Editorials

513 Nutrition as Medical Therapy in Pediatric Critical Illness
Timothy E. Bunchman
See related article on page 568.

515 Risk Factor Paradox in CKD and ESRD: Does a Healthy Lifestyle Matter?
Srinivasan Beddhu and Jo Abraham
See related article on page 602.

518 Making the Crooked Way Straight: Interpreting Geography and Health Care Delivery in CKD
Kevin C. Abbott, Robert Nee, and Christina M. Yuan
See related article on page 610.

520 Assessments of Causal Effects—Theoretically Sound, Practically Unattainable, and Clinically Not So Relevant
Wolfgang C. Winkelmayer and Georg Heinze
See related article on page 619.

Original Articles

Acute Kidney Injury /Acute Renal Failure

523 AKI Associated with Synthetic Cannabinoids: A Case Series
Gautam Kantilal Bhanushali, Gaurav Jain, Huma Fatima, Leah J. Leisch, and Denyse Thornley-Brown

527 Predictors of Death and Dialysis in Severe AKI: The UPHS-AKI Cohort
Francis Perry Wilson, Wei Yang, and Harold I. Feldman

Chronic Kidney Disease

538 Peginesatide for Maintenance Treatment of Anemia in Hemodialysis and Nondialysis Patients Previously Treated with Darbepoetin Alfa
Steven Fishbane, Simon D. Roger, Edouard Martin, Grant Runyan, Janet O’Neil, Ping Qiu, and Francesco Locatelli

546 TGF Expression and Macrophage Accumulation in Atherosclerotic Renal Artery Stenosis

Clinical Nephrology

554 Genetics and Outcome of Atypical Hemolytic Uremic Syndrome: A Nationwide French Series Comparing Children and Adults
Véronique Fremeaux-Bacchi, Fadi Fakhouri, Arnaud Garnier, Frank Bienaimé, Marie-Agnès Dragon-Durey, Stéphanie Ngo, Bruno Moulin, Aude Servais, François Provot, Lionel Rostaing, Stéphane Burtey, Patrick Niaudet, Georges Deschênes, Yvon Lebranchu, Julien Zuber, and Chantal Loirat

Clinical Pharmacology

563 Breastfeeding and Tacrolimus: Serial Monitoring in Breast-Fed and Bottle-Fed Infants
Kate Bramham, Gary Chusney, Janet Lee, Liz Lightstone, and Catherine Nelson-Piercy
Critical Care Nephrology

**Nutrition Support among Critically Ill Children with AKI**

Ursula G. Kyle, Ayse Akcan-Arikan, Renán A. Orellana, and Jorge A. Coss-Bu

See related editorial on page 513.

**Epidemiology and Outcomes**

**Preemptive Deceased Donor Kidney Transplantation: Considerations of Equity and Utility**

Morgan E. Grams, B. Po-Han Chen, Josef Coresh, and Dorry L. Segev

**Comparison of Serum Concentrations of β-Trace Protein, β2-Microglobulin, Cystatin C, and Creatinine in the US Population**

Stephen P. Juraschek, Josef Coresh, Lesley A. Inker, Andrew S. Levey, Anna Köttgen, Meredith C. Foster, Brad C. Astor, John H. Eckfeldt, and Elizabeth Selvin

**Hypothyroidism and Mortality among Dialysis Patients**

Connie M. Rhee, Erik K. Alexander, Ishir Bhan, and Steven M. Brunelli

**Adherence to a Healthy Lifestyle and All-Cause Mortality in CKD**

Ana C. Ricardo, Magdalena Madero, Wei Yang, Cheryl Anderson, Matthew Menezes, Michael J. Fischer, Mary Turyk, Martha L. Daviglus, and James P. Lash

See related editorial on page 515.

**The Associations between Race and Geographic Area and Quality-of-Care Indicators in Patients Approaching ESRD**

Guofen Yan, Alfred K. Cheung, Jennie Z. Ma, Alison J. Yu, Tom Greene, M. Norman Oliver, Wei Yu, and Keith C. Norris

See related editorial on page 518.

**ESRD and Chronic Dialysis**

**Comparing Mortality of Peritoneal and Hemodialysis Patients in the First 2 Years of Dialysis Therapy: A Marginal Structural Model Analysis**


See related editorial on page 520.

**Genetics**

**Screening of Male Dialysis Patients for Fabry Disease by Plasma Globotriaosylsphingosine**

Hiroki Maruyama, Takuma Takata, Yutaka Tsubata, Ryushi Tazawa, Kiyoe Goto, Jun Tohyama, Ichiei Narita, Hidekatsu Yoshioka, and Satoshi Ishii

**Simultaneous Sequencing of 24 Genes Associated with Steroid-Resistant Nephrotic Syndrome**

Hugh J. McCarthy, Agnieszka Bierzynska, Matt Wherlock, Milos Ognjanovic, Larissa Kerecuk, Shivaram Hegde, Sally Feather, Rodney D. Gilbert, Leah Krischock, Caroline Jones, Manish D. Sinha, Nicholas J.A. Webb, Martin Christian, Margaret M. Williams, Stephen Marks, Ania Koziell, Gavin I. Welsh, and Moin A. Saleem, on behalf of RADAR the UK SRNS Study Group

**Nephrolithiasis**

**1,25-(OH)2D-24 Hydroxylase (CYP24A1) Deficiency as a Cause of Nephrolithiasis**

Galina Nesterova, May Christine Malicdan, Kaori Yasuda, Toshiyuki Sakaki, Thierry Viboux, Carla Ciccone, Ronald Horst, Yan Huang, Gretchen Golas, Wendy Introne, Marjan Huizing, David Adams, Cornelius F. Boerkoel, Michael T. Collins, and William A. Gahl

**Attending Rounds**

**AKI in a Hospitalized Patient with Cellulitis**

Mark A. Perazella
Mini-Review

665 Antiplatelet Therapy in the Management of Cardiovascular Disease in Patients with CKD: What Is the Evidence?
Nishank Jain, S. Susan Hedayati, Ravindra Sarode, Subhash Banerjee, and Robert F. Reilly

Special Features

675 Communication Skills Training for Dialysis Decision-Making and End-of-Life Care in Nephrology
Jane O. Schell, Jamie A. Green, James A. Tulsky, and Robert M. Arnold

681 Introduction: Perspectives on Integrated Nephrology Care
Paul M. Palevsky

682 Considering an Integrated Nephrology Care Delivery Model: Six Principles for Quality
L. Lee Hamm, Thomas H. Hostetter, and Rachel N. Shaffer, on behalf of the ASN Accountable Care Organization Task Force

687 Nephrology Care in a Fully Integrated Care Model: Lessons from the Geisinger Health System
Evan Norfolk and James Hartle

694 Toward Population Management in an Integrated Care Model
Franklin W. Maddux, Stephen McMurray, and Allen R. Nissenson

Erratum

701 Correction

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On the Cover

What's the diagnosis? A middle-aged previously healthy patient was referred to the nephrology service for evaluation of acute kidney injury (AKI) and proteinuria. Serum free light chain test revealed an elevated kappa/lambda ratio while urine immunoelectrophoresis revealed elevated monoclonal kappa light chains. The patient underwent kidney biopsy, which demonstrated both cast nephropathy and light chain deposition disease (LCDD). Bone marrow biopsy revealed 15% abnormal plasma cells, consistent with a diagnosis of multiple myeloma. In the upper left panel, fractured casts with associated mononuclear cell and giant cell reaction are noted in two tubular lumens. This is consistent with myeloma cast nephropathy—the "myeloma casts" are comprised of kappa light chains bound to Tamm Horsfall proteins (uromodulin). The patient also had findings compatible with LCDD. In the upper right panel, a glomerulus with nodular mesangial expansion is present. Deposition of monoclonal light chains within the mesangium and glomerular basement membranes result in this glomerulopathy. LCDD does not show positive Congo red stain, while Amyloidosis, which may also cause nodular mesangial expansion, is usually Congo red positive. In the lower left panel an immunofluorescence stain demonstrates linear staining for kappa light chains along glomerular and tubular basement membranes (lambda light chain stain is negative). In the lower right panel, electron microscopy reveals granular, powdery electron dense light chain deposits along the glomerular basement membrane. This pattern of light chain deposition was also noted along tubular basement membranes and in mesangial nodules. In contrast to this granular pattern seen with LCDD, amyloidosis would show haphazardly arranged fibrillary substructure in the deposits. (Images and text provided by Gilbert Moeckel and Mark A. Perazella, Yale University, New Haven, Connecticut)