



# UNIVERSITY OF VIRGINIA

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## JOURNAL *of* MEDICINE

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# *Information for Authors:*

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## *Purpose*

The mission of the *University of Virginia Journal of Medicine* is to provide residents, fellows, and faculty members the opportunity to publish original materials generated from their experiences in patient care or patient care–related research. The journal will give housestaff at the University of Virginia Health System the opportunity to work with the faculty in writing medical case reports, thus providing a forum for learning about the process of journal article submission and revision. In addition, the journal offers referring physicians in the state of Virginia, alumni of the medicine training programs, and healthcare providers associated with the University of Virginia Health System the opportunity to learn from the breadth of clinically based educational experiences generated from patient care at the University of Virginia Health System.

## *Article Submission*

Only original, unpublished materials will be considered for publication. Submissions should be made electronically by e-mail to Terry Bennett (tl2e@hscmail.mcc.virginia.edu). When submitting a manuscript, authors should provide full disclosure of any duplicate publication of any content of the paper in a cover letter to the Editor. Funding sources and any potential conflicts of interest reported in the cover letter should also be included in the manuscript text file.

## *Manuscript Format*

- Authors are encouraged to follow the AMA writing style as outlined in *Writing and Publishing in Medicine*, 3rd Edition, Edward J. Huth, MD. Accepted manuscripts are edited in accordance with the *American Medical Association Manual of Style: A Guide for Authors and Editors*, 9th edition. Authors are also encouraged to refer to this guide when preparing manuscripts for submission.
- All submissions should include a title page, text, references, and as appropriate, figure legends, tables, and figures. For preparation of accepted manuscripts, a manuscript text file in Microsoft Word © must be submitted. Figure images should be submitted in separate files, with labels. Legends for all figures should be included at the end of the manuscript text file. Tables must be submitted as text, not images, and included in the manuscript text file.
- Abbreviations should not be used in the title or abstract, even commonly used abbreviations. Limit the use of abbreviation in the text, and expand all abbreviations at first mention in the text. All measurements should be expressed in SI units. Generic drug names are preferred.
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### *Abstracts*

A structured abstract of no more than 300 words for reports of original data. Structured abstracts should include the following sections: Background, explaining the clinical (or other) importance of the study and stating the objective or question addressed. Methods, describing the basic design of the study, patient or participant characteristics, and interventions. Results, reporting and quantifying the main outcomes of the study. Conclusions, providing conclusions of the study supported by the results, along with implications for clinical practice.

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### *References*

- All information not considered statements of common knowledge must be supported by citation of published articles in the medical scientific literature.
- Literature sources must be cited according to AMA guidelines. List all authors and/or editors up to 6; if more than 6, list the first 3 followed by "et al." Number references in the order they appear in the text; do not alphabetize. In text, tables, and legends, identify references with superscript Arabic numerals. Abbreviate names of journals according to PubMed guidelines.

### *Examples of Reference Style:*

Journal Article:

1. Crusher BC, McCoy LH, Bashir JS, et al. Extraterrestrial transfusion methods. *J Interplanetary Med.* 2800;13:53-65.

Book:

2. West H. *Reanimation in Theory and Practice*. Arkham, MA: Miskatonic University Press; 1923.

### *Guidelines for Article Review Process*

Manuscripts will be blindly reviewed by two members of the review board. Decisions regarding acceptance for publication will be based on the strength of the paper compared with other papers in the literature, the need for the *University of Virginia Journal of Medicine* to represent a balanced picture of important advances in internal medicine, and the number of accepted papers in the paper's category and topic area. In addition, reviewers will score submissions based on the following criteria.

- i. Originality of case presentation
- ii. Clarity of teaching points
- iii. Balanced and evidence-based representation of recommendations
- iv. Quality of the writing

**UVa Journal Article Categories:****Clinical Vignettes:** *length - 800-1600 words*

- Clinical vignettes describe patients with classic presentations of rare diseases or common diseases with unusual or interesting aspects. Authors are encouraged to present a brief review of pertinent literature and discuss salient parts of the patient diagnosis. Clinical Vignettes are coauthored by the resident or fellow and the attending physician who supervised the care of the patient and focus on one or two teaching points related to diagnosis, management, or treatment.

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- Presentation of a radiographic image or digital photograph of an intriguing patient case accompanied by a brief case report. Authors should focus on the diagnosis and management of underlying pathophysiology related to the presented image and associated medical condition.

**Medical Grand Rounds:** *length - 1600-3200 words*

- A review article written by an attending physician who recently presented during Medical Grand Rounds at the University of Virginia. Specifically, this article should provide readers a thorough overview of recent scientific and technologic advances, discussed during the Grand Rounds and developed at the University of Virginia, which have contributed to the overall understanding and management of specific conditions.

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- A comprehensive review article written by an attending physician based on a thorough assessment of the literature with the goal of outlining the current understanding of the pathophysiology and up-to-date practice guidelines for specific clinical topics.

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- The Clinical Commentary offers attending or resident physicians an opportunity to provide a unique clinical perspective on a component of patient care, education, or medical advancements. The scope of this submission is quite broad and may incorporate discussion of controversial issues in the practice of medicine, topics related to or examples of patient care that have affected the author's personal or professional outlook, and/or commentaries about health care policy or public health.

**The Academic Hospitalist Corner:** *length - 1600-3200 words*

- This section is dedicated to the emerging field of inpatient hospitalist medicine. Article submissions may be case reports, clinical reviews, perspective pieces, and/or commentaries on medical education and training as related to hospitalist medicine.

**Chief Resident Clinical Medicine Conference:** *length - 1600-3200 words*

- A report that describes a rare or unusual case, with an emphasis on processes of differential diagnosis, work-up, and management that are also applicable to commonly encountered medical conditions. The article should include a thorough discussion of several diagnostic dilemmas with the goal of addressing both the management of complex pathophysiology and the process of systematically arriving at difficult diagnoses.

**Tutorials in Medicine:** *length - 1600-3200 words*

- A classic presentation of a disease process with board-style questions about the case. This is followed by a discussion of one or more of the following: differential diagnosis, pathophysiology, management, or treatment. These should be authored by an attending physician with resident or fellow physician collaboration.

**Clinical Research :** *length - 1600-3200 words*

- Presentation of original data from clinical research conducted wholly or in part at the University of Virginia. Research accepted for publication must be current, well-executed, and applicable to patient care.

Errata

- Archbald-Pannone L, Alcantara-Warren C, Lyman J, Guerrant RL. *Increased Incidence of Clostridium difficile–Associated Diarrhea and Fluoroquinolone Use at the University of Virginia Health System*. UVA JOM. 2009;6:45-48.

In this article published in the University of Virginia Journal of Medicine, Dr Laurie Archbald-Pannone neglected to cite the proper funding source. She received funding in part by the following grants: NIH/NIAID Grant no. U01 AI070491 and NIH/NIAID Grant no. 1K23 AI074681. The author regrets this oversight.

- Enayat S, Mason PK. *A Familial Form of Wolff-Parkinson-White Syndrome: A Case Report and Management Considerations for Patients with PRKAG2 Mutations*. UVA JOM. 2009;6:3-6.

An error occurred in this article published in the University of Virginia Journal of Medicine. The figures were presented out of order. Figure 3 is actually Figure 1, Figure 1 is Figure 2, and Figure 2 is Figure 3. The University of Virginia Journal of Medicine regrets this error.

## ***Autoimmune Thyroiditis as a Complication of Polymyalgia Rheumatica***

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Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) seem to be associated with autoimmune thyroid disease. This rare association was first described in 1974, when a retrospective case series described 59 women with giant cell arteritis and reported that 8.5% of these women had a history of thyrotoxicosis.<sup>1</sup> Results of prospective studies performed since 1974 have demonstrated varying association strength for PMR and GCA. A first prospective study revealed that among 250 patients with autoimmune thyroid disease, 7 patients (2.8%) also had PMR or GCA. All of these patients were women older than 60 years.<sup>2</sup> In another prospective study of 200 patients who had thyroid disease at the time of enrollment, 5 patients (2.5%) also had PMR or GCA, and 1 of these was a man.<sup>3</sup> In a study of 29 GCA patients, however, investigators found no association of GCA with autoimmune thyroid disease.<sup>4</sup> Controversy persists regarding the true strength of any association between PMR and GCA, as well as the cause of the association if it exists. PMR and GCA may occur in the same patient because of an underlying immunologic relationship between the diseases or as a result of a treatment effect, such as corticosteroid administration for PMR or GCA that leads to Graves disease. Many questions remain to be answered. To highlight this phenomenon, we present the case of a patient with GCA confirmed by biopsy results who was also found to have autoimmune thyrotoxicosis.

### **CASE DESCRIPTION**

An 82-year-old white woman presented with a 3-week history of a persistent headache that started while she was on a trip to the British Isles. The patient stated that the discomfort began as tightness around her upper back and neck muscles and proceeded up the back of her neck to her forehead. She denied photophobia, tinnitus, dizziness, vertigo, visual changes, instability, numbness, tingling, difficulty speaking, and other neurologic complaints. She said that she had experienced a similar headache 30 years ago that had resolved spontaneously.

The patient's medical history included a glomus tumor of the left tympanic membrane, cystic lesions that had been identified when she underwent spinal magnetic resonance imaging for back pain, osteoarthritis in her hips and knees, and a history of chronic kidney disease. The patient's family history was notable because both of her parents had brain tumors. She had no family history of collagen vascular disease, diabetes mellitus, hypertension, stroke, bleeding disorders, anemia, or heart disease. Physical examination of the patient revealed normal vital signs and she denied scalp tenderness. The areas around her temporal arteries were normal and nontender bilaterally. Her pupils were equal and round and reacted to light and accommodation. The extraocular movements were full. There was no nystagmus or ptosis. The optic disks were flat bilaterally. Good venous pulsations were seen. No hemorrhages or exudates were noted. The left tympanic membrane showed a red vascular mass consistent with a paraganglioma. The right tympanic membrane was normal. Concentrations of electrolytes, glucose, and hemoglobin A1C were normal.

On the basis of these findings the patient's discomfort was diagnosed as a tension headache. The patient was advised to take acetaminophen every 6 hours for several days, and when she returned to the clinic a month later she reported that her symptoms had improved.

Four months later the patient again sought medical advice, this time for a chief complaint of fatigue that had progressed for several months. The patient also reported loss of appetite and an 8-pound weight loss over a 5-month period. She denied having experienced fever, chills, night sweats, gastrointestinal discomfort or distress, and she had noted no melena or hematochezia.

The patient did report that she felt tired on awakening. Laboratory studies revealed mild anemia, with a hematocrit of 29.5%, hemoglobin of 9.5 g/dL, and an increased platelet count of 465,000 per cubic millimeter. The patient's white blood cell count was 8400 per cubic millimeter with

*Ratnayake, Williams*

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a normal differential. A physical exam performed at the time revealed no new findings. The thyroid gland felt normal, with no palpable masses. A previously documented 2/6 systolic ejection murmur was heard at the left lower sternal border. No abdominal masses were palpable.

The patient was started on treatment with mirtazapine to stimulate her appetite as well as to treat any potential element of depression that may have been contributing to her symptoms. She returned for follow-up 3 weeks later and reported that although her appetite had improved her fatigue and weight loss had continued. She also stated that she had muscle stiffness in the morning and that she had experienced changes in her visual acuity, although she denied episodes of loss of vision in 1 eye (amaurosis fugax) or blindness. Her physical examination at this time revealed fullness in the left supraclavicular fossa, but no significant lymphadenopathy. Laboratory studies for inflammatory and collagen vascular diseases produced normal results. Total protein, albumin, and results of liver and renal function tests were normal. The patient's erythrocyte sedimentation rate and C-reactive protein concentrations were strikingly elevated, however, at 135 mm per hour and 14.2 mg/L, respectively.

The patient returned to the clinic, where physical examination revealed no tenderness or lack of pulsation over her temporal arteries. There was no obvious inflammation of the ocular vessels, and no flame hemorrhages were seen in the peripheral retina. No muscle atrophy or weakness was noted. A diagnosis of polymyalgia rheumatica was made, and the patient started a trial treatment with prednisone 10 mg twice daily, with recommendations for ophthalmologic evaluation and possible temporal artery biopsy, which was performed a few days later. Biopsy results confirmed giant cell arteritis. The patient was then given 1 g of methylprednisolone per day intravenously for 3 days and was started on 60 mg per day of oral prednisone.

After 2 days of treatment the patient reported that she noticed an increase in her energy level. However, 3 months later she returned to the clinic and reported a 2-week history of progressive sluggishness and exertional dyspnea. The patient had also noted midsubsternal chest discomfort early in the morning but no discomfort with exertion or associated breathlessness. She had no paroxysmal nocturnal dyspnea or orthopnea, but did complain of mild swelling of her ankles.

At this time she was taking 25 mg of prednisone daily. Physical examination performed at this time revealed that the patient was dyspneic. Examination of her hands showed palmar erythema and palmar and antecubital diaphoresis. Her thyroid was easily palpated and without palpable masses or nodules. Cardiac exam revealed no additional murmurs or gallops. There was no hepatojugular reflux and the spleen and liver were not enlarged. The patient did have trace amounts of pretibial edema. Electrocardiogram findings were normal. Results of laboratory studies of thyroid function showed thyrotropin concentration less than 0.01 mIU/L, free thyroxine 2.3 ng/L, and T3 uptake 41 with a free triiodothyronine value of 4.5 pg/mL, findings consistent with hyperthyroidism. The inflammatory indices were normal. Results of nuclear uptake confirmed the presence of thyroiditis.

**DISCUSSION**

Autoimmune thyroiditis is associated with many autoimmune processes, including rheumatoid arthritis, lupus, and polymyalgia rheumatica.<sup>5-8</sup> Although patients who present with both thyroiditis and polymyalgia rheumatica are rare,<sup>7</sup> some studies have found up to a 9% prevalence of polymyalgia rheumatica/giant cell arteritis in women older than 60 years who have autoimmune thyroid disease.<sup>6</sup> Whether PMR/GCA and autoimmune thyroid disease are associated is still debated. A growing body of scientific literature suggests that an association does in fact exist, but the cause of such an association between the disease processes is unknown.<sup>9</sup> However, clinicians should be alert to the possibility of this association, and a detailed clinical exam as well as thyroid laboratory assessment should be undertaken in symptomatic patients with PMR or GCA. In the particular case presented here, the observations of palmar erythema and increased palmar and antecubital sweat suggested the diagnosis of hyperthyroidism. Indeed, the potential association between PMR/GCA and thyroiditis could have raised the physician's index of suspicion for thyroiditis before its presence was confirmed by laboratory and imaging modalities.



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*Autoimmune Thyroiditis as a Complication of Polymyalgia Rheumatica*

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## Bronchopulmonary Sequestration

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**B**ronchopulmonary sequestrations (BPS) are rare congenital malformations found in the lower respiratory tract. The presentation can be varied, ranging from severe pulmonary symptoms to incidental detection on radiograph. We describe a case of intralobar BPS discovered in an adult.

### CASE DESCRIPTION

A 53-year-old man presented to clinic with a history of productive cough and recurrent pulmonary infections that began with an initial diagnosis of bacterial pneumonia 10 years prior. Since then the patient's cough had progressed and he had experienced 4 additional episodes of pneumonia. The patient was not a smoker, and his medical history was otherwise unremarkable.

The patient appeared well and his vital signs were normal. No abnormalities were revealed during physical examination. A chest radiograph (Figure 1, A and B) revealed a mass-like consolidation in the left lower lobe, best seen on the lateral projection. Chest computed tomography (C and D) with coronal reconstruction (E) confirmed an irregularly shaped, lobulated lesion in the left lower lobe. Computed tomographic angiogram (F-H) revealed that the blood supply to the mass originated from the celiac trunk via the left gastric artery.

### DIAGNOSIS

Taken together, the findings were consistent with an intralobar BPS. Given his symptoms, he underwent thoracotomy with segmental resection,

where the diagnosis was confirmed on pathologic examination.

### DISCUSSION

BPS are developmental anomalies composed of nonfunctioning pulmonary tissue lacking communication with the tracheobronchial tree. They typically derive a blood supply from the systemic circulation, often from a branch of the abdominal or thoracic aorta.<sup>1-4</sup> The pathogenesis is not well understood, but the lesion is thought to occur early in embryonic development during lung-bud formation.

Intralobar sequestrations most commonly present in late childhood or adolescence but may also present in older patients.<sup>3</sup> Symptoms include cough, recurrent infections, and heart failure due to blood flow through the anomalous vascular supply. BPS can also be discovered as incidental radiographic findings.<sup>3-5</sup> The differential diagnosis includes tumors and other space-occupying lesions, as well as other congenital pulmonary airway malformations.<sup>6</sup> In this patient, the symptoms and imaging characteristics were consistent with BPS. Treatment involves resection for symptomatic patients. Serial monitoring is an option for asymptomatic patients, although resection is often recommended to prevent recurrent infections for patients with intralobar BPS.<sup>4,7</sup> This patient did undergo resection, after which his postoperative course was uncomplicated and his symptoms improved.

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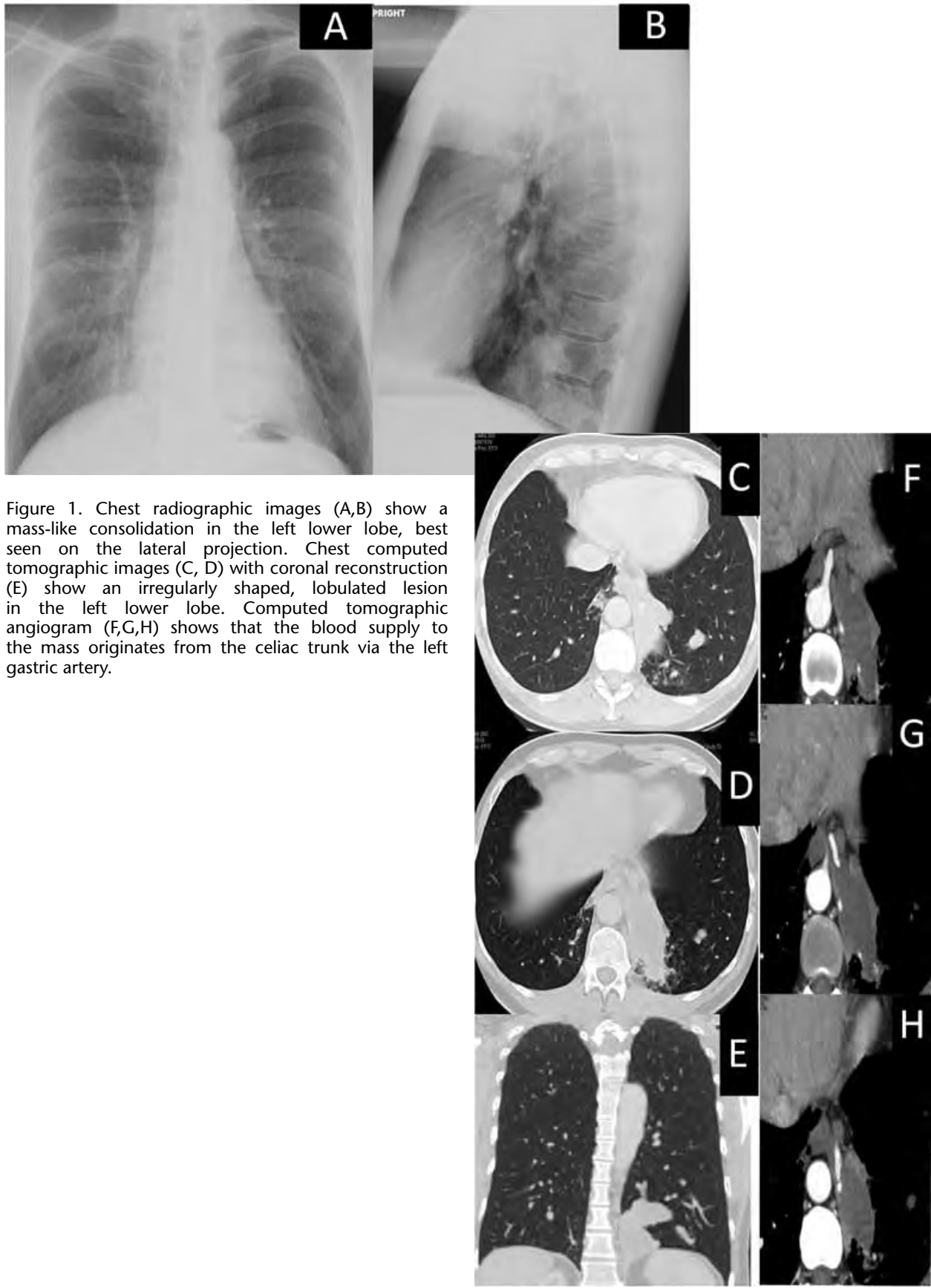
*Kapnadak, Donowitz*

Figure 1. Chest radiographic images (A,B) show a mass-like consolidation in the left lower lobe, best seen on the lateral projection. Chest computed tomographic images (C, D) with coronal reconstruction (E) show an irregularly shaped, lobulated lesion in the left lower lobe. Computed tomographic angiogram (F,G,H) shows that the blood supply to the mass originates from the celiac trunk via the left gastric artery.

## Concerns About Guidelines

*Peter P. Monteleone, MD, MS, Chief Resident, Department of Medicine*

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Previously published in revised form in the *Albemarle Medical News*, Winter 2009.

**P**ractice guidelines and comparative effectiveness research will be important parts of health care reform. The practice of evidence-based medicine (EBM) is certainly desirable, and many of us thought that we were practicing its methods even before “EBM” became a popular catchphrase. Guidelines are not perfect, however, and it behooves us as clinicians to be wary of the potential misuse of guidelines or we may become guilty of substituting “eminence-based medicine” (“Those guys are smart, they must be right.”) or, even worse, “arrogance-based medicine” (“We are really smart, how dare you contradict us.”) for EBM. The presence of guidelines never obviates the need for critical thinking. We thus discuss here several areas in which the use of guidelines should be carefully evaluated.

First of all, physicians should consider the source of any guidelines they use. Organizations work very hard to identify and eliminate, or at least reveal, possible conflicts of interest that may lead to inappropriate influences on guideline development and research promotion. The identification of conflicts of interest is usually achieved through self-reporting of financial relationships, but we are all aware of instances (eg, the Vioxx® Data Safety Monitoring Board) in which conflicts of interest were not apparent while a study was underway or developed after study completion. When conflicts of interest are not revealed, unforeseen motives may have a covert impact on published scientific data as well as on guidelines resulting from that data. The practice of ghost writing, in which a manuscript with an eminent physician listed as the author is actually prepared by a manufacturer, is a construct that can further conceal the impact of such conflicts of interest. Manuscript preparation that involves ghost writing or other undisclosed methods can introduce occult bias and, unfortunately, lead to “influence-based medicine.”

In the legislation for comparative effectiveness research (CER) proposed by the Senate Finance Committee as part of health care reform, CER would be managed (ie, funding would be awarded and

results would be published) by a panel that includes representatives of the pharmaceutical and medical device industries.<sup>1</sup> The prospect of such an obvious conflict of interest is truly frightening. Under this system the motives of external entities would be allowed not only to influence the development of a particular study, but also to have an impact on the selection of which studies are funded, which results are published, and which results are allowed to affect guideline development. Such power over medical research would allow influence-based medicine to directly affect the care of every patient. It would also represent a large step backwards in an era in which the medical scientific community has worked hard to prevent the pharmaceutical and device industries from having a covert impact on physician decision making.

A more subtle form of bias exists because guidelines are written principally by highly experienced specialists. Although these experts are very knowledgeable regarding their fields, their very expertise ensures that their clinical experience consists disproportionately of more complex cases, usually those for which initial management has failed. These cases often require more extensive workups, more sophisticated therapies, and the use of the newest diagnostic technology. This referral-filter bias makes recommendations based on these cases more likely to focus on high-technology and, unfortunately, high-cost approaches that may not be appropriate for patients seeking initial management for less complex health problems. Such overdependence on the most complex approach might be termed “elegance-based medicine.”

Authorship by a collection of disparate experts may, however, increase the applicability of produced work. Guidelines written by panels are often superior to textbook chapters, which are usually the opinions of one or two authors. Coauthors, who are often friends, close colleagues, and long-time collaborators, are likely to share biases, whereas panels consisting of experts of varying backgrounds may reflect an appropriate consensus among highly variant opinions.

*Monteleone, Rein*

The appropriate application of guidelines requires that we ask questions such as “how well do the collected data actually apply to my patient?” or “how closely does my patient approach the mean of the population that was studied?” Such questions are necessary to avoid the “ecological fallacy,” which assumes that all members of a group (eg, test subjects) are very much like the average members of the group. This assumption is of course not true but underlies the one-size-fits-all approach, one of the unfortunately persistent problems with the use of guidelines.

Transfer of conclusions from one population to another is a particularly treacherous practice when dealing with diagnostic tests. To enable investigators to obtain reasonable sample sizes, studies of such tests are usually conducted in artificial populations highly enriched with individuals who have the conditions under study. So, hypothetically, one might choose to evaluate a test on 100 people with tuberculosis and 100 healthy individuals. The test results could be shown to be correctly positive in 85 of the infected individuals (sensitivity = 0.85) and correctly negative in 95 of the healthy individuals (specificity = 0.95). Wow, what a great test! However, this is not the way we use tests, and the interpretation of results requires the use of an independent gold standard for diagnosis. Rather, we might ask, “if my patient has a positive test result, what is the likelihood that he or she has tuberculosis?” The answer depends not only on the sensitivity and specificity of the test but also on the probability that the patient actually has tuberculosis before the test is run.

Bayes theorem yields the conditional probability of an event, in this case the likelihood that a positive test result is a true positive, given the prevalence of disease in the population being tested, or the probability of disease in an individual patient. The probability is given by the formula:  

$$\frac{\text{Sensitivity} \times \text{Prevalence}}{(\text{Sensitivity} \times \text{Prevalence}) + [(1 - \text{Specificity}) \times (1 - \text{Prevalence})]}$$

This equation represents the ratio of true positives to total positives (the latter being the sum of true positives and false positives). Were one to look at the whole population of subjects in the study, in which 50% had tuberculosis, one would get 90 positive results, and 85 of the positive results would be true positives. So the probability that a patient from this population who tests positive for tuberculosis actually has tuberculosis would be 94%. Wow, what a great test; let’s put it in the guidelines!

But, let us now assume that a patient living in central Virginia is found to have a density on his or her chest radiograph, and a physician applies our screening test to this patient as the guidelines suggest. We live in the histoplasmosis belt, and other infections that affect the lungs, such as *Mycobacterium avium* complex and blastomycosis, are not rare, nor is lung cancer. Let us say that the likelihood that this lesion is tuberculosis is 1 in 20. We may get a positive test result, but Bayes theorem now tells us that the probability that the patient who has a positive test result actually has tuberculosis is only 47%. Thus this positive test result is potentially highly misleading<sup>2</sup> and no better than flipping a coin.

Enriched populations are also likely to consist of individuals with a particularly high level of risk factors for the condition in question. One must be careful about applying data collected in these populations to patients at lower risk. For example, the current television commercial for a platelet inhibitor specifically states that “if you have had a heart attack caused by a completely blocked artery” (cue the stretcher in the background), which characterizes the population in which the data were collected. Does a guideline based on these data expand its recommendations to other, lower-risk populations, either directly or by implication?

The evaluation of physician performance on the basis of guidelines is a process in which medical practice tends to be regarded simplistically, as black or white; were the guidelines followed or were they not? In practice, of course, clinical medicine is rarely an uncomplicated dichotomy. Our degree of certainty regarding a diagnosis is really a continuous variable, and an effective diagnostic and therapeutic approach to a patient depends on our understanding a good deal about that individual. One must appreciate highly quantitative assessments of multiple variables, such as the patient’s capacity to follow a regimen, willingness to tolerate adverse effects and outcomes, beliefs and fears regarding an illness, and general physical condition, age, and unfortunately, socioeconomic status. In addition, the variable capabilities of a treatment facility must also be incorporated into clinical decision making. One center may have world-class experts in one test or procedure (eg, cardiac stress magnetic resonance imaging), whereas another facility may be extremely proficient in a parallel procedure (eg, stress echocardiography). Unilateral guidelines do not take into account how optimal care provided by one facility differs from that provided by another.

One must also appreciate the findings of highly individual assessments, such as the degree to which disease is affecting patients' lives and the resulting lengths they are willing to undergo for treatment, the quality of life patients want to achieve with treatment, and the goals of care of the patients and their families. Guidelines cannot address all of these variables, because the studies on which EBM is based often focus on the treatment of a single condition in isolation, and thus cannot adequately consider the interaction of illnesses and characteristics that make patients so different from one another.<sup>3</sup>

If we evaluate physician performance on the basis of adherence to guidelines, we are apparently content to measure process rather than outcome, and the former is sometimes a poor substitute for the latter. True patient outcomes, however, are often difficult or expensive to measure. For example, consider the preservation of fertility through the optimal management of pelvic inflammatory disease or the prevention of cirrhosis and hepatic carcinoma in patients with chronic hepatitis B.<sup>4</sup> These outcomes usually develop years to decades after illness onset, which is the most favorable time for intervention. Studies of true outcomes would take decades and cost millions of dollars to perform. Dropout of study participants and losses of patients to follow-up might bias the results. Thus studies to evaluate the treatment of hepatitis B and serve as the source of guidelines<sup>4</sup> are based on surrogate markers<sup>5</sup> and usually involve shorter-term reduction in hepatic enzymes, reduction in circulating levels of viral DNA, and histological reversal. Unfortunately, the effect of short-term improvements on the incidence of true patient outcomes is often poorly defined.<sup>6</sup> The degree of confidence that can legitimately be inspired by data underlying guidelines should be clearly described, for failure to do this leads to "inference-based medicine," or worse, "overconfidence-based medicine." Guidelines, once formulated, tend to have an unfortunate permanence even in the face of new data. Their development and proliferation require time, and so, like textbook chapters, they are not based on the very newest information and thus may suffer acute obsolescence, often becoming outdated more rapidly than they are updated. The Centers for Disease Control and Prevention released their 2006 guidelines on the treatment of sexually transmitted diseases<sup>7</sup> and had to provide a major revision only about 6 months later,<sup>8</sup> because of new data on resistance patterns of gonococci. Let us avoid "persistence-based medicine."

Use of the very latest results may also lead to problems, however. Initial studies often promote more optimism and enthusiasm than does later understanding, for several reasons. In many statistical settings, data show regression to the mean, and results of subsequent, more extensive evaluations tend to resemble the mean of the population and provide less cause for enthusiasm than did the initial values. Thus, earlier results may inspire more optimism than later ones. In addition, one has to deal with "publication bias," in which positive results are more likely to be published and widely reported than negative results. Many of us have had patients ardently request the latest therapy on the basis of a widely disseminated story of initial results, only to learn several months later that the first blush of enthusiasm was not reproducible. Guidelines are susceptible to the same process.

A particularly dramatic example is the early termination of a study for benefit.<sup>9</sup> It seems ethically essential to stop enrolling subjects in a control group when the treatment has been shown to be superior. Thus many studies are equipped with stopping rules. If the difference in success rates between the treatment and control arms is sufficiently large, it becomes impossible for the study not to show statistical significance, regardless of any subsequent individual outcomes. This situation can occur early in a study if the initial differences are very large. However, if the study is then stopped, the estimate of the benefit is overly large, usually far larger than the benefit that would have been defined had the study proceeded to completion. This artifactual estimate, which may make the newly tested regimen look far better than it is, may underlie a guideline.

One must be particularly wary of guidelines based on subset analyses performed after the fact. Industry sponsors anxious for approval or investigators anxious for positive results to encourage publication may conduct multiple analyses of parts of their data. Some of these comparisons, perhaps 5%, may be statistically significant (traditionally  $P < .05$ ) on the basis of chance alone. One must apply corrections<sup>10</sup> for such multiple analyses, a practice less kindly referred to as "data dredging."<sup>11</sup>

In any case, statistical significance does not ensure clinical relevance. When one of us (MFR) was at the Centers for Disease Control and Prevention, we had access to studies of gonorrhea therapy involving many thousands of patients, and we could demonstrate statistical significance for differences in

*Monteleone, Rein*

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cure rates of only 2% to 3%. When a single patient is being treated, such “significant” differences are of no importance. Clinicians should note absolute as well as relative results of interventions. A 33% reduction in adverse events sounds much less impressive when it is described as a reduction of 2% to 3%. One should also consider the number of patients one would have to treat to obtain a single benefit or to avoid a single adverse outcome. This is an example of an effort-to-*yield* ratio,<sup>12</sup> which is an important consideration when the cost of applying guidelines may be considerable.

Guidelines are useful when they synthesize the data. They may also be valuable in clinical settings in which good information is lacking, but such situations must be clearly identified. Misapplication of poorly supported guidelines, which usually manifests as overreliance on these guidelines, will likely have rather dramatic adverse consequences. Insurance companies may be able to refuse coverage for approaches that deviate from published guidelines, even if such deviations are justified in the care of individual patients. One must also be concerned that deviation from published guidelines may leave practitioners open to malpractice actions. Blindly following guidelines to avoid such legal exposure, “avoidance-based medicine,” may be just one more instance of the defensive medicine that has for decades added to the cost of health care.

Practitioners must consider all of these elements of potential conflict of interest, bias, and statistical complexity whenever they choose to follow a guideline. The use of a guideline is thus a complicated art in itself rather than a straightforward simplification of medical practice. Guidelines in the past have been developed solely as means to aid the practitioner in improving patient care. But what will happen when guidelines are used to assess the practitioners’ use of this art? Who will pass judgment on whether a practitioner is following the correct guidelines, avoiding the incorrect guidelines, and following the correct guideline correctly? Will this be the task of the same panel proposed to manage CER, that same committee for which one fifth of the members were originally slated by the Senate Legislative Branch to be members of the pharmaceutical and device industry? Furthermore, once a deciding body is confirmed, how will effective guideline application be measured? And who will oversee the overseers? And how will the effectiveness of a CER panel be assessed? This centralization of CER will no doubt be a task costly in dollars and work-hours;

shouldn’t criteria for measuring the effectiveness or ineffectiveness of its implementation be in place before it is undertaken?

As practitioners, we constantly remind ourselves that every patient is an individual, that our focus must be on treating the particular patient in front of us and not on treating the generic disease process with which we have labeled a human being. The use of guidelines as an assessment tool will inherently pressure the hand of any physician away from doing what he or she deems best for the patient and toward what will best meet the demands of a governing body who will never lay hand or stethoscope on the patient at the center of the clinical decision. If done well, guideline-based assessment of providers can be an extremely important means to improve the baseline quality of care that our patients receive. If done poorly, however, it could further distance physicians from their patients and from their patients’ best interests. Health care reform will doubtless foster a proliferation of guidelines. In an ideal setting, these would indeed be applied as guidelines rather than as requirements, and their shortcomings would be clearly presented. We expect that most of these guidelines will be quite well crafted and useful. However, guidelines cannot replace critical evaluation and thinking about our individual patients. As the American College of Physicians states in *A Vision for ACP in 2015*, we should be using “evidence-based guidelines that emphasize the value of independent judgment based on an understanding of the patient as a person [emphasis ours].”<sup>13</sup>



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## *Tales from Uganda*

*William Knight, MD, Postgraduate Year 3, Internal Medicine*

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*An estimated 22.4 million adults and children were living with HIV in sub-Saharan Africa at the end of 2008. During that year, an estimated 1.4 million Africans died from AIDS. Around 14.1 million children have lost one or both parents to the epidemic. In Uganda, approximately 1 million people (7% of the population) are living with HIV infection, which has killed another million people and orphaned 1.4 million children.*

*The author and his fiancée Sarah Smith-Vaniz, MD, a pediatrics resident at the University of Virginia Health System, spent 4 weeks working at Masaka Regional Referral Center, a district hospital located in Masaka, a small city in Uganda. Both unnervingly frustrating and tremendously rewarding, their brief time there was packed with interesting stories and impressions, some of which are included here.*

**M**asaka is a small, sleepy city less than a 2-hour's drive from Uganda's capital city Kampala. Masaka is located at the intersection of 2 highways, one that leads to the nearby border with Tanzania, and one that connects Kampala with the mountainous regions in southwestern Uganda. The area surrounding Masaka is quite poor, but benefits from being near one of the main arteries leading to Kampala. Most people tend small family-owned farms, where they grow maize, bananas, and other crops.

At the end of each day, Sarah and I would eat a simple dinner in town. Dinner was often an assortment of matoke (mashed green banana), groundnuts (mashed boiled peanuts), "Irish" (white potato), beans, chicken curry, fish (caught in nearby Lake Victoria), goat, or beef. After dinner, it was never hard to find a motorcycle taxi, called a "boda-boda," to take us to the small hilltop guesthouse where we spent each night, just outside of town. The owner of the guesthouse, Joseph, had built the handful of guest rooms as additions to his own house, and so we shared the living space with his extended family. The family was constantly working: cooking over the outdoor fireplace, making improvements to the complex, washing clothes by hand, and making bark cloth, a beautiful traditional cloth made from bark that the family exports as tapestries to Germany. It seemed they almost never sat down, but could always be heard laughing as they worked.

Sarah worked in the pediatrics ward. The ward was intended for around 30 patients, but instead housed, on average, 120 patients and their mothers. As you made your way through the ward each step had to be carefully planned so as not to crush any delicate little fingers or toes. Many of the children were not seen by a doctor for days. Just a few nurses tended to the crowd. Children were not seen in the emergency department, so mothers simply brought their children directly to the ward, where they often had to wait for days to be seen by a physician, regardless of the severity of their illness. Sarah attempted to pick out the sickest children, but the situation was absolutely overwhelming. Children died almost daily. Many of the children who died had contracted HIV at birth. Others died from dehydration from diarrhea or from cerebral malaria. Their bodies were wrapped in the cloth they came in, and tied with IV tubing before being carried to the mortuary. With neither time nor energy to offer words of condolence to the grieving mother, the nurses moved on to the next patient. Sarah, unable to speak Luganda, looked on, speechless.

One day while I was walking between wards, a man implored me to see his cousin. I followed him to the patient's bedside and reviewed the chart. He was a 35-year-old man with HIV and a CD4 count of around 50, who had been admitted to one of the male medical wards a couple of days prior with slowly progressive fever, confusion, and neck stiffness. He had been treated for bacterial meningitis with ceftriaxone for the past 2 days, but his symptoms had progressed. The patient was somewhat cachectic, and he was lying in bed barely conscious. He was not responding to questions, was extremely febrile, and had a neck as stiff as a board. I performed a lumbar puncture and, later that day, the report from the laboratory showed completely normal cerebrospinal fluid, including a negative India Ink stain. Because India Ink is not highly sensitive for cryptococcal meningitis and the patient had not responded to ceftriaxone, I recommended treatment with amphotericin B for cryptococcal meningitis. The family was able to buy amphotericin at one of the private pharmacies in town for around \$12 per day and it was administered that afternoon. The next day I found the patient sitting up in bed, eating and

*Knight*

feebly smiling. Elated, I went and shook his hand, and spent a few minutes getting to know him. I decided his dramatic recovery made cryptococcal meningitis the most likely diagnosis, and prescribed lifelong fluconazole, which he could get for free from the local "Uganda Cares" HIV clinic.

Uganda Cares is the source of outpatient health care for most Ugandans with AIDS. It is a network of clinics funded by the Ugandan Ministry of Health



A patient with HIV and meningismus before treatment.



The same patient after treatment with amphotericin. Also pictured are the patient's family, the author, and the author's fiancée Sarah.

with help from the AIDS Healthcare Foundation, an international nonprofit organization. These clinics are well funded and well run. Until recently, they provided any new patients with free antiretroviral drugs. These medications are provided by the Ministry of Health primarily through the use of donated funds from the United States government and other sources. However, as reported in a recent article in the *New York Times*,<sup>1</sup> funds for

antiretrovirals have not kept up with the growing epidemic. Many clinics are starting to turn away new patients. The reason for the lack of increase in international funding for AIDS is partly due to the recent recession, but a shift in attitude is also partly responsible. Donors, such as President Obama's Global Health Initiative and the Bill and Melinda Gates Foundation, have decided to focus more on mother-and-child health. According to the Uganda AIDS Commission, to treat one Ugandan AIDS patient costs \$11,500 over the course of the patient's life. Donors have decided that more lives can be saved by increasing spending for infectious diseases that disproportionately kill children, such as malaria and diarrheal illnesses. Some would argue that measures such as bednets, antimalarial drugs, and deworming medications can save many more lives per dollar donated.

Sarah and I have always been interested in working abroad. People say that 90% of the world's health care expenditures are spent on 10% of the world's population. Whether this is true or not, I feel drawn to do my part in addressing such inequality. In addition, Sarah and I both enjoy the adventure and challenge of traveling in the developing world. Through the help of Dr Chris Moore and the Center for Global Health at the University of Virginia, we were able to arrange our trip to Uganda. Going to Uganda for a month was, among other things, an experiment for us, to see if we would enjoy working long-term as hospitalists in sub-Saharan Africa.

Accustomed to Western medical care, Sarah and I felt like Masaka Hospital was in a state of constant emergency. With such pressure, we were highly motivated and ready to help in any way possible. We took sera to the lab if the results were critical, we often bought medications and IV fluids at the private pharmacy in town when the hospital pharmacy was out, we bought missing parts for the inoperable oxygen tanks, and in the end, we felt like we had a positive impact during our short stay there. However, the overcrowding, understaffing, and recurring supply shortages quickly became exhausting. I want to go back for a longer period, but I can't be sure how long my energy would last. After our brief stay, I have even more respect for those heroes who devote their entire working lives to medical care in Uganda.

One such hero is Dr Patrick Banura, our host at Masaka. He is an internal medicine physician, trained in Uganda, who completed his master's of public health in Belgium. Dr Banura currently

does public health research and administration in association with Masaka Regional Referral Hospital, the Uganda Department of Health, and the World Health Organization. A few years after finishing his medical training, while working at a mission hospital around 20 miles north of Masaka, Dr Banura took out a loan and built a medical clinic in a poor area 15 miles north of the mission hospital. He had noted that many of the patients at the mission hospital who had come from this particular area would arrive too late. He concluded that a clinic within walking distance would help reduce the excess morbidity and mortality in this impoverished area. Dr Banura's wife and family warned him that it would not be profitable, given the low levels of income. He knew they were probably right, but felt he should build a clinic where the need was and not where the money was. Now, 8 years later, the clinic still only breaks even and Dr Banura is slowly paying back his loan by using his approximately \$4000 per year salary from the hospital plus income from the World Health Organization. He is able to work at his clinic only on Saturdays, often seeing around 60 patients between 7 AM and 10 PM. Dr Banura used to make the hour-long drive home at 10 PM after work, until one day he was almost killed by armed bandits during the trip. He now spends the night in one of the clinic's acute care beds. Another physician works there and sees patients full-time during the week.

Given his training and experience, Dr Banura could have easily made more money and worked in a more efficient and less resource-poor setting. He is not tied down by extended family—he grew up in western Uganda as part of the Banyoro tribe, far away from Masaka. Most people in Masaka and Kampala are from the Baganda tribe, the majority tribe of Uganda, and speak Luganda. Dr Banura learned Luganda as a second language, and people



Dr Patrick Banura is pictured on the right in front of the rural clinic he built. Also pictured are another physician who works at the clinic and the author's fiancée Sarah.

can tell by his accent that he is from a different tribe. So when elections approach, to be safe, he typically returns to his home region with his wife and children to avoid intertribal violence. Despite the risks of staying in Masaka, and despite the personal gains he could make by immigrating to wealthier neighboring countries, Dr Banura continues to devote himself to the people in and around Masaka, because he feels that is where the need is greatest. Playful, loving, humble, wise, and impressively knowledgeable, Dr Banura is one of the most remarkable people I have ever had the privilege to meet.

An elderly woman quickly straightened her husband's bed sheet and knelt on her bedside mat as I walked up to examine her husband. I had ordered a chest x-ray and a sedimentation rate a couple days before and had returned to review the results. He had made no improvement on antibiotics and was so weak he couldn't swallow. He was getting fluids and medications via a nasogastric tube. Though he was unable to produce sputum for acid-fast bacilli testing, the man's overwhelming cachexia, fevers, dyspnea, high sedimentation rate, and cavitary lung lesion on the chest x-ray made the diagnosis of pulmonary tuberculosis very likely. So I went over to the TB ward to register the patient, and returned with his first dose of HRZE (isoniazid, rifampicin, pyrazinamide, and ethambutol) combination therapy. With the help of the nurse as translator, I explained to his wife that her husband likely had TB, and that we should transfer him to the TB ward to carry out his treatment. The woman made effusive gestures of thanks. Then, unexpectedly, she shuffled toward me on her knees. Reaching out over the foot of the bed, she held her arms out to me, grabbed my forearm, and, pulling my hand toward her, placed a few crumpled bills in my hand, a day's salary. I accepted her offer with thanks, then handed the bills back to her. Rejuvenated by the woman's gratitude, I went on to the next patient.

#### **Acknowledgments**

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## *The End of the Beginning: Health Care Reform and the National Agenda*

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When presidential candidate Barack Obama made national health care reform a top campaign issue, he knew that the implementation of such a promise would be an uphill battle with potentially serious repercussions if he failed. After all, 60 years of attempts to enact national health insurance had been unsuccessful and had left proponents of reform politically vulnerable to accusations of advocating a fiscally irresponsible socialist agenda. However, Obama also knew that opportunities for wide-scale health care reform in the United States surface only every 20 years or so,<sup>1</sup> and that if he became president, his term would occur during an opportune time for his administration to attempt national health care reform. In addition, there were early indications that the public favored legislative action: in a public opinion poll taken shortly before the election, two thirds of respondents reported “it is more important than ever to take on health reform.”<sup>2</sup> After the election, public support of health reform accompanied Obama into the White House, but the honeymoon period was relatively short. Fourteen months after Obama’s inauguration, results of a national poll<sup>3</sup> indicated that the voters’ mood had shifted: only 29% of Americans still believed an overhaul of the US health care system would make the system better. Nevertheless, despite growing voter disenchantment and an acrimonious year-long congressional battle to enact health care reform, the legislative initiative ultimately passed, sealing for the president a historic victory. Now, in the legislative aftermath, there is every indication that implementation of the most significant social legislation since the passage of Medicare more than 40 years ago will be difficult at best, and likely fraught with challenges in the months and years ahead.

### *Elements of the New Legislation*

The Patient Protection and Affordable Care Act and its companion package of amendments, the Health Care and Education Reconciliation Act, were signed into law on Tuesday, March 23, and Tuesday, March 30, 2010, respectively. The passage of these bills culminated a year-long congressional effort in which each step of the process—from committee approval to overall support for the legislation—

lacked bipartisan support. Ultimately, political pragmatism and skillful leadership within the ranks of congressional Democrats prevailed, but not before compromises within the party were made on a range of issues, including abortion, cost control, and the exclusion of a Medicare-like government insurance program that would compete with private insurers. Yet, even as Democratic factions in Congress incrementally congealed around a final, albeit imperfect, bill, Republicans distanced themselves from the legislation, citing fears that the costs of the new national health program would worsen an already soaring federal deficit and insert burdensome government regulations into the lives of citizens and businesses. In the final analysis, passage of the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act did not garner a single Republican vote, the first time in US history that major social legislation of this magnitude was enacted along strictly partisan lines.<sup>4</sup>

The legislation promises expanded coverage of health insurance for uninsured working-age Americans through the enactment of state-based health insurance exchanges that offer individuals and small businesses comprehensive health coverage at group rates. Subsidies will be available for uninsured Americans whose incomes fall below 400% of the federal poverty level (\$43,320 in 2009). Within 10 years, an anticipated 32 million additional people will have gained health coverage, bringing the overall coverage rate of legal residents in the United States to 95%. Many new consumer-friendly regulations will be in place to oversee the administration of health insurance, including prohibiting health insurers from excluding individuals from coverage or charging higher premiums based on preexisting conditions, sex, or health status. Young adults, who make up 30% of uninsured Americans,<sup>5</sup> will be able to remain on their parents’ health plans until the age of 26. Medicaid, the public health program for the poor and disabled, will be reorganized from a categorical program (currently covering low-income pregnant women, children, the disabled, and the frail elderly) to one in which eligibility is extended to anyone whose income is less than 133% of the federal

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poverty level (\$14,404 in 2009). These additional Medicaid beneficiaries will comprise nearly half of the newly covered 32 million Americans.

The legislation also calls for investments in the training of primary care physicians (PCPs) and enhanced reimbursements for PCPs and health professionals working in medically underserved geographic areas. All public and private insurance plans will, over time, be required to offer first-dollar coverage for proven prevention and wellness services. An additional feature is the eventual elimination of the “doughnut hole” in Medicare’s prescription drug plan, a coverage gap of up to \$3000 for Medicare beneficiaries who, on an annual basis, exceed the first \$2250 in federally subsidized drug costs. Although some of the provisions will be implemented in the first year, the major insurance coverage expansion will not be phased in until 2014 and beyond.<sup>6</sup> Cost-control strategies within the new legislation include reducing payments to private Medicare Advantage plans, lowering payments to hospitals with high readmission rates, and empowering 2 new advisory boards to review and recommend innovative payment and delivery models in the Medicare program.

More than half of the \$940 billion cost of the new legislation will be paid for by reductions in the growth of Medicare payments to health care providers (except physicians); reductions in disproportionate share payments to hospitals, which will occur as expanded coverage leads to decreases in uncompensated care; and new fees on insurers, pharmaceutical manufacturers, tanning salons, and medical device suppliers. The remainder of the cost will come from new taxes that will affect wealthier Americans (those with incomes of \$200,000 for individuals and \$250,000 for families) and from penalties and fines. According to the Congressional Budget Office (CBO), the new legislation will not add to the federal budget deficit or accelerate the growth in health spending, but instead will lead to a reduction in the deficit by \$143 billion over a 10-year period.<sup>7</sup> In a later analysis, the Centers for Medicare and Medicaid Services challenged CBO’s numbers and suggested the new health care reform law will actually increase the deficit by \$251 billion during the next 10 years.<sup>8</sup> However, the Commonwealth Fund, a nonpartisan health policy research institute, supports the savings potential of the new law and projects that total health spending will slow under reform, from an annual rate of 6.6% to less than 6%. The Commonwealth Fund estimates that this reduction may save American

families \$2500 a year from 2019 onward.<sup>9</sup> Only time will tell which, if any, of these competing estimates is correct.

In return for the law’s new benefits and regulations, individual Americans will be required to have health coverage or pay a penalty. Similarly, fines will be imposed on businesses that do not offer employee health insurance and have more than 50 employees and at least 1 full-time employee eligible for a federal subsidy to purchase coverage on the exchange. Individuals without coverage will pay a penalty of \$95 or 1% of taxable income in 2014, with the penalty increasing to \$695 or 2.5% of taxable income by 2016. Some experts have asserted that the penalties are not burdensome enough and voiced the fear that healthy individuals will opt to pay the penalty rather than purchase coverage in the exchanges, which could lead to fewer insured Americans and more expensive insurance premiums.<sup>10</sup> Other experts have disagreed, citing the health insurance system in Massachusetts, the only state that mandates individual health coverage, where the uninsured rate is now less than 3%.<sup>11</sup> If the nation follows the example of Massachusetts, the subsidies in the new reform bill may lead to increased purchase of health insurance by price-sensitive healthy Americans who would contribute to the development of a stable risk pool, which in turn, would moderate premium levels. Nevertheless, even if the reform package covers the estimated cost of insuring an additional 32 million Americans by 2019, 5% of the population, or 23 million, will remain uninsured. One third of the individuals who still lack coverage will be undocumented immigrants, and the others likely will be individuals who are moving in and out of employer-based insurance, who are exempt from the mandate because of religious or economic hardship, or who have decided to pay the penalty rather than purchase coverage.

***Challenges Ahead for the Reform Effort***

Now that the historic health reform is law, the herculean task of implementation remains. Although the legislation lays out the guiding principles for what is needed, it does not offer specific ways and means to put the spirit of the law into practice. Even though the major coverage expansions do not take effect for several years, the building blocks of the redesigned system kick in much sooner, and federal and state agencies will be spending the next weeks and months implementing new provisions and programs. Rolling out the new provisions within the specified deadlines will be challenging and crucially

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important, because how the new programs and provisions are perceived and implemented will largely determine the public's view of the president's new plan. The first political testing ground will be the November 2010 midterm elections.

The immediate challenge, according to the implementation timeline, is the creation of insurance pools for people who are uninsured because of preexisting health conditions. High-risk pools will provide a safety net for these individuals. The new law targets \$5 billion for the establishment of a transitional high-risk pool (until the coverage expansions begin in 2014). Currently, 35 states cover 200,000 people in high-risk pools, but the rates and coverage provided to members of these insurance pools varies, and applicants may face long waiting lists. Another priority is to synchronize the new national benefit plan with state programs already in place and to set up coverage opportunities for eligible uninsured individuals in states without high-risk pools. The deadline for implementation of the national high-risk pool was July 1, 2010.

Other first-year deliverables include allowing dependent children to stay on family policies until age 26, beginning the elimination of the prescription drug doughnut hole in the Medicare program, requiring insurance companies to spend at least 80% of premium dollars on health care services (the annual average now is 73.6%),<sup>12</sup> providing businesses with fewer than 25 employees a tax credit to purchase health insurance, and increasing funding for community health centers and programs to expand the supply of primary care health professionals. Although these early initiatives will help only a modest number of Americans, they nonetheless will provide tangible benefits immediately and thus help stem confusion about the new law as well as mitigate to some extent the disappointment among supporters of reform who expected more dramatic changes in the short term.

***What the New Law Means for Physicians***

The new legislation will be successful only if physicians accept and adopt it, so it is important to examine how it will affect physicians. Certainly, having 32 million more Americans with health coverage will please physicians, who first and foremost advocate adequate health care coverage for their patients. But between compassion and coverage lies a burgeoning landscape of new insurance regulations, Medicare and Medicaid payment reforms, and escalating health care spending that is fueling the federal deficit.

Physicians are understandably guardedly optimistic but concerned about the future.

PCPs will be the big winners in the short term under the new legislation. The legislation authorizes specific programs to stabilize and expand the PCP workforce by providing for an immediate 10% increase in Medicare reimbursements and longer-term investment in programs to support workforce education and training. In addition, Medicaid will begin reimbursing general internists, family physicians, and pediatricians at Medicare rates, which are substantially more generous than current reimbursement. This increased funding for reimbursements, coupled with financial support for the expansion of community health centers, should begin to alleviate access problems for patients seeking primary care. The flip side of this benefit is the stress that 32 million new patients will place on the limited supply of generalist physicians. Although the legislation provides new funding to increase the number of PCPs and nurses, few believe it will eliminate or even significantly address the looming shortage of physicians, which the American Association of Medical Colleges has estimated will reach 124,000 to 159,000 by 2025.<sup>13</sup>

Another area of interest and possible concern to physicians is the probable change in Medicare's reimbursement methodologies. As mentioned previously, the new law calls for the establishment of several centers within the Centers for Medicare and Medicaid Services. The Center for Medicare and Medicaid Innovation will be charged with establishing pilot programs to test, evaluate, and expand various payment and service models in Medicare, including the patient-centered medical home and the establishment of accountable care organizations. These models provide financial incentives for physicians and physician groups to adopt integrated models of care that focus on increasing efficiency and value while demonstrating improved quality of care. Although these new payment models may hold great promise for bringing about improvements in patient care, the process of shifting Medicare reimbursements from the traditional volume-based fee-for-service system to bundled payment during an episode of care will be challenging for both physicians and patients. Physicians may worry that the change in payments will bring lower reimbursements from public programs,<sup>14</sup> and patients may fear that the emphasis on managing care will usher in a resurgence of the 1990s managed-care era that restricted access to services.<sup>15</sup>



*The End of the Beginning: Health Care Reform and the National Agenda*

Physicians may also be disappointed that medical liability tort reform was not more directly addressed in the health reform bill. Although the bill includes a provision for modest funding (\$50 million) for 5-year demonstration grants to states to develop, implement, and evaluate alternatives to current tort litigations, critics have said that this measure lacks any real power to combat the problems in the current medical malpractice system.<sup>16</sup> Although the overall costs of medical malpractice and defensive medicine may not be viewed as significant relative to the \$2.5 trillion annual spending on health care—cost estimates by the CBO and Harvard researchers have indicated that direct and indirect costs of malpractice litigation and defensive medicine are \$10 billion and \$60 billion per year, respectively<sup>17</sup>—physicians take little solace in those numbers when it comes to personal experience regarding their vulnerability to liability exposure and the necessity of practicing defensive medicine.<sup>14</sup>

The reform bill also does not address the continued chaos surrounding the correction of problems with the Sustainable Growth Rate (SGR), the formula used by Medicare to calculate physician reimbursement. Politicians and physicians alike have agreed that the SGR is a flawed system, but the \$371 billion price tag to update the SGR methodology proved too expensive to include in the final health care bill. In response, physician groups around the country have continued to pressure Congress to eliminate

the 21% reduction in Medicare reimbursements now delayed until December 1, 2010, and fix the SGR problem once and for all.<sup>18</sup>

*The End of the Beginning*

The recent passage of health care reform is historically significant, but it will take years for the real impact of its implementation to unfold. Although most Americans will see little or no change in their health care arrangements over the next few years, administrative challenges and burdens will be keenly felt by federal and particularly state agencies that must set up the new insurance exchanges for small businesses and individuals, enforce the new insurance reforms, and oversee the new Medicaid expansion. Over time, federal legislators will make corrections and improvements to this imperfect piece of legislation as they attempt to balance the dual challenges of encouraging universal health coverage and controlling ever-increasing health care spending.

As we stand on the precipice of momentous change in our health care system we are reminded of Winston Churchill's remarks in 1942 after a hard fought victory in battle during World War II: "Now this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning."<sup>19</sup> Churchill's words resonate now as we all wait to see what lies ahead in health care.

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## Wide Complex Tachycardia in an Unresponsive Patient

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### CASE PRESENTATION

A 57-year-old woman with a history of depression presented to the emergency department with pronounced lethargy. At presentation, no further details regarding her history were available. Initial vital signs included temperature 37.1°C orally, pulse 147 beats/min, respirations 16/min, blood pressure 104/68 mm Hg, and oxygen saturation of 97% on room air. During her physical examination the patient was disoriented and somnolent, and she would arouse only in response to painful stimuli. Her pupils were dilated at 7 mm bilaterally, with some reaction to light; mucous membranes were dry. Cardiopulmonary examination findings were significant only for tachycardia. The electrocardiographic (ECG) monitor in lead I demonstrated a tachycardic rhythm with minimal widening of the QRS complex (Figure 1).

**Query 1.** At this point in the evaluation, the ECG data in Figure 1 are best described by which of the following statements?

A. The rhythm is ventricular tachycardia likely secondary to an evolving acute coronary syndrome.

- B. The rhythm is sinus tachycardia resulting from an as yet unknown physiologic event.
- C. The rhythm is sinus tachycardia with additional findings strongly suggestive of a toxic insult.
- D. The rhythm is sinus tachycardia likely due to an evolving central nervous system (CNS) event.

The findings on examination of the patient's abdomen were unremarkable except for limited bowel sounds. The skin was dry. Results of laboratory tests indicated normal electrolytes, renal function, cell counts; a subsequent computed tomographic scan of the patient's brain revealed no acute abnormalities.

A 12-lead electrocardiogram was quickly obtained and revealed sinus tachycardia with a rate of 144/min, a QRS complex duration of 100 milliseconds, and a minimally prolonged QTc interval (Figure 2). Right axis deviation of the terminal QRS complex was also noted, as evidenced by a prominent S wave in lead I and a prominent R wave in lead aVR. Although not conclusive at this early stage of the evaluation, this constellation of clinical and ECG findings suggested sodium channel blockade likely resulting from a tricyclic antidepressant (TCA) ingestion.

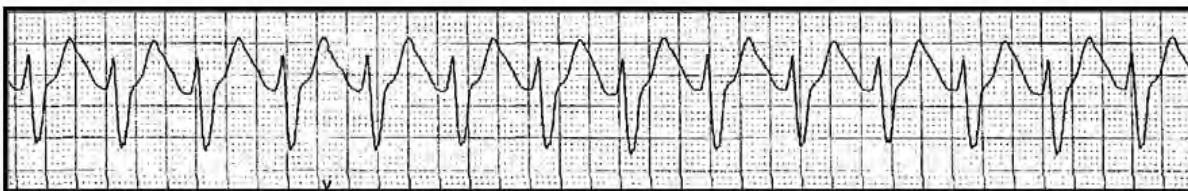


Figure 1. Lead I electrocardiographic rhythm strip early in presentation demonstrating sinus tachycardia, widened QRS complex, and deep S wave.

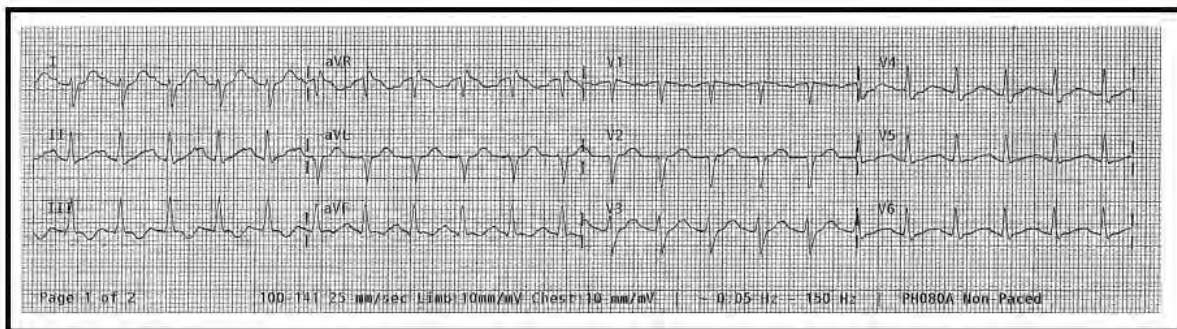


Figure 2. A 12-lead electrocardiogram showing sinus tachycardia, widened QRS complex, prolonged QTc interval, and terminal right axis deviation manifested by a deep S wave in lead I and R wave in lead aVR.

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**Query 2.** The ECG findings suggestive of the diagnosis include which of the following?

- A. Sinus tachycardia, inverted T wave in lead III, and nonspecific ST segment–T wave abnormalities.
- B. Sinus tachycardia, widened QRS complex, and R wave in lead aVR.
- C. Sinus tachycardia and prolongation of the QTc interval.
- D. Sinus tachycardia, pronounced QRS complex widening, and the S<sub>1</sub>–T<sub>III</sub> pattern.

A repeat ECG obtained approximately 20 minutes after the initial ECG (Figure 3) demonstrated progressive change. Based on the patient’s clinical presentation and the appearance of the ECG, empiric therapy was initiated.

**Query 3.** In addition to general resuscitative therapy and critical care, what specific interventions are needed in this patient with suspected TCA ingestion?

- A. Naloxone infusion with strict serum glucose monitoring.
- B. Sodium bicarbonate therapy with emergent hemodialysis.
- C. Empiric antibiotic administration for possible CNS infection, with sodium bicarbonate infusion.
- D. Sodium bicarbonate therapy with urgent paralysis-assisted endotracheal intubation and ventilatory support.

**DISCUSSION**

Patients with TCA-induced QRS complex widening are at risk for hypotension and cardiac dysrhythmias;

furthermore, signs of CNS toxicity, including coma and seizure, are not infrequently seen in this population. QRS complex abnormality in the poisoned patient is most often caused by myocardial sodium channel blockade; agents that cause myocardial sodium channel blockade produce a characteristic ECG pattern of terminal right axis deviation accompanied by a widening of the QRS complex (Figures 2 and 3). Recognizing this ECG constellation can help the physician narrow the differential diagnosis and adjust therapy. More importantly, QRS complex widening provides a clinical indication for the administration of sodium bicarbonate, which can be life-saving regardless of the specific offending poison.

Agents with a sodium channel blocking effect are a chemically diverse class of medications. Many xenobiotics act as sodium channel blockers and, in

Amantidine	Doxepin
Carbamazepine	Imipramine
Chloroquine	Nortriptyline
Class IA antidysrhythmics	Maprotiline
Disopyramide	Diltiazem
Quinidine	Diphenhydramine
Procainamide	Hydroxychloroquine
Class IC antidysrhythmics	Loxapine
Encainide	Orphenadrine
Flecainide	Phenothiazines
Propafenone	Mesoidazine
Citalopram	Thioridazine
Cocaine	Propranolol
Cyclic antidepressants	Propoxyphene
Amitriptyline	Quinine
Amoxapine	Verapamil
Desipramine	

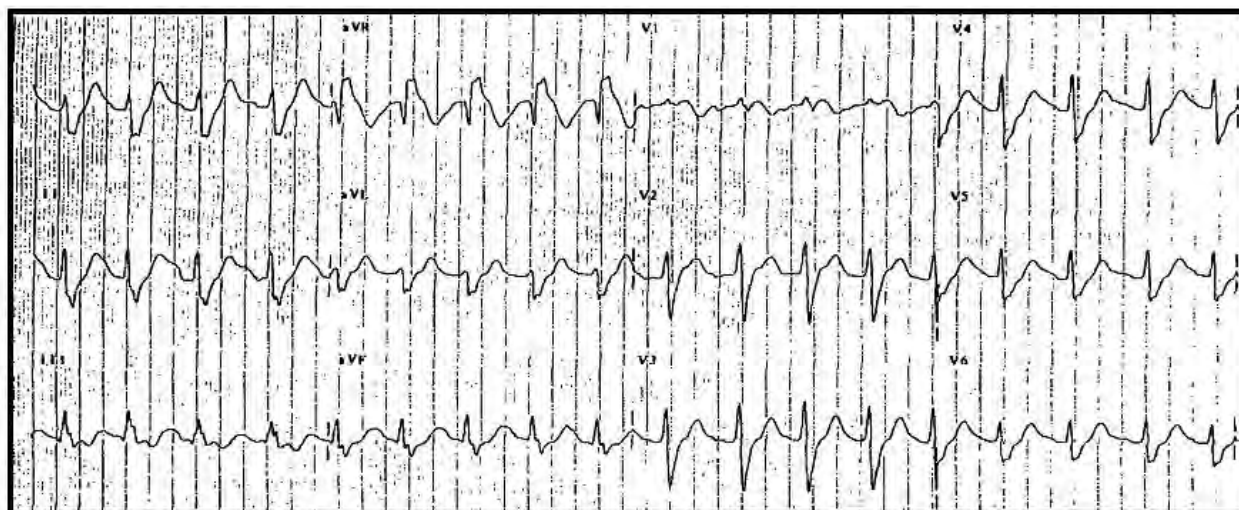


Figure 3. Progressive changes are seen in this electrocardiograph, including continued sinus tachycardia, further QRS complex widening, and increased terminal right axis deviation (deep S wave and very prominent R wave).

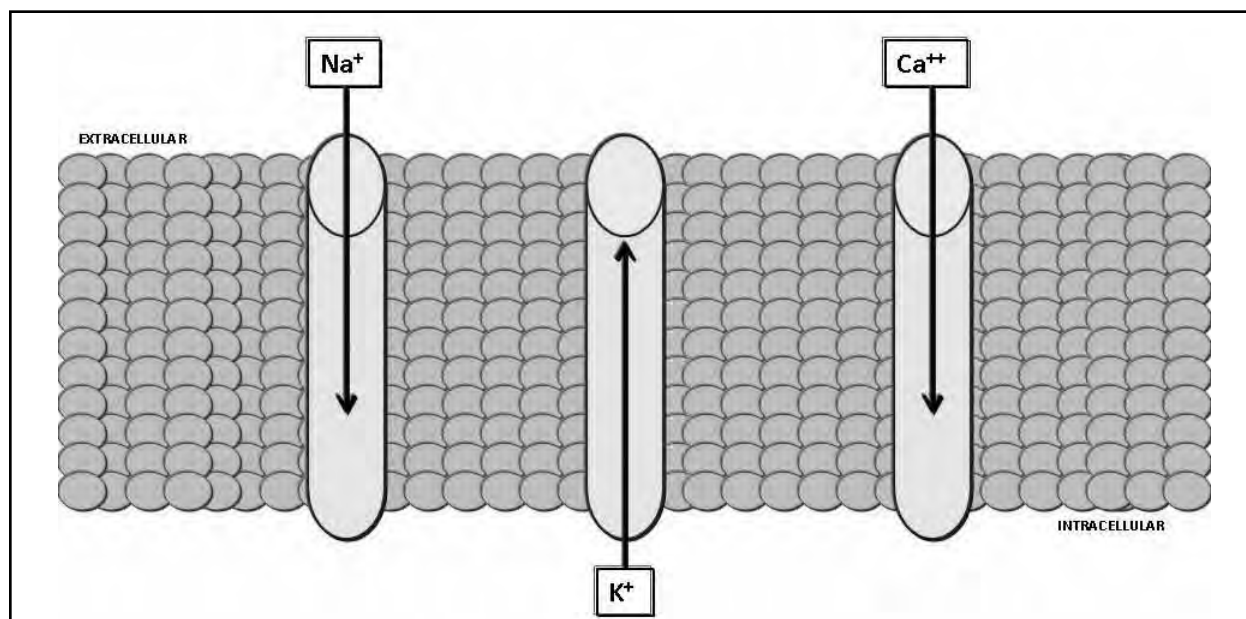


Figure 4. Cellular ion channels involving sodium, potassium, and calcium.

patients who have ingested a drug overdose, these effects are magnified. These agents range from cardiac antiarrhythmic agents and antidepressants to cocaine and certain narcotic medications. Table 1 provides only a partial list of such agents. A commonly encountered category of medications with sodium channel blocking ability are the Vaughan-Williams type I antiarrhythmic agents. In fact, the "prototypical" sodium channel blocking agent is quinidine. Many of the agents with sodium channel blocking ability are often referred to as having membrane-stabilizing, or "quinidine-like," effects. The TCA medications are another class of such agents and are perhaps the best known of all sodium channel blockers. Thus, much of this discussion focuses on the TCA as the offending agent in this patient. It must be remembered, however, that there are additional agents that have the potential to inhibit sodium flux across cell membranes and lead to a clinical syndrome similar to that seen with TCA-induced QRS prolongation.

#### **Pathophysiology**

To appreciate the cardiac complications of various xenobiotics, physicians must have a clear understanding of basic myocardial cell electrophysiology. Numerous ion channels (Figure 4) are found in the cell membrane; cyclic opening and closing of these channels produces the characteristic action potential (Figure 5) and, ultimately, the electrocardiographic signal depicted on the ECG.

Depolarization of the cardiac cell membrane is due to the rapid opening of sodium channels (Figure 4) and the subsequent massive sodium influx (phase 0 of the action potential; Figure 5). This sodium influx causes the rapid upstroke of the cardiac action potential as it is propagated through the ventricles; it is directly responsible for the QRS complex on the ECG. The peak of the action potential, and the end of phase 0, is caused by the closure of sodium channels; activation of the potassium efflux channels (phase 1) immediately follows. Concurrently, calcium influx occurs, allowing for

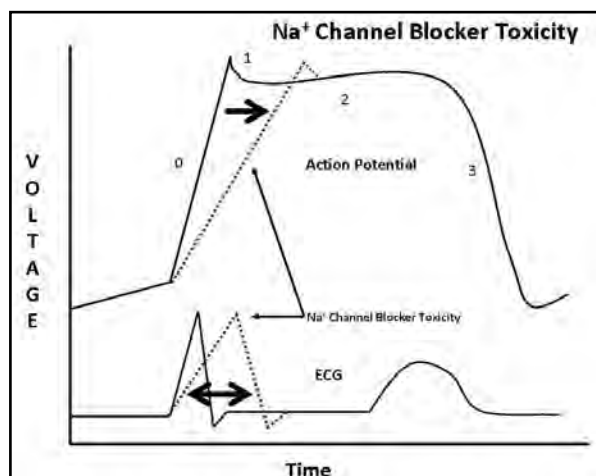


Figure 5. The cardiac action potential. Phase 0 is impacted by the blockade of the sodium channels, producing a delay in this rapid influx of sodium ions. The surface electrocardiogram (ECG) manifests this delay in phase 0 as a widened QRS complex.

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a plateau in the action potential (phase 2) and myocardial contraction.

The cardiac cycle ends with closure of the calcium channels and activation of rectifier potassium efflux channels, which return the membrane potential to  $-90$  mV (phase 3). It is this potassium efflux from the myocardial cell that is directly responsible for the QT interval as seen on the surface ECG (Figure 5). The sodium-potassium-ATPase pump actively moves 3 sodium molecules out of cardiac cells while pumping in 2 potassium molecules, to maintain a negative electric potential in the myocyte of approximately  $-90$  mV (phase 4).

Myocardial sodium channels exist in 3 phases: resting, activated, and inactivated.<sup>1</sup> Xenobiotics with sodium channel blocking activity generally bind to sodium channels in either the inactivated

or activated phase, slowing recovery of these channels and consequently decreasing the amount of sodium “moved” per unit time into the cell.<sup>1</sup> This reduction in sodium entry delays the upslope of depolarization, prolonging the time for the ventricles to depolarize, resulting in a widening of the QRS complex. The degree of widening depends on the number of sodium channels affected. As the heart rate increases, there are more channels in the activated and inactivated state, producing more channels “susceptible” to blockade; thus, increasing heart rate will produce a “more intense” blockade of the cellular sodium channels.<sup>6</sup>

In addressing this broad range of sodium channel blocking agents, clinicians must consider that multiple mechanisms of toxicity are at work at any given time for any given toxin; in other words, sodium channel blockade and its resulting clinical

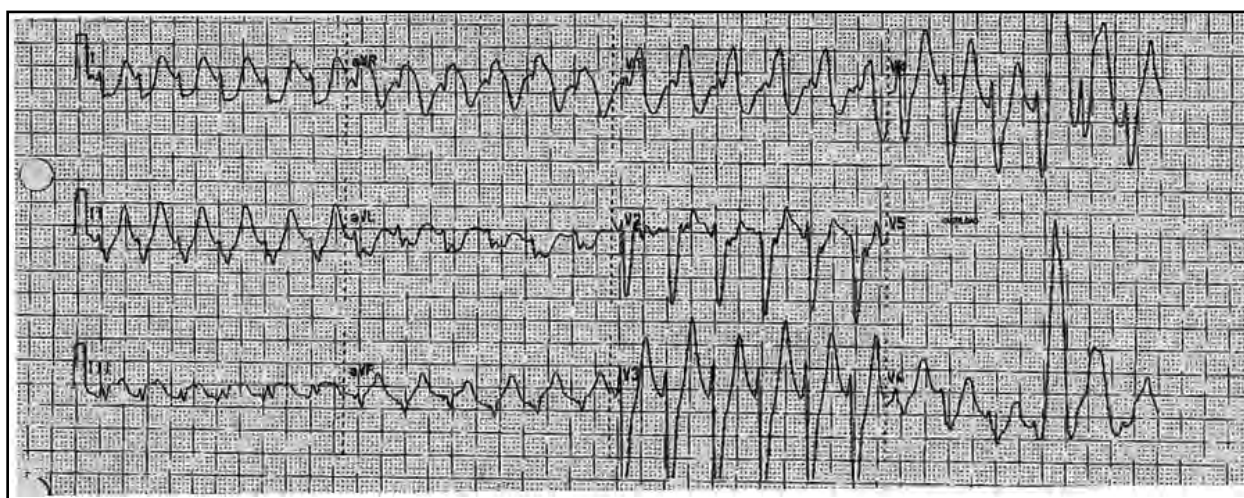


Figure 6. Toxin-mediated wide QRS complex tachycardia. This rhythm likely results from a combination of sodium channel blockade (QRS complex widening) and anticholinergic effect (tachycardia).



Figure 7. Wide complex tachycardia in patients with sodium channel blockade. A. The QRS complex width is approximately 0.12 seconds in this example. B. In this example, the QRS complex is markedly wider and more obviously shows a wide complex tachycardia.

*Wide Complex Tachycardia in an Unresponsive Patient*

effects can also be mediated by other pathways or mechanisms of toxicity. For example, the TCA class acts via a multitude of mechanisms, including anticholinergic effects, potassium efflux blockade,  $\alpha$ -1 antagonism, serotonin reuptake inhibition, and GABA ( $\gamma$ -aminobutyric acid) antagonism; cocaine manifests its toxicity via the sympathomimetic mechanism; and diphenhydramine acts via antihistaminic and anticholinergic mechanisms. Of course, all of these agents also demonstrate varying degrees of sodium channel blockade.

***Electrocardiographic Abnormalities***

Electrocardiographic findings are a very important source of clinical data in the poisoned patient. One such data point is the QRS complex; widening of the QRS complex is an ominous sign of significant toxicity. In a general sense, the consideration of the widened QRS complex usually occurs when durations are greater than 120 milliseconds. However, in the previously healthy patient

with a toxic ingestion, a QRS complex duration greater than 100 milliseconds is considered wide. In addition, the potential for dysrhythmia is present at this level and increases proportionally with increasing widths (Figures 1, 2, 3, 6, and 7).<sup>2</sup> More specifically, sodium channel blockers characteristically cause prolongation of the QRS complex; furthermore, the terminal 40 milliseconds of the QRS complex demonstrate a rightward axis deviation—in extreme cases, a right bundle branch block pattern is observed.<sup>3-5</sup>

The classic (and very specific) electrocardiographic pattern of a minimally widened QRS complex with terminal rightward axis deviation is suggestive of sodium channel cardiotoxicity; this terminal rightward axis shift is manifested on the ECG as a prominent R wave in lead aVR and a deep S wave in leads I and aVL (Figures 2, 3, and 8). Although the pathophysiology behind this pattern is not fully understood, it has been suggested that the

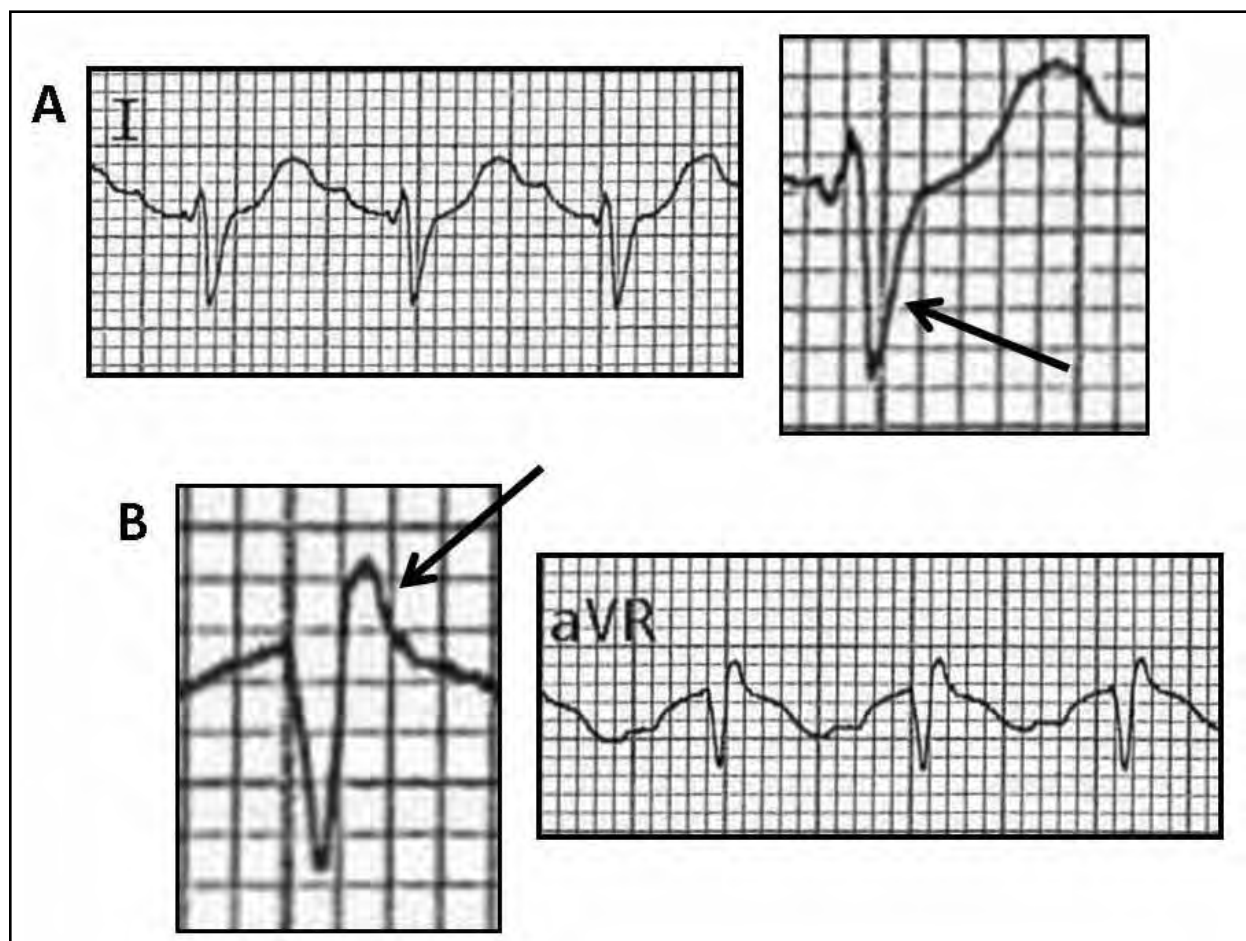


Figure 8. The  $S_1/R_{aVR}$  pattern seen in patients with significant cardiotoxic sodium channel poisoning. This pattern represents extreme rightward axis deviation of the terminal 40 milliseconds of the QRS complex and is strongly suggestive of sodium channel toxicity in poisoned patients.

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“smaller” right bundle becomes poisoned first, resulting in this right axis deviation—and the resultant ECG findings. Importantly, complete right axis deviation is not usually seen as a manifestation of sodium channel blocker toxicity; if found, either an extreme poisoning or other etiologies should be considered.

When a patient with suspected poisoning is being evaluated, a QRS complex duration longer than 100 milliseconds should alert the physician to the presence of a sodium channel blocker, particularly with the  $S_1/R_{aVR}$  pattern. This combination of findings—widened QRS complex with terminal rightward axis deviation—strongly suggests the possibility of sodium channel blockade in a poisoned patient. The magnitude of these findings can also be monitored with progressive ECG findings mirroring worsening toxic presentations (Figure 9).

***The ECG and Dysrhythmias***

Sodium channel blockade predisposes affected patients to reentrant arrhythmias, particularly ventricular tachycardia.<sup>1</sup> Unfortunately, with sodium channel blockade, the resultant ECG may appear similar to a preexisting conduction delay or bundle branch block pattern; in a tachycardic patient, it may be difficult to differentiate between sodium channel blockade and ventricular tachycardia (or supraventricular rhythm with aberrant conduction). Please refer to Figure 6 for an example of a toxin-

mediated form of wide complex tachycardia.<sup>2</sup> Although poisoned patients are often tachycardic secondary to other underlying mechanisms of the drugs ingested, pure sodium channel blockade may result in bradycardia and/or atrioventricular block due to overall depression of automaticity and disruption of conduction.<sup>6</sup>

In addition to diagnostic issues, this constellation of suggestive findings (widened QRS complex with terminal rightward axis deviation) assists the clinician to determine the degree of poisoning and, thus, the treatment options. For instance, the ECG is predictive of both seizures and dysrhythmias in TCA poisonings. In an often-cited study of acute TCA overdoses, Boehnert and Lovejoy found that no seizures or arrhythmias occurred in those poisoned individuals with a maximal QRS complex duration less than 100 milliseconds. TCA overdoses with a QRS complex duration greater than 100 milliseconds, however, had a 34% and 14% incidence of seizures and ventricular arrhythmias, respectively.<sup>11</sup> Furthermore, although seizures were seen with QRS complex duration greater than 100 milliseconds, ventricular arrhythmias were observed only with QRS complex widths greater than 160 milliseconds, with a 50% incidence in this study,<sup>11</sup> which suggests that the QRS complex duration could potentially be used to predict the risk of seizures and arrhythmias in acute TCA overdose. Liebelt et al demonstrated a similar correlation by using QRS complex considerations only in lead

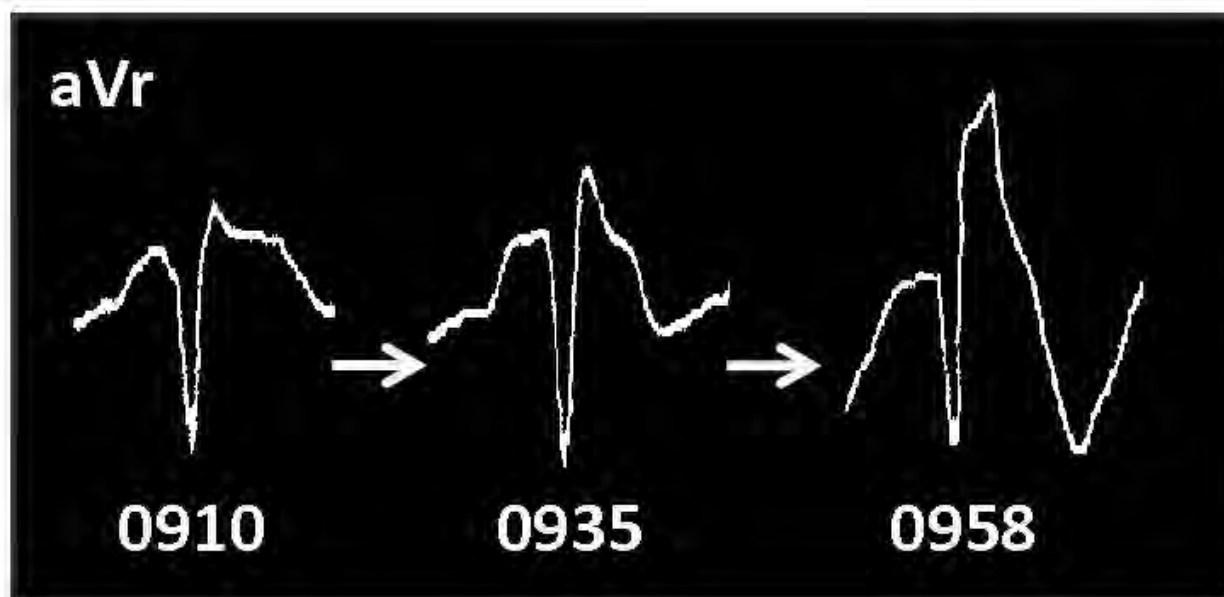


Figure 9. Progressive abnormalities observed in lead aVr in a patient with severe TCA poisoning. Note the progressive increase in the size of the terminal R wave in these 3 consecutive ECGs performed over a very short period of time. Interestingly, the QRS complex does not demonstrate a change in its width.



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aVR.<sup>4</sup> It is not unreasonable to extrapolate this TCA clinical experience to the greater issue of sodium channel blocker poisoning.

**Management Considerations**

The degree of QRS complex widening can guide therapy. Consequently, early consideration should be given to the administration of parenteral benzodiazepine and sodium bicarbonate in patients with TCA ingestion and other suspected sodium channel blocker poisonings with widened QRS complexes. As noted, patients with QRS complex widening beyond 100 milliseconds are at increased risk of seizures. The occurrence of seizures in these patients hastens the development of acidosis. It is very important to note that sodium channel blockers have been demonstrated to lead to increased cardiovascular toxicity (ie, dysrhythmias and hypotension) in an acidotic environment. The prevention of seizures with parenteral benzodiazepine therapy is an important initial step in avoiding acidosis. Early, invasive management of the airway with endotracheal intubation and mechanical ventilation is also encouraged; this approach can assist in avoiding acidosis and promoting alkalosis. The administration of intravenous sodium bicarbonate is yet another important intervention aimed at the prevention of acidosis.

The actual beneficial impact of sodium bicarbonate in the TCA-poisoned patient likely involves several different mechanisms, including not only the avoidance of acidosis and the production of alkalosis but also the overwhelming of the "blocked" sodium channels with sodium loading. In early studies

of TCA poisoning, both the administration of sodium chloride and the induction of alkalemia by hyperventilation have been shown to decrease the deleterious effects of sodium channel blockade.<sup>4</sup> In subsequent animal studies, the use of sodium bicarbonate appeared to exert beneficial effects via both sodium loading and the induction of alkalemia through narrowing of the widened QRS complex.<sup>4</sup> The majority of the animal and human studies were vetted in TCA-poisoned populations; multiple case reports, however, have documented the efficacy of sodium bicarbonate for other sodium channel blockers as well.

As sodium bicarbonate acts to overcome sodium channel blockade, it shortens the action-potential duration of the myocardial cell and increases calcium influx into the cell. This calcium influx improves both dromotropy and inotropy; therefore, sodium bicarbonate therapy can be used as a primary treatment for both tachydysrhythmias and hypotension in patients with a widened QRS.<sup>7-10</sup> In the poisoned hypotensive patient, administering sodium bicarbonate may increase cardiac output and directly improve hypotension. A typical practice is to administer sodium bicarbonate via an intravenous bolus, usually in 1-2 meq/kg increments, with frequent monitoring of the ECG until the primary end point of QRS complex narrowing is achieved. A 12-lead ECG should be obtained approximately 5 minutes after infusion ends. Depending on physician preference, a sodium bicarbonate drip may be started after the initial bolus in an attempt to maintain alkalemia and lessen cardiac toxicity.<sup>7</sup> Three ampoules of sodium bicarbonate can be placed in 1 L of 5% dextrose in water (D5W);

Table 2. Sodium Bicarbonate Therapy in Sodium Channel Blocker Toxicity

Agent	Therapeutic Goal	Dose and Administration	Comments
Sodium bicarbonate bolus	Initial treatment of QRS complex widening and/or hypotension.	1-2 mEq/kg body weight IV.	Assess QRS complex width and morphology 5 min after infusion.
Sodium bicarbonate, infusion	Maintenance of alkalemia and QRS complex narrowing.	150 mEq (3 standard ampoules) in 1000 mL D5W, infused at 1½-2 × maintenance rate. Add 40 meq KCl/L when urine output established.	Assess QRS complex width and morphology q 1 h until patient stabilized, then q 4 h. Monitor for hypokalemia, hypernatremia, and severe alkalemia.

*Charlton, Brady*

such a formulation will provide approximately 150 meq of sodium per liter. This infusion may then be run at 1½ to 2 times the maintenance rate. Once urine output is established, it is advised to include 40 meq of KCl because bicarbonate infusions will induce hypokalemia. An alternative practice is to forego the drip and follow serial ECGs, bolusing sodium bicarbonate as needed for QRS complex greater than 100 milliseconds. In either case, the ECG should be closely monitored for recurrent QRS complex widening. See Table 2 for a review of sodium bicarbonate therapy considerations in the patient with sodium channel blocker toxicity.

For continued cardiac toxicity that is unresponsive to the above measures, hyperventilation via mechanical ventilation and/or the use of 3% saline can be substituted for sodium bicarbonate infusions, assuming that alkalemia has been attained. In the unstable patient, standard advanced life support measures as suggested by the American Heart Association's Advanced Cardiac Life Support (ACLS) guidelines remain valid; the addition of sodium bicarbonate infusions are strongly urged in conjunction with standard ACLS management. Lastly, these patients should be admitted to an intensive care unit for close observation and therapy titration.

**CASE CLOSURE**

While the diagnostic studies were performed and interpreted, resuscitation was performed with attention to the patient's respiratory and circulatory status.

The patient's presentation with prominent anticholinergic findings coupled with the electrocardiographic abnormalities (tachycardia, widened QRS complex, and terminal right axis deviation) strongly suggested sodium channel blocker toxicity, likely caused by a TCA agent. Empiric "antidotal" therapy with sodium bicarbonate infusion was initiated while the patient underwent paralysis-assisted endotracheal intubation. Minutes after intubation, the patient's rate increased with further widening of the QRS complex, producing a wide complex tachycardia (Figure 6); this rhythm likely represented a toxin-mediated dysrhythmia and not ventricular tachycardia. The patient continued to receive sodium bicarbonate intravenously with improvement in the ECG.

**Query 4.** What are the indications for sodium bicarbonate therapy in such an ingestion?

- A. Unresponsiveness with tachycardia.
- B. Anticholinergic findings with QT interval prolongation.
- C. Suspected sodium channel blockade with hypertension.
- D. QRS complex widening.

A repeat ECG was performed 5 minutes later, which demonstrated an improvement in QRS complex duration. A sodium bicarbonate infusion containing 150 meq of sodium bicarbonate in 1000 mL of D5W was started at 200 mL/h.

The patient was admitted to the medical intensive care unit. Electrolyte panels were repeated every 2 hours, and results revealed mild hypokalemia that was replaced appropriately. Hourly ECGs were obtained initially for 6 hours to assess the need for additional sodium bicarbonate boluses. Once the patient was stabilized, the ECGs were performed every 4 hours. Serial blood gas measurements revealed a pH in the range of 7.45 to 7.50. The patient improved overnight; there was no apparent seizure activity, and mental status improved. Once the QRS complex duration returned to normal, the bicarbonate infusion was discontinued. No further QRS complex widening occurred. The patient was transferred to the medical floor and subsequently to the psychiatry service without further sequelae.

*Answers to Queries*

**Query 1.** At this point in the evaluation, the ECG data in Figure 1 is best described by answer C. The rhythm is sinus tachycardia with minimal widening of the QRS complex and deep S wave in lead I, which is strongly suggestive of TCA cardiotoxicity. The other answers are incorrect owing to the following: A, the rhythm is likely not ventricular tachycardia in that the QRS complex is minimally widened; B, the rhythm is sinus tachycardia yet more specific information suggestive of a diagnosis is present as noted in the correct answer, and D, although a CNS event is not unlikely, there is no specific information contained in the rhythm strip suggestive of such a diagnosis.

**Query 2.** The ECG findings suggestive of the diagnosis are included in answer B, sinus tachycardia, widened QRS complex, and R wave in lead aVR. The other answers are incorrect because although these findings are present they do not suggest the diagnosis.

**Query 3.** In addition to general resuscitative therapy and critical care, the treatment described

*Wide Complex Tachycardia in an Unresponsive Patient*

in answer D, sodium bicarbonate therapy with urgent paralysis-assisted endotracheal intubation and ventilatory support, is likely the best course of action. For answer A, although naloxone is an appropriate therapy, at this point in the evaluation, strict serum glucose monitoring is not a priority. Certainly, the determination that the serum glucose is not at the extremes of the range is appropriate at this time. In answer B, emergent hemodialysis is not an early intervention used in TCA poisoning. Regarding answer C, although empiric antibiotic therapy for a CNS infection is never incorrect if the diagnosis is suspected, this presentation does not

strongly suggest such a malady, whereas based on the data, ingestion of a cardiotoxic agent is likely.

**Query 4.** What are the indications for sodium bicarbonate therapy in such an ingestion? Answer D best describes a primary indication for sodium bicarbonate therapy in TCA ingestion—QRS complex widening; other indications for such therapy include significant hypotension and malignant dysrhythmia. The other findings are certainly encountered in the presentation but are not indications for sodium bicarbonate infusion.

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**ASSOCIATES' DAY**  
*January 23, 2010*  
*Norfolk, Virginia*



*Photos courtesy of Chris Lin, MD.*

**ABSTRACTS SELECTED FOR PRESENTATION AT  
ASSOCIATES' DAY  
VIRGINIA CHAPTER  
AMERICAN COLLEGE OF PHYSICIANS  
JANUARY 23, 2010  
NORFOLK, VIRGINIA**

The Virginia Chapter of the American College of Physicians holds an annual Associates' Day, at which medical students (Student Members) and Internal Medicine residents (Associate Members) present research abstracts and clinical vignettes. Our annual Associates' Day meeting was held on January 23, under the stewardship of Ranjodh Gill, MD, FACP and Nehemiah Thrash, Jr, MD, Associate Member. Over 140 research abstracts and clinical vignettes were received from our students and residents at: Eastern Virginia School of Medicine, Carilion Clinic-Virginia Tech, Naval Medical Center at Portsmouth, University of Virginia, Georgetown University, and Virginia Commonwealth University-Medical College of Virginia. The initial submissions, stripped of information regarding author and residency program, were reviewed by a panel of volunteer judges from throughout the state: John McGurl, M.D., Sidney Barritt III, M.D., FACP, Michael Rein, M.D., FACP, Mitchell Rosner, M.D., FACP, Michael Galitz, M.D., John Smith, M.D., Catherine Tsai, M.D., Edwin Landaker, M.D., John Lystash, M.D., Andrew Gentry, M.D., John Port, M.D., Puneet Katyal, M.D., Alyce Girardi, M.D., FACP, Thomas Kerkerling, M.D., FACP, Bruce Johnson, M.D., FACP, Deborah Henderson, M.D., FACP, Charles J. Schlepner, M.D., FACP, Andrew Rhinehart, M.D., FACP, and Chad DeMott, M.D., FACP. The forty excellent abstracts published here were chosen for oral presentation. We are particularly pleased that the submissions of three medical students were among those selected. The Virginia Chapter wishes to express its great appreciation to Robert Strieter, MD, MACP and Gerald Donowitz, MD, FACP for supporting the printing of this work. Although each abstract is the product of a collaboration and mentorship, only the names of the presenters appear with the abstract.

**WHEN A RUNNY NOSE NEEDS MORE THAN A TISSUE***Bonny Moore, M.D., Associate Member, Carilion Clinic – Virginia Tech Carilion*

Amongst internists, rhinorrhea is a common complaint. Many patients suffer from allergies or sinusitis and experience the typical “runny nose.” However, as this case illustrates, a common complaint can sometimes turn out to be an uncommon presentation of a more serious problem.

A 52 year old female with an extensive past medical history including hypertension, diabetes mellitus type 2, GERD, obstructive sleep apnea, depression, mild visual impairment, and panhypopituitarism presented with fever, leukocytosis, and dyspnea. She was admitted and subsequently diagnosed with pneumonia. Her panhypopituitarism and visual impairment were a consequence of two gamma knife radiosurgeries to the pituitary for Cushing’s disease six and nine years prior. During the hospitalization, she complained of increasingly copious right-sided rhinorrhea that increased with different positions of her head, had been present for several months, and seemed to worsen during admission. She stated the fluid had a salty taste. She had no other specific head, eyes, ear, nose, throat complaints nor any history of facial trauma or mechanical surgery to her head or sinuses. The patient was able to collect several mL of fluid at a time and a specimen was sent to the laboratory for testing. A CT of the sinuses was obtained with particular attention to the cribriform plate that showed an opacified right anterior ethmoid air cell lying immediately adjacent to the right side of the cribriform plate, indicative of mucosal thickening, mucous obstruction, or CSF obliterating the air cell. The fluid subsequently tested positive for Beta-2 transferrin, indicating a CSF leak. The patient then received neurosurgical and ENT evaluation for surgical repair.

CSF rhinorrhea can have a variety of causes including intracranial or intranasal surgeries, injury to the head or face, tumor that erodes the bone of the skull, or skull deformities. Beta-2 transferrin is a very specific (near 95%) and sensitive (near 100%) test in determining if fluid is indeed CSF. Beta-2 transferrin is a carbohydrate-free isoform of transferrin that is not present in serum, nasal mucus, or tears, but is present solely in CSF. Other methods of evaluating for possible CSF rhinorrhea include CT or MR imaging to look for signs of trauma or tumor, although in this case subsequent MRI did not show an obvious leak. While CSF leaks can resolve on their own, CSF rhinorrhea is often surgically managed to prevent the ascension of infections from the nasal cavity into the CSF. While this patient has no known risk factors for CSF rhinorrhea, she did receive radiosurgery for her pituitary tumor on two occasions that lead to panhypopituitarism and some optic nerve damage. To our knowledge this is the first report of the association of CSF rhinorrhea and gamma knife radiosurgery for Cushing’s disease.

**A CASE OF AN OPEN CHOLECYSTECTOMY LEADING TO ACUTE GALLSTONE PANCREATITIS 20 YEARS LATER.***George Pop, M.D., Associate Member, University of Virginia*

Suture material has been recognized as a focus for gallstone formation since late nineteenth century, with non-absorbable silk sutures regarded as being especially lithogenic in the common bile duct, postoperatively. Despite this, only 8 case reports of stone formation from a suture material nidus have been reported. Pathophysiologically, when a fragment of suture material is introduced into the CBD, it serves as a nucleus for stone crystallization. Over time the nucleus increases in size and moves slowly toward the distal common bile duct as a consequence of biliary duct activity, and eventually forms a sizable calculus. Here we present a case involving a large stone formed 20 years postcholecystectomy which led to acute gallstone pancreatitis.

A 46-year-old obese African-American female who underwent an open cholecystectomy in the 1980’s presented to our Emergency Department with a 4 day history of dull right upper quadrant pain, nausea, vomiting, and jaundice. Her pain was non-radiating, 8/10 in intensity and not alleviated by over the counter pain medication. In addition, she reported 3-4 emesis episodes daily, consisting of nonbilious and nonbloody material. She also noted diarrhea (3-4 greasy non-bloody loose stools per day) since the onset of her other symptoms. Her vital signs at presentation were significant for slight tachycardia. She was afebrile, normotensive and in no respiratory distress. Her physical examination was remarkable for obesity and moderate jaundice. She had a negative Murphy’s sign yet her abdomen was diffusely tender to palpation (slightly more accentuated in the right upper quadrant). She had no guarding or rebound. No organomegaly was appreciated. Her initial laboratory data showed a lipase of 932, amylase 670, alkaline phosphatase 197, alanine aminotransferase 800 and aspartate aminotransferase 399. She was subsequently admitted to our Digestive Health inpatient service for suspected gallstone pancreatitis. RUQ Ultrasound showed a dilated common bile duct (1.2cm at porta hepatis). Abdominal CT confirmed the suspected pancreatic inflammatory process as well as the dilated common bile duct. She underwent ERCP with biliary sphincterotomy and needle knife extraction of a large calculus, followed by balloon sweep of the common bile duct. The stone was notable for the presence of foreign body within it, which was consistent with suture material, likely from the patient’s prior cholecyst-ectomy. The patient tolerated the procedure well and her symptoms resolved during the next 3 days. She was discharged home subsequently. The described case gives us the opportunity to remind surgeons and endoscopists that biliary stones can be formed by surgery-related materials (sutures, clips etc.).

**ANY ORGAN NOT AFFECTED?**

*Shaun Bhatti, M.D., Associate Member, Virginia Commonwealth University/Medical College of Virginia*

**Case Presentation:** A 52 year-old man presented with abdominal pain. The pain began one week prior to presentation; it was diffuse and associated with nausea. Medical history was significant for stage III chronic kidney disease. Vital signs were significant for a blood pressure of 158/104 mm Hg. Cardiac exam was normal and without murmurs. Abdominal exam revealed diffuse tenderness. The patient's hands revealed sclerodactyly. Labs revealed anemia, leukocytosis, and worsening renal function with a creatinine of 5.0 mg/dl and blood urea nitrogen of 36 mg/dl. Further labs revealed normal complement levels, a urine protein: creatinine ratio of 2.5, negative anti-scl-70 and anti-SSB antibodies, and equivocal anti-Smith and anti-SSA antibodies. Abdominal ultrasound revealed calculous cholecystitis and bilateral medical renal disease without hydronephrosis. The patient underwent a laparoscopic cholecystectomy for acute calculous cholecystitis. His renal function continued to decline and hemodialysis was initiated. Scleroderma was diagnosed based on examination findings. During the hospital course, the patient developed pleuritic chest pain. Cardiac examination revealed a new 3/6 holosystolic murmur and S4. Workup was negative for ischemia and pulmonary embolism. Chest computed tomography revealed pericardial and pleural effusions, esophageal dilatation, and patchy ground glass opacities in the lungs. Transthoracic echocardiogram showed mild pulmonary hypertension. The patient was treated for pericarditis and his chest pain resolved. The acute renal failure persisted and the patient underwent a kidney biopsy due to increasing suspicion of scleroderma involvement. Biopsy was consistent with acute scleroderma renal crisis. The patient was started on an angiotensin converting enzyme inhibitor. A subsequent esophagram revealed esophageal dysmotility and reflux.

**Discussion:** Scleroderma disorders include a group of conditions linked by the presence of thickened sclerotic skin lesions. Systemic sclerosis constitutes the characteristic skin disorder associated with internal organ involvement. Clinical manifestations of diffuse systemic sclerosis involve multiple organ systems. The patient in this case exhibited the following features: sclerodactyly, Raynaud's phenomenon, pulmonary artery hypertension, scleroderma renal crisis, esophageal dysmotility, interstitial lung disease, hypertension, pericarditis, pericardial effusion, and renal findings of proteinuria and elevated plasma creatinine. Scleroderma renal crisis develops in 10 to 20% of patients with diffuse cutaneous systemic sclerosis and is characterized by acute renal failure, abrupt onset of hypertension, and a normal urinalysis with mild proteinuria. This case illustrates the importance of looking for a unifying diagnosis when patients present with multiple organ system abnormalities. The patient presented with classic features of scleroderma, and the constellation of findings prompted a renal biopsy, which confirmed the diagnosis and led to implementation of appropriate medical therapy.

**CRYPTOCOCCUS: A PHOENIX RISING**

*Susan Szulc, M.D., Associate Member, Eastern Virginia Medical School*

There are an estimated 957,900 cases/year of *Cryptococcus meningitis* in HIV patients worldwide, with about 624,000 deaths/year related to the disease. However, are we fighting a losing battle with standard antifungal therapies as this fungus adapts and reinvents itself? A 36-year-old male with HIV (CD4 200, 16.9%, undetectable viral load) on HAART, presents with complaints of a 2-week history of recurrent headaches. The headaches were described as 5/10, throbbing pain that was worsened by movement, especially with forward flexion. The patient denied any focal weakness, seizures, photophobia, or nausea/vomiting. Of note, the patient was diagnosed with *Cryptococcus neoformans meningitis* one-year prior. The patient had been maintained on fluconazole (FLU) 400mg daily, following induction with amphotericin B (AMB). However, the patient presented eight months after the initial diagnosis with similar complaints, but *Cryptococcus terreus* was isolated with titers of 1:810. Sensitivities revealed intermediate-resistance to FLU, with an MIC of 16. He underwent re-induction therapy with AMB and flucytosine. Titers decreased to 1:22, and the patient was discharged on an increased dose of FLU (800mg). Now, the patient presents 4 months after the second recurrence, with similar complaints. The patient was compliant with his medications, supported by his undetectable viral load and well-controlled CMV retinitis. Physical exam was significant only for mild meningismus. MRI revealed three intraventricular lesions consistent with *Cryptococcus. C. terreus* was again isolated, with titers of 1:79. The patient underwent an extended, four-week re-induction period with AMB and flucytosine. Titers subsequently decreased to 1:28. The patient was discharged on FLU 800mg daily. The emergence of a resistant species of *Cryptococcus* after treatment of *C. neoformans meningitis* has been documented in the literature.

However, to date, there are no cases of resistant *C. terreus* emergence after treatment for *C. neoformans*. *Cryptococcus terreus*, first identified in New Zealand soil in 1954, represents only about 10% of cases of all cryptococcal infections. Treatment of *Cryptococcus* has become increasingly difficult as the incidence of fluconazole-resistant *C. neoformans* steadily rises, currently at 12%. Species such as *C. terreus*, may also be associated with decreased azole susceptibility. Review of the literature shows that all cryptococcal species with a fluconazole MIC greater than or equal to 16 have an increased chance of treatment failure compared with MICs of less than 16. What are the options after treatment failure? Recent studies have shown posaconazole to be superior to fluconazole against *Cryptococcus* species. However, the solution remains unclear. Currently, there are no guidelines for the treatment of cryptococcal recurrence. The interval development of resistance or the emergence of a new species further compounds the problem. The best strategy is perhaps, to maintain a high suspicion for the emergence of resistance and allow sensitivities to guide therapy.

**LACRIMAL GLAND INJECTION WITH BOTULINUM TOXIN A TO QUELL CROCODILE TEARS***Ryan Fugate, M.D., Associate Member, Naval Medical Center, Portsmouth*

Bell's Palsy is a relatively common diagnosis encountered by primary care physicians. Its symptom severity ranges from unilateral facial weakness to complete paralysis with partial loss of taste, hyperacusis, and xerophthalmia. The spectrum of recovery is equally as diverse and patients are often left with silent reminders of their disease many years after initial presentation and treatment. Crocodile tears are the result of misdirected outgrowth of autonomic fibers during nerve regeneration. This causes tearing on the affected side when the salivary glands are stimulated. In this report we describe two such cases and their safe, effective treatment using botulinum toxin A (BTX A).

**Case 1:** A 40-year-old female presented with facial weakness, and spontaneous left eye tearing associated with chewing and yawning. She had left-sided Bell's palsy approximately ten years ago. At times her tearing was so severe it caused her social anxiety and even skin breakdown on the affected side. She was given a series of two injections of 2.5 and then 5 units of BTX A directly to the palpebral portion of the lacrimal gland. One week after the second injection she noted a 75% decrease in her tearing.

**Case 2:** A 36-year-old male presented with spontaneous right eye tearing associated with talking and ambient temperature changes, approximately one year following an episode of right-sided Bell's palsy. He was also given two injections of 2.5 and then 5 units of BTX A to the palpebral portion of the lacrimal gland with a resulting considerable improvement in his tearing symptoms one week following the second injection.

BTX A injection has come into favor for the management of several conditions over the past two decades. This is one of a growing number of reports to document the effectiveness of this underutilized procedure for crocodile tears. There is little consensus on the quantity of BTX A that should be used and doses ranging from 2.5 units up to 60 units have been reported with variable results. In most cases, complete albeit temporary resolution of symptoms can be obtained with escalating doses. We suggest a low dose initially, with frequent reevaluation and repeat injection with increased dose as needed. These two cases are presented to bring to light an uncommon but often debilitating sequelae to Bell's palsy and to show that safe and effective treatment modalities exist outside of lacrimal gland resection for these patients.

**HENOCH-SCHONLEIN PURPURA IN CONJUNCTION WITH CLOSTRIDIUM DIFFICILE COLITIS***Gregory Hong, M.D., Associate Member, University of Virginia*

Henoch-Schonlein purpura (HSP) is a systemic small vessel vasculitis characterized by pathognomonic IgA deposition in affected organs. Although predominantly a pediatric disease, up to 10% of cases present within the adult population with common manifestations including palpable purpura, arthralgias, abdominal pain, and renal impairment.

**Case:** A 77 year-old Caucasian male with chronic paraplegia secondary to polio as well as chronic osteomyelitis presented to the emergency room with 4 days of generalized malaise, decreased appetite, voluminous diarrhea, and a non-pruritic rash on his lower extremities. He had been maintained on chronic suppressive antibiotic therapy for osteomyelitis with moxifloxacin and rifampin. The diarrhea was described as watery without obvious blood or mucus. His rash had started on the anterior surface of his lower legs and per report had gradually spread proximally. He denied fever, headache, respiratory symptoms, and change in urine characteristics; subjective complaints of pain in his abdomen or joints were difficult to assess given the patient's lack of sensation.

Physical exam was notable for a normothermic temperature and soft & non-distended abdomen; palpable purpura was present on the anterior aspects of the patient's lower extremities with multiple lesions of ~1cm in diameter. Initial diagnostic work-up revealed a leukocytosis (white blood cell count >17,000 cells/microliter), acute renal failure (creatinine 1.6 mg/dl with a previous baseline 0.9 mg/dl), and positive clostridium difficile (c.dif) toxin in the stool. Biopsy was performed of the lesions on the lower extremities and initially revealed a leukocytoclastic vasculitis; subsequent biopsy revealed granular IgA deposition around superficial dermal vessels consistent with a diagnosis of HSP. During his initial hospital course the patient's renal function worsened despite adequate hydration; other work-up for causes of acute renal failure was equivocal. The decision was made to start a short course of systemic glucocorticoids for presumed renal involvement of HSP. Within 2 weeks of initiating glucocorticoids his skin lesions disappeared and his creatinine returned to baseline levels.

Although HSP is classically a pediatric condition, up to 10% of cases present within the adult population where it has a higher likelihood of causing significant and permanent renal impairment. The exact pathophysiology is unknown; however, it is thought that infectious agents trigger the immune complex mediated vasculitis that is responsible for end organ damage in HSP. This vignette presents a case of HSP associated with c.dif colitis. As it is a treatable entity, HSP should remain on the differential of any adult with palpable purpura and a recent or concurrent infection.

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**THE LIPOMA THAT WASN'T***Kimberly Span, MD., Associate Member, Eastern Virginia Medical School*

Melanoma is a serious disease and accounts for 75% of deaths due to skin cancer. A dangerous form of melanoma called amelanotic malignant melanoma occurs when the cancerous cells lack pigment, leading to a delay in diagnosis and higher mortality. Amelanotic melanoma reportedly accounts for 2-8% of all melanomas. It can be in the form of a primary skin lesion, usually presenting as a chronic, pruritic, or scaly area or as a metastatic lesion from another location. Primary amelanotic melanoma lesions have been known to metastasize in the same manner as pigmented melanoma, including to the lymph nodes, lung, liver and brain. Amelanotic malignant melanoma can also occur in unusual locations. Several cases of cutaneous, subungual, and female genital tract amelanotic melanoma have been reported in medical literature.

A 53 year-old Caucasian man presented to the outpatient clinic for a routine wellness check. During the history, he noted a subcutaneous soft tissue mass which had been slowly but progressively enlarging for approximately two years. The mass was located on his proximal right posterior forearm, was ovoid in shape, and measured 6.5 x 5.0 cm. It was firm, nontender, slightly mobile and lacked any overlying skin changes. Specifically, there was no erythema, scaling, or skin darkening present. The most likely diagnosis at the time was lipoma, but given the mass' large size and the fact it was progressively getting bigger, the patient was referred to a general surgery clinic for biopsy to rule out possible sarcoma. Core biopsy was taken, and pathology was significant for malignant melanoma. Subsequently, the patient underwent wide local excision of the mass along with sentinel lymph node biopsy. The mass was excised completely with deep margins negative for residual melanoma. Sentinel lymph node biopsy was also negative for melanoma. The patient was referred to oncology clinic, and further work-up, including MRI of the brain and CT scan of the chest, abdomen and pelvis, were negative for any evidence of metastatic disease.

Given the lack of any overlying sign of melanoma, this diagnosis could easily have been missed if the patient had not been referred for biopsy. A delay in diagnosing this condition could have easily led to a worse outcome if the disease were already metastatic. It is important to biopsy any suspicious or concerning mass to exclude rare but dangerous diagnoses.

**CRYPTOCOCCAL MENINGITIS MASQUERADING AS HEPATIC ENCEPHALOPATHY***Daniella Schwartz, M.D., Associate Member, Virginia Commonwealth University/Medical College of Virginia*

Cryptococcal meningoencephalitis is a requisite consideration in the differential diagnosis of altered mental status in HIV-infected and other immunocompromised patients. However, in non-HIV infected hosts, the diagnosis is often missed. This case describes a cirrhotic patient in whom altered mentation due to cryptococcal meningoencephalitis was wrongly attributed to hepatic encephalopathy.

A 47 year old male with a history of Hepatitis C, polysubstance abuse, and cirrhosis presented to a community hospital with abdominal distention and lower extremity edema. He was started on high doses of furosemide and spironolactone. His home medication of lactulose was stopped due to diarrhea and he was discharged. Three days later, he presented to the hepatology clinic with increased abdominal girth, headache, confusion, and paresthesias. He denied fevers/chills, neck pain, nausea/vomiting, and photophobia. On examination, he had a temperature of 99.6 and otherwise unremarkable vital signs. He was oriented to self, place, and time, but not to situation. He had moderate asterix and diffuse allodynia; no nuchal rigidity or focal neurologic deficits were noted. His abdomen was diffusely tender with no appreciable ascites. Laboratory studies were notable for a sodium of 128 mmol/L and an ammonia of 33 umol/L. Computed tomography scan of the head was unremarkable. Abdominal ultrasound revealed minimal ascites. Treatment was initiated with lactulose and cessation of diuretics. However, the patient's mental status continued to deteriorate, and his paresthesias and allodynia worsened. On hospital day #2, lumbar puncture was attempted unsuccessfully. Due to concern for meningoencephalitis, acyclovir, ceftriaxone, and vancomycin were administered. The patient's mental status deteriorated further, and on hospital day #3, lumbar puncture was successfully performed. CSF analysis revealed: 1225 leukocytes (61% poly, 36% lymph, 3% mono), protein 120 mg/dL, glucose 19 mg/dL, cryptococcal antigen positive. Treatment was initiated with amphotericin B and flucytosine, with return of mental status to baseline within 1 week.

This case demonstrates the importance of considering, and the challenge of diagnosing, cryptococcal meningitis in patients with cirrhosis. 70% of non-HIV infected patients with cryptococcal meningitis are immunocompromised, usually due to organ transplantation, malignancy, or glucocorticoid treatment. However, patients with cirrhosis are also at risk: multiple studies have demonstrated higher incidence and mortality of cryptococemia in patients with cirrhosis. Potential etiologies include opsonin, complement, and leukocyte dysfunction. However, as in other non-HIV infected patients, the diagnosis of cryptococcal meningitis in patients with cirrhosis is challenging: symptoms develop subacutely and are often nonspecific. 50% of patients are afebrile. Although this patient's presentation was confounded by his history of hepatic encephalopathy and hyponatremia, his headache, worsening mental status, and paresthesia/allodynia were all subtle markers of cryptococcal meningitis.

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**LOOKING BEYOND THE NUMBERS: "IDIOPATHIC" THROMBOCYTOPENIA IN A YOUNG ACTIVE DUTY MALE**

*Justin Lafreniere, M.D., Associate Member, Naval Medical Center, Portsmouth*

**Case Description:** A 27-year-old male, Active Duty E-4 with no significant past medical history was referred by his DMO for evaluation of thrombocytopenia discovered on routine laboratory screening. The patient denied any acute complaints, recent illness or surgery. He admitted to a lifelong history of slight mucosal bleeding with tooth brushing, but otherwise denied any easy bruising or excessive bleeding, even during a prior tooth extraction. He denied abdominal pain, early satiety, weight changes or night sweats. A review of rheumatologic symptoms was unrevealing. He used no prescription or over-the-counter medications. He reported a history of "low platelets" in his maternal grandmother and aunt.

His vital signs were unremarkable in the clinic. On physical exam there were no petechiae and no scleral icterus or jaundice. There was no lymphadenopathy. The abdomen was nontender and the spleen was not palpable. CBC revealed a normal hemoglobin and white blood cell count, but an automated platelet count of 64,000/mcL with a mean platelet volume of 10 fL. Review of recent CBC's revealed automated platelet counts ranging from 30-50,000/mcL and manual platelet counts ranging from 80-100,000/mcL. Complete metabolic panel was unremarkable. HIV-1 antibody was negative. An abdominal ultrasound excluded splenomegaly. Review of the peripheral blood smear revealed no blasts and normal RBC morphology with no schistocytes. Giant platelets were seen and multiple neutrophils were noted to contain spindle-shaped, basophilic Döhle bodies. The patient was diagnosed with May-Hegglin anomaly and was not thought to have any significant increased risk of bleeding. He remains on unrestricted active duty service.

**Discussion:** May-Hegglin anomaly is a rare congenital macrothrombocytopenia diagnosed by the triad of thrombocytopenia, giant platelets, and leukocyte inclusion bodies. It is part of a spectrum of diseases caused by mutations in the MYH9 gene responsible for encoding the nonmuscle myosin heavy chain IIA. We review the pathophysiology of May-Hegglin anomaly and explain the relationship between the genetic mutation and the spectrum of associated disease. We use this case to illustrate the importance of reviewing the peripheral blood smear when evaluating patients for thrombocytopenia, especially to avoid misdiagnosing idiopathic thrombocytopenic purpura and thereby exposing patients to the risks of unnecessary therapy with corticosteroids or splenectomy. This case also highlights the importance of accurate diagnosis in our active duty population and its resulting impact on duty status.

**DISSEMINATED BLASTOMYCOSIS WITH A THORACIC COMPRESSION FRACTURE:  
DELAYED DIAGNOSIS IN AN ENDEMIC REGION**

*Tuyet Nguyen, M.D., Associate Member, Virginia Commonwealth University/Medical College of Virginia*

**Case Description:** A 55-year-old man from Virginia with no significant medical history presented with right flank and back pain. The back pain began abruptly three weeks previously, when he lifted a car tire and felt a sharp, severe pain in his middle back. Initially, pain was localized to his mid-thoracic spine but subsequently radiated to his right flank. He denied abdominal pain, fevers, chills, or lower extremity weakness. Physical examination revealed unremarkable vital signs. There was no pain to palpation of his abdomen, flank, or spine. There were no neurological deficits. Dermatologic exam was notable for four, large, ulcerated lesions on his left nasal ala, right jawline, left posterior calf, and left posterior thigh. Upon further questioning, he reported that these lesions were present 3-4 months prior, and that initial biopsy by his primary care physician (PCP) was "negative." The lesions did not improve with antibiotics. Magnetic resonance imaging (MRI) revealed a pathologic T12 fracture with a paraspinal mass from T9 to L2. There was no spinal cord compression. Biopsies of both the skin lesions and the T12 vertebra were obtained, revealing broad-based budding yeast. Subsequent chest imaging showed diffuse nodular opacities in all lung lobes. He was started on itraconazole for presumed disseminated Blastomycosis and was discharged home. Two days after discharge, he returned to the hospital with acute lower extremity weakness and urinary incontinence. Repeat MRI revealed acute cord compression requiring emergent decompression and T10-L2 fusion. He was given amphotericin B and eventually regained continence and lower extremity strength. He was given amphotericin B for a total of 6 weeks, with plans to restart itraconazole for an additional 12 months. Fungal cultures from his skin biopsy eventually grew *Blastomyces dermatitidis* 1 month after his admission.

**Discussion:** *Blastomyces dermatitidis* is endemic to the Mississippi and Ohio river basins, encompassing many eastern and southern states. It has an annual incidence of 0.3-1.8 cases per 100,000 within endemic regions. Blastomycosis primarily starts as a pulmonary infection that spontaneously resolves. However 25-40% of cases result in dissemination to extrapulmonary organs such as skin and bone. Disseminated blastomycosis is not typically diagnosed until late in its course, consequently impacting morbidity. Early diagnosis and therapy can lead to resolution and prevent clinical relapse. This case serves to highlight the clinical manifestations of disseminated blastomycosis and to stress the importance of maintaining a high index of suspicion in an endemic region.

**A NEW RASH FOR AN OLD DISEASE**

*Michael Gonzales, M.D., Associate Member, Eastern Virginia Medical School*

Cutaneous vasculitis is a primary manifestation of rheumatologic disorders and is characterized by palpable purpura and nonspecific histopathologic findings. In rare cases however it may be a manifestation of a bacterial infection. A 61 year old male was found down and incoherent at home and was admitted to the ICU due to initial CT scan findings of petechial hemorrhage in the right frontal lobe. However, his past medical history revealed no stroke risk factors. He was afebrile, normotensive and cachectic. The rest of his examination was unremarkable except for generalized weakness, bipedal edema, and petechiae in both ankles. His CBC showed significant leucocytosis with neutrophilic predominance as well as severe microcytic anemia. Coagulation studies were normal. He also had newly discovered renal insufficiency, lactic acidemia and a nephritic urinary sediment. An MRI done showed that he had extensive subcortical infarcts scattered throughout the cerebrum. Blood cultures grew gram-positive cocci and transthoracic echocardiography confirmed the presence of a large mobile vegetation on the anterior leaflet of the mitral valve associated with severe mitral regurgitation. His cultures grew *Enterococcus faecalis* that was sensitive to penicillin and gentamicin. Accordingly a diagnosis of Sepsis due to Native valve endocarditis with septic emboli to the brain and perinfectious glomerulonephritis was made. Intravenous ampicillin and gentamicin was started accordingly and the patient was transferred out of the ICU. 3 days after starting antibiotics his platelets dropped and symmetric palpable purpura with some erosions and bullae formation were noted on his forearms, dorsal hands, and thigh. A HIT panel was negative and peripheral smear showed no schistocytes. A drug reaction was considered and ampicillin was changed to vancomycin and dermatology was consulted. Skin punch biopsy of two representative lesions showed mixed infiltrates of neutrophils and RBCs with necrosis of blood vessels and lack of any organisms. Immunofluorescent staining was strongly positive for IgG, IgA and IgM and weakly positive for C3. The final diagnosis was leukocytoclastic vasculitis. Dermatology recommended treatment of the underlying condition and did not recommend using steroids. The lesions eventually resolved with continued antibiotic treatment and supportive care. Infective Endocarditis has variable clinical presentations and classic cutaneous findings, but it may present with rheumatologic manifestations. In one study in Spain involving 172 adults with biopsy proven cutaneous vasculitis, majority were associated with HSP, Hypersensitivity vasculitis and Cryoglobulinemia and only 5 cases were related with a systemic bacterial infection, 4 of which were bacterial endocarditis. Although most clinicians associate endocarditis with septic emboli, Janeway lesions, and Osler's nodes, Cutaneous vasculitis should be recognized as a possible manifestation. In the same manner rheumatologists should also recognize that cutaneous vasculitis can be caused by bacterial infections especially endocarditis.

**A MATTER OF TASTE: PITUITARY MACROADENOMA PRESENTING AS DYSGEUSIA**

*Michelle Nalepa, M.D., Associate Member, Virginia Commonwealth University/Medical College of Virginia*

Gustatory dysfunction is a rare presenting complaint in a primary care practice. Although perceived taste disturbances are common in the elderly, truly altered taste (dysgeusia) may be a symptom of a much larger problem.

A 69-year-old white male presented to an outpatient clinic with the complaint of loss of taste for one week. He described being able to smell food but that everything tasted "like castor oil." Review of systems was significant only for nausea related to the bad taste, recent scant rhinorrhea, and daily headaches for forty years. He also had decreased libido and erectile dysfunction refractory to sildenafil for the past fifteen years. He denied any visual changes, numbness, tingling, weakness, syncope, seizures, heat or cold intolerance, hair changes, or nipple drainage. His past medical history included benign prostatic hypertrophy, migraine headache, low back pain, hypertension, and osteopenia. His medications included finasteride, hydrochlorothiazide, simvastatin, terazosin, and vitamin D; he had also recently been on lamisil for a fungal skin infection, which was discontinued two weeks prior to presentation. Physical exam was unremarkable except for the absence of taste to sweet, bitter, and salty foods. An MRI was obtained which showed a mass lesion in the sella extending into the suprasellar cistern, with expansion of the sella and erosion of the clivus. The lesion extended into the cavernous sinus on both sides, encasing the left internal carotid artery, and displaced the optic chiasm and proximal optic nerves superiorly. Hormonal work-up revealed a slight elevation in prolactin at 29.97 ng/ml (upper limit of normal was 13.13 ng/ml) as well as primary hypogonadism (low testosterone levels and elevated gonadotropins). The patient underwent transsphenoidal resection of the tumor, and at his three-month follow-up visit reported that his sense of taste was back to normal. Most alterations in taste perception are due to olfactory dysfunction, and true ageusia is rare. Primary care offices are often not equipped with the tools required to perform a complete examination of the olfactory and gustatory systems; however, the clinical history can often help guide diagnostic testing. In this case, the symptoms of daily headaches and loss of libido were concerning enough to warrant MRI, revealing the diagnosis.

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**INFERIOR SINUS VENOSUS ATRIAL SEPTAL DEFECT WITH ANOMALOUS RIGHT PULMONARY VENOUS RETURN:  
A RARE AND UNEXPECTED FINDING IN AN ACTIVE DUTY SAILOR**

*Rolf Graning, M.D., Associate Member, Naval Medical Center, Portsmouth*

**Introduction:** We present a rare type of sinus venosus atrial septal defect (SVASD) presenting in an adult male and review the anatomy, pathophysiology, and treatment of this condition.

**Case:** A 25 year old male who was noted to have an incomplete right bundle branch block on screening ECG was then referred to cardiology for further care. The patient was noted to have mild dyspnea on exertion, as well as physical exam and chest x-ray findings characteristic of right ventricular overload. Transesophageal echocardiogram revealed that the patient had a rare type of sinus venosus ASD with a defect in the inferior septum rather than the typical superior position, as well as partial anomalous pulmonary venous return of the right pulmonary vein into the right atrium. This abnormality was later confirmed with cardiac computed tomography and cardiac magnetic resonance imaging. The patient underwent surgical closure of this defect resulting in resolution of his right ventricular overload and clinical symptoms, and he was able to return to active duty.

**Discussion:** Congenital heart disease occurs in approximately 1% of live births and atrial septal defects (ASD) account for approximately 10% of these cases. ASDs are frequently not detected in childhood and therefore an understanding of the clinical presentation as well the anatomy and pathophysiology is pertinent to the Internist, as early diagnosis and treatment results in improved clinical outcomes. There are three main types of ASDs based upon the location on the atrial septum which include ostium primum, ostium secundum, and sinus venosus. Sinus venosus defects account for roughly 5-10% of all ASDs making them the rarest form of defect. The defect in this case is unique in that it is inferiorly located rather than the typical superior location found in over 95% of SVASDs. They are commonly associated with anomalous pulmonary venous return which adds to the left-to-right shunt, right ventricular volume overload, severity of symptoms, and complexity of repair. Clinical findings of a fixed split second heart sound with or without a pulmonary systolic flow murmur and right bundle branch pattern on ECG are highly sensitive for ASDs and should prompt further cardiac evaluation. Long term sequelae of uncorrected defects includes decreased exercise tolerance, pulmonary hypertension, and right ventricular failure, all of which are preventable if the underlying defect is diagnosed and treated early.

**AN ATYPICAL PNEUMONIA LEADS TO AN ATYPICAL DISEASE**

*Christine M. Lin, M.D., Associate Member, University of Virginia*

*Mycoplasma pneumoniae* is a well-recognized pathogen in community-acquired "atypical" pneumonia. Most infections are not diagnosed; however, in cases where a patient presents with persistent infections, an underlying cause should be sought.

A 19-year-old male with a past medical history significant for several past episodes of "walking pneumonia" presented to a student health clinic with a complaint of cough. He was diagnosed with bronchitis and given a prescription for azithromycin. Soon after finishing the antibiotic, he developed oral and urethral ulcerations, as well as conjunctivitis. He was then administered an intramuscular dose of ceftriaxone, and given a prescription for doxycycline as well as a prednisone taper. Nonetheless, his symptoms progressed and therefore, he was hospitalized for further work-up and treatment.

During his hospital course, he was placed on intravenous antibiotics and given his extensive mucosal disease, was started on high-dose intravenous steroids. His peripheral white blood cell count was normal at 8,100 cells/ $\mu$ L. A CT scan of the chest demonstrated bilateral patchy alveolar infiltrates, and bronchoscopy showed marked inflammation with purulent drainage. A tongue biopsy was performed, but only demonstrated fibrovascular tissue and chronic inflammation. A rheumatologic work-up yielded a negative anti-nuclear antibody, negative double-stranded DNA antibody, negative HLA-B27 antibody, and normal rheumatoid factor. CRP was normal at 0.7 mg/dL. Serologic testing, however, revealed positive *M. pneumoniae* IgG and IgM titers. Therefore, the patient was diagnosed with *M. pneumoniae* pneumonia with associated erythema multiforme.

Given his history of multiple pulmonary infections and a childhood history of persistent sinus/ear infections, quantitative immunoglobulins were checked. IgA, IgM, and IgG were within the normal range. However, the patient's CD4 count was low at 85 cells/ $\mu$ L. This test was repeated twice and demonstrated consistently low values, with the highest being 164 cells/ $\mu$ L. To rule out acute HIV infection, two HIV antibody tests, a Western blot, RNA level, and viral load were checked, which were all negative. Given the negative work-up to date, the final consensus was that the patient likely had idiopathic CD4+ T-cell lymphocytopenia, a rare condition which represents a variety of ill-defined immune disorders that currently has no identifiable cause.

The noteworthy aspect of this case rests in the fact that although the patient presented with a "common" disease, careful review of his history initiated further work-up. In idiopathic CD4+ T-cell lymphocytopenia, a low CD4 count (with no evidence of HIV infection) may be the only indication of this diagnosis and should prompt appropriate follow-up, education, and possible prophylaxis to prevent further illnesses and hospitalizations.

**PATHOGENIC PROBIOTIC? SACCHAROMYCES FUNGEMIA IN A PATIENT TAKING PROBIOTIC***Ursula Kelly, M.D., Associate Member, Eastern Virginia Medical School*

Probiotics are typically considered a safe product; however the possibility of a life threatening fungemia exists with their use. Composed of varying strains of bacteria or yeast and touted as “beneficial”, “natural”, and “non-pathogenic”, probiotics are available to the general public over the counter. They have been generally accepted as preventative therapy for antibiotic associated diarrhea as well as adjunctive therapy for infectious diarrhea, primarily focused on *Clostridium difficile*. Inclusion of these products into the already established and effective antibiotic treatment regimen for *C. difficile* infections may cause more harm than good. A 34 year old female with a history of Hirschsprung’s disease status post total colectomy with ileostomy had frequent hospital admissions for stricture of her ileostomy, requiring endoscopic dilatation by her Gastroenterologist. Along with these many hospitalizations, she was plagued by frequent infections with *C. difficile*. For this reason she was started on Florastor, a probiotic which utilizes *Saccharomyces boulardii* as its active yeast. Within weeks of its initiation she was again hospitalized for nausea, vomiting, and dehydration, which was found to be related to another stricture. She was hydrated through her mediport, which had been present for months, and again taken to the endoscopy suite for dilatation. Following the procedure she developed fever and chills. Blood cultures were drawn from her mediport which grew three fungal species, one of which identified as *Saccharomyces cerevisiae* later subspecies by molecular identification to *Saccharomyces boulardii*. Her fungemia was initially treated with Fluconazole, however subsequent to Infectious Disease consult she was changed to a 14 day course of Voriconazole and advised not to restart Florastor or consume other probiotics. While it is rare for probiotics to cause harm including potentially fatal fungemia, it does occur as this case illustrates. This patient was not an ideal candidate for probiotic use. She had several potential risk factors for *S. boulardii* fungemia including chronic central access via her mediport, frequent gastroenterological manipulations and alterations in the gastrointestinal barrier via her ileostomy. Physicians should be aware of the potential harms and risk factors and caution high risk patients against their use. Evidence shows that current antibiotic treatment regimens for *C. difficile* are effective and safe when used appropriately.

**RENAL CELL CARCINOMA PRESENTING AS SYNCOPE, DYSPNEA AND LIVER FAILURE***Smriti Sharma, M.D., Associate Member, Carilion Clinic – Virginia Tech Carilion*

**Introduction:** Renal Cell Carcinoma (RCC) classically presents as flank pain, hematuria and palpable abdominal mass. We present a case of syncope secondary to intra-cardiac obstruction as a result of cardiac extension of renal cell carcinoma.

**Case Presentation:** A 46-year-old man presented to the emergency department with recurrent exertional syncope with dyspnea in the preceding several days. His medical history included alcoholism with polysubstance abuse; he used an albuterol inhaler. The blood pressure was 118/86 mm Hg, pulse 96, respirations 18 and oxygen saturation 96%. He was alert but in some respiratory distress. Examination revealed a bulging right flank and leg edema but was otherwise unremarkable. The ECG showed NSR with low voltage and the CXR was unremarkable. Lab abnormalities included AST 275 U/L, ALT 68 U/L, INR 2.47, bilirubin 7.2 mg/dL, and alkaline phosphatase 341 U/L. Blood counts, kidney function and urinalysis were normal. Computed tomography showed a 13 cm right kidney mass extending into the IVC and right atrium (RA) with a pulmonary embolism (PE). Echocardiography confirmed a massively dilated RA nearly completely occupied by a 7 cm x 5 cm mass. The patient quickly developed multisystem failure and died on the fifth hospital day. Autopsy confirmed a large clear cell renal cell carcinoma with direct vascular extension into the hepatic veins, IVC and RA. There were not distant metastases and PE was not confirmed.

**Discussion:** Renal cell carcinoma accounts for 85% of malignant renal masses. It is considered a great mimicker in medicine, as it may cause diverse problems such as polycythemia, hypercalcemia, Cushing syndrome, leukemoid reaction, nonmetastatic hepatic dysfunction (Stauffer syndrome), and amyloidosis. Typical signs and symptoms include flank pain, hematuria and palpable abdominal mass, although this triad is present in only 10% of cases. In rare instances the tumor can directly invade the inferior vena cava and right heart, causing preload obstruction, hepatic dysfunction, and other evidence of right heart failure, as in this case. In the absence of detectable metastasis, about half of patients with intra-cardiac extension have prolonged survival after resection. This surgery is quite complex and associated with substantial morbidity and mortality. This was not feasible in this case due to the very rapid clinical decline.

**A HOMEMADE ELIXIR FOR DYSPEPSIA CAUSING SEVERE METABOLIC ALKALOSIS***Kelly Sibre, M.D., Associate Member, University of Virginia*

Despite many treatments available for dyspepsia such as H2 blockers and PPI, the cost of treatment is still considerable. As a result the use of a homemade treatment with baking soda is frequently used to alleviate symptoms. A 53-year-old male presented from home with family reporting altered mental status. The patient complained of three days of hiccups and six months of vomiting. Vomiting occurs post-prandially associated with solids but not liquids. He complains of pain with swallowing and food being stuck and a burning sensation that is worse at night. History was significant for gastro-esophageal reflux and severe erosive esophagitis diagnosed 3 years on EGD. On presentation he was afebrile, blood pressure 83/47, pulse 99, respirations 26, 95% on room air. He was a well developed male actively having hiccups. He was awake and oriented with normal neurologic exam. He had a 2/6 systolic murmur at the apex and non-tender abdomen, normal active bowel sounds, no organomegaly. Laboratory results were significant for hyponatremia 118, potassium 2.5, chloride 52, bicarbonate 44, anion gap 22, BUN 88, creatinine 4.4, phosphorus 6.8, serum osmolality 281, urine osmolality 323, FeNa 3.2. ABG on room air revealed pH 7.56/pCO2 55/pO2 67, base excess +22. Urinalysis had a specific gravity of 1.011, pH 8.0. On the basis of these findings of metabolic disarray and presumed significant volume contraction leading to acute kidney injury, moderate fluid hydration with normal saline was initiated with close monitoring of electrolytes. On recurrent labs the following day his sodium was 122, chloride 74, bicarbonate 33. On hospital day 2, further questioning of the patient uncovered chronic use of baking soda tonics for dyspepsia. He had increased use the last three days to drinking baking soda up to 8 times a day. Evaluation for the cause of his dysphagia was initiated with barium swallow showing significant esophageal dysmotility with global hypotonia of the esophagus; and mild smooth focal narrowing of the cervical esophagus. Swallow also showed aberrant right subclavian artery coursing posterior to the esophagus resulting in significant narrowing of the proximal thoracic esophagus and moderate non-reducible hiatal hernia. He underwent EGD and an upper esophageal web was found and dilated under fluoroscopy. He was also initiated on a proton pump inhibitor. Though he had been prescribed this in the past he reported not taking it due to expense. This case illustrates the importance of repeated history taking as a patient's status changes. Without the understanding of the cause of this gentleman's metabolic disarray we could not effectively prevent future recurrence, as this was actually his second presentation with the same metabolic picture.

**LYMPHATIC FILARIASIS FOUND AFTER SUSPECTED DIAGNOSIS OF TESTICULAR TORSION***Sean Cowley, M.D., Associate Member, Naval Medical Center, Portsmouth*

Lymphatic Filariasis is a disfiguring and potentially incapacitating disease affecting more than 120 million people around the world. The disease is caused by nematodes invading the lymphatic system, the most common species affecting humans being *Wuchereria bancrofti* and *Brugia malayi*. Many patients with filariasis are asymptomatic and the disease could take years to manifest itself. Lymphatic filariasis is transmitted by mosquitoes that deposit larvae into the skin. Treatment involves killing both adult nematodes and the larvae. We present a case of filariasis found on pathology after orchiectomy for suspected testicular torsion in a young adult male.

The patient is a 20-year-old male from India, with a medical history of latent tuberculosis on isoniazid therapy at time of presentation, who presented to sick call for acute onset of testicular pain following participation in an obstacle course. During evaluation he was found to have no evidence of blood flow on ultrasound and a diagnosis of testicular torsion was suspected. The patient was taken to the operating room for scrotal exploration and discovered no evidence of torsion. An orchiectomy was performed because blood flow could not be restored. Pathology revealed two adult nematodes within a lymphatic vessel and no microfilariae. The patient was then referred to the Infectious Disease clinic and the work up included collecting peripheral blood smears during the night due to microfilariae having a nocturnal periodicity. There was no evidence of microfilaria and no eosinophilia. From an infectious disease standpoint it was not necessary to treat with antiparasitic agents, no further workup was needed and there were no limitations placed on physical activity, travel or duty status.

All patients with acute scrotal pain should be evaluated for testicular torsion. When the history and physical examination strongly suggest that testicular torsion is present urgent surgical intervention is indicated. In our case, the patient's acute scrotal pain was caused not by torsion but by obstruction of blood flow from the nematode. The diagnosis of filariasis was only achieved by histological examination after surgery. Since it is a rare cause of acute scrotal pain in non-endemic areas and the disease can take years to manifest itself, it is important to keep the differential diagnosis broad and perform a good history and physical exam including travel plus background information on where the patient was raised. This is especially important for military personnel and recent immigrants to the United States.

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**MYELOPATHY AND WEAKNESS AFTER TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT***Daniel Markley, M.D., Associate Member, Virginia Commonwealth University/Medical College of Virginia*

Portosystemic myelopathy is a rare complication of cirrhosis after portosystemic shunting. It is typically characterized by progressive bilateral lower extremity paraparesis with an absence of sensory deficits. A 58-year-old male with a history of alcoholic cirrhosis presented to the hospital with two months of progressive weakness, dysarthria, and dysphagia. His first symptom was symmetric lower extremity weakness manifesting itself in two ground-level falls. At the time of presentation, he could no longer get up from a seated position without assistance. Two to three weeks before presentation his speech gradually became slower. He also began having problems swallowing solids, and eventually liquids. Five months before presentation he underwent transjugular intrahepatic portosystemic shunt (TIPS) for refractory ascites. The patient had no other significant past medical history. His cirrhosis was caused by alcoholism; however, he had abstained for the previous 6 years.

Physical examination revealed slow, scanning speech, symmetric lower extremity weakness, positive Babinski's reflex bilaterally, and brisk reflexes throughout. His gait was unstable, and Romberg's sign was positive. The patient had no sensory or cognitive deficits. Magnetic resonance imaging of the head revealed increased T1 signal intensity in the globus pallidus bilaterally with extension into the midbrain. The pons demonstrated extensive, somewhat symmetrical T2/FLAIR hyperintensity in a lobulated pattern with mild diffusion restriction and no enhancement. The cord demonstrated subtle increased T1 and T2 signal extending from the level of C3 through C5 without associated cord expansion or abnormal cord enhancement. MRA of the head and neck were essentially normal. Pertinent serum laboratory investigation included B12 (normal), RPR/VDRL (negative), HIV (negative), ceruloplasmin (normal), Lyme serology (negative), and ANA (negative). Serum ammonia was elevated (37  $\mu\text{mol/L}$ ), as well as Angiotensin Converting Enzyme (ACE) level (100U/L), and ESR (52mm/hr). Lumbar puncture revealed clear cerebrospinal fluid (CSF) with no white blood cells, normal protein (30mg/dL), normal glucose (92mg/dL), no oligoclonal bands, negative Lyme serology, negative Myelin Basic Protein, and a normal ACE level. Viral and bacterial cultures from the CSF were negative. A thorough medication and exposure history was negative for any causative agent. At this point, with all other possibilities excluded, the diagnosis of portosystemic myelopathy was made. The patient's neurologic deficits remained stable throughout his stay, and he was discharged to follow up on hospital day seven. At his neurology follow up two weeks later, the patient's gait had become slightly worse, and was described as spastic paraparesis.

This case brings attention to a rare, and poorly understood neurologic complication of portosystemic shunting in patients with cirrhosis. Most cases present with lower extremity spastic paraparesis, and a normal sensory exam. Although infrequent, the devastating effects of portosystemic myelopathy must be considered as medical advances are increasing the lifespan of patients with cirrhosis.

**LATE SECOND TRIMESTER ACUTE FATTY LIVER OF PREGNANCY: REDEFINING THE PARADIGM***Charles W. Shrode, M.D., Associate Member, University of Virginia*

Acute fatty liver of pregnancy (AFLP) is a disease characterized pathologically by microvesicular steatohepatitis. Clinically, patients may typically present with a nonspecific prodrome of nausea, vomiting, fatigue, and malaise. Jaundice may be present depending on the extent of the disease at the time of evaluation. Laboratory values vary on the severity of disease at the time of presentation but are typically consistent with elevated liver function tests. While a majority of patients present in the late third trimester during weeks 34-37, several case reports and case studies describe patients presenting throughout the third trimester. We present a case of AFLP occurring in the late second trimester.

Our case describes an otherwise healthy pregnant female, with a past medical history of a previously uneventful pregnancy and Lyme disease, who presented to her community hospital at 24 weeks gestation. The Lyme disease was treated with four weeks of antibiotics prior to her becoming pregnant. She reported a four-week history of cough, intermittent fever to 103.2°F, chills, and right upper quadrant pain. Prior to the onset of these symptoms, her pregnancy was uneventful. She reported rare acetaminophen use and denied alcohol use. Labs at presentation demonstrated significantly elevated liver function tests. Her alkaline phosphatase was 194 U/L, her AST was 730 U/L, and her ALT was 291. The patient presented to our facility during her 25th gestational week. Upon transfer to our facility her total bilirubin was 23.5 mg/dL, AST was 2929 U/L, ALT was 906 U/L. Viral hepatitis panels for hepatitis A, B, and C were completed at the outside facility and were negative. Liver biopsy at our facility was positive for findings consistent with AFLP. The patient underwent cesarean section on week 26.0 of her pregnancy. She clinically improved for a period of 72 hours before decompensating and expiring due to fulminant hepatic failure.

We present a unique case of acute fatty liver of pregnancy. Only one other case in the literature describes a patient presenting at a younger gestational age. This case demonstrates that the typical concept of acute fatty liver of pregnancy must be reconsidered. We propose that AFLP should be considered in all pregnant patients presenting with hepatic dysfunction in the late second trimester and throughout the third trimester.

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**HEADACHE AND A DEVIATED TONGUE IS REALLY A PAIN IN THE NECK:  
A CASE OF HYPOGLOSSAL NERVE PALSY RESULTING FROM INTERNAL CAROTID ARTERY DISSECTION**

*Michael R. Wagner, M.D., Associate Member, Naval Medical Center, Portsmouth*

Hypoglossal nerve palsy (HNP) not associated with other neurologic deficits is an unusual finding. The following case describes a patient with headache and tongue deviation caused by a spontaneous carotid artery dissection, a rare cause of HNP.

A 41-year-old male without significant past medical history initially presented to family practice with a two day history of severe headache. Neurological exam was normal and a non-contrast CT scan was negative for subarachnoid hemorrhage. He was re-evaluated at the emergency department two days later for continued headache and new onset dysarthria with an exam remarkable for left tongue deviation. Lumbar puncture was unsuccessful and MRI of the brain was normal. The next day in neurology clinic the patient described an initial 10/10 left supraorbital headache that evolved over 15-30 minutes without migrainous features. Over several days, his headache decreased to 2/10, shifted to the left temporoparietal region, and was characterized as scalp tenderness. The patient also described dysarthria, tongue biting and jaw pain with chewing. He denied fever, neck pain, pain with movement of the eyes, or changes in vision or taste. There was no history of trauma, neck manipulation, or strenuous exercise. Exam was remarkable for left tongue deviation but ability to move it in all directions and minimally dysarthric speech. The remainder of his physical exam was normal including absence of ipsilateral Horner's syndrome, carotid or vertebral bruits. ESR, D-dimer and coagulation studies were normal. Repeat MRI with cranial nerve protocol showed diminutive left internal carotid artery (ICA) flow void at the level of the petrous carotid canal. CT angiogram demonstrated dissection of the left ICA just above the left carotid bulb to the level of the petrous canal with 95% stenosis at the craniocervical transition. The patient was started on anticoagulation therapy and followed by neurology and neurosurgery with eventual resolution of tongue deviation.

HNP is a known complication of carotid surgery. Though blood supply to the hypoglossal nerve is predominantly from branches of the external carotid, it is probable that mural expansion of the ICA dissection caused compression of these smaller vessels resulting in ischemia to the hypoglossal nerve. This case is an example of a rare but increasingly recognized cause of isolated HNP and demonstrates the importance of considering carotidynia and referred neck pain in the differential diagnosis when evaluating patients with headache, especially those with focal neurologic deficits.

**BOTH CUSHING'S SYNDROME AND ADRENAL INSUFFICIENCY INDUCED BY RITONAVIR AND  
INTRAARTICULAR TRIAMCINOLONE ACETONIDE**

*Abhijeet Nakave, M.D., Associate Member, Eastern Virginia Medical School*

**Introduction:** Iatrogenic Cushing's syndrome (CS) cases have been reported recently with using injected, ingested, and inhaled glucocorticoids combined with drugs which inhibit hepatic cytochrome enzymes, including anti-fungals, macrolide antibiotics, and anti retrovirals, especially ritonavir, which is a profound inhibitor of CYP3A4 activity.

**Case Description:** We report here a 51 year old women with HIV diagnosed 13 yrs before with an absolute CD4 of 48, percent CD4 of 8 and viral load of 250,000 within 2 years. Ritonavir and saquinavir with tenofovir being added to regimen 3 years later kept her PCR RNA load and absolute CD4 count averaged <50 copies and >400 cmm, respectively, up until the present with no opportunistic infections. In January 2008, she was noted to have Cushing's syndrome with symptoms of 20 lb. weight gain, central fat deposition, HTN, hypokalemia, and edema. However, random serum cortisol was 0.5 mg/dL and 24 hr urine cortisol was undetectable, raising the issue of exogenous Cushing's. She denied topical, ingested or inhaled glucocorticoids but noted getting 2 doses of intra-articular triamcinolone, 20 mg, 7 and 4 months before January 2008, and that these preceded her symptoms. A low dose dexamethasone suppression test revealed undetectable cortisol and ACTH, and midnight salivary cortisols were 0.9 nmol both nights. CT scan of abdomen did not reveal any adrenal mass or hyperplasia. The enlightening data point which elucidated the pathophysiologic mechanism was the dexamethasone concentration during the suppression test, markedly elevated at 1150 (Normal 140-295 ng/ml). Cortisol levels showed prolonged suppression (0.5 to 1.7, 1.9, and 2.1) over a year with final rapid increase to 25.6 (16 months after last injection).

**Discussion:** This is the fifth described case of CS apparently caused by (usually) trivial triamcinolone doses, due to ritonavir inhibition of CYP3A, the most important cytochrome P450 isoform responsible for glucocorticoid metabolism and oxidative biotransformation. Steroids are metabolized by cytochromes converting them both to active (cortisone and prednisone to hydrocortisone and prednisolone) and inactive forms (dexamethasone, triamcinolone), while cytochrome CYP3A inhibitors like azole derivatives, macrolide antibiotics, protease inhibitors prevents this conversion. In addition to induction of CS, prolonged adrenal suppression has been noted in several, with this case demonstrating the longest interval until recovery of hypothalamic-pituitary-adrenal axis. Our case report cautions us of the potential for iatrogenic CS followed by adrenal suppression in patients receiving potent CYP3A4 inhibitors, and that absence of cortisol from the serum does not preclude a diagnosis of CS and further exploration in HIV patients with symptoms of Cushing's syndrome.



**A CASE OF PRIMARY ADRENAL INSUFFICIENCY AND POLYRADICULOPATHY DUE TO  
EXTRANODAL NK T-CELL LYMPHOMA, NASAL TYPE***Richard Hall, M.D., Associate Member, University of Virginia*

Extranodal NK T-cell lymphoma, nasal type is a rare non-Hodgkin's lymphoma infrequently encountered outside Asia. A 62 year old female presented to an outside hospital with a chief complaint of lower extremity weakness, low back pain, and fatigue. On admission she was hyponatremic to 122 mg/dl. An evaluation ensued and revealed a low morning cortisol at 3.6 µg/dl. The patient was diagnosed with primary adrenal insufficiency following a cosyntropin stimulation test and was initiated on hydrocortisone. Her fatigue and hyponatremia improved, however she continued to experience progressive right leg and back pain. A lumbar spine MRI was performed and unexpectedly revealed bilateral adrenal masses. She subsequently represented to an outside hospital with uncontrolled leg pain and weakness. A CT abdomen demonstrated enlargement of bilateral adrenal masses previously seen on MRI. A lumbar spine MRI was repeated and revealed diffuse nerve root enhancement, and a lumbar puncture was performed and notable for a protein at 95 mg/dL. She was diagnosed with Guillian-Barre syndrome and treated with IVIG prior to transfer to the University of Virginia. Once at the University of Virginia a CT guided biopsy of the patient's left adrenal gland was performed and was nondiagnostic. An extensive infectious work-up was performed and was unremarkable. Ultimately the patient underwent a left adrenalectomy that showed replacement with a diffuse lymphoid infiltrate. Immunohistochemical staining was positive for CD45, CD3, CD56, and TIA1, variable for CD4, and negative CD79a and CD5. FISH analysis for EBV was performed and showed diffuse nuclear staining. The pattern of staining, FISH analysis, and morphology yielded a diagnosis consistent with extranodal NK/T-cell lymphoma, nasal type. During the evaluation of the patients' neurological findings an EMG showed an L5-S1 polyradiculopathy with demyelination and excluded Guillian-Barre syndrome. The patient underwent an L3 laminectomy with distal nerve root and cauda equina biopsy that was nondiagnostic. Prior to the initiation of chemotherapy the patient developed a left peripheral CN VII palsy. MRI brain revealed nodular enhancement of the left facial nerve concerning for lymphomatous involvement. Induction chemotherapy was initiated with etoposide, prednisone, doxorubicin, and cyclophosphamide at a 25% dose reduction given her ECOG performance status of 4. The patient also received 2 doses of intrathecal methotrexate. CSF analysis failed to demonstrate lymphomatous cells throughout her hospital course. Despite administration of systemic and CNS chemotherapy, the patient experienced further clinical deterioration and was transitioned to comfort care. She was discharged home with Hospice care and died one week following discharge. This case demonstrated the convergence of a case of adrenal insufficiency and a polyradicular syndrome secondary to leptomeningeal lymphomatous infiltration of nerve roots into a single unifying diagnosis of a rare, aggressive non-Hodgkin's lymphoma.

**ACUTE MYOCARDIAL INFARCTION-LIKE SYNDROME: A CASE REPORT OF MYOCARDITIS***Imran Farooq, M.D., Associate Member, Virginia Commonwealth University/Medical College of Virginia*

Thousands of patients are admitted daily to the hospital for suspected acute coronary syndrome. The diagnosis is often supported by the evidence of myonecrosis (elevated troponin I levels). Nevertheless, myonecrosis is not synonymous with acute myocardial infarction. Here we describe the case of a 36 year old Caucasian male with history of a prior NSTEMI presenting with precordial chest pain, shortness of breath and nausea and vomiting ongoing for several days. At admission he had elevated troponin I levels (4.37ng/mL) and his ECG illustrated nonspecific ST segment abnormalities. A coronary angiogram was performed and revealed no obstructive coronary artery disease. A cardiac MRI was also performed and showed focal delayed enhancement of the epicardial anteroseptal wall confirming the diagnosis of myocarditis. Follow up serum Coxsackie virus Group B Antibody was positive at 1:64 (Neg: <1:8). Acute myocarditis, although uncommon may mimic acute myocardial infarction and lead to inappropriate treatment regimens. Cardiac MR represents a highly sensitive and specific non invasive tool to diagnose acute myocarditis and should be considered for patients with suspected myocarditis.

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**ATYPICAL TAKOTSUBO CARDIOMYOPATHY AS A COMPLICATION OF ACUTE ISCHMIC STROKE**

*An Bui, Medical Student, University of Virginia*

Takotsubo cardiomyopathy, also known as apical ballooning syndrome (ABS), stress cardiomyopathy, or Broken Heart Syndrome, is a distinct reversible cardiomyopathy that is often precipitated by acute medical illness or intense emotional or physical stress. Classically, it is a syndrome of postmenopausal women presenting with transient systolic dysfunction of the apical and/or mid segments of the left ventricle in the setting of absence of significant coronary artery disease. Takotsubo cardiomyopathy has a well-known association with subarachnoid hemorrhage (SAH). However, its occurrence as a complication of acute ischemic stroke remains to be determined. We describe a case of atypical takotsubo cardiomyopathy resulting as a complication of an acute ischemic stroke.

A 77-year-old woman with history of hypertension, pre-diabetes, and chronic kidney disease stage 3 presented to the Emergency Department with a three day history of unsteadiness with progressive shortness of breath. She had a 5-pack-year smoking history in which she quit 40 years ago. A 12-lead electrocardiogram (ECG) showed ST elevations in II, III, aVF, and V2-V6. The patient had an elevated cardiac troponin-I of 7.28mcg/L and brain natriuretic peptide level of 2953pg/mL. A transthoracic echocardiogram (TTE) showed severely decreased left ventricular systolic function with an estimated ejection fraction of 20-25%. To evaluate for acute coronary syndrome, the patient was urgently taken to cardiac catheterization that was significant for mild nonobstructive coronary artery disease, which raised suspicion for takotsubo cardiomyopathy. Due to the patient's persistent symptoms of unsteadiness and otalgia, a head MRI was obtained to rule out stroke; this revealed a new small infarct in the centrum ovale. Follow up TTE was done at 6 weeks which confirmed the diagnosis of takotsubo cardiomyopathy with normalization of ejection fraction to 55-60% and resolution of clinical symptoms.

Takotsubo cardiomyopathy is a distinctive reversible cardiomyopathy that can present as a complication of acute ischemic stroke. The clinical presentation of this syndrome is indistinguishable from a myocardial infarction, which contributes to its diagnostic challenge. Ischemic stroke appears to be a rare but important cause of takotsubo cardiomyopathy and should be on the differential diagnosis of patients presenting with neurologic dysfunction with suspected myocardial infarction. Acute ischemic stroke-induced takotsubo cardiomyopathy is an under-recognized phenomenon, and further studies are warranted to elucidate the pathophysiology behind this association.

**RHEUMATIC FEVER IN AN ADULT PATIENT**

*Shaun Bhatta, M.D., Associate Member, Virginia Commonwealth University/Medical College of Virginia*

**Case Presentation:** A 36 year-old man presented with sore throat and fevers. His symptoms were worsening over 12 days. A rapid strep antigen test was positive and he was started on azithromycin due to a penicillin allergy. He later developed redness and tenderness on his left shin and arthralgias of the ankles, knees, wrists, and back. He was started on erythromycin and aspirin and referred to an infectious disease clinic. In clinic, the patient reported swelling over his left ankle and a nonpruritic rash on both of his forearms. His sore throat had resolved. He denied fevers, chest pain, shortness of breath, cough, abdominal pain, involuntary movements, muscle weakness, or changes in his mood. Past medical history was significant for mitral valve prolapse. Allergies included cefazolin. Vital signs included a blood pressure of 138/85, heart rate of 73, respiratory rate of 14, and temperature of 95.9 degrees Fahrenheit. His oropharynx was nonerythematous and without lesions. He had a few small lymph nodes palpable in the inguinal region, but no palpable lymph nodes in the posterior cervical, supraclavicular, or axillary regions. Cardiac exam revealed a normal S1 and S2 without murmurs or extra heart sounds. Lungs were clear to auscultation. Skin exam revealed a morbilliform rash on the extensor surface of his forearms and an area of erythema and tenderness over the left shin. His left ankle was swollen, warm, tender, and had decreased range of motion. All other joints were normal. Labs were significant for an ESR of 45 mm in 1 hour, an elevated ASO titer, normal renal function, normocytic anemia, and a WBC of 9700 cells/mL. EKG had sinus bradycardia, PR interval of 152, and no conduction deficits. Transthoracic echocardiogram revealed no evidence of valvular lesions or systolic dysfunction. On a follow up visit, the patient developed a new erythematous rash with central clearing on the right anterior chest that was consistent with erythema marginatum. A diagnosis of rheumatic fever was made.

**Discussion:** Rheumatic fever is a delayed nonsuppurative sequela of a pharyngeal infection with group A streptococcus. The Jones criteria are used for diagnosing rheumatic fever. The patient in this case presented with a group A strep infection followed by the development of 1 major Jones criteria of erythema marginatum and three minor Jones criteria of fever, elevated ESR, and arthralgias. Rheumatic fever is most frequently seen in children from 4-9 years of age. Rheumatic fever is rare in adults, particularly adults over 40 years of age. Clinicians should be aware this condition and always include it in the differential of adults who present with fevers and arthritis.

**A RARE PRESENTATION OF A RARE TUMOR***Paul Schmidt, M.D., Associate Member, Naval Medical Center Portsmouth*

**Case:** A 45 y/o female complained of a right neck mass present for one year that had recently become painful. She reported two years of episodic hypertension associated with palpitations, headaches, blurry vision and feeling unbalanced. Balance problems resulted in falling at times, though she denied injury or losing consciousness. Episodes lasted up to 10 minutes and were occurring several times a day. She complained of extreme neck pain, but denied difficulty swallowing or breathing. Neck CT showed a lesion consistent with a vagal nerve mass. Otherwise CT imaging from head to pelvis was negative. She was referred to otolaryngology for possible resection. A fine needle aspiration showed pathology consistent with paraganglioma. 24 hour urine and plasma labs showed elevated vanillylmandelate, catecholamines, metanephrines, normetanephrine, and dopamine. Surgery was delayed pending a comprehensive endocrine evaluation. The patient's use of amitriptyline, which can elevate catecholamines and metanephrines, could have caused false positive results. Repeat labs, after two weeks off amitriptyline, showed persistently elevated values. An occult adrenal tumor was suspected as 85-90% of catecholamine-secreting tumors are intra-adrenal, while only 10-15% are extra-adrenal. MIBG (iodine-131-meta-iodobenzylguanidine) scan confirmed abnormal iodine uptake in her neck mass. The preoperative echocardiogram, to assess cardiac function that might affect anesthetic and surgical management, was normal. She was admitted for preoperative medical therapy to control hypertension and reduce the risk of hypertensive crisis during surgery. Alpha-blockade, with phenoxybenzamine, was instituted prior to initiating beta-blockade. Aggressive intravascular volume expansion must accompany induction of alpha-blockade, as profound hypovolemia is often unmasked by effective alpha-blockade. Beta-blockade, before alpha blockade, can precipitate a hypertensive crisis. Blocking vasodilatory peripheral beta-adrenergic receptors allows for unopposed alpha-adrenergic receptor stimulation.

Tumor manipulation during surgery caused significant blood pressure elevations. The procedure had to be interrupted several times for nitrate administration by the anesthesia. Pathologic evaluation of the resected tumor was consistent with a malignant paraganglioma, though lymph nodes were negative for metastasis. A week after surgery, a 24 hour urine collection showed catecholamines were within normal ranges. The patient continues to be followed by endocrinology.

This case illustrates the importance of a multi-disciplinary approach when evaluating and treating these rare tumors to maximize proper care and relief for these patients.

**INHALED NITRIC OXIDE USED TO STABILIZE ACUTE RIGHT SIDED HEART FAILURE***Douglas T. Summerfield, M.D., Associate Member, Eastern Virginia Medical School*

**Introduction:** Inhaled Nitric Oxide (iNO) has been shown to preferentially lower resistance in the pulmonary vasculature. In this vignette the vasculature selectivity of iNO was successfully exploited to treat acute pulmonary hypertension from a massive pulmonary embolism prior to mechanical thrombectomy.

**Case Description:** A 66 year old Caucasian female with shortness of breath, was transferred to the Intensive Care Unit after a V/Q scan revealed near absence of perfusion in her entire left lung, as well as the superior lobe of her right lung. Past medical history was significant for biopsy proven glioblastoma multiforme. The patient was realistic about her grim prognosis, however she had specific short term goals she wanted to realize. As such the decision was made to aggressively treat the patient. Thrombolytic therapy was contraindicated, but a heparin drip was started. Echocardiography revealed a pulmonary artery pressure of 57 mmHg, and a dilated right ventricle. The patient began to deteriorate as her blood pressure fell to 75/52 and her oxygen saturations decreased to the 70's. She was intubated and pressors were started. Despite pressors she remained unstable. iNO was started, after which her condition stabilized. She was able to remain on iNO without further hemodynamic collapse, until interventional radiology performed a mechanical thrombectomy. After two days the patient was transferred back to the floor where she realized some of her remaining goals.

**Discussion:** In acute pulmonary emboli, the right ventricle is unable to generate adequate pressures to overcome resistance imposed by clot burden in the pulmonary arteries. The right ventricle acutely dilates, cardiac output falls, and hemodynamic collapse ensues. In this setting, especially in patients unresponsive to conventional therapies, iNO has been used as a salvage therapy. iNO reduces pulmonary vascular resistance through smooth muscle relaxation by increasing cyclic guanosine monophosphate. The half life of iNO is 15 to 30 seconds, as it is quickly inactivated by hemoglobin. This quick inactivation makes iNO the only drug which selectively dilates the pulmonary artery, as all other medications have additional systemic effects. Once the pulmonary artery is dilated, pulmonary artery pressure is reduced, thus decreasing the afterload of the right ventricle and thereby improving cardiac output and stabilizing blood pressure. Side effects of iNO include methemoglobinemia, and cytotoxicity, the latter of which may reach targets further downstream from the lung by S-nitrosylation of hemoglobin. Rebound hypotension may also occur when iNO is discontinued, so iNO should always be tapered when treatment is done.

**βAgony: A CASE OF IATROGENIC DIABETIC KETOACIDOSIS CAUSED BY CONCURRENT ALBUTEROL AND HELIOX THERAPY**

*Marcus Walton, M.D., Associate Member, Naval Medical Center, Portsmouth*

Case: A 52 year old non-diabetic female with a history of asthma requiring previous intubations, presented to the Emergency Department with symptoms typical of an asthma exacerbation. After initial Emergency Department management with nebulized albuterol/ipratropium and intravenous methylprednisolone proved ineffective, she was treated with continuous nebulized albuterol (80 mg/hr) and heliox therapy. After several hours the patient's condition improved, however, a repeat laboratory evaluation was significant for new hyperglycemia with a blood glucose of 255 mg/dL, ketonuria and an anion gap metabolic acidosis with a serum bicarbonate of 18 mmol/L. Arterial blood gas analysis revealed a pH of 7.34 and pCO<sub>2</sub> of 37 mmol/L. These findings were consistent with mild diabetic ketoacidosis and were attributed to the combination therapy with continuous nebulized albuterol and heliox. Her laboratory abnormalities resolved with subcutaneous insulin and cessation of the continuous albuterol and heliox therapy.

Discussion: We present a case of iatrogenic diabetic ketoacidosis attributed to concurrent; β-agonist and heliox therapies. β-agonists are known to increase glycolysis and gluconeogenesis. It is thought that heliox potentiated this effect by increasing the delivery of nebulized albuterol. Furthermore, the dosing of the nebulized albuterol in this case was in excess of standard dosing parameters.

It is important for any physician who treats asthma exacerbations to recognize this potential complication of combination therapy with inhaled; β-agonist and heliox. We use our case to highlight the criteria for and classifications of diabetic ketoacidosis. In addition, we review the pharmacophysiological mechanisms thought to be responsible for the occurrence of diabetic ketoacidosis in this non-diabetic patient.

**MRSA: NAVIGATING THE ICEBERG**

*Susan Szulc, M.D., Associate Member, Eastern Virginia Medical School*

The incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections is on the rise. Management of these cases requires careful navigation around unseen complications that lay beneath the surface, complications that can be life-threatening. A 52-year-old female with end-stage renal disease on peritoneal dialysis, presents with complaints of right-sided flank pain and vomiting for one week. She had presented to the emergency department twice, earlier that week, with similar complaints. Peritoneal fluid cultures were drawn at that time and had returned positive for gram-positive cocci, prompting her return to the ED. The patient reported clear peritoneal fluid without purulent drainage from the catheter site, and denied fevers or chills. Of note, the patient was hospitalized four months prior for MRSA bacteremia associated with the peritoneal catheter. This episode was complicated by endocarditis and endophthalmitis. The patient had resumed peritoneal dialysis after completing six weeks of vancomycin treatment. On physical exam, the patient was afebrile, tachycardic, and hypertensive. The exam was significant for a 2/6 systolic ejection murmur at the LUS border with radiation to the axilla. The patient had rebound tenderness and tenderness to palpation in the right upper and lower quadrants. The patient also had right costovertebral angle tenderness. The patient was admitted for presumed secondary bacterial peritonitis and started on vancomycin and gentamicin. A CT of the abdomen/pelvis was ordered to rule out an abscess. The results showed an irregular aneurysmal dilation of the aorta, representing a contained aortic aneurysm rupture at the level of the diaphragmatic hiatus. Vascular surgery performed an emergent aneurysm repair. It was believed that this finding was related to the previous MRSA infection and she had likely seeded an aortic plaque that progressed to a mycotic aneurysm with rupture. Cultures from the aortic specimen grew MRSA. The patient was switched to vancomycin and rifampin for a 6-week course. Given the patient's extensive complications from the MRSA bacteremia, ID recommended continuing the patient on life-long suppressive antibiotic therapy. The patient tolerated the surgery well and was discharged home eleven days later.

This case serves to illustrate the impact MRSA infections and related complications have in the health care industry. In 2005 alone, 18,650 people died during a hospital stay related to a MRSA infection. 1 Approximately one-third of patients with *Staphylococcus aureus* bacteremia will develop metastatic complications from hematogenous seeding of distant sites or from local extension of disease. 2 Furthermore, a 2003 study showed that 33% of patients with an initial MRSA-positive culture will go on to develop a subsequent MRSA infection within 18 months. 3 With these staggering statistics, clinicians must be vigilant in the follow-up of patients with MRSA infections and related complications must be high on the differential.

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**ADEQUATE IMMUNE RECONSTITUTION IN RECIPIENTS OF UNRELATED DONOR HEMATOPOIETIC CELL TRANSPLANTS GIVEN RABBIT ANTI-THYMOCYTE GLOBULIN DURING CONDITIONING**

*Devon Fletcher, M.D., Associate Member,  
Virginia Commonwealth University/Medical College of Virginia*

**INTRODUCTION:** Anti-thymocyte globulin (ATG) is known to reduce the risk of developing acute graft vs. host disease following allogeneic hematopoietic cell transplant (HCT). Its effects on long-term immune reconstitution are less well defined, particularly in the adult population undergoing unrelated donor (URD) HCT.

**METHODS:** We performed a retrospective landmark analysis to compare immune reconstitution in patients who received ATG during conditioning vs. those who did not. Patients had to have completed at least 6 months of follow-up post transplant. Fifty six patients underwent matched related donor HCT and did not receive ATG (no ATG cohort); 30 patients received an URD HCT (ATG cohort).

**RESULTS:** Absolutelymphocytecountsat6,9and12monthsfollowingtransplantationwere(mean±SD)  $1.2 \pm 0.6 \times 10^3 / \mu\text{L}$  vs.  $1.0 \pm 0.8$  (T-Test,  $P=0.44$ ),  $1.5 \pm 0.9$  vs.  $1.3 \pm 1.0$  ( $P=0.51$ ) and  $1.6 \pm 0.9$  vs.  $1.3 \pm 0.9$  ( $P=0.23$ ) respectively in the no ATG cohort vs. ATG cohort. Lymphocyte subset enumeration data was obtained during the first year following HCT at the time of cessation of immunosuppression and was available for 32 and 12 patients in the no ATG and ATG cohorts respectively. Absolute CD3+ cell counts measured at a median of 278 days were  $1226 \pm 773$  vs.  $981 \pm 442 / \mu\text{L}$  in the no ATG vs. ATG cohorts ( $P=0.52$ ). Simultaneously measured absolute CD3+/4+ cell counts were  $483 \pm 231$  vs.  $242 \pm 122$  ( $P=0.001$ ), CD3+/8+ were  $717 \pm 627$  vs.  $701 \pm 444$  ( $P=0.94$ ), CD19+ were  $250 \pm 239$  vs.  $351 \pm 233$  ( $P=0.25$ ) and CD56+ were  $181 \pm 97$  vs.  $178 \pm 67$  ( $P=0.75$ ) in the no ATG vs. ATG cohorts. Surveillance for EBV and CMV reactivation was performed using PCR. No statistically significant difference was noted in rate of CMV reactivation between the two cohorts in the 6-12 month post-transplant period indicating equivalent functional cellular immune reconstitution. EBV reactivation did not occur in either cohort. During the same time period the incidence of culture proven fungal infections and viral infections was equivalent between the two groups, however there was a significantly higher number of patients who experienced bacterial infection episodes in the ATG group ( $P=0.004$ ). We are investigating the impact of ATG administration on the relative rate of relapse in these two cohorts.

**DISCUSSION:** We conclude that ATG administered during conditioning did not adversely impact cellular immune reconstitution in this cohort of patients. This effect could be explained by a reduction in the incidence of acute GVHD secondary to ATG use, which in turn reduces the overall immunosuppressive exposure these patients experience following transplantation. T helper cell reconstitution appears to be delayed and may contribute to the higher number of patients experiencing bacterial infections in the ATG cohort.

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**PARADOXES IN ADVANCE CARE PLANNING: THE COMPLEX RELATIONSHIP OF ONCOLOGY PATIENTS, ADVANCED MEDICAL DIRECTIVES, AND THEIR PHYSICIANS**

*Lindsay A. Dow, BS, Medical Student, Virginia Commonwealth University/Medical College of Virginia*

**Purpose:** Many seriously ill cancer patients do not discuss prognosis or advance directives (AD), which may lead to inappropriate and/or unwanted aggressive care at the end of life. Ten years ago, cancer patients said they would not like to discuss ADs with their oncologist, but would be willing to discuss them with an admitting physician. We assessed if this still held. **Methods:** Semi-structured interviews with 75 consecutively admitted cancer patients on the hematology-oncology inpatient service at an urban academic center.

**Results:** Of those enrolled, 41% (31/75) had an AD. Nearly all (87% (65/75)) thought it acceptable to discuss ADs with the admitting physician with whom they had no prior relationship, and 95% (62/65) thought that discussing AD issues was very or somewhat important. Only 7% (5/75) had discussed ADs with their oncologist. Only 23% (16/70) remaining would like to discuss ADs with their oncologist. When specifically asked which physician they would choose, 48% (36/75) of patients would prefer their oncologist, and 35% (26/75) their primary care physician.

**Conclusions:** Fewer than half of seriously ill cancer patients admitted to an oncology service have an AD. Only 23% (16/70) would like to discuss their ADs with their oncologist, but nearly all supported a policy of discussing ADs with their admitting physician. However, fully 48% (36/75) actually preferred to discuss advance directives with their oncologist if AD discussion was necessary. We must educate patients on why communicating the wishes that their ADs represent is beneficial, and train primary care physicians, housestaff, hospitalists and oncologists to initiate these difficult discussions.

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**GERD SYMPTOMS RESPOND TO AN ORAL APPLIANCE USED FOR THE TREATMENT OF OSAS***David W. Frate, D.O., Associate Member, Eastern Virginia Medical School*

**Introduction:** Existing evidence indicates Continuous Positive Airway Pressure (CPAP) reduces gastro-esophageal reflux disease (GERD) symptoms in patients with obstructive sleep apnea syndrome (OSAS). This study was designed to determine if another OSAS treatment modality, the oral appliance (OA), also improves GERD symptoms.

**Methods:** This prospective study of consecutive patients electing to use an OA for OSAS was performed at the EVMS/SNGH Sleep Disorders Center. Investigators utilized polysomnography (PSG) to establish the presence and severity of OSAS in adult (18-79 yr.) patients. OSAS patients electing OA therapy (N=56) visited 1 of 2 dentists skilled in OA use. No discussion regarding the potential utility of the OA in GERD occurred. Patients completed a validated GERD symptom questionnaire (Shaw, 2001) at the initial visit and after satisfactory use of OA. A score > than 15.5 (range 0-50) indicated GERD. The post questionnaire also queried subjective OA adherence. A group of bruxism patients visiting these same dentists, utilizing bruxism appliances and serving as the control group continues to be enrolled.

**Results:** A total of 56 patients with OSAS treated with the oral appliance completed the pre and post validated GERD questionnaire. (N=56, Male 32, Female 24, Mean age  $54 \pm 9$  and BMI  $31 \pm 5.4$ ), PSG data revealed an AHI  $22 \pm 19$  and low SaO<sub>2</sub>  $85 \pm 5.6$ .) Overall, there was a significant reduction in GERD symptoms. The overall pre-appliance GERD score revealed a mean of 5.8 and a post-appliance GERD score demonstrated a mean of 3.5. A Paired T Test p-value was significant at  $p = .01$ . There were eight patients manifesting pre-appliance GERD (score > 15.5) prior to the oral appliance and seven of these patients' symptoms improved. These patient's had a pre-appliance GERD score mean of 20.5 and a post-appliance GERD score mean of 10.6, the p value was significant at  $p = 0.04$ . Five of the eight patients with pre-appliance GERD symptom scores of >15.5 reduced their symptom scores to less than 15.5, which suggests not having GERD symptoms subsequent to oral appliance use. Regarding adherence, using a sensitivity/ specificity analysis, the reduction in GERD symptoms was best seen at >20 days/month and >6 hours/night.

**Conclusion:** The data suggest that the use of an oral appliance decreases GERD symptoms in patient with OSAS. This finding suggests that like CPAP, the OA improves GERD symptoms. The two dental practices continue their efforts to enroll the bruxism control group.

**PATIENT VARIABLES ASSOCIATED WITH POSITIONING OF THE INTERNAL JUGULAR VEIN***Olivia Gilbert, M.D., Associate Member, Georgetown University*

**Background:** The current study focused on patient variables - age, gender, height, weight, and number of previous access procedures - associated with varying locations of the internal jugular vein. Previous studies associating risk between the internal jugular vein and patient variables identified severe obesity, male gender, and age greater than 77 years as risk factors for complications. Implicit in such risk is more medial location of the internal jugular vein to the internal carotid artery. Accordingly, it was hypothesized that the internal jugular vein would be more medially located in male, heavier, older, and taller patients, while there would be little relationship between venous position and repeated numbers of procedures.

**Purpose:** By further defining anatomical sites and examining the relationship that exists between vein location and patient variables, this study sought to further clarify central venous access.

**Methods:** The location of the internal jugular vein was defined by nine points within the anatomical triangle between the two heads of the sternocleidomastoid muscle and the clavicle, consisting of three levels with three different positions, comprising a total of nine points. The levels were defined as shallow, medium, and deep. Within each level, three positions were identified as medial, middle, and lateral. Numbers one through nine were used to identify the nine different locations. For the 148 patients included in the study, internal jugular venous positions recorded by a single provider were retrieved from information cards kept for each patient receiving multiple cardiac biopsies within Sentara Norfolk General Hospital's cardiac catheterization laboratory. At the same time, demographic data was collected from patient charts.

**Results:** The most frequent positions were superficial and lateral. Based on these findings, a series of logistic regressions compared the superficial positions (one through three) with the deep positions (four through nine) in terms of age at procedure, gender, height, weight, and total number of procedures. Position was not significantly predicted by age at procedure, gender, height, or weight. However, patients who had undergone more procedures were significantly more likely to have a deep position with the odds of deep position being 1.8 times greater for every 10 procedures. Thus, results were opposite of the hypothesis.

**Conclusions:** This study made several achievements. First, it identified a relationship between deeper positioning of the internal jugular vein and repeated access attempts. Additionally, it identified the superficial and lateral locations as the most common points of access. This information may help guide physicians with patients who have undergone multiple cardiac biopsies, such as transplant patients, to attempt deeper rather than more superficial positions when attempting to gain access to the internal jugular vein as well as to provide a reference for the most common sites of access.

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## RECAPITULATING PANCREAS DEVELOPMENT IN EMBRYONIC STEM CELLS WITH CONTROLLED EXPRESSION OF PTF1A

*Robert Vincent, M.D., Associate Member, Virginia Commonwealth University/Medical College of Virginia*

**Introduction:** Embryonic stem cells (ESCs) are capable of limited differentiation into pancreatic progenitor cells and insulin-producing cells *in vitro*. However, beta-cell differentiation from ESCs occurs primarily in isolated populations without the occurrence of key morphogenetic developmental events. Recently, several studies have demonstrated that the pancreas specific transcription factor 1a (Ptf1a) is expressed in the early pancreatic bud in progenitor cells that give rise to all functional lineages of the pancreas and is essential for normal pancreas growth. Based on these findings, we explored whether regulated over-expression of Ptf1a in murine ESC differentiation cultures could impact the ability of ESCs to differentiate into endocrine and exocrine pancreas tissues as a model of development and tissue source for pancreatic research.

**Methods:** Through the modification of the Ainv15 murine ESC line, which contains a tetracycline transactivator and response element, we generated an ESC line capable of Ptf1a induction (TetPtf1a) upon exposure to doxycycline (Dox). TetPtf1a and control Ainv15 ESCs were differentiated into embryoid bodies (EBs) for 7 days followed by 28 additional days of differentiation on adherent substrate in medium containing 1% serum replacement (SR) allowing outgrowth of differentiated cells. Ptf1a transgene expression was then achieved through 1ug/ml Dox treatment. The differentiation status of the cells was assessed by quantitative RT-PCR, light microscopy and immunofluorescent staining.

**Results:** Upon induction of TetPtf1a ESCs, Ptf1a transcript levels increased 124 fold over uninduced control samples and protein expression was detected in 97% of cultured cells, compared to 0.5% of uninduced cells. Of the timed expression conditions tested, induced Ptf1a expression during a specific three-day window from day 11-14 resulted in the greatest increase in pancreas critical Pdx1 transcript levels and produced prominent PDX1+ buds. By 7 days after Ptf1a induction, the essential endocrine gene Ngn3 was expressed within the PDX1+ buds, but not in uninduced control cells. Endocrine cells subsequently emerged and migrated from the PDX1+ epithelium and formed islet-like clusters containing islet hormone+ cells. These neopancreatic buds also showed evidence of progressive branching into amylase+ pancreatic acinar-like tissue over time. Both the exocrine and endocrine cell number data were supported by hormone transcript levels. Furthermore, as the exocrine tissue matures with no outlet, the tissue expands and forms strings of exocrine lakes reminiscent of pancreatitis pathology.

**Conclusions:** These experiments describe the first differentiation of ESCs through morphological and cellular differentiation events characteristic of stereotypical pancreatic developmental stages. At this stage of the research the ESC-derived insulin+ cells appear to show incomplete functional maturation but the exocrine tissue demonstrates all normal structures except a complete outflow tract. These *in vitro* tissues represent a new potential model for pancreatitis and pancreatic cancer research.

## PROGNOSTICATION: CAN PALLIATIVE PERFORMANCE SCALE HELP?

*Neti N. Vora, M.D., Associate Member, Eastern Virginia Medical School*

**Background:** Prognostication, or prediction of life expectancy, is a challenge to most physicians. Not only do they avoid prognosticating but often are not accurate when doing so. The Palliative Performance Scale (PPS) is one tool available and validated to help physicians prognosticate. PPS is used by most hospice agencies when evaluating patients. Although several studies have examined PPS as a prognosticating tool, these studies have shown varying results and have failed to explain the predictive accuracy of PPS.

**Study:** Our retrospective study was focused on answering two questions 1) Does PPS accurately estimate survival of patients with end stage disease? and 2) Is there any difference in accuracy of PPS in prognostication when used for patients with cancer versus non-cancer diagnoses. We reviewed 115 patients' charts (74 Cancer and 41 Non-Cancer). Their PPS scores at admission, 3 months and 6 months were recorded. Patients with PPS of 60 or less were included. We compared the actual survival of these patients (avg. 80.96 days) to that predicted by PPS score. The data was further analyzed to compare accuracy of estimation of survival amongst patients with cancer and non-cancer diagnoses.

**Results:** The Cox Regression Model was applied to analyze survival time as a function of PPS scores. For our second question (comparing the estimation of survival amongst patients with cancer and non-cancer diagnoses), the variables of cancer and non-cancer were applied to the same model. Our study showed that PPS score at admission to hospice is a good independent predictor of survival time. We found that with every point increase in PPS score there is 5% decrease in hazard ratio ( $p < 0.001$ ). We also found that PPS performs differently in patients with cancer and non-cancer diagnoses. PPS provides some predictive value for patients without cancer but it is not a significant predictor of survival time for patients with cancer.

**Conclusion:** Our study indicates that PPS score at the time of admission is an independent predictor of survival irrespective of the type of diagnosis (i.e. cancer versus non-cancer) and those patients with higher PPS scores had longer survival time. These results reinforce the importance of PPS scoring in patients with end-stage disease. It also confirms that PPS is one of

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the more accurate tools available for prognostication. PPS provides physicians and health care professionals a useful tool when faced with the difficult question of prognostication. PPS may be used to identify patients who may benefit from hospice referral or who may benefit from additional hospice and palliative care services.

### ATORVASTATIN PREVENTS IL-1 SIGNALING AND ASSOCIATED SYSTOLIC DYSFUNCTION IN A MODEL OF SEPTIC CARDIOMYOPATHY INDEPENDENT OF IL-6 LEVELS

*Roshanak Robati, M.D., Associate Member, Virginia Commonwealth University/Medical College of Virginia*

**Purpose:** Sepsis is characterized by multiorgan dysfunction and high mortality. Left ventricular (LV) systolic dysfunction during sepsis (septic cardiomyopathy) is a common clinical feature associated with poor prognosis. Exogenous interleukin-1 $\beta$ ; (IL-1 $\beta$ ;) reproduces dynamic changes in LV ejection fraction and stroke volume, as seen in septic cardiomyopathy. As atorvastatin (ATV) is associated with more favorable outcome in septic patients, the current study evaluated whether ATV prevents IL-1 $\beta$ ; induced LV systolic dysfunction in a mouse model of septic cardiomyopathy and whether this effect was mediated through NF-kappa B pathway.

**Methods:** ICR mice were treated with intraperitoneal IL-1 $\beta$ ; 3mcg/Kg, and LV systolic function was assessed by transthoracic echocardiography at baseline and 4 hours after IL-1 $\beta$ ; challenge, measuring LV ejection fraction (EF) and stroke volume (SV). ATV was injected intraperitoneally 1 hour prior to IL-1 $\beta$ ; challenge. The mice were prospectively divided in 5 groups (N=6 per group): no pretreatment, ATV 0.02 mg/kg, ATV 0.2 mg/kg, ATV 2mg/kg, and ATV 20 mg/kg. Then the group treated with ATV 20mg/kg was sacrificed at 4 hours to obtain blood IL-6 levels.

**Results:** IL-1 $\beta$ ; significantly reduced LVEF and LVSV ( $P<0.001$  for all variables). Pretreatment with ATV lead to a significantly smaller reduction in LVFS, LVEF and LVSV (see Figure). The greatest effect was noted for ATV 20 mg/Kg, which fully prevented IL-1 induced systolic dysfunction. Although there was variation in the dose response, there seemed to be a linear correlation. The IL-6 levels were not significantly reduced in the mice pretreated with ATV 20mg/kg.

**Conclusions:** Atorvastatin prevents LV systolic dysfunction in murine model of septic cardiomyopathy. In this in vivo model, ATV prevents IL-1 signaling and the associated systolic dysfunction independent of IL-6 levels. Considering the safety profile of atorvastatin and the retrospective clinical data suggesting a clinical benefit of statins in septic patients, randomized clinical trials should be conducted.

### SHARPS INJURY AMONG ZAMBIAN HEALTHCARE WORKERS: URGENT NEED FOR PREVENTION

*Matthew J. Chung, Medical Student, University of Virginia*

Protecting healthcare workers (HCWs) in developing countries from exposure to bloodborne pathogens (BBP) is an issue that has largely been overlooked, partly due to the paucity of data. Zambian HCWs are at high risk for BBP exposure due to a population prevalence of 17 % for HIV, 30% for hepatitis B and 10% for hepatitis C. Our study sought to determine the frequency and mechanism of exposure of Zambian HCWs to blood and bodily fluids.

We conducted a retrospective survey of Zambian HCWs' sharps injuries and blood exposures to rapidly assess their BBP exposure risk, identify high-risk events and prioritize interventions. HCWs at various hospitals and clinics in Zambia completed 442 surveys in several institutional settings including general medical, surgery, delivery and labor, emergency, laboratory, housekeeping and security.

Respondents had been employed in healthcare for an average of 11 years and had worked an average of 40 hours per week. Job categories included 55% nurses/midwives, 14% physicians, 14% housekeepers/laundry workers/ward assistants, 8% lab workers and 5% security workers. Of all respondents, 89% had received no hepatitis B vaccine, yet 87% stated that HIV post-exposure prophylaxis was available. The average sharps injury rate was 1.4 injuries per year, 10 times higher than the average rate for United States HCWs (0.14 injuries/yr). The lowest rates were among lab workers (0.2 injuries/yr) and physicians and security workers (0.9 injuries/yr). Higher rates were reported among nurses and midwives (1.7 injuries/yr) and housekeepers, laundry workers and ward assistants (2.6 injuries/yr).

Of all devices, syringes caused the most injuries (53%). The majority of the syringes were used for injections (44%), while 19% were used for blood drawing. The rest were used for flushing lines, mixing drugs or unknown use. Of 157 injuries from hollow-bore needles, 22% were high risk injuries from needles used to access veins or arteries.



Zambian HCWs are at exceptionally high risk of percutaneous injury combined with an alarmingly high likelihood of exposure to BBP. Blood drawing and cannulation are the highest risk procedures. The introduction of safety-engineered IV catheters as well as “direct-draw” vacuum tube phlebotomy equipment may significantly reduce the risk of injury. A task-analysis of all blood-drawing procedures is needed to determine the safest equipment configuration. There is an urgent need to provide hepatitis B vaccination to all Zambian HCWs as early as possible and to improve waste disposal systems for the protection of housekeeping and laundry personnel. With these combined efforts, we may see a decrease in the alarmingly high sharps injury rate among Zambian HCWs.

### CLINICAL CHARACTERISTICS AND RADIOLOGIC PATTERNS OF ACINETOBACTER PNEUMONIA AT A TERTIARY CARE REFERRAL CENTER

*Walter E. James, M.D., Associate Member, Virginia Commonwealth University/Medical College of Virginia*

**Introduction:** Acinetobacter pneumonia is associated with prolonged hospitalization and significantly increased morbidity and mortality. A review of the literature shows that there have been no previous studies reviewing the radiographic features of Acinetobacter pneumonia. Our study was designed to identify characteristic clinical presentations and radiographic features of Acinetobacter pneumonia with the aim of assisting in earlier diagnosis and treatment.

**Methods:** Retrospective chart review was used to identify patients who met inclusion criteria - patients >18 years old who were diagnosed and treated for Acinetobacter pneumonia over a one year period. Diagnosis was based on the presence of positive respiratory and blood cultures for Acinetobacter and the radiographic appearance of pneumonia. All included patients had documented treatment for Acinetobacter pneumonia. Patients were excluded if they had polymicrobial cultures. A thoracic radiologist reviewed the relevant radiographs of patients who met inclusion criteria.

**Results:** 27 patients met inclusion criteria for radiograph review. The average age was 53 years old. Fifty-one percent of the patients were male and 52% of the patients were black. All included patients had positive respiratory cultures, with 6 of those also having positive blood cultures. Twenty-four patients were intubated at the time of diagnosis. There were 11 different admission diagnoses, the most common being trauma (6) and sepsis (6). Three patients were immunosuppressed. Nineteen (70%) of the patients had right lung predominance, with 18 (66%) of those patients having right lower lobe pre-dominance; only 4 (15%) patients had left lung predominance, with 3 being in the left lower lobe. The most common radiographic appearances were unilateral infiltrates (16; 59%) and patchy, non-segmental infiltrates (16; 59%). Seventeen (63%) patients had pleural effusions. None of the reviewed radiographs were described as nodular.

**Conclusion:** From our retrospective data analysis, Acinetobacter is primarily a ventilator-associated pneumonia with no significant association with sex, race or admission diagnosis. The radiographic characteristics were overwhelmingly unilateral and notable for having right lower lobe predominance, patchy non-segmental pattern, and associated pleural effusions.

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**SAVE THE DATE!**  
*Monday, May 2, 2011*

THE FIFTH ANNUAL  
*Carey, Marshall, Thorner*  
SCHOLARS' DAY

**Beginning at 12:00 pm with  
Medical Grand Rounds**

*Afternoon events feature oral and poster presentations by  
Department of Medicine residents, fellows, and post-docs, followed by  
awards and a reception.*

Location:  
Jordan Hall Auditorium, UVA Health System  
Jefferson Park Avenue  
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*For more information contact Karen Ward: 434-924-5725*