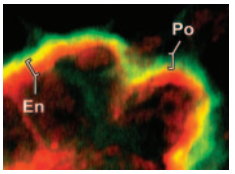
This Month's Highlights

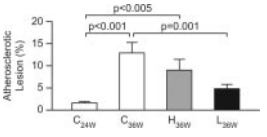
BASIC RESEARCH

Hybrid Glomeruli Provide Clues About Glomerulogenesis



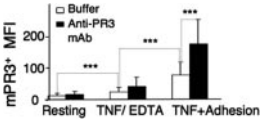
Laminins are integral components of glomerular basement membranes. Abrahamson and colleagues explored the role of laminins in glomerulogenesis by studying hybrid glomeruli comprising podocytes from laminin α5 knockout mice and endothelial cells from wild-type mice. By localizing the different isoforms of laminin expressed by podocytes and endothelial cells in these hybrids, the authors demonstrate that both cell types contribute significantly to the formation of the glomerular basement membrane, that the laminins remain attached to their cell of origin, and that proper development of podocyte foot processes requires normal composition of the underlying basement membranes. *See Abrahamson et al., pages 2285–2293.*

Angiotensin II Blockade Stabilizes Atherosclerotic Plaques



Atherosclerosis ravages patients with kidney disease. Blockade of the renin-angiotensin system reduces the associated morbidity and mortality, but the mechanisms underlying these effects are incompletely understood. Using apolipoprotein E–deficient mice with established atherosclerosis, Suganuma and colleagues found that treatment with the renin-angiotensin system inhibitor losartan not only slows progression of atherosclerotic plaques but also alters their composition. Losartan increases the relative amount of collagen in plaques and reduces the destruction of elastin in the arterial wall. Therefore, angiotensin II blockade may reduce the risk of plaque rupture in addition to reducing the atherosclerotic burden. *See Suganuma et al., pages 2311–2319.*

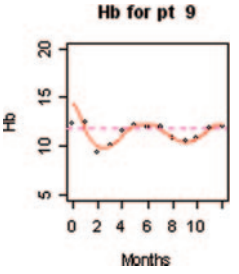
Anti-PR3 Antibodies Stimulate the Expression of Their Own Antigen



ANCA (anti-neutrophil cytoplasmic antibodies) directed against neutrophil proteinase 3 (PR3) are found in a subset of vasculitides, but their contribution to the pathogenesis of disease is not well understood. Brachemi and colleagues demonstrate that anti-PR3 interacts with membrane-bound antigen (mPR3) only after mPR3-expressing neutrophils have been activated by inflammatory cytokines and have adhered to vascular endothelial cells. Moreover, this antibody–neutrophil interaction stimulates additional translocation of PR3 to the cell surface, which may lead to a destructive positive feedback loop in the small vessels where neutrophils are known to wreak havoc in these autoimmune diseases. *See Brachemi et al., pages 2330–2339.*

CLINICAL EPIDEMIOLOGY

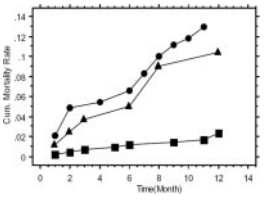
Mathematical Equations Assess Hemoglobin Trajectories



The hemoglobin concentration of a patient treated with epoetin often fluctuates around a target value as the drug regimen is adjusted in response to laboratory data. Using patient-level data from a previously published trial, West and colleagues describe a method by which a treatment algorithm can be evaluated for how well it achieves and maintains hemoglobin targets. They modeled individual trajectories of hemoglobin values over time with mathematical functions, and then analyzed these functions to assess how well protocol-driven adjustments in dosage stabilized hemoglobin levels at target. This type of approach may prove useful for the development of treatment protocols in clinical practice or future trials. *See West et al., pages 2371–2376.*

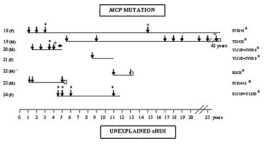
CLINICAL RESEARCH

Nondiabetics May Need to Worry about Fasting Glucose



Diabetic patients on hemodialysis are often chronically inflamed, malnourished, and at increased risk for cardiovascular death. The association of fasting glucose level with these characteristics has not received as much attention among nondiabetic patients on dialysis. Lin-Tan and colleagues prospectively assessed markers of both nutritional status and inflammation in 693 hemodialysis patients in Taiwan. Their analysis suggests that higher fasting glucose levels are associated with reduced serum albumin, increased high-sensitivity C-reactive protein, and increased 1-year mortality, even among nondiabetic patients. Whether interventions targeting glucose metabolism in these patients will affect outcome remains to be determined. *See Lin-Tan et al., pages 2385–2391.*

Mutations in Complement Pathway Affect HUS Course



Dysregulation of the complement cascade has been implicated in the pathogenesis of atypical hemolytic uremic syndrome (HUS). Sellier-Leclerc and colleagues studied 46 pediatric patients with atypical HUS and found associations between genetic susceptibility traits and clinical course. Half of the children had mutations in Factor H, Factor I, or membrane cofactor protein. Age at onset of symptoms, number of relapses during the first 10 years, and renal survival differed on the basis of which protein was mutated. In addition, triggering events were often identified in mutation carriers, suggesting that these mutations may modify risk rather than cause the syndrome. *See Sellier-Leclerc et al., pages 2392–2400.*