USE OF CRYOPRECIPITATE COAGULUM IN EXTRACTING RENAL CALCULI

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ABSTRACT — Human cryoprecipitated plasma can form an extractable coagulum which will effectively remove renal calculi in selected cases. We successfully used this blood product and a simplified injection technique in 30 patients undergoing surgery for upper tract calculi. Coagulum pyelolithotomy was performed in 24 cases with removal of all stones in 23 (96 per cent). In 6 patients incomplete stone removal by conventional operative methods was successfully completed by using the coagulum as an adjunctive procedure. In 10 of the 30 cases (33 per cent) radiographically "silent" calculi were recovered within the cryoprecipitate clot. The advantages of cryoprecipitate over previously reported blood products, certain technical simplifications, and the appropriate clinical indications for the coagulum procedure are discussed.

The removal of renal calculi by an extractable cast of the collecting system was first described in 1943 using pooled human fibrinogen and clotting globulin.[1] The technique was not widely used because of technical complexity, limited availability of the fibrinogen product, and a significant risk of hepatitis transmission. Several different blood products, formulations, and technical modifications have since been proposed.[2-4]

We recently investigated human plasma and cryoprecipitated plasma for potential use in coagulum formation.[5] Plasma alone did not form a coagulum of consistent or adequate strength to attempt calculi removal. However, cryoprecipitate when mixed with bovine thrombin and calcium chloride in a 1:2:1 ratio at body temperature formed a consistent coagulum of reproducible strength. Furthermore, it compared favorably to the strength of coagula formed with previously reported blood products and formulas. We also found the cryoprecipitate clot dissolved within twenty-four hours when submerged in sterile or infected urine. Similarly, instillation and removal of the cryoprecipitate coagulum in canine kidneys resulted in no untoward anatomic or physiologic changes in function.

Encouraged by our findings of safety, limited risk of hepatitis transmission in a readily available blood product, and a simplified operative method which evolved during our studies on dogs, we applied the cryoprecipitate coagulum to selected clinical cases, the results of which are herein reported.

Material and Methods

Thirty patients ranging in age from twenty-eight to seventy-six years, 12 females and 18 males, underwent surgery for upper tract calculi indicated for obstruction, persistent pain, or infection. In 24 patients the coagulum technique alone was used to extract the calculi. In 2 of the 24 patients an ipsilateral upper-third ureterolithotomy was performed prior to

coagulum pyelolithotomy. In the remaining 6 patients the cryoprecipitate clot was used as an adjunct to more conventional renal calculus operative procedures: anatrophic nephrolithotomy (5 patients), Gil-Vernet extended pyelolithotomy with heminephrectomy (1 patient).

The cases of primary coagulum pyelolithotomy were performed using the simplified injection technique and cryoprecipitate formula which we have reported previously[5] (Fig. 1). After appropriate dilutions as summarized in Table I, cryoprecipitate, bovine thrombin, and calcium chloride are placed into separate sterile syringes and placed in an intraoperative waterbath at 37° C.

While the constituent solutions are warming in the waterbath, appropriate exposure of the renal pelvis is secured, and a single 16-gauge angiocatheter is inserted proximal to the ureteropelvic junction. When a proximal ureterolithotomy is necessary prior to the pyelonephrolithotomy, a 14 F red Robinson catheter can be used. It is inserted through the ureterotomy and directed proximally into the renal pelvis. With either method, the ureter is occluded with polyethylene tubing. The pyelocalyceal system is then filled by injecting saline through the angiocatheter or the Robinson catheter. When the pelvis is distended and tense, the volume is recorded and the saline is aspirated. The volume of cryoprecipitate and corresponding concentrations of bovine thrombin and calcium chloride necessary for proper coagulum formation thus can be calculated. This formulation is based on the measured pyelocalyceal volume and the ratio of 1 cc. cryoprecipitate to 2 units thrombin to 1 mg. calcium chloride (Table II).

As outlined in Table I, the waterbath solutions are then transferred to sterile beakers on the operative field. The calculated volume of cryoprecipitate is aspirated into a sterile syringe. The corresponding thrombin and calcium chloride concentrations are drawn up and combined in a second syringe. This thrombin-calcium chloride solution is injected into the syringe containing the cryoprecipitate (Fig. 1B). This syringe is inverted a couple of times to ensure mixture, and the contents are injected via the angiocatheter within thirty seconds. After three minutes a pyelotomy is made and the coagulum withdrawn. An intraoperative radiograph of the clot is obtained in each case to confirm entrapment and removal of all calculi.

The patients undergoing anatrophic nephrolithotomy and extended pyelolithotomy also had the cryoprecipitate solution injected via an angiocatheter placed in the renal pelvis. The clot was extracted through nephrotomy in 1 patient and pyelotomy in the other 5 cases.

Results

No serious postoperative complications were encountered, and drains were removed by the tenth postoperative day. Disruption of the coagulum during extraction with retention of a clot fragment was not encountered. Failure of coagulum formation did not occur.

Twenty-three of 24 patients undergoing primary coagulum pyelolithotomy had complete entrapment of all calculi within the clot that was removed (96 per cent). The failure occurred in 1 patient when the coagulum removed only two out of three calculi. The retained calculus was trapped in a calyx with a stenotic infundibulum. Retrospectively, this represented an anatomic limitation of the coagulum when used as the only surgical technique, namely, a calyceal calculus larger than the infundibulum draining it.

In 6 of these 24 cases radiographically "silent" calculi (stones not seen on preoperative films) were found within the coagulum (25 per cent). An example of primary coagulum pyelolithotomy and extraction of unexpected calculi is shown in Figure 2. Three of the 5 patients undergoing anatrophic nephrolithotomy and adjunctive coagulum extraction had "silent" calculi, fragments, or debris entrapped in the clot (Fig. 3). Similarly, the patient who underwent extended pyelolithotomy with coagulum also demonstrated several unexpected calculi (Fig. 4). The heminephrectomy was performed because of segmental lower pole parenchymal atrophy and punctate calcifications within the papilla which were confirmed microscopically in the operative specimen.

The over-all incidence of "silent" stone retrieval directly attributable to the use of the coagulum technique, was 10 out of 30 (33 per cent). Each patient had postoperative plain films of the abdomen showing no residual calculi except for the patient in whom the procedure failed because of an anatomic limitation. Postoperative serum creatinine in each patient remained unchanged from preoperative values. Excretory urograms were obtained in 21 of the 30 patients, and each demonstrated prompt function and no structural aberrations attributable to the coagulum procedure.

TABLE I. *Preparation of coagulum constituents*

1. **$CaCl_2$: 1 gram per 10 ml (Upjohn ampoule) = 100 mg/cc.**
   a) aspirate contents into a sterile 10 cc. syringe and drop into waterbath
   b) warm at 37 ° C for 10 minutes
   c) transfer contents into sterile beaker on operative field
   d) draw required volume directly with a sterile tuberculin syringe — .25 cc. = 25 mg $CaCl_2$

2. **Topical Bovine Thrombin: 5000 units/vial (Parke-Davis) + 5 cc. of standard diluent = 1000 units/cc.**
   a) draw up 1 cc. and add 9 cc. saline (in a sterile 10 cc. syringe) = (100 units/cc.)
   b) put this syringe into waterbath
   c) warm at 37° C for 10 minutes
   d) transfer contents into sterile beaker on operative field
   e) draw required volume with a sterile tuberculin syringe .5 cc. = 50 units thrombin

3. **Cryoprecipitate - arrives from the blood bank thawed to room temperature**
   a) aspirate contents of enough packets to fill one sterile 50 cc. syringe and drop into waterbath
   b) warm at 37° C for 10 minutes
   c) transfer contents into sterile beaker on operative field
   d) draw required volume into a sterile syringe*

4. **The contents of the tuberculin syringes (thrombin - $CaCl_2$) are combined in a sterile 3 cc. syringe****

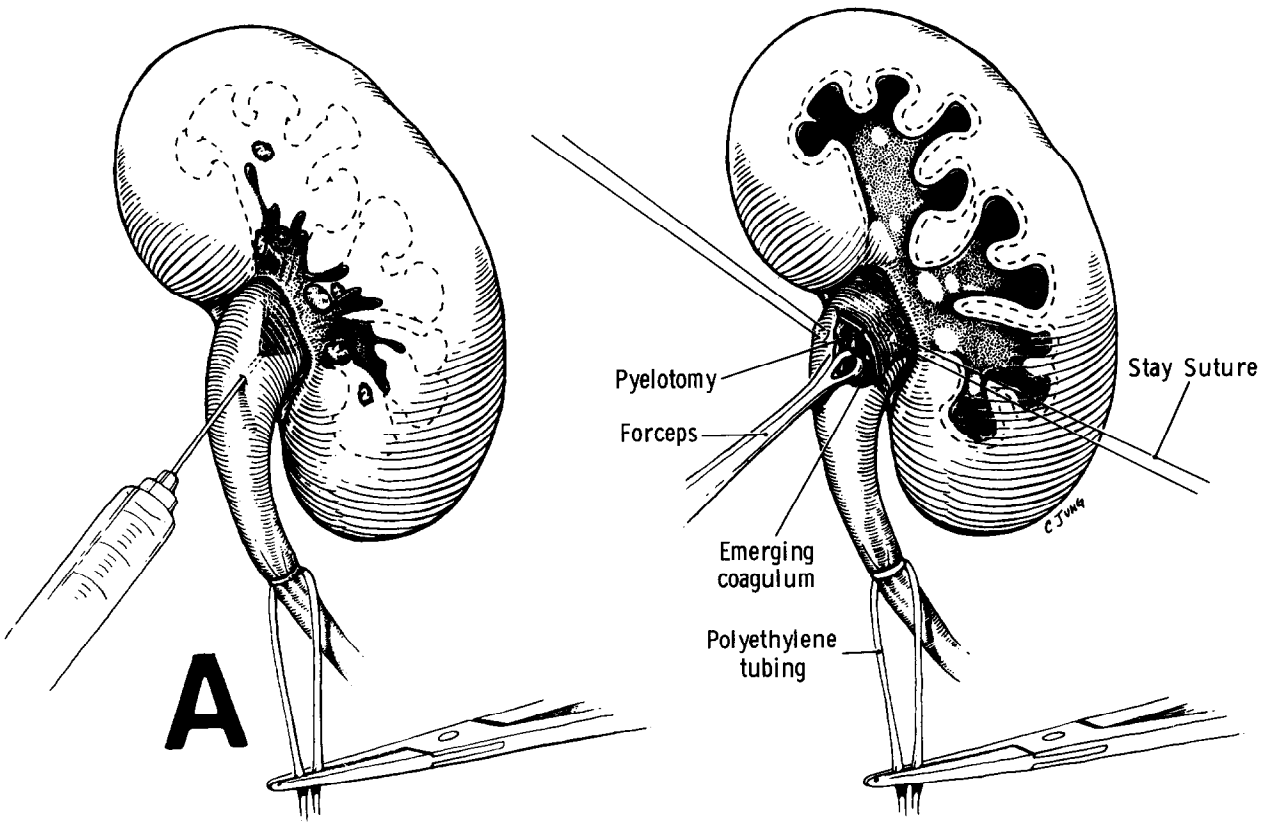

FIGURE 1. *(A) and (B) Sequence of cryoprecipitate coagulum technique.*

TABLE II. *Cryoprecipitate coagulum formulation*

Ratio of 1 ml Cryoprecipitate to 2 units Thrombin to 1 mg Calcium Chloride is maintained regardless of how large or small the pyelocalyceal capacity.

Measured Pyelocalyceal Capacity (ml)	Requires Cryoprecipitate (ml)	Requires mg $CaCl_2$ (100 mg/cc.)	Requires Units Thrombin (100 u/cc.)
10	9	9 (.10cc.)	18 (.20cc.)
15	14	14 (.15)	28 (.30)
20	19	19 (.20)	38 (.40)
25	24	24 (.25)	48 (.50)
30	28	28 (.30)	56 (.55)
35	33	33 (.35)	66 (.65)
40	38	38 (.40)	76 (.75)
45	43	43 (.45)	86 (.85)
50	48	48 (.50)	96 (1)
55	53	53 (.55)	106 (1.05)
60	58	58 (.60)	116 (1.15)
65	63	63 (.65)	126 (1.25)
70	68	68 (.70)	136 (1.35)
75	72	72 (.75)	146 (1.45)
80	77	77 (.80)	154 (1.55)
85	82	82 (.85)	184 (1.85)

[Q.S. with normal saline to make 1,2 or 3ml]

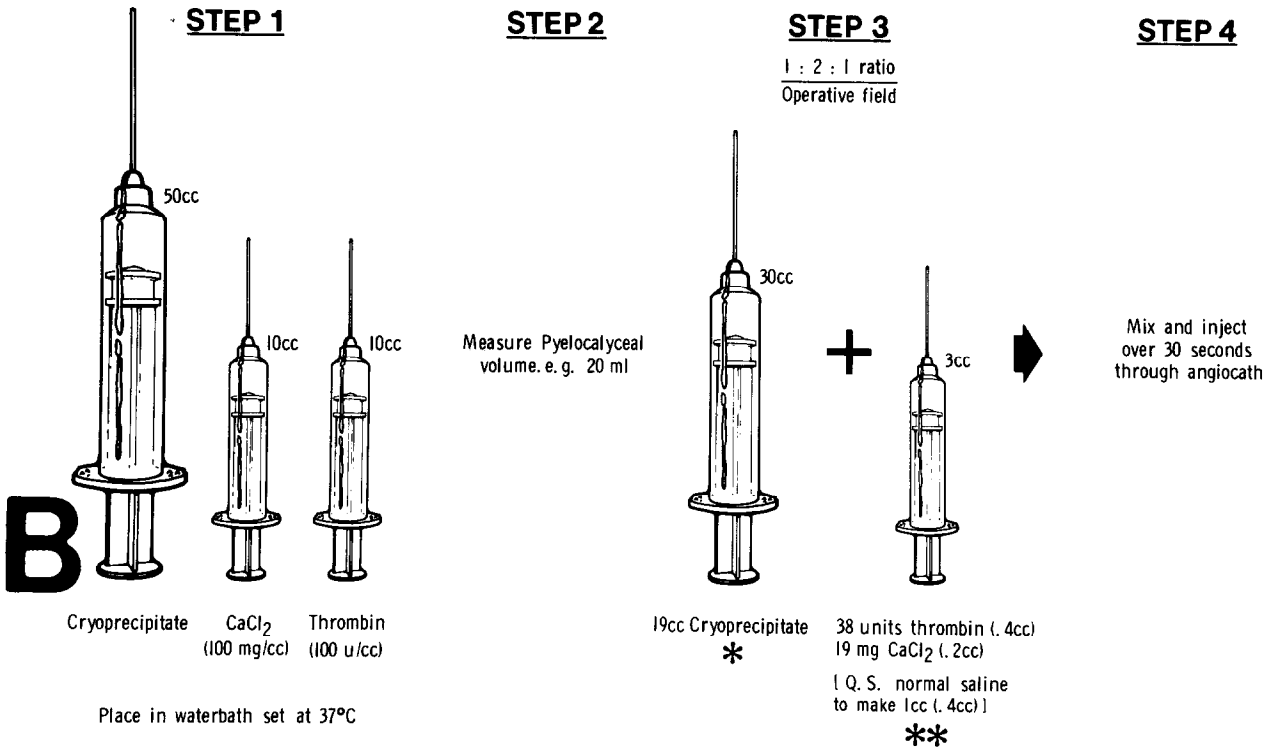

FIGURE 1. *Continued.*

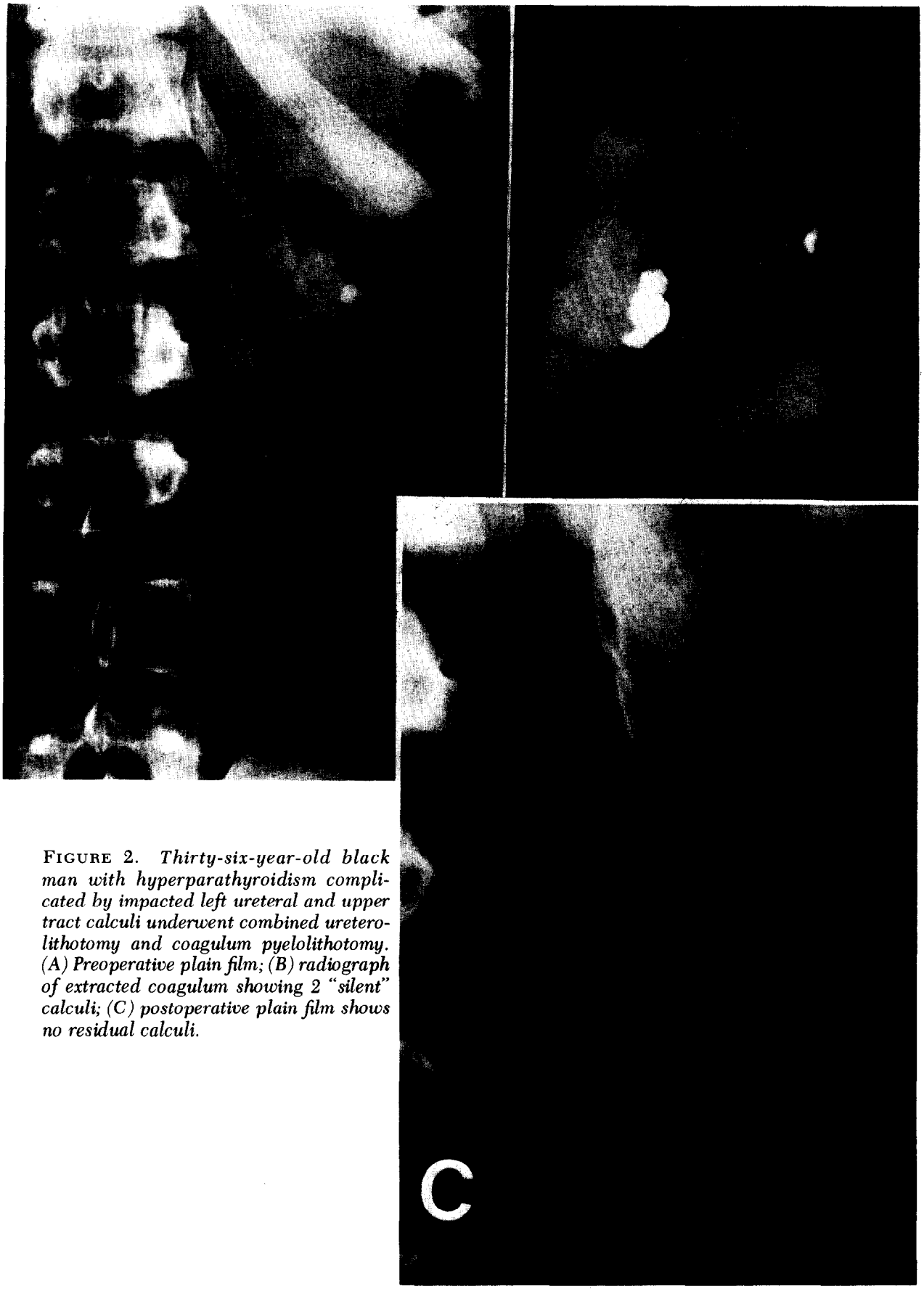

FIGURE 2. *Thirty-six-year-old black man with hyperparathyroidism complicated by impacted left ureteral and upper tract calculi underwent combined ureterolithotomy and coagulum pyelolithotomy. (A) Preoperative plain film; (B) radiograph of extracted coagulum showing 2 "silent" calculi; (C) postoperative plain film shows no residual calculi.*

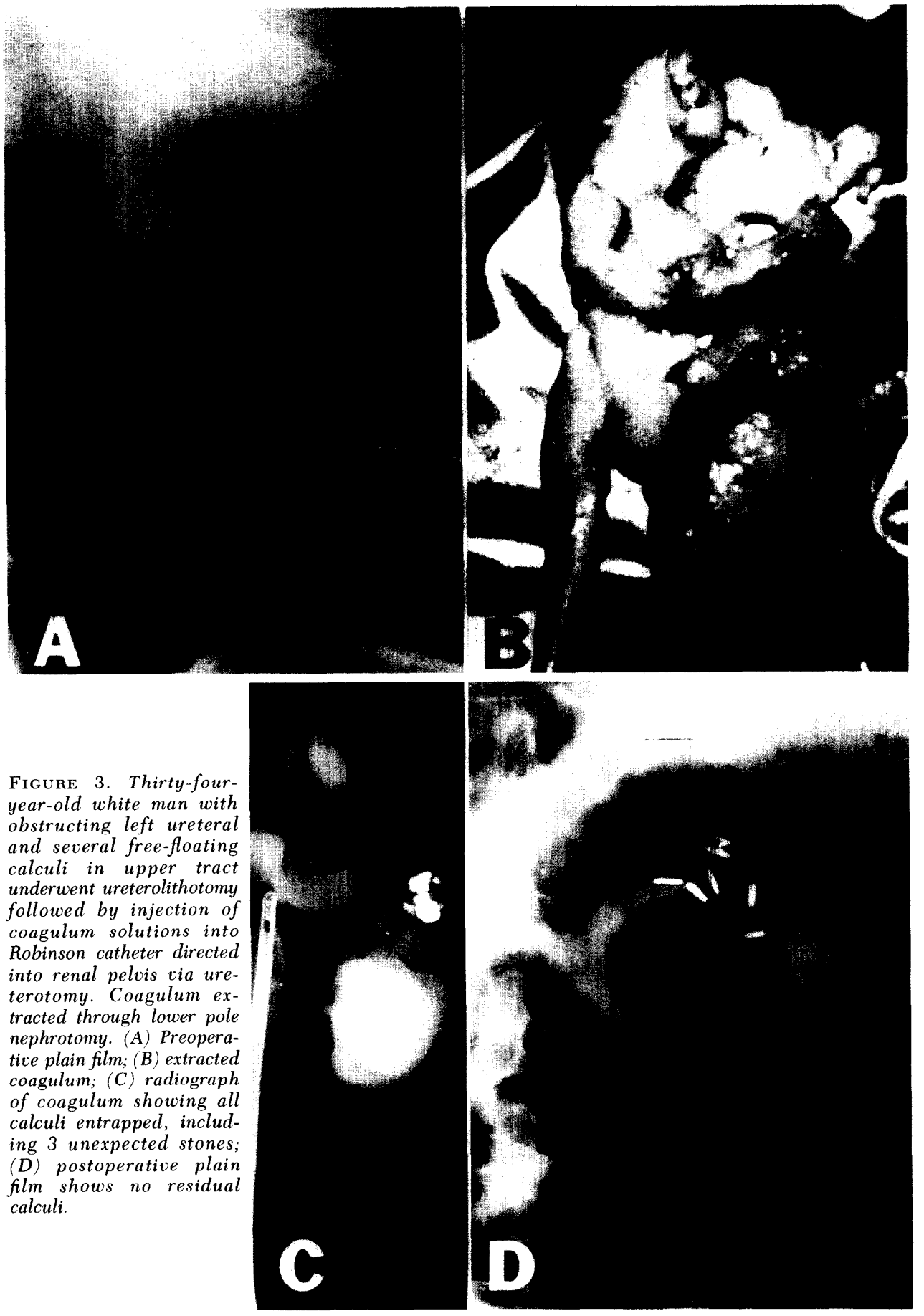

FIGURE 3. *Thirty-four-year-old white man with obstructing left ureteral and several free-floating calculi in upper tract underwent ureterolithotomy followed by injection of coagulum solutions into Robinson catheter directed into renal pelvis via ureterotomy. Coagulum extracted through lower pole nephrotomy. (A) Preoperative plain film; (B) extracted coagulum; (C) radiograph of coagulum showing all calculi entrapped, including 3 unexpected stones; (D) postoperative plain film shows no residual calculi.*

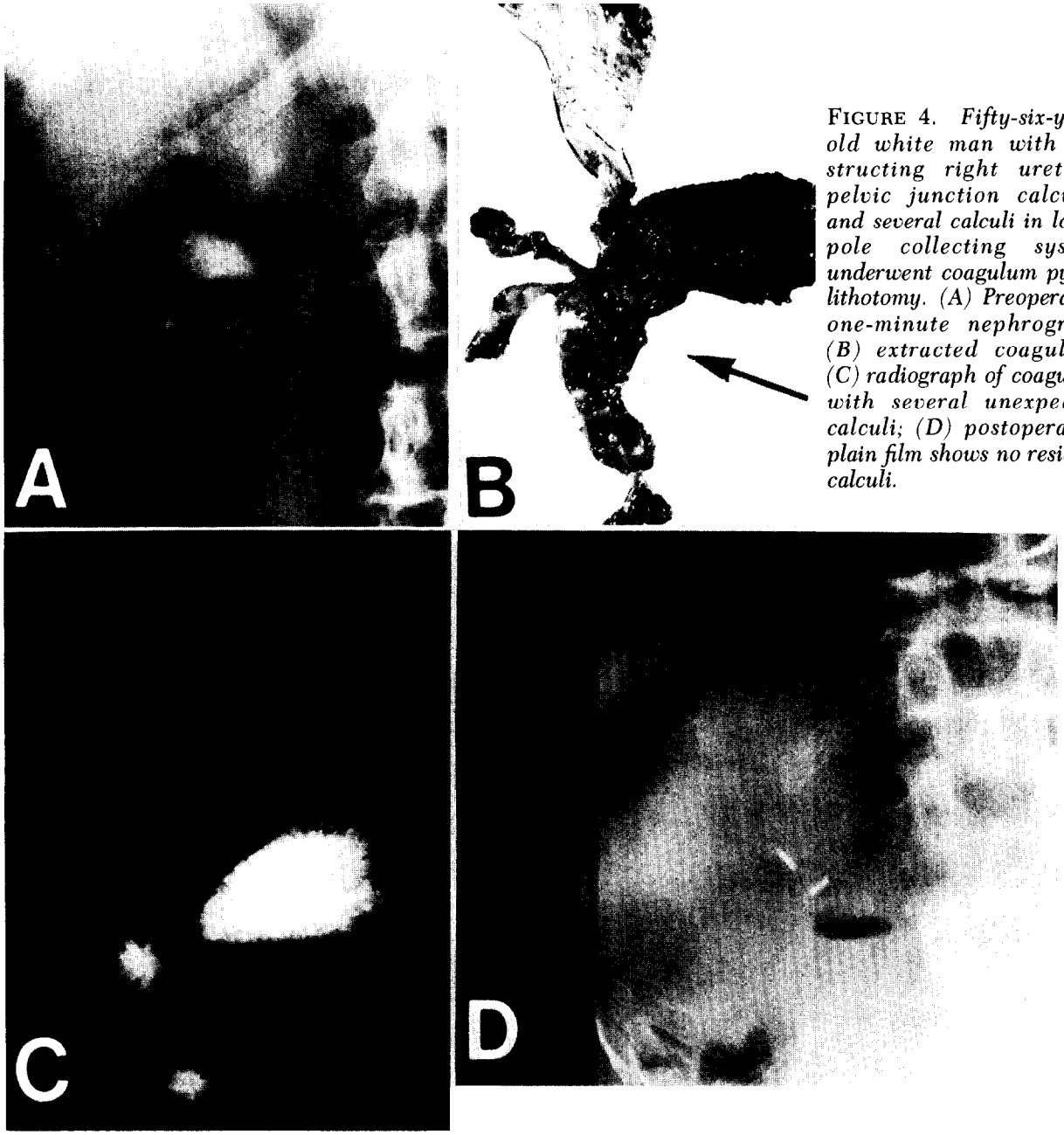

FIGURE 4. *Fifty-six-year-old white man with obstructing right ureteropelvic junction calculus and several calculi in lower pole collecting system underwent coagulum pyelolithotomy. (A) Preoperative one-minute nephrogram; (B) extracted coagulum; (C) radiograph of coagulum with several unexpected calculi; (D) postoperative plain film shows no residual calculi.*

Comment

A successful extraction rate of 96 per cent when using the coagulum for pyelolithotomy is gratifying and reflects proper selection of cases wherein favorable anatomic conditions exist, such as pyelocalyceal dilatation. This is best exemplified by our failure where a narrowed infundibulum did not allow extraction of a larger calyceal calculus.

Our 6 additional cases prove that the coagulum method can be a very useful adjunct to other renal stone procedures by allowing more complete evacuation of calculi. This is particularly true for small, free-floating stones, fragments, or poorly matured amorphous debris which otherwise would be difficult or impossible to localize accurately or remove. Occasionally an obstructing proximal ureteral calculus will be associated with additional upper tract calculi. If these stones are small or difficult to reach, only a ureterolithotomy normally would be performed. However, with the coagulum, these stones can be removed by combining a coagulum pyelolithotomy with the ureterolithotomy (Figs. 2 and 3).

The 33 per cent incidence of "silent" calculi within coagula is perhaps surprising but punctuates the potential frequency with which unsuspected calculi can occur. Virtually all of these additional stones were small (3 to 5 mm.) and, if left behind, could represent the nidus for persistent, recurrent, or progressive calculus formation. Thus, the cryoprecipitate technique

offers a new dimension to all forms of renal calculus surgery where the hallmark remains the removal of all stones and debris.

As described in our earlier study,[5] cryoprecipitate offers several advantages over previously reported blood products. It is available in virtually all blood banks and can be thawed in fifteen minutes, ready for use. All packets are screened for hepatitis B antigen by radioimmunoassay, and in many centers controlled donors who are known to be hepatitis-free provide the source for cryoprecipitate. Certainly the risk of hepatitis transmission is no greater than in a standard blood transfusion.

Autogenous cryoprecipitate can be prepared in elective cases. Two units of whole blood undergo plasmapheresis, yield 25 to 40 ml. of the concentrate, and the red blood cells can be reinfused during surgery. The process requires ten days' lead time but totally eliminates the risk of hepatitis. However, 40 ml. may not be sufficient for cases involving a large renal pelvis. Cryoprecipitate, commercial bovine thrombin, and calcium chloride are sterile products. The risk of introducing infection is low since sterility can be maintained by a series of sterile syringe exchanges from product container to waterbath to operative field. The cost of cryoprecipitate is not prohibitive, about $11 per packet which contains 15 to 20 ml. The number of packets needed will depend on the measured collecting system volume, but a minimum of four on hand is advised.

Our operative technique employs a single angiocatheter in the renal pelvis, premixing of the constituent solutions, and represents a simplification of previously described operative methods where one or two larger catheters are sutured into separate pyelotomies. With our modifications there is less renal dissection, the operative time is not prolonged, and premixing ensures more complete admixture with greater likelihood of calculi entrapment. Should the coagulum fail to remove the stones, other procedures still can be employed with no significant increase in difficulty or time lost.

Several points regarding the formulation and surgical technique require emphasis. The cryoprecipitate must be warmed to body temperature in an intraoperative waterbath to assure adequate tensile strength. Once the thrombin-calcium chloride solution is added to the cryoprecipitate, coagulation begins within fifteen to thirty seconds so injection via the angiocatheter must be immediate. The solution should be injected into a closed system. This requirement is not absolute. However, if a prior pyelotomy or nephrotomy has been made, it should be closed in a watertight manner before injecting the solution.

The cryoprecipitate can be colored to promote delineation of the coagulum from the collecting system. We did this by adding 0.5 cc. of methylene blue to the syringe containing the cryoprecipitate in 16 of our cases and found it to be helpful. When firm, the coagulum is opalescent, and an intraoperative radiograph should always be obtained to verify extraction of all calculi.

Certainly the key to successful use of the coagulum as a primary procedure is careful case selection with emphasis on calyceal structure. Limitations of the coagulum are entirely anatomic. It may not work as the sole maneuver for stone removal if there is an intrarenal pelvis with limited or no pyelocalyceal dilatation, or if stenotic infundibula drain calyces that contain larger calculi. However, even when the aforementioned anatomic circumstances do exist, injection of the coagulant can be combined with a standard stone procedure and be extremely beneficial. It will remove free-floating fragments, calculi, and sediment that are present or are created in the course of such calculi manipulations as in extended pyelolithotomy, segmental or anatrophic nephrolithotomy. Certainly our experience to date would support this.

We would hope that the availability of the cryoprecipitate blood product, the consistent formulation, the safety of the procedure with a less complex injection technique, and its successful use in several different forms of upper tract calculus disease would encourage general clinical application.

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