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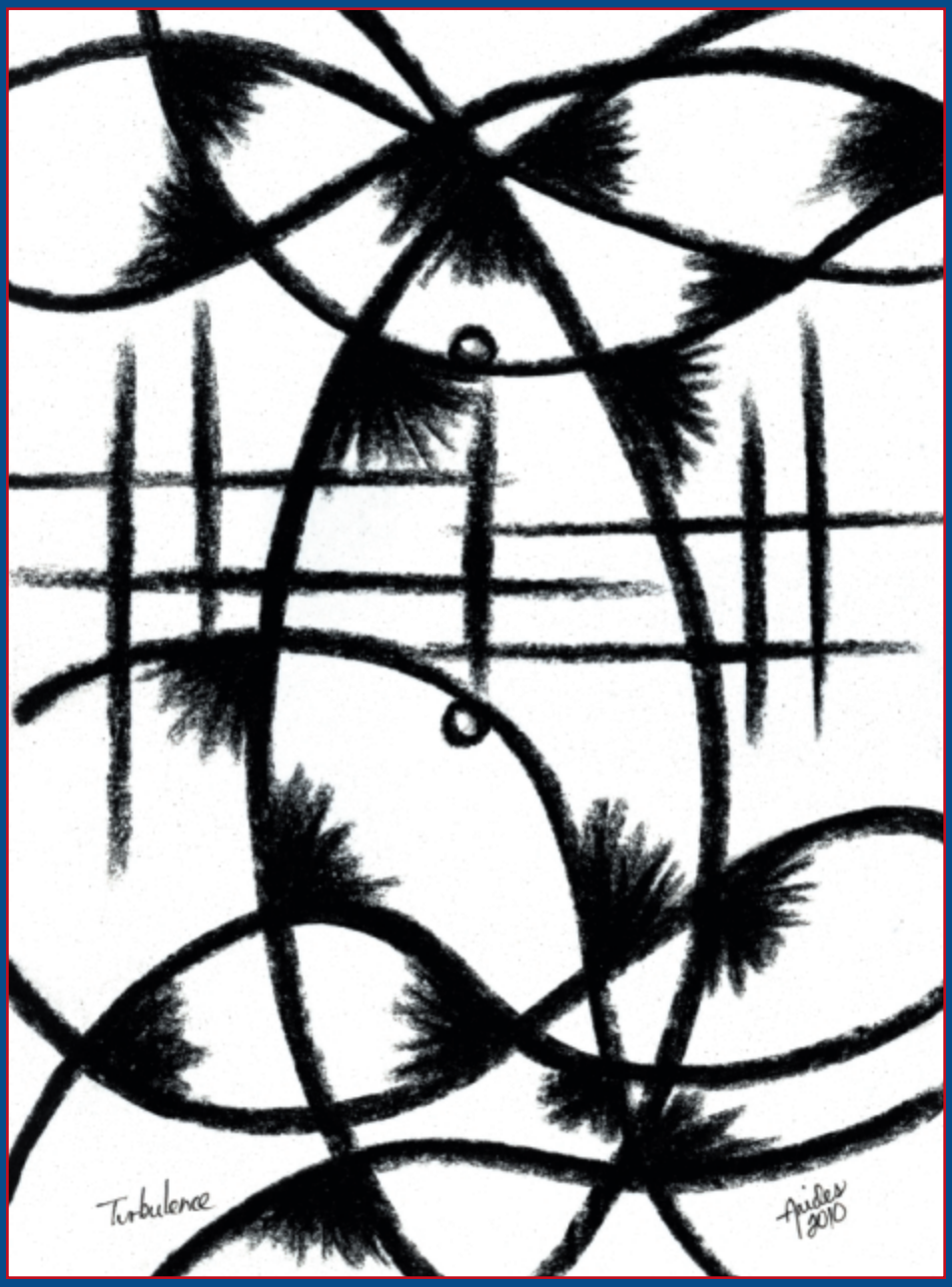

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Cover: "Turbulence," by Arides Pichardo, Originally from the Dominican Republic, the artist obtained a bachelor's degree in publicity, with a major in graphic design, from the Universidad Autonoma de Santo Domingo. In 2003 he immigrated to the United States. In Providence, he assisted in the creation of *Vision Moderna* Magazine and worked in the reconstruction of antique pictures. He has exhibited at Gail Cahalan Gallery, URI Feinstein Providence Campus, Gallery Z, and the Rhode Island Home Show. http://aridesfinearts.blogspot.com/.

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COMMENTARIES

CONTRIBUTIONS

COLUMNS

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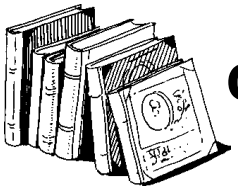

Commentaries

Continuing Medical Education (CME): Goals and Objectives

Many changes have occurred in the accreditation process for **continuing medical education** (**CME**) for doctors in the last 10 years, always under the guise of reform.

For one thing, drug companies are not allowed to pay speakers or their expenses directly. This change occurred about 10 years ago. The money must be laundered through the hospital. I recently discussed this with a colleague within the academic administration, who took offense at my use of "laundered." "That term is used for drug money and other illegal uses. Laundered money is made to look like it comes from another source. It's a pejorative term." I agreed. I used it purposely as a pejorative term. Under current guidelines, drug companies continue to pay the speaker and the speaker's expenses but must give the money to the hospital to give to the speaker. The money is given as an "unrestricted educational grant," but this unrestricted grant requires an application to the company, naming the speaker and the objectives, so that if the speaker or the objectives are not in keeping with the marketing goals of the company, the speaker is not funded. Although there is an "absolute fire wall" between the marketing and educational divisions of each company, companies seem less inclined to fund speakers who are not enamored of their drugs. When companies have been asked to give truly unrestricted educational grants, say to donate money to a general pool, the answer has been 100% negative in my department, although not so in some others. So what we have is a "restricted" educational grant, given as "unrestricted," using laundered money, with which the CME agencies are entirely complicit.

This is not to say that all companies behave badly. Some companies do, in fact, separate the marketing and educational parts of their companies. In Neurology, we have two or three corporate-funded talks per year, in which the majority are theoretically chosen from anywhere and in fact are chosen from lists approved by the corporation. The topics, however, are not, and the talks are not funded without review of the objectives.

The ACCME cannot guarantee quality. Its central mission is reducing bias. But it plays a role in quality assurance. One attempt to do this is by establishing standards for all talks. For example, all talks must list objectives before a talk is approved for CME credit. For my department this is an unnecessary requirement since all our speakers have been vetted in some way, either by virtue of their having academic appointments at well-known medical centers, because they are known in our community, or they have established reputations (especially for those sponsored by drug companies) and generally all three. They have been selected by the department.

I recently submitted a set of objectives for an unsponsored talk I was giving myself and was told that my objectives were not acceptable because I did not use language approved by the ACCME. I asked to review the documents that provided the language that was acceptable to the ACCME and was given the list of the acceptable descriptors. I was struck first by their length, a three-page document. I would have thought that two or three sentences would do. I was next struck by the apparently important distinction between "goals" and "objectives." Not having formal training in epistemology, I was unaware of the distinction. In case you aren't either, "Objectives should not be confused with goals, which are more general or global. Objectives are the action statements that operationalize a goal. For example, a goal for a CME activity may be "to help physicians provide the very best possible care to patients through improved communications." It turns out that objectives can only be met if they are introduced by particular verbs, 109 in number, for "communicating knowledge." There are 15 acceptable verbs for "imparting skills," four for "conveying attitudes," specifically excluding "appreciate", "understand" and "learn." For arcane reasons, "acquire, consider, exemplify and realize" are more "measurable as the direct outcome of a CME activity" than "appreciate, understand and learn." Thus I can have the audience "realize" the differences between A and B but I cannot plan to have them "learn" what the differences are.

Since I have been giving CME talks for a few decades I felt transformed from the person who had been speaking in prose his whole life without knowing it to the person who discovered that he really was supposed to have been speaking in poetry. My objectives were rejected for using unacceptable verbs. I had thought my talk would allow the audience to "understand" the differences between two problems, when I should have been planning to lead them to "realize" the differences. Perhaps by realizing the differences they would be more likely to remember these differences, since realization carries the implication of self discovery, that is, my talk would lead the listener to come to certain deductions, achieving an epiphany that would seem to be his own, rather than mine, and therefore more likely to stick in his memory.

I am reminded of a teaching rounds when I was a third-year student in internal medicine. We had a guest attending, an older distinguished doctor, who listened to a student case presentation and then proceeded to question us and discuss the case. At the end he said that when he was a student one of his professors had taught him that he should always learn at least one thing from every teaching session. He turned to a student and asked, "Can you tell me one thing you learned today?" The student was caught unawares. The discussion had been about a blood dyscrasia, and somewhere during the meandering discussion, probably having to do with lymph node enlargement, the professor had mentioned that in most people one foot was larger than the other, hypothesized, he thought, to be due to a venous asymmetry. So the student said that he learned that most people had one foot larger than the other. After his 90-minute discussion of blood dyscrasias the professor was temporarily speechless, but pulled himself together and replied, "Well, I guess that is one thing."

My first objective when I give a talk is keeping the audience awake. I rate my lectures by the number of people who stay awake. There are points deducted for myo-

clonic jerks from nodding heads. Imparting knowledge is my second objective, which I hope parallels the lack of nodding heads. I am unsure if "imparting knowledge" is an acceptable objective.

– Joseph H. Friedman, MD

Disclosure of Financial Interests

Joseph Friedman, MD, and spouse/significant other. Consultant: Acadia Pharmacy, Ovation, Transoral; Grant Research Support: Cephalon, Teva, Novartis, Boehringer-Ingelheim, Sepracor, Glaxo; Speakers' Bureau: Astra Zeneca, Teva, Novartis, Boehringer-Ingelheim, GlaxoAcadia, Sepracor, Glaxo Smith Kline, Neurogen, and EMD Serono.

Conflicts: In addition to the potential conflicts posed by my ties to industry that are listed, during the years 2001-2009 I was a paid consultant for: Eli Lilly, Bristol Myers Squibb, Janssen, Ovation, Pfizer, makers of each of the atypicals in use or being tested.

Superstition, Seizures and Science

When facing a terrible sickness, despairing therapies have always been society's response to the plea, "Do something!" But if you don't know your destination, the likelihood of getting there becomes remote. Similarly, if the underlying mechanism of a disease such as epilepsy remains elusive, the chance of finding an effective therapy becomes equally remote.

The history of the search for a meaningful therapy for those burdened by repeated convulsions has been a painful voyage through strange territories, a tale of failed interventions, desperate treatments and irrational measures. Indeed, most of those treatments resembled more the art of the fugue than exercises in intelligent reasoning.

Despite the secular teachings of Hippocrates, the dominant thinking in the Classical Era had been that epilepsy resulted from supernatural, evil forces. Indeed, its very name, epilepsy, is a Greek word defining the condition of being seized, captured or overcome, with the implication that the grasping was undertaken by a nameless, outside entity.

Effective therapy could only be achieved, then, by resorting to interventions that could overcome those unworldly, shadowy forces, forces that inevitably must have been evil. Thus appeals were made to such personages as St. Ignatius, who had driven the devils from many epileptic victims, St. Valentine (whose priory in Alsace was the goal of many pilgrimages undertaken by victims of epilepsy) and, of course, St. Vitus, whose very name defined a class of abnormal movement disorders in helpless humans. In general, people believed that evil could be vanquished solely by spiritual rather than material talent; therefore therapy, rendered with contriteness and humility, must be confined to prayer, instruction and fasting.

Alternatively, there were those, particularly in primitive cultures, who believed that the roots of epilepsy lay in the victim's head rather than in his spirit. Some early treatments were directed therefore to the victim's head, through cauterization of the scalp and even by boring holes (trephining) in the living skull. Indeed, many a prehistoric skull shows evidence of trephination.

If, on the other hand, epilepsy was caused by some ill-defined poison, a toxin perhaps, then efforts would be directed toward a search for some counteractive chemical. During the Middle Ages - and beyond the customary measures employed for the care of epileptics such as blood-letting, purging and the use of emetic agents - four botanicals were routinely prescribed in the vain treatment for epilepsy: mistletoe, garlic, peony and elderberries. The Scottish anthropologist J. G. Frazer (1854 – 1941) stated that many healers affirmed the value of mistletoe because it clung so resolutely to the branches of sturdy oak trees, did not fall to the ground and hence should obviously be used in epilepsy, the falling sickness. (Medieval therapies were often identified by seeking analogies in nature.)

Other known substances to combat the unnamed toxins with the epileptic have included boar's gall, powdered human skull, dragon's blood and the intestinal stones of hawks.

And when all else failed, there was always fresh human blood as a treatment. The blood of slain gladiators in the Coliseum of ancient Rome was routinely fed to epileptic children. Hans Christian Anderson, in his memoirs, recalled witnessing state executions in Copenhagen with parents making their epileptic children drink the shed blood.

By 1850 epilepsy had been consigned to the category of those diseases which, in the words of one contemporary neurologist, were "cryptogenic, inscrutable, and alas, incurable." In 1857, Dr. Charles Locock, obstetrician to Queen Victoria, published a brief commentary describing a trial with bromides that seemed to have suppressed the seizures in a group of young, epileptic women. And thus, gradually from an arena of vast ignorance, did earnest investigators gradually improvise effective, rational treatments for a disease previously thought to be incurable.

In 1920, the German scientist Hans Berger (1873 – 1941) devised the electroencephalograph (EEG), which detected brain waves emanating from the living brain. These electrical waves were captured by electrodes placed on the scalp, conveyed the intracranial impulses by wires to the instrument and expressed as oscillating waves on strips of moving paper. By inspecting these EEG-generated squiggles one can arrive at an objective diagnosis of epilepsy since, by the 20th Century, epilepsy was finally recognized as the systemic manifestations of abnormally discharging, anarchic, nerve cells. In the words of one neurologist, "What is greater magic than for the brain to write its own confession of wrongdoing on a sheet of moving paper?"

Most patients with epilepsy today have their convulsions safely controlled by medications and can lead normal, productive lives unencumbered by social isolation, superstition, ignorant bias, dangerous medicines or societal fear.

– Stanley M. Aronson, MD

Stanley M. Aronson, MD is dean of medicine emeritus, Brown University.

Disclosure of Financial Interests

Stanley M. Aronson, MD, and spouse/significant other have no financial interests to disclose.

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Rhode Island Chapter, American College of Physicians 2010 Annual Meeting Abstracts

In May 2010, the Rhode Island Chapter, American College of Physicians, hosted its annual Associates' Forum Competition at the Crowne Plaza Hotel in Warwick. More than 110 residents in Rhode Island's teaching hospitals submitted entries. A committee of program directors chose the following six winners. These six podium presenters each received a plaque and a cash award from the College Chapter. The Chapter and program directors applaud this year's Associates—they represent the future of medicine in the United States.

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Outcome of Hepatitis C Patients Treated with Pegylated Interferon and Ribavirin at Roger Williams Medical Center

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Purpose: This study retrospectively evaluated the outcome of a diverse population of Hepatitis C patients treated with pegylated interferon and ribavirin and compared actual real-life results to published clinical trials.

Materials and Methods: The medical records of a total of sixty seven Hepatitis C patients, treated by pegylated interferon and ribavirin, were retrospectively reviewed regarding their outcomes following treatment. The outcome variables considered in our analysis were: sustained virologic response (SVR), breakthrough, relapse, and no response. The different outcomes were plotted against the following variables: patients' age, ethnicity, gender, Body Mass Index (BMI), hepatitis C genotype, Human Immunodeficiency Virus (HIV) status and stage. We also reviewed the treatment-related side effects and compliance to treatment. Results: SVR was achieved in forty one out of sixty seven patients (61.1%). The majority of the patients were in the fifth to sixth decade from whom nineteen out of twenty eight (67.8%) achieved SVR; three out of five patients (60%) were non-white; females had better SVR compared to males (75% versus 54.5%); seventeen out of thirty six patients (47.2%) had genotype 1, thirteen out of fourteen (92.8%) genotype 2, nine out of thirteen (69.2%) genotype 3, and two out of four (50%) genotype 4; one patient had S0 and achieved SVR, four out of twelve (33.3%)S1, eleven out of sixteen (68.7%) S2, eight out of thirteen (61.5%) S3, one out of seven (14.2%) S4 and sixteen out of eighteen (88.8%) had no biopsy. The patients who had no biopsy were mainly genotype 2 and 3; we did not notice a difference in the SVR according to the patients' BMI. Ten out of sixty seven patients (14.9%) had relapse, two out of sixty seven (2.9%) had breakthrough, nine out of sixty seven (13.4%) did not respond, and twelve out of sixty seven (17.9%) did not complete the treatment. All patients developed side effects during their treatment, mainly fatigue (77.6%), flu like illness (32.8%), depression (26.3%) and insomnia (23.8%). Three patients out of the sixty seven (4.4%) developed serious side effects (pancytopenia, myocardial infarction, and suicidal attempt). Conclusion: Patients who have genotype 2 had better SVR compared to patients who have genotype 1. These results match with the statistical results shown in published clinical trials. BMI has no effect on SVR. The majority of nonresponders had genotype 1.

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Effectiveness of Pulsed Electromagnetic Field Therapy on Reducing Proteinuria

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As a major global health concern, proteinuria has been established as an important independent risk factor for cardiovascular disease and renal parenchymal damage leading to end-stage kidney failure. We investigated the efficacy of pulsed electromagnetic field (PEMF) therapy in reducing urinary protein excretion over a 2 week period in subjects with overt nephropathy while continuing optimal mechanisms to reduce proteinuria by inhibition of the renin-angiotensin system (RAS) using supramaximal doses of angiotensin receptor blockading (ARB) agents. Electrotherapeutic technologies has been demonstrated to modulate the calcium calmodulin-dependent, cGMP induced nitric oxide signaling pathway which may con-

fer anti-proteinuric and anti-fibrotic properties by working at the cellular level promoting nitric oxide release, creating a cascade of events including blood vessel dilation, growth factor secretion, angiogenesis and ultimately tissue remodeling.

As a result of activated changes in nitric oxide and intracellular mechanisms following ARB agents, we investigated whether there was a further reduction in proteinuria in subjects on ARB agents when administered PEMF therapy.

Methods: Four well controlled hypertensive volunteers with chronic macroalbuminuria applied low frequency PEMF therapy three times a day for 14 consecutive days, while continuing previously prescribed antihypertensive and RAS inhibitor medications.

No changes were made to drug regimens during the 28-day observation. Proteinuria was expressed as the ratio of protein to creatinine, as determined on adequate twenty-four hour urine collections at baseline, 14 and 28 days after initiation of therapy. Office blood pressure measurements along with serum creatinine, potassium and urea nitrogen concentrations collected at one central location were monitored at 7 day intervals from baseline to study endpoint. The glomerular filtration rate was estimated by means of the Modified Diet of Renal Disease (MDRD) formula. Collected data was analyzed with the use of paired Student's t-test.

Results: After 14 days of PEMF therapy, all participants demonstrated an arithmetic but not statistically significant decrease in urinary protein excretion. Mean urinary protein excretion was reduced by 36%, from 2.85 g of protein per gram of creatinine to 1.80 g of protein per gram of creatinine during the 2 week intervention period PEMF therapy was applied (p = 0.06). Proteinuria gradually increased again over time after discontinuation of PEMF therapy on day 15, resulting in a level of proteinuria that did not differ significantly from that at baseline. There were no significant changes in mean arterial pressures and serum creatinine concentrations during the 28 day observation. No adverse events were reported.

Conclusion: In this primary analysis, our observations demonstrate that additional and synergistic reductions in proteinuria were achieved with PEMF application in patients already receiving optimal pharmacological management to reduce proteinuria by RAS inhibition. Several limitations need to be taken into account such as small sample size and lack of long term follow-up. A larger study is currently in progress evaluating for persistent reductions in proteinuria, as well as the potential effect on possible preservation of renal function.

While the emphasis of our laboratory as well as other researchers have focused on reducing proteinuria through pharmacological means, the advent of electromagnetic fields may confer a new modality which may act synergistically with RAS antagonists to maximally reduce urinary protein excretion in patients already receiving optimal drug therapy and with limited treatment options.

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High Prevalence of Bone Demineralization and Vitamin D Insufficiency in a Cohort of HIV-infected Postmenopausal Women

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In the era of HAART, HIV-infected women will live longer and experience changes related to menopause. Osteopenia is prevalent in persons with HIV and is part of a normal sequence of aging in women. However, there are very little data on bone metabolism in HIV-infected postmenopausal women.

HIV-infected women age > 45 were referred to the HIV Menopause Clinic at the Miriam Hospital (Providence, RI). A woman was considered postmenopausal if she was status-post bilateral salpingo-oophorectomy with or without hysterectomy, or if she had no menses for more than 1 year with elevated FSH and/or LH. Bone mineral density (BMD) was assessed by dual-energy X-ray absorptimetry (DEXA) in the lumbar spine and hip. We then calculated 10-year fracture risk for postmenopausal women with osteopenia using the FRAX tool, which was developed by WHO based on models that integrate the risks associated with clinical risk factors and BMD at the femoral neck.

Thirty-five postmenopausal women were included. Median age was 52 years (range 38-72); 40% Caucasian, 34% African-American, 26% Latino. Median weight was 151 lb (range 99-261). Median follow-up since HIV diagnosis was 14 years. Median CD4 count was 373 cells/L (range 72-1260). 86% were on NRTI-based HAART: 40% with TDF, 28% with NNRTI, and 43% with PI. 63% of subjects had plasma viral loads (PVL) <75 copies/mL. 40% were current tobacco-smokers. 14% were on methadone maintenance. 17% had history of alcohol abuse. 40% self-reported their physical activity being inadequate. 54% did not consume sufficient amount of calcium. Mean serum level of calcium was 9.3 mg/dL and 25-OH Vitamin D was 25.8 ng/ml. 54% were vitamin D deficient (25-OH vitamin D level < 30 ng/mL). Based on WHO criteria, 18% were diagnosed with osteoporosis (t-score <-2.5 SD below normal) and 59% were osteopenic (t-score -1.0 to -2.5 SD below normal). Using FRAX, we found the average 10-year risk for major osteoporotic fracture was 7% and that for hip fracture was 1% for women with osteopenia. No patients in this cohort had a fracture since being infected with HIV.

This cohort-based cross-sectional survey of relatively young HIV-infected postmenopausal women showed a high prevalence of osteoporosis as well as Vitamin D deficiency. As this population ages, the clinical consequences (e.g. fractures) of bone demineralization and Vitamin D deficiency will become apparent. Studies are needed to investigate potential mechanisms and treatment options.

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Medical Residents Behind Bars: A Unique Clinical Experience and Linkage Project

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Prisoners have a high burden of chronic medical conditions. While incarcerated, prisoners are entitled to medical care, but often experience a discontinuity of primary medical services upon release. This leads to poor health outcomes, including an increased risk of death.

Background: In July 2008 a partnership was formed between the medical division of the Rhode Island Department of Corrections (RIDOC) and the Internal Medicine residency program of the Alpert School of Medicine of Brown University with the intention of exposing residents to correctional health, and promoting medical continuity for adult prisoners upon release into the community. In the men's division of the Adult Correctional Institute (ACI), clinic sessions were developed to target inmates with chronic medical problems who were at risk of discontinuity of care upon release. Residents were precepted by RIDOC Board Certified internists at clinics sessions one half day a week and provided medical services to soon-to-be-released inmates. Those without identified plans for community medical follow up were seen by a social worker and referred to the medical residents' clinics at Rhode Island Hospital (RIH) and The Miriam Hospital (TMH) upon release.

Methods: We conducted a review of all inmates seen at the medical residents' clinic sessions held at the minimum security prison during Jan 1-Dec. 31, 2009. Baseline data were self-reported at initial pre-release visits. Patients were then searched against the data repository of RIH / TMH to identify clinical encounters occurring during the period following release. The RIDOC database was also searched for any activity of re-incarceration during the patients' post-release period. Descriptive statistics were generated for demographic and clinical data.

Results: A total of 146 patients were seen over the period. The mean age was 44 years. The most prevalent conditions were hepatitis C (21.2%), injection drug use (19.9%), depression (14.4%) and hypertension (13.0%). Patients were seen at a mean of 35 days prior to release from prison; 76% were referred to residents' medical clinic. A search of the RIH / TMH / RIDOC databases during the post-release period found 29 (19.9%) patients had outpatient medical encounters at a mean of 38 days after release, 26 (18%) had Emergency Department (ED) encounters at 69.5 days, and 41 (26%) had re-encounters with the ACI at 87 days.

Conclusions: Early data suggest our patients are less likely to encounter the ED within 60 days of release than in the general population of released prisoners. Our project represents a novel collaboration incorporating correctional health with medical residents' ambulatory experience and may serve as model of transitional care for adults released from prison. Further studies are needed to better understand the impact of this program on the health outcomes and resource utilization of its patients.

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Characteristics of Adults Hospitalized with Novel 2009 influenza A (H1N1) in a Community Hospital

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Background: Results from studies of the novel 2009 H1N1 influenza early on during the pandemic suggest that the majority of symptomatic patients are young, and clinical disease is mostly mild. Data on patients hospitalized with H1N1 disease in community hospitals are scarce.

Objective: To describe the epidemiological and clinical characteristics of adult patients hospitalized with pandemic influenza A (H1N1) during the peak of the pandemic in a community hospital.

Methods: Review of medical records from adults admitted with laboratory-confirmed novel 2009 influenza A (H1N1) between October 31 and December 9, 2009 at Memorial Hospital of Rhode Island – a teaching community hospital.

Results: A total of 23 (70%) of the laboratory-confirmed adult patients admitted with pandemic influenza H1N1 during this time period consented to study enrollment. Among these, 74% were women, and 26% were men. The median age was 54 (range 22 – 81), and the mean Charlson comorbidity index was 3.7. The majority (91%) of these patients had underlying chronic lung disease, and 57% of the patients were obese (BMI = 30). The diagnosis of novel H1N1 influenza was confirmed by a positive RT-PCR in all cases. The sensitivity of our rapid nucleoprotein antigen test for detecting pandemic H1N1 influenza was only 32%. The median duration of clinical symptoms was 9 days (range 3-22 days), and the median length of hospital stay was 7 days (range 2-19 days). Patients whose symptoms lasted = 10 days were more likely to have a prolonged hospitalization (P = 0.02), and tended to be = age 65 (P = 0.07). Radiological pulmonary infiltrates were present in 61% of the patients. These patients were more likely to have multiple underlying comorbidities (Charlson index = 5, P = 0.06) and hospital stays = 7 days (P = 0.02). The median duration between onset of clinical symptoms and laboratory confirmation of pandemic H1N1 influenza was 6 days (range 2-20 days).

Conclusion: Our preliminary findings suggest that during the peak of the 2009 pandemic, novel H1N1 influenza was associated with significant morbidity in the hospitalized elderly and adult patients with underlying comorbid illnesses. Interestingly, in some hospitalized patients, nasopharyngeal viral samples were positive for influenza by RT-PCR for 6 or more days from clinical onset. Further research addressing risk factors associated with prolonged H1N1 viral shedding would have important infection control implications.

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Oseltamivir Resistant 2009-2010 Pandemic Influenza A (H1N1) in an Immunocompromised Patient

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Although neuraminidase inhibitors are active against most 2009-2010 pandemic influenza A (H1N1) swine-origin strains, since April of 2009, 54 total cases of oseltamivir-resistant H1N1 swine-origin have been reported in the US (as of February 1st, 2010). We report a patient with an underlying hematologic malignancy who was hospitalized with influenza A (H1N1) swine-origin and whose strain developed oseltamivir resistance during therapy.

Case Report: A 26 year-old woman with ALL was admitted to our hospital on November 18, 2009 for re-induction chemotherapy. On admission, her absolute neutrophil count (ANC) was 800 cells/μL. On hospital day 3, she developed a non-productive cough and had a temperature of 102.6 °F with an ANC of 300 cells/μL. She was started on antibiotics and oseltamivir 75mg twice daily. A nasopharngyeal swab sent for a respiratory viral panel revealing probable influenza A (H1N1) swine-origin and rhinovirus. She continued to have fever so antifungal coverage was added, antibiotics were changed, and oseltamivir was continued. Fevers persisted, and bronchoscopy was performed. Viral culture derived from the bronchoscopy specimen grew influenza A (H1N1) swine-origin. The patient continued to have daily fever in the setting of prolonged neutropenia. On hospital day 17, a nasopharyngeal swab again revealed H1N1, as well as rhinovirus, despite 13 days of oseltamivir, and the concern for resistance was raised. Antiviral coverage was changed to zanamivir, and a nasopharyngeal swab culture was sent for resistance testing. A nasopharyngeal swab was used for respiratory viral panel testing on day 20 which was negative. On day 23, viral cultures from a nasopharyngeal swab done on day 17 returned positive for oseltamivir-resistant influenza A with the H275Y mutation. Despite aggressive therapy, she died on hospital day 40. After her death, we performed resistance testing on a stored sample of the initial influenza strain isolated on hospital day 3; it was sensitive to oseltamivir. Additional testing was also performed on the bronchoscopy specimen from hospital day 11, which demonstrated that resistance to oseltamivir had developed after eight days of oseltamivir therapy.

Discussion: To our knowledge, this is the first case of oseltamivir-resistant, swine-origin influenza A (H1N1) that was associated with death. In the United States, 42 of 54 individuals with resistance had documented exposure to oseltamivir, suggesting that resistance develops under selective pressure to the drug and not as a natural variant. We have shown that resistance developed during oseltamivir treatment in our patient who was receiving the recommended dosing of 75mg twice a day. Recent literature suggests that an increased dose of 150mg twice a day may be preferable for critically ill patients. Oseltamivir resistance should be a consideration when treating critically ill or immunocompromised patients.

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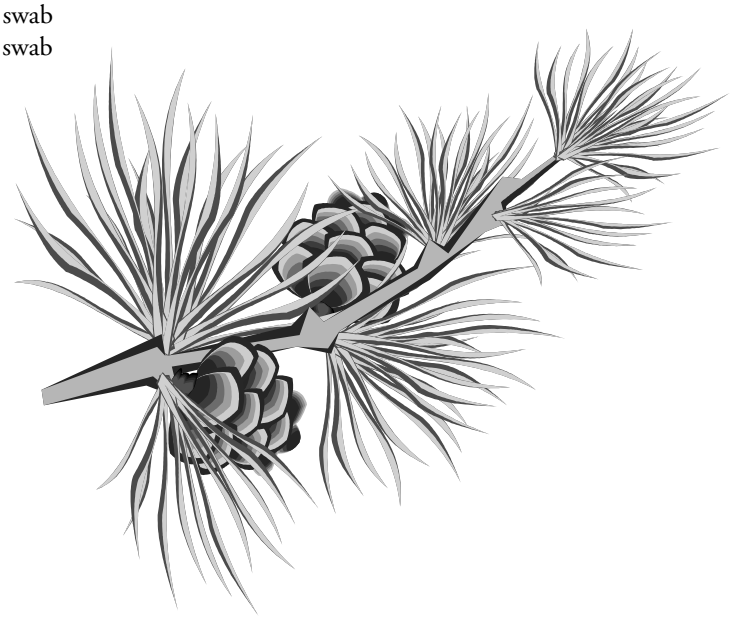


Teen Pregnancy In Rhode Island: Policies To Improve Outcomes

Susanna R. Magee, MD, MPH, Melissa Nothnagle, MD, MSc, Mary Beth Sutter, MD

The United States has one of the highest rates of teen pregnancy among industrialized countries, with more than 750,000 pregnancies each year among women less than 20 years of age.[1] Though teen pregnancy rates in the US had declined each year since 1991, the most recent national data show that rates of teen pregnancy, abortion, and birth are on the rise.[1] Rhode Island has 2,430 teen pregnancies per year, the highest prevalence among the New England states. In Rhode Island, 51% of these pregnancies result in live births and 35% in abortion.[2] Rates of teen pregnancy in Rhode Island vary by region: the highest rates from 2003-2007 were seen in Central Falls (95.5 births per 1,000 teens), followed by Woonsocket (65.2 births per 1,000 teens), Pawtucket (58.7 births per 1,000 teens), and Providence (48.0 births per 1,000 teens). [3]

Births to teens have long been associated with adverse outcomes, including individual and familial poverty and reduced educational attainment.[4,5,6] Children born to adolescent parents experience higher rates of behavioral and developmental disorders, substance abuse, depression, early sexual activity, and teen pregnancy.[7] Nationally, about 20% of births to teens are repeat births, which place additional socioeconomic and health pressures on teen parents.[8] In Rhode Island, the repeat birth rate in 2004 was 19% for women ages 15-19.[8]

Prevention of Teenage Pregnancy and Birth

Sexual education in schools

Comprehensive sexual education is an important tool to prevent teen pregnancy. From 1996 to 2009, federal funding of sexual education programs was available only for abstinence-only programs, which exclusively teach the benefits of abstaining from sexual activity.[9] Comprehensive sexual education programs promote abstinence but also provide information on contraception for pregnancy prevention and condoms for prevention of sexually transmitted infections. Well-designed studies of abstinence-only sexual education programs have found no significant impact on teen sexual activity or rates of unprotected sex.[9, 10] However, a population-based study of US sexual education programs found that teens who received comprehensive sex education were significantly less likely to become pregnant than those who received abstinence-only or no sex education.[11]

State law mandates that Rhode Island schools offer sexual education, including instruction on sexually transmitted infections and HIV, but requires abstinence to be emphasized and permits parental opt-out from participation.[12] From 2003-2007, Rhode Island received federal money to support abstinence-only education; the majority of this funding was distributed to community-based organizations. In 2008, Rhode Island declined Title V federal funding for abstinence-only-until-marriage programs. [13] Currently there is no standardized sexual education curriculum for Rhode Island schools and little teacher training or supervision.

Access to Contraception

Rhode Island is one of 27 states that require insurers to provide coverage of the full range of FDA approved contraceptive options.[14] However, approximately 62,670 reproductive-age, sexually-active Rhode Island women are in need of publicly-funded contraceptive services.[15] Among these, 19,660 (31.4%) are teens. A sexually active teen not using contraception has a 90% chance of pregnancy within one year.[16] In 2005, only 23% of Rhode Island teenagers in need received care from publically funded clinics.[17] In 2006, Rhode Island's family planning clinics received $3,778,000 from federal and state governments, or approximately $60 per woman in need of services.[18] These clinics are expected to deliver sexually transmitted infection screening and treatment, cervical cancer screening, education, contraceptive methods, and counseling to ensure consistent and correct use of contraception.

In addition to funding barriers, issues of consent may limit teens' access to contraceptive services in Rhode Island. While Connecticut allows confidential contraceptive access to married minors, and Massachusetts funds a statewide program to give all minors access to confidential contraceptive care, Rhode Island is one of only four states with no explicit policy on minors' authority to consent to contraceptive services.[19] As a result minors in Rhode Island are not assured confidentiality regarding contraceptive care and may have difficulty obtaining contraception if they are afraid to inform their parents of their sexual activity. Furthermore, Rhode Island lacks an emancipated minor law for parenting teens, so even those who already have children may need parental consent to obtain contraception to prevent repeat pregnancies.

Federal law requires access to confidential contraceptive services for all teens covered by Medicaid. While Rhode Island law does not prohibit physicians from providing contraceptives to minors without parental consent, there is no law protecting those who prescribe contraception to teens. Rhode Island's silence on this issue may discourage physicians from providing teens with confidential access to contraception. Programs such as California's comprehensive teen pregnancy prevention program which expand free confidential contraception and comprehensive sexual education for all teens are associated with reduced rates of teen sexual activity as well as substantially fewer births to teens.[20]

Another potential barrier to effective contraception for teens is lack of awareness among primary care providers about the safety of long-acting reversible contraceptive methods such as in-

trauterine contraception among teenagers. Historically, intrauterine devices were recommended only for monogamous women who had already given birth, but current evidence supports their safety and efficacy in nulliparous women.[21,22] Intrauterine devices and contraceptive implants are the most effective methods of reversible contraception available and should be discussed with all sexually active adolescents.

In addition, emergency contraception offers a chance to prevent pregnancy to women who have had unprotected intercourse or contraception failure or who have experienced sexual assault. Teens can use it correctly, and access to emergency contraception does not increase risky sexual behavior.[23]

Federal law recently made levonorgestrel-containing emergency contraception available to all women ages 17 and older without a prescription, as it has no contraindications or drug interactions, does not cause birth defects, and is nontoxic.[23]

Ten states including Massachusetts have laws allowing pharmacists to dispense emergency contraception without a prescription through collaborative-practice agreements.[24] These laws now apply specifically to minors under age 17, given the recent federal legislation. As mentioned above, Rhode Island lacks any such policy regarding contraceptive access for minors.

Access to abortion

In addition to accessible and effective contraception, access to abortion is essential in reducing unwanted births to teens. In 2005 in Rhode Island, 5,290 women obtained abortions including 1,620 teens; in the same year, 22 of every 1,000 teen pregnancies in Rhode Island ended in abortion, compared with 19 per 1,000 teen pregnancies nationally. [25,26]

Rhode Island law creates multiple barriers for teens seeking to end unwanted pregnancies. First, Rhode Island is one of 32 states that prohibit the use of public funds (including Medicaid) to pay for abortion, except in cases of rape, incest or life endangerment.[25] This restriction also applies to insurance policies for public employees in Rhode Island. The federal Hyde Amendment prohibits use of federal Medicaid funds for abortion, and allows states to determine whether state Medicaid funds will be used to pay for abortions for low income women.

Second, Rhode Island is one of 35 states that require parental consent or notification for abortion.[25] Parental consent laws have little effect on rates of abortion among minors; they do, however, result in delays (with increases in cost and associated risk) and increase the number of minors who travel to another state for abortions.[27-28] Massachusetts also requires parental consent for abortion, but allows an exception for medical emergencies, and Connecticut does not require parental consent for abortion.[29] The number of Rhode Island teens who travel out of state to avoid parental consent laws is not known.

Intrauterine devices and contraceptive implants are the most effective methods of reversible contraception available and should be discussed with all sexually active adolescents.

Recommendations

We recommend the following actions:

1.) *Provide comprehensive sexual health education in schools.*

Rhode Island schools should provide a comprehensive, age-appropriate sexual health curriculum, including information on contraception and sexually transmitted infection prevention for middle and high school students. Our Commissioner on Education, district superintendents, and leadership at the Department of Health must implement a system of teacher training and oversight in order for this to be effective.

2.) *Improve access to contraception for adolescents.*

Legislative barriers prevent many Rhode Island teens from accessing effective contraceptive services. Minors in Rhode Island should be guaranteed confidential access to contraceptive services through primary care providers and family planning clinics. Education for primary care providers should emphasize the safety and efficacy of long-acting reversible contraceptive methods, including intrauterine contraception, in teenage women. Given its safety and potential to reduce unplanned pregnancy when used in a timely manner, emergency contraception should be made available to women under 17 without a prescription, as it is currently in 10 other states including Massachusetts.

3.) *Improve minors' access to abortion.*

As parental consent requirements have little impact on abortion rates, but result in delays in care and increase the number of teens who travel to other states to get abortions, parental consent for abortion should not be required for minors. Use of state funds such as Medicaid to pay for abortions for low-income women should also be permitted.

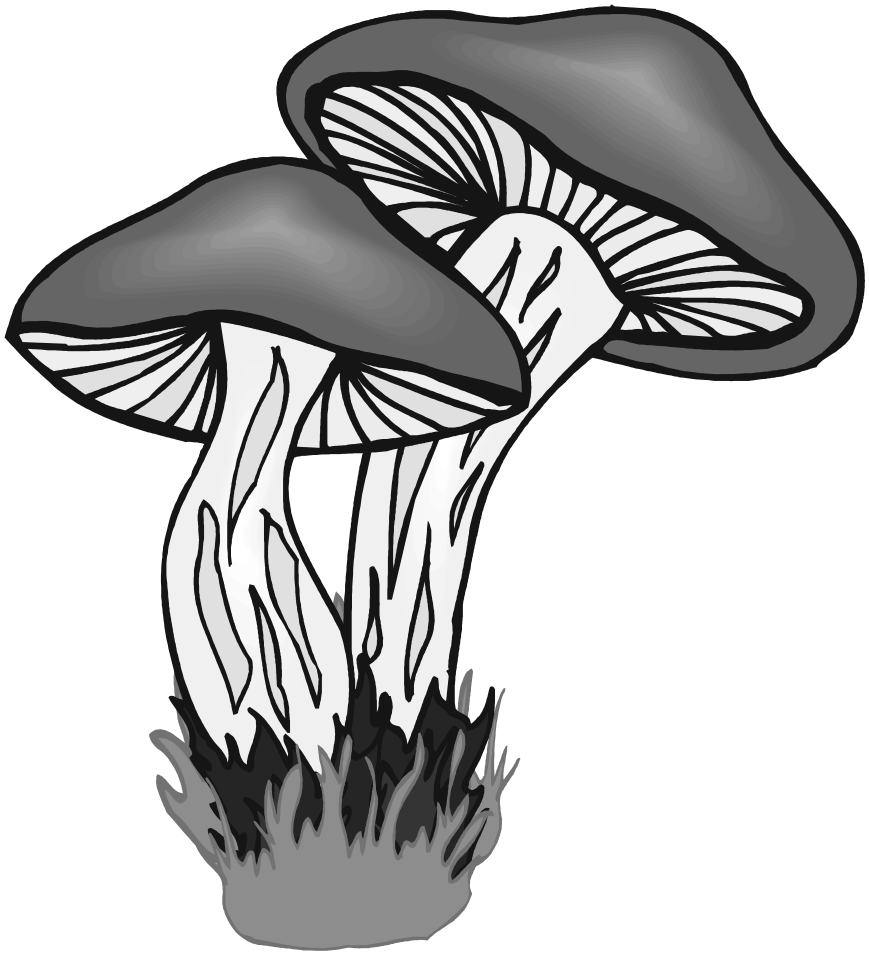
4.) *Provide educational opportunities to pregnant and parenting teens.*

Teens who become pregnant are less likely to graduate high school and more likely to live in poverty. Likewise, the children of these teen moms are more likely to grow up in homes where the income is significantly below the national poverty level. Pregnant teens should be encouraged to remain in school as long as possible and return to school after delivery as soon as possible. Day care programs based on site at schools have had success, yet in recent years these programs have been cut rather than expanded. [30] State funding should support programs that help teens complete their education.

Rhode Island's small size allows state-level initiatives to make great differences in the lives of its citizens. We must promote healthy teens; young people are the future of our state and their success or failure is in our hands.

References

1. Kost K, Henshaw S, Carlin L. *U.S. Teenage Pregnancies, Births and Abortions: National and State Trends and Trends by Race and Ethnicity.* 2010. http://www.guttmacher.org/pubs/USTPtrends.pdf
2. Guttmacher Institute. *Contraception Counts: Rhode Island*. 2006. http://www.guttmacher.org/pubs/state_data/states/rhode_island.pdf
3. Rhode Island KIDS COUNT. 2010 Rhode Island Kids Count Factbook: Births to teens. http://www.rikidscount.org/matriarch/documents/10_Factbook_Indicator_30.pdf
4. Hofferth SL, Moore KA. *Amer Sociolog Review* 1979;44:784-815.
5. Klepinger DH, Lundberg S, Plotnick RD. *Fam Plann Persp* 1995;27:23-8.
6. Moore KA, Myers DE, et al. *J Res Adolescence* 1993;3:393-422.
7. Klein JD. *Pediatrics* 2005; 116:281-6.
8. Schelar E, Franzetta K, Manlove J. *Repeat teen childbearing: Differences across states and by race and ethnicity.* 2007. Washington, DC: Child Trends. http://www.childtrends.org/Files//Child_Trends-2007_11_27_RB_RepeatCB.pdf
9. Santelli J, Ott MA, et al. *J Adolesc Health* 2006;38:72-81.
10. Trenholm C, Devaney B, et al. *J Policy Anal Manag* 2008;27:255-76.
11. Kohler PK, Manhart LE, Lafferty WE. *J Adolesc Health*. 2008;42:344-51.
12. Rhode Island General Law 16-22-18: Health and family life courses. http://www.rilin.state.ri.us/Statutes/TITLE16/16-22/16-22-18.HTM
13. Sexuality Information and Education Council of the United States. *A Portrait of Sexuality Education and Abstinence-Only-Until-Marriage Programs in the States*. http://www.siecus.org/index.cfm?fuseaction=Page.viewPage&pageId=487&parentID=478
14. Guttmacher Institute. *State Policies in Brief. Insurance Coverage of Contraceptives*. 2010. http://www.guttmacher.org/statecenter/spibs/spib_ICC.pdf
15. Frost JJ, Henshaw SK, Sonfield A. *Contraceptive Needs and Services: National and State Data, 2008 Update*. May 2010. http://www.guttmacher.org/pubs/win/contraceptive-needs-2008.pdf
16. Harlap S, Kost K, Forrest JD. *Preventing pregnancy, Protecting Health: A New Look at Birth Control Choices in the Unites States*. New York: Alan Guttmacher Institute; 1991.
17. Guttmacher Institute. *Contraception Counts Rhode Island*. 2006. http://www.guttmacher.org/pubs/state_data/states/rhode_island.pdf
18. Sonfield A, Alrich C, Gold RB. *Public Funding for Family Planning, Sterilization and Abortion Services, FY 1980-2006*. January 2008. http://www.guttmacher.org/pubs/2008/01/28/or38.pdf
19. Guttmacher Institute. State Policies in Brief. Minors' Access to Contraception Services. 2010. http://www.guttmacher.org/statecenter/spibs/spib_MACS.pdf
20. Brindis CD, Geierstanger SP, Faxio A. *Health Educ Behav* 2009;36:1095-108.
21. Prager S, Darney PD. *Contraception* 2007;75(6 Suppl):S12-5.
22. Allen RH, Goldberg AB, Grimes DA. *Am J Obstet Gynecol* 2009;201:456.e1-5.
23. Harper CC, Weiss DC, et al. *Contraception* 2008;77:230-3.
24. Guttmacher Institute. *State Policies in Brief: Emergency Contraception*. 2010. http://www.guttmacher.org/statecenter/spibs/spib_EC.pdf
25. Guttmacher Institute. *State Facts on Abortion: Rhode Island*. 2008. http://www.guttmacher.org/pubs/sfaa/pdf/rhode_island.pdf
26. Guttmacher Institute. *US Teenage Pregnancies, Births and Abortions: National and State Trends by Race and Ethnicity*. January 2010. http://www.guttmacher.org/pubs/USTPtrends.pdf
27. Colman S, Joyce T. *Perspect Sex Reprod Health* 2009;41:119-26.
28. Dennis A, Henshaw SK, et al. *The Impact of Laws Requiring Parental Involvement for Abortion: A Literature Review*. New York: Guttmacher Institute, 2009.
29. Guttmacher Institute. State policies in Brief: Parental Involvement in Minors' Abortions. 2010. http://www.guttmacher.org/statecenter/spibs/spib_PIMA.pdf
30. Sadler LS, Swartz MK, et al. *J Sch Health* 2007;77:121-30.



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Cardiac Manifestations of Lyme Disease

Thomas J. Earl, MD

Case 1

A 15-year old man with no significant medical history presented to the emergency department following two episodes of syncope. He was in his usual state of good health until earlier on the day of admission when he awoke with a severe headache, shortly followed by a syncopal episode with brief loss of consciousness. Later that same day, he experienced a second syncopal episode and subsequently sought medical attention.

On arrival to the emergency department, he was afebrile and hemodynamically stable. Physical examination was notable for irregular and bradycardic heart sounds without murmurs, rubs, or gallops. **Electrocardiogram (ECG)** (Figure 1) revealed complete heart block with a narrow QRS complex. Transthoracic echocardiogram showed normal biventricular size and function and mild mitral regurgitation. There was no pericardial effusion visualized. He was given intravenous ceftriaxone for presumed Lyme carditis and transferred to the Coronary Care Unit for monitoring and treatment.

Shortly after admission, telemetry monitoring revealed progressively lower heart rates requiring transcutaneous and eventual transvenous pacing. He was continued on ceftriaxone. Subsequent ECGs showed progression from complete heart block, to 2:1 **atrioventricular (AV)** block, and eventually sinus rhythm with first degree AV block. (Figure 2) Subsequent laboratory data revealed elevated Lyme IgM and IgG antibodies.

With improvement in his native conduction the transvenous pacing wire was removed. He was discharged home to complete a twenty-eight day course of ceftriaxone and remained well in follow-up.

Case 2

A 34-year old man with no significant medical history presented to the emergency department with pleuritic chest pain. Approximately five weeks prior to presentation he developed fevers, a "bull's-eye" type rash, and Bell's palsy. Serologic workup at an outside hospital was notable for elevated Lyme antibody titres. He was prescribed doxycycline but discontinued it after 3 days after experiencing nausea and vomiting.

On presentation to our institution, initial workup was notable for an ECG (Figure 3) showing diffuse, upsloping ST-segment elevations without reciprocal depressions along with subtle PR-segment depressions. Serial cardiac biomarkers were negative. Transthoracic echocardiogram revealed normal biventricular size and systolic function without a pericardial effusion.

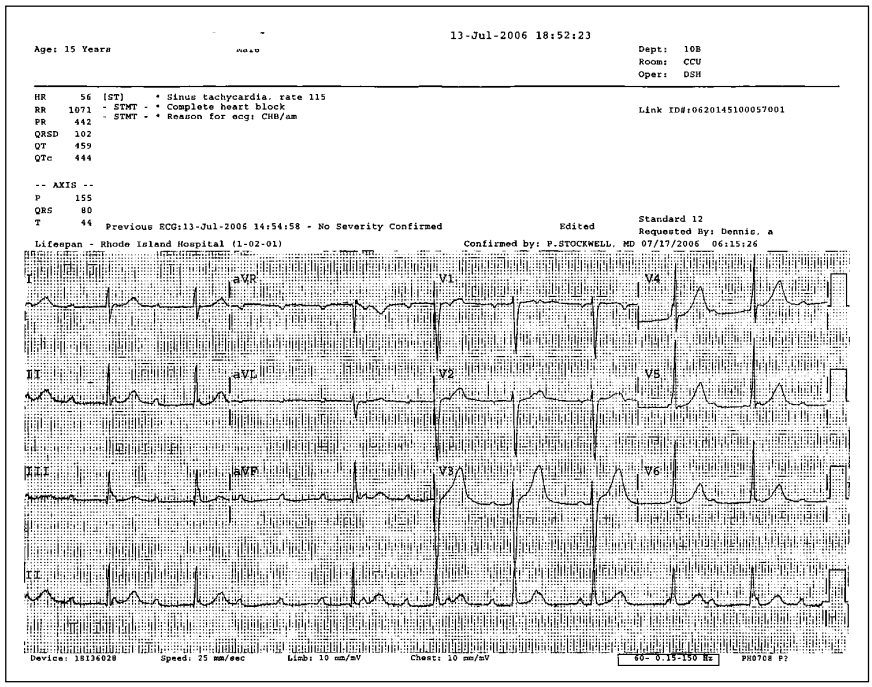

Figure 1. 12-lead ECG showing complete heart block with a narrow QRS complex.

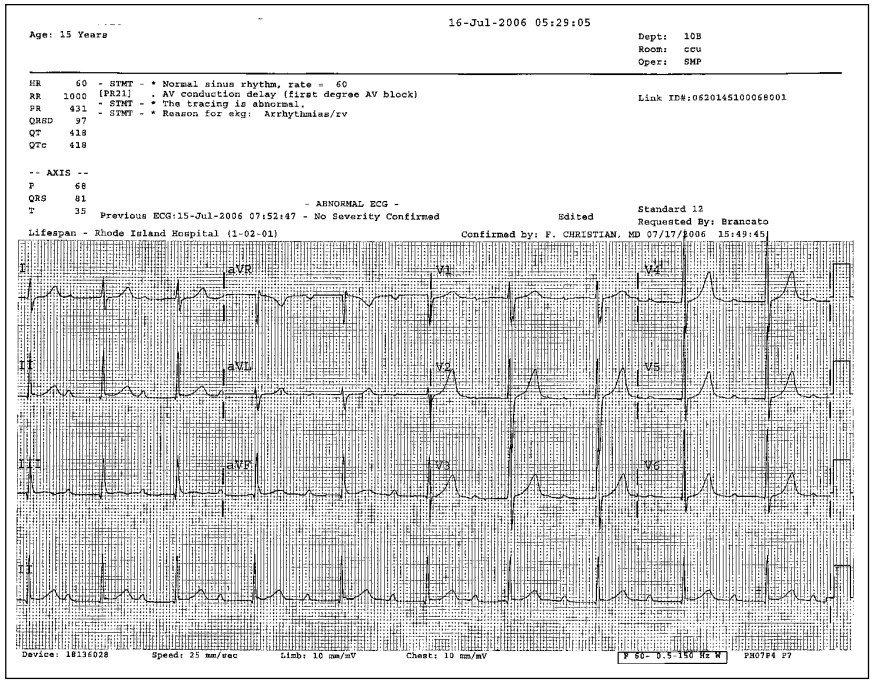

Figure 2. 12-lead ECG showing sinus rhythm with a first-degree AV block.

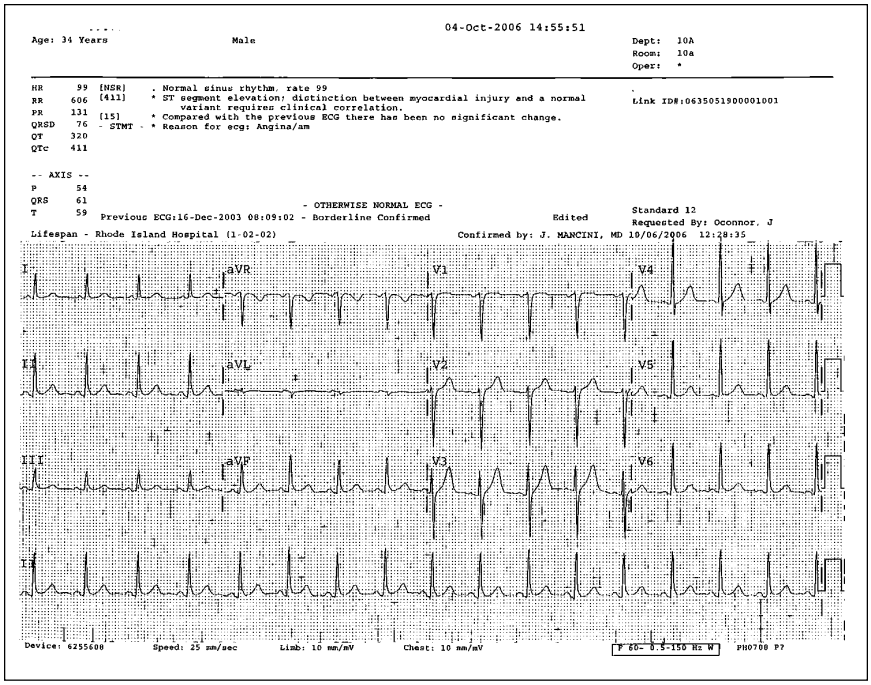

Figure 3. 12-lead ECG showing sinus rhythm with diffuse, upsloping ST-segment elevations as well PR-segment depressions in the inferior leads.

Given his clinical presentation and recent serologic data he was started on intravenous ceftriaxone for a diagnosis of Lyme pericarditis. Treatment was continued for a total of twenty-eight days. He was treated with NSAIDs and opiate analgesics with eventual relief of his pain. At the time of completion of antibiotic therapy he was without chest pain.

Discussion

Lyme disease, a tick-borne illness first described in Connecticut in 1977, is currently the most commonly reported vector-borne illness in the United States. In this country, Lyme disease is caused by the spirochete Borrelia burgdorferi, which is transmitted by the bite of Ixodes tick. According to the Centers for Disease Control and Prevention (CDC), the incidence of Lyme disease in Rhode Island in 2008 was 17.7 (confirmed cases per 100,000 persons), with peak reporting in the mid and late summer months.1,2 The majority of patients present with the classic rash of Lyme disease, erythema migrans, and/or arthritis, while a small minority experience cardiac manifestations of the disease.3

Cardiac manifestations of Lyme disease are typically seen in the early-disseminated phase (Stage 2) of the illness, with approximately 5% of untreated patients having cardiac involvement within the first few weeks after disease onset.4 Despite a slightly higher incidence of Lyme disease in females, there is a 3:1 male-to-female predominance of Lyme carditis. The spectrum of cardiac involvement in Lyme disease is highly variable, ranging from asymptomatic to severe manifestations. Notably, early recognition of infection and prompt administration of antibiotic therapy is thought to decrease the likelihood of cardiac involvement, although to my knowledge there are no randomized trials demonstrating a clinical benefit of antibiotics in terms of duration or severity of cardiac symptoms.5 Clinical manifestations of Lyme carditis include syncope or pre-syncope, palpitations, dyspnea, and/or chest pain. Cardiac abnormalities in Lyme disease most commonly include varying degrees of AV block and/or myopericarditis.

Steere et al reported twenty patients with cardiac manifestations of Lyme disease in 1980. Within this group, eighteen patients developed fluctuating degrees of AV block, with eight patients developing complete heart block. Interestingly, the degree of AV block was noted to fluctuate even over the course of minutes.6 Electrophysiology studies performed on select patients with Lyme carditis from van der Linde's series revealed diffuse conduction system involvement, with the majority of patients demonstrating prolonged A-H intervals suggestive of AV nodal involvement.7 There is typically no response to atropine in acquired AV block attributed to Lyme disease, suggesting direct involvement of the conduction system as opposed to increased vagal tone.

Fortunately, acquired AV block in Lyme carditis is typically transient and resolves with antibiotic therapy. This is demonstrated in Case 1 in which a rapid improvement in native conduction was observed. The need for temporary pacemaking is not uncommon, but persistent AV block necessitating permanent pacemaker placement is rare. In a retrospective study of 105 patients with documented Lyme carditis, 35% of patients required temporary pacing, while only five patients went on to receive a permanent pacemaker. Among these patients receiving a permanent pacemaker, four were noted to have resolution of their conduction system disease, while one remained pacer-dependent.7

Following conduction system disease, Lyme carditis most commonly manifests as myopericarditis. Steere et al described ECG abnormalities suggestive of myocardial involvement such as ST-segment depressions, T-wave inversions, and/or intraventricular conduction delays in thirteen of twenty patients. Of note, all of the observed abnormalities resolved over time. Furthermore, three patients were observed to have mild left ventricular (LV) systolic dysfunction by radionuclide imaging during the active phase of the disease; all had normalization of LV systolic function on repeat imaging when the disease was in remission.6 Several case reports and small cohort studies have additionally described patients with clinical and ECG evidence of pericarditis.8-11 Finally, Lyme disease has been purported to play a causative role in the development of a dilated cardiomyopathy and/or chronic congestive heart failure following small European studies showing higher rates of seropositivity in patients with an idiopathic dilated cardiomyopathy as compared to controls as well as the ability to grow B burgdorferi from endomyocardial biopsy specimens taken from a small cohort of patients with an idiopathic dilated cardiomyopathy.12,13 To date, similar findings have not been replicated in the United States.

The diagnosis of Lyme carditis is typically established through a combination of clinical presentation, serologic data, and non-invasive cardiac testing. A directed history should focus on potential tick exposures as well as current or antecedent erythema migrans. In Steere's cohort, eighteen of the twenty patients described erythema migrans at some point in the disease course, while fifteen had the classic skin manifestation at the time that cardiac involvement was recognized.6 Of note, cardiac disease as the sole manifestation of Lyme disease has also been reported.14 Suspicion of Lyme carditis is confirmed with serologic testing.

Guidelines from the Infectious Diseases Society of America suggest that patients with Lyme disease and AV block and/or myopericarditis be treated with either oral or parenteral antibiotics for fourteen days. For hospitalized patients, a parenteral antibiotic is the preferred initial choice. Preferred oral antibiotics include amoxicillin, doxycycline, or cefuroxime axetil, while ceftriaxone is the suggested parenteral antibiotic of choice.15

In summary, Lyme disease is an uncommon but readily reversible cause of a variety of cardiac complications, most notably AV block. The diagnosis of Lyme carditis requires a high index of suspicion, especially in the absence of the antecedent skin rash typically seen in Lyme disease. For clinicians practicing in an endemic area, the differential diagnosis of newly recognized AV block should include Lyme disease. As demonstrated by our two patients, cardiac manifestations of Lyme disease are typically reversible and patients recover completely without any long-term sequelae.

References

1. Reported Lyme disease cases by state, 1999-2008. Division of Vector-Borne Infectious Diseases. www.cdc.gov.
2. Reported Cases of Lyme Disease by Month of Illness Onset United States, 1992-2004. Division of Vector-Borne Infectious Diseases. www.cdc.gov.
3. Reported Clinical Findings Among Lyme Disease Patients, 1992-2004. Division of Vector-Borne Infectious Diseases. www.cdc.gov.
4. Steere AC. Lyme disease. *NEJM* 1989;321:586-96.
5. Sangha O, Phillips CB, et al. Lack of cardiac manifestations among patients with previously treated Lyme disease. *Ann Intern Med* 1998;128:346-53.
6. Steere AC, Batsford WP, et al. Lyme carditis. *Ann Intern Med* 1980;93:8-16.
7. van der Linde MR. Lyme carditis. *Scan J Infect Dis Suppl* 1991;77:81-4.
8. Horowitz HW, Belkin RN. Acute myopericarditis resulting from Lyme disease. *Am Heart J* 1995;130:176-8.
9. Lorcerie B, Boutron MC, et al. Pericardial manifestations of Lyme disease. *Ann Med Interne (Paris)* 1987;138:601-3.
10. Bruyn GA, De Koning J, et al. Lyme pericarditis leading to tamponade. *Br J Rheumatol* 1994;33:862-6.
11. Veyssier P, Davous N, Kaloustian E, et al. Cardiac involvement in Lyme disease. 2 cases. *Rev Med Interne* 1987;8:357-60.
12. Stanek G, Klein J, et al. Borrelia burgdorferi as an etiologic agent in chronic heart failure? *Scand J Infect Dis Suppl* 1991;77:85-7.
13. Lardieri G, Salvi A, et al. Isolation of Borrelia burgdorferi from myocardium. *Lancet* 1993;342:490.
14. Kimball SA, Janson PA, LaRaia PJ. Complete heart block as the sole presentation of Lyme disease. *Arch Intern Med* 1989;149:1897-8.
15. Wormser GP, Dattwyler RJ, et al. The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2006;4:1089-134.

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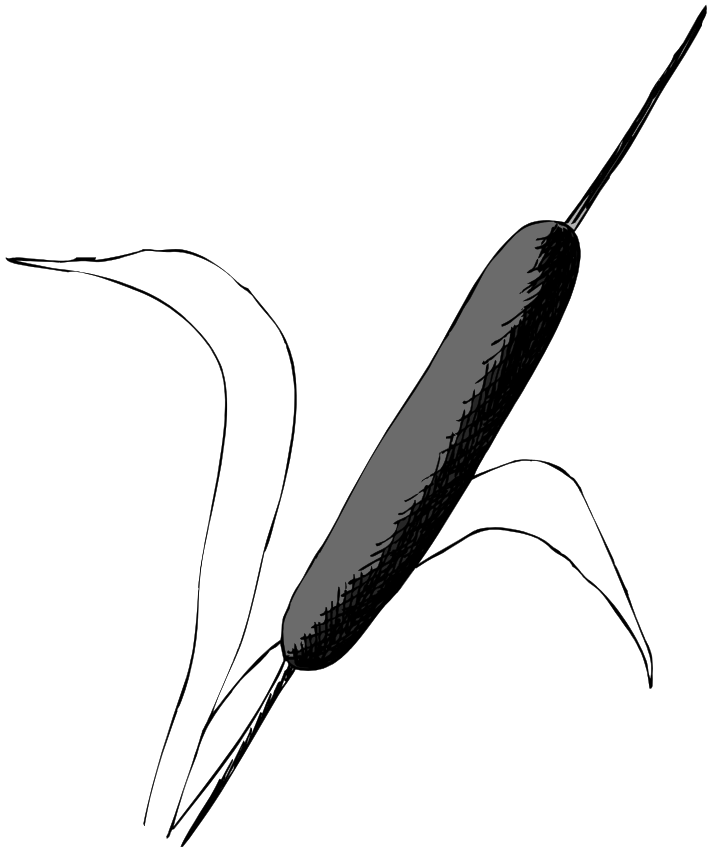

Evaluation and Management of Vesicoureteral Reflux: A Decade of Change

Zachary N. Gordon, Anthony Caldamone, MD, FACS, FAAP, Pamela Ellsworth, MD, FACS, FAAP

Vesicoureteral reflux (VUR) is the most common urinary tract abnormality in children,[1] yet the optimal diagnostic and therapeutic approach remains controversial. Studies over the past decade have raised significant questions regarding all aspects of VUR management, including the approach to the evaluation of childhood **urinary tract infection (UTI).** Determining which children will actually benefit from diagnosis and treatment is the greatest challenge to VUR management.

Definition, Etiology, and Incidence

VUR, the retrograde flow of urine from the bladder up the ureter toward the kidney, is the result of an incompetent antireflux mechanism at the **ureterovesical junction (UVJ).** VUR is considered primary or secondary depending on the main etiology. Primary VUR, the most common, is caused by a congenital maldevelopment of the UVJ antireflux mechanism.[2] Secondary VUR results when abnormally increased bladder pressures, as seen in posterior urethral valves, neuropathic bladder, or voiding dysfunction, overwhelm and/or destabilize the normal UVJ.[3]

VUR is estimated to occur in ~1-3% of otherwise healthy children. In children with a febrile UTI, the incidence increases to ~30-40% and there is a female predominance of ~4:1.[1] Nearly 80% of VUR cases are diagnosed after UTI.[3] Approximately 10-20% of infants with a history of prenatal hydronephrosis have VUR.[4] A strong inheritance pattern exists for primary VUR, with an incidence of ~32% in siblings[5] and ~65% in offspring of a patient with a history of VUR.[6]

Reflux Nephropathy

The clinical significance of VUR is its association with renal parenchymal scarring, also referred to as **reflux nephropathy (RN).**[7] Historically, RN was postulated to be due to a "water-hammer" effect, resulting from the direct transmission of bladder pressures to the renal pelvis via sterile refluxing urine.[8] While VUR associated with abnormally elevated bladder pressures may cause renal damage, in 1975 Ransley and Risdon demonstrated that, at physiologic bladder pressures, renal scarring occurs only in the presence of UTI.[9] In the presence of UTI, reflux facilitates the transport of infected urine from the bladder to the kidney, potentially leading to bacterial invasion of the renal parenchyma (i.e., pyelonephritis). The inflammatory response, in turn, leads to focal ischemia, interstitial damage, fibrosis, and potentially irreversible renal scarring.[10]

The primary concern regarding RN is the potential for serious long-term sequelae, including hypertension, chronic kidney disease, and end-stage renal disease. The risk of developing such complications may vary with age, degree of renal scarring, and unilaterality/bilaterality of damage.[11] Retrospective studies have demonstrated that the incidence of hypertension in the setting of RN is ~15-20% in children, but ~30-40% in adults.[12] In the United States and Canada in 2008, RN was the fourth leading diagnosis in pediatric transplant (5.2%), dialysis (3.5%), and chronic kidney disease (8.5%) patients, and, in Italy, VUR remains a leading cause of end-stage renal disease in children and young adults, accounting for 25% of all cases.[11] Few prospective, longitudinal studies of RN-associated complications exist; thus, clear incidences and actual risks of the late clinical sequelae remain poorly defined.

Historical Approach to Evaluation and Treatment

The American Academy of Pediatrics recommends both renal **ultrasonography (US)** and **voiding cystourethrography (VCUG)** following first febrile UTI in all children between 2 months and 2 years of age, as the prevalence of VUR and risk of renal scarring following pyelonephritis is highest in this age group.[1] US is a safe, noninvasive, highly sensitive screening test for collecting system dilatation. However, because its sensitivity for detecting VUR or renal scarring is low, it should primarily be regarded as a screening tool to detect patients at risk of these or other abnormalities.[11] The traditional gold standard diagnostic study for detecting VUR is fluoroscopic VCUG, in which contrast material is instilled into the bladder through a catheter, and intermittent fluoroscopy is utilized during filling and voiding. VCUG allows for both visualization of urethral and bladder anatomy, as well as grading of VUR severity if present.[13]

The initial grade of VUR is correlated with both the likelihood of spontaneous reflux resolution as well as the risk of renal scarring.[1] Grades I and II VUR, non-dilating "low-grade" reflux, are found in over half of children diagnosed with VUR after UTI, and, regardless of age at presentation, spontaneously resolves within 5 years in 92% and 81%, respectively.[14] In contrast, grades IV and V, "high-grade" reflux, involve moderate (IV) to severe (V) dilation of the collecting system, blunting of the calyces, and tortuosity of the ureter,[15] and are unlikely to spontaneously resolve.[14]

VCUG requires urethral catheterization, in most cases of the non-sedated child, and ionizing radiation exposure. Direct **radionuclide cystography (RNC)** is an alternative to VCUG in which a radionuclide, rather than contrast material, is instilled into the bladder under a gamma camera detector. RNC involves 100 times less ionizing radiation than traditional VCUG and is highly sensitive for detecting VUR; however, it does not allow for anatomical assessment or precise VUR grading, and still requires catheterization.[13] Thus RNC is not recommended as the initial diagnostic study in a child with suspected VUR, but may be used in follow-up studies.[1]

The primary goal of VUR treatment is prevention of reflux-related febrile UTIs to reduce the risk of renal scarring and long-term consequences.[14] Historically, the initial approach to VUR man-

agement was via open surgical correction of the UVJ abnormality, "ureteral reimplantation," performed using either an intravesical, extravesical, or combined approach.[2] Intravesical approaches have a 98-100% success rate; however, these procedures are associated with transient postoperative hematuria and bladder spasm. In contrast, extravesical approaches have similar success rates, but avoid opening the bladder, and thus, are associated with less postoperative morbidity. However, due to an increased risk of acute urinary retention after bilateral extravesical procedures, this approach is more commonly performed in children with unilateral VUR.[16]

In 1979 Smellie et al.[17] challenged the concept that surgery is necessary in all children with VUR. Their seminal study demonstrated the role of medical therapy via continuous low-dose antibiotic prophylaxis in reducing the rate of UTI while awaiting reflux resolution or surgical correction. This led to widely divergent opinions regarding the optimal initial management of VUR, and two **randomized, controlled trials (RCTs)**, the International Reflux Study[18] and the Birmingham Study,[19] compared the outcome of surgical versus medical treatment of grade III-IV VUR. A 50% decrease in the incidence of clinical pyelonephritis in the surgical group was noted;[18] however, there were no differences in the incidence of cystitis or renal scars between the two management arms.[18, 19]

Based on these findings and the high resolution rates in low-grade reflux, in 1997 the American Urological Association recommended the initial management of children with grades I-IV VUR consist of antibiotic prophylaxis until either spontaneous reflux resolution, or surgery is indicated. Indications for surgical correction included: (1) recurrent UTIs despite prophylaxis (i.e., breakthrough UTIs); (2) persistent VUR after a variable period of observation; (3) poor compliance with prophylaxis; and (4) development of new renal scarring.[14] A relative indication for surgery is if the parents are felt to be unreliable in terms of seeking treatment immediately at the first sign of infection, and thus, placing the child at risk for pyelonephritis and renal scarring.

Technetium-99m labeled **dimercaptosuccinic acid scintigraphy (DMSA scan)** is the gold standard technique for the detection and evaluation of acute pyelonephritis and renal scarring. When performed at the time of UTI, sensitivity and specificity for detecting pyelonephritis are both 92-95%,[20] and, when performed at 6-month follow-up, are 96% and 98%, respectively, for detection of renal scarring.[21] Although follow-up DMSA scan may help identify those at risk for long-term sequelae, its routine use is controversial, as the incidence of scarring after first febrile UTI is only ~15%.[22]

Children without pyelonephritis are not at risk for scarring, regardless of the presence of reflux.

Changes in Evaluation

Until recently a common assumption was that VUR is an absolute prerequisite for new or acquired renal scarring following UTI; however, over the past decade this assumption has been questioned. DMSA scintigraphy has demonstrated that pyelonephritis, rather than VUR, is the prerequisite for acquired renal scarring,[21] and that low-grade VUR is of low clinical significance.[23, 24] Evidence supporting these conclusions include: (1) only about two-thirds of children with a febrile UTI actually have acute pyelonephritis, and only about one-third of those have VUR;[23] (2) there is no significant difference in the risk of pyelonephritis or acquired renal scarring between children with low-grade VUR and those without VUR, whereas children with high-grade VUR have a significantly increased risk of pyelonephritis as well as renal scarring;[23] and (3) once pyelonephritis occurs, the rate of subsequent renal scarring (~30-60%)[23, 25] is independent of the presence of reflux; children without pyelonephritis are not at risk for scarring, regardless of the presence of reflux.[21, 26]

Recently, a new diagnostic strategy for the evaluation of childhood UTI, the **"top-down" approach (TDA)**, has been proposed.[27] In contrast to the traditional "bottom-up" approach, in which the initial diagnostic concern is detection of VUR via VCUG, the TDA focuses first on detecting pyelonephritis via a DMSA scan performed at the time of infection.[28] Since children with pyelonephritis are more likely to have high-grade VUR, the TDA recommends a VCUG be performed only in those with an abnormal DMSA.[27]

Both retrospective and prospective studies have confirmed the validity of the TDA. Hansson et al.[29] and Preda et al.[30] found that the sensitivity and negative predictive value (NPV) of initial DMSA scan after febrile UTI to predict VUR were 73% and 87%, respectively. The incidence of VUR missed with this strategy was ~10%, all of which were low-grade, and both the sensitivity and NPV of DMSA to predict high-grade VUR were 100%. Thus, if VCUG is only performed in those children with DMSA-confirmed pyelonephritis, then *all* cases of clinically significant high-grade VUR would be detected and ~40% of VCUGs could be avoided.[27]

Changes in Management

Increasing concerns regarding antibiotic-resistant bacteria, poor patient compliance with prophylaxis (reported to be as low as 40%[31]), and recent challenges to the clinical benefit of prophylaxis have questioned the role of antibiotic prophylaxis as the initial management in all VUR patients.[32] A major limitation of prior RCTs was the lack of a placebo or "observation-only" arm with which to compare the efficacy of antibiotic prophylaxis; however, four recently published RCTs, all of which included a control group,[24, 33-35] failed to demonstrate a reduction in the rate of UTI in children with low-grade reflux treated with prophylaxis. As these studies were limited by insufficient statistical power, enrollment primarily of children with grades I-III VUR, and lack of categorization regarding voiding patterns, the question remains whether antibiotic prophylaxis is indeed an effective treatment for reflux, particularly in children with grades III-V.

Despite the high success rate of antireflux surgery, concerns regarding the invasive nature and morbidity of these procedures have led to less invasive alternatives for VUR correction.[36] Both intra-

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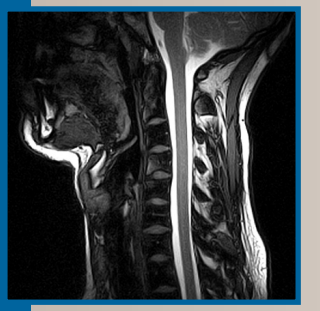

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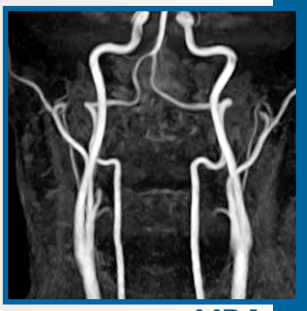

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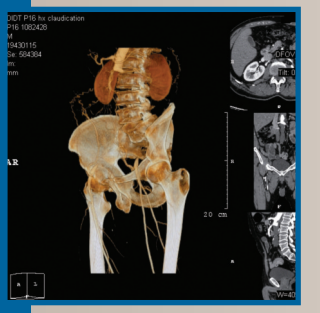

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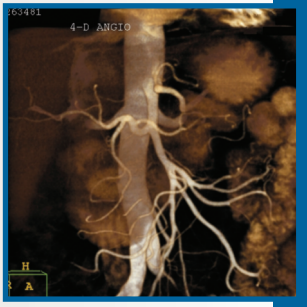

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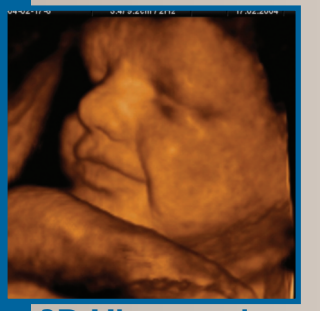

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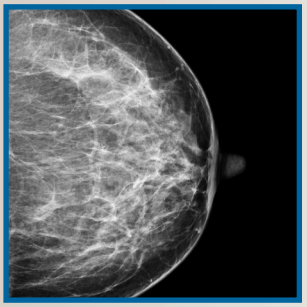

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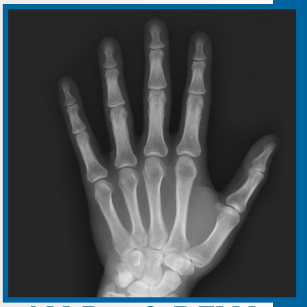

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vesical and extravesical procedures have been approached laparoscopically, which offers the benefits of improved cosmesis due to smaller incision(s), shorter hospital stay, and decreased postoperative bladder spasm and analgesia requirements.[37] Although success rates are comparable to open surgical correction,[38] a steep learning curve, increased postoperative complications, and increased operating time have led few to embrace the laparoscopic approach.

In 2001, dextanomer/hyaluronic acid (Dx/HA) (Deflux®, [Oceana Therapeutics Ltd, USA]) was approved as an injectable gel for endoscopic correction of grades II-IV VUR. Comprised of cystoscopy and subureteric injection of Dx/HA under general anesthesia, endoscopic treatment is a minimally invasive outpatient procedure, generally lasting less than 20 minutes, and the child may resume preoperative activities immediately after. The likelihood of initial success after Dx/HA injection, in terms of VUR resolution, is correlated with preoperative VUR grade.[39] On average, success rates for low-grade reflux are ~85%, and ~75% and ~60% for grade III and IV, respectively.[40] The long-term durability of Dx/HA is unclear, with long-term success rates ranging from 74-87% after 1-5 years.[41] Nevertheless, some have begun to recommend it as a first-line treatment alternative to prophylaxis or surgery.[39] In the absence of rigorous comparisons between the different treatment modalities, however, the indications for endoscopic treatment should currently remain the same as open surgery.[14]

Over the past decade, the evaluation of childhood UTI and nearly all aspects of VUR management have experienced a large paradigm shift. In some centers, the initial diagnostic study in children presenting with febrile UTI has changed from VCUG for detection of VUR to DMSA scan to assess for pyelonephritis. Under this new "top-down" approach, a VCUG is only ordered in those with DMSA-confirmed pyelonephritis. Antibiotic prophylaxis is currently the mainstay of initial VUR management, with surgical correction being reserved for select cases. Traditional viewpoints regarding the clinical significance of low-grade VUR as well as its management with prophylactic antibiotics have also recently been challenged. Many authorities now consider low-grade VUR clinically insignificant, and recent RCTs strongly suggest that antibiotic prophylaxis is ineffective at reducing the rate of febrile UTI in low-grade VUR. Given the unclear effectiveness of antibiotic prophylaxis, a long-term, multicenter, double-blind, randomized, placebo-controlled trial was designed in 2005 and is currently underway: the **Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR)** study. This large trial of 600 children should have the necessary statistical power to assess the efficacy of antibiotics in reducing the rate of febrile UTI and renal scarring.[42]

In the meantime, the recently published results from the Swedish Reflux Study, a prospective, multicenter RCT, have addressed some of the questions regarding the management of grade III-IV reflux. In this study, 203 children between the ages of 1 and 2 years with grade III-IV VUR were randomized to treatment with either antibiotic prophylaxis, endoscopic treatment with Dx/HA, or surveillance with antibiotics only for symptomatic UTI.[32] After 2 years of follow-up they demonstrated: (1) reflux resolution or downgrading to low-grade was significantly more common in the endoscopic group (~70%) compared to the prophylaxis and surveillance groups (~40-45%); (2) recurrent dilating reflux occurred in 20% of those initially treated successfully with Dx/HA; (3) when compared to the control group, prophylaxis and endoscopic treatment both decreased the rate of recurrent febrile UTI in females by ~60%; neither treatment reduced the rate of febrile UTI in males; and (4) the rate of new scarring in females was significantly less in the prophylaxis group compared to the control group, whereas in males the rate of new scarring was low in all groups.[43-45] While these results must be validated, hopefully by the RIVUR study, this is the largest RCT to date investigating children with dilating reflux, and the first to provide convincing evidence that antibiotic prophylaxis is effective in reducing the rate of febrile UTI and renal scarring in children with dilating reflux, albeit only in females.

Conclusion

The evaluation and management of VUR is evolving. The historical philosophy of evaluating for VUR in all children presenting with UTI and managing all children with VUR with antibiotic prophylaxis or surgical correction has evolved to identifying those children at greatest risk for renal scarring via the use of DMSA scintigraphy and the "top-down" approach. Endoscopic treatment has emerged as a new promising management option and results of the RIVUR study are likely to lead to further modification of VUR management in the coming decade.

References

1. American Academy of Pediatrics, Committee on Quality Improvement, Subcommittee on Urinary Tract Infection. *Pediatrics*. 1999;103(4 Pt 1):843-52. Erratum in: *Pediatrics* 1999 May;103(5 Pt 1):1052, 1999 Jul;104(1 Pt 1):118. 2000 Jan;105(1 Pt 1):141.
2. Hutch JA. *J Urol* 2002;167:1410-4.
3. Elder JS. *Curr Urol Rep* 2008;9:143-50.
4. Nguyen HT, Herndon CD, et al. *J Pediatr Urol* 2010;6:212-31.
5. Hollowell JG, Greenfield SP. *J Urol*. 2002;168:2138-41.
6. Noe HN, Wyatt RJ, et al. *J Urol* 1992;148:1869-71.
7. Bailey RR. *Clin Nephrol* 1973;1:132-41.
8. Hodson CJ, Edwards D. *Clin Radiol* 1960;11:219-31.
9. Ransley PG, Risdon RA. *Urol Res* 1975;3:105-9.
10. Roberts JA. *J Urol*. 1992;148(5 Pt 2):1721-5.
11. Ismaili K, Avni FE, et al. *EAU-EBU Update Series* 2006;4:129-40.
12. Farnham SB, Adams MC, et al. *J Urol* 2005;173:697-704.
13. Lee RS, Diamond DA, Chow JS. *Pediatr Radiol* 2006;36 Suppl 2:185-91.
14. Elder JS, Peters CA, et al. Pediatric *J Urol* 1997;157:1846-51.
15. Lebowitz RL, Olbing H, et al. *Pediatr Radiol* 1985;15:105-9.
16. Palmer JS. *Urol* 2009;73:285-8.
17. Smellie J, Normand IC. Reflux nephropathy in childhood. In: Hodson J, Kincaid-Smith P, eds. *Reflux nephropathy*. New York: Masson Publishing USA; 1979:14-20.
18. Jodal U, Smellie JM, et al. *Pediatr Nephrol* 2006;21:785-92.
19. Birmingham Reflux Study Group. *Br Med J (Clin Res Ed)*. 1987;295:237-41.
20. Majd M, Nussbaum Blask AR, et al. *Radiol* 2001;218:101-8.
21. Rushton HG. *Pediatr Nephrol* 1997;11:108-20.
22. Montini G, Zucchetta P, et al. *Pediatrics* 2009;123(2):e239-46.
23. Merguerian P, Sverrisson E, et al. *Current Urol Reports* 2010;11:98-108.
24. Garin EH, Olavarria F, et al. *Pediatrics* 2006;117:626-32.
25. Peters C, Rushton HG. *J Urol* 2010;184:265-73.
26. Hoberman A, Charron M, et al. *NEJM* 2003;348:195-202.

27. Pohl HG, Belman AB. *Adv Urol* 2009;783409.
28. Herz DB. The top-down approach: an expanded methodology. *J Urol.* 2010;183(3):856-857.
29. Hansson S, Dhamey M, et al. *J Urol.* 2004;172:1071-3; discussion 1073-4.
30. Preda I, Jodal U, et al. *J Pediatr* 2007;151:581-4, 584.e1.
31. Copp HL, Nelson CP, et al. *J Urol* 2010; 183:1994-9.
32. Brandstrom P, Esbjorner E, et al. *J Urol* 2010;184:274-9.
33. Montini G, Rigon L, et al. *Pediatrics* 2008;122:1064-71.
34. Pennesi M, Travan L, et al. *Pediatrics* 2008;121:e1489-94.
35. Roussey-Kesler G, Gadjos V, et al. *J Urol* 2008;179:674-9; discussion 679.
36. Simforoosh N, Radfar MH. *Adv Urol* 2008;536428.
37. Kutikov A, Guzzo TJ, et al. *J Urol* 2006;176:2222-5; discussion 2225-6.
38. Capolicchio JP. *Adv Urol* 2008;567980.
39. Cerwinka WH, Scherz HC, Kirsch AJ. *Adv Urol* 2008;513854.
40. Routh JC, Inman BA, Reinberg Y. *Pediatrics* 2010; 183:1994-9.
41. Lackgren G, Wahlin N, et al. *J Urol* 2001;166:1887-92.
42. Keren R, Carpenter MA, et al. *Pediatrics* 2008;122 Suppl 5:S240-50.
43. Holmdahl G, Brandstrom P, et al. *J Urol* 2010;184:280-5.
44. Brandstrom P, Esbjorner E, et al. *J Urol* 2010;184:286-91.
45. Brandstrom P, Neveus T, et al. *J Urol* 2010;184:292-7.

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A Pilot Retrospective Comparison of Fondaparinux and Enoxaparin For the Prevention of Venous Thromboembolism (VTE) In Patients With Stroke

Jon A. Mukand, MD, PhD, and Nita H. Mukand

Stroke is a leading cause of morbidity and mortality in the world, with an annual incidence of fifteen million cases each year, of which 5 million people die and 5 million are permanently disabled.[1] In addition to myriad neurologic deficits, people with stroke are susceptible to a variety of medical complications, including **venous thromboembolic disease (VTE)**. The analysis of pro-thrombotic factors in a small population of patients with stroke revealed elevated levels of biochemical markers of coagulation activity or fibrinolysis, in comparison to the levels of healthy control adults.[2] Clinical risk factors for VTE in patients with stroke include age, paralysis, immobility, and infections such as urinary tract infections and pneumonia.[3]

As a major source of morbidity and mortality after stroke, VTE has received a great deal of attention in terms of screening, prophylaxis, and treatment. In the absence of preventive measures, the incidence of **deep venous thrombosis (DVT)** after a stroke is 24 to 55%.[4-6] If the DVT is untreated, the mortality rate resulting from a **pulmonary embolus (PE)** is as high as 25%.[7,8] Even with treatment of a DVT, the mortality rate is still 6%.[9] Pulmonary embolus is the leading cause of mortality in the first 2-4 weeks after a stroke, based on autopsy studies.[10] Although the highest incidence of VTE diagnosis after a stroke is in the first four weeks, there is a significant continued risk of these events until the eighth week, and some patients at high risk will develop VTE more than three months after the stroke.[2]

In the setting of stroke rehabilitation units, the prevalence of DVT is almost 20%.[11] A recent cost-effectiveness study of routine Doppler ultrasound screening for DVT in patients with ischemic stroke was in favor of routine screening for only certain subgroups on admission for rehabilitation.[12]

Patients with stroke due to cardiac emboli are given warfarin for secondary stroke prevention, which reduces the risk of VTE. Warfarin is contraindicated for patients with intracranial hemorrhage, and they receive pneumatic compression sleeves to improve blood flow and reduce the risk of VTE.[2] Patients with ischemic strokes remain at high risk of VTE, in spite of treatment with anti-platelet agents such as aspirin and clopidogrel. All patients with acute neurologic conditions should receive prophylaxis for VTE, according to the **American College of Chest Physicians (ACCP)** consensus.[13]

A study of DVT prevention, in which 360 rehabilitation patients with stroke were randomized into four groups (heparin, intermittent pneumatic compression, functional electrical stimulation, or placebo), found no significant difference in the development of DVT.[14] In contrast, other studies of prophylaxis with **unfractionated heparin (UFH)** have

Table 1: Patient Demographics by Drug Group

	Fondaparinux	Enoxaparin
Mean Age ± SD	72.4 ±13.9	75.7±10.7
Gender n (%)		
Male	14 (46.7%)	12 (40.0%)
Female	16 (53.3%)	18 (60.0%)
Race n (%)		
White	23 (76.7%)	27 (90.0%)
Black	6 (20.0%)	1 (3.3%)
Hispanic	1(3.3%)	1(03.3%)
Asian	0 (00.0%)	1 (3.3%)
Mean Weight ± SD (kg)	74.7 ± 15.3	74.5 ±17.8
Mean LOS ± SD (days)	28.6 ± 3.1	30.0 ±13.2
Discharged n (%)		
Home	13 (43.3%)	15 (50.0%)
Nursing Home	11 (36.7%)	8 (26.7%)
Subacute Unit	4 (13.3%)	4 (13.3%)
Acute	2 (6.7%)	3 (10.0%)

shown effectiveness in reducing the rates of DVT/PE by about 60%.[4-5] In comparison with UFH, **low-molecular-weight heparin (LMWH)** appears more effective in preventing VTE among patients with stroke.[5,15] A Cochrane database analysis (2005) suggested that LMWH decreases the incidence of DVT, when compared to UFH, but there were insufficient data to comment on other outcomes including intracranial hemorrhage and death.[16]

Most recently, a randomized controlled trial of almost eighteen hundred patients with acute ischemic stroke found that daily enoxaparin reduced the risk of VTE by 43% in comparison with UFH (68 vs. 121 patients, P = 0.0001). The bleeding rates, a composite of major extra-cranial and clinically significant intracranial hemorrhage, were slightly higher in the enoxaparin group (11 vs. 6, P = 0.23).[17]

Fondaparinux (Arixtra), made by GlaxoSmith Kline, is the latest therapeutic option for DVT/PE prevention and treatment. This small, synthetic pentasaccharide is a potent inhibitor of Factor Xa, via its action on Antithrombin III. It does not significantly bind to plasma proteins or affect platelet function, and has a predictable pharmacokinetic profile that allows for daily dosing without routine monitoring of levels.[18-20]

Fondaparinux has been shown to be superior to enoxaparin, with comparable safety, in preventing VTE in patients after hip fracture, hip replacement, and knee replacement surgery.[21-23] Fondaparinux is also approved for the prevention of VTE in patients after abdominal surgery, who are at risk of VTE.[24] Finally, fondaparinux is approved for the treatment of VTE, in conjunction with warfarin; a comparative study with enoxaparin (for DVT) showed similar efficacy and safety.[25] Due to its efficacy and safety in comparison with current therapies, fondaparinux appeared to be a potentially valuable option for preventing VTE in patients with stroke. Therefore we compared it to enoxaparin.

Methods

After approval by the rehabilitation center's Research Oversight Committee, we conducted a retrospective chart review of adults with strokes admitted over three years who received enoxaparin (40 mg subcutaneously daily) or fondaparinux (2.5 mg subcutaneously daily) for VTE prevention. The first group included 30 consecutive admissions until 2005, when our rehabilitation center started using fondaparinux as the preferred agent for VTE prophylaxis. Thirty patients in the second group were also consecutive admissions. In effect, these patients were randomly assigned to the two drugs as there was no selection process. Both groups included only patients with non-hemorrhagic strokes, no active bleeding, and a calculated creatinine clearance of 30 ml/min or above, since both drugs are cleared by the kidneys. Patients received either drug until they consistently walked a total of 100-150 feet each day. All patients were assessed on a daily basis for DVT by examination of the legs and for PE by clinical signs such as chest pain and dyspnea; an ultrasound was obtained if indicated to diagnose a DVT.

Table 2: Clinical Characteristics by Drug Group

	Fondaparinux	Enoxaparin	
Location of Stroke			
Left	14 (46.7%)	19 (63.3%)	
Right	16 (53.3%)	11 (36.7%)	
Ultrasound	4 (13.3%)	4 (13.3%)	
Aspirin	18 (60.0%)	14 (46.7%)	
Clopidogrel	3 (10.0%)	1 (3.3%)	
Aspirin and Clopidogrel	4 (13.3%)	8 (26.7%)	
Aspirin and Dipyridamole	5 (16.7%)	4 (13.3%)	
Any Anti-platelet Agent	29 (96.7%)	26 (86.7%)	
Leg Edema	5 (16.7%)	3 (10.0%)	
Calf Tenderness	0 (0.0%)	0 (0.0%)	
Transfers (FIM)	2.7 ± 1.2	2.9 ± 2.5	
Ambulation (FIM)	1.7 ± 1.2	2.6 ± 0.3	T=2.7 P=0.01
Ambulation (Feet)	27.1 ± 49.4	23.2 ± 43.4	
Dorsiflexors	1.3 ± 1.6	2.2 ± 2.1	
Hip Flexors	1.8 ± 1.2	2.2 ± 1.3	
Knee Extensors	2.1 ± 1.5	2.6 ± 1.7	
Tone	-0.1 ± 0.7	0 ± 0.7	

*FIM scores, ambulation distance, strength, and tone are Mean ± SD. Other values are n (%).

The data set included demographics (age, sex, race), length of stay, weight, location of stroke (right vs. left), admission **Functional Independence Measure (FIM)** scores for transfers and ambulation; distance of ambulation on admission; lower extremity strength (hip flexors, knee extensors, ankle dorsiflexors graded on a scale of 0 - 5); lower extremity tone; presence of leg edema and calf tenderness on admission; risk factors for DVT/PE based on the discharge summary and rehabilitation medicine evaluation; duration of enoxaparin or fondaparinux; concomitant use of anti-platelet agents including aspirin, clopidogrel, or aspirin/dipyridamole; calculated creatinine clearance; initial hemoglobin and platelets; hemoglobin and platelets obtained closest to the discharge date; presence of an ultrasound study to diagnose a DVT; and discharge disposition. Patients admitted with concomitant anti-platelet agents received them throughout the study. The outcome measures were occurrence of DVT and PE,

Table 3: Lab Characteristics by Drug Group

	Fondaparinux	Enoxaparin	
Initial Hemoglobin (gm/dl)	12.8±1.8	13.0±1.7	
Final Hemoglobin	12.3± 1.8	11.9± 2.9	
Mean Hemoglobin Change	-0.49± 0.8	-1.1± 2.8	
Initial Platelets (k/cumm)	232.5± 96.0	293.2± 111.9	T=2.3 P=0.03
Final Platelets	233.1± 63.6	258.2± 126.9	
Mean Change in Platelets	+0.5± 57.0	-35.1 ± 92.2	T=1.8, P=0.07
Creat. Clearance (ml/min)	71.8± 33.4	61.8± 51.0	

*All values are Mean ± SD.

Table 4: Presence of Risk Factors by Drug Group

	Fondaparinux	Enoxaparin
Age (n, %)	23 (76.7%)	27 (90.0%)
Weight	13 (43.3%)	9 (30.0%)
Infection	19 (63.3%)	24 (80.0%)
Paralysis	19 (63.3%)	15 (50.0%)
Edema	3 (10.0%)	3 (10.0%)
IBD	0 (00.0%)	1 (3.3%)
Cancer	0 (00.0%)	2 (6.7%)
History of DVT	0 (00.0%)	1 (3.3%)
Mean Total Risk Factors ± SD	2.6 ± 1.2	2.7 ± 0.8

*All values are n (%), except for the last variable.

as well as bleeding complications. All patients were closely monitored for bleeding complications. Bleeding was classified as either minor or major; the latter included bleeding that was fatal, in a critical organ, or with a bleeding index (decline in hemoglobin + units transfused) greater than 2.

The rationale for selecting these variables was as follows. In order for an unbiased comparison of the two drugs, we wished to ensure that the two groups were similar in terms of risk factors for VTE: age (over 60), obesity (weight > 120% of ideal body weight), paralysis (strength of = 1/5 at lower extremity muscles), immobility (FIM scores of 1 for transfers and ambulation, or initial ambulation < 5 feet), leg edema, and calf tenderness. In addition, other risk factors such as inflammatory bowel disease and hormone replacement therapy were noted, to obtain the total number of risk factors. The length of stay and discharge dispositions were indicators of stroke severity. Duration of enoxaparin or fondaparinux, creatinine clearance, initial platelet count, and the use of antiplatelet agents could all increase the risk of bleeding complications. Initial and final platelets and hemoglobin were laboratory indicators of bleeding complications, the outcome measure for safety.

Statistical analysis using cross tabulation was used to determine whether there was a significant difference in the frequency of PEs, DVTs, and bleeding complications between those patients taking fondaparinux versus those taking enoxaparin. Bivariate analysis, including difference of means test and Chi-square, was used to examine whether there were significant differences between groups that may affect the statistical significance of DVT/PE and bleeding complications after stroke.

Results

There were no significant (NS) differences between the groups in almost all demographic characteristics (Table 1); clinical features, anti-platelet agents, and level of disability related to the stroke (Table 2); lab characteristics (Table 3); and risk factors for DVT/PE (Table 4). The mean duration of treatment was 21.1 ± 14.1 days with enoxaparin and 20.6 ± 15.0 days with fondaparinux. Significant differences occurred only with FIM scores and platelets. Mean FIM scores for ambulation were higher among the enoxaparin group (2.6 ± 0.3, 95% CI, 2.05 - 3.1) vs.1.7 ± 1.2 (95% CI, 1.2-2.1) with fondaparinux (T=2.7, P=0.01). The enoxaparin group had higher mean admission platelets than the fondaparinux patients (293.2 ± 111.9 k/cumm, 95% CI, 251.5 - 335.0) vs. 232.5 ± 96.0 k/cumm (95% CI, 196.7 - 268.4; P = 0.03). There was also a greater mean decline in the platelet count at discharge with enoxaparin (- 35.1, 95% CI, -69.5 to -0.6) vs. + 0.5 k/cumm (95% CI, -20.8 - 21.8; T = 1.8, P = 0.07, NS).

Among the fondaparinux patients, the greatest decline in platelets was from 622 to 371 k/cumm and with enoxaparin the worst decline was from 474 to 301 k/cumm. The major bleed with fondaparinux was a decline in hemoglobin that required transfusion, and the one with enoxaparin required transfer to the acute care hospital.

The number of patients on antiplatelet agents was higher in the

fondaparinux group (29, or 96.7% vs. 26, or 86.7%, P = 0.16), but the combination of aspirin and clopidogrel was higher in the enoxaparin group (8, or 26.7 % vs. 4, or 13.3 %, P = 0.16); neither of these findings was significant. The fondaparinux group had a decline in hemoglobin of 0.49 (from a mean of 12.8 gm/dl ± 1.8), but the enoxaparin patients had a decrease of 1.1 (from a mean of 13.0 gm/dl ± 1.7, P =0.28, NS).

More patients in the fondaparinux group had leg edema (5 vs. 3), but this was not a significant finding (P=0.58). The mean total number of risk factors for DVT/PE was higher in the enoxaparin patients (2.7 vs. 2.6), and this was also not significant (P=0.53).

There were no significant differences between the two drugs in the safety and efficacy outcomes (Table 5). Neither group had a PE. The incidence of DVTs was 3.3% (1) with enoxaparin and no patient on fondaparinux had a DVT (P= 0.31, NS). There were 3 (10%) minor and one major bleeding incidents 1 (3.3%) among the fondaparinux group, and 4 (13.3%) minor and 1 (3.3%) major bleeding incidents among the patients on enoxaparin. With the minor bleeding episodes, the fondaparinux group had two instances of hematuria and one of epistaxis. With enoxaparin, the patients had one subconjunctival hemorrhage, one knee effusion, and two instances of gastrointestinal bleeding.

Bivariate analysis of the impact of those traits that significantly differed by group showed no significant relationship to the outcome measures. For instance, the ambulation FIM did not change the statistical significance of the difference in DVT incidence.

Table 5: Outcomes by Drug Group

	Fondaparinux	Enoxaparin
PE (n, %)	0 (0%)	0 (0%)
DVT	0 (0%)	1 (10%)
Minor Bleeding	3 (10%)	4 (13.3%)
Major Bleeding	1 (3.3%)	1 (3.3%)
Mean Drug Duration (Days ± SD)	20.6 ± 15.0	21.1 ± 14.1

*All values are n (%), except for the last variable.

Discussion

There was no DVT in the fondaparinux group and one occurred in the enoxaparin group, but this difference was not statistically significant. The two groups were similar in terms of age, gender, race, weight and risk factors for VTE, except for the ambulation FIM score at admission, which was significantly lower in the fondaparinux group.

Safety assessment in both groups revealed no significant differences. Major bleeding in the fondaparinux group involved a patient who was on two medications that significantly increase the risk of gastrointestinal bleeding: aspirin and clopidogrel. The patient on enoxaparin with a major bleeding episode was on aspirin. Both the creatinine clearance and platelet count were normal in these two patients.

Platelets declined among the enoxaparin group by a mean of 35.1 k/cumm, a difference that approached significance (P = .07, NS). This finding may be consistent with the pharmacology of these two drugs in relation to **heparin-induced thrombocytopenia (HIT)**. An in vitro study (platelet aggregation test) of 25 patients with HIT showed that 19 (76%) samples of serum cross-reacted with enoxaparin, but none interacted with fondaparinux.[26]

A randomized controlled trial of enoxaparin and heparin in 212 patients revealed that VTE, major bleeding, and death within three months of stroke occurred in 37.7 % of patients on daily enoxaparin and 49.1 % of patients on thrice daily heparin (P = 0.127).[15] A larger study of almost 1,800 patients showed a 10.2 % incidence of VTE with enoxaparin and 18.1 % for those given heparin (P = 0.0001), although bleeding occurred more often with enoxaparin. [17] Enoxaparin seems to be superior to heparin for VTE prevention in the stroke population.

The ACCP guidelines for VTE prevention were updated in 2008. Unfractionated heparin, low molecular weight heparin, and fondaparinux all received the highest recommendation of Grade 1A for acutely ill medical patients who are confined to bed and have an acute neurological disease.[27]

Limitations of our study include the small sample size and lack of randomization. In addition, mandatory venography was not performed (as was done for the orthopedic studies comparing the two drugs), so there was the possibility of undiagnosed DVTs.

Conclusion

Based on this retrospective chart review, fondaparinux appears as effective and safe as enoxaparin in preventing DVTs and PEs in patients with stroke. There were no DVTs with fondaparinux, but one occurred in the enoxaparin, and minor bleeding was slightly higher with enoxaparin. These differences in efficacy and safety were not significant. A randomized controlled trial with a sufficient number of patients is needed to determine if one of these medications is superior.

References

1. Mackay J, Mensah G. *The Atlas of Heart Disease and Stroke.* Part three: The burden. World Health Organization. http://www.who.int/cardiovascular_diseases/resources/atlas/en/.
2. Harvey RL. *Topics Stroke Rehabil* 2003;10:61-9.
3. Wolozinsky M, Yavin YY, Cohen AT. *Am J Cardiovasc Drugs* 2005;5:409-15.
4. Geerts WH, Heit JA, et al. *Chest* 2001;119(1 Suppl):132S-175S.
5. Turpie AG, Gent M, et al. *Ann Intern Med* 1992;117:353-7.
6. Gitter MJ, Jaeger TM, et al. *Mayo Clin Proc* 1995;70:725-33.
7. Kelly J, Rudd A, et al. *Stroke* 2001;32:262-7.
8. Byrne JJ. *NEJM* 1995;253:579-86.

9. Salzman EW, Davies GC. *Ann Surg* 1980;191:207-18.
10. Vitanen M, Winblad B, Asplund K. *Acta Med Scand* 1987;222:401-8.
11. Desmukh M, Bisignani M, et al. *Am J Phys Med Rehabil* 1991;70:313-6.
12. Wilson RD, Murray PK. *Arch Phys Med Rehabil* 2005; 86:1941-8.
13. Geerts WH, Pineo GF, et al. *Chest* 2004;126(3 Suppl):338S-400S.
14. Pambianco G, Orchard T, Landau P. *Arch Phys Med Rehabil* 1995;76:324-30.
15. Hillbom M, Erila T, et al. *Acta Neurol Scand* 2002; 106:84-92.
16. Sandercock P, Counsell C, Stobbs SL. Update of: Cochrane Database Syst Rev. 2001;(4):CD000119, Cochrane Database Syst Rev. 2005;(2):CD000119.
17. Sherman DG, Albers GW, et al. *Lancet* 2007;369:1347-55.
18. Prescribing information, Arixtra.
19. Donat F, Duret JP, et al. *Clin Pharmacokinet* 2002;41 Suppl 2:1-9.
20. Nutescu EA, Helgason CM. *Pharmacotherapy* 2004;24(7 Pt 2):82S-87S.
21. Eriksson BI, Bauer KA, et al. *NEJM* 2001;345:1298-304.
22. Lassen MR, Bauer KA, et al. *Lancet* 2002;359:1715-20.
23. Bauer KA, Eriksson BI, et al. *NEJM* 2001;345:1305-10.
24. Agnelli G, Bergqvist D, et al. *Br J Surg* 2005;92:1212-20.
25. Buller HR, Davidson BL, et al. *Ann Intern Med* 2004;140:867-73.
26. Elalamy I, Lecrubier C, et al. *Thromb Haemost* 1995;74:1384-5.
27. Hirsh J, Gordon G, et al. *Chest* 2008;133:71S-105S.

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Injury Visits To Emergency Departments and Hospital Discharges In Rhode Island, 2005–2009: Focus On Falls

Patricia M. Burbank, DNSc, RN, and Edward F. Donnelly, RN, MPH

The number of emergency department (ED) visits in the United States reached 119.2 million visits in 2007. [1] The largest percentage of these visits was for people with injury-related diagnoses (42.4 million visits),[1] with falls accounting for 76% of these among adults age 65 and older. [2] Hospital discharge data for injury-related admissions reflects those patients visiting the ED whose injuries were so severe that they warranted admission.

Beginning January 1, 2005, hospitals in Rhode Island have reported patient-level data on visits to EDs to the Rhode Island Department of Health.[3] This report presents summary information for 2005 - 2009 on hospital ED visits and hospital in-patient discharges in Rhode Island for injuries and poisonings, together referred to as "injuries," with emphasis on falls.

Methods

Under licensure regulations, the eleven acute-care general hospitals and two psychiatric facilities in Rhode Island report to the Department of Health's Center for Health Data and Analysis a defined set of data items on each ED visit beginning with visits occurring January 1, 2005. Submission of similar records of hospital discharges began in 1992. The data include patient-level demographic and clinical information. This analysis covers five years of ED visits occurring January 1, 2005 - December 31, 2009, including those where the patient received treatment only in the ED, was held for observation, and was admitted as an inpatient. Principal diagnosis and cause of injury for each patient were extracted from the ED record where available, otherwise from the inpatient record or observation stay record. Diagnoses are coded in ICD-9-CM[4] and were grouped as for published national data.[3] ICD-9-CM external cause of injury codes ("E-codes") used to record the mechanism of injury were grouped according to national standards.[5] Denominators used in the calculation of rates were derived from US Census estimates of the state population for each of the five event-years.

Results

During this five-year period, 2005 – 2009, there were 2,466,757 total visits to hospital EDs in Rhode Island. Of these, 665,773 visits (28%) suffered an injury or poisoning, making injury the most frequently occurring diagnosis for ED visits. Annual ED visits from all diagnoses steadily increased in number from 473,847 in 2005 to 507,331 in 2009. Of the total 723,380 hospital discharges during the five years, 58,895(8%) of these involved an injury.

The highest rates of injury ED visits occurred in persons 85+ years of age with slightly higher rates among females. Many of these injuries were severe and resulted in hospital admissions for those in age groups 65 years and older; those ages 85+ had the highest actual number and the highest rate of injury discharges from hospitals. (Figure 2) Falls were the most commonly reported injury among patients seen in hospital EDs, which resulted in 26%

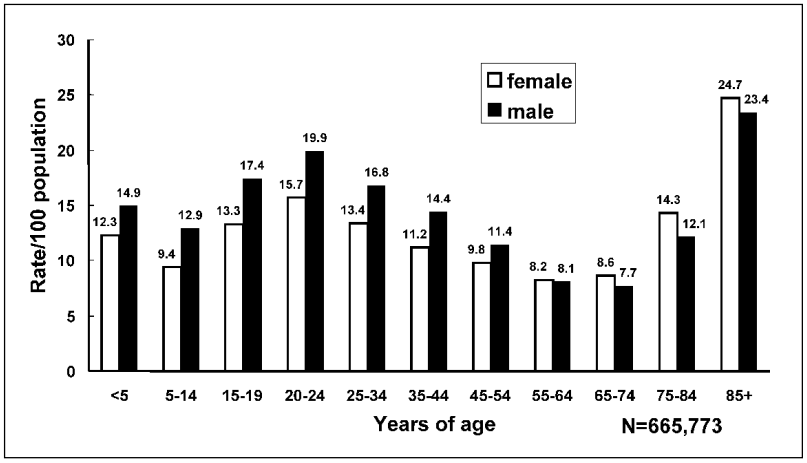

Table 1. Sex and Age group-specific average annual rates of injury ED visits per 100 population, Rhode Island, 2005-2009

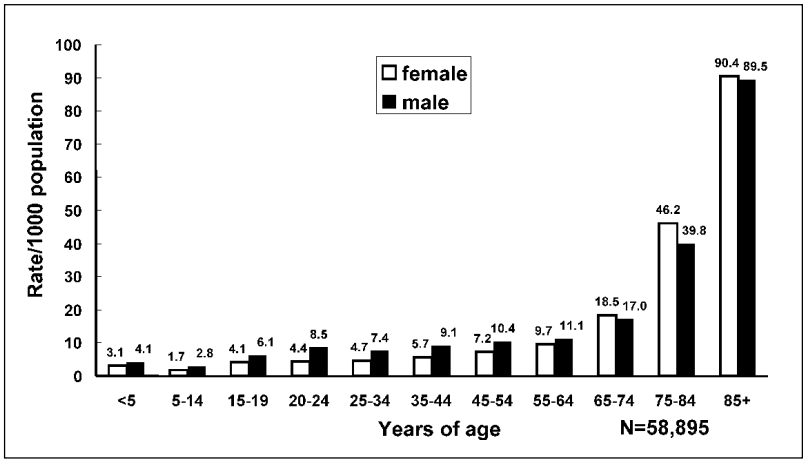

Table 2. Sex and Age group-specific average annual rates of injury discharges per 1,000 population, Rhode Island, 2005-2009

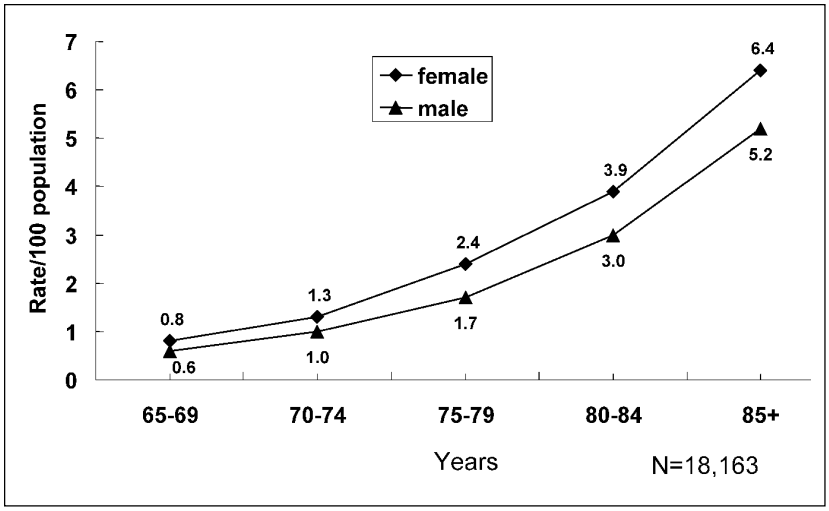

Table 3. Specific rates of fall discharges in older persons per 100 population by sex by age group, Rhode Island, 2005-2009

of all visits in Rhode Island from 2005 - 2009 and 43% of hospital discharges due to injury. Next most common were poisoning (10%) and motor vehicle and other transport injuries (7%). [Children are a major part of poisonings seen in the ED but not in discharges. Over 25% of poison visits and about 22% of poison discharges are in males 25-64. The poisoning category includes drug overdoses regardless of the source of the drug, thus the high numbers in middle age males. If an older person takes too many pills, it's an overdose. If the pills are taken as intended, resulting adverse effects are not included in poisonings in this analysis.]

Specific rates of ED visits for falls and fall hospital discharges increase dramatically with age, both following the same pattern. Figure 3 illustrates the increased rate of fall discharge with slightly higher rates among females in all the older age groups.

Discussion

The availability of statewide patient-level records on hospital ED visits and hospital discharges in Rhode Island has broad implications for public health efforts in our state. Studies have shown fall prevention measures such as exercise and Vitamin D are effective in reducing falls by as much as 30%. [6,7,8] It is hoped that future analyses will show a reduction of injury-related visits to EDs and hospital discharges, reflecting statewide success at reducing falls and preventing injuries.

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References

1. CDC FASTSTATS – Emergency Department Visits. 2010. www.cdc.gov/nchs/fastats/ervisits.htm
2. National center for health statistics, Health, United States, 2009: With special feature on medical technology. Hyattsville, MD, 2010. www.cdc.gov.nchs/data/hus/hus90.pdf#090
3. Williams KA, Buechner JS. Utilization of hospital emergency departments, Rhode Island, 2005. *Medicine & Health / RI* 2006; 89:415-6.
4. Public Health Service and Health Care Financing Administration. *International Classification of Diseases, 9th Revision, Clinical Modification*, 6th ed. Washington: Public Health Service, 1996.
5. National Center for Injury Prevention and Control, Centers for Disease Control and Prevention. Recommended framework of E-code groupings for presenting injury mortality and morbidity data (February 1, 2007). http://www.cdc.gov/ncipc/whatsnew/matrix2.htm.
6. Tinetti ME, Baker DI, et al. A multifactorial intervention to reduce the risk of falling among elderly people living in the community. NEJM *1994; 331*:821-7.
7. Day L, Finch CF, et al. Modelling the population –level impact of tai-chi on falls and fall-related injury among community –dwelling older people. *Injury Prevention* 2010;July 19.
8. Kalyani RR, Stein B, et al. Vitamin D treatment for the prevention of falls in older adults. *J American Geriatrics Soc 2010;* 1299–310.

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Fecal Incontinence

Leslie Roth, MD

A 74-year old woman with a medical history of hypertension, diabetes, and urinary incontinence comes for an annual exam. She feels well, has no physical complaints, and has been healthy since her last visit. She reports her urinary incontinence has improved, but mentions that she sometimes has "accidents" with stool. Her obstetrical history is significant for 3 vaginal deliveries, one with a 3rd degree tear. She had no difficulties with fecal control when she was younger. She reluctantly admits this has been going on for many years but she has been too embarrassed to talk about it. When asked how often this happens, she says often enough that she has adjusted her lifestyle. She tries to stay home as much as she can, has her friends come to her, and avoids going any place where a bathroom is not readily accessible.

Introduction

Fecal incontinence affects an estimated 2-20% of the general population, and up to 50% of the elderly and institutionalized population.[1] Patients with incontinence tend to suffer in silence; they often do not seek help because of embarrassment and stigma. They often become confined to their homes because they are afraid of having an "accident". Although this is not a life-threatening condition, the psychological, emotional, and social impact can be devastating.

Background & Anal Physiology

Normal bowel control involves the coordinated interaction among multiple different neuronal pathways and the pelvic and perineal musculature. Normal defecation is started by distention of the rectum which stimulates pressure receptors located on the puborectalis and pelvic floor muscles. This stimulates the **rectoanal inhibitory reflex** (**RAIR**) which causes relaxation of the internal anal sphincter. Defecation occurs unless there is voluntary contraction of the external anal sphincter and levator ani muscles.

Etiology & Differential Diagnosis

Decreased ability to control bowel movements may be related to: alterations in bowel motility; stool volume and consistency; compliance of the rectum; mental awareness; neural pathways; pelvic floor muscles; and anal sphincters. Incontinence occurs when one or more of these are altered without adequate compensation.

There are numerous etiologies of fecal incontinence, some of which may be reversible. It is important to determine all possible sources in order to offer appropriate management.[2,3]

Common causes include:

1. Medications: Many medications can alter bowel motility causing diarrhea or constipation, resulting in incontinence.
2. Obstetrical injury: Direct tear of the sphincters occur in 0.6% of deliveries, but occult injuries can be seen on ultrasound in 20-35% of all deliveries. These patients can compensate when they are younger, but as they age, continence decreases.
3. Trauma: Pelvic fractures, insertion of foreign bodies, spinal injuries, or perineal lacerations.
4. Diabetes
5. Radiation
6. Stroke/Brain tumors
7. Dementia
8. Multiple sclerosis/Muscular dystrophies/Myasthenia gravis
9. Amyloidosis

Evaluation and Work-Up

A thorough history should include:

1. Incontinence to gas, liquid, and/or solid stool
2. Frequency of stools
3. Frequency of incontinent episodes
4. Consistency of stools
5. Awareness of the incontinent events
6. Obstetrical history (episiotomies, forceps, multiparity)
7. Previous surgery (prolapse, urinary incontinence, hemorrhoids, fissure, bowel resection)
8. Sexual history (anal sex, causing dilation or injury of internal anal sphincter)
9. CNS disorders (peripheral neuropathy, back injury)
10. Chronic diseases (Diabetes, Crohn's, Ulcerative Colitis, Irritable bowel syndrome)
11. Medications

The physical exam should include a detailed inspection of the anus. The exam should seek evidence of scarring, trauma, fistulas, or prolapse. During the digital rectal exam, the patient should be asked to squeeze and relax during exam to allow assessment of squeezing and resting sphincter tone. The work-up should begin with evaluation of the rectal mucosa with a rigid or flexible procto-sigmoidoscope to look for tumors, inflammation, prolapse, hemorrhoids, or infectious coli-

tis. Once these are ruled out, a specialist can do further testing to delineate other causes of fecal incontinence.

Diagnostic Testing

Anal Manometry: A small catheter is inserted in the anus to measure the resting and squeeze pressures of the sphincters. A small balloon on the end of the catheter can test for the RAIR and compliance of the rectum.

Defecography: Radiologic imaging of the act of defecation, allowing visualization of the anorectal angle; degree of evacuation; and the presence or absence of rectal prolapse, rectoceles, enteroceles, and internal intussusception.

Ultrasound: Allows 3-dimentional visualization of the anal sphincters. This is a useful test which can demonstrate defects or scars in the anal sphincters, as well as the thickness of the perineal body.

Pudendal Nerve Latency Time: Used to evaluate nerve damage to the pelvic floor. Measures the time from the electrical stimulus of the pudendal nerve to the onset of the electrical response of the pelvic floor muscles.

Treatment

The choice of therapy depends on the cause of incontinence, any anatomical defects, and the degree of neurologic damage. Treatment should be tailored for each patient and realistic goals should be set.[1]

Initial steps should usually include dietary modification. Patients should be encouraged to keep a food and bowel movement diary, looking for connections between foods and accidents. Patients should avoid foods that cause diarrhea or accidents. All patients should be encouraged to avoid caffeine, which increases colonic motility and augments fluid secretion in the small bowel.[1]

Next, patients can increase their stool consistency and decrease stool frequency by eating more fiber, which helps bulk up stool, making it firmer and easier to control. Patients with diarrhea should consume fiber with limited water to increase stool consistency. Additionally, anti-diarrheal agents can help slow intestinal transit time, allowing for increased fluid absorption and increased stool consistency. Loperamide (Imodium) in low dose (one every other day) has been shown to increase the resting internal anal sphincter pressure and can help with minor fecal incontinence.[4]

Biofeedback, or pelvic floor physical therapy, can give the patient better information about physiologic activities that are under the control of the nervous system but not always clearly or accurately perceived by the patient. The three components of biofeedback include: exercising the external sphincter muscle, discrimination training of rectal sensation, and training synchrony of the internal and external sphincter responses during rectal distension. Beneficial effects of biofeedback can be seen in up to 75% of patients and the therapy is noninvasive. However, biofeedback requires a dedicated therapist and a competent, motivated patient for optimal outcomes.[5]

Surgical treatment can be an option for many patients who are not satisfactorily helped by medical therapy, or for whom specific indications exist. For example, patients with anterior sphincter defects and adequate residual muscle mass (usually caused by obstetrical injury) can be offered an overlapping sphincteroplasty, a low-cost operation with a relatively short hospital stay. The most commonly noted adverse reaction is pain from the perineal wound. Sphincteroplasty has an immediate post-operative 50-80% success rate for solid and liquid stool control, but deteriorates to 26-57% at 3-4 year follow-up. The declining function may be attributed to degeneration with aging, stretching of the scar, or progressive pudendal nerve deterioration. Prior to choosing surgical intervention, patients need to be aware that the resulting control will never equal the level prior to injury.[6]

Another option is an artificial anal sphincter, an implantable silicone cuff balloon filled with fluid that encircles the anus. A pump is placed in the scrotum or labia that can be deflated for defecation. This is the best option for patients with substantial sphincter injury for whom other repairs are not possible. The success rate is 49-82% but there is a removal rate of 19-38%. The intention-to-treat success rate is 53%.[7]

Sacral Nerve Stimulator is used for urinary incontinence and was found to be helpful in fecal incontinence as well. An electrode is placed through S2, S3, S4 sacral foramina to stimulate the pelvic floor muscles. Numerous studies have shown its effectiveness, and **the Federal Drug Administration (FDA)** approval for use in fecal incontinence is anticipated in the near future. Patients are first evaluated, using a temporary electrode that is left in place for 3 weeks. If incontinence has significantly improved during this period, a permanent stimulator is placed subcutaneously in the gluteal area. The mechanism of action is unclear as it not only works on the pelvic floor but also on the entire colorectum and anus. An advantage over the external anal sphincter is that this device does not have to be turned "off" to defecate. There is a 70-90% success rate with minimal morbidity although long term follow-up is not yet known. This may be a very good option in the near future.[8]

For patients who are not suitable candidates for surgery or have failed other options, a trial of daily suppositories or enemas is reasonable to clean out the lower colon and rectum to help avoid or eliminate accidents. This simple solution may allow a patient to resume activities without the fear of an accident.

A permanent stoma is an option for patients who have experience failed attempts at sphincter-preserving procedures, radiation, or who have major comorbidities. A permanent stoma can provide patients with relief from the symptoms associated with fecal incontinence. It can drastically improve quality of life if patients are accepting of a stoma. Some patients with a permanent stoma can irrigate their colostomy and have scheduled function, allowing them to wear a colostomy cap instead of an appliance. Eighty-three percent of patients with permanent colostomy report substantial improvement in lifestyle, and 84% of patients would choose to have the stoma again.

Conclusion

This 74-year old woman underwent testing and was found to have a sphincter tear. She was started on fiber supplements and experienced improved control, but continued to have ac-

cidents. She underwent a successful sphincteroplasty and has not had an accident of solid or liquid stool in the past 2 years. She is happy that she spoke with her doctor, and her life has improved greatly.

Most patients will avoid discussing fecal incontinence. It is imperative to put patients at ease to elicit open, honest communication about this under-reported condition. Asking about fecal and urinary incontinence routinely as part of the annual review of systems is strongly encouraged. A careful and thoughtful history is the important first step in the evaluation of fecal incontinence. The key to helping patients lies in eliciting the symptoms and educating patients that fecal incontinence is treatable, that diagnostic tests exist, and that treatment strategies (other than a permanent stoma) are available.

References

1. Tan, JJY, Chan, M, Tjandra, JJ. Evolving therapy for fecal incontinence. *Dis Colon Rectum* 2007; 50:1950-67.
2. Damon H, Bretones S, et al. Long-term consequences of first vaginal delivery-induced anal sphincter defect. *Dis Colon Rectum* 2005; 48: 1772-6.
3. Galandiuk S, Roth LA, Greene QJ. Anal incontinence - Sphincter ani erepair. *Langenbeck Arch Surg* 2009; 394:425-33.
4. Ehrenpres ED, Chang BA, Eichenwald BS. Pharmacotherapy for fecal incontinence. *Dis Colon Rectum* 2006; 50:641-9.
5. Heymen S, Scarlett Y, et al. Randomized controlled trial shows biofeedback to be superior to pelvic floor exercises for fecal incontinence. *Dis Colon Rectum* 2009; 52: 1730-7.
6. Bravo Gutierrez A, Madoff RD, et al. Long term results of anterior sphincteroplasty. *Dis Colon Rectum* 2004; 47: 727-32.
7. Wong DW, Congliosi SM, et al. The safety and efficacy of the artificial bowel sphincter for fecal incontinence. *Dis Colon Rectum*; 45:1139-53.
8. Michelsen HB, Thompson-Fawcett M, et al. Six years of experience with sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum* 2010; 53:414-21.
9. Jorge JMN, Wexner SD. Etiology and management of fecal incontinence. *Dis Colon Rectum* 1993; 36: 77-97.
10. Matsuoka H, Mavrantonis C, et al. Postanal repair for fecal incontinence. *Dis Colon Rectum* 2000;43:1561-1567.
11. Devesa JM, Rey A, et al. Artificial anal sphincter. *Dis Colon Rectum* 2002;45:1154-63.
12. Osterberg A, Graf W, et al. Persults of neurophysiologic evaluation in fecal incontinence. *Dis Colon Rectum* 2000;43:1256-61.
13. Gooneratne ML, Scott SM, Lunniss PJ. Unilateral pudendal neuropathy is common in patients with fecal incontinence. *Dis Colon Rectum* 2007; 50:449-85.
14. Fang DT, Nivatvongs S, et al. Overlapping sphincteroplasty for acquired anal incontinence. *Dis Colon Rectum* 1984;27:720-2.
15. Varma MG, Brown JS, et al. Fecal incontinence in females older than aged 40 years. *Dis Colon Rectum* 2006; 49:841-51.
16. Venkatesh KS, Ramanujam PS, et al. Anorectal complications of vaginal delivery. *Dis Colon Rectum* 1989;32:1039-41.
17. Rasmussen OO, Buntzen S, et al. Sacral nerve stimulation in fecal incontinence. *Dis Colon Rectum* 2004;47:1158-63.
18. Belmonte-Montes C, Hagerman G, et al. Anal sphincter injury After vaginal delivery in primiparous females. *Dis Colon Rectum* 2001;44:1244-8.

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Discussion of product not labeled for use under discussion or investigational:

Sacral nerve stimulator

9SOW-RI-GERIATRICS-112010

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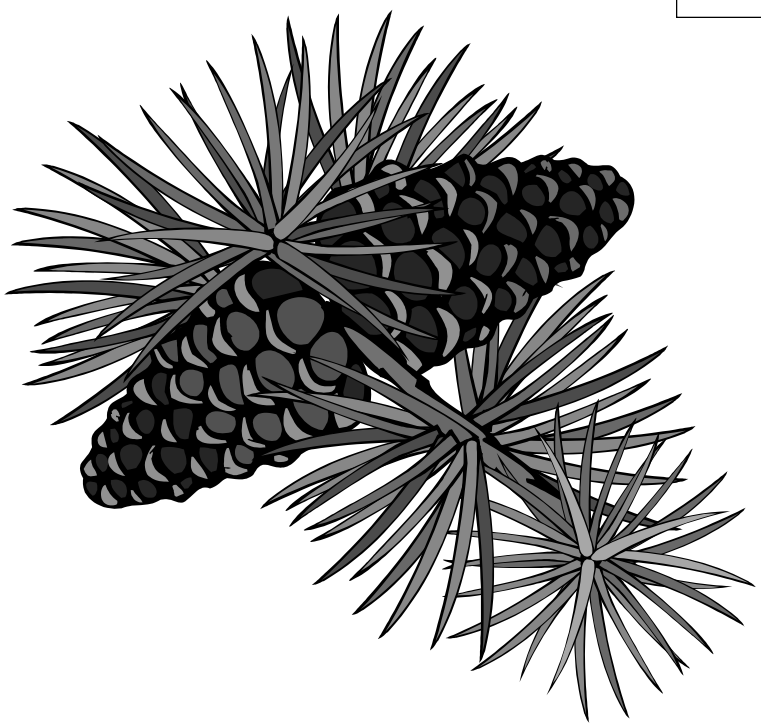

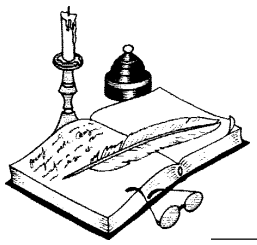

Physician's Lexicon

Ten You Can Count On

As unlikely as it may seem, the digital examination and the digital computer share a linguistic ancestor: *digitus*, the Latin word for finger. It is the descendent of an Indo-European root meaning 'to show', from which we also get such words as indicate and index. Time and technology have obscured the ancestral line from the ten fingers to the decimal counting system and ultimately to the ones and zeros forming a binary number, which employs only one of the nine Arabic numerals but is nevertheless said to comprise a series of digits. The word, finger, comes from a root meaning five, which also begat *penta* in Greek and *quintus* in Latin.

Students of anatomy know the little finger as *digitus quintus*, but tradition has given to the fingers names richer in meaning than their numerical designations. The little finger was known to the Romans as the auricular finger because of its utility in cleaning the ear. In Old English it is the *earclænsend* finger. The Dutch word for this finger, *pinkje*, found its way into the Scottish dialect as pinkie, a term used to indicate something very small.

A Roman belief held that the heart receives blood directly from a *vena amoris* arising from the fourth finger on which one traditionally places a wedding band. In his *Etymologies*, Isidore of Seville observes that physicians use this ring finger or gold finger to apply salves, hence *digitus medicinalis* or, in Old English, *læce* or leech finger.

The middle finger, the *digitus summus* or tallest finger in Latin, has acquired a colorful reputation from its use in gestures of derision, hence the nickname *digitus impudicus*, the shameless finger. Borrowed by the Anglo-Saxons, the name appears in Old English as the *æwiscberend* finger, the shame-bearer.

The index finger; so named from its use in pointing (*L. indicare*), is the *scytefinger* or shooting finger in Old English, presumably from its role in pulling the bow-string. The name might well apply today when the fingers form a make-believe pistol with the *scytefinger* extended.

The word, thumb, can be traced to an Indoeuropean root meaning 'to swell', from which we also get thigh, tumor, and thousand. The Romans called it *digitus pollex*, the powerful finger (from *pollere*, to be powerful), figuratively deployed to subjugate those under it.

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Rhode Island Department of Health
David Gifford, MD, MPH
Director of Health

Vital Statistics

Edited by Colleen Fontana, State Registrar

Rhode Island Monthly Vital Statistics Report Provisional Occurrence Data from the Division of Vital Records

Underlying Cause of Death	Reporting Period			
	November 2009	12 Months Ending with November 2009		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	200	2,356	224.2	3,324.5
Malignant Neoplasms	179	2,238	213.0	6,317.5
Cerebrovascular Diseases	41	433	41.2	834.5
Injuries (Accidents/Suicide/Homicde)	54	586	55.8	9,873.5
COPD	30	521	49.6	312.5

Vital Events	Reporting Period		
	May 2010	12 Months Ending with May 2010	
	Number	Number	Rates
Live Births	1,010	12,137	11.4*
Deaths	805	9,123	8.5*
Infant Deaths	(6)	(77)	6.3#
Neonatal Deaths	(4)	(63)	5.3#
Marriages	549	6,030	5.6*
Divorces	160	3,153	3.0*
Induced Terminations	363	4,225	348.1#
Spontaneous Fetal Deaths	42	693	57.1#
Under 20 weeks gestation	(38)	(620)	51.1#
20+ weeks gestation	(4)	(73)	6.0#

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,067,610.

(c) Years of Potential Life Lost (YPLL).

Note: *Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.*

* Rates per 1,000 estimated population
\# Rates per 1,000 live births

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Ninety Years Ago, November 1920

The year 1920 marked an era before malpractice suits. In "Diagnosis and Treatment of Gall Bladder Disease," Charles O. Cooke, AM, MD, advised readers to conduct routine physical examinations. "I recall one patient whom I anaesthetized for another surgeon in which failure to examine the heart led to a needless exploratory operation on a normal gall bladder."

In "Case Report: Salivary Calculus," James W. Leech, MD, described a 52-year old woman who complained of "swelling and sores in the right neck of a few days' duration." When, eighteen months before, she had had swelling in her jaw, a physician in another state advised "extraction of teeth, followed by vaccine injections, the nature not known." The swelling subsided in 2 to 3 weeks. This time, "with lachrymal probes the opening was enlarged and a Eustachian whale-bone bougee introduced the entire length of the duct into the gland where a grating sensation made certain the presence of a salivary calculus." A few days later, healing was complete.

Harvey B. Sanborn, MD, in "Analysis of Wasserman Reactions," discussed the interpretation of partial readings.

Fifty Years Ago, November 1960

Alfred A. Argrist, MD, Professor and Chair, Department of Pathology, Albert Einstein College of Medicine, presented the 13th Annual Doctor Isaac Gerber Oration: A Pathologist's Experience with Death." He concluded: "Let us foster a rational satisfying equanimity for the event of death" and strive to "live a creative life and do some good which will live after us."

Hyman Goldman, MD, Orthopedic Surgeon, Poriah Government Hospital, Israel, presented at the 149th Annual Meeting of the Rhode Island Medical Society: "Report of an Orthopedic Survey of 5,000 Israeli children." Discussing scoliosis, he noted the U shape of Israeli classrooms: no child has a front seat. But children who habitually sat to the right of the teacher showed scoliosis to the right; children who sat to the left showed scoliosis to the left. As to whether the curve followed a political bent, Dr. Goldman concluded: "..we must confess that we did not discover more curves to the left in the pink-tinged kibbutzim."

J. Merrill Gibson, Jr, MD, described "Spontaneous Rupture of an Umbilical Hernia Manifested by Severe Hemorrhage" in a 40-year old man.

Robert A. Brogan, MD, and Howard J. Morrison, MD, in "Fanconi-De Toni-Delire Syndrome," described a boy who died at 4 year, 5 months. The autopsy "revealed crystalline deposits in liver, spleen, kidney and lymph areas."

Twenty-Five Years Ago, November 1985

Seebert J. Goldowsky, MD, Editor, discussed "The Next Great Need;" specifically, the need for long-term care insurance. President Reagan had just announced a plan to spur private insurers to enter this market.

In "Case Records: Rhode Island Hospital Clinicopathological Case," Tom J. Wachtel, MD, George F. Meissner, MD, and David O. Williams, MD, Editors, presented the case of a 77-year old retired painter, admitted with fractures of the left hip. He had received radiation therapy on his face for basal cell carcinomas, and had developed right facial palsy. Three months before, he developed hoarseness, dysphagia with solids, and impaired vision in his right eye. After 106 days in the hospital, he died. The diagnosis after autopsy: "poorly differentiated squamous cell carcinoma, probably of nasopharyngeal or nasal sinus origin…"

Toussaint A. Leclerq, MD, and Rosalie Bolton, MD, in "Indications for CT Scanning in Benign Head trauma," urged a liberal policy toward CT evaluations of head trauma.

Michael L. Linenberger, MD, and Robert E. Knisley, MD, discussed the "rare occurrence" of "IgD Myeloma with Plasma Cell Leukemia."

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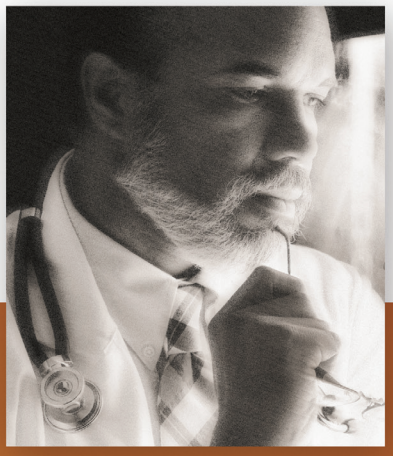

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