The History of Kidney Stone Dissolution Therapy: 50 Years of Optimism and Frustration With Renacidin

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Abstract

Background and Purpose: Over the last 50 years, chemolysis as a primary or adjuvant treatment for urinary stones has fallen in and out of favor. We review the literature for a historical perspective on the origins and chronology of Renacidin therapy, focusing on landmark studies and impracticalities that have seemingly condemned it to history.

Materials and Methods: A MEDLINE search was performed on the topic of chemolysis of urinary calculi. Historical literature was reviewed with regard to stone composition, treatment modalities, outcomes, and complications.

Results: A total of 61 articles were reviewed, 40 of which were case series, representing a total of 817 patients studied. Mulvaney first introduced Renacidin in 1959 as a modification of Suby and Albright’s 1943 solution. Because of an overabundance of nonstandardized irrigation protocols, six deaths were reported in the early 1960s resulting in a Food and Drug Administration ban on the practice of upper urinary tract stone dissolution. Over time, Renacidin returned to the urologist’s arsenal, appearing first as an adjunct to dissolve catheter and bladder calculi and later (1990) as an approved agent for renal pelvis and ureter use. This feat was almost single-handedly the result of a successful hemiacidrin case series published in 1971 by Nemoy and Stamey. By using daily urine cultures, prophylactic antibiotics, and meticulous intrarenal pressure monitoring, Nemoy and Stamey virtually eliminated all major irrigation complications, paving the way for a flurry of studies. More importantly, they established the link between residual struvite stones, persistent infection, and recurrent staghorn stone formation.

Conclusions: Dissolution of urinary calculi by chemolysis has been shown to be safe and effective if performed with sterile urine cultures, prophylactic antibiotics, and low intrapelvic pressures. The pioneers of this therapy are remembered for their attempts to develop an alternative to open surgery, and, in the process, solidified the “stone-free” concept for infection-based stones.

Introduction

“In the future, it is likely that irrigations of the urinary tract with various solutions designed to dissolve stones will be an important part of the practice of urology.”

—Arthur R. Israel, 1981

“Any urologist who treats stone disease should be familiar with the fundamentals of chemolysis and its potential role in the management of urinary calculi.”

—Arthur D. Smith, 2000

For years, urologists have dreamed of using chemicals and solutions to turn insoluble kidney and bladder stones into more water-soluble forms. This process, known as dissolution or chemolysis, seems plausible for a number of reasons. First, a variety of dissolution products have been found to be effective in laboratory and animal studies. Second, the urothelium of the renal pelvis and bladder is designed for fluid transit. Thus, as long as the system is adequately drained, the chemicals used for dissolution should pass out of the urinary tract with minimal absorption. Finally, open kidney stone surgical procedures of the mid-20th century were quite morbid. Stone dissolution would obviate the need for flank incisions to relieve renal colic and obstruction. With these factors in place, human trials of stone dissolution ensued.

The closest realization of dissolving stones came in the form of a solution called Renacidin (10% hemiacidrin). The triumphs, catastrophes, and controversy that surrounded Renacidin’s use and seeming downfall will be chronicled in this review. In the peak of its popularity, Renacidin was being used to achieve stone-free status in recurrent struvite stone formers as a means of eradicating bacterial infection, a...
concept that is still relevant today. Although it is impossible
to fully catalog 60 years of Renacidin’s history, the novelty of
its use in urology deserves mention and gives perspective
for potential future therapies in the endourologists’ arma-
mentarium.

Materials and Methods

Relevant studies were searched from electronic databases
including Cochrane Central Register of Controlled Trials (The
Cochrane Library), MEDLINE, and EMBASE. Reference lists
were also made from urology and nephrology textbooks and
review articles. An on-line Google search was also used to
identify legal documents and other pertinent materials.
Search terms included all forms and abbreviations of re-

nacidin, hemiacidrin, chemolysis, dissolution, urologic solu-
tion G, Suby’s solution, ethylenediaminetetraacetic acid, and
Guardian Chemical Corporation.

A total of 61 papers were reviewed. Of these, 21 were
identified as basic science inquiries, case reports, or lower
uroinary tract investigations. The remaining 40 focused pri-
marily on upper urinary tract stones, totaling 817 patients. All
40 upper tract stone studies were case series. Prospective
clinical trials or cohort studies were not identified nor were
any detailed Renacidin protocols before 1971. No data were
present on patient selection criteria in these case series, and
clear-cut variables (irrigation time, length of stay in hospital,
stone analysis, etc.) were often lacking. From these 40 papers,
15 were chosen to be presented in tabular form.

The Beginning of Dissolution

The first reported case of stone dissolution was by Crowell4
in 1924. Using a primitive retrograde catheter, Crowell
methodically filled a young cystine stone former’s renal
pelvis with an alkaline antiseptic lavage of mercurochrome
every other day. Along with oral sodium bicarbonate for urinary
alkalinization, Crowell repeated these weekly lavages for a total
of 10 months until the roentgenogram was clear of stones. After
this success, Hellstrom5,8 (1938) used 1% phosphoric acid with a
mixture of boric acid and potassium permanganate to acidify
alkaline salts associated with Staphylococcus-associated lithiasis.

A year later, Albright and coworkers6 dissolved human cal-
cium phosphate bladder stones using isotonic citrate solutions
(pH = 4.0).2 This acidic solution, however, caused painful mu-
mosal bleeding for the patient, so a rabbit model was developed
to study dissolution speed using decalcified teeth. Their work
culminated in 1943, when Drs. Suby and Albright7 reported a
reduction in bladder mucosal irritation and bleeding by adding
magnesium to the citric acid solution (Table 1).7 This product
(isotonic citrate, magnesium oxide, and sodium carbonate) be-
came known as urologic solution G or Suby solution (Table 2).7
Although effective, the use of this solution was soon to be
overshadowed by the establishment of Renacidin.

Development and Introduction
of Hemiacidrin (Renacidin)

In 1955, Guardian Chemical Corporation began manufactur-
ing a liquid product to dissolve calcium deposits that fre-
cently clogged milk pasteurizing equipment and tubing. In
1957, Dr. William P. Mulvaney (urologist at the University of
Cincinnati) approached Dr. Alfred E. Globus (founder of
Guardian Co. and biochemist who developed the solution) and
suggested that the product may be useful in dissolving
urinary catheter calcium deposits and encrustation.

After the product was renamed Renacidin, Dr. Mulvaney
presented his preliminary data at the 1957 American Uro-
logical Association meeting. The solution itself was similar in
pH and buffering capacity to the Suby G solution but con-
tained malonic and gluconic acids (Table 2). The protons of
these acids were believed to complex with phosphate (phos-
horic acid) and calcium (calcium citrate) to form soluble
compounds at a pH of 4.0. Because struvite stone solubility
increased at pH < 5.5, Dr. Mulvaney believed Renacidin
would be useful in dissolving struvite stones. For commercial
purposes, Guardian began producing the product in powder
form, where 100 g Renacidin could be reconstituted in
1000 mL distilled water. Once in solution, Renacidin was
stable for long periods and could be autoclaved or boiled
without losing its potency.8

In 1959, Dr. Mulvaney published the first study describing
the in vitro properties of Renacidin (10% hemiacidrin) on 50
human calculi as well as in three human case reports.9 He and
his colleagues found that Renacidin sequestered 400% more
mineral than any single organic acid alone, such as citric acid.10
They thought that the added magnesium salts (roughly four
times the elemental magnesium of the Suby G, Table 2) pro-
vided ion exchange with stone calcium and enhanced dissolu-
tion with the added benefit of decreased mucosal irritation.9,11–14
It appeared to act as an excellent solvent for calcium phos-
phate, calcium carbonate, and magnesium ammonium phos-
phate stones. Cholesterol, uric acid, and calcium oxalate
stones, however, were relatively insoluble to Renacidin.

Their “proof of concept” experiment was a small case series
of three patients who had significant kidney and bladder
stones along with catheter encrustation. Despite a reported
100% success rate (Table 1), this series was limited by lack of
stone composition, follow-up data, and the need for indefinite
daily 10% hemiacidrin catheter irrigation to ensure removal of
calcifications.9,10

Based on Dr. Mulvaney’s initial reports, several large case
series with modest results were published using Renacidin
irrigations to treat catheter encrustation and a variety of renal
and bladder stones compositions, not just struvite (Table 1).8,13,15–20
This increase in clinical use also unveiled some
limitations. First, because Renacidin solution contained high
levels of magnesium and phosphate, its use was contrain-
dicated in patients with advanced renal disease (creatinine
clearance < 10 mL/min).21–27 Second, as if foreshadowing fu-
ture catastrophes, Mulvaney reported in 1960 that debris and
sand tended to obstruct single ureteral catheters, resulting in
patient discomfort and obstruction.15 Years later, the develop-
ment of percutaneous nephrostomy puncture techniques
would lead to improved irrigation and drainage (Fig. 1).28

In the early 1960s, however, haphazard Renacidin delivery
protocols through ureteral catheters were associated with six
patient deaths that would take Renacidin almost 30 years to
surmount.29,30

Banned by the Food and Drug Administration (FDA)

The safety of Renacidin irrigation first came into question
when Kohler30 reported a patient mortality during irrigation
use. He described postmortem renal infarction, necrosis, and
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>N</th>
<th>Agent</th>
<th>Delivery method</th>
<th>Composition (n)</th>
<th>Mean duration</th>
<th>Dissolution results</th>
<th>Mean F/U</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suby and Albright 1943</td>
<td>7</td>
<td>Solution G</td>
<td>Intermittent</td>
<td>CaP (2)</td>
<td>45 days</td>
<td>Complete: 4/7</td>
<td>NR</td>
<td>+ hematuria and lower urinary tract symptoms; air pyelography used to ensure stone-solution contact</td>
</tr>
<tr>
<td>Mulvaney 1959</td>
<td>3</td>
<td>Renacidin</td>
<td>Intermittent</td>
<td>Mixed (2)</td>
<td>NR</td>
<td>Complete: 3/3</td>
<td>NR</td>
<td>This report includes results of in vitro dissolution of 50 stones</td>
</tr>
<tr>
<td>Mulvaney 1960</td>
<td>46</td>
<td>Renacidin</td>
<td>Continuous</td>
<td>Mixed</td>
<td>NR</td>
<td>Success:</td>
<td>NR</td>
<td>First report of staghorn stone dissolution; success defined as stone reduction or disappearance on radiography</td>
</tr>
<tr>
<td>Timmerman and Kallistratos 1966</td>
<td>260</td>
<td>EDTA</td>
<td>Continuous</td>
<td>90% calcium</td>
<td>NR</td>
<td>Complete:145/260</td>
<td>NR</td>
<td>Largest reported dissolution series; success defined as reduction or disappearance of stone on radiography; DVT rate, 3.8%</td>
</tr>
<tr>
<td>Comarr et al 1971</td>
<td>119</td>
<td>Renacidin</td>
<td>Intermittent</td>
<td>Struvite</td>
<td>70 days</td>
<td>Complete: 51/119</td>
<td>NR</td>
<td>Series consists of spinal cord injury patients only</td>
</tr>
<tr>
<td>Nemoy and Stamey 1971</td>
<td>14</td>
<td>Renacidin (8); Antibiotics (14)</td>
<td>Continuous</td>
<td>Struvite</td>
<td>11 days</td>
<td>Complete: 8/8</td>
<td>3 years</td>
<td>Standardized dissolution protocols, antibiotics, and sterile urine; no stone recurrence in follow-up</td>
</tr>
</tbody>
</table>

Before the 1970s, all percutaneous nephrostomy tubes were placed open or at the time of open lithotomy.
PNT = percutaneous nephrostomy tube; UC = ureteral catheter; CaP = calcium phosphate; NR = not recorded; SPT = suprapubic tube; EDTA = ethylenediaminetetraacetic acid.
purulent kidney infection in a stone patient with high inflow pressures over 80 mm Hg during Renacidin irrigation therapy. Fostvedt and Barnes29 added four cases of sudden death from suspected pyelovenous backflow with postmortem findings ranging from papillary necrosis to cerebral edema.29 Finally, Auerbach and associates31 followed with a case of severe pyelonephritis, ureteritis, and chemical pyelitis in a patient with bilateral renal calculi. The patient’s ultimate cause of death was ruled pulmonary embolus, but the striking renal findings were attributed to Renacidin.31

Based on these six deaths, on June 13, 1963, the FDA banned the use of Renacidin irrigation for the upper urinary tract and bladder.28,32 The FDA acknowledged that inconsistencies in protocols and user mistakes likely led to the Renacidin mortalities and pointed to sepsis, rather than direct toxicity of the agent, as the cause of death in all cases. Not surprisingly, Mulvaney came out in defense of the solution, attributing the deaths to obstructed ureteral catheters leading to increased intrapelvic pressures and sepsis. He pointed to the safety of the procedure at renal pressures below 24 to 30 cm H2O and even advocated adding neomycin directly to the solution to prevent infectious complications.19 The intrapelvic pressures he described were subsequently validated by other investigators to be high enough for stone fragmentation but low enough to minimize pyelovenous backflow.33 Finally, Mulvaney noted that most adverse events seemed to occur at night when nursing care was scarce, and his safety frustrations were echoed by multiple other authors.3,8,17,23,34

Based on Mulvaney’s comments, on August 8, 1963, less than 2 months after their first decision, the FDA approved Renacidin to “prevent formation of and to dissolve calcifications in catheters in the urinary bladder.” Interestingly, the ruling on the upper urinary tract remained in place until October 1990, when Renacidin was approved as an “orphan drug” for the treatment of renal and bladder calculi of the apatite or struvite variety (United-Guardian Inc., U.S. patent #4,962,208). The term orphan drug refers to a drug or biologic intended for use in a rare disease or condition (defined as affecting fewer than 200,000 Americans) whose sponsor receives certain governmental benefits in exchange for drug development. Therefore, for almost 30 years, Renacidin’s use in the upper tract was classified as investigational and needed informed patient consent, approval by a hospital human ethics committee, and occasionally permission from the FDA.18,35 Undoubtedly, this drug would have retreated into history had it not been for two advocating urologists and a new protocol.

Table 2. Comparison of Renacidin with Urologic Solution G

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Renacidin (10% hemiacidrin)</th>
<th>Urologic solution G (Suby)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First urology publication</td>
<td>Mulvaney1959</td>
<td>Suby and Albright 1943</td>
</tr>
<tr>
<td>pH</td>
<td>3.9</td>
<td>4.0</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Guardian Lab (Hauppauge, NY)</td>
<td>Baxter International, Inc (Deerfield, IL)</td>
</tr>
<tr>
<td>Constituent (g in 1 L water)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citric acid</td>
<td>28.2</td>
<td>32.4</td>
</tr>
<tr>
<td>Magnesium carbonate</td>
<td>14.8</td>
<td>0</td>
</tr>
<tr>
<td>D-gluconic acid</td>
<td>5.0</td>
<td>0</td>
</tr>
<tr>
<td>Sodium carbonate</td>
<td>0</td>
<td>4.3</td>
</tr>
<tr>
<td>Magnesium oxide</td>
<td>0</td>
<td>3.8</td>
</tr>
<tr>
<td>Magnesium acid-citrate</td>
<td>2.5</td>
<td>0</td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td>1.0</td>
<td>0</td>
</tr>
</tbody>
</table>

FIG. 1. (A) Left-sided struvite kidney stone by plain film with indwelling nephrostomy tubes; (B) plain film after 17 days of Renacidin irrigation showing complete stone dissolution. Reprinted with permission from Massaro and colleague. Pharmacotherapy.27
New Life for Renacidin

In 1971, Nemoy and Stamey14 published a landmark article on the adjuvant use of Renacidin through percutaneous nephrostomy tubes (PNT) after open pyelolithotomy in patients harboring infectious stones, specifically *Proteus mirabilis* and *Klebsiella*.14 More than any previous dissolution article, Nemoy and Stamey highlighted the concept of a formal protocol for dissolution therapy in the setting of infectious stones after open stone surgery (Table 3). First, they outlined absolute contraindications to Renacidin, including infected urine, fever, or persistent flank discomfort. Their pre-surgical guidelines emphasized daily urine cultures for proper antibacterial selection and confirmation of sterility before surgery or irrigation.14

During open surgery, the renal pelvis and collecting system were irrigated copiously with saline to flush out stone fragments. Renacidin irrigation began on the fourth or fifth postoperative day with saline irrigation to test for complete healing of the pyelotomy incision. If no leakage, fever, or flank discomfort occurred, 10% Renacidin was then started at 120 mL/hr through nephrostomy tube. Once there was absence of visible particles on tomography, the irrigations would cease after an additional 24 to 48 hours. Interestingly, they even allowed patients to have control over their irrigations by instructing them on “...how to disconnect the inflow tube at the first sign of flank discomfort, even before notifying the nurse. This important precaution allows immediate reduction of intrarenal pressure in the presence of temporary outflow obstruction.”14

Table 3. Abbreviated Nemoy and Stamey Protocol for Renacidin Irrigation (1971)14

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Contraindications and requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Preoperative laboratory studies: blood count, metabolic panel, calcium, uric acid, liver function tests.</td>
<td>Absolute contraindications: UTI, fever, and/or persistent flank discomfort.</td>
</tr>
<tr>
<td>2. Abdominal x-ray, IVP.</td>
<td>1. One week preoperative penicillin G or ampicillin. Sterile urine during irrigation.</td>
</tr>
<tr>
<td>4. Copious irrigation during open stone surgery.</td>
<td>3. Halt irrigation if nephrostomy tube site leaks.</td>
</tr>
<tr>
<td>5. Low pressure saline irrigation on post-operative day 4 to test for leak. If negative, start 10% Renacidin at 120 mL/hr through nephrostomy tube.</td>
<td>4. Patients disconnect inflow tube at the first sign of flank discomfort, even before notifying the nurse.</td>
</tr>
<tr>
<td>6. Once tomograms are negative, continue irrigations for an additional 24–48 hours.</td>
<td>5. For patients with vesical irritation, reduce Renacidin to 50 mL/hr or alternate Renacidin and saline solution (1 liter) each hour and place a urinary catheter.</td>
</tr>
</tbody>
</table>

UTI = urinary tract infection; IVP = intravenous pyelography.

During open surgery, the renal pelvis and collecting system were irrigated copiously with saline to flush out stone fragments. Renacidin irrigation began on the fourth or fifth postoperative day with saline irrigation to test for complete healing of the pyelotomy incision. If no leakage, fever, or flank discomfort occurred, 10% Renacidin was then started at 120 mL/hr through a nephrostomy tube. Once there was absence of visible particles on tomography, the irrigations would cease after an additional 24 to 48 hours. Interestingly, they even allowed patients to have control over their irrigations by instructing them on “...how to disconnect the inflow tube at the first sign of flank discomfort, even before notifying the nurse. This important precaution allows immediate reduction of intrarenal pressure in the presence of temporary outflow obstruction.”14

FIG. 2. Irrigation equipment configurations for direct chemolysis I. (A) Retrograde ureteral catheter with computer-driven inflow/outflow; (B) retrograde ureteral catheter with computer inflow and nephrostomy outflow. Reprinted with permission from Bernardo and Smith. Urol Clin North Am.2
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>N</th>
<th>Delivery method (n)</th>
<th>Stone composition (n)</th>
<th>Mean duration (d)</th>
<th>Dissolution responses</th>
<th>Reported complications</th>
<th>F/U (mos)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blaivas et al 1975³</td>
<td>9</td>
<td>PNT</td>
<td>Struvite (8)</td>
<td>11</td>
<td>Complete 6/9</td>
<td>UTI 4/19</td>
<td>12</td>
<td>Intrapelvic pressure kept below 25 cm H₂O by Y-tubing between nephrostomy, irrigation, and manometer; no recurrence during short follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Apatite (1)</td>
<td></td>
<td>Partial 2/9</td>
<td>Fever 3/9</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Failure 1/9</td>
<td>Pain 3/9</td>
<td></td>
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</tr>
<tr>
<td>Fam et al 1976²⁶</td>
<td>11</td>
<td>PNT after OL (6); UC (5)</td>
<td>Struvite/apatite</td>
<td>OL 12–120 UC 14–115</td>
<td>Complete: -UC 4/5</td>
<td>Fever 4/11</td>
<td>12</td>
<td>10/11 patients had spinal cord injuries; stone sizes for UC and residual stones all &lt;2 cm</td>
</tr>
<tr>
<td>Jacobs and Gittes 1976³⁷</td>
<td>11</td>
<td>PNT after OL</td>
<td>Struvite (7)</td>
<td>7</td>
<td>Complete 9/11</td>
<td>Hematuria 3/11</td>
<td>17</td>
<td>Adjuvant therapy after open lithotomy in 11 patients; dissolution failed in calcium-based stones</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calcium (2)</td>
<td></td>
<td>Failure 2/11</td>
<td>Recurrence 2/11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dretler et al 1979²⁸</td>
<td>8</td>
<td>PNT</td>
<td>Struvite (presumed)</td>
<td>16</td>
<td>Complete 6/8</td>
<td>Flank pain 3/8</td>
<td>NR</td>
<td>Patient allowed to disconnect PNT; 2/8 patients needed additional PNT because of ureteral obstruction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Partial 2/8</td>
<td>Fever 3/8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sant et al 1983³⁵</td>
<td>21</td>
<td>PNT after OL (19); PNT (2)</td>
<td>Struvite</td>
<td>13</td>
<td>Complete 18/21</td>
<td>Back pain 9/21</td>
<td>66</td>
<td>Consecutive open series with adjuvant Renacidin that included two patients with nonsurgical PNT dissolution; long follow-up</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Partial 2/21</td>
<td>Recurrence 2/21</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Failure 1/21</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silverman and Stamey 1983⁴⁰</td>
<td>46</td>
<td>PNT after OL (46)</td>
<td>Struvite/apatite (46)</td>
<td>4.5</td>
<td>Complete 40/46</td>
<td>NR</td>
<td>84</td>
<td>All patients placed on Renacidin irrigation after OL regardless of stone status; 1/46 patients had documented stone recurrence in mean 7 years</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>Failure 6/46</td>
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<tr>
<td>Dretler and Pfister 1984⁴⁶</td>
<td>28</td>
<td>PNT</td>
<td>Struvite (presumed)</td>
<td>2–30</td>
<td>Complete 19/28</td>
<td>Fever 8/28</td>
<td>3–84</td>
<td>Hospital stay 5–60 days; stone recurrence documented in 3/19 patients complete stone clearance</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>Partial 6/28</td>
<td>Candiduria 6/28</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Failure 3/28</td>
<td>Sepsis 1/28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palmer et al 1987⁴⁶</td>
<td>15</td>
<td>PNT (1); PNT after OL (6) or MIS (8)</td>
<td>Struvite (12); apatite (3)</td>
<td>28</td>
<td>Complete 11/15</td>
<td>Leakage 15/15</td>
<td>NR</td>
<td>Highly motivated patients who performed outpatient PNT irrigation after stone removal; stones recurred in 3/15; cost approximated a 1-day inpatient hospitalization</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Partial 1/15</td>
<td>Fever 14/15</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Failure 3/15</td>
<td>Admission 3/15</td>
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<td></td>
<td>Pain 2/15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spimak et al 1988⁴⁵</td>
<td>11</td>
<td>PNT after SWL</td>
<td>Struvite (presumed)</td>
<td>6</td>
<td>Complete 9/11</td>
<td>Pyelo 2/11</td>
<td>NR</td>
<td>Case series of complex struvite stone patients managed by irrigation after SWL; average 12-day hospital stay</td>
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<td>Partial 2/11</td>
<td>Candiduria 2/11</td>
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PNT = percutaneous nephrostomy tube; UTI = urinary tract infection; OL = open lithotomy; UC = ureteral catheter; NR = not recorded; MIS = minimally invasive surgery; SWL = shockwave lithotripsy.
In response to the controversy surrounding Renacidin-associated deaths, Nemoy and Stamey reasoned they were secondary to pyelovenous backflow of untreated urinary tract infections and stated, "It is abundantly clear from these reports that if the physician is unwilling to assume responsibility for a sterile renal urine prior to and during irradiation...he should not attempt dissolution of infection stones."14

With safe and effective protocols in place, clinical applications for Renacidin irrigation and struvite stones intensified (Fig. 2). During the next 15 years (1973 to 1988), Renacidin reached its pinnacle of publications with its use described through PNT after open lithotomy, through ureteral catheters for chronically ill or spinal cord injury patients, and even as primary therapy through fluoroscopic PNT techniques (Table 4).3,33,35–38 Many of these investigators also contributed refinements to the protocol, such as irrigating for an additional 48 hours after radiography has shown disappearance of stones or halting irrigation altogether if a week of treatment did not result in a 50% reduction in size.3,33,36–38

More than their attention to dissolution safety, Nemoy and Stamey14 are credited with observing the relationship between small residual stones, incomplete infection eradication, and high struvite recurrence rate. They theorized that urea-splitting organisms were deeply embedded within struvite stones, protecting them from the action of antibacterial agents. Unlike many others, they stated that small stones could lead to persistent infection and stone recurrence and strongly advocated for complete stone-free results after pyelolithotomy for struvite stones.30 Silverman and Stamey40 went on to prove the theory by placing 46 struvite stone patients with bacteriuria on a "total therapeutic program." (Table 4) After open surgical debulking and culture-sensitive antimicrobial therapy, they placed all patients on adjuvant dissolution therapy, with Renacidin through a Hemovac tube for at least 48 hours or until stone fragments were dissolved. With years more follow-up than any other series, Stamey boasted a 2.5% stone recurrence rate while his peers at that time reported stone recurrences of 30% in 6 years.41 Stamey concluded that "...the urologist has no choice but to use Renacidin in the kidney when residual struvite or apatite fragments are left in the kidney postoperatively."

**Declining Popularity**

Even in light of Nemoy and Stamey’s protocols, the shortcomings of Renacidin seemed to outweigh its advantages (Table 5). First, stone analysis was necessary for the proper selection of the irrigant, and this was not always available. Second, vigilance in maintaining flow and proper equipment was frustrating. Constant nursing care was needed for most patients, and placement of additional ureteral catheters or PNT was needed if obstruction occurred. The protocols were labor intensive, necessitating prolonged antibiotics, daily urine cultures, serum magnesium levels, bi-weekly radiography, and complete absence of fever or pain.

Deep venous thrombosis prophylaxis was considered mandatory because of patient immobility during therapy.28,31,42 In 1979, Dretler and colleagues28 (Table 4) chronicled these concerns by reporting frequent irrigation cessations for elevated intrapelvic pressures, repeated fluoroscopy trips to radiology, and psychologically taxing lengths of immobility and hospitalization in patients on Renacidin irrigation.

With the introduction of percutaneous nephrolithotomy (PCNL) in 197643 and shockwave lithotripsy (SWL) in 1980,44 the era of minimally invasive surgery (MIS) for stone disease began. Urologists were eager to learn new procedures that reduced patient morbidity and, most importantly, were not banned by the FDA. As MIS popularity expanded, Renacidin began to be used in an adjuvant setting. Spirnak and coworkers45 described an 80% stone-free rate when Renacidin was combined with SWL in a group of patients with complex struvite stones. Palmer and colleagues46 detailed a group of patients who completed months of daily outpatient renacidin irrigations through a PNT after PCNL or SWL with only three patients needing inpatient hospital admission during 365 total outpatient days (Table 4). Although they reported total outpatient daily cost equal to that of one hospital day stay, several others documented that adjuvant Renacidin added 11 days to hospital stay and up to 3 months of outpatient therapy.3,30,33

In October 1990, the ban on Renacidin’s upper tract use was lifted, but it was too little, too late. Since 1990, only 20 Renacidin articles have been published, and most of these are in vitro studies. The era of managed care and cost containment did to Renacidin what a 30-year FDA ban could not. Perhaps Rodman47 was right when he wrote these sentiments, “One has to wonder whether the advent of managed care and the consequent emphasis on shortening hospital stays did not adversely affect the management of struvite stone disease.”

Renacidin is not completely gone. United-Guardian Inc. continues to report annual Renacidin U.S. sales from $1.2 to 1.5 million, primarily from lower urinary and catheter irrigation use. As recent as Medicare contract year 2010, Renacidin has a Healthcare Common Procedure Coding System code and continues to be listed in the Federal Register as a paid outpatient service to Medicare beneficiaries. Certainly, stone dissolution by Renacidin is not a panacea, and discretion must be exercised when considering its use. After reviewing the literature, Renacidin appears to be a valuable addition to the urologic armamentarium if used within its narrow clinical setting and with cautious vigilance.

**Conclusions**

Renacidin has had a complex history marked with promise and frustration. Although it survived an FDA ban, it could not survive the era of MIS, cost containment, and managed care. Renacidin will be remembered as a novel therapy for patients who were poor surgical candidates and made headway in struvite stone formers, sparing them morbidity and stone
recurrence after primary surgical interventions. For patients with colonized urinary tracts and infectious stones, postoperative and prophylactic irrigations with Renacidin were shown to eliminate the nidus for recurrent infection and serve as a potential long-lasting cure. This, at least in theory, should be considered when its higher healthcare costs are discussed.

The importance of Renacidin in the discovery and achievement of stone-free status for the infected stone patient cannot be overstated. Patients with complex struvite stone disease who are not cured by stone removal alone still exist. In these patients, it may be time to reconsider the role of Renacidin irrigation therapy.

**Disclosure Statement**

No competing financial interests exist. Funding for this study was obtained through grant R01 DK061666-06 (Canales).

**References**


Abbreviations Used

FDA = Food and Drug Administration
MIS = minimally invasive surgery
PCNL = percutaneous nephrolithotomy
PNT = percutaneous nephrostomy tube
SWL = shockwave lithotripsy