

# Contents

## SECTION 1: Characteristics and Formation of Kidney Stones

*Section Editor: Andrew P Evan*

|  |           |
|--|-----------|
| <b>1. Epidemiology of Kidney Stones</b>  | <b>3</b>  |
| <i>Eric N Taylor, Gary C Curhan</i>  |           |
| ▪ Overview   | 3         |
| ▪ Prevalence, Incidence, and Recurrence  | 3         |
| ▪ Kidney Stone Type  | 4         |
| ▪ Cost   | 5         |
| ▪ Nondietary Risk Factors  | 5         |
| ▪ Diet and Stone Disease   | 7         |
| ▪ Beverages and Calcium Stones   | 11        |
| ▪ Urinary Factors  | 13        |
| <b>2. Nonclassical Crystallization Processes: Potential Relevance to Stone Formation</b>                     | <b>18</b> |
| <i>Stephan E Wolf, Joe Harris, Archana Lovett, Laurie B Gower</i>  |           |
| ▪ Prolog   | 18        |
| ▪ From Idealized to Real Crystallization Systems:<br>Classical Versus Nonclassical Crystallization Processes | 18        |
| ▪ General Considerations of Stone Formation  | 28        |
| ▪ Mineralogical Signatures of Nonclassical Mineralization<br>Processes Occurring in Stone Formation          | 30        |
| ▪ Renal and Urinary Constituents that might be Potential<br>Candidates in Promoting Nonclassical Processes   | 46        |
| <b>3. Biology and Clinical Relevance of Urine Crystallization Inhibitors</b>                                 | <b>55</b> |
| <i>Kristin J Bergsland</i>   |           |
| ▪ Small Molecules  | 55        |
| ▪ Macromolecules   | 57        |
| <b>4. Characteristics of Human Kidney Stones</b>   | <b>77</b> |
| <i>Michel Daudon, James C Williams Jr</i>  |           |
| ▪ Calcium Oxalate Stones   | 77        |
| ▪ Calcium Phosphate in Stones  | 83        |
| ▪ Infection Stones   | 89        |
| ▪ Purines in Stones  | 91        |
| ▪ Cystine Stones   | 92        |
| ▪ Other Forms of Urinary Stone   | 94        |
| ▪ Concluding Comments  | 94        |

**5. Crystals in Human Kidneys 98***Andrew P Evan*

- Patterns of Tissue Mineralization 98
- Papillary Stones Fixed to Sites of Interstitial (Randall's) Plaque 99
- Patterns of Mineral Deposit in Specific Clinical Stone Phenotypes 127
- Idiopathic Calcium Oxalate Stone Forms (ICSF) 127
- PHPT 131

**6. Calcium Oxalate and Calcium Phosphate Crystal Interactions with Renal Cells 143***Benjamin A Vervaeke, Patrick C D'Haese, Marc E De Broe, Anja Verhulst*

- The (Molecular) Phenotype of Crystal-Binding Epithelia 143
- Crystal Adhesion as Cause or Consequence of Epithelial Phenotypical Changes 147
- Postadhesion Renal Crystal Clearance 154

**7. Animal Models of Urolithiasis 162***Orson W Moe, David A Bushinsky*

- General Considerations 162
- Animal Species Currently Used in Urolithiasis Research 164
- Monogenic Models of Stone Risk 168
- Polygenic Rat Model of Urolithiasis 168
- Effects of Diet on Rodent Stone Risk 171
- Effects of Medications on Rodent Stone Risk 174
- Effects of Hypercalciuria on Rodent Bone 176

---

**SECTION 2: Mineral Metabolism and Stone-Forming Diseases**

---

*Section Editor: Elaine M Worcester***8. Vitamin D, PTH and Regulation of Mineral Metabolism 187***Murray J Favus*

- Mineral Distribution of Calcium, Magnesium, and Phosphorus 187
- Mineral Homeostasis 189
- Organs 195
- Calcium Homeostasis and Adaptation: Human Studies 196
- Phosphorus Transport 198
- Magnesium Transport 200

**9. Gastrointestinal and Renal Mineral Transport and Regulation 204***Anke L Lameris, Joost GJ Hoenderop, René JM Bindels*

- Epithelial Transport of  $\text{Ca}^{2+}$  204
- $\text{Ca}^{2+}$  Homeostasis 207
- Important Regulators of  $\text{Ca}^{2+}$  Transport 210
- Hereditary Disorders of Mineral Balance and Nephrolithiasis 215

|  |            |
|--|------------|
| <b>10. Renal Citrate Metabolism and Transport: Physiology and Pathophysiology</b>  | <b>226</b> |
| <i>Kathleen S Hering-Smith, Lee Hamm, Orson W Moe</i>  |            |
| ▪ Evolutionary Origins of Urinary Citrate  | 226        |
| ▪ Renal Citrate Handling   | 230        |
| ▪ Physiologic Regulation of Urinary Citrate Excretion  | 233        |
| ▪ Clinical Pathophysiology of Hypocitraturia   | 236        |
| ▪ Citrate Therapy in Nephrolithiasis   | 238        |
| <b>11. Urine pH: Relationship to Integrative Physiology of Calcium, Phosphate and Magnesium, and Prevention of Calcium Phosphate Precipitation</b> | <b>246</b> |
| <i>Mitchell L Halperin, Orson W Moe</i>  |            |
| ▪ Determinants of UpH  | 246        |
| ▪ Preventing Formation of $\text{CaHPO}_4$ in Sites Other than Bone  | 248        |
| ▪ Incomplete Distal RTA  | 252        |
| ▪ Pathophysiology of Incomplete RTA  | 254        |
| <b>12. Acid-Base Balance, Hypercalciuria, and Bone</b>   | <b>259</b> |
| <i>Kevin K Frick, Nancy S Krieger, David A Bushinsky</i>   |            |
| ▪ Hypercalciuria and BMD   | 259        |
| ▪ Effects of Acid on Hypercalciuria <i>In Vivo</i>   | 259        |
| ▪ Effects of Metabolic Acid on Bone <i>In Vivo</i>   | 260        |
| ▪ Population Studies   | 260        |
| ▪ Effects of Metabolic Acids on Bone <i>In Vitro</i>   | 261        |
| ▪ Acute Effects of Acidosis  | 261        |
| ▪ Chronic Effects of Acidosis  | 263        |
| ▪ Hypothesis   | 268        |
| <b>13. Idiopathic Hypercalciuria</b>   | <b>276</b> |
| <i>Fredric L Coe, Elaine M Worcester</i>   |            |
| ▪ What is Idiopathic Hypercalciuria?   | 276        |
| ▪ Idiopathic Hypercalciuria is Familial and can be Bred for in Animals   | 277        |
| ▪ Gastrointestinal and Bone Contributions to IH  | 278        |
| ▪ Renal Calcium Handling in IH   | 281        |
| ▪ Hormones and Receptors   | 287        |
| ▪ Absorptive Hypercalciuria  | 290        |
| ▪ Lessons about Pathogenesis from Treatment  | 292        |
| ▪ Creation of an Effective Treatment Plan  | 297        |
| <b>14. Bone Histopathology and Disease in Hypercalciuria</b>   | <b>303</b> |
| <i>Ita Pfeferman Heilberg, Aluizio Barbosa Carvalho</i>  |            |
| ▪ Epidemiological Studies  | 303        |
| ▪ Clinical Studies   | 304        |
| ▪ Potential Pathophysiological Mechanisms for Bone Alterations in Hypercalciuric Stone Formers   | 308        |
| ▪ Treatment of Bone Disease  | 313        |

## **15. Idiopathic Stone Formers 321**

*Fredric L Coe, Elaine M Worcester*

- Calcium Stone Formers 321
- Clinical Evaluation of Stone Formation 321
- Calcium Stones from Systemic Diseases 324
- Comprehensive Metabolic Evaluation 330
- Idiopathic CaOx Stone Formers 336
- Idiopathic Calcium Phosphate Stone Formers 347

## **16. Primary Hyperparathyroidism and Renal Stone Disease 355**

*Edwin L Kaplan, Megan K Applewhite, Raymon H Grogan*

- Historical Perspective 355
- Symptoms 356
- Diagnosis 356
- Indications for a Parathyroidectomy 357
- Pitfalls for the Surgeon 358
- Pathology of Primary Hyperparathyroidism 361
- Localization Procedures 361
- Operative Approach 365
- Success of Minimally Invasive Parathyroidectomy Versus Routine Four-Gland Explorations 367
- Surgery for Parathyroid Cancer 370
- Results of Parathyroidectomy for Primary Hyperparathyroidism 371

## **17. Bowel Disease and Urolithiasis 374**

*John R Asplin*

- Gastrointestinal Anatomy and Physiology 374
- Disease of the Colon and Colectomy 378
- Enteric Hyperoxaluria 384
- AmU Stones 403

## **18. Primary Hyperoxaluria 412**

*Dawn S Milliner, Jane S Matsumoto*

- Primary Hyperoxaluria Types 412
- Pathophysiology 415
- Diagnosis 415
- Stones 419
- Nephrocalcinosis 431
- Kidney Damage and Kidney Failure 433
- Medical Management 434
- Future Directions 436

## **19. Renal Tubular Acidosis and Urolithiasis 443**

*Daniel G Fuster, Orson W Moe*

- Brief Primer on Renal Acidification and Acid-Base Homeostasis 443
- Acid Buffering: Temporizing Measure 443

|  |            |
|--|------------|
| ▪ Renal Acid Excretion: Definitive Defense   | 444        |
| ▪ Cellular Mechanisms of H <sup>+</sup> Excretion                                  | 445        |
| ▪ Three Key Entities in Distal Acidification                                       | 445        |
| ▪ Definition, Classification, and Causes of RTA                                    | 446        |
| ▪ Epidemiology of dRTA and Urolithiasis  | 451        |
| ▪ Clinical Manifestations of dRTA  | 452        |
| ▪ Pathophysiology of Urolithiasis in dRTA  | 455        |
| ▪ Evaluation and Treatment of dRTA and dRTA-Associated Urolithiasis                | 456        |
| <b>20. Medullary Sponge Kidney and Human Monogenic Hypercalciurias</b>             | <b>464</b> |
| <i>Giovanni Gambaro</i>  |            |
| ▪ Medullary Sponge Kidney  | 464        |
| ▪ Human Monogenic Hypercalciuria   | 471        |
| ▪ Primary dRTA   | 476        |
| <b>21. Cystine and Uncommon Organic Stones</b>                                     | <b>482</b> |
| <i>David S Goldfarb</i>  |            |
| ▪ Cystinuria   | 482        |
| ▪ APRT Deficiency  | 491        |
| ▪ Xanthinuria  | 495        |
| <b>22. Drug-Induced Stones</b>   | <b>501</b> |
| <i>Lama Nazzal, David S Goldfarb</i>   |            |
| ▪ Diagnosis of Drug-induced Nephrolithiasis  | 501        |
| ▪ Epidemiology   | 501        |
| ▪ Management of Patients with Drug-induced Calculi                                 | 509        |
| <b>23. Uric Acid Stones: Epidemiology, Pathophysiology and Treatment</b>           | <b>514</b> |
| <i>Khashayar Sakhaee</i>   |            |
| ▪ Epidemiology of Uric Acid Nephrolithiasis and its Link to the Metabolic Syndrome | 514        |
| ▪ Etiologic Causes: Acquired, Congenital and Idiopathic                            | 515        |
| ▪ Clinical Basis of Impaired Renal Ammonium Excretion                              | 518        |
| ▪ Clinical and Cellular Basis of Increased Endogenous Acid Production              | 522        |
| ▪ Diagnosis  | 522        |
| ▪ Treatment Approach   | 524        |
| <b>24. Pediatric Kidney Stone Disease</b>  | <b>530</b> |
| <i>David J Sas</i>   |            |
| ▪ Epidemiology   | 530        |
| ▪ Pathophysiology  | 531        |
| ▪ Medical Evaluation   | 532        |
| ▪ Treatment and Follow-up  | 536        |
| <b>25. Chronic Kidney Disease and Stone Disease</b>                                | <b>544</b> |
| <i>Andrew D Rule, John C Lieske</i>  |            |
| ▪ Kidney Stones as Risk Factors for CKD  | 544        |
| ▪ Kidney Stones as Risk Factors for ESRD   | 545        |

- Risk of CKD by Stone Characteristics 547
- Acute Kidney Injury with Kidney Stones 547
- Long-term Effects of Stone Removal Procedures 549
- Crystalline Nephropathy 549

### SECTION 3: Surgical Management of Kidney Stones

*Section Editor: James E Lingeman*

- 26. The Natural History of Kidney Stones** 559  
*Jubilee Tan, Dean G Assimos*
- Natural History of Untreated Calyceal Stones 559
  - Natural History of Untreated Staghorn Stones 560
  - Natural History of Residual Fragments after Stone-Removing Procedures 560
  - Spontaneous Ureteral Stone Passage 562
- 27. Stone Factors Affecting Treatment Choices (Anatomy, Composition, etc.)** 565  
*Aaron D Benson, Nicole L Miller*
- Surgical Treatment Options 565
- 28. Preoperative Preparations for Stone Surgery** 588  
*Daniel Schneider, William A Critchlow, Mitchell R Humphreys*
- Unique Demographics of Stone Patients 588
  - Patient Presentation with an Acute Ureteral Stone Episode 588
  - Pathophysiology of Urinary Tract Obstruction 591
  - Imaging 594
  - Workup for Complex Stone Disease 601
  - Infections of the Urinary Tract and the Stone Patient 604
  - Symptom Management in the Stone Patient 610
- 29. Radiological Imaging of Nephrolithiasis: Emerging Technologies and Radiation Safety** 618  
*Cynthia H McCollough, Joshua H Grimes*
- Imaging Modalities Used in Nephrolithiasis 618
  - Appropriateness of Each Imaging Modality 619
  - Controversies Regarding Radiation Safety 619
  - New and Emerging Clinical Applications 621
- 30. Contemporary Outcomes for Shock Wave Lithotripsy, Ureteroscopy, and Percutaneous Nephrolithotomy** 624  
*Yung-Khan Tan, Keng-Siang Png, Yew-Lam Chong, Michael YC Wong*
- Management of Ureteral Stones 624
  - Management of Renal Stones 627
  - Complications in PCNL 631
  - Complications in URS 631
  - Complications in SWL 633

|   |            |
|---|------------|
| <b>31. Shock Wave Lithotripsy in Management of Stones</b>   | <b>638</b> |
| <i>Michelle Jo Semins, Brian R Matlaga</i>  |            |
| ▪ Contemporary Instruments  | 638        |
| ▪ Range of Uses   | 641        |
| ▪ Complications   | 643        |
| <b>32. Ureteroscopy in the Management of Stones</b>   | <b>649</b> |
| <i>Fernando Cabrera, Michael Lipkin, Glenn M Preminger</i>  |            |
| ▪ History and Development   | 649        |
| ▪ Indications for Ureteroscopy  | 649        |
| ▪ Contraindications   | 653        |
| ▪ Preoperative Preparation  | 653        |
| ▪ Intraoperative Instruments, Technology and Technique  | 657        |
| ▪ Intracorporeal Lithotripters  | 660        |
| ▪ Postoperative Considerations  | 664        |
| ▪ Tips and Tricks   | 664        |
| ▪ Complications   | 666        |
| ▪ Future of Ureteroscopy  | 669        |
| <b>33. Percutaneous Nephrolithotomy in Management of Stones: Present Role, Approaches, Outcomes and Complications</b> | <b>674</b> |
| <i>Arvind P Ganpule, Mohan Kumar, Mahesh Desai</i>  |            |
| ▪ Present Role of Percutaneous Nephrolithotomy  | 674        |
| ▪ The Approach  | 675        |
| ▪ Newer Concepts in Percutaneous Surgery  | 677        |
| <b>34. Special Considerations in Ureteroscopy</b>   | <b>683</b> |
| <i>Mitra R de Cógáin, Amy E Krambeck</i>  |            |
| ▪ Urinary Diversion   | 683        |
| ▪ Calyceal Diverticula  | 685        |
| ▪ Horseshoe Kidney  | 687        |
| ▪ Ureteral Reimplantation   | 689        |
| ▪ Renal Transplantation   | 690        |
| ▪ Pregnancy   | 691        |
| <b>35. Role of Laparoscopic, Robotic Assisted and Open Surgery in Management of Urolithiasis</b>                      | <b>698</b> |
| <i>Amit Bhattu, Mihir M Desai</i>   |            |
| ▪ Indications for Open Surgery for Urolithiasis   | 698        |
| ▪ Role of Laparoscopic and Robotic Surgery  | 698        |
| <b>36. Surgical Management of Stones in Children</b>  | <b>704</b> |
| <i>Stephen Scott Sparks, Craig A Peters</i>   |            |
| ▪ Epidemiology  | 704        |
| ▪ Presentation  | 705        |
| ▪ Evaluation  | 705        |
| ▪ Management  | 707        |
| <b>Index</b>  | <b>717</b> |