Athens Kidney Center
1440 North Chase Street
Athens, GA 30601

RETURN SERVICE REQUESTED

ZERO CENTRAL LINE-RELATED BACTEREMIA IS POSSIBLE

It is as simple as 1, 2, 3: use a check-list based on federal guidelines for catheter care; foster and improve communication amongst ICU staff; get administration to help promote a culture of overall patient safety. As reported by Lipitz-Snyderman et al, *Arch Intern Med*, 2011 in a study of ICUs participating in the Michigan Keystone Project, 60% of participant ICUs had no line-related infection in 1 year, and 26% had none in 2 years. Which makes us think that perhaps, 1 day central-line infections would be as rare (and shocking) as wrong-limb amputations...

PROGRESSIVE LOSS OF VISUAL FIELD IN TREATED GLAUCOMA

A retrospective study published by De Moraes et al, Arch Ophthal, 2011 for the Glaucoma Progression Study (GPS) showed that both intra-ocular pressure (especially peak IOP) as well as other variables affected visual field progression in those with treated glaucoma: thinner (central) corneal thickness, disc hemorrhage, parapapillary atrophy in beta-zone as well as exfoliation syndrome and older age (the last 2 only significant in a univariable model).

OVER-SELLING ROBOTICS IN HOSPITALS

From Johns Hopkins comes an interesting (and altogether, not too surprising) report by Jin et al, J HealthCare Quality, 2011, that hospitals tend to make inaccurate claims about robotic surgery. Even though to date, there is no randomized controlled trial showing patient benefit from robotic surgery vs "conventional" surgery, such a little detail has not tempered the enthusiasm of either vendors or the general public, resulting in a 400% spike in use over the last 4 years. Analyzing 400 randomly selected hospital websites, Jin et al found 41% of hospitals which provided a patient-centered description of robotic surgery. Unfortunately, the benefits of robotic surgery were routinely exaggerated whilst its risks were inversely minimized by those hospitals, with over two-thirds of such hospitals actually using text/stock images from machine vendors, whilst a third of hospitals went "the extra mile" by directly linking the visitor/patient to the vendor/manufacturers' websites. Now, that's what I call "full service" advertising.....

the
SECOND OPINION

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FROM THE EDITOR

It's all about economics. Really. In one of the most difficult weeks for American democracy since the Watergate debacle, we all bore witness to governmental dysfunction in high places. Political compromise and middle-of-the-road moderation was held hostage by the Tea Party caucus, an irreverent, back-to-fundamentals movement, which had sounded like a good idea at the beginning. The casualties, of course, were the tax-payers, those dispossessed "men-in-the-street" on whose backs the budget will eventually be balanced, and common sense, whose transcendent and immanent goddess, Iris of pharaonic mythology, briefly deserted our congressional halls. Not one to let a good opportunity for show-boating go by, Standard & Poor in an act of monumental hubris, quickly downgraded America's credit rating despite clear evidence that their math was at the very least suspect, to the tune of 2 trillion (!!!) dollars. We are expected to believe that Singapore, Liechtenstein, Guernsey, Isle of Man and goodness knows where else is more credit-worthy than the United States? *Puhleeze*. Sadly enough, 30 of our best and bravest, members of the storied DEVGRU Navy Seals, were lost in a horrific helicopter implosion over the eastern Afghan highlands. Meanwhile, Congress is engrossed in the energizing debate on who really "owns" the credit downgrade: Obama, Tea Party or Boehner? Even as the reinvigorated Tea Party prepares to unleash all new manner of mischief on the prostrate economy, all in the name of 2012 politics. Welcome to the world's greatest democracy.

Economics equally permeates and pervades all that we do as doctors, both in public and private. By avoiding central line infections in hospitals, we stand to save at least 480 million dollars yearly in treatment-related costs. If prior CT scans help us limit DEXA scan use for the diagnosis of osteoporosis, we add another 80 million dollars to our credit. Imagine how many more people (and dollars) could be saved with a cup of coffee added to our pegylated interferon protocol for hepatitis C? Any takers for making oral statin use more tolerable and more universally employed for those at high cardiovascular risk? The data shows that hospitals may already be way ahead of the economics curve, if the study from Marty Makary's group from Johns Hopkins is to be believed: our hospitals shilling for robotics vendors? Not in these United States!

As always, dear folks, I'll see you Friday lunchtime, at the CME lounge.

Beze Adogu, MD, Ph.D, FACP

PREVENTING DIABETES MELLITUS: YES, WE CAN

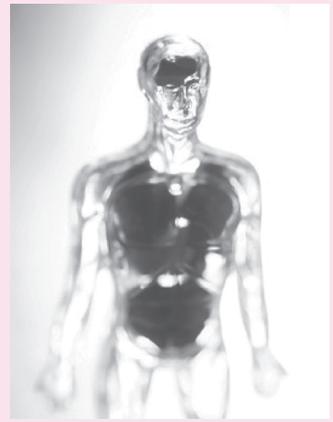
High risk adults (who are defined by either an impaired oral glucose tolerance test, elevated but still pre-diabetic fasting blood glucose levels [100-125 mg/dL], or obesity associated with insulin resistance) can be prevented from developing type 2 diabetes mellitus. And the choices are multiple: thiazolidinediones (such as pioglitazone) reduce risk by 75% at the cost of increased weight gain and water retention; weight loss by 60%; metformin by <50% with the added benefit of weight reduction though at the risk of rare but potentially fatal lactic acidosis in the susceptible. Saito et al, *Arch Intern Med,* 2011 expand our knowledge base by showing that diabetes risk reduction was greatest amongst those closest to actual development of clinical diabetes (i.e. hemoglobin A1c > 5.6%) and the more the number of risk factors, the greater the potential impact of risk reduction strategies.

CAN WE EVER BE SURE CHEST PAIN ISN'T ACUTE CORONARY SYNDROME?

Chest pain is common and often benign. Acute coronary syndrome isn't (common or benign). Differentiating the two ought not require a 3-year cardiology fellowship. To help triage chest pain, ED physicians have come up with 2 useful algorithms.

The Vancouver Chest Pain Rule has 100% sensitivity (does not miss anyone with an acute coronary syndrome) and 18% specificity (may incorrectly include 18% of those who actually do not have an acute coronary syndrome): if the initial EKG is non-ischemic, and ultra-sensitive troponin levels on arrival and after 2 hours are not elevated, the patient in question is younger than 50 years, has no previous history of coronary artery disease, has no prior prescription or treatment with nitrates, and the pain is reproduced with precordial palpation, then you can be certain this is not myocardial ischemia.

The North American Chest Pain Rule also has 100% sensitivity and 21% specificity: if patient is aged 50 years or less, chest pain is not typical of angina, there is no known history of coronary artery disease, there are no (acute) ischemic changes on EKG, ultra-sensitive cardiac troponin is within normal limits, you can rule out myocardial ischemia.



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STATIN-RELATED MUSCLE ACHES: WHAT YOU MUST KNOW

1. Statins (3 HMG Co A reductase inhibitors) are the most widely prescribed drugs world-wide (over 35 million people use statins in USA, at out-patient cost of over $20 billion).

2. Indications for statin use are steadily expanding, in part because of its non-lipid, anti-inflammatory pleiotropic effects.

3. Statins are generally well-tolerated; however, 50% of those who ought to be on statins are not, because of concerns relating to intolerance.

4. Most statin-induced intolerance is either neuromuscular or hepatotoxic.

5. About 50% of statin-treated patients discontinue the drug within 1-2 years because of intolerance.

6. The most common side effect of statin use is myopathy: an "umbrella" term for myalgias (i.e. symptoms of muscle damage such as achiness, cramps, weakness, pain/soreness with/without CK elevation), myositis(elevated CK levels with/without symptoms), rhabdomyolysis (extreme CK elevation at least 10x above normal, with risk of acute renal failure).

7. Several drugs can independently cause myopathy or exacerbate statin-related myopathy: diuretics, biphosphonates, raloxifene (Evista), emetine, protease inhibitors/zidovudine, vitamin E, alcohol, steroids, red yeast rice (lovastatin).

8. Cause(s) of statin-induced myopathy is uncertain, but likely related to inhibition of (target) protein farnesylation and prenylation (such target proteins include Coenzyme Q10), which in turn leads to muscle apoptosis.

9. Over 10 percent of statin users will experience muscle complaints; as this is a relatively uncommon and unpredictable for individual patient (in contrast to steroid-induced myopathy which is predictable at high doses for all exposed patients) it is thought that there is an idiosyncratic element (genetic? metabolic?) to statin-use myopathy.

10. Risk factors for statin myopathy include old age >70 y.o., female gender, small size, frailty, Asian ancestry, family history of myopathic disease, hypokalemia/hypophosphatemia, personal history of prior muscle complaints/dysfunction, unaccustomed/repeated muscle stress, concurrent liver/kidney disease, acute illness/ICU care, diabetes mellitus, hypothyroidism, alcohol misuse, concurrent drug exposure (especially myotoxic drugs or drug that interfere with cytochrome P450 system, particularly 3A4: fibrates, niacin, coumadin, colchicine, digoxin, macrolide antibiotics, protease inhibitors, azole antifungals, verapamil/diltiazem calcium antagonists, amiodarone, cyclosporin/tacrolimus, nefazoline, H2-blockers, grapefruit juice).

11. All statins can cause myopathy, though risk is associated with higher drug doses, better lipid-lowering potency, higher lipophilicity (e.g. Lovostatin, Simvastatin, Cerivastatin) and higher risk of cytochrome P450 interactions (Pravastatin does not interact with cyt P450 system).

12. Least myotoxic statins are Fluvastatin and Rosuvastatin (crestor).Safest statins use of , but only 0-.1% identified in most prospective trials.

13. If muscle symptoms occur in statin-treated patient: consider statin as putative cause (myopathic symptoms not related to drug will usually resolve spontaneously within 2 weeks); check CK level (if elevated, hold statin x 6 weeks); if minor symptoms with normal CK, adjust correctable risk factors (e.g. stop concurrent high-risk medicines) and continue treatment (as symptoms often resolve in few weeks); if symptoms persist, stop statin, switch to Zetia (ezetimide) or bile acid resin (cholestyramine or colesevelam), consider low-dose Crestor used BIW/TIW, reassess serum lipid targets.

THE FUTURE OF OSTEOPOROSIS DIAGNOSIS

Cancellous bone mineral density can be estimated with "routine" CT scans (ordered for other purposes, and not specifically for either osteoporosis screening or diagnosis) using Hounsfield units, which correlate very well with DEXA scores (dual-energy x-ray absorptiometry) as well as bone compressive strength, reports Schreiber et al, J Bone Joint Surg, 2011. Hounsfield units on CT declined with age and showed an excellent correlation with mineral density, making it a useful test for osteoporosis and clinical evaluation for fracture risk. We think the future is nigh.....

COFFEE PLUS PEG-IF KILLS HEPATITIS C

As anyone who has dealt with treating hepatitis C will tell you, the therapeutic options are, well, bloody. Virologic response to the standard treatment with pegylated interferon plus ribavirin is only modest, but now comes data from Freedman et al, *Gastroenterology*, 2011, that drinking 3 or more cups of coffee a day substantially improves virologic response (as measured by hepatitis C RNA titers) and were also more likely to tolerate full doses of pegylated interferon. Neither myself nor Dr. Freedman has any idea how come, but you can be sure that I'll be sending packages of Maxwell's to my favorite patients.

SHOULD WE CATHETERIZE THE VERY ELDERLY?

Percutaneous coronary intervention as part of the evaluation of suspected acute coronary syndrome was retrospectively studied in nonagenarians (mean age 92 years old) by Chait et al, Am J Cardiol, 2011. Mortality and morbidity figures were comparable to those posted for younger subjects, 86% had no post-procedural complications and in-hospital mortality was 7.8%. Notable procedural complications included acute cardiac decompensation (6.7%), kidney failure (5.6%) and cardiogenic shock (2.2%). More importantly, actuarial survival was 61% at 24 months and 32% at 48 months, whilst a quality of life audit suggested similar outcomes with the general (healthy) population as corrected for age and gender. This timely report provides needed reassurance that age per se should not be a barrier to aggressive medical care, especially where the potential for functional rehabilitation is great.

FIBROBLAST GROWTH FACTOR-23 CORRELATES WITH POOR OUTCOMES IN CKD

FGF-23 is an important hormonal regulator of phosphate metabolism, which excretion is progressively restricted in chronic kidney disease. High levels of FGF-23 are common in CKD, and a new study by Isakova et al, *JAMA* 2011, shows a correlation between hormone levels and adverse outcomes (defined as death or end-stage renal failure) in patients with CKD. Surprisingly, FGF-23 was a more powerful independent predictor of outcomes in CKD than serum phosphorus or parathyroid hormone levels, and was a better predictor of (cardiac) death than either traditional (Framingham) cardiac risk factors, severity of kidney failure (GFR) or proteinuria.

BARIATRIC SURGERY IN OLDER MALES

Bariatric surgery has become an established intervention in treating morbid obesity even though its long-term outcomes are still unclear. Previous survival studies in young Caucasian females are difficult to interpret, in part because baseline obesity-related mortality is very low in that cohort. To remedy that defect, Maciejewski et al, *JAMA* 2011, selected a higher mortality group of older male Veterans from a huge hospital data-base. Though crude mortality rates appeared to be lower in these patients post-bariatric surgery, any statistical advantage quickly evaporated using propensity-matched patient controls followed through a mean of 6.7 years. The authors speculate that high peri-procedural mortality associated with the more invasive Roux-en-Y gastric bypass surgery might be complicit in these findings.

THERAPEUTIC HYPOTHERMIA IS NOT OF UNIVERSAL BENEFIT

Therapeutic hypothermia has become a common ICU intervention in the management of coma following out-of-hospital cardiac arrests. It is thought to protect against anoxic brain damage by reducing glucose/oxygen consumption in the brain, reducing nerve cell metabolism (and avoiding metabolic consequences of reduced perfusion), reducing the release of excitatory amino-acids such as glutamate as well as reactive oxygen species, and maintaining the integrity of neuronal cells, intracellular pH and the blood-brain barrier. Laish-Farkash et al, Am J Cardiol, 2011 report on 110 consecutive patients treated following cardiac arrest: 66% of coma due to ventricular fibrillation had successful outcomes, whilst only 8% of those with non-VF as cause of cardiac arrest (including asystole and pulseless electrical activity) had successful outcomes. Predictors of poor outcomes within groups include older age, ejection fraction <35%, seizure activity at presentation, hemodynamic instability at presentation or prolonged anoxic time (before restoration of spontaneous circulation). Death was commonly from severe neurologic dysfunction (all groups), cardiogenic shock (in VF group) and sepsis (in VF group). Morbidity during therapeutic hypothermia is related to progressive dyscoagulopathy, nosocomial/ventilator-associated infections, arrhythmias, cold-induced diuresis (with resultant hypokalemia, hypomagnesemia, hypophosphatemia) and pancreatitis.

USING SODIUM BICARBONATE TO PREVENT CONTRAST NEPHROPATHY

The advantage of sodium bicarbonate to simple volume expansion with sodium chloride has been endlessly debated by nephrologists. Based on the effect of reactive oxygen radical scavengers (such as superoxide dismutase in experimental animals and acetylcysteine in man) in preventing contrast nephrotoxicity, Motohiro et al, *Am J Med*, 2011 re-visits sodium bicarbonate prophylaxis through a multi-center, prospective randomized clinical trial. Using sodium bicarbonate at 1 mL/kg/hr for ~10 hours (3 hours before procedure until 6 hours after procedure) they showed that bicarbonate in addition to saline infusion reduced contrast-related nephrotoxicity by 4x compared to saline infusion alone. This study validates the earlier results of Merten et al, *JAMA* 2004, Ozcan et al, *Am Heart J* 2007 and Briguori et al, *Circulation* 2007, but refutes the findings of Maioli et al, *J Am Coll Cardiol* 2008.

BEWARE OF LONG QT INTERVALS

Prolonged QT interval is more likely to be acquired (commonly from medications or electrolyte abnormalities) than familial (genetic), but both risk cardiac arrest. Diagnosis is based on duration of corrected QT intervals of >440 msec in men and 460 msec in women. Drugs commonly associated with prolonged QT include macrolide/quinolone antibiotics, anti-arrhythmic drugs (including amiodarone), anti-histamines/anti-cholinergics/anti-congestants, amphetamines/sympathomimetics, SSRIs/tricyclic antidepressants, phenothiazine anti-psychotic drugs (including Haldol) and protease inhibitors.

IMPROVING HOW WE PRESCRIBE

Most physician-patient interactions end with a prescription. Problem is that many prescriptions are potentially hazardous, especially amongst vulnerable sub-groups of patients. Hamilton et al, Arch Intern Med, 2011 explores potentially inappropriate drug use amongst the elderly. Using both Beers criteria and STOPP criteria, the most common potentially inappropriate medications prescribed were: (1) Use of PPIs for uncomplicated peptic ulcer for >8 weeks, (2) Use of aspirin in absence of cardiac/peripheral vascular disease, (3) use of benzodiazepines or opiates or neuroleptic agents in patients with repeated falls, (4) Duplicate use of drugs in same drug class, (5) Use of long-term (>1 month) benzodiazepines or long-acting benzodiazepines or benzodiazepines with long-acting metabolites, (6) use of loop diuretics for treating hypertension (in those with normal/mildly abnormal renal function), (7) long-term use of NSAIDs (>3 months) in treating mild arthritis, (8) use of benzodiazepines or sympatholytics (methyldopa, reserpine) in patients with clinical depression, (9) Use of anticholinergics, tricyclic antidepressants or calcium channel blockers in patients with constipation, (10) Use of anti-platelet drugs or NSAIDs or ASA in patients on oral anticoagulants or with bleeding disorder, (11) Any use of doxazosin (Cardura) or flurazepam in the elderly.

SAFETY ALERT #1: BENZOCAINE AND METHEMOGLOBINEMIA

The FDA has recently issued an alert concerning methemoglobinemia developing in children and adults exposed to benzocaine products. Benzocaine is found in non-prescription gel/liquids or sprays such as Orajel, used in relieving mucosal discomfort and oral inflammation.

SAFETY ALERT #2: STATINS AND ICH

Statins are of proven benefit in vascular disease, both for primary and secondary prevention, but may be associated with a predisposition to intracranial hemorrhage. For those patients surviving a deeply-located intracranial bleed, a Markov decision model predicted a gain of 2.2 quality-adjusted life-years by avoiding statin use (Westover et al, *Arch Neurol*, 2011).