Editorials

1105 Pathophysiological Implications of Variability in Blood Tacrolimus Levels in Pediatric and Adolescent Kidney Transplant Recipients
Rachel Becker-Cohen
See related article on page 1194.

1107 Physiology of the Aging Kidney: We Know Where We Are Going, but We Don’t Know How …
Pierre Delanaye, Hans Pottel, and Toralf Melsom
See related article on page 1119.

1110 Health Care for Older Adults with Kidney Failure
Jorge I. Fonseca-Correa and S. Vanita Jassal
See related article on page 1159.

1113 Novel Approaches for the Removal of Uremic Solutes
Mengyao Tang and Sahir Kalim
See related article on page 1168.

1116 Calamari, Hyperkalemia, and Renin-Angiotensin System Blockade
Emily Janak and Holly Kramer
See related article on page 1139.

Original Articles

Chronic Kidney Disease

1119 Age and the Course of GFR in Persons Aged 70 and Above
Elke S. Schaeffner, Natalie Ebert, Martin K. Kuhlmann, Peter Martus, Nina Mielke, Alice Schneider, Markus van der Giet, and Dörte Huscher
See related editorial on page 1107.

Clinical Nephrology

1129 Prevalence and Risk Factors for Kidney Disease and Elevated BP in 2-Year-Old Children Born Extremely Premature
Sangeeta Hingorani, Robert Schmicker, Kaashif A. Ahmad, Ivan D. Frantz, Dennis E. Mayock, Edmund F. La Gamma, Mariana Baserga, Janine Y. Khan, Maureen M. Gilmore, Tonya Robinson, Patrick Brophy, Patrick J. Heagerty, Sandra E. Juul, Stuart Goldstein, and David Askenazi, for the PEnUT Trial Consortium

1139 Short-Term Changes in Serum Potassium and the Risk of Subsequent Vascular Events and Mortality: Results from a Randomized Controlled Trial of ACE Inhibitors
Toshiaki Ohkuma, Katie Harris, Mark Cooper, Diederick E. Grobbee, Pavel Hamet, Stephen Harrap, Giuseppe Mancia, Michel Marre, Anushka Patel, Anthony Rodgers, Bryan Williams, Mark Woodward, and John Chalmers, on behalf of the ADVANCE Collaborative Group
See related editorial on page 1116.

Glomerular and Tubulointerstitial Diseases

1150 Short- and Long-Term Progression of Kidney Involvement in Systemic Lupus Erythematosus Patients with Low-Grade Proteinuria
Shudan Wang, Allan Spielman, Mindy Ginsberg, Michelle Petri, Brad H. Rovin, Jill Buyon, and Anna Broder
Maintenance Dialysis
1159 Quality of Life before and after the Start of Dialysis in Older Patients
Esther N.M. de Rooij, Yvette Meuleman, Johan W. de Fijter, Saskia Le Cessie, Kitty J. Jager, Nicholas C. Chesnaye, Marie Evans, Agneta A. Pagels, Fergus J. Caskey, Claudia Torino, Gaetana Porto, Maciej Szymczak, Christiane Drechsler, Christoph Wanner, Friedo W. Dekker, and Ellen K. Hoogeveen, on behalf of the EQUAL study investigators
See related editorial on page 1110.

1168 Removal of Uremic Solutes from Dialysate by Activated Carbon
Seohyung Lee, Tammy L. Sirich, Ignacio J. Blanco, Natalie S. Plummer, and Timothy W. Meyer
See related editorial on page 1113.

1176 Long-Term Effect of Physical Exercise on the Risk for Hospitalization and Death in Dialysis Patients: A Post-Trial Long-Term Observational Study
Francesca Mallamaci, Graziella D’Arrigo, Giovanni Tripepi, Nicola Lamberti, Claudia Torino, Fabio Manfredini, and Carmine Zoccali

Mineral Metabolism
1183 Association of Genetically Predicted Fibroblast Growth Factor-23 with Heart Failure: A Mendelian Randomization Study

Transplantation
1194 Patterns in Tacrolimus Variability and Association with De Novo Donor-Specific Antibody Formation in Pediatric Kidney Transplant Recipients
See related editorial on page 1105.

1204 Association of HLA Mismatches and Histology Suggestive of Antibody-Mediated Injury in the Absence of Donor-Specific Anti-HLA Antibodies
Aleksandar Senev, Eyevine Lerut, Maarten Coemans, Jasper Callemeen, Hannah Charlotte Copley, Frans Claas, Priyanka Koshy, Vasilis Kosmokaptsis, Dirk Kuypers, Ben Sprangers, Amaryllis Van Craenenbroeck, Elisabet Van Loon, Vicky Van Sandt, Marie-Paule Emonds, and Maarten Naesens

Research Letter
1216 Anxiety, Comorbid Depression, and Dialysis Symptom Burden
Daniel Cukor, Stephanie Donahue, Sri Lekha Tummalapalli, Andrew Bohmart, and Jeffrey Silberzweig

Errata
1218 Correction: Fractional Excretion of Sodium (FENa): An Imperfect Tool for a Flawed Question
1219 Correction: CRRT Fluid Choices: A Solution for a Common Problem?

Critical Care Nephrology and Acute Kidney Injury
1220 Drug-Induced Acute Kidney Injury
Mark A. Perazella and Mitchell H. Rosner
1234 Radiographic Contrast Media and the Kidney
Winn Cashion and Steven D. Weisbord

Kidney Case Conference: How I Treat
1243 How I Treat IgA Nephropathy
Heather N. Reich and Jürgen Floege

Perspectives
1247 Prescribing Nirmatrelvir/Ritonavir for COVID-19 in Advanced CKD
Swapnil Hiremath, Michaeline McGuinty, Christos Argyropoulos, K. Scott Brimble, Pierre Antoine Brown, Zain Chagla, Rebecca Cooper, Stephanie Hoar, David Juurlink, Darin Treleaven, Michael Walsh, Angie Yeung, and Peter Blake
vasculature is patchy, and the diagnosis may be missed if not enough sections are examined. There is no speci-

Left image (light microscopy, H&E [400x])—glomerulosclerosis.

cholesterol embolization in the kidney and acute tubular necrosis superimposed on advanced chronic kidney injury with features of diabetic

and kidney ultrasound, was normal/negative. Kidney biopsy showed severe small arterial cholesterol clefts, suggestive of extensive

initiated during the same admission. Extensive workup for AKI, including hepatitis panel, serum and urine electrophoresis, immunofixation

and kidney ultrasound, was normal/negative. Kidney biopsy showed severe small arterial cholesterol clefts, suggestive of extensive

cholesterol embolization in the kidney and acute tubular necrosis superimposed on advanced chronic kidney injury with features of diabetic
glomerulosclerosis.

Cholesterol crystal embolism is a common cause of kidney failure in older patients with atherosclerosis, and most of them were older than 70

years.1 The risk factors for cholesterol crystal embolism include male sex, White race, tobacco use, cardiovascular disease, cerebrovascular
disease, hypertension, hyperlipidemia, diabetes, hypercoagulability, abdominal aortic aneurysm, peripheral vascular disease, and family

history of vascular disease.2 The exact incidence of cholesterol crystal embolism is often underdiagnosed with at least 4% of all inpatient

admission.3 It is estimated that about 30%–85% of patients with cholesterol crystal embolism have a history of invasive vascular procedure in

the preceding 3 months, while only 4.3% had cholesterol embolism in age-matched controls that did not have invasive vascular procedure.4

Clinical presentation includes AKI, CKD, renal infarction, uncontrolled hypertension, and allograft failure. Kidney biopsy is usually
diagnostic, and the characteristic lesion is occlusion of cholesterol emboli in the lumina of arcuate, interlobular arteries, and glomeruli. The

emboli of cholesterol crystals generally are defined by the empty, biconvex, and needle-shaped clefts, appearing as “ghosts,” because

cholesterol crystals usually dissolve during routine histologic preparation procedures. However, in frozen sections, the crystals are

birefringent under polarized light and give positive histochemical reactions for lipids.5 Interlobular and arcuate arteries usually show

perivascular polymorphonuclear and eosinophilic infiltration. Glomeruli can have normal morphology in the initial stage, but ischemic

retraction of podocyte foot processes, focal segmental glomerulosclerosis (FSGS), interstitial fibrosis, perivascular fibrosis around the

occluded vessels, and tubular atrophy can be seen frequently due to ongoing ischemic injury in the later stages of the disease. Generally,
immunofluorescence staining for immunoglobulins are negative. Kidney biopsy has a sensitivity of about 75%. Involvement of renal

vasculature is patchy, and the diagnosis may be missed if not enough sections are examined.6 There is no specific therapy for cholesterol
crystal embolism. Withdrawal of any form of anticoagulants, postponing aortic catheterization, and surgery should be considered first to

avoid recurrence of cholesterol crystal embolism. The aim of treatment is to prevent the progression of tissue ischemia and further showering of

cholesterol crystals or provide supportive care in the event of kidney failure.7

References:

(Images and text provided by Mohankumar Doraiswamy, Division of Nephrology, The Ohio State University Wexner Medical Center, Columbus, Ohio; Sampath Thiruvedi, Division of Nephrology, Kettering Medical Center, Kettering, Ohio; and Anjali Satoskar, Division of Pathology, The Ohio State University Wexner Medical Center, Columbus, Ohio)