Medicine & Health
RHODE ISLAND

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ALLIANCE - affiliation, association, marriage, relationship

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COLUMNS

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Commentaries

The Surgeon General: Why not have one?

I realized recently that I didn't know the name of the US Surgeon General. This is a political statement, both by me and by the Bush administration. They like their appointees to keep out of the limelight. They like their administrators to focus on issues that can't attract attention. First Ladies support reading, not combating teen pregnancy or health ignorance. Surgeon generals support good health. In the recent past they took on the cigarette industry, sexual mores that led to pregnancy and venereal disease, the effects of poverty on health and other issues that are the heart of public health in the United States. Nowadays the focus is different. The goal is to avoid publicity that reveals anything amiss. It is a policy of corruption of the soul.

The office of Surgeon General was created in 1798 to attend to the health of the merchant marines. In 1870 it became a position similar to that of today. The current Surgeon General advises the Under Secretary of Health. Exactly what advice he gives may be evident by the positions he's so boldly staked out. As best I can tell from reviewing the Surgeon General's website, he supports the importance of obtaining a family history when evaluating a patient. That took the calendar year 2003. And he supports being a good parent. In fact, the Surgeon General declared 2005 to be The Year of the Healthy Child, a bold political move that undoubtedly attracted a lot of raised eyebrows. He even pioneered "whole world without tobacco day." Who said this was a man afraid of controversy? Having advanced these two forays into the public realm, he's either resting or thinking up another mind-boggling sally into the morass of public platitudes.

The current Surgeon General, the first in 30 years or so whose name I couldn't think of, has an interesting background. He was a high school dropout from my own neighborhood, who went to community college in the Bronx, and ended up graduating at the top of his class from UCSF, a distinguished medical school. He then trained there, did a fellowship, obtained an MPH, and became a general surgeon with an interest in trauma. This Horatio Alger story is an inspiration. His bio-sketch on the official website notes that he has a "large number of publications" to his credit and was a professor of surgery at the University of Arizona. Since this large number of publications in the peer-reviewed realm was 8, somewhere in the ballpark of beginning assistant professor, I assume that his promotion to full professor either reflected a lot of non-academic credits, or weak academic criteria. Since his administrative public health roles have been quite impressive, I assume the professorship reflects his contributions to the Arizona community. This would be irrelevant if there was some justification for this person's promotion to Surgeon General other than his impressive rise from high school dropout to leader of the Public Health Service of our country. Being an accomplished administrator in Arizona and being given the bully pulpit in Washington, DC, are different.

The year of the healthy child includes 12 important ideas. These include (and, to quote Dave Barry, the humor writer, "I am not making this up") fathers should be role models; children shouldn't be exposed to violence; children should have pediatricians and get their vaccinations; they should have healthy diets; they shouldn't smoke; they should begin a "habit of good oral health;" they should be given positive feedback; they should be put in safety belts in cars; etc.

I'm not sure where poverty, violent neighborhoods, poor schools, lack of health insurance, absent dental care, AIDS and single parent households fit in. The fact that 44 million Americans, most of whom work, have no health insurance and that over 60 million are underinsured isn't as big a problem as it seems. The notion of a baby without food, health care or a viable future is apparently too unpleasant to consider. The idea that a public official, one who wears a uniform representing the US Public Health Service, should have to deal with such an indelicate problem would go against the grain. It might mean having to confront a faulty system, maybe making some suggestions for improving it. Announcing to the world that our system is flawed.

Our health care system, in crisis and chaos for a decade, careens from bad to worse. We are a model to the world of how to cater to the rich and trample on the poor. We waste more money on health care than most countries pay for public health. Our Surgeon General, no role model to the medical world, faced with a disaster getting worse, takes on the role of "father knows best." Health problem? What problem? Kids just need some strong guidance and role models. No role models? Well, that's not good. Get some.

The problem is that this Surgeon General may be a role model. He's the role model we see denounced in "Enemy of the People" by Ibsen. He's the complicit, "go along to get along" person. He's the epitome of a public policy focused on not making waves rather than making things better. And I don't even know him! I've never seen him, heard him speak. I've read his *New England Journal of Medicine* article, but it's hard to take advice from someone who is so far removed from the medical world.

Maybe in real life he's an ardent advocate for the poor, sick and helpless and he fears that if he's replaced, it might be by someone who may advocate *against* the downtrodden.

Joseph H. Friedman, MD

A consumptive finds salvation in Nature

Tuberculosis (TB) accounted for about one-fourth of all deaths in greater London during the early decades of the 19th Century. While the disease was substantially more common, and certainly more rapidly fatal, in those living in the impoverished, intensely congested inner precincts of the city, even the wealthy of London were occasionally afflicted. And when they were diagnosed with TB, many were advised to seek warmer, more congenial climates. When the poet John Keats (1795-1825), a physician himself, became fully aware of his TB, he left England to seek a cure in sunny Italy. Anton Chekhov (1860-1904), the Russian playwright-physician, fled to the Southern Crimea to alleviate his TB. And Robert Louis Stevenson (1850-1894) even voyaged to the southwest Pacific in attempting to subdue his disease.

Some consumptives sought hot, dry climates; others, isolated islands; still others the cold, crisp air of remote Alpine villages. Susan Sontag, in *Illness as Metaphor*, commented on this geographic assortment and concluded that "their very diversity suggests what they have in common: the rejection of the city."

But when did the curious notion arise that moving to another site might be curative? The Hippocratic writings, over two millennia old, certainly mention the rehabilitative value of furloughs to the sacred temples of Esclapius, and vacations were always intuitively regarded as a means of restoring health, but it was not until the 19th Century that the formal idea of "a rest cure" took hold.

A German botanist, Herman Gustav Brehmer, developed mild TB as a young man. He wisely abstained from the more drastic forms of therapy such as repeated blood-letting, mercurials or the use of harsh cathartics - and elected, instead, to take an ocean voyage. His travels took him, ultimately, to the Himalayan mountains where he rested for months. And whether it was the hillside climate, the stress-free existence, the fresh air, his Buddhist readings or just a natural remission of the disease, Brehmer returned to Germany clinically cured of his consumptive disorder. He was convinced that he had discovered a novel way of combating TB. He returned to his medical studies with renewed vigor. His 1854 doctorate thesis defended his new therapeutic conjectures.

Brehmer explored the mountainous region of Southern Germany seeking a site that would combine both remoteness from the stresses of urban existence and natural beauty. He finally selected a mountainous village, Gorbersdorf, in the Prussian province of Silesia. And in 1859, he established a retreat "away from the physical and moral ills of the town."

He chose the Latin word, *sanare,* meaning to heal, to define his establishment, calling it a sanatorium. He zealously attended to the smallest environmental details. The result was an intricate complex of mountainside gardens, picturesque walks through the neighboring forests, grottos, ponds stocked with trout, carriage paths through dense woods and even a model dairy farm to provide an atmosphere of uninterrupted tranquility. A nurturing, benevolent Nature was to be the guardian healer of Brehmer's patients.

Brehmer's new horticultural concepts departed from the established European principles of gardening. Instead of rectangular flower beds, geometrically distributed shrubs, benches, paths and fountains, the sanatorium gardens employed curved boundaries, undulant land profiles, meadows abundant with wild flowers and, in general, a landscape that enhanced rather than replaced the natural features of an unsullied preserve.

Brehmer's remote Eden recruited his patient's need for spiritual renewal. As part of their therapeutic regimen, patients were encouraged to walk, sun bathe, (later to be called heliotherapy) and undertake some modest gardening. They slept in unheated porches with an abundance of cold, fresh air. Diet was prudent and uncomplicated, free of spices, heavy foods or alcohol. Smoking was forbidden. Any dancing, or any other factor which might excite the carnal senses, was also enjoined. Brehmer's retreat became a huge commercial success and the Black Hills of Bavaria as well as the Alps were soon congested with resorts designed expressly for those seeking a more humane form of tuberculosis cure – and who could afford it.

The concept of the sanatorium, as a means of exploiting nature, spread rapidly. In the United States, the first such establishment was created by Edward Trudeau in 1882 in his Adirondack Cottage Sanatorium on Saranac Lake in upper New York. Within a few decades, there were more than 400 establishments in the United States catering to the needs of a large tuberculous population. In Rhode Island, an impressive colony for those suffering from TB was constructed within the state forest in the northwestern corner of the state adjacent to Wallum Lake.

The sanatorium movement in the United States, often funded by public funds, was necessarily more egalitarian than its European counterpart; and in conjunction with other public health measures, TB gradually receded in this country (although in recent years the incidence rate of TB in the larger cities has sharply increased).

The sanatoria provided a restful, unstressed sanctuary for the TB patient. The process functioned well, but sooner or later the former TB patient had to return to the squalor from whence he came; and without support systems he frequently relapsed.

The sanatoria helped to sanitize the prevailing image of TB; and the dawn of the 20th Century witnessed a new body of fictional literature based upon the imagined lives of those confined to isolated communities called the sanatoria. These patients, however, were the privileged few; the overwhelming majority of TB sufferers, in truth, lived within the stark realities of a slow, relentless pestilence which drained their lives of energy and spirit. In Dickens' words, it is a disease which "day by day, and grain by grain, the mortal part wastes and withers away, so that the spirit grows light and sanguine with its lightening load, and, feeling immortality at hand, deems it but a new term of mortal life – a disease in which death takes the glow and hue of life, and life the gaunt and grisly form of death."

Stanley M. Aronson, MD

Abstracts. Rhode Island Chapter American College of Physicians, 2005

The following abstracts, in order of acceptance, were selected for oral presentation at the ACP Conference on May 11, 2005, in Warwick, RI.

A Chronic Care Model for Diabetic Care at a Resident Clinic

Catherine Malone, MD; Lynn Bowlby, MD
Rhode Island Hospital and Miriam Hospital

Background: A recent cross-sectional study of 6700 Americans found that patients with chronic illnesses receive only half of the recommended care.[1] Wagner et. al. developed a **Chronic Care Model (CCM)** to improve care of chronic disease, particularly congestive heart failure, asthma and diabetes.[2] The CCM multidisciplinary approach combines community resources, patient self-management support, and clinical information systems. At the Rhode Island Hospital resident clinic (MPCU) we care for 800 patients with type II diabetes. Chronic disease management is challenging in our setting because of socioeconomic barriers, multiple providers, and large numbers of active medical problems. However, clinics similar to ours have improved their treatment of chronic disease using a CCM.

Methods: We created a pilot CCM program to improve treatment of type II diabetes at the MPCU. Ninety-nine patients, identified using ICD-9 codes and resident input, were enrolled in a computerized registry. After each visit, data were updated and a printed summary report was placed in the chart. The reports graphically depict trends in lab values and designate care that is due in a bold font. We educated residents about the program at a noon-conference lecture, in small groups, and via electronic mail. Patients were given educational and self-management materials and received a printed report at each visit. If overdue for an appointment, they were called and rescheduled. The pilot program continued for 6 months.

Results: At baseline, 30% of patients had a HgA1C of less than 7% and 54% met cholesterol treatment guidelines. These values did not significantly change over the course of this intervention but the number of patients who had these labs checked increased. Other parameters of care improved. Diabetic education increased from 14% to 23% and nutritional education from 8% to 16%. Documented foot exams improved from 33% to 38%. The number of patients on an ACE-I or ARB increased from 76% to 90% and the number of patients on aspirin went from 42% to 50%. The retinal exam rate did not change.

Conclusions: Our data are concordant with national data showing that while our providers are knowledgeable about the guidelines for diabetic treatment, a minority of patients receive the recommended treatment. By organizing each patient's diabetic information into an easily updated report we improved several parameters of care in a short time. This program will now expand to include all diabetic patients in the MPCU.

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Marked Improvements in In-Hospital Outcomes Following Contemporary PCI in Patients with Diabetes Mellitis

Andrew M. Freeman, MD; J. Dawn Abbott, MD; Alice K. Jacobs, MD; Helen A. Vlachos, MS; Faith Selzer, PhD; Warren K. Laskey, MD; Katherine M. Detre, MD, PhD; David O. Williams, MD
Miriam Hospital and Rhode Island Hospital

Introduction: Patients with diabetes undergoing coronary revascularization have worse outcomes when compared to patients without diabetes. Over the past decade, **percutaneous coronary intervention (PCI)** has evolved to include mechanical stents and potent adjunctive antiplatelet agents. It is unknown if these features of contemporary PCI impact morbidity and mortality in patients with diabetes.

Objective: To determine if advances in PCI, including stents and pharmacologic adjuncts, result in improved outcomes for patients with DM

Design: Database cohort study of two registries from 1985-6 (PTCA registry) using angioplasty only and 1997-2001 (Dynamic registry) using stents

Setting: Fifteen cinical centers in North America

Patients: 943 adults with diabetes; 325 from the PTCA registry; 618 from the Dynamic registry

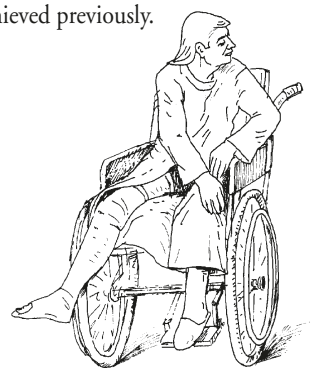
Intervention: PCI using balloon angioplasty only versus PCI

using stents

Measurements: Outcomes in-hospital and one-year post-discharge

Results: Dynamic registry patients were older, had more comorbidities, lower EF (50.4% vs. 57.8%, p<0.0001) and more complex coronary lesions. While fewer lesions were attempted (1.4 vs. 1.7, p<0.001) in the Registry, the stenosis severity immediately after intervention was lower (7.8% vs. 34.4%, p<0.001) with more success. Following PCI, incidences of in-hospital **myocardial infarction (MI)** (1.0% vs. 7.4%, p<0.001), **coronary artery bypass grafting (CABG)** (0.2% vs. 3.1%, p<0.001) and death (1.9% vs. 4.3%, p<0.05) were less in the contemporary Dynamic registry. One year rates of MI (4.80% vs. 11.02%, p<0.001), CABG (6.30% vs. 15.04%, p<0.001) and repeat revascularization were lower in the Dynamic registry.

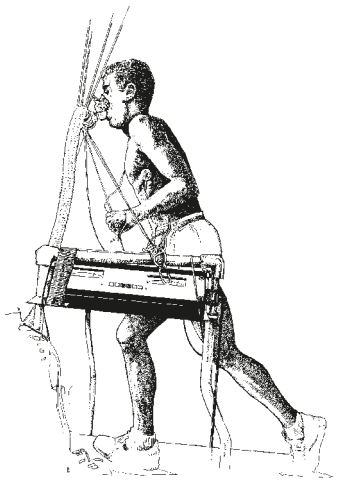
Conclusions: Although patients with diabetes in the Dynamic registry had ore advanced coronary disease, PCI success rates were higher and in-hospital and late adverse events were lower. Thus, contemporary PCI results in better outcomes for patients with diabetes than achieved previously.



CELLULAR IMMUNOTHERAPY UTILIZING LOW DOSE IRRADIATION, BONE MARROW TRANSPLANTATION AND DONOR LYMPHOCYTE INFUSIONS FOR REFRACTORY MALIGNANCIES: A PHASE II STUDY

SHEILA PASCUAL, MD; SAMUEL CHUNG, MD; MEHRDAD ABEDI, MD; LAWRENCE LUM, MD; RITESH RATHORE, MD; KAREN K BALLEN, MD; BIMAL R DEY, MD; GERALD A. COLVIN, DO; PETER J. QUESENBERRY, MD
Roger Williams Medical Center; Massachusetts General Hospital

The quest for effective, yet less toxic means of treating advanced diseases has led physicians searching for the optimal balance between host immune suppression, stable chimerism, effective graft versus tumor response and overall survival. We asked the question "how low can you go?" and approached this from the minimalist view. Born out of murine studies, mini-HLA-identical **bone marrow transplantation (BMT)** using 100cGy as host conditioning followed by non-mobilized peripheral blood **lymphocyte infusion of 1×108 CD3 cells/kg was successful in achieving a complete** responses (CR) in 4 of 11 refractory hematologic malignancy pts (Blood 100:442, 2002). This study has been extended using HLA-haploidentical donors. We evaluated CD3+ cell dose escalation with BMT in pts with refractory malignancies. We have performed a total of 41 HLA-haploidentical BMT with escalation of the CD3+ cell dose up to 2x108cells/kg using G-CSF primed product, with 100cGy total body irradiation. Ages ranged from 16-82 yrs. One treatment related death occurred from grade IV aGVHD. Most patients had a transient infusional haploimmunostorm syndrome believed to be cytokine or immunologically modulated. Of the 29 patients with hematologic malignancies there were a total of 13 responses, with 6 major responses. Three of 6 patients with NHL responded to treatment with 2 of three in a CR and 1 with minimal residual disease, 41+, 31+ and 37+ months respectively. We observed several encouraging responses in pts with refractory AML. We treated 13 pts with AML and have obtained a durable CR in 3 of 12 and transient PR in 7 of 12 evaluable pts. All responses occurred outside of persistent detectable donor chimerism (<5%). Donor cells labeled with indium111analyzed after BMT in one pt showed persistent signal in the bone marrow and spleen. Serial bone marrow biopsies performed in several pts show evidence for large tumor reduction and early resumption of hematopoiesis. In summary, TBI of 100cGy followed by HLA-mismatched transplant is a biologically active therapy for refractory AML and NHL. This well-tolerated outpatient treatment produced minimal toxicity for the majority of patients. Theories on biological effect include an initial graft vs. tumor cell kill, altered host immune response breaking host tumor tolerance, persistent non-detectable microchimerism or a combination of any of the three.



NOVEL PROGNOSTIC FACTOR IN CHRONIC LYMPHOCYTIC LEUKEMIA

Alex V. Danilov, MD; Andreas K. Klein, MD
Memorial Hospital; New England Medical Center

Chronic lymphocytic leukemia (CLL) is a unique malignancy characterized by the accumulation of quiescent lymphocytes in the peripheral blood. Clinical outcomes in CLL are very heterogenous. Multiple efforts have been undertaken to better predict prognosis in each individual case of the disease. In this respect, assessment of the IgV_H mutational status has become the gold standard. Recently, it has been shown that high ZAP-70 (Zeta-chain associated protein kinase – 70 kDa) expression level correlates with low IgV_H mutational status and predicts poor outcome in B-CLL. A variety of molecular pathways (such as bcl-2 and p53) involved in cell cycle control have been investigated in an effort to explain this phenomenon. Dipeptidyl Peptidase 2 (DPP2) is a serine protease known to maintain cells in the quiescent state. In this study we investigated if DPP2 is involved in cell cycle control in B-CLL.

The study included 38 patients with B-CLL and 20 healthy controls. Median age of CLL patients was 67 years. Median time from diagnosis to enrollment in the study was 102 months. 21 patients (55.3%) received treatment before enrollment in the study. Standard Ficoll-Hypaque techniques were used to isolate peripheral blood mononuclear cells from healthy donors and CLL patients. Cells were treated with Val-boro-Pro, an inhibitor of DPP2, harvested after 16-24 hours and resuspended in propidium iodide (PI) buffer. PI uptake was immediately assessed by flow cytometry to evaluate apoptosis. Expression of CD38 in CLL was assessed by flow cytometry, ZAP-70 – real-time reverse-transcription polymerase chain reaction, bcl-2 and p53 – western blot analysis.

In this study specific inhibition of DPP2 resulted in caspase-dependent apoptosis of lymphocytes from all healthy subjects. In individuals with CLL, death of B-lymphocytes (and rescue by caspase inhibitors) was observed in 22 cases (57.9%). In the remaining 16 cases (42.1%) malignant B-cells did not undergo apoptosis upon inhibition of DPP2. We found that CLL cells resistant to DPP2 inhibition-induced apoptosis demonstrated higher levels of expression of ZAP-70. Those patients exhibited worse disease prognosis such as shorter treatment-free period ($p<0.001$), more frequent treatment failure and earlier attainment of the advanced stage of the disease. Between the two groups, we identified no differences in expression of p53 and bcl-2.

Thus, resistance vs. susceptibility to DPP2 inhibition-induced apoptosis can be employed as a novel prognostic factor in CLL.

Assessing Predictors and Colon Cancer Screening in the Insured Population

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Miriam Hospital and Rhode Island Hospital

Purpose: Screening for colorectal cancer has been clearly shown to reduce colorectal cancer incidence and mortality, however many adults remain unscreened. While there have been a few studies published on this subject, mainly using national **Behavioral Risk Factor Surveillance system (BRFSS)** data, there are not many studies on who is getting colon cancer screening in the insured population, where access to medical services is not a major issue. The purpose of this study is to identify characteristics of people who are screened, compared to those who are not screened, in the insured population, age 50 and over.

Methods: Data were collected from Blue Cross Blue Shield members of Rhode Island. Participants were asked to fill out a general health assessment questionnaire while attending a work wellness health fair. The survey was given out from 2003-2004. Database had a total of 4571 records; 1394 records came from participants age 50 or older. Demographical information, cancer screening information and risk factors for colon cancer were analyzed. Bivariate analysis was performed using the chi-square test between the selected factors and colon cancer screening, and multivariate analysis was performed with logistic regression to assess the effects of the factors on screening, adjusting for potential confounders.

Results: Persons age 50 and over who reported having had colorectal cancer screening in the past was 57.2%, versus 42.8% who reported never having had colorectal cancer screening. This is compared to 75 to 89% of people reported having had a recent prostate, pap smear and mammogram test. Controlling for age, sex, income, education, race, and marital status, some of the factors that were associated with colon cancer screening included a personal history of cancer (OR=2.1, CI=1.2-3.7), family history of cancer (OR=1.5, CI=1.1-2.1), physician visit in the last 12 months (OR=3.9, CI=2.3-6.7), current mammogram screening(OR=6.1, CI=2.1-18.1), rectal exams in females (OR=3.7,CI=2.4-6.0), and prostate exam in males (OR=3.8; CI=1.6-9.1).I f demographic factors are looked at separately, age had a strong association to colon cancer screening, with age>=65 having an OR=2.6

(CI=1.5-4.4). Gender also was statistically significant, with females 30% less likely to have had colon cancer screening than males.

Conclusion: Far fewer people are reporting that they have had a colon cancer screening, compared to other cancer screening, such as prostate, breast and cervical cancers. Interventions should be looked at to target those individuals who are less likely to be screened. Health care providers and insurance companies could do more to encourage patients to participate in colon cancer screening.

In Vitro Conversion of Murine Bone Marrow To Muscle

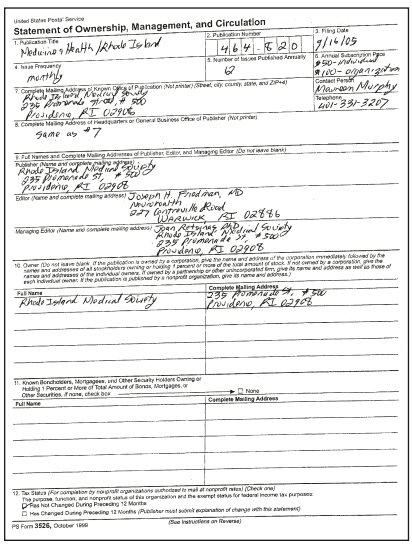
Cannon Milani, MD; Mehrdad Abedi, MD; Deborah A Greer; Bethany Foster; Mark S. Dooner; Peter J. Quesenberry, MD
Roger Williams Medical Center

Background and Objective: There is profound interest in the concept of skeletal muscle regeneration following genetic and environmental insults that render the muscle incapable of proper function. The potential utility of stem cell transplantation for the treatment of muscular dystrophies, disuse atrophy, mitochondrial myopathies, and muscle injury secondary to trauma or athletics is at its infancy. In principle new muscle formation can be described as a process in which mononucleated muscle precursor cells, myoblasts, become activated, differentiate, and fuse to form multinucleated cells called myotubes. The myotubes undergo further differentiation and subsequent innervation to mature into functional muscle fibers. Data suggest that bone marrow cells can differentiate into other non-hematopoietic tissues and participate in regeneration of those organs. Our team along with others have shown that marrow cells following transplantation can differentiate into the cardiotoxin injured skeletal muscle fibers. The signals and the type of the cells involved in this process are not clear. As a result in vitro models can be very helpful.

Experimental Design: In our experiment we employed the C2C12 skeletal myoblast cell line of murine origin to induce myoblast differentiation. C2C12 cells are capable of growing, fusing, and differentiating up to the formation of myotubes in culture. The cell line was obtained from the **American Tissue Culture Collection (ATCC)** and routinely maintained in tissue culture grade flasks. Cells were maintained in growth medium consisting of **Dulbecco's Modified Eagle's Medium (DMEM)** supplemented with 10 % **fetal bovine serum (FBS)** and a 1 % Pen/Strep solution for expansion. However for cell differentiation a 2 % FBS was used. In this media and when confluent, the cells lose their myoblastic potential and differentiate rapidly into contractile myotubes. The differentiation of myoblasts into fused myotubes is stimulated by cell contact and the lack of poorly understood growth factors in fetal bovine serum. Once the C2C12 cultures had been established, 1 million **Whole Bone Marrow (WBM)** cells from **Green Fluorescent Protein (GFP)** transgenic mice were introduced to the culture.

Results: For 2 weeks via the utilization of deconvolutional microscopy, we observed for tube formation and fusion of GFP cells into the myotubes. We noted an incidence of 3 to 10 GFP positive myotubes per chambered slide. The GFP positive myotubes expanded in size and fused with other adjacent fibers.

Conclusion: Similar experiments using fresh myoblast cells to induce muscle differentiation in marrow cells have demonstrated analogous results. These experiments confirm our previous data that there is a population of marrow cells capable of differentiating into muscle fibers, and establishes a new *in vitro* model for further characterization of this phenomenon.



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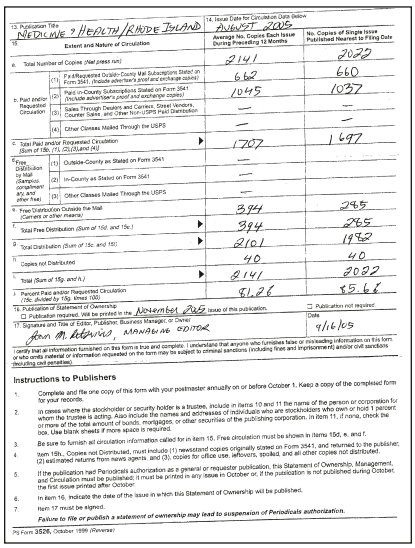

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Neurologic Consequences of Cardiac Arrest and Preventive Strategies

Michelle L. Mellion, MD

Cardiovascular disease is the world's leading cause of morbidity and death. The incidence of cardiac arrest is rising despite use of proven and effective medical and surgical therapies. In the US alone, over 700,000 cardiac deaths will occur this year and half will be related to cardiac sudden death. Approximately 86% of these victims will experience cardiopulmonary resuscitation (CPR). **Return of spontaneous circulation** (**ROSC**) will occur in 17-49%, but most victims will expire at the scene.[1] Despite these dismal statistics, more victims are admitted to the hospital for advanced treatment because of improvements in the quality of the "chain of survival", bystander CPR, establishment of effective police/firefighter responder programs and public availability of automated external defibrillators.[2] Of those patients who are admitted to the hospital, half will die within hours of cardiac causes or other comorbidities. If the victim survives, morbidity and mortality are more likely to be the result of neurologic rather than cardiac injury.[1]

In those patients successfully resuscitated and admitted to the hospital, almost 80% will be in a coma for varying lengths of time, making cardiac arrest the third leading cause of coma. Approximately 40% will enter a persistent vegetative state and 80% die within one year.[3] The overall survival to hospital discharge is 20%.[2] If a patient does survive to discharge without significant neurologic injury, meaning that s/he can participate in rehab or go home, that patient can expect a fair to good quality of life. Studies have shown no significant difference in anxiety, depression, vitality, and general wellbeing between patients and controls. There are, however, significant differences in energy levels, emotional reactions and sleep patterns. Additionally, 11-28% of patients discharged will be cognitively impaired with problems in memory, attention and executive function.[4] These consequences of cardiac arrest are the result of neuronal injury.

Neuronal injury is the result of ischemia and hypoxia which leads to necrotic and apoptotic cell death. Animal models and limited human studies of neonatal hypoxia and cerebral hypoperfusion during cardiopulmonary bypass have shown that brain injury occurs during the event and evolves even after ROSC. The primary sources of cerebral injury are perfusion failure, reoxygenation injury and blood stasis leading to the formation of microthrombi. At the time of arrest, there is perfusion failure. A stop of cerebral circulation depletes the neuronal oxygen stores within 20 seconds and consciousness is lost.[1] Within 5 minutes of complete cerebral ischemia and hypoxia, brain glucose and ATP stores are depleted. Dysfunction of neuronal membrane pumps leads to membrane depolarization, influx of calcium, and activation of lytic enzymes. The loss of cerebral autoregulation leads to prolonged global and multifocal hypoperfusion and to transient global hyperemia due to vasoparalysis.[5]

"...the physical exam, performed at 24 hours and at regular intervals thereafter, is the best tool for predicting meaningful recovery in patients in coma after cardiac arrest"

With the ROSC there are reoxygenation-induced chemical reactions that cause excitotoxicity, mitochondrial damage, and DNA fragmentation that results in primary necrosis or programmed cell death (apoptosis).[1] Cerebral microcirculation is compromised because of increased blood viscosity, endothelial cell swelling, and coagulation activation with subsequent mircrocirculatory fibrin deposition that contributes to prolonged ischemia.[6]

The extent of neuronal injury depends on the duration of ischemia/hypoxia and on premorbid function. Neuronal injury manifests clinically as amnesia, focal or multifocal motor and sensory deficits, spinal cord compromise, seizures, myoclonus, persistent vegetative state or brain death. Patients with a short duration of ischemia/hypoxia, usually less than five minutes, are unlikely to have permanent neurologic deficits and will usually return to their previous functional level.[7] However, patients who have longer events may have seizures, watershed infarcts, or spinal cord infarction. A patient who suffers prolonged, severe, global hypoxic/ischemic insult that results in widespread death of neurons and necrosis of the cerebral cortex will have myoclonus, be in a persistent vegetative state or possibly be brain dead.[7]

Given the range of neurological outcomes, prognosis has a significant effect on the choice of medical treatment and on the family. If a patient wakes up within 24 hours after the event, their neurological prognosis is good. For those who remain comatose, early prognosis can be difficult. Many studies have attempted to validate a reliable method for the correct prediction of outcome. Earlier studies of prognosis in coma after cardiac arrest focused on the initial examination and whether the patient would wake up. One even formulated a mathematical equation (motor response + 3Xpupillary light response + spontaneous eye movements + blood glucose on admission)

to help with early prognosis.[8] The **Glasgow Coma Scale (GCS)**, which is used to evaluate trauma patients, has been easily adapted to aid in early prognosis in nontraumatic coma patients. Unfortunately, an indeterminate GCS (5-9) means an indeterminate prognosis. The GCS does not have a high specificity for determining if the patient will wake up until 3-5 days after admission.[7] Functional recovery was not taken into account until 1985 when Levy and Caronna, et al. followed 210 patients with nontraumatic coma, 150 following cardiac arrest. They performed clinical examinations at days 1,3,7 and 14 and assessed functional recovery at 1,3,6 and 12 months. They observed that the neurologic signs most reliably linked to outcome within the first 24 hours were pupillary light reflex, spontaneous eye movements, and corneal reflex. The presence or absence of a motor response did not make a difference in prognosis until 72 hours after the event.[10] A meta-analysis showed that the absence of the corneal reflex, pupillary response, withdrawal response to pain at 24 hours and no motor response at 72 hours was consistent with a poor prognosis 97% (95% **confidence interval (CI)** 87-100%) of the time.[11] The variables not associated with outcome were verbal response, which is one of the cornerstones of the GCS, age, sex, site of onset (meaning whether the event occurred in the home or in the hospital ICU), cause of coma and paroxysmal activity.[10] No clinical findings strongly predicted good clinical outcome.[11] Even though simple physical examination techniques strongly predicted death or poor outcome in coma patients after cardiac arrest, the clinical exam was useful in prognosis 24 hours after presentation and not beforehand. The reason the clinical exam was not useful acutely is that the exam itself may be difficult to interpret because of sedating medications, paralytics or a patient's comorbidities.[11] In this situation, it is best to try to minimize these confounding factors, by reducing sedation, the effects of paralytics and the use of pain medications; by correcting underlying metabolic abnormalities, and by stabilizing the patient from a cardiopulmonary standpoint. If it is not possible to control confounding factors, objective tests may be helpful, but should not be performed before the clinical examination at 24 hours unless there is suspicion of *status epilepticus* or a structural lesion.

The EEG is not a good tool for prognosis because it is easily contaminated by the use of sedating medications, the ICU environment and the metabolic state of the patient.[12] It is useful in ruling out the possibility of status epilepticus. Additionally, imaging is only useful in ruling out the possibility of stroke or other structural abnormalities. The most reliable objective tool for prognosis is the **somatosensory evoked potential (SEP)**. This test is not influenced by medications, environment or the metabolic state of the patient and it is easy to perform in the ICU. If both cortical responses are absent, that the chance of the patient awakening is less than 1%.[12,13] However, caution needs to be exercised because this test does not take into account functional recovery. Biochemical markers, such as S-100 protein and **neuron specific enolase (NSE)** that assess neuronal tissue injury are under investigation.[14] The physical exam, performed at 24 hours and at regular intervals thereafter, is the best tool for predicting meaningful recovery in patients in coma after cardiac arrest.

A meaningful recovery in survivors of coma after cardiac arrest depends not only on cardiopulmonary resuscitation, but also on cerebral resuscitation. Studies have suggested that just as patients have "stunned" myocardium after cardiac arrest, there may also be "stunned", viable neurons after ischemic/hypoxic cerebral injury.[15] Many different neuroprotective strategies have been tested and are still being developed to help mitigate neuronal injury that occurs during the event and continues to evolve after the ROSC. Pharmacological agents that seemed promising in animal studies, but failed in controlled trials include corticosteroids, barbiturates, inhalational anesthetics and calcium channel blockers. Corticosteroids were used to reduce cerebral swelling; however, in clinical trials they were shown to be ineffective and in fact may worsen cerebral damage because of elevation of serum glucose. Steroids are NOT recommended after arrest even if the head CT shows swelling. Barbiturates reduce cerebral metabolic requirements and have neuroprotective effects when given immediately after cardiac arrest, but are no longer used because of their tendency to produce hypotension and arrhythmias. Calcium channel blockers were believed to improve cerebral blood flow and reduce calcium entry into cells; however, in clinical trials they failed to demonstrate any improvement. [15] Other pharmacologic agents under investigation include inhibitors of neuronal apoptosis, like antiapoptotic proteins Bcl-2 and Bcl-Xl, excitatory amino acid receptor blockers, such as blockade of glutamate with NMDA and AMPA receptor antagonists, and free radical scavengers, such as superoxide dismutase and the use of normoxic ventilation after cardiac arrest.[16] The canine model showed that resuscitation with 21% versus 100% inspired O2 resulted in lower levels of oxidized brain lipids and improved neurological outcome after 24 hours of reperfusion.[17] Also under investigation are agents that improve microcirculation by inhibiting vasocontrictive mediators, leukocytes and coagulation. Improvement in neurologic outcome was achieved in animals with heparin, dextran and rTPA.[6]

Hypothermia is perhaps the most promising neuroprotective strategy. Hypothermia is "a state of body temperature which is below normal in a homeothermic organism". Small clinical trials were performed in the 1960s, but because of management problems and adverse reactions such as arrhythmia, coagulopathy, and sepsis it was not widely used. At that time it was believed that hypothermia must be moderate, <32C. In the late 1980s, animal models showed that mild

Determination of Prognosis in Patients After Cardiac Arrest

Presentation	Cardiopulmonary stabilization Minimize sedation, paralytics and pain medication Correct underlying metabolic abnormalities NO ELECTROPHYSIOLOGIC EXAMS unless suspect status epilepticus or cerebral structural abnormality Document initial clinical exam
24 Hours	Assess pupillary light reflex Corneal reflex ➡ ABSENT = POOR prognosis Withdrawal response to pain
24-48 Hours	If patient still comatose and confounding factors (ie. use of sedation, paralytics, pain meds or unable to correct underlying metabolic abnormalities) may consider SEP If Cortical SEP absent bilaterally ➡ < 1% chance of awakening If GCS < 8 + absent cortical responses ➡ 97% predictive for POOR prognosis
72 Hours	No motor response ➡ POOR prognosis

**No clinical findings strongly predict good outcomes

hypothermia (32-34C) is clinically safe and can improve neurologic outcome.[18] Controlled, meaning avoidance of our defense mechanisms such as shivering and catecholamine release, mild hypothermia (a body temperature between 32-34 C) has been shown to provide a neuroprotective effect. Neuromuscular blocking agents are used to prevent shivering, and sedation is maintained with fentanyl and midazolam.[18]

Therapeutic hypothermia acts on many different targets of this damaging ischemic/hypoxic cascade. The protective effects include the slowing of the destructive enzymatic processes, protection of lipid membrane fluidity, reduction in oxygen requirements without impairing microvascular blood flow, inhibition of lipid peroxidation, attenuation of brain edema and reduction of intracellular acidosis. Animal studies have shown that mild hypothermia reduces cell death and has beneficial effects on white matter injury and astroglial cell proliferation.[18]

In 2002, two prospective randomized studies showed that hypothermia may be an effective neuroprotective strategy. The Australian trial included 77 comatose survivors from cardiac arrest with a primary rhythm of **ventricular fibrillation (VF)** or pulseless **ventricular tachycardia (VT)**. Patients were randomly assigned to hypothermia (33C, 12 hours; achieved with ice packs) or normothermia. The primary outcome measure was survival to hospital discharge with sufficiently good neurologic function to be discharged home or to rehab. Twenty-one of the 43 patients (49%) treated with hypothermia survived and had favorable neurological recovery, compared to nine of the 34 patients (26%) treated with normothermia (P=0.046). After adjustment for baseline differences, the odds ratio for good outcome with hypothermia compared with normothermia was 5.25 (95% CI 1.47-18.76).[19] The European multicenter trial included 275 patients who were seen in the emergency department. They were known to have either VF or VT as the cause of their arrest. They were randomly assigned to receive therapeutic hypothermia (32-34 C, 24 h; achieved with cold air) or to standard treatment with normothermia. The primary outcome measure was favorable neurologic out come at 6 months. Seventy-five of the 136 patients (55%) in the hypothermia group had favorable neurological recovery after six months, compared with 54 out of 137 patients (39%) in the normothermia group. This translates to a number needed to treat of 6. In addition, there was a significant reduction in mortality at six months in the hypothermia group, compared to normothermia.[20] In both studies, age, gender and time from collapse to spontaneous circulation did not have a significant effect. There was no difference between the two groups in adverse events.

Many strategies have been developed to initiate and control cooling; e.g., ice bags, blankets containing circulating coolant, cold artery infusion, a cooling helmet and endovascular convection cooling using a balloon tipped catheter. Despite these innovations there are still many questions that need to be answered about the use of hypothermia. such as when is the optimal time to initiate cooling, what is the optimal time to keep a patient cooled, is there permanent benefit and what is the best strategy for rewarming the patient?

With improvements in CPR, neurologic morbidity and mortality will continue to be a consequence of cardiac arrest. Accurate prognosis is possible, but the care of the patient should not stop there. Continued research into neuroprotective agents and strategies is necessary to improve the neurologic short and long term outcomes of victims of cardiac arrest.

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Doctors As Athletes —Review & Commentary

Melvin Hershkowitz, MD

Recently Dr. Joseph Friedman, Editor of this Journal, and I discussed the topic of this essay as a reflection of our mutual interests in medical education and sports. As a neurologist, Dr. Friedman immediately identified one of the most famous doctor-athletes of all time, London neurologist Dr. Roger Bannister, who in 1954 was the first man to run one mile in less than 4 minutes.

My interest in Doctor-Athletes arose when, as president of my undergraduate class ('42) at Columbia University and editor of our class newsletter, I wrote reviews of Columbia's great quarterbacks and basketball captains. To my surprise, I discovered that three quarterbacks had become physicians: Dr. Don Kasprzak,'45 (Thoracic Surgery); Dr. Claude Benham, '57 (Family Practice); and Dr. Arthur (Archie) Roberts, '65 (Cardiac Surgery)). Archie Roberts was an All-American, drafted by the Cleveland Browns, but he chose medical school at Case Western Reserve over a pro football career. Among the basketball captains were Dr. Lester Martens, '44 (Internal Medicine) and Dr. Ken Benoit, '66 (Surgery). Other Columbia athletes who became doctors were Dr. Gerald Klingon, '42 (Neurologist and Baseball First Baseman); Dr. Felix DeMartini, '43 (Internist & CEO at Columbia Presbyterian Hospital, Football Guard); Dr. William Sinton, '43 (Orthopedist and Football End); Dr. Richard Donelli, '59 (Dentist & Quarterback); and Dr. Russell Warren, '62 (Orthopedic Surgeon, consultant to the NY Giants Pro Football Team, and All-East Halfback).

While running (slowly) on the Columbia Cross-Country Team, 1938-1939, I had three teammates who became physicians: Dr. Michael Bonfiglio, '40 (Professor of Orthopedics and Chief at University of Iowa); Dr. Alan Goulding, '42 (Internist and one of the founders of the Billings Clinic in Montana); and Dr. Solomon Papper, '42 (Nephrologist and Professor of Medicine and Chief at the University of Oklahoma).

The following list does not claim to be comprehensive. I invite readers to suggest additional names of Doctor-Athletes.

ROGER BANNISTER, born in 1929, grew up in Bath, where his running and academic skills earned him a scholarship to Oxford. In 1951 he was the British Champion Miler, but finished a disappointing 4th in the 1952 Olympics in Helsinki. At St. Mary's Hospital Medical School, Bannister continued running, limited to 45 minutes daily because of the academic demands. His goal was to become the first man to break the 'Four Minute Barrier' for the mile run. With the help of friends and fellow runners Chris Brasher and Chris Chataway, he made the attempt on May 6, 1954, at Oxford. Brasher and Chataway set a fast pace for the first 3⁄4 mile, hoping to pull Bannister along to reach that mark in 3 minutes or less. Behind them, Bannister summoned a mighty effort to run the final quarter mile in less than 60 seconds. He collapsed at the finish line, as his historic success was proclaimed by the announcer's official time of the race: 3:59.4! One month later, the Australian John Landy broke Bannister's record, but in the British Summer Games in Vancouver, Bannister defeated Landy. Since then, the one-mile record has been pushed far below Bannister's original goal. College milers often run the mile in less than 4 minutes; and the world record, set by Moroccan runner Hicham El Guerrouj in 1999, is 3.43.13.

Dr. Bannister was Editor of Brain's *Textbook of Neurology* (now known as *Brain & Bannister's Clinical Neurology*, revised by Bannister in 1992). In 1983 he was Editor of *Autonomic Failure*, which he revised for the 1999 edition. After two decades of practice and research, he was knighted in 1975. As Sir Roger Bannister, he became Director of the National Hospital For Nervous Diseases in London and Chairman of the Editorial Board of Clinical Autonomic Research.

TENLEY ALBRIGHT, born in 1935, was the daughter of Boston surgeon Dr. Hollis Albright. At age eleven, she contracted poliomyelitis and for a short time could not walk. Four months after taking up ice skating for recreational therapy, she won the United States Junior Ladies Championship. At age 13, she won the US National Novice Championship, the US National Junior Title at 14, and the US Women's Championship at 16. In the 1952 Winter Olympics in Oslo, she won the Silver Medal. At age 17, she became the first American woman to win the World Figure Skating Championship. Tenley then entered Radcliffe as a pre-medical student, where she arose at 4 AM for skating practice, sometimes devoting as much as 7 hours per day to training. She won the United States Championships in 1954 and 1955, the World Championship in 1955,and the Gold Medal in the 1956 Olympics in Italy, despite a gash on her right ankle from a training accident. She then retired from competition, entered Harvard Medical School, and completed her training to become a general surgeon. She married, had three daughters, and became a member of the Executive Committee of the United States Olympic Committee. In 1988, she was inducted into the US Olympic Hall of Fame.

BOBBY BROWN (Robert William Brown), Yankee Third Baseman and cardiologist, was born in 1924, graduated from Tulane University School of Medicine, practiced in San Francisco and Fort Worth, Texas, from 1959-1984, and reported that in 26

years he never missed a day in his office because of illness. From 1946-1954, Bobby Brown played third base for the Yankees, with time out to serve in a MASH Unit in Korea in 1952-1953. He played on four Championship Yankee teams, with a career batting average of .279. He had an unsurpassed World Series batting average of .439 in 17 games. After eight seasons with the Yankees, Bobby Brown left baseball for cardiology. After retiring from medical practice, Bobby Brown was appointed President of the American League, from 1984-1994. While traveling with the Yankees, Bobby Brown's roommate was Yogi Berra. While Yogi read comic books, Bobby studied medical books. On one occasion, Yogi is rumored to have asked Bobby: "How did yours come out"??

ERIC HEIDEN, winner of five speed skating events in the 1980 Winter Olympics at Lake Placid, was born in Madison, Wisconsin, the son of an orthopedic surgeon. Eric graduated from the Stanford University Medical School, completed Orthopedic Residency training, and became a member of the Orthopedics Faculty at the University of California-Davis Medical School in Sacramento. Eric was just 21 years old in 1980, when for the first time in Olympic history, he won all five speed skating events at distances of 500, 1000, 1500, 5000 and 10,000 meters. This feat has not been equaled. Eric then showed his execptional versatility when, in 1985, he won the United States Professional Cycling Championship. Eric serves as the Orthopedic Consultant to the Sacramento Kings basketball team.

LES HORVATH, '45 Ohio State University Dental School, was a dental student when he won the Heisman Trophy as the best collegiate football player in the nation in 1944. In that year, he led OSU to an undefeated season. He played briefly for the Cleveland Browns and LA Rams, before embarking on a 41-year career of dental practice in Los Angeles. A member of the National Football Foundation Hall of Fame, he died in 1995.

DAVID JOYNER graduated from Penn State School of Medicine in 1976. As an undergraduate at Penn State, Joyner was an All-American offensive tackle and co-captain of the 1971 Penn State Football team, which had an 11-1 record. That same year he was an All-American Wrestler in the heavyweight division, ranking second in the nation. After medical school, Joyner did residencies in general and orthopedic surgery at Milton Hershey Medical Center, then began his practice of Sports Medicine. In 1992 he founded the Joyner Sports Medicine Institute ,and worked at the University Orthopedic Center in State College. Joyner received the NCAA Silver Anniversary Award in 1997.

JIM LONBORG was born in California in April, 1942. After graduating from Stanford University, he signed as a pitcher with the Boston Red Sox. He pitched for the Red Sox from 1965-1971, and in 1967 won the Cy Young Award with a record of 22-9 and a 3.16 ERA. In the 1967 World Series he pitched a one-hitter. After hurting his knee in a skiing accident, he lost much of his effectiveness. Traded to Milwaukee in 1972, he finished his career with the Philadelphia Phillies, 1973-1979. His lifetime won-loss record for 15 years in the major leagues was 157-137. Always interested in health and medicine, Lonborg followed his wife's suggestion and entered Tufts Dental School after his baseball career was over. He finished in three years, and now at age 63, practices dentistry in Massachusetts.

GEORGE MEDICH was born in Aliquippa, PA, in 1948. From the University of Pittsburgh, he was drafted by the New York Yankees as a pitcher in 1970. In 1972 he began both his medical studies at the University of Pittsburgh and his Major League baseball career with the Yankees. In 1973 he was voted Rookie Pitcher of the Year. In 1974 he won 19 games for the Yankees, going on to pitch 32 complete games in the 1974-1975 seasons while intermittently continuing his medical studies. He retired from baseball in 1982, having won 124 games for the Yankees, Pittsburgh Pirates, Oakland Athletics, Texas Rangers, Seattle Mariners, New York Mets and Milwaukee Brewers. He then devoted full time to medicine, and in 1986 completed an Orthopedics Residency at the University of Pittsburgh. His recent Certification in Orthopedic Surgery was from 1995-2005. In 1999 he was sentenced to nine years of Probation for writing twelve false narcotics prescriptions in the names of patients for his personal use. His lawyer stated that Dr. Medich had struggled with drug addiction for many years.

CARY MIDDLECOFF was born in Memphis in 1921, the son of a dentist and Club Golf champion. Cary graduated from the Tennessee College of Dentistry ('44) and inherited his father's golf-skills. As an amateur Cary won the North & South Open in 1945. As an Army Dentist in WW II, he estimated that he filled 12,000 teeth, which might have entered into his decision to abandon dentistry and become a professional golfer. He had his first Pro Tour win in 1947, then won the US Open in 1949,the Masters in 1955, the US Open again in 1956, and played on three US Ryder Cup Teams. He retired as an active player in 1961, became a golf critic and commentator, and was elected to the PGA Hall of Fame in 1986. He died in 1998 at age 77 of congestive heart failure.

GEORGE SHEEHAN was born in Brooklyn in 1918, the son of a cardiologist. At Manhattan College, he was a track star, winning the Metropolitan Indoor Mile Championship in 1940. He entered the Long Island College of Medicine ('43) (now Downstate), in the WW II accelerated program. After a brief internship, he served in the Navy from 1944-1946 in the South Pacific as a medical officer aboard the Destroyer USS Daly . In 1949, after residency, he practiced internal medicine and cardiology in Red Bank, NJ. In 1963, at age 45, he resumed running and racing, and in 1964 ran in his first Boston Marathon, continu-

ing to run this race for 21 years until 1984. In 1969, at age 50, he set an age-group record of 4:47 for the mile run, and in 1979, at age 60, he ran the Marine Corps Marathon in 3:01.In 1970, Dr. Sheehan wrote his first column for *Runners World Magazine*, beginning a long affiliation as an editor and commentator His 1978 book,"Running And Being",was a New York Times Best Seller. His last book,"Going The Distance",was published posthumously,after he succumbed to prostate cancer in 1993, four days before his 75th birthday.He had endured seven years of metastatic disease before his death, keeping active and exhortative for running. In 1998, he was elected to the National Distance Runners Hall of Fame.

JOHN SIEGAL, born in 1918 in Pennsylvania, entered Columbia University in 1935. He was a classmate of Columbia's All- American and later All-Pro Quarterback, Sid Luckman. John played End on the Columbia Football teams of 1936, 1937 and 1938, in an era of two-way Football, when the niceties of Tight End, Split End, Defensive End, etc were not yet in vogue. He was a major pass receiver for Luckman at Columbia, and went with Luckman in 1939 to the Chicago Bears. Playing End with the Bears, John contributed to their three Professional Championships in the 1940s, and simultaneously obtained his DDS degree in 1943 from Northwestern University Dental School. He then retired from football and served as a Dentist in the US Navy before entering private practice in Plymouth, PA. In an interview several years ago, John modestly disclaimed the rumor that as a Dentist and Pro Football player, he had invented the Mouth Guard.

DEBI THOMAS, born in New York City in 1967, became the first African-American figure skater to win a medal at the Winter Olympics (1988, the Bronze Medal, Calgary). In 1986, at age 19 while an undergraduate at Stanford University, Thomas won the US National and World Figure Skating Championships. She graduated from Stanford in 1991 with a degree in Engineering, and toured for a few years as a professional skater before entering Northwestern University Medical School ('97). In 1996 she married Christopher Bequette, a Sports Attorney, and completed an Orthopedic Surgery Fellowship in 2001 at the University of Arkansas School of Medicine. Thomas was inducted in to the US Figure Skating Hall of Fame in 2000.

JENNY THOMPSON, a Third Year Medical Student at Columbia University, is a 31 year-old Olympic Champion swimmer,. She won two gold medals at the Pan-Am Games in 1987, then won 26 US National titles,and in 1999 set a World Record of 57.88 seconds in the 100 meter butterfly.In four Olympic Games between 1992 and 2004, Thompson won eight Gold Medals,a record for an American woman.Thompson graduated from Stanford University with a major in Human Biology,but did not enter medical school immediately.She entered Columbia University School of Medicine in 2000,c ontinuing to train while attending classes. After the 2004 Olympic Games, Thompson retired from competitive swimming, and focused on her Third and Fourth Year clinical rotations.

ERNEST VANDEWEGHE, born in Montreal in 1928, was an All-American Basketball player at Colgate University ('49). Drafted by the New York Knicks, he was a Guard-Forward for six seasons. (1949 – 1956). At the same time, he attended medical school at Columbia (MD'53). He completed an internship at Bellevue Hospital from 1953-1954,and a Residency in Pediatrics at Columbia's Babies Hospital from 1954-1956. Vandeweghe married Colleen Hutchins, an athletic Miss America. Among their four children, Heather, became a physician. A son, Kiki, born in Wiesbaden while Vandeweghe was on military duty as a Pediatrician, became an even more accomplished professional basketball player than his father. Kiki Vandeweghe played on a UCLA National Championship team, averaging 19.7 PPG in a 13-year career in the NBA. Dr. Ernest Vandeweghe, Associate Clinical Professor of Pediatrics, Adolescent Medicine, and Sports Medicine at UCLA Medical Center, practiced for three decades, while serving on the President's Council On Physical Fitness And Sports. He helped develop Title IX legislation and remains an advisor to corporations and professional athletes.

The following Doctor-Athletes are members of the Brown Medical School Faculty:

DR. GREG AUSTIN, Orthopedic Surgeon, played for three years on Princeton's Soccer Team, and was Captain in 1975-1976. Dr. Austin graduated from the University of Pittsburgh Medical School in 1980 and completed Residencies in Orthopedic Surgery and Hand Surgery at Tufts New England Medical Center. He specializes in hand surgery in Rhode Island.

DR. RICHARD BESDINE, a graduate of Haverford College and the University of Pennsylvania School of Medicine, was recently Interim Dean of the Brown Medical School,. While on the Harvard faculty, he won the Massachusetts State Squash Championship in 1979 as a member of the Harvard Medical School Team, won the Hartford Open in 1986, reached the round of 16 in the US Over 55 National Championship in 1998, was finalist in the over 60 RI State Championship in 2001, and won the University Club Hard Ball Championship in 2003.While at Harvard, he co-founded, with Dr. John Rowe, the Harvard Program in Geriatric Medicine. He went to the University of Connecticut School of Medicine as Director of the Division of Geriatrics, before coming to Brown in 2000 as Greer Professor of Geriatrics. He still plays squash daily.

DR. CHARLES CARPENTER, Professor of Medicine and internationally recognized consultant in HIV-AIDS therapy and research,

played end on the 1951 Princeton football squad, practicing with their star halfback,Dick Kazmaier, who won the Heisman Trophy. In 1950-51 Princeton had two consecutive undefeated seasons, with 22 victories, and was ranked 6th in the Nation by the AP & UPI. At Johns Hopkins Medical School, he was Chief Resident in the Department of Medicine and Director of the Division of Infectious Diseases. He became Physician-in-Chief and Professor of Medicine at Case Western Reserve School of Medicine (1973-1985), before coming to Brown as Professor of Medicine. Dr. Carpenter, acclaimed for his work in controlling cholera epidemics in India, is a member of the BRUNAP Program in HIV-AIDS research and therapy.

DR. EDWARD FELLER, Clinical Professor of Medicine, former Director of the GI Division at Miriam Hospital, one of the most honored teachers in the Brown Medical School during the past decade, and editorial chair of *Medicine & Health/Rhode Island*, graduated from the University of Pennsylvania, and from the UMDNJ-Newark in 1973. He did his medical residency from 1973-1976 at Royal Victoria Hospital in Montreal, followed by a GI Fellowship in 1976-1978 at Harvard-Massachusetts General Hospital, before coming to Brown. Dr. Feller, a well-known marathon and ultramarathoner, completed the 100 mile Ultramarathon around the Grand Canyon.

Summary And Comments

What qualities enable a Doctor or Dentist to become an accomplished athlete, and a talented athlete to become a Doctor or Dentist? Some answers are obvious: intellectual distinction,physical strength, skills in hand-eye coordination, speed, anticipation, courage, stamina, tolerance of pain and fatigue, and the thrills of competition and triumph. To these qualities, one must add a willingness to sacrifice some of the ordinary pleasures of daily life to pursue intensive training. Efficient time management to fulfill the obligations of Doctor and Dentist to patients, family, and friends, and to his or her sport, is an essential but often elusive factor in this complex equation.

These eighteen Doctor-Dentist Athletes have been active across a spectrum of sports:

1 Basketball player
1 Golfer
1 Soccer player
1 Speed Skater
1 Squash Player
1 Swimmer
2 Figure Skaters
3 Baseball Players
3 Runners
4 Football Players

There are no Tennis players in this group. Among our expectations for the future, we can hope that a Doctor or a Dentist will emerge as a star in this popular sport.

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A HISTORICAL PERSPECTIVE ON UPPER ENDOSCOPY AT RHODE ISLAND HOSPITAL

JOSEPH D. DIMASE MD, AND WALTER THAYER MD

Endoscopy, a word derived from the Greek endo (within), and scope (view), began with Hippocrates (460-375 BC), who made reference to a rectal speculum using a natural light source. In the Pompeii ruins (70 AD) a three-bladed speculum was found similar to the current day vaginal speculum. Consequently, interest in exploration of internal organs has its origins from the beginning of medicine.

Technical difficulties confronting researchers included design of the instrument and suitable material of construction. However the greatest impediment was a suitable light source. The latter was obviously an essential quality to accurately gain information by precise visual inspection. Over the last 2000 years, endoscopy has relied on a light source progressing from natural light, to candle light, to light from alcohol, turpentine, gas, electric, fiberoptic, and most recently to a video chip.

For a detailed history of the development of gastroenterology, with photos of historic gastroscopes, the reader is referred to "The History of Gastroenterology," by L. Walk. (1) As noted in this article, numerous modifications of the gastroscope took place, but the basic instrument remained a rigid one with a high rate of perforations. In 1928, Wolf, a German electro-optician, and Rudolph Schindler, a German clinician, devised a semi-flexible instrument, with a series of lenses having short focal distances, allowing the image to be passed through the curved tube.[2] In 1932, the instrument was presented to the medical society of Munich. Gastroscopy was reborn and streaked across the world. In 1934, Schindler was invited to the University of Chicago, where he established an endoscopic clinic and trained many endoscopists. He can rightly be called the father of American gastroscopy. He was one of the original founders of the American Society for Gastrointestinal Endoscopy.

A few years after Schindler came to the US, Dr. Russell Bray began practicing his specialty as a gastroenterologist in Rhode Island, after receiving training in Philadelphia. A field of endoscopic excellence had developed in that city under the leadership of Dr. Henry Bockus. To our knowledge Dr. Bray was the first clinical gastroenterologist in this state.

The Schindler gastroscope, made by Wolf in Berlin, was purchased by Dr. Bray. He performed his first gastroscopies using local procaine anesthesia. Later he set up a clinic at Chapin Hospital and still later the first GI clinic at Rhode Island Hospital. There gastroscopies were performed "anywhere I could find a darkened room." [3] The Schindler instrument was replaced by the Eder-Hufford scope, (photo), which had a hot light bulb tip and a hand bulb attachment for gastric distention.

In 1854, a British physicist, John Tyndall, described that light would follow a curved path.[4] Ingenius inventions followed,[5] and one hundred years later, an undergraduate physics student, Laurence Curtiss, invented the fiber glass bundle conveying an entire image.[6]

In 1958, Basil Hirshowitz et. al. demonstrated the prototype fibergastroscope at the University of Michigan (photo).[7] This was a side viewing instrument which required blind introduction into the stomach.

In 1965 Dr. Walter Thayer who, trained as a gastroenterologist and endoscopist under Dr. Howard Spiro at Yale University, was appointed the first Chief of Gastroenterology at Rhode Island Hospital. Upon Dr. Thayer's arrival, the Rhode Island Hospital purchased an Eder-Hufford gastroscope, a "flexible" esophagoscope, and subsequently the Hirshowitz gastroscope. The Eder-Hufford gastroscope was equipped with a series of prisms and lenses. The distal half had a rubber exterior with a hot light source at its tip. Because it could only be flexed 15 degrees forward and because it was a side viewing instrument, the esophagus, posterior stomach, fundus and antrum could not be seen. Gastric biopsies had to be taken blindly with a Woods tube, a device with a circular blade and a hole. Suction pulled a piece of mucosa into the opening which was then cut with the circular blade.

The esophagoscope was a straight stainless steel hollow instrument with a distal hot light source and a flexible obturator, useful for insertion into the upper esophagus. Both instruments required a trained assistant who positioned the head of the patient for insertion. Although the eye piece had some magnification, viewing with this instrument was just like looking through a pipe. Esophageal biopsies could be obtained with forceps, which were advanced through the instrument.

Gastroenterology was fundamentally changed with development of the Hirshowitz fiberoptic gastroscope, made commercially available in 1961. Principal advantages included flexibility, better visualization, and an outside cold light source. It required blind introduction into the stomach. Controls at the proximal end of the instrument were added later. This allowed the endoscopist to manipulate the distal tip. In the late 60's, forward viewing fiberoptic endoscopes were designed and permitted complete visualization of the esophagus and easy entry into the duodenum. The instrument had a separate channel which allowed the endoscopist to take biopsies and cytologic specimens.

The prototype fiberoptic instruments were rather cumbersome with large circumferences. It was only a matter of time before pediatric endoscopes appeared and were quickly adapted to adult use, allowing easier and more comfortable passage. These newer instruments allowed visualization of the hypopharynx, as well as vocal cords as they were introduced under direct vision. Head holding by an attendant was no longer necessary and biopsy of the small intestine became easier, eliminating the need of a blind biopsy with either the Crosby capsule or Quinton tube.

At Rhode Island Hospital the first forward viewing instrument became available in the early 70s, initiating a rapid advancement in the sub-specialty of gastroenterology. The site of upper GI hemorrhage could immediately be identified and later treated endoscopically with electrocoagulation or injection of vasoconstrictive agents. The diagnosis of upper bowel disease could easily be obtained by a well chosen biopsy.

Sclerosing agents were developed for the treatment of esophageal varices. Later this was replaced by esophageal banding. Uni and bipolar electrocautery allowed the endoscopist to effectively treat upper tract bleeding and allowed polyp removal.

In 1970, Oi and co-workers reported on their historic development of ampullary canulation of the biliary and pancreatic ducts that rapidly expanded diagnostic and therapeutic aspects of biliary and pancreatic diseases.[8] This technology became available at Rhode Island Hospital after the purchase of a side viewing duodenoscopes, made possible through a generous private donation. Biliary and pancreatic stone removal eventually followed. Esophageal, pyloric, biliary, and pancreatic stenting for benign as well as malignant lesions added other dimensions to therapeutic endoscopy. To facilitate resident teaching a fiberoptic teaching attachment could be attached to the endoscope.

In the early 90s, Rhode Island Hospital acquired videoscopes, allowing images to be conveyed to a TV monitor permitting large images and all in the examining room to see the clear pictures.

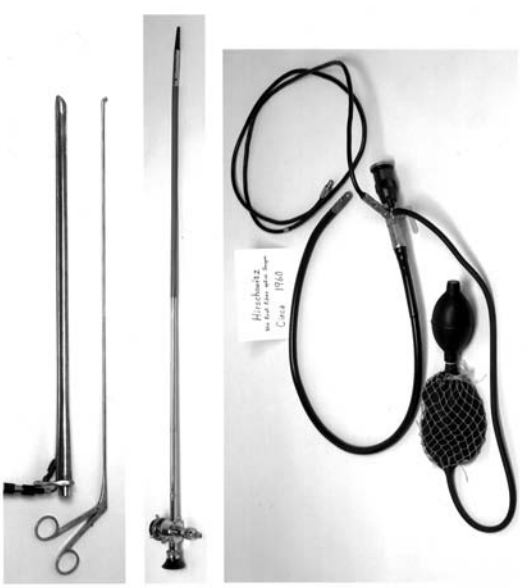
Endoscopic ultrasonography with fine needle aspiration became available at Rhode Island Hospital in the late 90s. In the past five years more exciting studies have led to the development and use of endoscopic techniques for treating reflux disease as well as endoscopic mucosal resection of benign and early malignancies.

More recently capsule endoscopy was developed. During this procedure the patient swallows a small pill sized capsule containing a video monitor which transmits images to a receiver that stores the pictures enabling the gastroenterologist to visualize the entire stomach and small bowel.

Pioneering persists at other institutions around the world with both ends of the spectrum of gastrointestinal endoscopy in a state of accelerated evolution. Transluminal techniques are being developed and include endoscopic appendectomy, cholecystectomy and fallopian tube ligation.

New modalities for studying the mucosa, such as magnification endoscopy, light-induced fluorescence,[9] and optical coherence tomography[10] are being developed, which will allow us to make the histologic diagnosis and define depth of penetration of the lesion in the near future.

To conclude, allow a quote from W.S. Haubrick: "To know the history of endoscopy is to pay tribute to those who have cleared the path we now tread, to understand the impediments that have been overcome, to appreciate more fully the facility we now enjoy, and to point to the prospects of still more marvelous advances to come." [11]



1 2 3

1. Rigid Esophagoscope with biopsy forcepts 2. Eder-Hufford Gastroscope
3. Hirshowitz Gastroscope

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Last Day

Edward H. Wu, MD

Last Day

It is the day before July 1.
"Congratulations!" they all say.
"How does it feel?" they all ask.
I visit my final morning report, to learn something new,
But it's the end of the month, so no clinical case today;
Instead, we play medical "Jeopardy!" Our team wins!
Though I pity one resident, on-call her last day;
Good thing I cancelled my clinic.
Handshakes and hugs from my program directors,
"Good luck, keep in touch, this is not goodbye."
Smile and pride from my research mentor,
We still have to write our manuscript.
The new Chief Residents wish me well;
Once fellow green interns, we grew into residents,
Now they're in charge of another set of new faces.
I turn in my pager, and I am 6497 no longer;
I turn in my Debitek card, no more free meals;
I turn in my key, now I can't even open the call room;
I turn in my ID badge, and I am housestaff no more.
One last look at the resident lounge:
Three years of agony and excitement,
Numerous admissions, feeling overwhelmed,
Fumbling through rounds, asking questions, trailing my residents;
Growing more comfortable, amassing knowledge,
Providing answers, leading my interns, commanding confidence;
Checking e-mail at 3am, watching TV during night float,
Sizing up the lunch food, gossiping about each other;
Then, paralyzing code bells interrupting the camaraderie,
Frozen as we await the overhead page instructions,
The adrenaline rush propelling us as we race to a code,
Or the peculiar sense of relief with a fire drill announcement,
At least, until we hear the sirens.
This was my life; this was my home, away from home.
The final walk to my car, and I drive out of lot E-7 one last time,
With hope that someday, after the boards, after fellowship,
I will return, and park in the attending lot.

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Bio-Emergency Preparedness in Rhode Island: A Role for Urgent Care Centers?

Matthew J. Finn and Marguerite A. Neill, MD

Since 1971 when a Rhode Island emergency medicine physician opened the first American emergency care center, urgent care centers have grown rapidly, particularly in the past decade.[1] They have doubled from 8,700 centers five years ago to about 15,000 today.[2] This growth reflects the changes in the landscape of acute medical care in the U.S.

This project was undertaken to understand whether and how urgent care centers in Rhode Island might be incorporated into overall planning for clinical and public health responses to bio-emergencies, whether intentional or naturally occurring. The massive regional disruption and destruction from Hurricanes Katrina and Rita illustrate the need for such planning and the need for clinical surge capacity.

Acute Care in the United States

In the United States the number of emergency departments has decreased even as the volume of patient visits has risen. From 1998 to 2002, total visits to emergency rooms increased 23%, from 89.8 million to more than 110.2 million, despite a 15% decrease in emergency departments over the same period.[3]

Changes in office-based medical practice have resulted in less time and resources to devote to acute medical problems. These limitations in traditional practice settings and the constraints on emergency department access have provided the impetus for the development of urgent care centers since these entities theoretically can provide both access to, and rapidity of, evaluation and diagnosis. In 2003 alone, urgent care centers across the nation had 150 million visits,[4] 36% more than the total number of emergency department visits during the previous year.

A bioterrorist attack or outbreak of an infectious disease would overwhelm the nation's already strained emergency departments. If urgent care centers were incorporated into the planning framework, these centers could accept particular types of patients and trauma victims. Urgent care centers could see those exposed but not yet ill, the walking sick, and, what is likely to be a majority of those seeking medical attention after a biologic terrorist attack, the worried well. Many of these elements were seen in the rapid evolution of clinical care for persons displaced by Hurricane Katrina to crowded shelters in Houston and Baton Rouge. Medical clinics were established on site to treat patients with acute illnesses, infections and post-traumatic stress disorders to the extent possible with on-site resources, which allowed those cities' emergency departments to function despite extreme strain.

Acute Care in Rhode Island

Following the national trend, the number of urgent care centers in Rhode Island is increasing. Rhode Island hospitals have not escaped the "squeeze" of increased demand and resource constraints. Rhode Island hospitals are projected to be operating at or above capacity in 2006.[5] Urgent care centers in Rhode Island have already absorbed some of the overflow of minor and moderate care patients. Dr. Daniel Halpren-Ruder, an urgent care center physician, estimated that 70% of his clinics' patients would have gone to an emergency department if his centers were not available.[6]

The **Center for Biodefense and Emerging Pathogens (CBEP)** at Memorial Hospital of Rhode Island, in conjunction with the Rhode Island Department of Health, surveyed the urgent care centers in Rhode Island to profile their performance characteristics, staffing patterns, and interest in education and training relevant to bioterrorism and emerging pathogens. Twenty-four urgent care centers were identified and sent a two-page questionnaire by e-mail or fax. Fourteen completed the survey (a response rate of 58%). In geographic distribution, urgent care centers are highly concentrated in central Rhode Island. They fall into three groups based on how they are set up and regulated. (Table 1)

"The urgent care centers could be used to monitor for emerging pathogens at the community level."

The type of facility is shown in Figure 1; the majority of urgent care centers in Rhode Island are operated under a physician's license and deliver episodic, need-based care for acute medical problems. Although physicians in this type of center typically have training in emergency medicine, family practice or internal medicine, some are radiologists, pathologists or other professional disciplines. The proportion that is board certified in their discipline is not known.

The urgent care centers in Rhode Island vary in size, patient volume, and staffing patterns. (Table 2) All indicated that they are busiest on Mondays, regardless of whether they are in service on the weekends. Typical patient turn-around time (from registration to final disposition) is less than one hour. Of the centers that completed the survey, 79% provided care for all patient types regardless of age; 21% did not provide care for pregnant women. Urgent care centers cannot, by law, accept ambulances, but if medical acuity is high, the clinics will stabilize patients for transfer.

Table 1. Types of Urgent Care Centers in Rhode Island

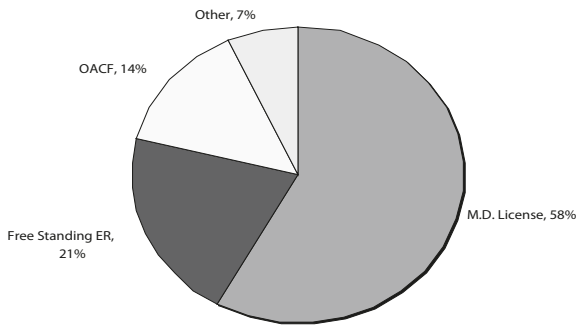
Designation	Description	Regulation Requirement
Urgent Care Center (self-designated)	Provides prompt care for illness or injury	Not currently regulated; centers operate under the physician license of the owner or operator
Free-Standing Emergency Facility	Operates separately from a hospital; provides prompt emergency care for acute illness or injury which seriously impairs health unless immediate attention is rendered	Regulated under the Department of Facilities Regulation of the Department of Health; can be privately owned by individual(s) or investor(s)
Organized Ambulatory Care Facility (OACF)	Provides outpatient health care, including services for acute, minor, non-life threatening illnesses or injuries	Regulated under the Department of Facilities Regulation of the Department of Health under separate regulations from those for free-standing emergency rooms; can be privately owned by individual(s) or investor(s)

The urgent care centers are not networked for communication, neither formally to manage daily patient flow (as the emergency departments are with the Nextel Hospital Emergency Communication System), nor through a statewide professional society. Reasons for this include their relatively recent emergence onto the medical landscape, their heterogeneity, and that they do not fall under a uniform regulatory standard.

Potential Roles for Urgent Care Centers in a Bioterrorism Event or Bio-emergency

How could urgent care centers be used as an asset to our state and communities in a bioterrorist threat, during a widespread increase in an infectious disease like influenza, or in the aftermath of a natural disaster such as a hurricane? Urgent care centers could be a valve to decompress the hospitals, relieving the pressure on emergency departments and doctors' offices, increasing the efficiency and effectiveness of medical care at times of crisis. They are already in place, concentrated in the central portion of the state that corresponds to the state's population distribution. The local community could be familiar with the facility and thus more accepting of it as a designated site for care in an emergency.

Figure 1. Category of Urgent Care Facility in Rhode Island



Although it varies among urgent care centers, they have some resources (medical personnel, lab and x-ray capacity) to evaluate the sick and stabilize the injured. With triage algorithms and planning for patient flow, the urgent care centers could be used to rapidly evaluate those potentially exposed to infectious agents and initiate post exposure prophylaxis. Of equal importance, they could provide on site care for some types of trauma and acute illness. Handling groups of patients like these at their local urgent care center rather than the closest emergency room would help to maintain patient flow, improve the overall utilization of medical workers, and keep the hospitals functional. For this to succeed, however, the urgent care centers need to be networked for communication so that information specific to them and their patients could be disseminated quickly and effectively. This communication network could also serve as a "first look" public health needs assessment for the type of patients affected and the illnesses seen in an attack, a biological emergency or a natural disaster.

Potential Role of Urgent Care Centers in Surveillance

The urgent care centers could be used to monitor for emerging pathogens at the community level. These walk-in centers are likely locations for patients with acute infectious diseases to seek medical assistance and thus urgent care centers might provide the first hint of an event, functioning as sentinels for disease occurrence in a population. A communication network between urgent care centers would allow them to share information quickly on disease occurrence

Table 2. Functional Characteristics of Rhode Island Urgent Care Centers

Category	Average	Range	Median
No. of exam rooms	7.54	1 to 13	7.5
No. of full-time physicians	2.07	1 to 6	2
No. of part-time physicians	3.71	0 to 10	3.5
Average patients per day	56.07	20 to 100	62.5
Interest in bioterrorism*	1.82	1 to 3.5	1.5
Interest in pandemic influenza*	1.71	1 to 3	1

* On a scale from 1 to 5, with 1 being "very interested" and 5 being "not interested"

so that proper infection control precautions could be taken. Early detection is invariably a pre-requisite for control of most infectious agents whether from a common source exposure which is continuing (such as from contaminated food) or from person-to-person spread. Such real-time trends in disease syndromes would allow federal and state agencies to know if control measures are working.

With a bi-directional communication channel between these centers and the state, the Department of Health could communicate with the urgent care centers to provide guidance on evaluation and treatment, and incorporate them into surveillance networks for "real-time surveillance."

Future Planning

Incorporating urgent care centers into emergency preparedness planning offers the potential to bring on-line a previously unidentified resource for use in both surveillance and response. To do this, a better understanding is needed of the medical care delivery and practices within urgent care centers and their interaction with traditional sites of acute medical care. A detailed assessment needs to categorize urgent care center personnel in terms of their professional background and training in order to target educational efforts aimed at ensuring particular core competencies relevant to bioterrorism and emerging pathogens. Other important areas are to determine the maximum capacity in patient volume that the existing urgent care centers can handle and the on-site availability of resources, like laboratory and x-ray. Establishment of a communication network, particularly a bi-directional one, should involve urgent care centers early on in the planning process to judge the feasibility of options under discussion. With training and education to urgent care staff, and their assumption of roles in surveillance and response, urgent care centers could be an asset in the portfolio of bio-emergency preparedness, in Rhode Island and regionally.

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CREATINE KINASE: A REVIEW OF ITS USE IN THE DIAGNOSIS OF MUSCLE DISEASE

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Measurement of serum enzymes is a widely used screening diagnostic test for suspected muscle disease. **Creatine kinase (CK),** otherwise known as **creatine phosphokinase (CPK)**, is the preferred screening tool because, unlike other enzymes found in skeletal muscle (e.g., lactate dehydrogenase, aldolase, and transaminases), CK has relative predominance in skeletal muscle, is not falsely elevated by hemolysis, and being unbound in cell cytoplasm is readily released in cellular injury.[1,2] Despite these advantages, CK may create diagnostic uncertainty when an elevated level is found in a mildly symptomatic or asymptomatic patient. Not only are myopathy and cardiac disease among possible causes of the elevated CK, but a false positive CK elevation must be considered, such as in transient non-pathological situations (e.g., cramps, post-exercise) or in those with normally high baseline CK levels. To address diagnostic uncertainty in the use of serum CK levels, this paper will describe the structure and function of CK, summarize common reasons for elevated CK levels in normal individuals as well as those with myopathy or neuropathy, and finally develop a diagnostic strategy for mildly symptomatic or asymptomatic patients suspected to have myopathy. Additionally, a strategy for suspected myopathy in statin-treated patients will be addressed.

Structure and function of CK

Cytoplasmic CK, a protein-product of chromosome 19, is an 86,000 molecular weight dimer molecule that produces adenosine triphosphate for use in muscle cells by catalyzing the transfer of a high energy phosphate bond from creatine phosphate, the major storage reservoir of energy during muscle at rest, to adenosine diphosphate.[3] CK exists in relatively tissue-specific forms called isoenzymes, allowing for greater diagnostic precision. CK-MM makes up over 95% of total CK in skeletal muscle, whereas CK-BB comprises most of the total CK in brain tissue.[4,5] Although CK-MB is a useful measure of cardiac muscle infarction, CK-MM is the most abundant isoenzyme (over 60%) in the myocardium.[4,5] Total CK content is largely contained in skeletal muscle, exceeding the myocardial concentration by as much as two-fold.[4] Consequently, serum normally contains CK provided predominantly from skeletal muscle, almost exclusively as the CK-MM isoform.[5]

Aldolase, present in skeletal muscle, liver, and erythrocytes, is not considered a particularly good screening test for myopathy because the enzyme is not released readily with muscle injury and is often technically compromised by serum sample hemolysis.[1,2] However, approximately 10% of active inflammatory myopathies may have normal CKs and elevated aldolase.[6] We have had a case in which a patient with isolated persistent elevated serum aldolase levels was found to have florid vasculitis and myositis on muscle biopsy in the face of a normal examination and electromyography, and near-normal CK levels. Therefore, aldolase may be useful in those situations with a high clinical suspicion of myopathy and normal CK levels.

Elevated serum CK levels in the normal population

Normal values of CK are difficult to estimate due to individual and population variation in serum levels. Persistent high levels of CK may be seen in blacks compared with other races, males compared with females, and in those with large muscle mass.[7,8] In one study of normal adults, reported mean total CK was 147 U/L (range of 7 to 284 U/L) for 57 black males, 61 U/L (range 35 to 87 U/L) for 44 white males, 66 U/L (range 16 to 116 U/L) for 90 black females, and 37 U/L (range 19 to 55 U/L) for 99 white females.[7] This study highlighted a lack of specificity when laboratory reference values for serum CK do not consider race.

Transient elevations in CK levels are common after reversible causes of muscle injury such as trauma (including injections or needle electromyography), vigorous exertion, or even muscle cramping. A serum sample drawn after electromyography (EMG) in a normal patient will increase up to three fold within the next 24 hours and may show a false positive CK result suggesting myopathy. Therefore, it is important to draw CK levels before EMG studies. In one report, CK levels rose from a mean baseline of 53 U/L in 10 patients to a maximum mean CK of 91 U/L 12 to 24 hours after an EMG; a return to baseline occurred after 48 to 72 hours.[9]

Vigorous exertion may increase serum CK levels transiently. After a marathon, CK levels in 7 runners were reported to maximally increase 24 hours after the race to a mean of 1404 U/L (range 683 to 2261 U/L).[10] In this study, mean CK levels approached baseline after about 1 week. In general, one week of avoidance of exertional activity should be sufficient to ensure accurate measurement of CK levels in a frequently exercising patient. Excessive skeletal muscle exertion resulting in CK elevations can also be seen in certain non-neuromuscular pathological events such as neuroleptic malignant syndrome, convulsive seizures, acute psychosis and violent behavior.[2]

A single non-pathological cramp can also cause a substantial rise in CK levels. In one published case, [11] after a single severe cramp in a gastrocnemius muscle lasting several minutes, serum CK elevated from 117 IU/L (normal <220 IU/L) to 229 IU/L within 6 hours after the cramp and to a peak of 534 IU/L by 30 hours. Serum CK levels returned to normal after 5 days.

Serum CK levels in muscle disease

The degree of CK elevation in muscle disease largely reflects the underlying disease process, and is predominantly due to myonecrosis or membrane defects[2, 5] (Figure 1: *Serum CK level and time course of various myopathies* and Table 1: *Expected serum CK levels amongst common myopathies*).

Table 1: **Expected serum CK levels amongst common myopathies**

Normal CK: mitochondrial, steroid-related, hyper- and hypothyroid myopathies, channelopathies

Mildly Elevated CK: amyotrophic lateral sclerosis, spinal muscular atrophy, post-polio syndrome, Guillan Barre syndrome

Moderately Elevated CK: fascioscapulohumeral muscular dystrophy, inclusion body myositis

Markedly Elevated CK: dystrophinopathies (e.g., Duchenne's & Becker's muscular dystrophy), polymyositis, rhabdomyolysis, neuroleptic malingnant syndrome, malignant hyperthermia

Highest elevations of CK are seen with conditions causing muscle fiber necrosis as in dystrophinopathies (e.g., Duchenne and Becker muscular dystrophy), rhabdomyolysis, malignant hyperthermia, neuroleptic malignant syndrome, and severe polymyositis. More indolent myopathies, such as fascioscapulohumeral muscular dystrophy, myotonic dystrophy, and inclusion body myositis usually have lesser degrees of CK elevation. Disorders causing muscle atrophy without cell membrane damage often have normal CK levels, as in steroid-induced myopathy, hyperthyroidism, channelopathies and mitochondrial myopathies.

Most inflammatory myopathies (i.e., polymyositis, dermatomyositis) will have abnormal CK levels during the disease course, although the extent of CK level elevation can be quite variable.[12] In polymyositis and dermatomyositis, CK levels improve on steroids, usually regardless of whether weakness improves and are not particularly useful to monitor success or failure of treatment.[12] An acute increase in CK levels in these disorders, however, may be a harbinger of relapse. As patients with chronic myopathies lose muscle mass and strength, CK levels will drop and may approach normal in later stages of muscular dystrophy[2, 12] (Figure 2: *CK values in a large population of autosomal recessive Limb-girdle muscular dystrophy by duration of disease*).

Diagnostic confusion sometimes occurs in destructive myopathies as regenerating fibers may release a larger proportion of the CK-MB fraction compared with mature muscle cells, which primarily release CK-MM when injured.[1, 5, 13] In these cases, higher serum levels of CK-MB do not necessarily indicate coexisting cardiac disease in the presence of destructive myopathies.

Serum CK levels in nerve disease

Serum CK levels are not commonly thought to be elevated in neurogenic disease such as mononeurpathy or polyneuropathy, and for the most part, this is true. However, in certain neurogenic diseases, such as amyotrophic lateral sclerosis[14], spinal muscular atrophy and Guillan Barre syndrome,[15] there may be an elevation of CK, though usually no more than five times normal. One proposed mechanism is damage due to increased work requirement on muscle fibers in weakened muscle,[2] though this seems doubtful given that other causes of weakness do not cause elevations of CK. These neuropathies cause denervation of muscle fibers and the ongoing entrophic changes to the muscle fiber membrane may result in leakage of CK. Another possibility would be elevation of CK secondary to frequent cramping, a common symptom in acute neurogenic diseases such as amyotrophic lateral sclerosis and Guillain-Barre syndrome.[11]

Commonly encountered primary care situations involving elevated CKs

Three situations commonly confront primary care providers: the patient complaining of myalgias (muscle pain or tenderness) without weakness, the asymptomatic patient found to have elevated CK levels, and suspected myopathy in a patient taking cholesterol-lowering medications. A proposed diagnostic algorithm is presented in Figures 3 and 4.

Situation 1: Myalgias

Muscle pain is common in normal individuals. One-third to 80% of the population reports muscle pain at some point and many of these patients will have no abnormal test findings.[16] Since few cases of myalgia will likely be due to myopathy, screening tests with high specificity are useful to select those few patients in whom more sensitive (and more

Figure 1: **Serum CK level and time course of various myopathies.**

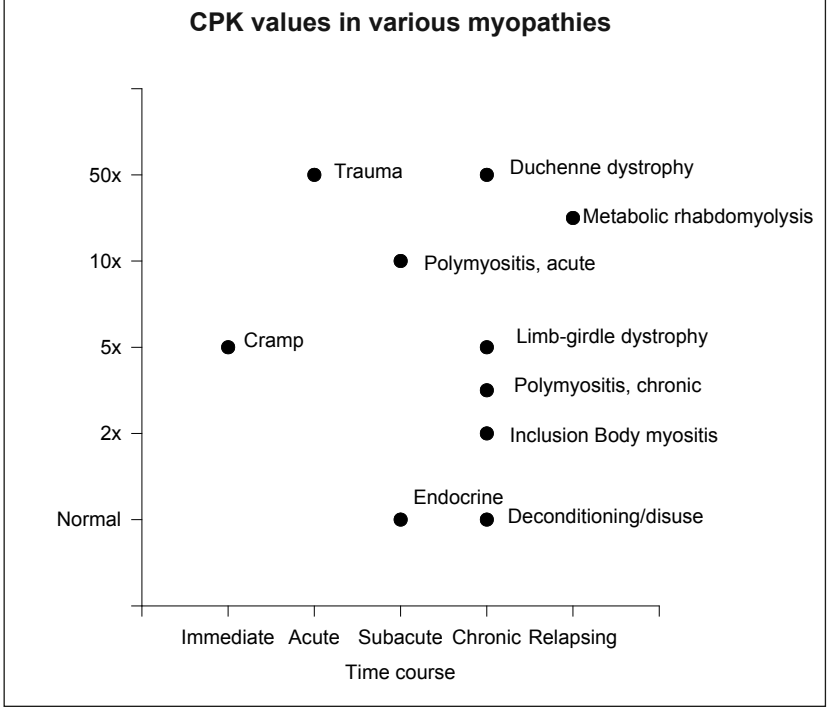
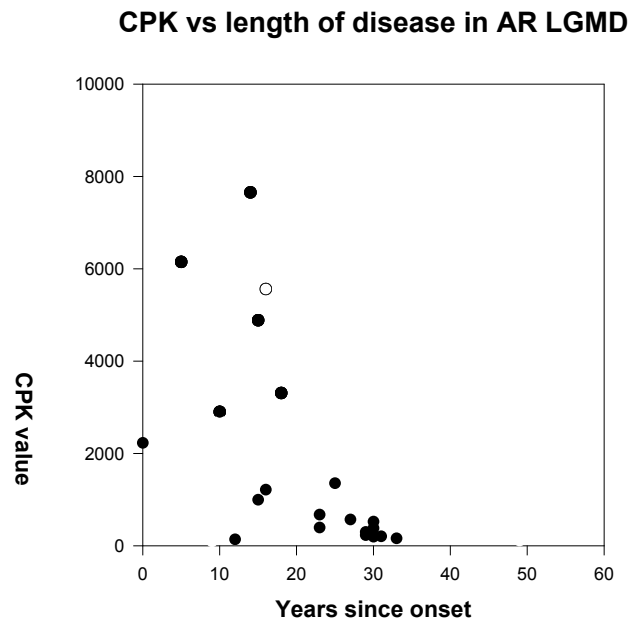


Figure 2: **CK values in a large population of autosomal recessive Limb-girdle muscular dystrophy by duration of disease** (shows reduced serum CK levels with reduction in muscle mass in limb girdle muscular dystrophy).



invasive) testing will be necessary.[17] Common screening tests for myopathy include serum CK and erythrocyte sedimentation rate (ESR), which have been shown to be highly specific (81% and 93%, respectively) for suspected myopathy.[17] ESR, while less sensitive than CK in diagnosing myopathy,[17] is helpful in evaluating common causes of myalgias that do not cause elevated CKs, e.g., polymyalgia rheumatica. Other potentially useful initial serum testing includes aldolase and thyroid stimulating hormone (TSH). Patients with thyroid disease may show myopathic clinical manifestations that may or may not result in elevated CK levels.

If these screening blood tests are abnormal, further investigation should then proceed to EMG testing and possibly, to muscle biopsy as well as other tests (e.g., ischemic exercise testing and DNA evaluation). EMG and muscle biopsy are more invasive tests and typically the second and third line diagnostic tests in screening and confirming muscle disease. Muscle biopsy is the most sensitive diagnostic test for myopathy (81%[17]) and should be employed in patients with a positive screening test (e.g., confirmed weakness, elevated CK or ESR, abnormal EMG). With normal screening tests, the yield for a significant finding on muscle biopsy is low. One study reported that among 20 patients with modest elevations of CK, a normal neurologic examination and nondiagnostic EMG, only one was found to have a diagnostic muscle biopsy.[18]

Other tests may also be helpful, including genetic testing for those with a significant family history of myopathy (to test for dystrophinopathy or carrier state, for example) or ischemic exercise testing for those with exercise-related myalgias or weakness, suggesting a possible metabolic myopathy.

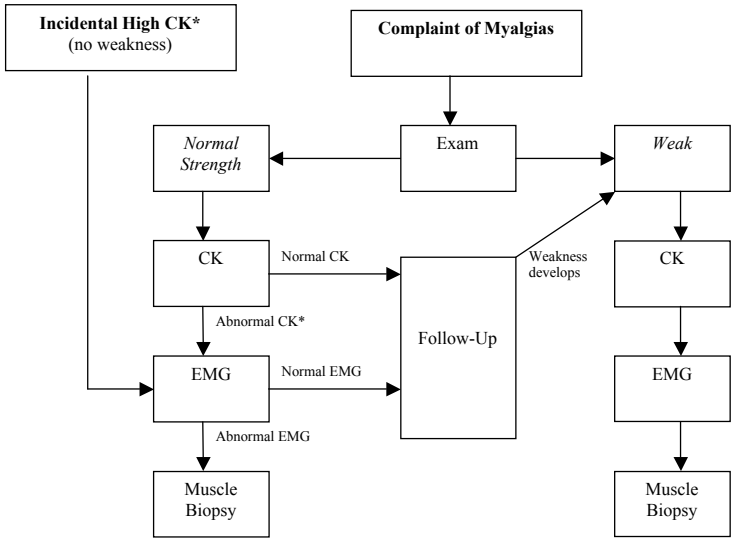
Situation 2: Asymptomatic increased levels of CK

Mild CK elevations are often detected during evaluation of heart disease or routine testing for other medical conditions. Out of 100 consecutive patients seen with elevated CKs after admission to an Austrian medical service, [19] the diagnosis was acute myocardial infarction (32%), drug-related (32%), trauma after a fall (24%), hematoma (17%), intramuscular injection (16%), and malignancy (11%). Only 2% of the CK elevations were explainable by neuromuscular disease. Gender, race, age and recent exercise must also be considered in the situation of mildly elevated CK.

A persistent unexplained elevated CK level, usually three- to 10-times above normal, in an otherwise strong healthy asymptomatic individual with a normal EMG and muscle biopsy is termed idiopathic hyperCKemia.[2] Numerous studies report the results of detailed neuromuscular evaluation in patients with suspected idiopathic hyperCKemia. After considering common causes of asymptomatic elevated CK levels, such as exertion, thyroid disease or other nonpathological reasons of raised CK levels, identifiable causes for suspected idiopathic hyperCKemia are found in approximately one out of every six cases after extensive testing, including EMG and muscle biopsy.[20,21] Neuromuscular diseases subsequently diagnosed in patients with idiopathic hyperCKemia included inflammatory, mitochondrial, and metabolic myopathy among other causes.[20,21] The prognosis of idiopathic hyperCKemia is good: a long-term (mean 7 years, range 4-18 years) follow-up study of 31 patients diagnosed with idiopathic hyperCKemia reported no clinical deterioration in 74% of the patients who had a final evaluation.[22]

For unexplained elevations in CK, we generally perform an EMG. If this is normal, and the patient remains without weakness or significant symptoms, a muscle biopsy is best deferred. The diagnostic yield of muscle biopsy in this setting is low, and even if a diagnosis were made, it would be difficult to make an asymptomatic patient feel better than they already are, thus providing little benefit to the patient. Uncommonly, elevated CK in an asymptomatic individual may be an indicator of either pre-symptomatic or carrier status for an inherited muscle disease, such as muscular dystrophy. The same ethical considerations come into play in this situation as for any asymptomatic patient seeking genetic

Figure 3: Diagnostic Algorythm for incidental high CK and myalgias



* Elevated serum CK levels in these scenarios assumed to not be due to other medical conditions (i.e., cardiac disease), nonpathologic causes of elevated CK levels (i.e., black, male, large body mass, exertional activities or occuopation), and with normal ESR and TSH levels.

testing, as for example, Huntington's disease[23] and referral to a center with genetic counseling is appropriate before any genetic testing is done. Continued follow-up of the patient for the development of symptoms or signs suggestive of myopathy is important, though regular testing for CK levels is uncommonly useful as further testing will be predicated not on the already known elevation of CK, but rather on the history and exam.

Situation 3: Elevated CK while on a cholesterol-lowering and other drugs

Various medications have been associated with elevated CK levels[24, 25] (Table 2: *Commonly used medications associated with elevated CK levels*). Although most medications that lower cholesterol have been associated with muscle disease, the statins, being the most common cause of **cholesterol-lowering agent myopathy (CLAM),** will be our primary concern. Statins (HMG CoA reductase inhibitors) are considered first line therapy in reducing low density lipoprotein levels, [26] however, concerns about adverse effects, including CLAM, may be behind reports of underutilization of statins in populations that would benefit from such medications.[27] Moreover, concerns of myopathy have led to extensive monitoring of asymptomatic statin-users, leading to increased costs and discontinuation of a medically important therapy.[27]

CLAM is clinically variable, manifesting in its most acute state as rhabdomyolyisis, or in a more indolent manner as isolated elevations in serum CK levels or subjective complaints of myalgias. The mechanism of statin-induced muscle injury is not completely understood, although a leading theory proposes that statins may create unstable myocytes by reducing the cholesterol content in muscle cell membranes.[28]

Statin-induced rhabdomyolysis was highlighted by the recent withdrawal of Baycol (cerivastatin) after an association with deaths due to rhabdomyolysis.[29] Rhabdomyolysis is a syndrome of myalgias, weakness and muscle swelling associated with acute elevation of CK greater than 10 times the upper limit of normal, usually accompanied by myoglobinuria, hyperkalemia and potentially, acute renal failure.[30] The risk of rhabdomyolysis from statins has been extensively studied retrospectively, through voluntary reporting data as well as clinical trials, and is real, although the absolute risk is rare.[28,29,30]

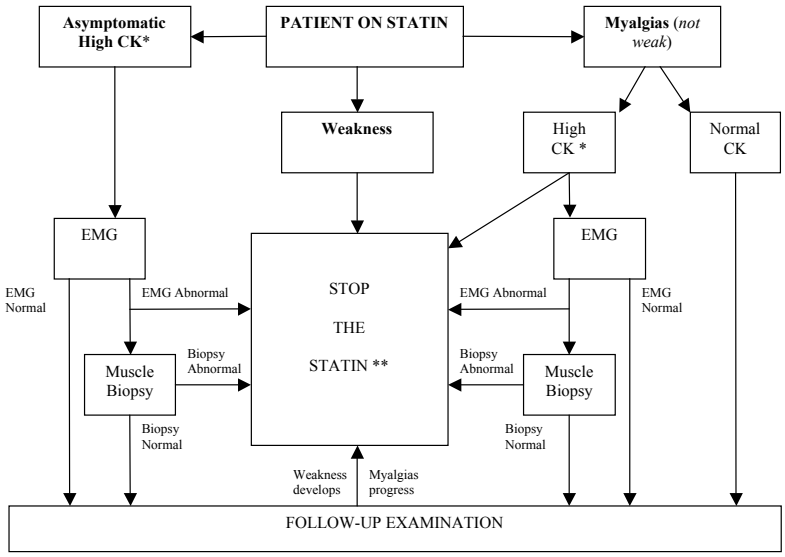
A widely cited analysis summarizing reported adverse events found the incidence of fatal statin-related rhabdomyolysis to be only 0.15 deaths per 1 million prescriptions, although voluntary reports likely underestimate actual occurrences.[29] In a review of randomized clinical trials of statin therapy, only 49 cases of myopathy and 7 cases of rhabdomyolysis were noted among the 42,323 patients on statins, numbers virtually identical to the 41,535 control patients.[28] One retrospective study of approximately 250,000 patients treated with lipid-lowering medications reported that only 24 required hospitalization for rhabdomyolysis, a risk of 1 in 10,000.[31]

Statins may also cause low-grade myopathic symptoms, characterized by muscle pain (myalgias) with or without elevated CK levels.[32] However, other than individual cases showing a temporal relationship between statins and muscle pain, statin-induced myalgias have been difficult to prove as many studies have shown quite low rates of myalgias in statin-treated patients (in many studies only as high as about 5%) and not significantly different than controls.[28,33] Statins do

Table 2: **Commonly used medications associated with elevated CK levels**

Alcohol
Amiodarone
Antipsychotics (typical and atypical classes)
Chloroquine
Cholesterol-lowering agents (HMG CoA reductase inhibitors, fibric acid derivatives, bile acid sequestrant, nicotic acid)
Colchicine
Cyclosporine
D-penicillamine
Isotretinoin
Labetolol
Procainamide
Vicristine
Zidovudine (AZT)

Figure 4: *Diagnostic Algorythm for Suspected CLAM*



* Elevated serum CK levels > 5 fold normal limit assumed to not be due to other medical conditions (i.e., cardiac disease), nonpathologic causes of elevated CK levels (i.e., black, male, large body mass, exertional activities or occuopation), and with normal ESR and TSH levels.
** EMG and muscle biopsy should be done.

appear to have a real pathological effect on muscle in some cases, however. One report recently documented myopathy by biopsy in four patients with myaglias and normal CK levels while on statin therapy.[34]

Isolated asymptomatic elevated serum CK associated with statin-use, generally less than 10 times normal, is usually detected incidentally.[28] Here again, the incidence has been difficult to determine formally with extremely low rates (<1% to 2%) of statin-induced CK elevations without muscle-related symptoms reported in clinical trials and retrospective studies.[27,35]

General recommendations[30, 33] regarding the use of statins reflect the increased risk of myopathy associated with certain patients and elevated statin serum concentrations. These recommendations include: starting statins at a low dose, especially when used with concomitant medications that affect liver metabolism and using the lowest dose possible to meet cholesterol goals; using statins more cautiously in high risk groups such as the elderly, those with renal insufficiency, liver disease, alcoholism or hypothyroidism, and those on multiple medications; and, possibly withholding statins prior to expected stressful periods such as major surgery. Medications that may be associated with increased risk of CLAM when used concomitantly with a statin include fibrates, cyclosporine, azole antifungals, macrolide antibiotics, protease inhibitors, nefazadone, verapamil, diltiazem, and amiodarone.[33] When combination therapy is required, a new inhibitor of intestinal cholesterol absorption, ezetimibe, can be considered which appears to be safe to use in combination with statins without an increased risk of myopathy.[28]

Routine measurements of CK levels in asymptomatic patients are not required although a baseline CK level is helpful in evaluating subsequent muscle complaints.[33] CK levels should be checked for any new muscle complaint while on statins and considerations made to discontinue or lower the dose if myaglias progress or CK levels are found to be over 10 times normal.[33] Once statins are discontinued, improvement may occur as early as a few days to a week,[36] or recovery may be prolonged. In one report, CK returned to normal after 12 days but weakness persisted for over two months.[37] Therefore, if myalgias continue to worsen or persist off statins for one to two months, another cause of myopathy is possible.

Conclusion

Serum CK is a useful screening test for suspected myopathy. Diagnostic challenges occur when symptoms are mild (isolated myalgia) or there are no symptoms (isolated rise in serum CK levels). Additionally, statin medications offer many neuromuscular diagnostic challenges. We have briefly reviewed the structure and function of CK, and developed a treatment algorithm for common situations in which CK, as well as follow-up neuromuscular testing, are useful.

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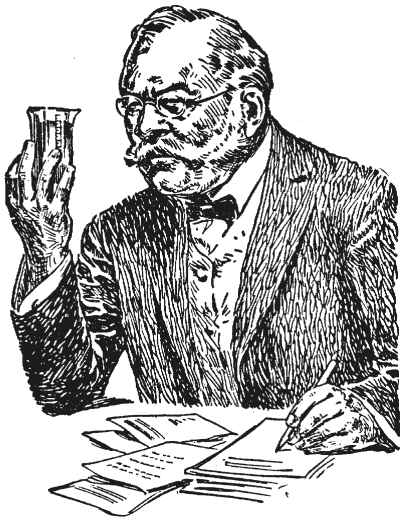

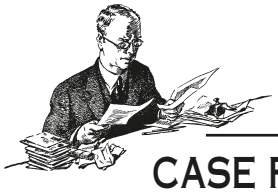

Hospital Case Files

CASE PRESENTATIONS OF THE BROWN UNIVERSTY DEPARTMENT OF MEDICINE MIRIAM HOSPITAL MORBIDITY AND MORTALITY CONFERENCE: A CASE OF CARDIAC SARCOIDOSIS

ANA C. TUYA, MD, AND MARY H. HOHENHAUS, MD

Chief Complaint: Shortness of breath

History of Present Illness: This 46-year-old African-American man, with a past medical history significant for end-stage renal disease, first noted increasing dyspnea 2 weeks earlier. After several days of progressive symptoms, he was admitted to the Miriam Hospital, where he was treated for community-acquired pneumonia and volume overload. He was discharged 5 days later, but did not fill prescriptions for furosemide or levofloxacin.

Four days after discharge, the patient again noted dyspnea. Onset was acute and occurred both at rest and with exertion. By the following morning, he had developed a productive cough, chest pain, fever, and chills. The patient called rescue. Pulse oximetry revealed an oxygen saturation of 71%. He was transported to the Miriam Hospital emergency department.

Review of Symptoms: Positive for sweats, subjective fevers and chills, and mild nausea with abdominal bloating. He denied vomiting, rigors, weight change, rash, and lower extremity edema.

Past Medical History: End-stage renal disease secondary to focal segmental glomerulosclerosis, on dialysis for 1 year. Hypertension, hepatitis C with cirrhosis, gout, hypercholesterolemia, pericarditis. 2D echocardiogram 9 months prior showed ejection fraction of 55% with normal left ventricular systolic function.

Medications: Labetolol 300 mg bid, amlodipine 10 mg qd, candesartan 32 mg qd, clonidine 0.3 mg bid, aspirin 325 mg qd, atorvastatin 10 mg qd, colchicine 0.6 mg qd, multivitamin, and metoclopramide 5 mg prn

Allergies: Amoxicillin, penicillin

Social History: 90 pack-year smoking history, quit 3 years ago.

Family History: Mother with hypertension, father died of a myocardial infarction.

Physical Exam:
Vital signs: Temp = 39.2 BP = 150/90 (120/78 after diuresis) HR = 124 RR = 24 SaO2 = 99% 2L nasal cannula
General: Adult male, no acute distress
HEENT: No jugular venous distension, sclerae anicteric
CVS: Tachycardic, normal S1/S2, no murmur, rub, or gallop
Lungs: Fine crackles halfway up bilateral lung fields
Abdomen: Normoactive bowel sounds, soft, nontender, no organomegaly
Extremities: Trace bilateral lower extremity edema, left upper extremity arteriovenous fistula without redness, warmth, or edema
Neurologic: Nonfocal

Labs:
CBC:
WBC count: 6,800 per mL
Hemoglobin: 11.3 g/dL
Hematocrit: 36%
Platelet count: 111,000 per mL
Differential: 78% neutrophils, 8% lymphocytes

Chem 7:
Sodium: 133 mmol/L
Potassium: 6.4 mmol/L
Chloride: 96 mmol/L
Bicarbonate: 21 mmol/L
BUN: 42 mg/dL
Creatinine: 6.8 mg/dL
Glucose: 105 mg/dL

EKG: Sinus tachycardia, rate 120, left anterior fascicular block
Chest X-ray: Low lung volumes with an enlarged cardiac silhouette. Engorged hilar vasculature, haziness in the perihilar region and over the left hemidiaphragm.

Hospital Course: In the emergency department, the patient was treated for hyperkalemia. His dyspnea was attributed to incompletely treated pneumonia and volume overload, and he was admitted to the medical service. Treatment included furosemide, albuterol, azithromycin, and ceftriaxone.

Despite aggressive fluid removal, the patient continued to require supplemental oxygen. He complained of dry cough and mild dyspnea on exertion. Fine crackles persisted on pulmonary exam. High resolution **computed tomography (CT)** of the chest, obtained to evaluate for interstitial lung disease, was significant for honeycombing and bronchiectasis in the lower lobes, as well as extensive hilar and mediastinal lymphadenopathy.

The patient underwent thoracoscopic biopsy of the right lung. Mediastinal biopsy was not performed because the patient became hypoxic and hypotensive. He was extubated and admitted to the postanesthesia care unit. Phenylephrine was continued for persistent hypotension. Several hours later, he developed a wide complex irregular cardiac rhythm with a heart

rate in the 90s. Within minutes, he became bradycardic and lost consciousness.

Cardiopulmonary resuscitation was begun. The patient was intubated and a transvenous pacer was placed. Scant fluid was obtained from pericardiocentesis. Per protocol, he received alternating boluses of atropine and epinephrine. Defibrillation performed for ventricular fibrillation was unsuccessful. Calcium, insulin, dextrose, and bicarbonate were administered for suspected hyperkalemia. The patient became asystolic, and resuscitation efforts were suspended after 45 minutes. Chemistries drawn during resuscitation were significant for potassium of 9.4 mmol/L.

An autopsy revealed extensive pulmonary, cardiac, and gastric sarcoidosis. Given the degree of cardiac involvement, it was hypothesized that the patient suffered a lethal arrhythmia. Hyperkalemia would have contributed, although chemistries obtained during resuscitation may not accurately reflect potassium levels immediately prior to the inciting event.

Discussion:

1. What are the clinical manifestations cardiac sarcoidosis? How is it treated?

Sarcoidosis, a multisystem disorder involving formation of noncaseating granulomas, frequently affects the heart. Although cardiac involvement is documented in up to 30% of patients at autopsy, it is clinically evident in only 5%. Sudden cardiac death may be the first manifestation. Cardiac involvement can occur at any point and may precede pulmonary findings. Presentation depends on the cardiac site involved. Manifestations include rhythm and conduction disturbances, repolarization abnormalities, papillary muscle dysfunction, infiltrative cardiomyopathy with congestive heart failure, and pericarditis. Conduction abnormalities, ranging from first-degree atrioventricular block to complete heart block, are the most common findings in large case series. Rhythm disturbances most commonly take the form of sustained or non-sustained ventricular tachycardia (VT). VT is the second most common presentation of cardiac sarcoidosis and is believed to cause the majority of sudden deaths.

A high index of suspicion is essential in the diagnosis of cardiac sarcoidosis. Testing may include endomyocardial biopsy, echocardiography, radionucleotide imaging, and magnetic resonance imaging (MRI). Treatment focuses on reducing the inflammatory response. Corticosteriods can slow the progression of fibrosis, although reversal of existing fibrosis is unlikely. Resolution of conduction and repolarization abnormalities with steroid treatment has been reported. Pacemakers and automated defibrillators may be indicated. Anti-arrhythmic drugs generally are not used, with recent reviews demonstrating a strong association with increased arrhythmia recurrence and incidence of sudden death.

2. What is the typical radiographic appearance of sarcoidosis?

The lungs are the most common site involved in sarcoidosis, affecting 90% of patients. The radiographic appearance can vary considerably, but three patterns are described. Pattern I is typified by bilateral hilar adenopathy; pattern II has bilateral hilar adenopathy with concomitant interstitial infiltrates (usually in the upper lung zones); pattern III is characterized by receding hilar adenopathy and increasing interstitial infiltrates. Advanced fibrosis without adenopathy is considered a subtype of pattern III.

High resolution CT of the chest is used increasingly to evaluate the patient presenting with interstitial lung disease. In sarcoidosis, the CT demonstrates hilar adenopathy and varying degrees of ground glass opacities and fibrosis with distortion of the underlying lung architecture. The distinguishing feature is that these changes are more prominent in the upper lung zones. This patient's presentation was unusual, as the underlying changes were mostly in the lower lung zones.

3. Is there an association between sarcoidosis and focal segmental glomerulosclerosis (FSGS)?

Increased calcium absorption with nephrocalcinosis is the most common cause of chronic renal failure in sarcoidosis. Interstitial nephritis with granuloma formation is seen in approximately 20% of cases, but renal insufficiency is uncommon. The course is rapidly progressive when such patients present with renal failure.

Glomerular disease is rare in sarcoidosis. The underlying pathology is diverse, including membranous nephropathy, FSGS, IgA nephropathy, and proliferative or crescenteric glomerulonephritis. FSGS can present late in the course; the pathogenesis may be related to T-cell dysfunction. Renal sarcoidosis is usually treated with corticosteriods.

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THE RHODE ISLAND HEALTH WEB QUERY SYSTEM

ANNIE GJELSVIK, PHD

The Rhode Island HEALTH Web Query System is a new resource on the Department of Health website that allows health professionals, community agencies, Department personnel, and the general public to produce aggregated health data for the state to their own specifications. This system provides health professionals and community organizations with valuable information with which to improve the health of Rhode Islanders through data-driven programs and policies. The RI HEALTH Web Query System is one of the Department of Health's responses to the ever-increasing public expectation for reliable and trustworthy online health data and information. The system is publicly accessible and requires no sign-in or registration.

The HEALTH Web Query System currently contains seven years (1998-2004) of data from Rhode Island's **Behavioral Risk Factor Surveillance System (RIBRFSS)** covering over twenty topics. (Table 1) The BRFSS is a national telephone survey of randomly selected non-institutionalized adults (ages 18 and older). The BRFSS monitors the prevalence of behavioral risks that contribute to the leading causes of disease and death among adults in the United States. It is administered in all 50 states and four US territories with funding and methodological specifications provided by the **Centers for Disease Control and Prevention (CDC).**[1]

Within the twenty topics, the system includes one hundred variables and allows users to obtain up-to-date information, view time trends, and combine years in order to obtain stable estimates. The system became operational in September 2004 on the Rhode Island Department of Health intranet and in September 2005 over the Internet. The project will expand access to other databases in phases, beginning with those required for monitoring the Healthy Rhode Islanders 2010 Leading Health Indicators,[2] then moving to other databases that reside in the Rhode Island Department of Health, and finally to certain external databases. In the next year the system will add Youth Risk Behavior Survey data,[3] death certificate data, and state population data from the 2000 Census and subsequent population estimates and projections.

HOW TO USE THE SYSTEM

Rhode Island's HEALTH Web Query System features a simple step-by-step process to request data for a single year, for multiple years in sequence, or for multiple years combined, to select independent and dependent variables, and, if desired, to subset the output by demographic or geographical variables. Users can also select whether to have estimates of the population at risk displayed with the prevalence rate data. After submitting a request the user is shown a confirmation screen to review the selections that have been made prior to processing of the request. Results are displayed in tabular form and, if selected, graphical form. Users can download these results in one of three formats: Excel format, maintaining all title and footnote information; Comma Separated Value format; and Rich Text format, which can be opened by word processing programs or copied and pasted directly into a PowerPoint presentation.

SYSTEM APPLICATIONS

This versatile system can be used to identify target populations for interventions, evaluate programs, track Healthy Rhode Islander 2010 objectives among sub-populations, and provide estimates of populations at risk and of risk factor prevalence for funding applications.

For example, in November 2004 the Department's Oral Health Program used the HEALTH Web Query System to obtain data for a successful grant application to implement the *Providence Senior Smiles Project*, an oral health surveillance and health promotion/disease prevention project to be conducted at selected sites serving non-institutionalized elders in Providence. According to Dr.

Table 1.

Topics Currently Available on Rhode Island's HEALTH Web Query System – BRFSS

Alcohol Consumption	Asthma
Body Mass Index (BMI)	Cholesterol
Colorectal Cancer Screening	Demographics
Diabetes	Disability
Firearms	Fruits and Vegetables
General Health	Geography
HIV/AIDS	HIV/AIDS Beliefs
Health Care Access	Healthy People 2010
Hypertension Awareness	Immunizations
Oral Health	Physical Activity
Prostate Cancer Screening	Seatbelts
Smoking	Weight Control
Women's Health	

Table 2.
How to access Rhode Island's HEALTH Web Query System – BRFSS

Direct link to the system	http://www.health.ri.gov/webquery/index.html
Link to RI's BRFSS page	http://www.health.ri.gov/chic/statistics/brfss.php
Sample query	http://www.health.ri.gov/webquery/Sample%20query.htm

Deborah Fuller, Dentist Consultant, Office of Primary Care, "The system provided an instantaneous result which we incorporated into our grant application immediately. Using the system allowed us to access the data at our convenience (based on our timeline) using our program staff as opposed to requesting assistance from other offices (Health Statistics)."

Development Process

The development of this system has been supported by a Cooperative Agreement under the Assessment Initiative of the CDC. During the first year of the Agreement, project staff held several focus sessions with stakeholders, partners, and data users to assess interactive web-query systems for health data maintained by other states and by federal agencies. The goal of these sessions was to have an inclusive design process that maximized the utility and flexibility of the system implemented here. Based on the results of these sessions, the software program SAS IntraNet was selected to implement Rhode Island's web-query system in October 2003. Initially, five years of RIBRFSS data were converted into the data format for the system; currently, seven years (1998-2004) of RIBRFSS data are accessible on the system.

In addition, during the first year of the project, project staff and the Office of Health Statistics jointly undertook a comprehensive review of the RIBRFSS using *Updated Guidelines for Evaluating Public Health Surveillance Systems: Recommendations from the Guidelines Working Group,*[4] including a survey of RIBRFSS data users. This work is summarized in a report on the current needs of RIBRFSS users and recommendations for improving the RI-BRFSS.[5] Progress towards these recommendations and improvements is reviewed yearly.

How to Access the System

Users can access the system through the HEALTH web site in two ways: directly at http://www.health.ri.gov/webquery/index.html or by navigating there from the RIBRFSS web page (http://www.health.ri.gov/chic/statistics/brfss.php). Instructions for use of the system, with graphics and examples of result interpretation, are provided on a sample query page (http://www.health.ri.gov/webquery/Sample%20query.htm). (Table 2)

Annie Gjelsvik, PhD, is Project Coordinator of the Assessment Initiative Grant and Investigator, Department of Community Health, Brown Medical School.

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5. A copy of this report is available from the author at annieg@doh.state.ri.us.

Lifestyles of Retired Rhode Island Physicians

Medicine & Health/Rhode Island would like to publish an issue devoted to discussions of the lifestyles of retired Rhode Island physicians.

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A Physician's Lexicon

The many words of diabetes mellitus

Aretaeus the Cappadocian, the immortal Alexandrian physician of the second Century, was confronted with a patient exhibiting excessive urination. He chose a Greek word, *diabetes* (meaning that which passes through), to define what he considered to be the dominant clinical sign in his patient. The Greek prefix, *dia-*, means through or entirely, (as in words such as diagnosis, dialect, dialysis, and diadochokinesis) and is appended to the Greek stem, *baino-*, meaning to go.

The word *mellitus*, however, is a word of Latin origin. *Mellis,* in Latin, means honey (and also refers to the bee). Melliferous, mellifluous and Melissa are all derivative, but not words such as melody and melodrama which are descended from a Greek word meaning song. Another Latin word for sweet is *dulcis,* which forms such English words such as dulcet, dulcimer and Dulcinea, Don Quixote's girlfriend.

Willis, in 1670, distinguished between those with a sweet-tasting urine, (diabetes mellitus) and those with polyuria without taste (diabetes insipidus).

A Greek root, *glyco-*, meaning sweet, forms the basis for English words such as glycogen, glycosuria, glycerin and hyperglycemia. The word licorice, meaning a sweet-tasting leguminous root, had originally been spelled glycyrrrhiza and is hence derived from the same Greek root. The root *gluco-*, as is words such as glucose and glucosamine, represents an ancient misspelling of the Greek root, *glyco-*. The Latin suffix, *-ose,* meaning full of (as in adipose) usually denotes a carbohydrate such as amylose, hexose or lactose.

The Greek adjectival prefixes, *hypo-* and *hyper-* (as in hyperglycemia) mean less than or more than. Their Latin equivalents are *super-* and *sub-*.

The neologism, insulin, (suggested by Schaefer in 1913) is derived from the Latin *insula*, meaning island (and represents an allusion to the source of the hormone in the pancreatic islands of Langerhans.)

The word pancreas, first used by Herophilus in about 300 BC because of the meaty quality of the organ, is taken from the Greek prefix, *pan-*, meaning all (as in words such as pandemic, panacea, panorama and pandaemonium) and a Greek root, *kreas,* meaning flesh. This root also appears in English words such as creatine, creature, creative, and recreation.

-Stanley M. Aronson, MD

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

Vital Statistics

Edited by Roberta A. Chevoya, State Registrar

Rhode Island Monthly Vital Statistics Report

Provisional Occurrence Data from the Division of Vital Records

Underlying Cause of Death	Reporting Period			
	November 2004	12 Months Ending with November 2004		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	246	2,989	279.4	4,779.0
Malignant Neoplasms	207	2,498	233.5	6,941.5
Cerebrovascular Diseases	46	488	45.6	782.5
Injuries (Accident/Suicide/Homicide)	35	453	42.3	7,216.0
COPD	37	463	43.3	377.5

Vital Events	Reporting Period		
	May 2005	12 Months Ending with May 2005	
	Number	Number	Rates
Live Births	1313	13,617	12.7*
Deaths	826	10,180	9.5*
Infant Deaths	(5)	(81)	5.9#
Neonatal deaths	(5)	(66)	4.8#
Marriages	669	7,902	7.4*
Divorces	232	3,179	3.0*
Induced Terminations	367	5,384	395.4#
Spontaneous Fetal Deaths	81	1,016	74.6#
Under 20 weeks gestation	(78)	(934)	68.6#
20+ weeks gestation	(3)	(82)	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 1,069,725

(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 1915

Twenty years ago the Rhode Island Medical Society had lobbied for a law making it a misdemeanor "for failure to report within 6 hours by anyone who has charge of a new-born infant any redness or inflammation of the eyes." "The moral effect of the law and its attempted enforcement was sufficient to decidedly lessen the number of cases of gonorrheal ophthalmia for a number of years, but we have become somewhat careless and the profession itself is to blame for many of the cases of blindness, as well as ignorant midwives." A Boston study linked more cases of blindness from *opthalmia neonatorum* to physicians than midwives. In Providence, the Editorial cited one instance where a physician ignored the observation of a district nurse: "The district nurse had called his attention to the fact of the child's having a sore eye, but he assured her it was nothing at all serious." She, though, took it on herself to send the child to the hospital. In 1910-11, 23.9% of pupils entering school were blind [in at least one eye] from this disease; in 1914-5, 15.1%.

Jay Perkins, MD, in "The Case of the Tuberculous," recounted the history of St. Joseph's Tubercular Hospital at Hillsgrove. It began in September 1904 with tents (one for patients, one for the Sisters). When the tents blew down, the sisters and patients sought shelter in a nearby farmhouse. Soon afterward a building was erected on site. Dr. Perkins praised the Sisters: "Perhaps they will be boycotted by the 8 –hour-a-day labor union when I tell you that they frequently work from 3 or 4 o'clock in the morning until 8 o'clock at night." The hospital averaged 70 patients a day, with 6 sisters, 3 nurses, 2 orderlies "and some help from the patients themselves." "The main remedies are the physiological ones of fresh air, good nourishment and a proper regimen of exercise and rest."

FORTHCOMING

Medicine & Health/Rhode Island

DECEMBER 2005

Forensic Medicine, Part II

Guest Editor:

Barry Wall, MD

Fifty Years Ago, November 1955

Jose M. Ramos, MD, in "Rheumatoid Arthritis: Fifteen Years' Experience with Chrysotherapy," gave statistics on 36 patients treated in the past 15 years at Newport Hospital. He praised the efficacy of the treatment.

Seebert Goldowsky, MD, in "The Beginnings of Medical Education, Part III," traced the development of hospitals in Rhode Island. The earliest ones were for the military, for seamen, and for quarantine. In 1716, Newport erected a smallpox hospital on a harbor island; in 1732 Bristol used a house for a smallpox hospital. In 1711 Tiverton had a military hospital for injuries expected in the Battle of Rhode Island. From 1752-6 Providence had 3 smallpox hospitals; in 1798 Providence established a yellow fever hospital; in 1824 Providence bought property at Fields Point for a smallpox hospital; in 1910 the Providence City Hospital for Contagious Diseases (later renamed the Charles V. Chapin Hospital) opened. In 1868 Rhode Island Hospital opened. On the efforts to start a medical school at Brown, the author recounted William Osler's 1899 talk before the Rhode Island Medical Society: "The conditions are singularly favorable for a small first class school."

Twenty-Five Years Ago, November 1980

Alan B. Weitberg, MD, in "Laboratory Testing in Teaching Hospitals: Impact on Cost of Health Care," noted that "A simple audit can produce results in reducing costs." Specifically, at Roger Williams General Hospital, a review of patients on the medical service showed "unnecessary" tests dropping from 199 one week in November to 33 on a week in January. Among the strategies to reduce costs, was a discussion of those costs.

Pasquale F. Finelli, MD, James Reimer, MD, Mary Ambler, MD, discussed "Intracerebral Hemorrhage reported in patients with CNS disease receiving TPN."

Charles E. Millard, MD, contributed "The Effect of Modern Therapeutics on the Human Gene Pool," the winner of the 1979 Fiske Fund Prize Essay.

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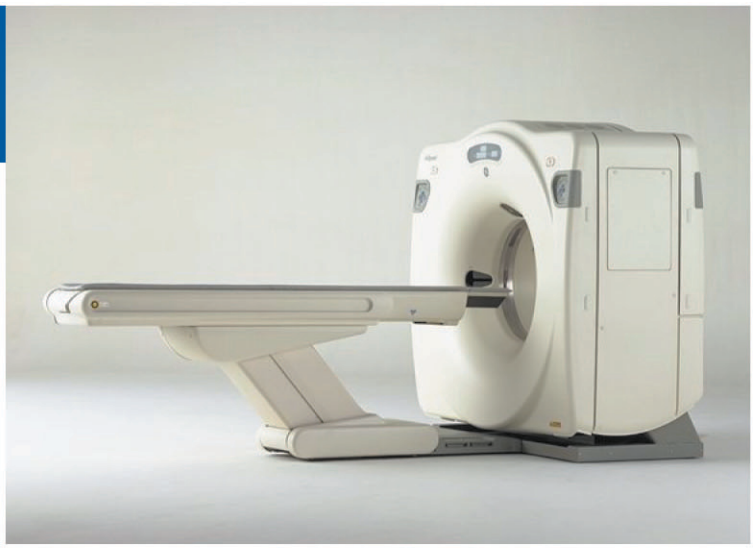

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