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Editorials

- 1** **CJASN: Turning the Page**
Rajnish Mehrotra
- 3** **Predicting Risk of RRT in Patients with CKD**
Morgan E. Grams and Josef Coresh
See related article on page 87.
- 5** **Screening Women with CKD for the Emperor of All Maladies**
Deidra C. Crews and Waseem Khaliq
See related article on page 95.
- 7** **Early Steroid Withdrawal in Black Transplant Patients: A Selective Process**
Joshua J. Augustine
See related article on page 131.

Original Articles

- Acute Kidney Injury**
- 10** **Association of Preoperative Urinary Uromodulin with AKI after Cardiac Surgery**
Pranav S. Garimella, Bertrand L. Jaber, Hocine Tighiouart, Orfeas Liangos, Michael R. Bennett, Prasad Devarajan, Tarek M. El-Achkar, and Mark J. Sarnak
- Chronic Kidney Disease**
- 19** **Cardiovascular Phenotypes in Children with CKD: The 4C Study**
Franz Schaefer, Anke Doyon, Karolis Azukaitis, Aysun Bayazit, Nur Canpolat, Ali Duzova, Ana Niemirska, Betül Sözeri, Daniela Thurn, Ali Anarat, Bruno Ranchin, Mieczyslaw Litwin, Salim Caliskan, Cengiz Candan, Esra Baskin, Ebru Yilmaz, Sevgi Mir, Marietta Kirchner, Anja Sander, Dieter Haffner, Anette Melk, Elke Wühl, Rukshana Shroff, and Uwe Querfeld for the 4C Study Consortium
- 29** **Interlaboratory Variability in Plasma Creatinine Measurement and the Relation with Estimated Glomerular Filtration Rate and Chronic Kidney Disease Diagnosis**
Elizabeth Lee, Christine P. Collier, and Christine A. White
- Clinical Immunology and Pathology**
- 39** **Staphylococcus Infection–Associated GN – Spectrum of IgA Staining and Prevalence of ANCA in a Single-Center Cohort**
Anjali A. Satoskar, Sarah Suleiman, Isabelle Ayoub, Jessica Hemminger, Samir Parikh, Sergey V. Brodsky, Cherri Bott, Edward Calomeni, Gyongyi M. Nadasdy, Brad Rovin, Lee Hebert, and Tibor Nadasdy
- Clinical Nephrology**
- 50** **Pathogenic Variants in Complement Genes and Risk of Atypical Hemolytic Uremic Syndrome Relapse after Eculizumab Discontinuation**
Fadi Fakhouri, Marc Fila, François Provôt, Yhsou Delmas, Christelle Barbet, Valérie Châtelet, Cédric Rafat, Mathilde Cailliez, Julien Hogan, Aude Servais, Alexandre Karras, Raifah Makdassi, Ferial Louillet, Jean-Philippe Coindre, Eric Rondeau, Chantal Loirat, and Véronique Frémeaux-Bacchi

Epidemiology and Outcomes

60 Associations of Conventional Echocardiographic Measures with Incident Heart Failure and Mortality: The Chronic Renal Insufficiency Cohort

Ruth F. Dubin, Rajat Deo, Nisha Bansal, Amanda H. Anderson, Peter Yang, Alan S. Go, Martin Keane, Ray Townsend, Anna Porter, Matthew Budoff, Shaista Malik, Jiang He, Mahboob Rahman, Jackson Wright, Thomas Cappola, Radhakrishna Kallem, Jason Roy, Daohang Sha, Michael G. Shlipak, and the CRIC Study Investigators

69 Filtration Markers as Predictors of ESRD and Mortality: Individual Participant Data Meta-Analysis

Lesley A. Inker, Josef Coresh, Yingying Sang, Chi-yuan Hsu, Meredith C. Foster, John H. Eckfeldt, Amy B. Karger, Robert G. Nelson, Xun Liu, Mark Sarnak, Lawrence J. Appel, Morgan Grams, Dawei Xie, Paul L. Kimmel, Harold Feldman, Vasam Ramachandran, Andrew S. Levey, for the CKD Biomarkers Consortium

79 Diet Soda Consumption and Risk of Incident End Stage Renal Disease

Casey M. Rebholz, Morgan E. Grams, Lyn M. Steffen, Deidra C. Crews, Cheryl A. M. Anderson, Lydia A. Bazzano, Josef Coresh, and Lawrence J. Appel

87 Predicting 5-Year Risk of RRT in Stage 3 or 4 CKD: Development and External Validation

Emily B. Schroeder, Xiuhai Yang, Micah L. Thorp, Brent M. Arnold, David C. Tabano, Amanda F. Petrik, David H. Smith, Robert W. Platt, and Eric S. Johnson
See related editorial on page 3.

95 Patterns and Predictors of Screening for Breast and Cervical Cancer in Women with CKD

Germaine Wong, Jade S. Hayward, Eric McArthur, Jonathan C. Craig, Danielle M. Nash, Stephanie N. Dixon, Deborah Zimmerman, Abhijat Kitchlu, and Amit X. Garg
See related editorial on page 5.

ESRD and Chronic Dialysis

105 Peritoneal Dialysis Access Revision in Children: Causes, Interventions, and Outcomes

Dagmara Borzych-Duzalka, T. Fazil Aki, Marta Azocar, Colin White, Elizabeth Harvey, Sevgi Mir, Marta Adragna, Erkin Serdaroglu, Rajiv Sinha, Charlotte Samaille, Juan Jose Vanegas, Jameela Kari, Lorena Barbosa, Arvind Bagga, Monica Galanti, Onder Yavascan, Giovanna Leozappa, Maria Szczepanska, Karel Vondrak, Kei-Chiu Tse, Franz Schaefer, and Bradley A. Warady, for the International Pediatric Peritoneal Dialysis Network (IPPN) Registry

113 Monocyte Chemoattractant Protein-1 Levels and Postangioplasty Restenosis of Arteriovenous Fistulas

Chih-Cheng Wu, Tsung-Yan Chen, Mu-Yang Hsieh, Lin Lin, Chung-Wei Yang, Shao-Yuan Chuang, and Der-Cheng Tarng

Renal Transplantation

122 Dialysis Vintage and Outcomes after Kidney Transplantation: A Retrospective Cohort Study

Maria C. Haller, Alexander Kainz, Heather Baer, and Rainer Oberbauer

131 A Comparative Effectiveness Analysis of Early Steroid Withdrawal in Black Kidney Transplant Recipients

David J. Taber, Kelly J. Hunt, Mulugeta Gebregziabher, Tittle Srinivas, Kenneth D. Chavin, Prabhakar K. Baliga, and Leonard E. Egede
See related editorial on page 7.

Glomerular Diseases: Update for the Clinician

140 Patient-Reported Outcomes in Glomerular Disease

David T. Selewski, Aliza Thompson, Sarrit Kovacs, Elektra J. Papadopoulos, Noelle E. Carlozzi, Howard Trachtman, Jonathan P. Troost, Peter A. Merkel, and Debbie S. Gipson

Evidence-Based Nephrology

149 Biomarkers for the Early Detection and Prognosis of Acute Kidney Injury

Rakesh Malhotra and Edward D. Siew

Commentary

174 **Commentary on Biomarkers for Early Detection and Prognosis of AKI**

Bryan Kestenbaum and Stephen L. Seliger

Mini-Review

176 **Renal Toxicities of Novel Agents Used for Treatment of Multiple Myeloma**

Rimda Wanchoo, Ala Abudayyeh, Mona Doshi, Amaka Edeani, Ilya G. Glezerman, Divya Monga, Mitchell Rosner, and Kenar D. Jhaveri

Public Policy Series

190 **Facility Practice Variation to Help Understand the Effects of Public Policy: Insights from the Dialysis Outcomes and Practice Patterns Study (DOPPS)**

Douglas S. Fuller and Bruce M. Robinson

200 **The Healthy People 2020 Objectives for Kidney Disease: How Far Have We Come, and Where Do We Need to Go?**

James B. Wetmore, Jiannong Liu, Suying Li, Yan Hu, Yi Peng, David T. Gilbertson, and Allan J. Collins

210 **ESRD Databases, Public Policy, and Quality of Care: Translational Medicine and Nephrology**

William M. McClellan, Laura C. Plantinga, Adam S. Wilk, and Rachel E. Patzer

On the Cover

What is the diagnosis? A 54-year old man presented with shortness of breath, fatigue and rash on his arms and legs. The patient was an active cocaine user, and last used four days prior to presentation. The patient's rash was an angulated purpuric rash with erythematous rims that were tender to touch (left image). Serum creatinine was 2.1 mg/dL (baseline 0.9 mg/dL). Urinalysis demonstrated 3+ blood, trace leukocyte esterase, and 2+ protein with protein/creatinine ratio of 0.76. Urine sediment revealed dysmorphic red blood cells (middle image) and mixed cellular casts. Other labs include positive anti-MPO, positive IgM antiphospholipid antibodies, elevated rheumatoid factor, negative ANA, and normal complement levels. Kidney biopsy (right image) revealed fibrinoid necrosis of the glomerulus. Immunofluorescence and electron microscopy were negative, consistent with levamisole-induced vasculitis. The patient improved with supportive care and did not require renal replacement therapy.

Cocaine-induced vasculitis is caused by the adulterant, levamisole, which is found in 60-80% of cocaine sold in the United States. In the past, levamisole was employed as an adjuvant treatment for colon cancer and an immunomodulator for various conditions. However, the drug was removed from the market due to agranulocytosis. It is now used in veterinary practices as an anthelmintic agent. The most common clinical manifestations of levamisole-induced vasculitis are arthralgias and skin lesions. Other manifestations include fever, night sweats, myalgias, weight loss, or other constitutional symptoms. Urinalysis positive for protein, blood and cellular casts suggests kidney involvement. MPO-ANCA is positive in all patients and 50% may also have positive PR3-ANCA, which is a tip off to levamisole-associated vasculitis. While urine toxicology can confirm cocaine use within the preceding 2-3 days, testing for levamisole in serum or urine is of limited utility due to the drug's short half-life (approximately 5 hours). Treatment hinges on discontinuation of levamisole and supportive care. Data on treatment are limited but steroids have been used for skin lesions and severe nephropathy with variable results. It is imperative to avoid levamisole re-exposure as there is a greater than 25% risk of recurrence. (*Images and text provided by Bryan Tucker, DO and Mark A. Perazella, MD, Yale University School of Medicine, New Haven, Connecticut*)