Athens Kidney Center
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RETURN SERVICE REQUESTED

TREATMENT OF SIADH

Euvolemic hyponatremia, often secondary to SIADH, is the most common trigger for in-hospital nephrology consultations to address an electrolyte problem. In this situation, despite a low serum osmolality the patient is unable to excrete a maximally dilute urine (failure of "free water" excretion). Consequently, ADH secretion is said to be "inappropriate" and "independent" of intravascular volume status, being commonly due to excessive release of ADH (from non-osmotic stimuli, such as pain or biochemical aberrancy, in which case the relationship between ADH levels and plasma tonicity is lost), exaggerated ADH receptor suprasensitivity (to minimal levels of circulating ADH, in which case the "set point" for osmotic release of ADH is lower than usually obtains) or (activating) mutations of the intra-renal ADH receptor and/or defects in intracellular signaling post ADH receptor activation (resulting in ADH release despite zero levels of circulating ADH). SIADH, as is well recognized, is a diagnosis of exclusion; the diagnostic confirmation relies on quick exclusion of endocrinopathy (in this instance, forget the medical school aphorism that *"uncommon complications of common conditions are more common than common complications of uncommon complications"*: though hypothyroidism is a more common clinical problem, hyponatremia due to adrenal insufficiency is a more common cause of SIADH), protein-calorie malnutrition (extremely low protein diet as found in food faddists, diluted infant formula feeds, jam-toast diets of the elderly-impaired, and extreme poverty) and low urine solute excretion in beer-potomania syndrome. To support the diagnosis of SIADH, confirm normal volume status on exam with absence of clinical dehydration or volume retention (ascites, raised JVD, peripheral edema), urine sodium is >30 mmol/L (though this may later drop if the patients becomes dehydrated), low BUN level, low serum uric acid level, and search for evidence of CNS/pulmonary or neoplastic/HIV-related disease.

Treatment: (1) Stop causative drugs (which either stimulate ADH release from pituitary such as anti-depressants/anti-psychotics and nicotine; potentiate ADH effects on kidneys such as NSAIDs, oxytocin, DDAVP; or have an indeterminate effect on ADH biochemistry such as cyclophosphamide/vincristine, anti-epileptics, ACE inhibitors, clofibrate, omeprazole); (2) consider "therapeutic trial" with 1 liter of isotonic saline (if hyponatremia is due to hypovolemic causes [cerebral salt wasting syndrome, "third spacing", diarrheal diseases, excessive sweating, diuretics/salt-wasting nephropathy, obligate/osmotic diuresis from ketonuria/glycosuria/bicarbonaturia], it will correct without developing signs of volume overload, and urine sodium will certainly rise to be consistently >30 mmol/L as dehydration is corrected; conversely, note that urine osmolality in SIADH is in the 400-600 mOsm/kg range whilst osmolality of isotonic saline is 308 mOsm/kg [Na + Cl], therefore IV isotonic saline is actually more likely to worsen hyponatremia in SIADH); (3) Vaptans (vasopressor/ADH receptor antagonists, i.e. vaptans, are the future of hyponatremia treatment: vaptans cannot be used in anuric patients, pregnancy, hypovolemic states and/or dehydration, and are too slow for routine use in acutely decompensated/symptomatic hyponatremia; the choices include the "ambidexterous" conivaptan which blocks both V2/V1a receptors and is available both orally/parenterally, all other vaptans which can only block the V2 receptor and are only available orally); (4) fluid restriction at 800 mL/day (not an effective long-term strategy); (5) hypertonic 3% saline in symptomatic patients with/without loop diuretics to avoid secondary hypervolemia (slow correction of hyponatremia is the rule and should be stopped at serum Na 130 mmol/L, infused at approximately [weight in kg] mL/hr, but serial plasma sodium monitoring is always critical to avoid "over-correction" and risk of pontile myelinolysis which are probably more common in the elderly, anorectics, hypokalemic and undernourished); (6) diabetogenics (demeclocycline and lithium both induce nephrogenic diabetes insipidus, but either can lead to long-term renal failure, making them unattractive options).

POST-CARDIAC ARREST SYNDROME

Stub et al, *Circulation*, 2011, provide a useful clinical summary of post-cardiac arrest syndrome. Only 24% of out-of-hospital cardiac arrests survive to hospitalization, and about 7.5% make it home from hospital. Survival is related to acuity of hospital care, with best outcomes within specialized cardiac centers (Carr et al, *Intensive Care Med*, 2009). Amongst survivors, morbidity is high, in large part from prolonged visceral hypo-perfusion and whole-body tissue ischemia leading to hypoxic brain injury, myocardial ischemia/ischemic cardiomyopathy and systemic reperfusion injury. Management should focus on: (1) appropriate ventilatory status with adequate oxygenation (including avoidance of hypoxemia or hyperoxemia, either of which is deleterious; avoidance of hypocarbia, which triggers cerebral vasoconstriction; avoidance of hyperventilation which can reduce cardiac output); (2) hemodynamic support, using colloids/crystalloids with/without vasotonic drug therapy to maintain a mean arterial pressure of 65-100 mmHg (though the higher range of 80-100 mmHg might provide superior outcomes); (3) neuroprotection with therapeutic hypothermia, phenytoin-based seizure prophylaxis, and possibly, thiopentone anesthesia; (4) coronary angiography with percutaneous angioplasty, as underlying coronary artery disease is thought to account for the majority of cardiac arrests. Overall, absence of pupillary and/or corneal reflexes at day 3 post-arrest is prognostic of a poor clinical outcome.

SECONDARY STROKE/TIA PREVENTION

Furie et al, *Stroke*, 2011, report on current strategies to prevent a second stroke (at least, 25% of all strokes are "second" or recurrent strokes/TIAs): (1) CT imaging to differentiate ischemic vs hemorrhagic stroke, and EKG/vascular studies to identify modifiable risk factors for recurrence such as atrial fibrillation (Coumadin to INR 2-3) and carotid stenosis (surgery indicated if >50% ipsilateral stenosis where major surgical complication rate is <6%) and valvular heart disease; (2) general strategies (control BP to recommended goal, start anti-platelet therapy with low-dose ASA vs Ticlid vs Aggrenox, correct dyslipidemia with statins to reach LDL cholesterol goal of <100 mg/dL); (3) Behavioral modification (moderate-intensity physical exercise, stop smoking, limit alcohol use).

the
SECOND OPINION

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FROM THE EDITOR

If you were an alien visitor to planet Earth, and happened to stumble upon National Ambulatory Medical Care Survey (NAMCS) data, you'd be forgiven for thinking our civilization was peopled by chronically depressed, dyslipidemic, dyspeptics in perpetual pain. The data shows that 48% of the American population- and that includes teenagers and children- are on at least, 1 prescription pill. Word on the "street" is that the majority of those not on prescription pills are already on non-prescription drugs, mostly of the illicit kind. But I digress. The point is that over three-quarters of all non-institutional physician contacts (in the consulting clinics, out-patient departments and emergency rooms) conclude with a drug prescription, the most frequently written being analgesics, anti-depressants, anti-hyperlipidemic and anti-ulcer drugs.

In the state of Georgia, we face an epidemic of prescription drug-fueled mortality, with six times more deaths from analgesic or hypnotic-sedative overdose than all other medications, licit or illicit, combined. In this state, the chief culprits are alprazolam (marketed as Xanax), methadone, oxycodone (marketed as Percocet, Endocet, Roxicodone and Oxycontin) and hydrocodone (marketed as Lortab and Vicodin). Based on CDC estimates, for every confirmed prescription pill-related mortality, there are at least 35 emergency room visits, and 161 reports of inappropriate drug use. Still, those numbers, shocking as they might be, only represent the tip of a huge iceberg.

Part of the problem is medical training itself, with its reflexive prescription habits, reaching for a prescription pad as the culmination of its non-secular sacrament of consultation. Cultural acceptance of prescriptions as being somehow more honorable as a route to addiction than, say, marijuana or alcohol, complicates the picture. Throw in a black market of filial drug exchange, where prescriptions are routinely swapped between family and friends; aggressive "doctor shopping" by the addicted, dependent, habituated and chronically impaired; diversion and other forms of criminal access to potentially harmful medications; the metastatic spread of "pain clinics" at the edge of misery and suburban dislocation; physician complacency masquerading as empathy; lack of stringent prescription drug monitoring in most jurisdictions, and soon, there is a problem stalking every local neighborhood corner.

Still, the problem of prescription drug misuse is a complex one. As a physician, I am constantly uneasy about under-treating my own patients and subjecting chronic sufferers to a life of pain and anxiety. On the other hand, I am very reluctant to extend- and possibly, support- a drug habit that needs proper evaluation and treatment. Perhaps, it is a reflection of the sad reality of my own chosen sub-specialty, but I recognize that for most of my patient encounters, the buck does stop at my front door. Most often, my decision rests on judgment rather than science or certainty. It is frustrating, and possibly inept, and I am sure many physicians face the same quandary: we do not want to be harbingers of unintended death through sloppy prescription habits, but we also do not want to be purveyors of unending misery.

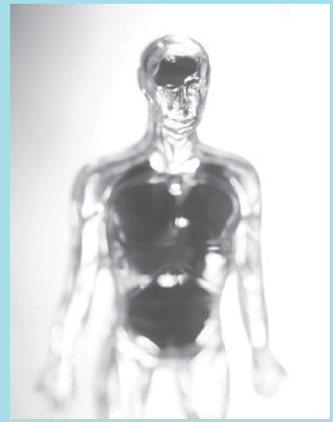
....And speaking of misery, after the blizzard of proposed Medicare vouchers, budget-neutral politricks, trillion-dollar debt-ceilings, hurricane-strength devastation sweeping across the Southeast, threats of government shut-down, sky-rocketing fuel prices, the shibboleth of foreign birth (a.k.a. "birther" controversy), creeping involvement in another foreign war (Libya, that is), a jobless economic recovery, and- horror of horrors- no American of note invited to the royal wedding at the house of Windsor, it was oddly reassuring to see the President complete a hat-trick over 1 weekend. After consoling the bereft and bereaved in Alabama, the commander-in-chief took the scalp of the birther-in-chief, Mr. Donald Trump himself, at the usually light-hearted White House correspondent's dinner, and for an encore, did a Herod Antipas by laying the head of you-know-whom at his country's feet. Maybe its just me, but I sense a new swagger in the American stride.

As always, I'll see you Friday lunch-time, at the CME lounge.

Beze Adogu, MD, Ph.D, FACP

TIMELY REMINDER: UNUSUAL CAUSES OF ST-SEGMENT ELEVATION

Heath et al, *Archives Intern Med*, 2011 present an EKG challenge with syncope, atypical chest pain and ST-segment elevation. A review of causes of ST-segment elevation was presented: transmural myocardial ischemia/infarction, pericarditis, hyperkalemia, ventricular aneurysms and hereditary sodium channelopathies such as Brugada syndrome (autosomal dominant defect characterized by a loss of function mutation in gene encoding the alpha subunit of cardiac sodium channel, with variable expressivity in both time [generation] and location [cell type/cardiac chamber], resulting in heterogeneity of ventricular repolarization and predisposition to arrhythmias often arising from the RV).



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ACTOS: ACTING OUT IN DIABETES PREVENTION

DeFronzo et al, *N Engl J Med*, 2011, report that pioglitazone (Actos), the thiazolidinedione "insulin sensitizer" taken once daily in the morning, was able to reduce the progression of pre-diabetes (individuals at high risk for future development of type 2 diabetes mellitus based on obesity, positive family history of diabetes, and impaired glucose tolerance established through a formal glucose tolerance test) to "full-blown" type 2 diabetes mellitus by 72% amongst study participants. In the randomized, double-blind, placebo-controlled ACT Now Trial, 602 participants were followed for a mean duration of 2.4 years, with only 2.1% of Actos recipients developing diabetes per annum in contrast to 7.6% per annum amongst those on placebo. This is, so far, the largest published reduction in diabetogenesis by any medical intervention, either through diet, exercise or medications. However, this anti-diabetic effect was at the price of weight gain and peripheral edema, a factor in early discontinuation of the drug by about a fifth of participants. Importantly, hemoglobin A1c levels did not increase with time amongst study participants on Actos (in contrast to the finding in the placebo group, where a steady rise in hemoglobin A1c was noted over time). Hemoglobin A1c levels stayed "stable" with Actos, inferring that hypoglycemia was probably uncommon with its extended use in this context. Lipid profiles were less atherogenic (higher levels of HDL cholesterol and lower levels of serum triglycerides) than in the placebo arm of the trial, diastolic BP was lower in the Actos group, fracture rates were roughly equivalent in both arms (in contrast to other studies suggesting that thiazolidinediones might be associated with a higher fracture risk) and progression of carotid artery intima thickness was slower than was seen in the placebo sub-group. NNT (numbers needed to treat) to prevent 1 case of diabetes mellitus per year was 18.

DRUG-INDUCED LUPUS

Many drugs can trigger autoimmune reactivity, presumably by acting as haptens to induce immunoreactivity (or more insidiously, disrupting or otherwise perverting central immuno-tolerance through effects of drug metabolites or T-cell stimulation), often triggering ANA (anti-nuclear antibodies) production. The few cases of drug-induced lupus entail more than simply ANA production: there has to be added clinical features such as fever, arthritis, pleuritis/serositis, mucositis, hepatitis or skin rashes. Notable drugs associated with lupus causation, the so-called "PHAICOPS regimen" are: Procainamide/Penicillamine/Practolol, Hydralazine, Aldomet (alpha-methyldopa)/alpha-interferon/anti-TNF/anti-convulsants, Isoniazid, chlorpromazine, oral pill (estrogen) and sulfa drugs. Two other drugs that are commonly indicted as etiologic for drug-induced lupus are Diltiazem (for hypertension control) and Minocycline (for acne treatment). Drug-induced lupus has specific characteristics: (1) No gender-bias (male = female incidence); (2) Absent renal or neuro-psychiatric features; (3) Common photosensitive scaly rash (similar to subacute cutaneous lupus erythematosus); (4) Positive anti-histone antibodies (in 95% cases if drug-induced, in ~75% of SLE); (5) Negative anti-double stranded DNA antibodies (antibodies to single-stranded DNA are positive); (6) Resolution of disease within 6 months of drug withdrawal; (7) Often associated with a slow acetylator phenotype; (8) absence of hypocomplementemia.

PLEIOTROPISM: STATINS AS NEW-AGE ASPIRIN

Statins block the rate-limiting step of cholesterol biosynthesis by inhibiting HMG Co A reductase, the enzyme which converts HMG CoA to mevalonic acid. That critical step also controls the "down-stream" synthesis of isoprenoids/pyrophosphates, which contribute to the post-translational modification of G-proteins (guanosine triphosphate-binding proteins, such as ras and rho) used for intracellular signaling, and therefore are important effectors of inflammation, proliferation, immunoreactivity and apoptosis. Therefore, statins also have immuno-modulatory, anti-proliferative, anti-inflammatory and anti-atherogenic properties. Several trials have suggested a role for statins in preventing lung and/or colon cancer (Farwell et al, J Natl Cancer Institute, 2008), controlling COPD (Keddissi et al, *Chest*, 2007), avoiding contrast-associated nephropathy (Khanal et al, *American J Med*, 2005), treating polycystic ovary syndrome (Banaszewska et al, *J Clin Endocrinol Metab*, 2007), preventing Alzheimer-type dementia (Jick et al, *Lancet*, 2000) and modulating sepsis (Gao et al, *British J Anaesth*, 2008). It should be emphasized that none of these studies have been universally replicated so far.

Statins are thought to exert their cellular effect by inhibiting several vulnerable pathways simultaneously: for example, blocking the isoprenylation of ras and rho in tandem with reduced cytokine synthesis (such as TNF, IL-6, gamma-interferon), reduced expression of cell surface adhesion molecules and inhibition of transcription factors such as nuclear factor-kappa B (NF-kB) result in potent anti-inflammatory and anti-proliferative effects. Such properties are beneficial in apoptosis and may explain the the anti-proliferative effects of statins demonstrated in cancer cells. By inhibiting protein isoprenylation, statins could limit formation of beta-amyloid fibrils in the brain. Furthermore, statins are thought to arrest mitosis at G1/S phase particularly in dysfunctional neuronal cells, which might be prone to secreting amyloidogenic plaque.

HOSPICE & THE ART OF PREDICTING MORTALITY

Current hospice care in the United States is predicated on the presumption of death within 6 months. Prognostication is difficult, though robust estimates are in development. Schonberg et al, *J General Intern Med*, 2009, developed an 11-point system to predict death within 5 years amongst community-dwelling retirees. Using the NHIS data-base, they subjected 24,115 respondents to 39 risk factors, which were in turn subjected to a multivariate Cox proportional hazards model. Eleven (11) variables were predictive: age (>74 y.o.), male sex, BMI <25, self-perception of health status, history of cancer, history of emphysema, history of diabetes mellitus, past or present smoking, dependent status for ADL (activities of daily living), difficulty walking and hospitalization within past 1 year.

Perhaps more relevant is the retrospective cohort study amongst institutionalized patients with advanced dementia (Mitchell et al, *JAMA*, 2004). Utilizing the minimum data set (MDS) the study found a better prognostic power than FAST 7c (Functional Assessment STaging scale: loss of ambulatory ability) based on a point-score system: (1) Activities of Daily Living (score 1.9), (2) Male Sex (score 1.9), (3) Cancer (score 1.7), (4) Heart Failure (score 1.6), (5) Oxygen therapy in last 2 weeks (score 1.6), (6) Dyspnea (score 1.5), (7) Typically Eats <25% Meals (score 1.5), (8) Clinically Unstable (score 1.5), (9) Bowel Incontinence (score 1.5), (10) Bedfast (score 1.5), (11) Age >83 y.o. (score 1.4), (12) Asleep Most Of Day (score 1.4); if score is 0, risk of dying in next 6 months is 8.3%; for score of 1-2 the risk of death is 10.8%, for score of 3-5 the risk is 23.2%, for score of 6-8 the risk is 40.4%, for score of 9-11 the risk is 57%, for score >12 the risk of death within 6 months is 70%.

EPIGENETIC CHANGES IN DIABETES: THE CASE FOR METABOLIC MEMORY

Diabetic microvascular complications manifest as nephropathy (often leading to kidney failure), neuropathy (causing distal sensory loss) and retinopathy (as a leading global cause of blindness). Those dreaded complications are closely linked to genetic predisposition, duration and severity of chronic hyperglycemia, hypertension and hyperlipidemia. By triggering an accelerated synthesis of superoxide radicals and other cellular mediators (including endothelial/transforming and insulin-like growth factors), the cellular response to chronic hyperglycemia includes microvascular inflammation, microvascular expansion (with endothelial cell proliferation) and activation of the NFkB pathway. However, epidemiological studies indicate that even after correction of hyperglycemia, those cellular and biochemical changes that define "hyperglycemic stress" persist. That persistence of non-heritable changes within the genomic repertoire of previously distressed cells is known as "metabolic memory", or if you will, the "legacy effect". This very poorly-understood phenomenom was recently highlighted by Zhong & Kowluru, *Diabetes*, 2011, in a study on streptozotocin-induced diabetic rats. They were able to show that chronic hyperglycemia x 4 months led to persistent changes in the enhancer and promoter regions of the mitochondrial manganese superoxide dismutase gene (sod2) in the rat retina, which in turn led to increased gene transcripts for nuclear transcription factor NFkB and post-translational modification of histone fragments within the chromatin thread, both hypothesized as active precursors of diabetic retinopathy. Interestingly, those changes (as well as increased levels of cellular mediators) did not normalize on return to euglycemia. In other words, metabolically speaking, your past is your future!

MANAGING CHRONIC ORTHOSTATIC HYPOTENSION

Absolute or relative hypotension (defined as a drop of >20/10 mmHg on assuming an erect posture from recumbency), with or without symptoms of cerebral hypoperfusion whilst standing, occur from loss of intravascular volume or failure of regulatory (autonomic) reflexes from medications, geriatric frailty, loss of baroreceptor sensitivity, loss of vascular (arterial) compliance or peripheral neuropathy.

Once diagnosis has been made, it is important to perform a drug screen to identify any causative or contributory drugs. Typically, those include vasodilatory drugs (anti-hypertensives such as nitrates, hydralazine, minoxidil, sildenafil, and renin-aldosterone angiotensin system antagonists) and dopaminergic agents (including anti-psychotics and tricyclic antidepressants). Next, correct any volume deficits as might be suggested by sinus tachycardia and signs of clinical dehydration. Improve orthostatic tolerance by elevating the head of bed approximately 20-30 degrees, wearing waist-high compression pants/hosiery, and assuming the erect posture "in stages". Post-prandial exacerbation of hypotension can be improved by eating small, frequent meals, drinking coffee with food, and avoiding extremes of temperature. It is also helpful to avoid alcohol consumption, hot baths/spas, vigorous exercises, straining/coughing bouts, rapid ascent to high altitudes, hyperventilation, as well as immediately treat fevers. There are few effective pharmacological strategies in treating chronic orthostatic hypotension; published interventions include erythropoetin (in cases associated with anemia, oftyen started at 25-75 IU/kg given SQ weekly [Hoeldtke & Streeten, N Engl J Med, 1993]), midodrine 2.5 mg p.o. TID (slowly increasing as needed to a maximum of 10 mg p.o. TID [Low et al, JAMA, 1997]), fludrocortisone 0.1 mg p.o. QD (slowly increasing as needed to a maximum of 0.5 mg daily [Robertson & Davis, Neurology, 1995]) and pyridostigmine 30 mg p.o. QD (increasing as needed to a maximum of 60 mg p.o. TID [Singer et al, Archives Neurol, 2006]).

THE SCIENCE OF SPERM ACTIVATION: HOW FERTILIZATION REALLY WORKS

Thanks to Lishko et al, *Nature*, 2011 and Strunker et al, *Nature*, 2011, we are ever closer to understanding the biochemistry of fertilization. Progesterone, which is released by cumulus cells surrounding the oocyte, activates a sperm-specific and pH-sensitive calcium channel (CatSper), in turn leading to a rapid influx of calcium with practically no latency (suggesting that this biological phenomenom is not mediated by "second messengers" such as cAMP). Intracellular calcium fluxes within sperm is the biochemical signal for sperm chemotaxis (moving towards the ovulated egg), hyperactivation and acrosomal exocytosis. It is hypothesized that the CatSper channel might actually be the progesterone receptor on sperm cells, the implication being that blocking this "receptor" could provide a novel pathway for non-hormonal contraception. The question is, of course, would you trust any lothario who murmurs in flagrante: "Darling, I always remember to take my Catsper blocker?".

(NOT) FOLLOWING GUIDELINES, PART III

Rotjanapan et al, *Archives Intern Med*, 2011, highlight discrepancies in UTI management in 2 nursing homes, using a retrospective chart review. Urinalysis in long-term care facilities was found not to meet accepted consensus criteria for antibiotics therapy in 85% of cases (McGreer et al, American J Infect Control, 1991: fever >100.4 degrees F, new or worsening of burning dysuria/frequency/urgency, new flank/suprapubic pain or tenderness, change in urine character, worsening of mental or functional status) yet antibiotics were often started (in 56% of cases), which was the wrong drug anyway in over 72% of cases, wrong dosage in 46% of cases (based on renal function), and wrong duration in 67% of cases, with those receiving antibiotics when they did not meet treatment criteria being 8.5x more likely to develop C. difficile infection in the following 3 months.

As a reminder, treatment of asymptomatic bacteriuria in the elderly is a fraught topic: symptoms may not be classic, but manifest as confusion, incontinence, lethargy, weakness or agitation; asymptomatic bacteriuria in non-catheterized elderly folks is typically transient and benign, and does not require antibiotic therapy; antibiotic treatment will not improve mortality or morbidity, will not maintain a sterile urine, is associated with drug-related adversity and multiple side-effects, will foster emergence of resistant strains, and is associated with higher re-infection rates. However, a case may be made to treat elderly folk who are non-communicative (from dementia or other neurologic illness), are culture-positive for urease-splitting organisms (such as Proteus or Pseudomonas spp.), have corroboration of active urologic inflammation such as leucocyturia, or suffer from chronic immuno-compromise (e.g. poorly-controlled diabetics and patients on immunosuppressant drugs).

ANOTHER OPTION IN FIGHTING HEMODIALYSIS CATHETER INFECTIONS

The major challenge of renal replacement treatment is a functional vascular access. A major problem in access provision is maintaining both patency and asepsis. Maki et al, *Crit Care Med*, 2011, writing for the AZEPTIC Trial investigators show that a triple combination of 7% sodium citrate plus 0.15% methylene blue plus 0.15% methylparaben plus 0.015% propylparaben (C-MB-P) as a catheter-lock solution was well tolerated, prevented intraluminal thrombosis (in the same order as heparin) and reduced the risk of catheter-associated infections by 71%. Those that work with the ESRD population will recall that infections are the #2 most common cause of death amongst dialysis patients, the majority being due to bacterial sepsis. Catheter-related bloodstream infections have been noted in prospective trials to occur at ~2-5 cases per 1000 catheter-days (Labriola et al, *Nephrol Dial Transplant*, 2008).

CLINICAL ALERT: ABDOMINAL WALL DEFECTS IN ATHENS, GA

In the Athens community, we have recently seen an unusual number of fetuses with abdominal wall defects. In the past year, there have been 11 cases of either omphalocele or gastroschisis. The reported incidence of ompahlocele varies from 0.74-3.9/10,000; for gastroschisis, it ranges from 0.47/10,000 in Japan to 4.4/10,000 in England. Regardless, considering that Athens has approximately 3,500 deliveries/year, 11 cases is clearly more than would be ordinarily expected. This case clustering does not necessarily imply any direct causation.

Of the two types of abdominal wall defects, ompalocele carries a worse prognosis generally because of the associated anomalies that occur in 67-88% of reported cases. Also, there is a 30-40% chance of an underlying chromosomal abnormality. If the defect is isolated (i.e. with no other associated structural anomalies) and the chromosomes are normal, the prognosis is much better. Neonatal surgery would be necessary, and sometimes, this is offered as a staged procedure if there is more than bowel involved within the hernia sac. Delivery is usually by Cesarean section to avoid trauma to the (exposed or herniated) abdominal organs.

Gatroschisis is much less likely to be associated with other anomalies, and there is not an increased risk of chromosomal abnormalities. It is usually the result of a right-sided paraumbilical defect that allows the bowel to be out and free floating within the amniotic fluid. Exposure to amniotic fluid over time can result in damage to the bowel, and frequently there will be dilatation of the bowel wall near term. If the bowel is dilated or there is liver involvement, caesarean delivery is recommended. We usually deliver abdominal wall defects here in Athens, and stabilize the neonate before transfer to a tertiary medical center for surgery.

The diagnosis of these conditions is relatively straightforward: an image showing normal umbilical cord insertion into the fetal abdomen essentially rules out an abdominal wall defect. If there are abdominal contents outside of the abdomen, if those contents are contained in a hernia sac and the defect is central, it is an omphalocele. If there are free loops of bowel which are not contained in a sac, and the defect is right sided, it is a gastroschisis. An important diagnostic pitfall is that until 12 weeks gestational age, bowel contents can still be found extracorporeally in normal pregnancy.

We are currently investigating this unusual case cluster and will update you if any significant cause is discovered.

Contributed by Rich Rosemond, MD, Materno-Fetal Medicine