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Editorials

1273 Is There Clinical Value in Measuring suPAR Levels in FSGS?

Sanja Sever, Howard Trachtman, Changli Wei, and Jochen Reiser
See related article on page 1304.

1276  What Determines Whether a Patient Initiates Chronic Renal Replacement Therapy?

Michael J. Germain and Lewis M. Cohen
See related article on page 1327.

1279 Pulmonary Congestion in Hemodialysis: An Old Chestnut Worth Screening For?

Austin G. Stack and Liam F. Casserly
See related article on page 1343.

1282 Fracture Risk in CKD

Kristine E. Ensrud
See related article on page 1367.

Original Articles

Acute Kidney Injury /Acute Renal Failure

1284 Impaired Kidney Function at Hospital Discharge and Long-Term Renal and Overall Survival in Patients Who Received CRRT

Susanne Stads, Gijs Fortrie, Jasper van Bommel, Robert Zietse, and Michiel G.H. Betjes

Chronic Kidney Disease

1293 Cardiac Resynchronization Therapy in CKD: A Systematic Review

Neha Garg, George Thomas, Gregory Jackson, John Rickard, Joseph V. Nally Jr., W.H. Wilson Tang, and Sankar D. Navaneethan

Clinical Nephrology

1304 Serum Soluble Urokinase-Type Plasminogen Activator Receptor Levels and Idiopathic FSGS in Children: A Single-Center Report

Margret E. Bock, Heather E. Price, Lorenzo Gallon, and Craig B. Langman
See related editorial on page 1273.

1312 Relation between Asymptomatic Proteinase 3 Antibodies and Future Granulomatosis with Polyangiitis

Stephen W. Olson, David Owshalimpur, Christina M. Yuan, Charles Arbogast, Thomas P. Baker, David Oliver, and Kevin C. Abbott

Clinical Pharmacology

1319 Lipoprotein Kinetics in Male Hemodialysis Patients Treated with Atorvastatin

Johannes P. Schwaiger, Yoshinobu Nakada, Ramona Berberich, Katsunori Ikewaki, Benjamin Dieplinger, Emanuel Zitt, Ulrich Neyer, Hermann Salmhofer, Florian Kronenberg, Paul Koenig, and Hans Dieplinger

ESRD and Chronic Dialysis

1327  Factors Associated with Initiation of Chronic Renal Replacement Therapy for Patients with Kidney Failure

Labib I. Faruque, Brenda R. Hemmelgarn, Natasha Wiebe, Braden J. Manns, Pietro Ravani, Scott Klarenbach, Rick Pelletier, and Marcello Tonelli, for the Alberta Kidney Disease Network
See related editorial on page 1276.

1336 Temporal Trends in the Incidence, Treatment, and Outcomes of Hip Fracture in Older Patients Initiating Dialysis in the United States

Sumi Sukumaran Nair, Aya A. Mitani, Benjamin A. Goldstein, Glenn M. Chertow, David W. Lowenberg, and Wolfgang C. Winkelmayr

1343 Asymptomatic Pulmonary Congestion and Physical Functioning in Hemodialysis Patients

Giuseppe Enia, Claudia Torino, Vincenzo Panuccio, Rocco Tripepi, Maurizio Postorino, Roberta Aliotta, Marianna Bellantoni, Giovanni Tripepi, Francesca Mallamaci, and Carmine Zoccali, on behalf of the Lung Comets Cohort Working Group
See related editorial on page 1279.

Genetics

1349 Association between Genotype and Phenotype in Uromodulin-Associated Kidney Disease

Jonathan L. Moskowitz, Sian E. Piret, Karl Lhotta, Thomas M. Kitzler, Adam P. Tashman, Erin Velez, Rajesh V. Thakker, and Peter Kotanko

1358 Candidate Gene Analysis of Arteriovenous Fistula Failure in Hemodialysis Patients

Jeffrey J.W. Verschuren, Gurbey Ocak, Friedo W. Dekker, Ton J. Rabelink, J. Wouter Jukema, and Joris I. Rotmans

Mineral Metabolism/Bone Disease

1367 Estimated GFR and Fracture Risk: A Population-Based Study

Meghan J. Elliott, Matthew T. James, Robert R. Quinn, Pietro Ravani, Marcello Tonelli, Luz Palacios-Derflingher, Zhi Tan, Braden J. Manns, Gregory A. Kline, Paul E. Ronksley, and Brenda R. Hemmelgarn
See related editorial on page 1282.

1378 Parathyroidectomy and Heart Rate Variability in Patients with Stage 5 CKD

Jing Zhang, Xiangbao Yu, Bin Sun, Jianling Bai, Yongyue Wei, Xiaoming Zha, Yiyao Cui, Ming Zeng, Jingjing Zhang, Jia Liu, Huijuan Mao, Bo Zhang, Haibin Ren, Yifei Ge, Xueqiang Xu, Zhixiang Shen, Changying Xing, Kejiang Cao, and Ningning Wang

Nephrolithiasis

1389 Soda and Other Beverages and the Risk of Kidney Stones

Pietro Manuel Ferraro, Eric N. Taylor, Giovanni Gambaro, and Gary C. Curhan

Renal Transplantation

1396 Comparison of Regulatory T Cells in Hemodialysis Patients and Healthy Controls: Implications for Cell Therapy in Transplantation

Behdad Afzali, Francis C. Edozie, Henrieta Fazekasova, Cristiano Scottà, Peter J. Mitchell, James B. Canavan, Shahram Y. Kordasti, Prabhjoat S. Chana, Richard Ellis, Graham M. Lord, Susan John, Rachel Hilton, Robert I. Lechler, and Giovanna Lombardi

Commentaries

1406 The Unjustified Classification of Kidney Donors as Patients with CKD: Critique and Recommendations

Arthur J. Matas and Hassan N. Ibrahim

1414 GFR Estimating Equations: Getting Closer to the Truth?

Andrew D. Rule and Richard J. Glasscock

Ethics Series

1421 Considerations in Starting a Patient with Advanced Frailty on Dialysis: Complex Biology Meets Challenging Ethics

Mark Swidler

Mini-Review

1429 Systematic Review of Structural and Functional Neuroimaging Findings in Children and Adults with CKD

Divya G. Moodalbail, Kathryn A. Reiser, John A. Detre, Robert T. Schultz, John D. Herrington, Christos Davatzikos, Jimit J. Doshi, Guray Erus, Hua-Shan Liu, Jerilynn Radcliffe, Susan L. Furth, and Stephen R. Hooper


Special Features

1449 Digital Pathology Evaluation in the Multicenter Nephrotic Syndrome Study Network (NEPTUNE)

Laura Barisoni, Cynthia C. Nast, J. Charles Jennette, Jeffrey B. Hodgin, Andrew M. Herzenberg, Kevin V. Lemley, Catherine M. Conway, Jeffrey B. Kopp, Matthias Kretzler, Christa Lienczewski, Carmen Avila-Casado, Serena Bagnasco, Sanjeev Sethi, John Tomaszewski, Adil H. Gasim, and Stephen M. Hewitt

1460 American Society of Nephrology Quiz and Questionnaire 2012: Glomerulonephritis

Fernando C. Fervenza, Richard J. Glassock, and Anthony J. Bleyer

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On the Cover

What's the diagnosis? A 60-year-old man with remote history of lower extremity DVT (on warfarin) presented with diffuse joint pains, and erythematous rash on his right hand and wrist that extended to his forearm. A purpuric rash subsequently developed on his left arm and bilateral thighs. He was initiated on intravenous antibiotics for cellulitis at a community hospital and transferred to Yale-New Haven Hospital. The purpura progressed to hemorrhagic bullae. Biopsy of the rash was consistent with leukocytoclastic vasculitis with negative IgA staining. Abdominal pain and bloody stools developed during hospitalization. The nephrology service was consulted after urinalysis showed 2+ protein and large blood on dipstick and serum creatinine increased from 0.9 mg/dL to 2.0 mg/dL. Nephrologist performed urine microscopy demonstrated 2-5 dysmorphic RBCs/HPF, 1-3 WBCs /HPF and 1-2 RBC casts/LPF (upper left panel). A kidney biopsy was performed revealing a proliferative glomerulus with necrosis on light microscopy (upper right panel). Immunofluorescence staining (lower left panel) revealed dominant IgA staining in the mesangium and capillary loops. Electron microscopy demonstrated electron dense deposits in the mesangium and subendothelium (lower right panel). The clinical presentation and kidney biopsy findings are consistent with Henoch-Schonlein Purpura (HSP) or IGA vasculitis. The patient was treated with intravenous methylprednisolone 1 gram daily for 3 days followed by oral prednisone 60 mg daily. Within a few days, he felt much improved with resolution of arthralgias and abdominal pain, while the rash started to fade over the next week. Kidney function stabilized and improved back to baseline over the next 2 weeks.

HSP, which is more commonly a disease of childhood, is characterized by the tetrad of palpable purpura, arthritis/arthralgias, abdominal pain, and kidney disease. Clinical manifestations, which result from the deposition of IgA-containing immune complexes, typically develop over a period of days, often starting with joint symptoms and purpuric skin rash. Skin biopsy reveals a leukocytoclastic vasculitis with IgA positive staining; however, IgA can be negative in 25%, especially in older lesions. Urinalysis often reveals proteinuria, hematuria, and leukocyturia, while urine microscopy demonstrates an active urine sediment with dysmorphic RBCs and RBC casts (upper left panel). Kidney biopsy reveals a spectrum of glomerular changes ranging from isolated mesangial proliferation, focal and segmental proliferation, to glomerular necrosis with severe crescentic glomerulonephritis. Immunofluorescence reveals prominent IgA staining in the mesangium (lower left panel). IgG, IgM, C3 and fibrinogen may also be present. Electron dense deposits are often found in the mesangial area, which can extend to the peripheral capillary loops (lower right panel). Supportive care is typically sufficient in most cases; however, glucocorticoids enhance the rate of resolution of arthralgias and rash. Intravenous methylprednisolone followed by oral prednisone (for 6 months) are used when glomerular necrosis and crescentic glomerulonephritis are present.

(Images and text provided by Gilbert Moeckel, MD and Mark A. Perazella, MD, Yale University School of Medicine, New Haven, Connecticut)