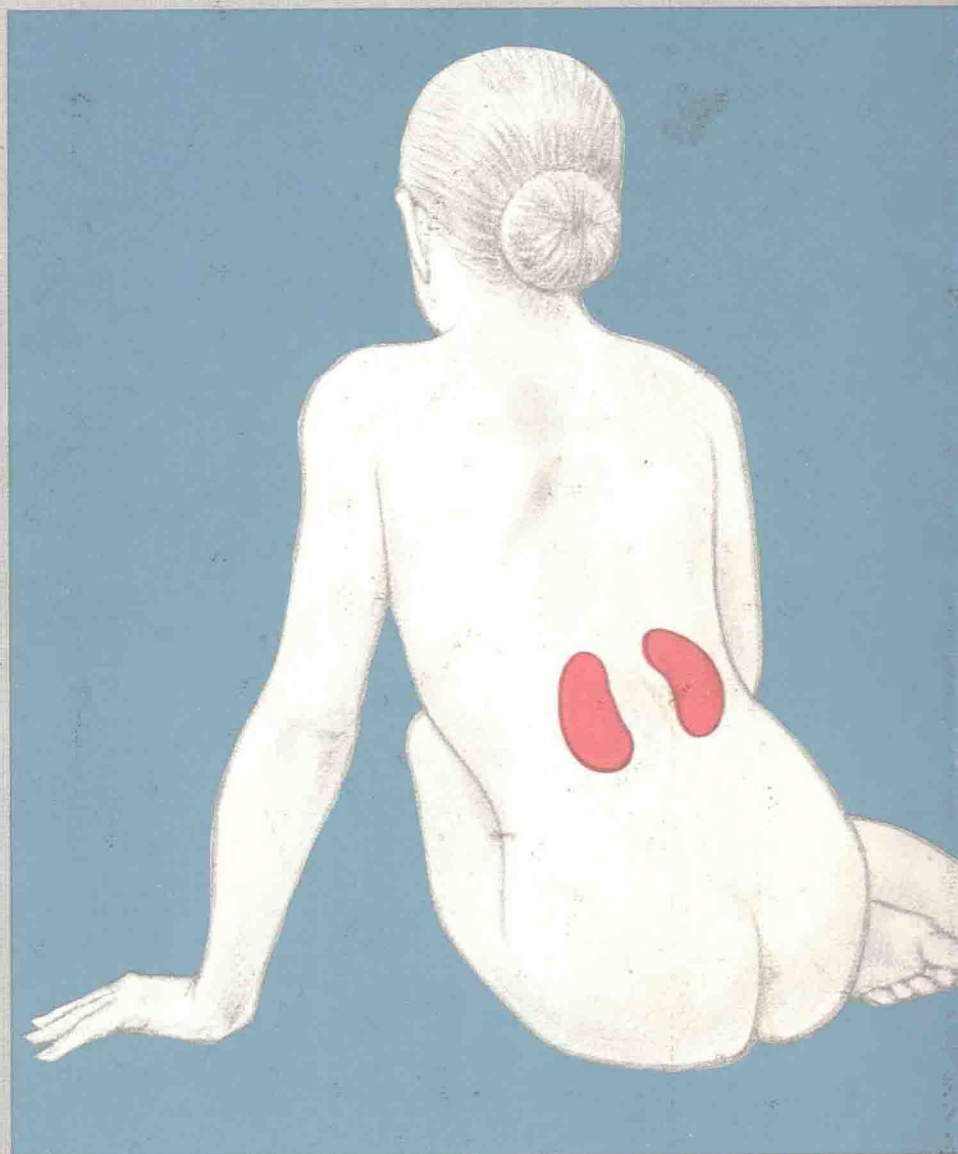


# NEPHROLITHIASIS: PATHOGENESIS AND TREATMENT



FREDRIC LAWRENCE COE  
JOAN HUNT PARKS

SECOND EDITION

# **Nephrolithiasis**

## **Pathogenesis and Treatment**

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**SECOND EDITION**

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**For our families**

***Eleanor Coe and Brian and Laura Coe  
and  
Gregory, Dana, and Leslie Parks***

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# Preface: A Whim of the Tenth Moon

But while the moon is rounding towards the full  
He follows whatever whim's most difficult  
Among whims not impossible, . . .<sup>1</sup>

Imagine yourself writing a protocol for stone disease. You plan to measure what of blood and urine chemistry the causes of stones can distort, so that from what is abnormal or normal you can infer the probable cause and choose a treatment. Your protocol, constructed at leisure and over a long time, inspected by colleagues, drawn from what the most experienced or expert say is best to do, must exceed in verity—verity to what is thought best—what any doctor could contrive in practice. After all, a doctor can spend only so much of his time on one patient, or on the few he will encounter with stones, whereas someone who writes a protocol writes for everyone. He may set practice for a nation of doctors, and can afford, for a time, to give up to the effort the main energies of his life. Like the craft of one physician, the protocol tests itself and can be perfected. As patients are studied, their results confirm or disprove what is said in books—they have certain kinds of abnormal traits, not others, for example—and the protocol is changed to emphasize what is found. Because it is on paper the protocol forgets nothing, omits nothing, changes only as, and as much as what is known changes. It is a map in place of the explorer's rich, vague mind.\*

Because it holds the truth, and can perfect itself, your protocol is full of promise, like a seed, and like a seed is lifeless by itself; it is a waking dream. Architect plans, musical scores, instructions for dance, scripts, medical protocols in turn, all are merely dreams, less than dreams because merely writings. The dreams become real only when people

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\*These two enchanting adjectives were, of course, used by Yeats, who put them into the mouth of Cuchulain in his death speech to queen Aoife<sup>3</sup>; they referred, there, to the sea, with which Cuchulain had fought after he went mad toward the end of "On Baile's Strand."<sup>4</sup> They are, through some foolishness, missing from the play in the author's own edition of 1934,<sup>4</sup> and must be sought by those who would seek them where I say to look.<sup>3</sup> Death of Cuchulain was added to the 1934 plays after Yeats had died, and the publisher used a text without either word.

who can perform what they say to do take them up and use them; and the shapes the dreams assume, the effects that they have upon people depend upon the performers, upon whether or not they are passionate, have talent, and love their craft.

Is your protocol all about measurement—as mine is? Then the quality of what the protocol becomes in life depends upon the laboratory. If the measurements are difficult, as they are, the laboratory must be special for them, committed to accuracy, and stable over the years so a measurement today can be compared to one made 10 years hence. Too stringent? Well, then, accept less for your patients. I have read how angry Sebastian Bach was with the choirboys at Leipzig who performed his weekly cantatas, though the results were music. I know a nephrologist and department chairman who can build a house, my coauthor in this book dances, I play piano, almost everyone reads plays; it is not hard to bring the dreams to life for oneself, but very hard to do it so it has its full effect—ideal care, for example—on others. Your protocol, being a dream and an ideal, must widen the difference between the best care and the ordinary, because a few will enact it with talent and passion, and others, most, perhaps, will—or must—content themselves with what is mundane: data that are imprecise, variable, and uncertain.

This vision of the dream and its performers, of the protocol and the laboratory, captivated me years ago, at the start of my career; and I, in thrall to the vision, set out to make a program in its image. I wrote protocols in Nephrology. I built a laboratory around a few excellent people who were excited by the vision and we began to enact my dream in our clinical theater. Doctors sent their patients. Data accumulated in our new charts. Letters and telephone calls began. The vision condensed into a material form. It took on the firmness of real life. And as it became real, the program displayed a size and complexity I had not imagined, that dawned upon me as an unwelcome revelation. Protocols were so complex, needed so many measurements, required so much scheduling, collating, calculating, comparing of results to normal results, keeping up of records, that I was unable to use them by myself and also be a doctor.

The complexity provoked a crisis; I needed more people, but I also wanted my program to support itself. Where was I to find the income within the program to pay for the people I needed? Medical fees could not support other people to help me; Universities need them to support their faculty, and doctors in practice for themselves. Grants for research are not for patient care. The only source was laboratory income, which by tradition goes almost always to hospitals or clinical pathologists,

not to the medical unit that cares for the patient; so I, with great reluctance, became the proponent of an unpopular cause. I cajoled, fought, wrangled, and argued with everyone who had authority and would listen, hospital managers, medical directors, deans, senior faculty, telling them that for the sake of an experiment the hospital corporation should give up money it considered its own. I fell by stages from dreamer to partisan to soldier to fanatic.

Ultimately, perhaps because the idea itself was irresistible, I got my way. The laboratory, the protocol, the doctor, and people to gather and maintain the information all came together into one unit that used its income to support itself; I called this mundane innovation of protocol, laboratory and staff, and altered financial arrangements wrested from an unwilling institution a 'Diagnostic Unit,' and made up my mind that to its development and proliferation I would devote my main energies. The idea of the unit was meant to be revolutionary, to create a change in medical practice; if units were built, and successful, others would follow.

Perhaps because I was young, somewhere between the first quarter moon and the full, or because I am by nature immoderate, I set out to reform all of Nephrology at once even though each protocol was daunting. The signs and symptoms of patients with kidney and urinary tract diseases group themselves into ten clusters, called syndromes,<sup>2</sup> which doctors recognize by direct perception and simple testing; I wrote protocols for evaluating patients with each one. The first was for hypertension, common, serious, and due—sometimes—to curable causes detected by laboratory testing. Eric Reiss, Chairman of the Department of Medicine I then worked in, suggested stone disease as the second protocol. He thought the field of hypertension was a crowded one for a young clinical scholar, and knew that because most people were hypertensive for no obvious cause except heredity, the yield of causes from the protocol evaluation would be low. Stone disease is common, was studied then—as now—by only a small band of scientists, and has yielded up a rich harvest to those who before me had cultivated it. Besides that, Eric studied mineral metabolism and wanted company. I knew nothing about the diseases that cause stones, cared less, and ignored the idea; but after a few months, and on impulse, I decided to set up the measurements for a good stone laboratory.

For several years, my unit studied both patients with stones and patients with hypertension, and even began to study some—using the protocol method and the laboratory—who had primary renal diseases. Nephrology seemed small at that age, so why not do it all? I began to use a computer for the volumes of data we amassed; of course, patients

were plentiful. I soon responded to my computer's seductive nature: could not protocols be written into computer programs? My career itself gradually turned into an experiment: which of the protocols would work best? Would computers be useful? Would the whole idea prove important? Would I find that Nephrology was too small a field to be interesting, or too large to handle?

It is hard to place the exact time, but if the 14th moon is full it must have been near the tenth moon, or about when I was 35 that I decided to limit my work to stones. That decision was not rational. Partly, I was not publishing enough to stay in Academic Medicine; partly, no one believed I was anything but insane to work on so global an issue as the reform of an entire medical specialty; certainly, no agency wanted to fund research based on the units because plausibility was in doubt; perhaps I was guided by an instinct for self-preservation. Whatever the true cause—which I shall never know—I decided all at once, in an instant, to commit all of my energies to patients with stones, and I have continued to do this ever since.

The main question I pursued was unchanged, but limited to the one example of stone disease: was the unit idea a good one; would it be an important model for medical care? I thought of many tests I could use to find the answer, each a question of its own. Would a unit made of a protocol, a special laboratory, a doctor, and several others be practical, support itself, allow one doctor to do all of the clinical work and other things as well? Would we discover in most patients the diseases causing their stones? Would our diagnoses lead us to treatment that prevented stones? Would new clinical patterns display themselves?

Because I had begun to study only one problem, my interest in research increased; I saw how the unit could foster research. Since the laboratory, protocol, staff, and income were together; since the patients were studied uniformly in what was meant to be the best way possible; since the data were precise, stable, and accurate, and there was support for data collation, maintenance, and calculation, all that was needed to do research was to add people supported by research grants who could use the data. Since the unit was built to support itself, research subsidies could be much smaller, and the long-term stability of the unit for patient care much more certain than in a system for clinical research that depended mainly upon grants. I reasoned that if the unit proved attractive as a core for a funded center for research in stone disease, basic science work might gradually surround the clinical core because patients were available. It was, I suppose, simple chance that at about the right time the National Institutes of Health proposed funding a few



centers of stone research, and I know that it was our excellent fortune to win one.

By now, the moon has passed the full; the adventure and the dream are altered by experience. What the unit has contributed we have gathered here, in this volume, and we offer it up as the only answer we will ever have for all of our many questions. Will any other disease be like this one? Will any other people follow a whim so difficult, and will it be one that is possible? Is our result the curious outcome of a singular passion, or does it tell us that one part of medicine, that part which is about matters of craft, can be done like science is done and become part of science yet stay useful as medical practice? In all of our writings, we have never spoken of the unit itself, never about its real intent, about the whim and the dream; and we barely speak of it now, and only here, in this private and nearly invisible place.

FREDRIC L. COE

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# Acknowledgments

This book is for physicians who treat patients with renal stones and nephrocalcinosis. It is a comprehensive and practical book, personal and opinionated, and written in a style that is meant to please. The tables and figures summarize our own large experience of more than 1,400 patients, and compare what we have found to what is said by others. The references are as extensive and as complete as we could make them. We have written case reports of patients whose diseases are instructive because unusual. We have added a primer of mineral metabolism, stone radiographs and crystal photomicrographs, and a brief chapter on cystinuria, which was omitted from the first edition. The Preface is a story about how the Stone Program began, and what the results of its 17 years may mean about how medicine can be practiced.

Our colleagues elsewhere who study stone disease and mineral metabolism we have honored in the best way possible, by using their data, citing their papers, and arguing with their conclusions. Most of our collaborators in the program, in Chicago, speak for themselves, in their papers, which we quote liberally. We mention a few to whom our indebtedness is incalculable. Murray Favus and David Bushinsky study vitamin D and bone metabolism; Y. Nakagawa purified and has led our work on nephrocalcin, what we believe is the main urine inhibitor of calcium oxalate crystallization; Sergio DeGanello has given us what insights into crystallography we possess; Mary Soik Le Dunn has directed the Stone Laboratory almost since it opened, in 1969; Lisa Sandin is who our patients talk to most of the time.

Drs. Donald P. Griffith, Dennis J. Levinson, and Leif B. Sorenson contributed to or wrote chapters in the first edition on uric acid stones and struvite stones, and portions of what they wrote are retained here as a valued legacy. Much has changed, especially our own experience, so we have written—we hope as well as they did—what we now think and believe we know about the topics.

Although we suspect he rarely thinks about the matter, Dr. Franklin Epstein is the godfather of this book; he engendered its first edition by introducing me to its publishers and telling me to write it, he wrote its Foreword, and he edited the text. Dr. Nancy B. Cummings, when she was at the National Institutes of Health, established an initiative for specialized centers of research in stone disease, and we were fortunate

## **xiv / Acknowledgments**

enough to win one of the five grant awards. The five centers brought together the few investigators who study this common illness, and made possible the creation of our mineral research group at Chicago. We who study stone disease are forever in debt to her vision.

FREDRIC LAWRENCE COE  
JOAN HUNT PARKS

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# Contents

Preface      vii

<b>1 / Clinical Approach</b>	<b>1</b>
General Features	1
Analysis of Kidney Stones	1
Appearances of Kidney Stones	2
Microscopic Appearance of Crystals	6
Manifestations of Stone Disease	7
Activity of Stone Disease: An Illustrative Case	12
Natural History of Stones	18
Natural History in Selected Groups	19
Causes of Stones	25
Clinical and Laboratory Evaluation of Patients With Stones	27
Clinical History	28
Physical Examination	31
How to Decide Who Has Stones	31
Laboratory Evaluation	32
Sequence of Evaluation	34
Something About Lithotripsy	35
<b>2 / Physical Chemistry of Calcium Stone Disease</b>	<b>38</b>
Structure of Calcium Oxalate Monohydrate	39
Supersaturation	42
Basic Concepts	42
Ion Concentrations	44
Ions in Water	45
Calculation of Supersaturation	46
Empirical Measure of Supersaturation	47
Heterogeneous Nucleation	49
Clinical Nucleators	51
Measurement of Nucleation in Urine	51
Inhibitors	53
Citrate	54
Magnesium	54
Pyrophosphate	54
Glycoproteins	55

Glycosaminoglycans	56
<b>3 / Primary Hyperparathyroidism</b>	<b>59</b>
Etiology of Primary Hyperparathyroidism	60
Regulation of Normal Parathyroid Hormone Secretion	60
Response to Chronic Hypocalcemia: Secondary Hyperparathyroidism	62
Primary Hyperparathyroidism	62
A Reasonable View of Etiology	64
Normal Mineral Physiology	65
Physiologic Effects of Parathyroid Hormone	65
Parathyroid Hormone Effects on Bone	71
Calcitriol Regulation	71
Intestinal Transport	72
General Features of Primary Hyperparathyroidism	72
Blood and Urine Chemistry	72
Observations in Our Patients	78
Biochemistry	78
Stone Disease	80
Bone Disease	80
Other Clinical Manifestations	83
Association With Other Endocrine Abnormalities	83
Diagnosis	84
Establishment of Hypercalcemia	84
Exclusion of Other Hypercalcemic States	84
Role of Parathyroid Hormone and Urine Cyclic Adenosine Monophosphate Assays	88
Ionized Calcium	88
Other Measurements	88
Normocalcemic Primary Hyperparathyroidism	89
An Overview	89
Surgical Treatment	90
Localization Techniques	90
Parathyroid Surgery	90
Postoperative Care	94
Long-Term Results	96
Medical Treatment	99
Choice of Patients	99
Types of Treatment	99
<b>4 / Familial (Idiopathic) Hypercalciuria</b>	<b>108</b>
Diagnosis and Occurrence	108
What is Hypercalciuria?	108

When is Hypercalciuria Idiopathic?	109
Etiology	110
Report of a Case	110
Pathogenesis of Hypercalciuria	113
Contrasting Theories	113
Evidence for a Disorder of Calcitriol Metabolism	113
Clinical Implications	116
Unresolved Issues	119
Clinical Features of Familial Hypercalciuria	122
Laboratory Findings	123
Clinical Consequences of Hypercalciuria	123
Treatment	125
Thiazide	125
Low Calcium Diet	131
Cellulose Phosphate	131
Orthophosphate	131
Magnesium	132
<b>5 / Calcium Phosphate Stones and Renal Tubular Acidosis</b>	<b>139</b>
Calcium Phosphate Stones in General	142
Supersaturation With Respect to Calcium Phosphate Salts	144
Characteristics of Patients With Calcium Phosphate Stones	144
Clinical Features	144
Laboratory Findings	145
Normal Acid-Base Physiology	149
Bicarbonate Equilibria	150
Reclamation	153
Normal Physiologic Variations of Urine pH	155
Response to Alkali Loading	155
Response to Acid Loading	156
Renal Tubular Acidosis	157
Types of Renal Tubular Acidosis	157
Consequences of Distal Renal Tubular Acidosis	159
Basic Defect in Distal Renal Tubular Acidosis	162
Comparison of Proximal and Distal Renal Tubular Acidosis	163
Clinical Aspects of Renal Tubular Acidosis	165
Incomplete Renal Tubular Acidosis	168
<b>6 / Hyperoxaluric States</b>	<b>172</b>
Types of Hyperoxaluria	172
Consequences of Surplus Oxalate	174

Hyperoxaluria	174	
Systemic Oxalosis	175	
Synthesis of Oxalate	178	
Ascorbic Acid Pathway	178	
Glyoxylate Pathway	179	
Summary	181	
States of Oxalate Overproduction	182	
Type I Hyperoxaluria	182	
Type II Hyperoxaluria	183	
Thiamine Deficiency	185	
Pyridoxine Deficiency	185	
Ethylene Glycol Ingestion	185	
Methoxyflurane Anaesthesia	186	
Treatment of Oxalate Overproduction	186	
A Patient With Primary Hyperoxaluria	187	
Absorptive Hyperoxaluria	187	
Ileal Resection	188	
Intestinal Bypass	190	
Our Experience With Intestinal Disease and Stones	192	
Dietary Oxalate Excess	192	
Cellulose Phosphate	193	
Patients With Dietary Hyperoxaluria	197	
Treatment of Absorptive Hyperoxaluria	197	
Clinical Overview of Hyperoxaluria	200	
<b>7 / Uric Acid and Calcium Oxalate Stones</b>	<b>205</b>	
Mechanisms of Hyperuricosuria	206	
Role of Diet	206	
Role of Overproduction	207	
Possible Renal Tubule Disturbance	208	
Urine Supersaturation in Hyperuricosuric Patients	210	
Clinical Features of Hyperuricosuric Calcium Oxalate Nephrolithiasis	212	
Mixed Calcium Uric Acid Stone Disease	212	
Interactions Between Calcium Oxalate and Uric Acid Crystals	214	
Epitaxy	215	
Heterogeneous Nucleation	217	
Overview of Crystal Interactions	221	
Reduced Urine Inhibitors	222	
Allopurinol Treatment	224	
Patients With Hyperuricosuria and Calcium Stones	227	

Summary	228
<b>8 / Idiopathic Stone Formers</b>	<b>232</b>
Diagnostic Criteria	232
Excretion Rates	232
Supersaturation	233
Heterogeneous Nucleation	235
Inhibitors	235
Treatments	243
High Fluid Intake	243
Low Calcium Diet	243
Effect of Fluids and Low Calcium Intake	244
Orthophosphate	244
Thiazide and Allopurinol	247
<b>9 / Uric Acid Stones</b>	<b>250</b>
Factors That Control Uric Acid Crystallization	250
Urine pH	250
Uric Acid Excretion	255
Urine Volume	257
Clinical Expression of Uric Acid Crystallization	258
Stones	258
Crystalluria	259
Obstruction	260
Clinical Settings for Uric Acid Stones	260
Idiopathic Uric Acid Stones	260
Gout	261
Neoplastic Diseases	262
Gastrointestinal Disease	262
Excessive Dermal Water Losses	262
Hyperuricosuria Without Hyperuricemia	263
Purine Gluttony	263
Treatment of Uric Acid Stones	263
Unusual Radiolucent Stones	265
<b>10 / Cystine Stones</b>	<b>269</b>
Pathogenesis of Cystinuria	269
Pathogenesis of Stones	270
Natural History	271
Treatment	272
Water	272
Alkali	272
Diet	272



**xx / Contents**

D-Penicillamine	272
Thiola	274
Glutamine and Low Salt	274
<b>11 / Struvite Stones</b>	<b>276</b>
Pathogenesis and Etiology	276
Urea Hydrolysis	276
Organisms With Urease	278
Clinical Course	278
General Experience	278
Our Experience	278
Treatments	284
Surgery	284
Lithotripsy	285
Medical Treatment	285
A View of Treatment	290
<i>Index</i>	294