Editorials

1467 AKI Is Around the World but Public Recognition Is Lacking
Bruce A. Molitoris
See related article on page 1482.

1469 Diet: The “Keys” to Longevity
Holly Kramer
See related article on page 1548.

1471 Peritonitis in the Patient on Peritoneal Dialysis: Does the Composition of the Dialysis Fluid Make a Difference?
Danica Lam and Joanne M. Bargman
See related article on page 1556.

1474 Time to Improve Fluid Management in Hemodialysis: Should We Abandon Clinical Assessment and Routinely Use Bioimpedance?
Adrian Covic and Mihai Onofriescu
See related article on page 1575.

Original Articles

Acute Kidney Injury/Acute Renal Failure

1476 Regional Variation in the Incidence of Dialysis-Requiring AKI in the United States
Raymond K. Hsu, Charles E. McCulloch, Elaine Ku, R. Adams Dudley, and Chi-yuan Hsu

1482 World Incidence of AKI: A Meta-Analysis
Paweena Susantitaphong, Dinna N. Cruz, Jorge Cerda, Maher Abulliara, Fahad Alqahtani, Ioannis Koulouridis, and Bertrand L. Jaber, for the Acute Kidney Injury Advisory Group of the American Society of Nephrology
See related editorial on page 1467.

Chronic Kidney Disease

1494 Effects of Exercise and Lifestyle Intervention on Cardiovascular Function in CKD
Erin J. Howden, Rodel Leano, William Petchey, Jeff S. Coombes, Nicole M. Isbel, and Thomas H. Marwick

1502 Association of Nocturnal Hypoxemia with Progression of CKD
Yusuke Sakaguchi, Tsuguru Hatta, Terumasa Hayashi, Tatsuya Shoji, Akira Suzuki, Kodo Tomida, Noriyuki Okada, Hiromi Rakugi, Yoshitaka Isaka, and Yoshiharu Tsubakihara

1508 Renal Clearance and Intestinal Generation of p-Cresyl Sulfate and Indoxyl Sulfate in CKD
Ruben Poesen, Liesbeth Viaene, Kristin Verbeke, Kathleen Claes, Bert Bammens, Ben Sprangers, Maarten Naesens, Yves Vanrenterghem, Dirk Kuypers, Pieter Evenepoel, and Björn Meijers

Clinical Immunology and Pathology

1515 Renal Amyloidosis: Origin and Clinicopathologic Correlations of 474 Recent Cases

Clinical Nephrology

1524 Comparison of Risk Factors and Outcomes in HIV Immune Complex Kidney Disease and HIV-Associated Nephropathy
Matthew C. Foy, Michelle M. Estrella, Gregory M. Lucas, Faryal Tahir, Derek M. Fine, Richard D. Moore, and Mohamed G. Atta
Original Articles (Continued)

1533 Extracorporeal Therapy for Dabigatran Removal in the Treatment of Acute Bleeding: A Single Center Experience
Tripti Singh, Thin Thin Maw, Brian L. Henry, Nuria M. Pastor-Soler, Mark L. Unruh, Kenneth R. Hallows, and Thomas D. Nolin

Epidemiology and Outcomes
1540 Differences in Progression to ESRD between Black and White Patients Receiving Predialysis Care in a Universal Health Care System
Tessa O. van den Beukel, Moniek C.M. de Goeij, Friedo W. Dekker, Carl E.H. Siegert, and Nynke Halbesma, for the PREPARE Study Group

1548 Mediterranean Diet, Kidney Function, and Mortality in Men with CKD
Xiaoyan Huang, Jose Juan Jimenez-Moleon, Bengt Lindholm, Tommy Cederholm, Johan Arlonov, Ulf Riserus, Per Sjogren, and Juan Jesus Carrero
See related editorial on page 1469.

ESRD and Chronic Dialysis
1556 Association of Biocompatible Peritoneal Dialysis Solutions with Peritonitis Risk, Treatment, and Outcomes
Yeoungjee Cho, Sunil V. Badve, Carmel M. Hawley, Stephen P. McDonald, Fiona G. Brown, Neil Boudville, Kym M. Bannister, Philip A. Clayton, and David W. Johnson
See related editorial on page 1471.

1564 Association of Left Ventricular Longitudinal Strain with Mortality among Stable Hemodialysis Patients with Preserved Left Ventricular Ejection Fraction
Yen-Wen Liu, Chi-Ting Su, Junne-Ming Sung, Saprina P.H. Wang, Yu-Ru Su, Chun-Shin Yang, Liang-Min Tsai, Jyh-Hong Chen, and Wei-Chuan Tsai

1575 Bioimpedance-Guided Fluid Management in Hemodialysis Patients
Ulrich Moissl, Marta Arias-Guille, Peter Wabel, Nestor Fontsered, Montserrat Carrera, Jose Maria Campistol, and Francisco Maduell
See related editorial on page 1474.

Hypertension
1583 Prevalence of Apparent Treatment-Resistant Hypertension among Individuals with CKD
Rikki M. Tanner, David A. Calhoun, Emmy K. Bell, C. Barrett Bowling, Orlando M. Gutierrez, Marguerite R. Irvin, Daniel T. Lackland, Suzanne Oparil, David Warnock, and Paul Muntner

Mini-Review
1591 Dabigatran and Kidney Disease: A Bad Combination
Felix Knauf, C. Michael Chaknos, Jeffrey S. Berns, and Mark A. Perazella

Special Features
1599 Kidney Research National Dialogue Overview and Commentary
Krystyna E. Rys-Sikora, Christian J. Ketchum, and Robert A. Star, on behalf of the Kidney Research National Dialogue (KRND) Editorial Board

1603 Diabetic Nephropathy: A National Dialogue

1606 AKI: A Path Forward
Joseph V. Bonventre, David Basile, Kathleen D. Liu, Dianne McKay, Bruce A. Molitoris, Karl A. Nath, Thomas L. Nickolas, Mark D. Okusa, Paul M. Palevsky, Rick Schnellmann, Krystyna Rys-Sikora, Paul L. Kimmel, and Robert A. Star, on behalf of the Kidney Research National Dialogue (KRND)
Special Features (Continued)

1609  Fostering Innovation, Advancing Patient Safety: The Kidney Health Initiative
Patrick Archdeacon, Rachel N. Shaffer, Wolfgang C. Winkelmayer, Ronald J. Falk, and Prabir Roy-Chaudhury

1618  Prevention of Contrast-Induced AKI: A Review of Published Trials and the Design of the Prevention of Serious Adverse Events following Angiography (PRESERVE) Trial
Steven D. Weisbord, Martin Gallagher, James Kaufman, Alan Cass, Chirag R. Parikh, Glenn M. Chertow, Kendrick A. Shunk, Peter A. McCullough, Michael J. Fine, Maria K. Mor, Robert A. Lew, Grant D. Huang, Todd A. Conner, Mary T. Brophy, Joanne Lee, Susan Soliva, and Paul M. Palevsky

1632  American Society of Nephrology Quiz and Questionnaire 2012: Renal Replacement Therapy
Rajnish Mehrotra, Richard J. Glassock, and Anthony J. Bleyer

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On the Cover
What’s the diagnosis? Nodular glomerulosclerosis has classically been described in patients with long-standing diabetes mellitus. High blood glucose levels are toxic for mesangial cells, resulting in mesangial matrix overproduction and diffuse mesangial and eventually nodular glomerulosclerosis. A similar effect on mesangial cells can be seen in monoclonal immunoglobulin deposition diseases (most commonly kappa light chain deposition disease) or in heavy smokers where some unidentified components in cigarette smoke have a toxic effect on mesangial cells in predisposed patients. Nodular expansion and glomerulosclerosis can also be seen in chronic immune complex-mediated glomerulonephritides, such as a membranoproliferative glomerulonephritis and lupus nephritis; in such instances, one can still detect immune complex deposition by immunofluorescence and electron microscopy studies. Thrombotic angiopathies that have resulted in significant mesangiolysis can present with a nodular type of glomerulosclerosis as the lesions heal and sclerose. Amyloidosis does not cause nodular sclerosis, although the mesangium may show nodular expansion by amorphous and acellular material; these do not contain collagen and therefore the basement membrane silver stains will be negative, unlike in above-mentioned causes of nodular glomerulosclerosis. (Image and text provided by Dr. Vanesa Bijol, Brigham and Women's Hospital)