violent tetany when fed this milk.

2. *Calcium Administration.* On the other hand, if an amount of soluble calcium salt was given corresponding to the Ca in the

amount of milk, which prevents tetany, the dogs kept normal on any diet; now when meat was given in excess, the dogs increased in weight and were normal in all their actions. It was possible by giving large amounts of calcium lactate by stomach tube to restore the calcium content of the blood almost to the normal level. From this condition it took a longer time than usual to produce tetany on a milk free diet and when tetany occurred serum calcium was always found lowered again. If tetany was produced from the latent stage a single dose of calcium lactate (5-10 grams) usually checked all the symptoms. Analysis of serum calcium then always showed that at the moment, when the symptoms were relieved, there was an increase in the calcium content of the blood, showing that it is the actual absorption of calcium which cures the symptoms. The same increase in serum calcium was seen when milk checked the symptoms. Concerning the relation between the blood calcium and phosphorus during latent tetany and the clinical symptoms, the findings may be summed up as follows: (a.) Whenever the animals were brought into tetany from a symptom free condition, the blood calcium was always still further lowered; (b.) When the animals by administration of calcium or milk were made normal again, the blood calcium was always higher than during the symptoms of insufficiency. (c.) The level of blood calcium at which tetany occurred seemed to vary and seemed to depend upon at what level of blood calcium the tetany producing diet was started. Inorganic phosphorus showed no regularity; it usually was higher than normal.

3. The protein metabolism in dogs with latent tetany on a milk diet and without symptoms was normal. The non protein nitrogen and blood urea were normal both in the latent state and during tetany.

4. Carbohydrate metabolism. The blood sugar was unchanged in these dogs both during the latent stage and during tetany. The tolerance for glucose given orally was lowered; when calcium in the blood was increased by calcium feeding, the tolerance was distinctly increased. When the dogs were brought into tetany by milk free diet the tolerance was lowered. The urine in one experiment contained 10 per cent. of sugar during the test. The blood sugar curves indicate that the lowered tolerance is not due

to increased permeability of the kidneys, but to a functional disturbance of the glycogen-forming organs. The results indicate that there is a relation between sugar tolerance and blood calcium in these animals.

5. Guanidin injections in a normal dog in amounts large enough to produce violent convulsions did not alter the serum calcium but produced hyperglycemia and lowering of the alkali reserve; phosphates remained normal.

These experiments show that the characteristic feature in the chemistry of parathyroid insufficiency is the drop in blood calcium, which is more marked the more parathyroid tissue is removed. They suggest that the parathyroids control the calcium metabolism and by doing so they influence the function not only of the muscle and nerve tissue, but probably of all organs. When the parathyroids are removed, the threshold for the excretion of calcium in the intestines is lowered. The behavior of the blood calcium indicates that the actual recovery of completely parathyroidectomized dogs in these experiments is not due to compensatory hypertrophy of accessory glands, as the action of these would have been to restore the blood calcium to the normal level; the "adaptation" to a low calcium level, which in the beginning causes tetany, is not explained.

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Experimental diabète gras.

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French authors, especially Lancereaux,[1] have described two types of diabetes mellitus: diabète maigre and diabète gras. Lancereaux believed that the former was due to pancreatic dis-

[1] Lancereaux, quoted by E. L. Opie, Diseases of the Pancreas, 1903, p. 308.