Editorials

1311 The Golden Hours of AKI: Is Oxygen Delivery the Key?
Jay L. Koyner
See related article on page 1340.

1314 Medication Safety + Mobile Health = Patient Engagement in CKD
Bryan N. Becker
See related article on page 1364.

1316 Preparing for Disasters for Patients on Dialysis
Michael Davis and Jeffrey B. Kopp
See related article on page 1389.

1318 Lower Dialysate Temperature in Hemodialysis: Is It a Cool Idea?
Maria-Eleni Roumelioti and Mark L. Unruh
See related article on page 1408.

1321 Timing of Dialysis Initiation—Do Health Care Setting or Provider Incentives Matter?
Venkat Ramanathan and Wolfgang C. Winkelmayer
See related article on page 1418.

Original Articles

Acute Kidney Injury

1324 A Prospective International Multicenter Study of AKI in the Intensive Care Unit
Josée Bouchard, Anjali Acharya, Jorge Cerda, Elizabeth R. Maccariello, Rajasekara Chakravarthi Madarasu, Ashita J. Tolwani, Xinling Liang, Ping Fu, Zhi-Hong Liu, and Ravindra L. Mehta

1332 Biomarker Enhanced Risk Prediction for Adverse Outcomes in Critically Ill Patients Receiving RRT
Francis Pike, Raghavan Murugan, Christopher Keener, Paul M. Palevsky, Anitha Vijayan, Mark Unruh, Kevin Finkel, Xiaoyan Wen, and John A. Kellum for the Biological Markers for Recovery of Kidney (BioMaRK) Study Investigators

1340 Low Systemic Oxygen Delivery and BP and Risk of Progression of Early AKI
Mario Raimundo, Siobhan Crichton, Yadullah Syed, Jonathan R. Martin, Richard Beale, David Treacher, and Marlies Oertmann
See related editorial on page 1311.

Chronic Kidney Disease

1350 GFR in Patients with β-Thalassemia Major
Gai Milo, Revital Feige Gross Nevo, Idit Pazgal, Anat Gaftor-Gvili, Ofer Shpilberg, Uzi Gaftor, Arie Erman, and Pinhas Stark

1357 Advanced Parameters of Cardiac Mechanics in Children with CKD: The 4C Study
Marcello Chinali, Maria Chiara Matteucci, Alessio Franceschini, Anke Doyon, Giacomo Pongiglione, Gabriele Rinelli, and Franz Schaefer
Epidemiology and Outcomes

1364 Remote Usability Testing and Satisfaction with a Mobile Health Medication Inquiry System in CKD
Clarissa J. Diamantidis, Jennifer S. Ginsberg, Marni Yoffe, Lisa Lucas, Divya Prakash, Saurabh Aggarwal, Wanda Fink, Stefan Becker, and Jeffrey C. Fink
See related editorial on page 1314.

1371 Risk Prediction for Early CKD in Type 2 Diabetes
Daniela Dunkler, Peggy Gao, Shun Fu Lee, Georg Heinze, Catherine M. Clase, Sheldon Tobe, Koon K. Teo, Hertzel Gerstein, Johannes F.E. Mann, and Rainer Oberbauer on behalf of the ONTARGET and ORIGIN Investigators

ESRD and Chronic Dialysis

Seychelle Yohanna, Ali M.A. Alkatheeri, Scott K. Brimble, Brendan McCormick, Arthur Iansavitchous, Peter G. Blake, and Arsh K. Jain

1389 Disaster Preparedness and Awareness of Patients on Hemodialysis after Hurricane Sandy
Naoka Murakami, Hira Babu Siktel, David Lucido, James F. Winchester, and Nikolas B. Harbord
See related editorial on page 1316.

1397 An Incident Cohort Study Comparing Survival on Home Hemodialysis and Peritoneal Dialysis (Australia and New Zealand Dialysis and Transplantation Registry)
Annie-Claire Nadeau-Fredette, Carmel M. Hawley, Elaine M. Pascoe, Christopher T. Chan, Philip A. Clayton, Kevan R. Polkinghorne, Neil Boudville, Martine Leblanc, and David W. Johnson

1408 Randomized Controlled Trial of Individualized Dialysate Cooling for Cardiac Protection in Hemodialysis Patients
Aghogho Odudu, Mohamed Tarek Eldehni, Gerry P. McCann, and Christopher W. McIntyre
See related editorial on page 1318.

Health Services Research

1418 Trends in Timing of Dialysis Initiation within Versus Outside the Department of Veterans Affairs
Margaret K. Yu, Ann M. O’Hare, Adam Batten, Christine A. Sulc, Emily L. Neely, Chuan-Fen Liu, and Paul L. Hebert
See related editorial on page 1321.

1428 Satisfaction with Care of Patients on Hemodialysis
Michelle M. Richardson, Susan S. Paine, Megan E. Grobert, Christine A. Stidley, Ezra Gabbay, Antonia M. Harford, Philip G. Zager, Dana C. Miskulin, and Klemens B. Meyer

Renal Transplantation

1435 Capillary C4d and Kidney Allograft Outcome in Relation to Morphologic Lesions Suggestive of Antibody-Mediated Rejection
Željko Kikić, Alexander Kainz, Nicolas Kozakowski, Rainer Oberbauer, Heinz Regele, Gregor Bond, and Georg A. Böhmig

Renal Physiology

1444 Urea and Ammonia Metabolism and the Control of Renal Nitrogen Excretion
I. David Weiner, William E. Mitch, and Jeff M. Sands

Renal Immunology

1459 How the Innate Immune System Senses Trouble and Causes Trouble
Takashi Hato and Pierre C. Dagher
Role of the Medical Director

Managing Disruptive Behavior by Patients and Physicians: A Responsibility of the Dialysis Facility Medical Director
Edward R. Jones and Richard S. Goldman

Attending Rounds

Lactic Acidosis in a Patient with Type 2 Diabetes Mellitus
Lawrence S. Weisberg

Public Policy Series

Shortage of Peritoneal Dialysis Solution and the Food and Drug Administration’s Response
Valerie Jensen and Douglas C. Throckmorton

Special Feature

CKD as a Model for Improving Chronic Disease Care through Electronic Health Records
Paul E. Drawz, Patrick Archdeacon, Clement J. McDonald, Neil R. Powe, Kimberly A. Smith, Jenna Norton, Desmond E. Williams, Uptal D. Patel, and Andrew Narva

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On the Cover

What’s the diagnosis? A 42 year old renal transplant patient presented with a painful, swollen left leg. A plain radiograph revealed muscle calcification consistent with nephrogenic systemic fibrosis (NSF) (cover image). The patient has Von Hippel-Lindau syndrome and was previously on hemodialysis following bilateral nephrectomies for renal cell carcinoma. During this time he had multiple gadolinium-enhanced MRI scans for resection of cerebellar haemangioblastomas.

NSF results from CD34 positive fibrocyte infiltration, causing thickened and hard skin and muscles. Gadolinium has been implicated as a causative agent. The pathogenesis of NSF is incompletely understood however one of the proposed mechanisms suggests that a number of factors, including circulating iron and hyperphosphataemia, lead to an increased dissociation of free gadolinium (Gd3+) from its chelate. Both free Gd3+ and poorly soluble precipitates such as GdCl3 can cause a release of profibrosing cytokines such as TGFβ and MCP-1. Different preparations of gadolinium contrast agents confer different risk: the Royal College of Radiologists advises the lowest volume of the most stable agent least likely to release Gd3+. Currently the only treatment for NSF is recovery of renal function. Our patient received a kidney transplant, but despite this his muscle and skin changes have worsened.

(Image and text provided by Emma O’Lone and William White, Royal London Hospital, Renal London, London, United Kingdom and Muhammad Magdi Yaqoob, William Harvey Research Institute, Translational Medicine and Therapeutics London, London, United Kingdom)