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Editorials

1061 Preeclampsia and Subsequent Cardiovascular Disease: Villain or Innocent Bystander?

Sharon E. Maynard

See related article on page 1126.

1064 Cholecalciferol in Chronic Dialysis Patients: Not Strong Enough?

Bryan Kestenbaum and Ian H. de Boer

See related article on page 1143.

1066  Oh! What a Tangled Web We Weave

Neiha Arora and Glenn M. Chertow

See related article on page 1151.

1068 Sodium Thiosulfate: Mythical Treatment for a Mysterious Disease?

W. Charles O'Neill

See related article on page 1162.

Original Articles

Acute Kidney Injury/Acute Renal Failure

1070 Adverse Drug Events during AKI and Its Recovery

Zachary L. Cox, Allison B. McCoy, Michael E. Matheny, Gautam Bhave, Neeraja B. Peterson, Edward D. Siew, Julia Lewis, Ioana Danciu, Aihua Bian, Ayumi Shintani, T. Alp Ikizler, Erin B. Neal, and Josh F. Peterson

1079 Performance of Kidney Injury Molecule-1 and Liver Fatty Acid-Binding Protein and Combined Biomarkers of AKI after Cardiac Surgery

Chirag R. Parikh, Heather Thiessen-Philbrook, Amit X. Garg, Deepak Kadiyala, Michael G. Shlipak, Jay L. Koyner, Charles L. Edelstein, Prasad Devarajan, Uptal D. Patel, Michael Zappitelli, Catherine D. Krawczeski, Cary S. Passik, and Steven G. Coca, for the TRIBE-AKI Consortium

Chronic Kidney Disease

1089 Segmentation of Individual Renal Cysts from MR Images in Patients with Autosomal Dominant Polycystic Kidney Disease

Kyungsoo Bae, Bumwoo Park, Hongliang Sun, Jinhong Wang, Cheng Tao, Arlene B. Chapman, Vicente E. Torres, Jared J. Grantham, Michal Mrug, William M. Bennett, Michael F. Flessner, Doug P. Landsittel, and Kyongtae T. Bae, for the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP)

1098 Association of Plasma Des-acyl Ghrelin Levels with CKD

Rohit K. Gupta, Tamil Kuppasamy, James T. Patrie, Bruce Gaylinn, Jianhua Liu, Michael O. Thoner, and Warren K. Bolton

1106 Glomerular and Tubular Damage Markers in Individuals with Progressive Albuminuria

Ferdau L. Nauta, Lieneke Scheven, Esther Meijer, Wim van Oeveren, Paul E. de Jong, Stephan J.L. Bakker, and Ron T. Gansevoort

Clinical Immunology and Pathology

1115 Association of Urinary Laminin G-Like 3 and Free K Light Chains with Disease Activity and Histological Injury in IgA Nephropathy

Maria Teresa Rocchetti, Massimo Papale, Anna Maria d'Apollo, Ida Valentina Suriano, Anna Maria Di Palma, Grazia Vocino, Eustacchio Montemurno, Leonarda Varraso, Giuseppe Grandaliano, Salvatore Di Paolo, and Loreto Gesualdo

Epidemiology and Outcomes

1126 Preeclampsia and Prevalence of Microalbuminuria 10 Years Later

Miriam Kristine Sandvik, Stein Hallan, Einar Svarstad, and Bjørn Egil Vikse
See related editorial on page 1061.

1135 Short-Term Pretransplant Renal Replacement Therapy and Renal Nonrecovery after Liver Transplantation Alone

Pratima Sharma, Nathan P. Goodrich, Min Zhang, Mary K. Guidinger, Douglas E. Schaebel, and Robert M. Merion

ESRD and Chronic Dialysis

1143 Effects of Cholecalciferol on Functional, Biochemical, Vascular, and Quality of Life Outcomes in Hemodialysis Patients

Nathan A. Hewitt, Alicia A. O'Connor, Denise V. O'Shaughnessy, and Grahame J. Elder
See related editorial on page 1064.

1151  Disentangling the Ultrafiltration Rate–Mortality Association: The Respective Roles of Session Length and Weight Gain

Jennifer E. Flythe, Gary C. Curhan, and Steven M. Brunelli
See related editorial on page 1066.

1162 Sodium Thiosulfate Therapy for Calcific Uremic Arteriopathy

Sagar U. Nigwekar, Steven M. Brunelli, Debra Meade, Weiling Wang, Jeffrey Hymes, and Eduardo Lacson Jr.
See related editorial on page 1068.

1171 Geographic Variation in Black–White Differences in End-of-Life Care for Patients with ESRD

Bernadette A. Thomas, Rudolph A. Rodriguez, Edward J. Boyko, Cassianne Robinson-Cohen, Annette L. Fitzpatrick, and Ann M. O'Hare

Genetics

1179 Severe Prenatal Renal Anomalies Associated with Mutations in *HNF1B* or *PAX2* Genes

Leire Madariaga, Vincent Morinière, Cécile Jeanpierre, Raymonde Bouvier, Philippe Loget, Jelena Martinovic, Pierre Dechelotte, Nathalie Leporrier, Christel Thauvin-Robinet, Uffe Birk Jensen, Dominique Gaillard, Michele Mathieu, Bruno Turlin, Tania Attie-Bitach, Rémi Salomon, Marie-Claire Gübler, Corinne Antignac, and Laurence Heidet

Health Services Research

1188 Quality of Care for First Nations and Non-First Nations People with Diabetes

Vinay Deved, Nathalie Jette, Hude Quan, Marcello Tonelli, Braden Manns, Andrea Soo, Cheryl Barnabe, and Brenda R. Hemmelgarn, for the Alberta Kidney Disease Network

Hypertension

1195 Vascular and Renal Hemodynamic Changes after Renal Denervation

Christian Ott, Rolf Janka, Axel Schmid, Stephanie Titze, Tilmann Ditting, Paul A. Sobotka, Roland Veelken, Michael Uder, and Roland E. Schmieder

Mineral Metabolism/Bone Disease

1202 24-Hour Urine Phosphorus Excretion and Mortality and Cardiovascular Events

Heather L. Palomino, Dena E. Rifkin, Cheryl Anderson, Michael H. Criqui, Mary A. Whooley, and Joachim H. Ix

Moving Points in Nephrology


- 1211** **Interventional Nephrology: What the Nephrologist Needs to Know about Vascular Access**
Micah R. Chan
- 1213** **Vascular Access Morbidity and Mortality: Trends of the Last Decade**
Charmaine E. Lok and Robert Foley
- 1220** **Interventional Nephrology: Physical Examination as a Tool for Surveillance for the Hemodialysis Arteriovenous Access**
Loay Salman and Gerald Beathard
- 1228** **Interventional Nephrology: When Should You Consider a Graft?**
Aris Q. Urbanes
- 1234** **Interventional Nephrology: Catheter Dysfunction—Prevention and Troubleshooting**
Vandana Dua Niyyar and Micah R. Chan
- 1244** **Interventional Nephrology: Novel Devices that Will One Day Change Our Practice**
Alexander S. Yevzlin and Amanda M. Valliant

Public Policy Series

- 1252** **The Coming Fiscal Crisis: Nephrology in the Line of Fire**
Martin J. Andersen and Allon N. Friedman
- 1258** **Future of Medicare Immunosuppressive Drug Coverage for Kidney Transplant Recipients in the United States**
Bekir Tanriover, Patricia W. Stone, Sumit Mohan, David J. Cohen, and Robert S. Gaston

Special Feature

- 1267** **American Society of Nephrology Quiz and Questionnaire 2012: Transplantation**
Daniel C. Brennan, Richard J. Glassock, and Anthony J. Bleyer

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On the Cover

What's the diagnosis? This electronmicrograph (original magnification $\times 20,000$) is from the renal biopsy of a 53 year-old woman with nephrotic syndrome. It shows fibrillar material in the glomerular basement membrane, and also in parallel “spicules” which are surrounded by podocyte cytoplasm. These fibrils measured 12 nm in average thickness. A Congo red stain showed red-green birefringent staining under polarized light microscopy and the deposits stained for lambda light chain, consistent with amyloidosis, AL lambda type. The differential diagnosis of fibrillar deposits in the kidney includes amyloidosis, fibrillary glomerulonephritis, diabetic fibrillosis, collagenofibrotic glomerulopathy, and fibronectin glomerulopathy. A combination of Congo red stain (and other amyloid stains), immunohistochemical stains, and electron microscopy permits distinction of these entities. Specifically, the thickness and distribution of the fibrils is important, with amyloid fibrils usually having a random orientation. However, amyloid deposits in the glomerular basement membrane may occasionally form distinctive spicules arranged perpendicular to the surface, mimicking the basement membrane spikes of membranous nephropathy. In this case, the spicules appear to be engulfed by the podocyte but this is likely an artifact. The pathogenesis of this peculiar arrangement of amyloid fibrils at the interface of the of the glomerular basement membrane and overlying podocyte is unknown. $63\times 39\text{mm}$ (600×600 DPI)