Athens Kidney Center
1440 North Chase Street
Athens, GA 30601

RETURN SERVICE REQUESTED

CHECK-LIST FOR INSOMNIA

1. Insomnia is often a symptom of another unrecognized medical problem: search deep, search broadly, search thoroughly.
2. Confirm the patient's description through an independent history obtained from the patient's sleep partner/spouse.
3. Characterize the pathology of insomnia: duration? associated daytime impairment/dysfunction? sleep-time routines/habits? social factors (depression, loss, unfamiliar environment, anxiety)? aggravating factors? triggering factors? relieving factors?
4. Underlying medical illness: post-nasal drip/sinusitis; COPD; GERD/irritable bowel syndrome; CAD/heart failure/palpitations; polyuria/urinary frequency/incontinence; arthritis/neuropathy; seizures/myoclonus; dementia/delirium/stroke; psychiatric disease.
5. Medications audit: illicit drugs; alcohol; anti-depressants & CNS psychostimulants (e.g. caffeine, sympathomimetics, nicotine); steroids; thyroid supplements; anti-histamines; phenytoin; L-dopa; cimetidine; beta/alpha blockers; diuretics; methyldopa.
6. Treat sparingly: antihistamines trigger cholinergic side-effects (palpitations, dry mouth, visual blurring, agitation, glaucoma) and cognitive dysfunction including delirium/hallucinosis; benzodiazepines may cause respiratory depression, paradoxical agitation/rebound insomnia, psychomotor impairment/falls and memory loss; anti-depressants (e.g. Trazodone) may cause weight fluctuations.
(7) Preferred drugs (especially in the elderly and those with COPD or recent strokes, but could still risk parasomnias [e.g. sleep walking] and drug-drug interactions with other sedatives) are (a) Zaleplon (Sonata) 5 mg p.o. QHS (may repeat 1 extra tablet deep into night, on arousal) but watch for myalgia, nausea and altered color vision; (b) Ramelteon (Rozerem) 8 mg p.o. QHS (a non-sedating melatonin receptor agonist, probably safest drug in formulary, but can cause dizzy spells and fatigue/headache); (c) Zolpidem (Ambien) 5 mg p.o. QHS (watch for abdominal pain and somnolence/rebound insomnia) but as effects wane rapidly, it is less effective for "maintaining" sleep except if given as 6.25 mg of an extended-release ER formulation; (d) Eszopiclone (Lunesta) 1 or 2 mg p.o. QHS (watch for headache, somnolence, impaired memory, dry mouth and bitter dysgeusia).
8. Ask your patients if they are already taking herbal remedies (melatonin and/or valerian root): they do not mix well with prescription pills.

MANAGING DIABETES IN RENAL FAILURE PATIENTS

A 27 y.o. gentleman with a long-standing history of "brittle" type 1 diabetes mellitus and dialysis-dependent renal failure presented to the ER with gastroparesis, non-anion gap metabolic acidosis and florid hyperglycemia. He was placed on a glucommander insulin protocol and soon lapsed into hypoglycemia. The pitfalls of diabetes management in renal failure were highlighted:
1. Kidney failure increases the risk of hypoglycemia in diabetics through (a) loss of renal gluconeogenesis; (b) extended half-life of oral hypoglycemic drugs, largely due to reduced renal elimination; (c) loss of renal "insulinase" activity which extends effective half-life of insulin formulations; (d) reduced effect of so-called Vallance-Owens anti-insulin blood factors in uremic serum.
2. Lack of hypoglycemia awareness is rife: this reflects the long-standing history of microvascular attrition with resultant peripheral and autonomic neuropathy, as was demonstrable in this case; note that oral beta-blocker therapy (often advocated for underlying cardiac disease) can exacerbate this tendency.
3. High clinical predilection to GI symptoms, including (a) nausea & vomiting (mediated by autonomic neuropathy leading to chronic gastritis, acute gastric dilatation typically found in DKA, high prevalence of H pylori gastritis in uremic patients, and peptic ulcer diathesis; (b) pancreatitis mediated by chronic pancreatitis, malnutrition-related pancreatitis (so-called Zuidema disease), Fredericksen type IV hyperlipidemia, alcohol use and medication-related pancreatic damage; (c) progressive abdominal discomfort secondary to fatty infiltration of liver (NASH), cholecystitis, mesenteric ischemia (true infarction is relatively rare) and obstructive uropathy with bladder distention (from dysautonomia, prostatic disease or luminal obstruction/fibrosis).
4. Poor therapeutic compliance associated with (a) dialysis/uremic dementia, (b) inability to read labeled instructions or glucometer arising from severe diabetic retinopathy (and rarely, macular edema during DKA episodes, as well as significant intraocular bleeding from vitreous hemorrhage and/or rubeosis iridis).
5. Loss of "overflow" protective function of osmotic polyuria in uncontrolled diabetics (as well as those with low renal tubular threshold for glucose).
6. Alteration in insulin sensitivity/resistance mediated by (a) endocrinopathy (typically adrenal insufficiency/Cushing's syndrome, dysthyroidism or hypopituitarism/acromegaly); (b) malabsorption syndromes and celiac disease; (c) liver failure/hepatitis; (d) fluctuations in weight/adiposity, with insulin resistance manifesting in obesity; (e) medications, including diuretics and beta-blockers (which may block hepatic glycogenolysis); (f) electrolyte abnormalities (e.g. hypokalemia is associated with insulin resistance).
7. Development of "occult" medical complications including (a) psychiatric illness (leading to factitious insulin administration, parasuicidal gestures, et cetera); (b) sepsis syndrome (may present as unexplained hypoglycemia); (c) neoplasia (including islet-cell tumors as well as hepatoma and mesenchymal tumors provoking chronic hypoglycemia).

the SECOND OPINION

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FROM THE EDITOR

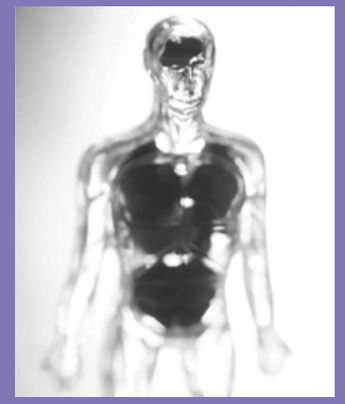
The political season is once more upon us (in truth, it never really left us, not even for a day): all manner of gubernatorial gladiators and presidential pretenders currently stalk the land, offering platitudes and snake oil instead of solutions to seemingly intractable problems. The central issues of our social malaise- high unemployment, entanglement in foreign wars, the vexing issue of healthcare reform and, of course, the perennial charge for fair taxation- will only be sporadically mentioned, pretty much as afterthought. Most of the debate- or theater- will focus on personalities- of the "me against them" variety- and very likely, the sotto voce declensions of class and race. I tell you, my friend, our politics is not for the faint of heart.
As a physician, I am concerned about the future of healthcare. This is not simply a matter for politicians or party activists, and if I may say so, not really an issue for legal interpretation by the Supreme Court. Healthcare is too important, too central to our way of life, and too fundamental a right to be hoisted on any party platform as a right or artifice. As we speak, the Supreme Court is weighing the constitutionality of requiring every American to purchase healthcare insurance, the so-called "individual mandate". Based on a layman's interpretations of oral arguments before the august court, Obamacare (as it is derisively called by the loyal Conservative opposition) is not destined for longevity. Almost all parties agree that our healthcare system is not as inclusive, affordable or efficient, as it perhaps should be. We differ largely on our prescriptive intent: should we overhaul, reform or let "market forces" correct our structural lapses? What should have been an invigorating debate has been lost in the maelstrom of ideology and partisan politics. There will be no winners in this fight.

Consider: in 1844, a barely known cleric of the Anglican tradition, John Henry Newman, well-versed in Latin, Greek and English as was expected of Oxford professors of his day, published a moving essay on The Development Of Christian Doctrine. In that narrative which was to precede the even more seismic Apologia pro Vita Sua (Defense of His Own Life), John Newman sought to trace the development of Christian canonical doctrine, which as anyone with a passing knowledge of early Christian liturgy would tell you, is an invidious task. His brilliant analysis was shorn of emotion, the true antithesis of logic, and despite his own prejudices, he never allowed preconceptions eclipse his intellectual (and spiritual) insight. He reached the startling conclusion, despite his original belief system and Oxbridge esthetics, that a "guiding hand" must have midwifed the contentious progress of early Christianity, overcoming notable controversies such as adoption of pagan rituals, concept of Trinity, Virgin birth, and a whole catalogue of ecclesiastical incongruity. Based on his scholarship, he reached what was then considered (at least, amongst his fellow Oxford academics) the impossible conclusion that Roman Catholicism was the only true path of Christian doctrine. Whilst we may not all necessarily agree with Cardinal John Henry Newman (he was, after all, pilloried by both Anglicans and Catholics alike in his day, the former for his alleged heresy against the Anglican faith, the latter on accusations of wanton hypocrisy and opportunism), we can at least agree on his brutal honesty, faith- and yes, scholarship. Our issues will not be solved by mere scholarly disquisition, but it would be an important first step. As a wise old man once reminded me: "it is far better to open your eyes and say you do not understand, than to close your eyes and say you do not believe it".
Will the next Cardinal John Henry Newman please stand up?

I'll see you Friday lunch-time, at the CME lounge. *Beze Adogu, MD, Ph.D, FACP*

HEIGHT AND RISK OF HEART FAILURE: TALLER IS BETTER

Height- or more precisely, the lack of it- has previously been linked to heart disease, including coronary artery disease as documented by Walker et al, Int J Epidemiol, 1989. This study by Akinkuolie et al, Am J Cardiol, 2012, from Boston, using the Physicians' Health Study data-base confirmed the inverse relationship between height and heart failure. Height was self-reported, and incident heart failure was ascertained by serial questionnaires. Cox proportional hazard model was utilized in computing hazard ratios at 95% confidence interval: physicians at higher height categories were less likely to suffer heart failure after adjusting for age, weight, and the presence of hypertension and/or diabetes mellitus. The paper provides a less-than-convincing mechanistic explanation for why height might predict cardiovascular stress; a role for gravity in vascular distensibility was canvassed.



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PROSCRIPTION OF COMPETITIVE SPORTS IN HEART DISEASE

Walker et al, *Am J Med*, 2010, provide a readable treatise on cardiac arrhythmias amongst athletes and others involved in competitive or contact sports. Exercise, as the authors carefully point out, is rarely the cause of cardiac disease; however, acute symptoms following exercise-induced surges in cardiac output/LV afterload and associated sympatho-adrenal discharge, could assay sudden death. The underlying cardiac disorders include valvular heart disease, Marfan's syndrome and a host of nonarrhythmogenic disorders, but those with a propensity to cardiac arrhythmia in the athlete include: (1) autosomal dominant hypertrophic cardiomyopathy (HOCM); (2) arrhythmogenic R ventricular dysplasias (with fibro-fatty enlargement of RV resulting in T-wave inversion in V1-V3 and/or epsilon EKG waves at rest); (3) long QT syndrome (of prolonged cardiac repolarization); (4) short QT syndrome (of abbreviated cardiac repolarization, often associated with atrial fibrillation); (5) autosomal dominant Brugada syndrome (associated with ST segment elevation in R-sided precordial leads); (6) autosomal dominant catecholaminergic polymorphic ventricular tachycardia (where exercise triggers polymorphic VT or VF) and (7) anomalous origin of major coronary artery (leading to myocardial hypoperfusion). All these 7 conditions require strict proscription of competitive sports and consideration to defibrillator placement (except for anomalous origin of coronary arteries where surgery, not defibrillator therapy, may be indicated if myocardial perfusion is limited). Beta-blockers may be of value in treating catecholaminergic polymorphic VT and arrhythmogenic RV dysplasia. The other 4 arrhythmogenic conditions which do not necessarily imply a complete avoidance of high-intensity sports are: (8) commotio cordis (VF triggered by blunt precordial chest trauma); (9) idiopathic ventricular tachycardia (best treated by catheter ablation); (10) atrial flutter/fibrillation (treat with rate control, anticoagulants, and consider catheter ablation); (11) Wolff-Parkinson-White syndrome (characterized by delta wave on EKG and A-V node re-entrant tachycardia on EP studies, best treated by catheter ablation).

DOOR-TO-BALLOON TIMES: DELAY & MORTALITY IN STEMI

Outcomes in ST-elevation myocardial infarction is dependent on total ischemic time: the time from onset of symptoms (or first medical/EMT contact) until myocardial reperfusion is successfully completed. The accepted standard in the United States is 90 minutes. However, such indices are rarely achieved when patients present to outlying (district) hospitals without percutaneous coronary intervention (PCI) facilities. Miedema et al, *Circulation*, 2011, analyze the root causes and prognostic impact of delayed angioplasty amongst such patients who first present to outlying hospitals with chest pain. A total of 2034 patients who presented at 11 peripheral hospitals between 2003 and 2009 were included in the study. Delays were attributable to (1) Delay in completing ED evaluation at local hospitals (especially where initial EKGs were non-diagnostic of STEMI or investigations were carried out for other causes of chest pain); (2) Delay whilst awaiting Emergency ambulance transportation to central referral center (which were often attributable to inclement weather, long distance or staffing issues); (3) Delay at central hospital PCI facility (most commonly attributable to catheterization team delays/staffing issues and complexity of coronary artery lesions). The worst delays were often encountered amongst the elderly, patients in cardiogenic shock, non-smokers and diabetics. Those treated outside 120 minutes of medical contact were statistically more likely to die (6.4% mortality vs 4.1% mortality, p = 0.023). The study provides an interesting but viable breakdown of alloted times in STEMI referral: (a) referring (local) hospital door in-door out (DIDO) time of 45 mins or less; (b) between-hospitals transfer time of 45 mins or less; (c) referral (central) hospital door-to-balloon time of 30 mins or less: total time = 120 mins or less. Miedema et al achieved a contact-balloon time of 90 mins or less in 30% of their cases, and 120 mins or less in 66% of cases, even though some of the distances were over 60 miles outside the central referral facility. This study in effective regional cardiology cooperation proves that for proper STEMI management, it's all about logistics and forward planning. For the unlucky few hospitals uinable to meet these impressive targets, the fall-back option of fibrinolytic therapy to achieve reperfusion can still be managed at all peripheral hospitals.

REPAIR OF RENAL ARTERY STENOSIS: ARE WE THERE YET?

Renal artery stenosis (RAS) is common, but its clinical diagnosis can be elusive: underlying risk factors include advanced age, female gender, presence of chronic arterial hypertension or diabetes mellitus, evidence of atherosclerotic vascular disease elsewhere (peripheral vascular disease or coronary artery disease), smoking and presence of chronic kidney disease. Therefore, RAS may be found in over 20% of patients with either peripheral artery disease, abdominal aneurysms or refractory hypertension rising to 40.8% amongst incident dialysis patients (de Mast & Beutler, *J Hypertens*, 2009). At least, 10% of patients undergoing coronary angiograms have radiologic evidence of RAS depending on criteria used for diagnosis. Over 90% of renal artery stenosis in adults is due to atherosclerosois. RAS is often asymptomatic, but can present as CKD (chronic ischemic nephropathy) and less commonly, as renovascular hypertension (1 of the most common causes of secondary hypertension in adults) and "flash" pulmonary edema. Conventional treatment involves either medications vs surgical bypass vs balloon angioplasty/stenting. Though stenting has become the "preferred" therapy, randomized trials such as STAR, ASTRAL and CORAL did not show any benefit of stents above optimal medical treatment.

EARLY PREDICTION OF KIDNEY FAILURE IN "NORMAL" DIABETICS

Gohda et al, *J Am Soc Nephrol*, 2012, provide data supporting the predictive value of inflammatory markers in diabetic nephropathy. They showed that elevated serum levels of tumor necrosis factor receptors 1 and 2 predicted the future development of kidney failure in patients with type 2 diabetes but without proteinuria or other evidence of ongoing kidney damage. The investigators followed two cohorts of 628 patients with type 1 diabetes, normal renal function, and absence of proteinuria. Over 12 years, 69 patients developed CKD stage III, defined as glomerular filtration rate <60 mL/min per 1.73 m2 (16 per 1000 person-years). Concentrations of tumor necrosis factor receptors 1 and 2 were strongly associated with early renal decline, but renal decline was only modestly linked to total tumor necrosis factor (TNF)α concentration and was unrelated to levels of free TNFα. Using Cox proportional hazards analysis, patients with the highest levels of tumor necrosis factor receptor 2 were thrice more likely to experience renal decline than other patients; the risk of kidney damage associated with high tumor necrosis factor receptor 1 values was slightly less than the risk associated with high tumor necrosis factor receptor 2 levels.

STABLE ISCHEMIC HEART DISEASE: WHY ARE WE STILL STENTING?

There is a "cognitive dissonance" in the world of chronic stable angina: our head affirms optimal medical treatment whilst our hearts lurch towards percutaneous coronary intervention (PCI) even though we know it does no (added) good to medical therapy. PCI works well in acute coronary syndromes, the literature does not support any role in chronic stable angina, as it offers no benefit for prevention of death, nonfatal MI, unplanned revascularization or persistent angina (Stergiopoulos et al, Arch Intern Med, 2012). Each year, physicians deploy over 1 million coronary stents for coronary artery disease, at huge cost (and effort) with no return on our investment. Editorializing in the February 27 edition of Archives, William Boden, *Arch Intern Med*, 2012, lays out the case against PCI in stable coronary artery disease, citing the stout clinical data from COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive drug Evaluation: Boden et al, *N Engl J Med*, 2007), BARI-2D (Bypass Angioplasty Revascularization 2 Diabetes Trial: Frye et al, *N Engl J Med*, 2009) and JSAP (Japan Stable Angina Pectoris: Nishigaki et al, *JACC Cardiovasc Interv*, 2008) trials. Commendably, Dr. Boden finally attempts to finally kill the dragon of conflation- a statistical mirage in the comparative meta-analyses of Jeremias et al, *Am J Med*, 2009 and Schomig et al, *J Am Coll Cardiol*, 2008, where stable CAD was comingled with acute coronary syndromes as well as post-MI cases- by waving the white flag of Wijeysundera & Ko, *Circ Cardiovasc Qual Outcomes*, 2009). Bolden comes close, but fails to call for a total proscription of "elective" PCIs. Now, that would have been ONTARGET (The ONTARGET Investigators, *N Engl J Med*, 2008).

PREDICTING EVENT-FREE EXTENDED SURVIVAL FOLLOWING A HEART ATTACK

This paper by Berton et al, *Am J Cardiol*, 2012, analyzees clinical factors that may predict long-term event-free survival following an acute MI in Italy. A total of 37 clinical variables (including demographic information, known CVS risk factors, serologic findings and hospital characteristics) were examined. Only 19% of survivors were event-free at 10 years. Independent predictors identified by logistic and Cox regression models were: young age at event, no history of angina pectoris, no history of previous MI, normal renal function, low urinary albumin/creatinine ratio and high/normal LV ejection fraction. This model appeared to improve upon traditional Framingham risk prognostication.

CANADIAN MODEL: YOU GET WHAT YOU PAY FOR

An interesting study by Stukel et al, *JAMA*, 2012, explores the relationship between quality of care offered to acute-care patients and overall hospital spending in Ontario, Canada. Using an adult population admitted either for an acute MI, congestive cardiac failure, hip fracture or colon cancer between 1998 and 2008, the investigators analyzed 30-day and 1-year mortality, readmissions and major cardiac complications (acute MI, unstable angina, cardiac failure or death) during the 1 year of follow-up. Patients who had been admitted to hospitals in the highest- vs lowest-spending intensity groups had lower rates of all adverse outcomes; indeed, in the highest vs. lowest spending hospitals, the age/sex-adjusted 30-day mortality rate was 12.7% vs 12.8% for AMI, 10.2% vs 12.4% for CHF, 7.7% vs 9.7% for hip fracture, and 3.3% vs 3.9% for CHF; fully adjusted relative 30-day mortality rates were 0.93 (95% CI, 0.89-0.98) for AMI, 0.81 (95% CI, 0.76-0.86) for CHF, 0.74 (95% CI, 0.68-0.80) for hip fracture, and 0.78 (95% CI, 0.66-0.91) for colon cancer. Similar but not identical results were noted for 1-year mortality, readmissions, and major cardiac events. The investigators found that higher-spending hospitals tend to have higher nursing staff:patient ratios, more inpatient specialist consultations, more interventional procedures, better overall medical/cardiac therapies, better preoperative specialty care and improved post-discharge collaborative care with specialist/primary MD. This study carried out in a relatively low-spending healthcare market, might seem to contradict the American experience as outlined in the Dartmouth Atlas, which suggests that care in resource-rich hospital settings was not superior to low-resource hospital settings amongst Medicare beneficiaries. Stay tuned: Atul Gawande's work is not yet done.

OBESITY & CVS MORBIDITY

Obesity, which is defined as BMI >30 kg/m2 is linked to premature atherosclerosis (which is thought to be mediated by chronic inflammation, insulin resistance, hyperlipidemia, chronic arterial & pulmonary hypertension, adverse cardiac remodeling, increased sympathetic tone, endothelial dysfunction and arrhythmias). Consequently, patients are at risk for cardiac death resulting primarily from ischemic heart disease and congestive heart failure. A useful review by Apovian & Gokce, *Circulation*, 2012, outlines the CVS consequences of extreme obesity. It is thought that the clinical phenotype of obesity may be modified by fat distribution, degree of ectopic/visceral fat burden, ill-defined genetic factors, gender and degree of pro-inflammatory activation (of cytokines derived from the adipose-hepatic axis). Long-term treatment of obesity is fraught, as dietary and exercise regimen typically do not sustain weight loss above 5-10% of initial weight over 6 months. Successful therapy must include behavioral approaches, including low calorie diets and regular exercise, in addition to appetite suppressants such as phentermine (a norepinephrine-releasing agonist and central hypothalamic appetite suppressant) and diethylpropion (another sympathomimetic agent), and orlistat, a peripherally-acting lipase inhibitor, which blocks absorption of ~25% of ingested fats, but only has a mild weight-loss effect. Bariatric surgeries- either Roux-en-Y gastric bypass, laparoscopic gastric banding or bilio-pancreatic diversion with/without duodenal switch- are now more commonly performed in the morbidly obese (i.e. BMI > 40%), and have become correspondingly safer, with 30-day mortality of 0.3% and early complication rates of ~4%. In the future, medical therapy of obesity would likely incorporate incretin hormones, glucagon-like peptide 1 agonists (such as exanatide and liraglutide), leptins (such as metreleptin, which are adipocyte-derived hormones that signal satiety within the hypothalamus), endocannabinoid receptor blockers (such as rimonabant) and opiate receptor blockers (such as naltrexone).

PREDICTING AIDS-RELATED DEMENTIA: THE WAIST HAS IT

A cross-sectional study by McCutchan et al, *Neurology*, 2012, based on the CHARTER (CNS HIV Anti-Retroviral Therapy Effects Research) cohort of 130 patients showed that neuro-cognitive deficits (as found in 40% of study participants based on 12 neuropsychological tests of identified cognitive domains commonly impaired in HIV-AIDS) were associated with markers of long-term HIV infection and/or cardio-metabolic disease, but not necessarily the severity of HIV infection/disease: older age, longer reported duration of HIV seropositivity, premorbid diagnosis of diabetes mellitus or glucose intolerance and larger waist circumference. Interestingly, cognitive impairment was not found to aggregate in accordance to CD4 count, anti-retroviral treatment or HIV viral load (in plasma or cerebrospinal fluid). In another study, researchers at Stony Brook, NY, studied psychiatric illness and cognitive dysfunction amongst young folks with perinatally-infected HIV disease as published by Nachman et al, *Arch Pediatr Adolesc Med*, 2012. A cross-sectional analysis of participants recruited through the IMPAACT (International Maternal Pediatrics Adolescent AIDS Clinical Trials Group) study across the United States and Puerto Rico supported the contention that psychiatric morbidity (social skills, cognitive abilities and academic learning) was associated with markers of disease severity, namely low CD4 counts and high viral load. To differentiate Alzheimer-type dementia from HIV-associated neurocognitive disorder (HAND), Ances et al, *Arch Neurol*, 2012, suggest the use of carbon-11 labeled Pittsburgh compound B (an amyloid-binding compound) which is avidly taken up in cortical/subcortical amyloid plaques of Alzheimer's disease but not in HAND.

ASYMPTOMATIC BACTERIURIA: TOO MUCH TREATMENT ALREADY

A retrospective study of patients at 2 academic medical centers in 2009, by Lin et al, *Arch Intern Med*, 2012, analyzed contemporary antibiotic use for enterococci-positive urine samples. A total of 339 positive urine samples were identified as meeting study criteria; 54% were classified as asymptomatic bacteriuria and 46% were classified as true UTIs. Urinalysis was commonly but not universally performed; pyuria was noted in 70% of UTIs but only in 42.3% of asymptomatic bacteriuria. Antibiotics were wrongly prescribed in 32.8% of such cases of asymptomatic bacteriuria, usually triggered (odds ratio, 3.27) by the concurrence of pyuria in UA. Subsequent bacterial infections were uncommon following enterococci-positive urine cultures, occurring in 2.1% of all 339 culture-positive cases, and were even rarer (1.1%) in those with asymptomatic bacteriuria. Moral: do not treat asymptomatic bacteriuria.

NEUROLOGIC (STROKE) COMPLICATIONS IN ADULT ECMO

ECMO (extracorporeal membrane oxygenation) is the therapy of last resort in severe cardio-pulmonary failure. A Mayo Clinic study by Mateen et al, *Arch Neurol*, 2011, prospectively analyzed adult ECMO participants for neurologic sequelae. A total of 87 patients between 2002 and 2010 who received ECMO for >12 hours were assessed for injury: 42 patients suffered neurologic events, including subarachnoid hemorrhage, watershed (ischemic) infarcts, hypoxic encephalopathy, unexplained coma and brain death. Mortality was associated with older age (odds ratio being 1.24 per decade of life) and low arterial oxygen pressures. Most of the autopsied brains showed severe vascular lesions consistent with ischemic or hemorrhagic stroke. The authors conclude that ECMO may be instrumental in provoking neurovascular events in the susceptible.

TIGHT SKIN PLAQUES: WHAT ARE THE CLINICAL CONSIDERATIONS?

1. Nephrogenic systemic fibrosis (NSF) in patients with stage 5 or 6 chronic kidney disease who have been exposed to gadolinium contrast during MRI scans; there is also some probable etiologic link to erythropoietin in advanced CKD.
2. Eosinophilia-myalgia syndrome (EMS) may result from toxic exposure to L-tryptophan (used for treating insomnia) or adulterated rapeseed oil leading to a non-pitting edema and/or induration with peau d'orange picture; this syndrome is characterized by eosinophilia, visceral involement (pulmonary infiltrates), myalgias and neuropathy/arthropathy.
3. Scleromyxedema is a paraneoplastic disease (but can also occur de novo) associated with mucinous deposits in skin dermis; another related condition is palmar fasciitis and polyarthritis syndrome (PFAPS) which is another paraneoplastic condition associated with ovarian cancer, manifesting as a rapidly progressive dactylitis (indurated digital swelling) which has a uniformly poor prognosis; other "look-alikes" include local sclerosants (e.g. silica, vinyl chloride, bleomycin), localized amyloid plaques, carcinoid syndrome and graft-versus-host-disease.
4. Eosinophilic fasciitis describes deep tissue eosinophil infiltration with skin induration of limbs (characteristically sparing the hands/feet), eosinophilia and polyclonal hypergammaglobulinemia.
5. Systemic sclerosis is suggested by visceral complications such as bibasilar pulmonary fibrosis/pulmonary hypertension, esophageal dysmotility, renal crisis and auto-antibodies, including positive (nucleolar/anti-centromere) ANA titers; localized scleroderma may be associated with Raynaud's reaction, sclerodactyly, telangiectasias, calcinosis cutis in addition to the tell-tale skin lesions.