# CHEMICAL, CLINICAL, AND IMMUNOLOGICAL STUDIES ON THE PRODUCTS OF HUMAN PLASMA FRACTIONATION.

## XVIII. FIBRINOGEN COAGULUM AS AN AID IN THE OPERATIVE REMOVAL OF RENAL CALCULI [1]

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In spite of the fact that the surgeon operating to remove stones from the kidney has at his command the invaluable aid of either the fluoroscope or the x-ray film used at the operating table as a means of determining the number of stones present and their location in the ramifications of the renal pelvis, he still may find their extraction difficult and accompanied by an undesirable degree of injury to the renal parenchyma. The use of grasping forceps is difficult at times or even dangerous because of the chance of crushing the stone and leaving unsuspected minute fragments to serve as nuclei for further growth. Irrigation of the pelvis with sterile saline solution followed by negative pressure suction through a tube inserted into the various compartments may also fail to remove all concretions.

Still another aid in the removal of fugitive or inaccessible calculi has been devised by means of a coagulum of fibrinogen, caused to form in the pelvis, which on removal will bring away the calculus incorporated within itself (Figure 1).

The preparation and properties of the coagulum, as well as the first five clinical cases, have been described elsewhere (1 to 3). Subsequently, fibrinogen separated in Fraction I in course of large scale plasma fractionation (4, 5) has been employed to prepare coagula with mechanical properties (6) adapted to the procedure. Fibrinogen dissolved in a buffer solution is injected into the renal pelvis in an amount sufficient to fill it fully while at the same time a small amount of thrombin ("clotting globulin") is simultaneously injected. The resultant clot is complete after the expiration of 4 to 5 minutes and is then withdrawn. The coagulum has a tensile strength from 10 to 20 times greater than that of a blood clot, and is unaffected by the presence of small amounts of urine or of blood. After from 6 to 24 hours, however, at body temperature, the clot becomes disintegrated by the action of urine. Postoperative observation of patients, as well as that of the experimental animal, shows that the coagulum has no irritative effect whatever on the pelvic epithelium.

The use of such a coagulum has the following advantages: (*1*) All free stones, regardless of size, number, or position within the renal pelvis, should be removed. (*2*) Fragmentation of calculi during removal is avoided. (*3*) Trauma to the kidney is reduced to a minimum. (*4*) Complete surgical mobilization of the kidney may be unnecessary, as exposure of the renal pelvis alone provides adequate exposure for the procedure. The coagulum cannot be expected to remove a calyceal calculus of larger diameter than that of the infundibulum through which it must pass, nor a calculus imbedded in or adherent to the wall of the pelvis.

In clinical cases where infection was absent, or only moderate, the coagulum has been almost uniformly successful in incorporating all free stones. In instances where severe infection was present and the urine had become mucoid, slimy, and thick, the clot has failed to incorporate a certain number of free stones. We have felt that these failures were due to a difference in surface tension of fibrinogen solution and mucoid urine which prevented complete dissemination of the injected fluid throughout the pelvis and around

[1] Certain of the products of plasma fractionation employed in this work were developed from blood, collected by the American Red Cross, by the Department of Physical Chemistry, Harvard Medical School, Boston, Massachusetts, under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

CALCULI REMOVED WITH COAGULUM

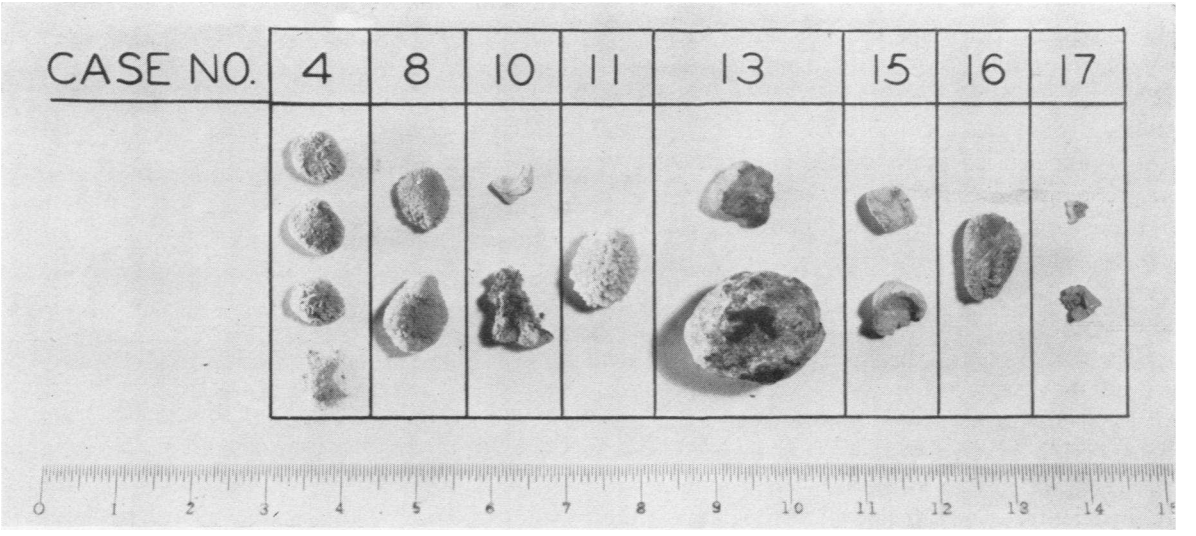


FIG. 1. PHOTOGRAPH OF RENAL STONES REMOVED BY MEANS OF COAGULUM

each calculus. To overcome this difficulty, a number of wetting agents and detergents have been investigated, the most satisfactory so far examined being Aerosol O.T.[2] Toxicity experiments, to be reported elsewhere, indicate that the use of this substance in the kidney pelvis, as herein described, is without ill effect. *In vitro* experiments and its use in 5 clinical cases strongly suggest that preliminary irrigation of the kidney pelvis with 0.1 per cent Aerosol solution greatly improves the distribution of fibrinogen solution throughout the pelvis.

The steps in the operative procedure in use at the present time are as follows: (*1*) After surgical exposure of the kidney pelvis and upper ureter, the lumen of the ureteropelvic junction is gently occluded with a suitable instrument or tape to prevent escape of the coagulable material down the ureter. (*2*) A small incision, 4 mm. in length, is made in the renal pelvis. (*3*) A No. 12 French rubber urethral catheter with two eyes is introduced through the small incision until the second eye lies just within the renal pelvis. If it does not fit the opening snugly, it may be made to do so by grasping one end of the incision with a mucosa clamp. Urine is then aspirated from the pelvis. (*4*) The kidney pelvis is next filled with normal saline solution and completely aspirated by means of a graduated syringe. The amount of normal saline necessary to distend the pelvis fully may be taken as the pelvic capacity. The catheter should be so adjusted that it irrigates perfectly. (*5*) The pelvis is next lavaged with a solution of 0.1 per cent Aerosol, in an amount not exceeding two-thirds of its predetermined capacity. (*6*) Lavage is next carried out with a solution of fibrinogen to insure complete distribution of this material throughout the pelvis and around the calculi. It is then withdrawn by aspiration. (*7*) Fibrinogen solution in an amount equal to approximately 90 per cent of the predetermined capacity of the renal pelvis is next injected through the urethral catheter into the pelvis. Simultaneously, by means of a 2 cc. syringe and needle, an assistant injects one-tenth that amount of 2 per cent clotting globulin[3] through the wall of the urethral catheter into its lumen, so that the two materials are intimately mixed as they enter the renal pelvis. The fibrinogen solution should be approximately 37° C. at the time of injection. (*8*) Four minutes are allowed to elapse. (*9*) After removing the urethral catheter, the usual pyelotomy incision is made by

[2] The di-octyl ester of sodium sulfasuccinic acid, a product of the American Cyanide and Chemical Corporation, New York City.

[3] I am indebted to Lederle Laboratories, Inc., for generous quantities of clotting globulin.

extending the initial small incision as desired. (*10*) The coagulum partially extrudes through the pyelotomy opening, and may be grasped with ring forceps and slowly but firmly withdrawn. It should remove, enmeshed within itself, all free stones from the renal pelvis. (*11*) The pyelotomy incison is usually closed only partially to insure against ureteral obstruction during the first postoperative day by any portion of the clot which might remain in the pelvis. Several cases have been closed completely, however, without ill effect.

The clinical results in 21 patients for whom the coagulum was used are as follows: In 13 patients, all stones were removed; and in 3 of these patients, additional tiny stones, not demonstrated in the pre-operative x-ray film, also came away. In 6 patients, some but not all of the stones were removed. In 2 instances, the coagulum failed to remove free stones.

An illustrative case history is that of a 27-year-old man who had an irregular calculus, measuring 12 × 9 × 6 mm., partially obstructing the right lumbar ureter which had been producing intermittent symptoms for 8 months. In addition, a very faint opacity suggestive of calculus was visible by x-ray in the region of the lower calyx of the kidney above (Figure 2A). The renal pelvis was moderately hydronephrotic. At operation, the ureteral calculus was removed through a ureterotomy incision made directly over the stone. Then, by exposing the extrarenal portion of the pelvis, coagulum pyelolithotomy was carried out, the capacity of the pelvis being 25 cc. On removing the coagulum, 2 irregular small calculi were found imbedded within it (Figure 2B). One calculus measured 4 × 4 × 2 mm.; the second stone measured 3 × 2 × 1 mm.

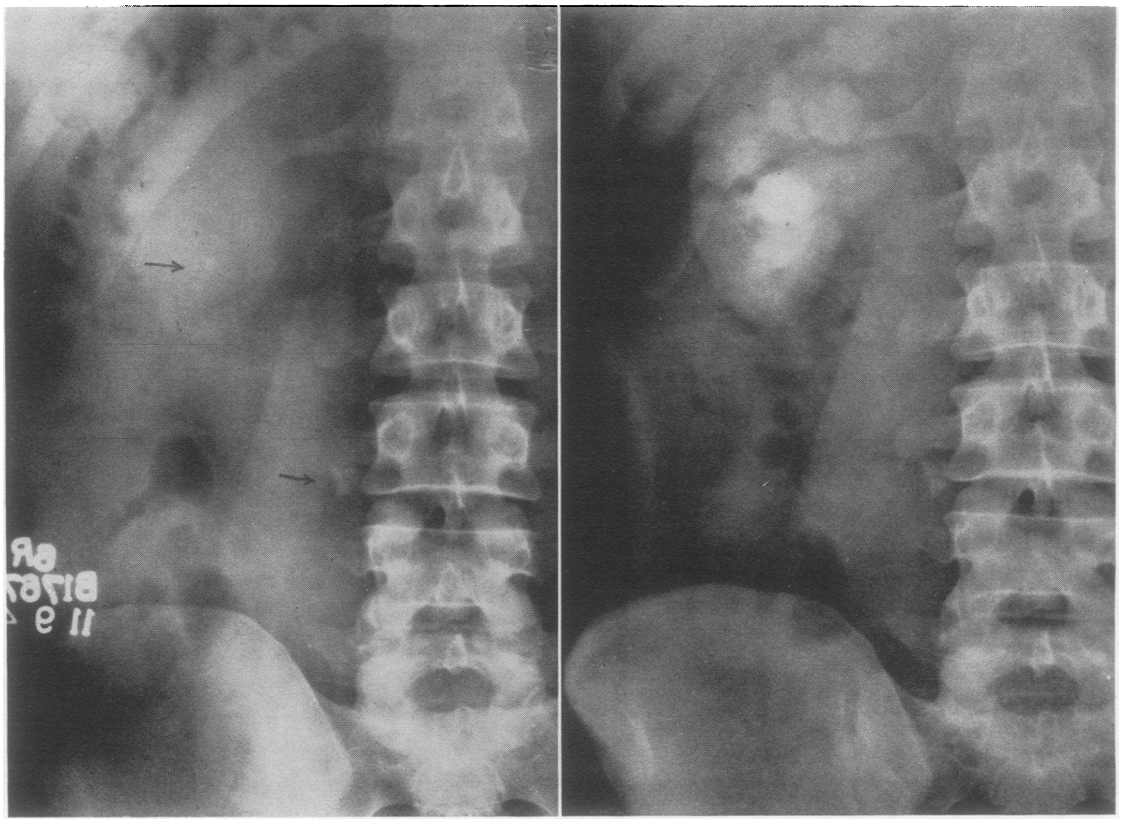

FIG. 2A. PLAIN X-RAY AND INTRAVENOUS UROGRAM SHOWING LUMBAR URETERAL CALCULUS, HYDRONEPHROSIS, AND FAINT OPACITY, SUGGESTIVE OF CALCULUS IN REGION OF LOWER RENAL CALYX

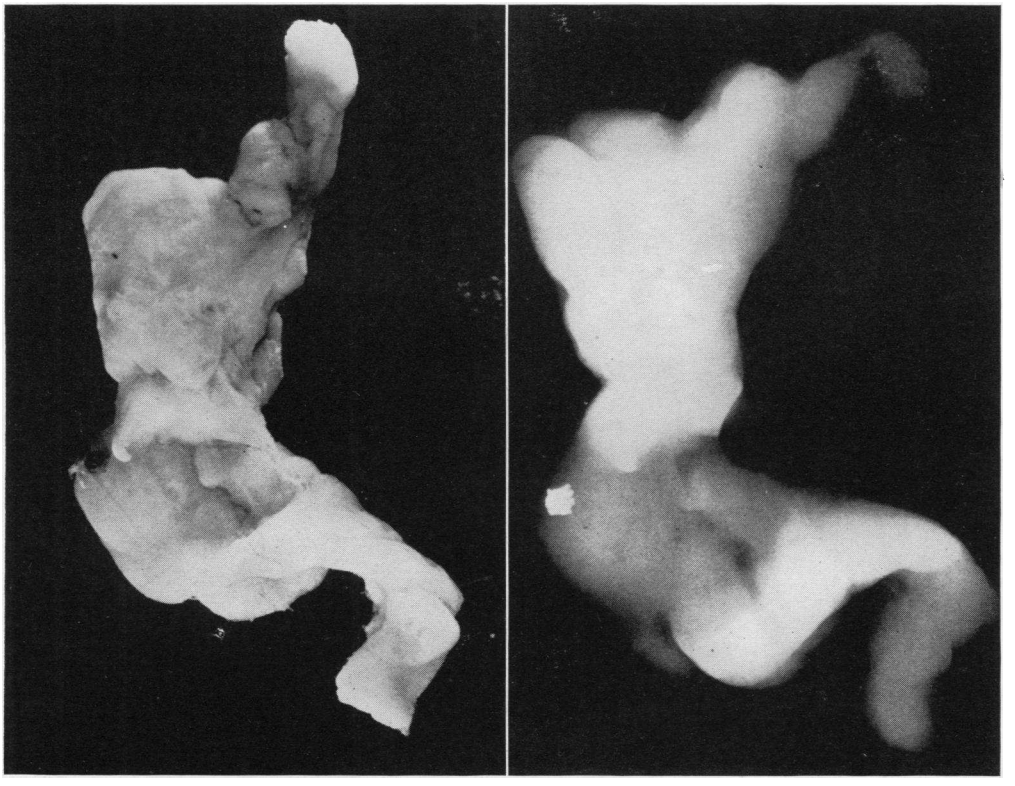

FIG. 2B. PHOTOGRAPH AND X-RAY OF COAGULUM SHOWING REMOVAL OF 2 TINY STONES FROM RIGHT KIDNEY PELVIS (URETERAL CALCULUS REMOVED SEPARATELY)


## SUMMARY

A new aid in the removal of small free stones from the renal pelvis at open operation is described. By the simultaneous injection of solutions of fibrinogen and thrombin, a strong coagulum which completely fills the pelvis and enmeshes all free stones is produced. On withdrawing this coagulum through the usual pyelotomy incision, all free stones should be removed. Fragmentation of calculi and trauma to the kidney are thus avoided. This operative procedure has been carried out in 21 patients without demonstrable ill effect. The operative results herein reported, although still imperfect, are improving as additional experience with the method is acquired. It is hoped that this procedure will be of distinct aid in the problem of the surgical removal of renal calculi.


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