Radioactive Phosphorus (P^{32}) Used to Study Phosphate Exchange between Urine in the Renal Pelvis and Renal Calculi Containing Phosphate[1]

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In 1948, Cristol *et al.* (*2*) reported the surgical removal of a bladder stone from a patient receiving P^{32} therapy for polycythemia vera, and demonstrated radioactivity in the calculus. It occurred to us that P^{32} might be another tool to use in an investigation of the phosphate exchange between urine in the renal pelvis and renal calculi containing phosphate as PO_4. From a review of the literature, it appears that this is the first time that renal calculi containing phosphate and the urine bathing them have been studied for radioactivity after administration of P^{32}.

TABLE 1

QUANTITATIVE CHEMICAL ANALYSIS OF TWO STONES FROM PATIENT C. G.

	%
Calcium oxalate	21.6
Calcium + phosphate (22.7 + 34.6)	67.3
Moisture	6.0
Carbonate	trace

In the present study, the test patient, a female aged 23 years, had unilateral renal calculi containing phosphate as PO_4 (Table 1) in the right renal pelvis (Fig. 1). The control patient, a female 33 years old, gave a negative history for urinary tract calculi. In both patients the levels of nonprotein nitrogen, serum calcium, phosphorus, and vitamin A were normal, as were the urea and phenolsulfonphthalein clearances. Cystoscopy and bilateral ureteral catheterization were carried out under local anesthesia with 1% solution of procaine.

The P^{32} was administered orally as acid sodium phosphate, the test patient receiving an activity of 7,920,000 cpm, and the control an activity of 10,000,000 cpm (70 and 130 μc, respectively). Urine specimens from both patients were then collected directly from the renal pelves at various time intervals over a period of 700 min (Fig. 3a and b).

Twenty-four hours after oral administration of P^{32}, 16 renal calculi weighing a total of 0.850 g were removed surgically. Two of these were analyzed chemically (Table 1) according to the procedures described by Thompson *et al.* (*8*). Five stones were tested for radioactivity by use of a Geiger-Müller counter, and the radioactive measurements are recorded in Table 2. Radioautographs were made by placing five of the stones directly in contact with an occlusal film (Fig. 2). The five stones shown here were not washed in water before the autoradiographs were made.

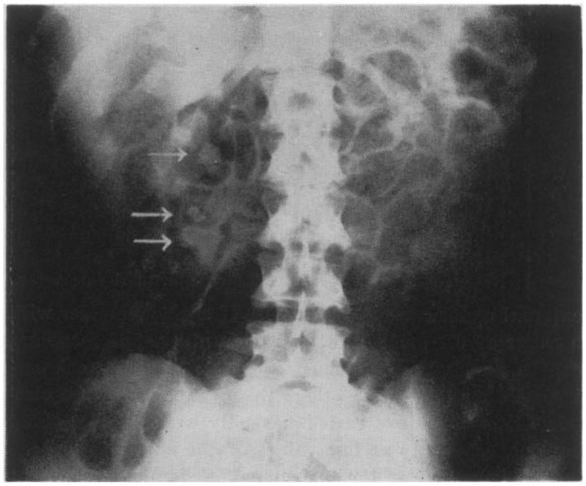

FIG. 1. The arrows on the roentgenogram point to the stones in the right kidney pelvis in the patient C. G., none being present in the left kidney.

The urine was prepared for radioactivity measurements in the following manner. Urine specimens were hydrolyzed in 5*N* H_2SO_4 for 1 hr–2 hr at 90° C prior to analysis by either the Fiske and Subbarow (*4*), or Kuttner and Lichtenstein (*6*) methods. The samples were taken directly or diluted with distilled water and counted with an all-glass dipping Geiger-Müller tube (*1*) supplied with a commercial scaling circuit[4] (scale of 64). Sufficient counts were accumulated to reduce the error of measurement below 5%. Results are expressed in terms of specific activity or cpm/mg of phosphorus. In the two experiments it was not possible to give exactly equal doses.

TABLE 2

WEIGHTS AND RADIOACTIVITY MEASUREMENTS OF FIVE KIDNEY STONES

Stone	Weight in mg	Cpm/mg	Total cpm (corrected)
1	84.7	0.542	45.9
2	90.0	0.713	64.1
3	48.6	1.56	75.8
4	66.9	0.885	59.0
5	79.7	1.13	90.3

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[4] Obtained from Radiation Counter Laboratories, Inc., Chicago, Illinois.

The data have been corrected, therefore, so that they correspond to the administration of a total dose of exactly 10^7 cpm.

The results obtained from the study of the two patients receiving P^{32} are presented in Fig. 3a and b. The effect of the kidney stones in patient C.G. on the radio-

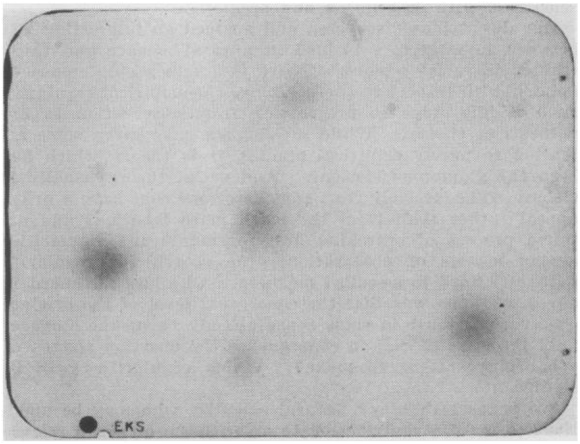

FIG. 2. Radioautograph of five renal calculi, obtained by placing the stones directly on an occlusal film, which is exposed for 15 days and then developed for 8 min.

activity was quite striking. Shortly after administration of P^{32}, the specific activities of urine specimens from the kidney containing the stones rose more slowly than did those of the control kidney, and remained elevated at later time intervals (Fig. 3a). It is clear that both kidneys of the control patient E.M. excreted phosphate of the same specific activity. There were no consistent differences in the activity of the phosphate obtained from either the right or the left kidney at a given time interval and the slight variations that were observed were within permissible experimental error (Fig. 3b). These are the expected results, consistent with the accepted view that living cells cannot differentiate between isotopes of the same element.

The most rational explanation of the radioactivity in the renal calculi is as follows: A highly radioactive phosphate passes by the nonradioactive stones, an ionic exchange takes place, radioactive phosphate from the urine replacing nonactive phosphate in the surfaces of the stones. This lowers the specific activity of the urine reaching the renal pelvis and imparts radioactivity to the stones. Later, as the specific activity of the newly formed urine falls below the activity of the stones, the reverse process takes place, the stones contributing radioactive phosphate for nonisotopic phosphate and thus producing an elevated activity of the urine obtained 10 hr

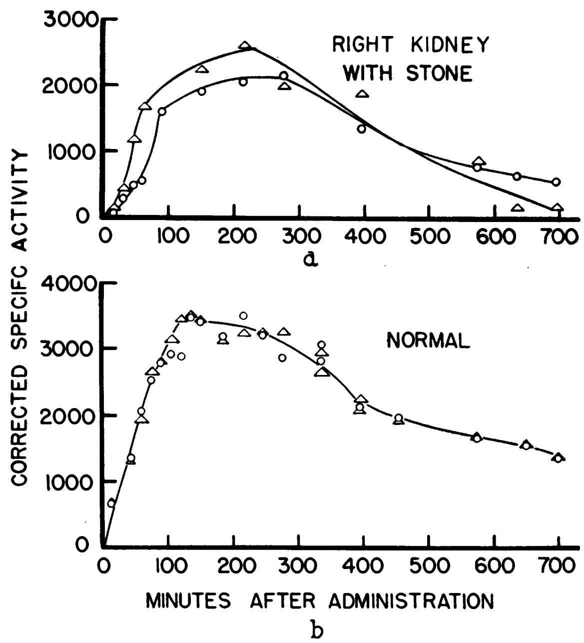

FIG. 3a and b. Radioactivity results from the two patients. In both cases circles represent the data obtained from study of the right kidney, triangles from the left. The curves in Fig. 3a show the results from the study of the urines from either renal pelvis in patient C. G., who had stones in the right kidney. The lower curve shows results of the same type of study on patient E. M., who had normal kidneys.

or more after administration. The proposed ionic exchange mechanism is not a new concept. The exchange of radiophosphate of solution for nonisotopic phosphate of a solid has been well studied in the case of bone (*3*, *5*, *7*).

This is a preliminary report and further studies are planned with respect to glomerular filtration rates and to phosphorus excretion.

References

1. BALE, W. F., HAVEN, F., and LEFEVRE, M. L. *Rev. sci. Instr.*, 1939, **10**, 193.
2. CRISTOL, DAVID S., BOTHE, ALBERT E., and GROTZINGER, PAUL W. *New Eng. J. Med.*, 1948, **239**, 427.
3. FALKENHEIM, M., NEUMAN, W. F., and HODGE, H. C. *J. biol. Chem.*, 1947, **169**, 713.
4. FISKE, C. H. and SUBBAROW, Y. *J. biol. Chem.*, 1925, **66**. 375.
5. HODGE, H. C. and FALKENHEIM, M. *J. biol. Chem.*, 1945, **160**, 637.
6. KUTTNER, THEODORE and LICHTENSTEIN, LOUIS. *J. biol. Chem.*, 1930, **86**, 671.
7. NEUMAN, W. F. and RILEY, R. F. *J. biol. Chem.*, 1947, **168**, 545.
8. THOMPSON, H. E. *et al.* *J. Urol.*, 1944, **51**, 259.