Editorials

235 World Kidney Day 2011: Protect Your Kidneys, Save Your Heart
William G. Couser and Miguel C. Riella

239 Source Matters: From Phosphorus Load to Bioavailability
Masafumi Fukagawa, Hirotaka Komaba, and Ken-ichi Miyamoto
See related article on page 257.

Original Articles

Chronic Kidney Disease

241 FGF-23 as a Predictor of Renal Outcome in Diabetic Nephropathy

248 Vascular Risk Factors and Cognitive Impairment in Chronic Kidney Disease: The Chronic Renal Insufficiency Cohort (CRIC) Study

257 Vegetarian Compared with Meat Dietary Protein Source and Phosphorus Homeostasis in Chronic Kidney Disease
Sharon M. Moe, Miriam P. Zidehsarai, Mary A. Chambers, Lisa A. Jackman, J. Scott Radcliffe, Laurie L. Trevino, Susan E. Donahue, and John R. Asplin
See related editorial on page 239.

Diagnosis

265 Urinary Cystatin C as a Potential Risk Marker for Cardiovascular Disease and Chronic Kidney Disease in Patients with Obesity and Metabolic Syndrome
Noriko Satoh-Asahara, Takayoshi Saganami, Takaumi Majima, Kazuhiko Kotani, Yasuhisa Kato, Rika Araki, Kazunori Koyama, Taiichiro Okajima, Makito Tanabe, Mariko Oishi, Akihiro Himeno, Shigeo Kono, Akira Sugawara, Masakazu Hattori, Yoshihiro Ogawa, Akira Shimatsu, and the Japan Obesity and Metabolic Syndrome Study (JOMS) Group

Dialysis

274 Hyperfiltration Affects Accuracy of Creatinine eGFR Measurement
Shih-Han S. Huang, Ajay P. Sharma, Abeer Yasin, Robert M. Lindsay, William F. Clark, and Guido Filler

281 Role of Residual Renal Function in Phosphate Control and Anemia Management in Chronic Hemodialysis Patients
E. Lars Penne, Neelke C. van der Weerd, Muriel P.C. Grooteman, Albert H.A. Mazairac, Marinus A. van den Dorpel, Menso J. Nubé, Michiel L. Bots, Renée Lévesque, Piet M. ter Wee, and Peter J. Blankestijn, on behalf of the CONTRAST investigators

290 Contribution of Residual Function to Removal of Protein-Bound Solutes in Hemodialysis
Ilian O. Marquez, Shouieb Tambra, Frank Y. Luo, You Li, Natalie S. Plummer, Thomas H. Hostetter, and Timothy W. Meyer
Abandoning Peracetic Acid-Based Dialyzer Reuse Is Associated with Improved Survival
Eduardo Lacson, Jr., Weiling Wang, Ann Mooney, Norma Olsthun, J. Michael Lazarus, and Raymond M. Hakim

Large Artery Calcification on Dialysis Patients Is Located in the Intima and Related to Atherosclerosis
Blai Coll, Angels Betriu, Montserrat Martínez-Alonso, María Luisa Amoedo, María Vittoria Arcidiacono, Merce Borras, Jose Manuel Valdivielso, and Elvira Fernández

Continuous Flow Peritoneal Dialysis: First Experience in Children with Acute Renal Failure
Renske Raaijmakers, Cornelis H. Schröder, Priya Gajjar, Andrew Argent, and Peter Nourse

Cystatin C Reduction Ratio Depends on Normalized Blood Liters Processed and Fluid Removal during Hemodialysis
Shih-Han S. Huang, Guido Filler, Abeer Yasin, and Robert M. Lindsay

Epidemiology and Outcomes

Opioid and Benzodiazepine Use in End-Stage Renal Disease: A Systematic Review
Ahraaz Wyne, Raman Rai, Meaghan Cuerden, William F. Clark, and Rita S. Suri

Primary Care-Specialist Collaboration in the Care of Patients with Chronic Kidney Disease

Hereditary Disease

Clinical Value of NPHS2 Analysis in Early- and Adult-Onset Steroid-Resistant Nephrotic Syndrome
Sheila Santín, Bábara Tazón-Vega, Irene Silva, María Ángeles Cobo, Isabel Giménez, Patricia Ruiz, Rafael García-Maset, José Ballarín, Roser Torra, and Elisabet Aris, on behalf of the FSGS Spanish Study Group

Renal, Ocular, and Neuromuscular Involvements in Patients with CLDN19 Mutations
Stanislas Faguer, Dominique Chauveau, Pascal Cintas, Ivan Tack, Olivier Cointault, Lionel Rostaing, Rosa Vargas-Poussou, and David Ribes

Copeptin, a Surrogate Marker of Vasopressin, Is Associated with Disease Severity in Autosomal Dominant Polycystic Kidney Disease
Esther Meijer, Stephan J.L. Bakker, Eric J. van der Jagt, Gerjan Navis, Paul E. de Jong, Joachim Struck, and Ron T. Gansevoort

Magnetic Resonance Imaging of Kidney and Cyst Volume in Children with ADPKD
Melissa A. Cadnapaphornchai, Amirali Masoumi, John D. Strain, Kim McFann, and Robert W. Schrier

Mineral Metabolism/Bone Disease

Breast Arterial Calcification: A Marker of Medial Vascular Calcification in Chronic Kidney Disease

Effects of Dietary Phosphate and Calcium Intake on Fibroblast Growth Factor-23
Marc G. Vervloet, Frans J. van Ittersum, Rahel M. Büttler, Annemieke C. Heijboer, Marinus A. Blankenstein, and Piet M. ter Wee

Policy

Race Disparities in U.S. Nephrology Fellowship Training
Chavon Onumah, Paul L. Kimmel, and Mark E. Rosenberg

Renal Transplantation

Thrombotic Microangiopathy and Peritubular Capillary C4d Expression in Renal Allograft Biopsies
Shane M. Meehan, Joseph Kremer, Farah N. Ali, Jessica Curley, Susana Marino, Anthony Chang, and Pradeep V. Kadambi

Early Steroid Withdrawal in Repeat Kidney Transplantation
Muhammad A. Mujtaba, Tim E. Taber, William C. Goggins, Muhammad S. Yaqub, Dennis P. Mishler, Martin L. Milgrom, Jonathan A. Fridell, Andrew Lobashevsky, John A. Powelson, and Asif A. Sharfuddin
Autologous Mesenchymal Stromal Cells and Kidney Transplantation: A Pilot Study of Safety and Clinical Feasibility
Norberto Perico, Federica Casiraghi, Martino Introna, Eliana Gotti, Marta Todeschini, Regiane Aparecida Cavinato, Chiara Capelli, Alessandro Rambaldi, Paola Cassis, Paola Rizzo, Monica Cortinovis, Maddalena Marasà, Josee Golay, Marina Noris, and Giuseppe Remuzzi

Single Time Point Immune Function Assay (ImmuKnow™) Testing Does Not Aid in the Prediction of Future Opportunistic Infections or Acute Rejection
Janna Huskey, Jane Gralla, and Alexander C. Wiseman

Switching from Calcineurin Inhibitor-based Regimens to a Belatacept-based Regimen in Renal Transplant Recipients: A Randomized Phase II Study
Lionel Rostaing, Pablo Massari, Valter Duro Garcia, Eduardo Mancilla-Urrea, Georgy Nainan, Maria del Carmen Rial, Steven Steinberg, Flavio Vincenti, Rebecca Shi, Greg Di Russo, Dolca Thomas, and Josep Grinyó

Mini-Review
Prevention and Control of Phosphate Retention/Hyperphosphatemia in CKD-MBD: What Is Normal, When to Start, and How to Treat?
Kevin J. Martin and Esther A. González

In-Depth Review
Peritoneal Dialysis First: Rationale
Kunal Chaudhary, Harbaksh Sangha, and Ramesh Khanna

Special Feature
Dialysis at a Crossroads: 50 Years Later
Thomas Parker III, Raymond Hakim, Allen R. Nissenson, Theodore Steinman, and Richard J. Glassock

On the Cover
What’s the Diagnosis? Renal biopsy reveals osmotic nephropathy associated with intravenous Ig (IVIG). Osmotic nephropathy describes a morphologic pattern with vacuolization and swelling of the renal proximal tubular cells, which can result from sucrose (stabilizer in IVIG), hydroxyethyl starch, dextran, mannitol, and contrast media. The clinical spectrum includes both AKI and CKD, but the process can develop and resolve without any obvious kidney injury. Patients with preexisting acute kidney disease or CKD are at greatest risk to develop this lesion because of their decreased ability to degrade and excrete the causative agent. Primarily straight and sometimes convoluted proximal tubules are involved, whereas distal tubules and collecting ducts are spared. The exogenous substances enter cells through pinocytosis whereupon the pinocytotic vacuoles fuse with each other and lysosomes, which fill the cellular cytoplasm. Cell swelling was initially thought to be caused by osmotic effects of the pinocytosed hyperosmolar substance but was subsequently shown to result from the large number of vacuoles and lysosomes. Over time, vacuolization resolves; however, it may persist and be associated with tubular atrophy, interstitial fibrosis, and inflammation. Osmotic nephropathy should be considered when AKI develops in patients who received infusions of the above noted exogenous solutes. (Photo courtesy of Mark A. Perazella Yale University, New Haven, Connecticut)

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