XLII. ON THE ACTION OF PARATHORMONE. II.

BY HECTOR KENNETH GOADBY
AND REGINALD STEPHEN STACEY.

*From the Medical Unit Laboratories, St Thomas's
Hospital, London.*

(Received December 19th, 1935.)

It has been shown by numerous investigators that the administration of parathormone results in an immediate phosphate diuresis followed some hours later by a rise in the serum calcium. In a previous paper Goadby and Stacey [1934] showed that the phosphate diuresis was not accompanied by a rise in plasma inorganic phosphate and could not therefore be considered as the result of a liberation into the blood-stream of phosphorus held elsewhere in the body, and they brought forward evidence which suggested that parathormone produced this effect by direct action on the kidney.

The present work was undertaken to examine this point further, by observing whether or not parathormone produces a phosphate diuresis when the kidneys are severely damaged. Experiments similar in all respects to those previously recorded were carried out on patients in an advanced stage of renal insufficiency due to chronic nephritis.

Methods.

The patient was allowed a normal breakfast at 8 a.m., no lunch and a normal tea at 4 p.m. The experiment was conducted from 6 a.m. to 6 p.m., during which time half a pint of fluid—lemonade or water—was taken every 2 hours to ensure adequate urine excretion. The urine was collected during a preliminary period every 2 hours, *viz.* 6–8 a.m., 8–10 a.m., 10 to midday. At midday blood was taken from the antecubital vein and immediately afterwards 100 units of parathormone (Lilley) were injected intramuscularly. The urine was collected every hour after this up to 6 p.m. Blood was taken again at 2.30 p.m., which corresponded to about the maximum phosphate diuresis previously found in normals; a further sample was taken 24 hours after the injection. The following estimations were performed.

Plasma inorganic phosphate. Blood was drawn into a 10 ml. centrifuge-tube containing 2 drops of 20% potassium oxalate solution and the plasma separated at once. The method of Youngburg and Youngburg [1930] was used for this estimation.

Serum calcium. This was estimated by Clark and Collip's [1925] modification of the Kramer-Tisdall technique.

Urine inorganic phosphate. When albumin was present this was precipitated by the addition of an equal volume of 20% trichloroacetic acid to an aliquot portion of the urine. The estimation was done on the filtrate by the Youngburg technique.

Experiments were done on 3 cases of chronic nephritis with severe nitrogen retention, 1 case of congenital cystic kidneys with nitrogen retention, 1 case of acute nephritis during nitrogen retention and again during convalescence. Experiments were also done on 3 cases of renal disease without gross derangement of renal concentrating power, as shown by normal blood ureas and normal urea concentration tests, *viz.* 1 case of congenital cystic kidneys without

nitrogen retention, 1 case of acute nephritis during convalescence (*vide supra*), and 1 case of nephrosis. In none of the cases was there sufficient circulatory failure to prevent absorption of the parathormone.

DISCUSSION.

The experimental findings are given in the figure and tables and show clearly that when the renal function is grossly impaired parathormone does not produce a phosphate diuresis in any way comparable with that obtained in

Fig. 1.

normal persons. Furthermore if the phosphate diuresis in normals were secondary to a rise in blood phosphate mobilised from the reserve stores, this rise would be very marked in those persons in whom the diuresis did not occur owing to renal damage. No such rise was observed, the small changes seen were insignificant compared with the amount of extra phosphorus excreted by normal persons after parathormone.

Further confirmation of our hypothesis is given by case 5, acute nephritis: during the stage of acute renal failure (blood urea 115 mg./100 ml.) the phosphate diuresis was small: after recovery, when the blood urea was normal, the phosphate diuresis was increased fourfold. (No such increase has been seen in normal persons when given parathormone injections at similar intervals of time.)

It will be seen that there is a rise in the serum calcium 24 hours after parathormone injection both in the normal and in the nephritic series: this suggests

Table I. *Response of normal and nephritic individuals to 100 units of parathormone.*

Case	Plasma phosphate variation in 6 hours + or - mg./100 ml.	Extra phosphate excretion in 6 hours mg.	Serum Ca rise in 24 hours mg./100 ml.
1. Chronic nephritis B.P. 210/130, B.U. 160	+0.4	27.3	1
2. Chronic nephritis B.P. 150/80, B.U. 150, U.C.T. 0.87	+0.4	32.9	2.4
3. Congenital cystic kidneys B.P. 185/105, B.U. 134, U.C.T. 1.2	+0.2	7.7	1.0
4. Arteriosclerotic kidneys B.P. 182/84, B.U. 170	+0.1	6.8	0.7
5. Acute nephritis B.P. 144/106, B.U. 115, U.C.T. 1.35	+0.1	76.0	1.0
5. Acute nephritis, recovered B.P. 116/70, B.U. 31, no albuminuria	-0.56	285.0	4.3
6. Congenital cystic kidneys B.P. 160/95, B.U. 115, no albuminuria	-0.15	166.0	1.2
7. Nephrosis. Plasma cholesterol 640 B.P. 124/72, albuminuria, casts ++	+0.02	325.0	1.8
8. Normal	-0.23	225.8	0.9
9. Normal	-0.59	415.4	2.0
		Extra phosphate excretion in 4 hours mg.	
10. Normal	-0.25	215.0	—
11. Normal	+0.13	138.0	—
12. Normal	+0.08	312.0	—
13. Normal	-0.36	135.6	—
14. Normal	-0.15	138.0	—

B.P. = Blood pressure in mm. Hg. B.U. = Blood urea in mg./100 ml. U.C.T. = Maximum % concentration of urine-urea in urea concentration test.

that the actions of parathormone in raising the blood calcium and in causing increased excretion of phosphorus are independent, for the Ca rises whether there is the initial large phosphate diuresis or not. These findings are in accordance with the observations of Ellsworth and Fitcher [1935], who showed that parathormone produces a rise in the blood calcium of nephrectomised dogs. Collip *et al.* [1934] also demonstrated that in nephrectomised animals the bones were depleted of calcium by injection of parathormone in the same way as in normal animals.

SUMMARY.

1. In persons in whom the excreting power of the kidneys is grossly impaired, parathormone fails to cause the same increased excretion of phosphorus in the urine as occurs in normal persons.

2. This was true in all 5 cases of renal damage, due to various causes, that have been examined.

3. In no case was there a large rise in the plasma inorganic phosphate after parathormone.

4. The hypothesis that parathormone acts directly on the kidneys to produce a phosphate diuresis is thus confirmed.

5. In the same 5 cases, the blood calcium rose in the 24 hours after the injection to the same degree as in normal persons.

6. It is therefore suggested that parathormone has at least two actions: one on the kidney, the other on the calcium stores of the body.

We wish to express our gratitude to the Physicians of St Thomas's Hospital for permission to use their cases.

REFERENCES.

- Clark and Collip (1925). *J. Biol. Chem.* **63**, 461.
Collip, Pugsley, Selye and Thompson (1934). *Brit. J. Exp. Path.* **15**, 335.
Ellsworth and Fitcher (1935). *Bull. Johns Hopkins Hosp.* **57**, 91.
Goadby and Stacey (1934). *Biochem. J.* **28**, 2092.
Youngburg and Youngburg (1930). *J. Lab. Clin. Med.* **16**, 158.