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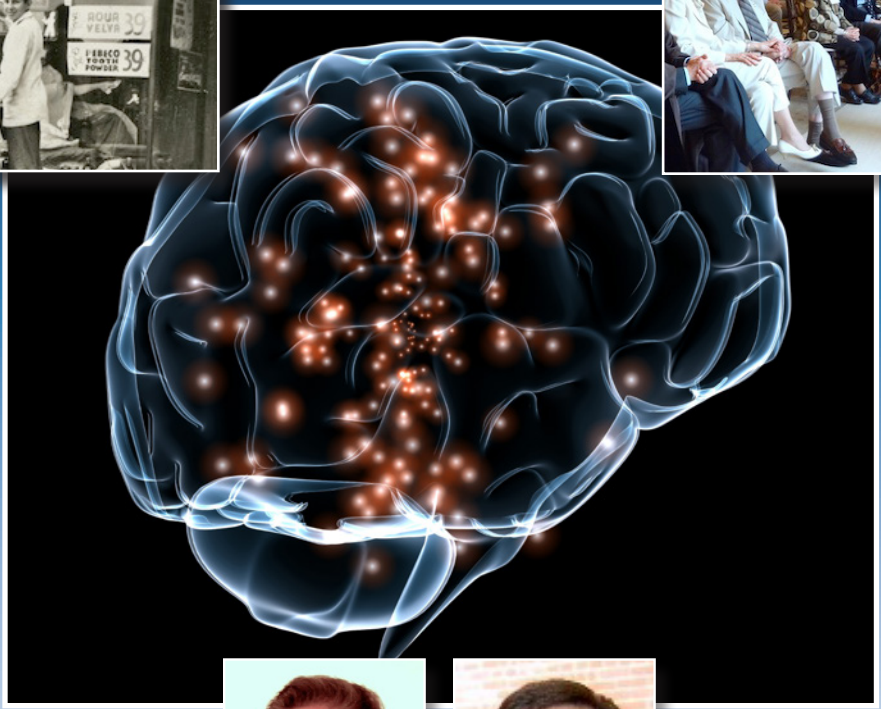

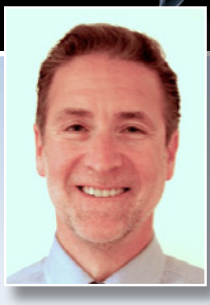

SPECIAL SECTION

IDENTIFYING *and* MANAGING PSYCHIATRIC EMERGENCIES

COLIN J. HARRINGTON, MD; ROBERT BOLAND, MD; GUEST EDITORS

JUNE 2014 VOLUME 97• NUMBER 6 ISSN 2327-2228

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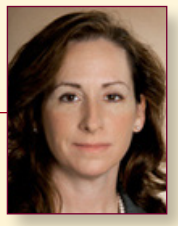

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The Brown university traumatic brain injury research consortium and the Norman Prince Neurosciences Institute.

Rogg J, Lafrance WC Jr, Wilcox E, Correira S, Chodobski A, Szmydynger-Chodobska J, Raukar N, Ellermeier A, Spader H, Machan JT.
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This article provides an overview of the Brown University Traumatic Brain Injury Research Consortium (TBIRC) and summarizes the multidisciplinary basic and clinical neuroscience work being conducted by investigators at Brown University and the affiliate hospitals in association with the Norman Prince Neurosciences Institute (NPNI).
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Retirement: For Better or Worse?

JOSEPH H. FRIEDMAN, MD
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"The doctor told him not to retire. He said that retirement would kill him."

I'm often amazed by what doctors tell patients and what patients believe. Usually the quote is more like, "if you waited another 10 minutes he'd have been dead." As if we can forecast the future. This quote came from the wife of a patient of mine, a 72-year-old man with Parkinson's disease who was continuing to work three days a week in his family business, and rather ambivalent about giving it up. He mostly wanted to give it up but his friend, a man of about the same age, had recently gotten the advice quoted above. I told the patient and his wife, who apparently believe that the doctor really does know best, that, "I never said anything like that to you. In fact, I've never said anything like that to any of my patients. My patients tell me what they want to do and we discuss what they can and cannot do, and the patient makes a decision. I can't predict the future. I just try to help you make a decision." Of course, who knows what the doctor really said? The gap between what is said in the doctor's office and what is heard has been studied and may be enormous.

I often ask my retired patients about their retirement. Some rejoice in their emancipation from the daily schedule and their ability to do things they really enjoyed much more than work. "I'm so busy I don't know how I had time to work!" Others are adrift. One of my physician colleagues, recently retired due to illness, and still adjusting, reported that he met another retired doctor, who summed up his retirement this way: "I used to be important."

Retirement and disability are quite different but may overlap. The person who retires because of a disability is in a very different mindset than the one who has looked forward to stopping work for years in order to do something prized more highly than their vocation. Sometimes disability provides the impetus for a long-considered retirement, a little, or not so little, nudge over the line. Since I deal only with patients with movement disorders I mostly see people with Parkinson's disease. For those who begin their illness during their working years, which is, in fact, the majority, the notion of retirement or disability is a very big deal. Over all I encourage people with PD who want to continue working and think they can, to continue. Some need job modifications, of course, like the guys who climb utility poles and fix overhead wires, or roofers or firemen, or secretaries who spend a lot of time on the phone but have failing voices from their illness. But, unlike the situation of the patient with chronic pain who needs "work hardening" therapy to live with the pain and restore meaning and financial support in their lives, PD is a progressive disorder. Work now takes longer, is harder, and may not be performed at the same level as before, and therefore less rewarding. Furthermore the most disabling aspects of PD for many are the "non-motor" symptoms, problems such as fatigue, sleepiness, loss of ability to perform two tasks at the same time. This complements the difficulties induced by physical slowness, reduced dexterity, tremor and imbalance. These problems are impossible to assess from the outside. When a PD patient asks me for a disability or an early retirement letter, I always agree. Most people want to continue working.

One of my physician colleagues, recently retired due to illness, and still adjusting, reported that he met another retired doctor, who summed up his retirement this way: "I used to be important."

I've often thought about retirement, but can't actually imagine doing it. I've reached "retirement age," and could get social security now. My brother is retired and a close friend from medical school has set a firm date for his retirement, but I can't see what I'd do, not just to keep busy and avoid boredom, but how I'd give structure and meaning

to my life. I can easily see sliding into the gloomy retrospection of, "I used to be important." Of course, I'm not "important" now, so I don't expect to be looking back to the days when I was important, but I do have a clearly defined role in society, and to some people I am important. People now ask for my opinion, patients for example. I'm asked to teach, to lecture, to evaluate articles, to evaluate patients. I have value. The real issue with retiring (aside from the not-so-small financial issues) is that my pleasure in life comes primarily from my work. This is not necessarily a good thing. I think the world would agree that it was a good thing for Charles Dickens and Louis Pasteur to work until they died, but I'm much more easily replaced. My problem is the lack of substitute for the work. I like to be on the go. I need projects. When I'm at work I worry when I'm not too busy, and I worry when I am too busy that I'm not doing a good job. There's no good in-between. But I'm always on the go, always doing something.

My main dread is reaching a point where I have to retire even when I don't want to, and, even worse, being forced to retire due to skill or mind erosion, and losing the insight into recognizing it.

I've given a lot of thought to being "not important" anymore, and I have decided that it does not sit well with me. I'd like to think that my achievements were not motivated by a desire to become "important," but rather to actually accomplish something tangible, and of value. I really suspect I'm more motivated by fear of failure than competition for success.

As my neuronal count slowly but inevitably declines, I pray that the decline is not accelerated by some hideous disease. Each day as I drive to work I wonder how I'll handle the day when I won't be able to do this anymore. ❖

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Joseph H. Friedman, MD, is Editor-in-chief of the *Rhode Island Medical Journal,* Professor and the Chief of the Division of Movement Disorders, Department of Neurology at the Alpert Medical School of Brown University, and chief of Butler Hospital's Movement Disorders Program.

Disclosures

Dr. Friedman's conflicts of interest can be obtained by request.

Rhode Island Medical Journal Submissions

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Contributions report on an issue of interest to clinicians in Rhode Island. Topics include original research, treatment options, literature reviews, collaborative studies and case reports.

Maximum length: 2000 words and 20 references.

PDFs or Jpegs (300 dpis) of photographs, charts and figures may accompany the case, and must be submitted in a separate document from the text. Color images preferred.

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The writer shares a perspective on any issue facing clinicians (eg, ethics, health care policy, patient issues, or personal perspectives). Maximum length: 600 words.

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Authors submit an interesting image or series of images (up to 4), with an explanation of no more than 500 words, not including legends for the images..

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The Moral Heritage of the Corner Drugstore

STANLEY M. ARONSON, MD
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No community of humans, no matter how primitive, had been without someone who possessed a special skill in identifying plants, someone knowing which were poisonous and which, when consumed, yielded a particular and purposeful effect. And so, as nomadic groups became increasingly attached to the land, this casual botanical skill evolved into a beneficial profession, often called herbalism, and typically practiced by women.

By the medieval era, herbalism as a mercantile specialty evolved into the chemist's domain; and by the 16th Century most British communities possessed such a retail establishment, now divorced from the grocers and called the apothecary shop. They were sanctioned by their own professional guild and guided by governmental regulations. And by the opening years of the 19th Century, apothecaries were respected professionals. John Keats was a licensed apothecary when he began his career as a poet. One critic declared: "'Tis better to be a starved apothecary than a starved poet."

In the centuries following the era of the medieval chemist's stores and the apothecary's establishments – but before the advent of strip malls, mega-pharmacies and health-related retail chains – there arose the neighborhood drugstore. In upscale 20th-Century communities, they were called pharmacies; but in inner Brooklyn, it was merely the corner drugstore.

Few events were more disquieting than being summoned to the drugstore telephone by the pharmacist's boy.

Since the 1920s, the drug stores have evolved dramatically, first, by establishing linear, sit-down counters to dispense ice cream sodas and other non-alcoholic beverages; then, by

Photograph shows the interior of a soda fountain/drugstore taken circa 1910; man on left, wearing dark suit, stands behind drugstore counter; man on right, in white jacket, stands behind soda fountain counter.

offering an ever-expanding variety of over-the-counter, prepackaged medications including a bewildering spectrum of vitamins, other micronutrients, unproven nostrums for a spectrum of ailments and even contraceptives. The tradition of the drugstore as a health-engendering establishment withered when it took to dispensing children's toys, cosmetics, packaged foods and even automobile tires.

In the 1920s, a time that historians considered the epitome of American pride in itself, the drugstore became the anchor establishment of the lower-class neighborhoods, frequently situated at the intersection of two major streets. Its windows displayed a few medically-oriented symbols such as mortars and pestles, perhaps an ancient microscope but were otherwise austere and uncommunicative.

The drugstore on Union Street was owned and operated by a white-coated, registered pharmacist whose father had managed the store before him. Like the savings bank and the local police station, the drugstore represented a basic community resource, an indispensable institution, an anchor that seemed more forbidding than friendly, more imperishable than welcoming; yet it was vital for the functioning of that microcosm called 'the neighborhood.' In some neighborhoods the drugstore was the pole-star of the community. ("I live just two blocks west of Harrison's Drug Store.")

A completed prescription was the penultimate event when a physician made a house call. And so, with trembling hands, this life-saving bit of paper was brought to the drugstore. Opening the pharmacy's front door activated a bell announcing the arrival of a customer.

One then entered into a poorly illuminated room; and to one side, the Bell Telephone public booth, with its folding doors, all in funereal mahogany. Since most neighborhood apartments in the 1920s had no telephones, this drugstore telephone booth became an indispensable part of the local business of living. Making a phone call, in those days, was never a frivolous happening. Rather, it summoned the family physician or it notified relatives of the birth, death or mortal sickness of a family member. And when a call came in for one of the neighborhood residents, the pharmacist would dispatch one of his sons to beckon Mrs. Schwartz who lived on the fourth floor, back apartment, in the second tenement around the corner. Few events were more disquieting than being summoned to the drugstore telephone by the pharmacist's boy.

Behind the counter sat the pharmacist's wife with all the congeniality of Lady Macbeth. She was accompanied by her notebook, pencil, her ancient Remington typewriter and the cash register. She rarely spoke, but the gravity of the illness that had provoked the prescription would be clearly evident in her facial expressions.

In the back room was the pharmacist with his mortars, pestles, an array of empty bottles, a scale to weigh powders, a shelf with containers holding dried herbs, a microscope for urinalysis, a hand-press to make pills, and an assortment of elixirs, nostrums, decoctions and placebos to fill the complex formulations of the physician's prescriptions.

The inner city of America, in the decade of the 1920s, was a fragile patchwork of immigrant families striving to merge with the mainstream middle class. This resident population was in constant flux with new families arriving and second- generation families planning to move elsewhere. Tenancy, for these mobile families, rarely persisted for more than a year or two. And in a sea of instability, then, the drugstore served as a monument of cohesion and stability. ❖

Author

Stanley M. Aronson, MD, is Editor emeritus of the *Rhode Island Medical Journal* and dean emeritus of the Warren Alpert Medical School of Brown University.

Disclosures

The author has no financial interests to disclose.

Working on the Family 'Pharm'

MARY KORR
RIMJ MANAGING EDITOR

The *Rhode Island Medical Journal's* graphic designer, Marianne Migliori, became intrigued by Dr. Stanley Aronson's story of neighborhood drugstores in his commentary this month. She provided the accompanying photos of her father-in-law, the late **JULIUS C. MIGLIORI, MD**, in front of the establishment started by his maternal grandfather, Antonio Cardi.

Julius' brother, **JOSEPH L. MIGLIORI, MD**, a retired Cranston ophthalmologist, recalled the family business in response to questions from RIMJ. It is truly an American, a Rhode Island and a Cranston story. Thank you 'Uncle Joe' for sharing a glimpse from the past.

PHOTOS COURTESY OF THE MIGLIORI FAMILY

The late Julius C. Migliori, MD, who was the Chief of the Department of Anesthesia for 40 years at St. Joseph's Health Services, washes the window of his uncle's pharmacy in Cranston circa 1940..

Q. When did the pharmacy first open?

A. The drug store, called the Medical Arts Pharmacy, was built by my grandfather (Antonio Cardi) to accommodate his son and my uncle, **Alfred Cardi**, who graduated from the R.I. College of Pharmacy (now URI's College of Pharmacy) in about 1925. My grandfather thought it would be a good idea to have him practice in Knightsville where the family was well-known.

Eventually, **Mary Cardi-Longo** (Alfred's sister) also worked there as a pharmacist upon her graduation from the same college 13 years after her brother.

Q. Was the clientele mostly immigrants?

A. The workers were mostly first-generation, bilingual Italo-Americans; but the clients they served were the Italian immigrants from Itri, Italy, newly settled in Knightsville and very much interdependent for survival. The Medical Arts Pharmacy was very successful because of this. The pharmacy was a thriving business until Alfred's death in 1977. His children tried to maintain the drugstore but with competition from the big chain pharmacies, it was doomed without Alfred and his devoted Knightsvillers.

Q. Other than pharmaceuticals, what else did the pharmacy sell?

A. Besides the pharmacy, there was a full-service soda fountain with store-made ice cream and several booths where one could enjoy an ice cream soda, etc. Available for sale were various sundries and hygiene products, the newspaper, perfumes (to be wrapped as presents if wished,) penny candy, cigarettes and cigars, liniments, bandages, soda-pop, etc. About 1960, a special section for liquor was added, not to be sold on holidays.

The Medical Arts Pharmacy circa 1936; the building still stands at 1701 Cranston Street in Cranston. At left, Alfred Cardi poses with three of his brothers-in-law, [unidentified], in the center, Giuseppe Migliori with son Julius as a child, at right, brothers Michael and Albert Perrino.

Q. Did you work there as a boy?

A. I worked at the drugstore from 1954, when I was in Jr. High, until 1968, when I was in medical school. When my brother Giulio (Julius) went to high school, he quit the drugstore to play varsity football. It was a family business!

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HARRY SCHWARTZ, MD

ISRAEL – Janine Schwartz, RN, of Providence, and her daughter, Alanna Schwartz, a research associate at the UCSF School of Medicine in San Francisco, check out the May issue of RIMJ while visiting Jerusalem.

Editor's Note: Please take RIMJ on your travels (easily downloadable to your mobile device at rimed.org), snap a photo for publication, and send to mkorr@rimed.org.

MICHAEL MIGLIORI, MD

FRANCE – RIMJ designer Marianne Migliori at the Louvre, Paris with a 2nd-century Roman statue of Hygeia, daughter of Aesclepius, and the figure symbolized in the RIMS seal.

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Identifying and Managing Psychiatric Emergencies

COLIN J. HARRINGTON, MD; ROBERT BOLAND, MD
GUEST EDITORS

Most U.S. medical schools require only five core clinical rotations in the third year – internal medicine, surgery, pediatrics, obstetrics and gynecology, and psychiatry. Despite the growing number of medical-surgical subspecialties, there are fundamental reasons that psychiatry remains a core clinical requirement for medical school graduation and physician training: psychiatric disease is highly prevalent, extremely distressing to patients and families, associated with high levels of disability and health care costs, linked to significant reductions in quality of life, and has adverse effects upon the course of many illnesses with which it is co-morbid, including diabetes mellitus, cardiovascular disease, and stroke, amongst others.

Despite great advances in the understanding of the neurobiological underpinnings of psychiatric disease and the development of more effective and better tolerated medications, patients with severe and persistent mental illness (SPMI) such as schizophrenia and bipolar disorder have a life expectancy that is 15-20 years shorter than that of the general population. This reduction in life expectancy is due not only to suicide but to co-morbid substance abuse and the more aggressive course of associated medical illnesses driven by suboptimal adherence with care, inadequate attention to modifiable risk factors for disease, metabolic side effects of psychotropic medications, and other still poorly understood psychophysiologic mechanisms that affect other organ systems.

Psychiatry as a specialty has its roots in neurology. Their theoretical, diagnostic, and therapeutic paths, however, diverged through much of the 20th Century. After years of treating psychiatric and neurologic disease separately, the pendulum has swung and the specialties find themselves comfortably and appropriately reconnected. Perhaps better considered as *neuropsychiatry*, today's psychiatry is poised at the interface of medicine and neurology and seeks to understand the brain basis of behavior, the neurologic roots of psychiatric disease, the behavioral presentations of neurologic disease, and the psychosomatic and psychophysiologic relationships between medical and psychiatric illness.

No less important to a *newer* neuropsychiatric conceptualization of mental illness is a *renewed* emphasis on the fundamental and traditional bio-psycho-social factors that inform the presentation and course of medical and psychiatric disease – such as access to care, employment status, community supports, interpersonal relationships, family function, and specific personality factors.

This issue of the *Rhode Island Medical Journal* (RIMJ) is dedicated to a discussion of psychiatric emergencies and frequently encountered urgent behavioral problems. It includes articles on delirium diagnosis and treatment, management of neuropsychiatric symptoms in dementia, recognition and treatment of serotonin syndrome, toxidromes related to newer designer drugs, and practical approaches to the management of the behaviorally dysregulated "problem patient."

CONTRIBUTIONS

- In "Delirium Diagnosis and Treatment: Parts I and II," I have joined with my co-author, **KALYA VARDI, MD**, to review the presentation, causes, pathophysiology, evaluation, and treatment of delirium. Delirium is highly prevalent and is associated with multiple adverse patient and systems outcomes. It is often under-recognized and can be difficult to treat. Behavioral and pharmacologic treatments and preventative strategies are discussed.
- In "The 'Problem Patient': Modest Advice for Frustrated Clinicians," **ROBERT BOLAND, MD**, provides a discussion of personality constructs and abnormal illness behaviors that often interfere with the effective and efficient delivery of care. These patients and behaviors can challenge even the most even-tempered of physicians, nurses, and hospital staff. Dr. Boland discusses issues of countertransference and offers practical suggestions regarding staff approach to these patients – with the specific goals of optimizing patient engagement in care and avoiding responses that can escalate behavioral dysregulation.
- "Serotonin Syndrome: A Concise Review of a Toxic State" by **DWAYNE HEITMILLER, MD**, focuses on the presentation, implicated drugs, pathophysiology, and management of this iatrogenic toxidrome. Differential diagnosis, including neuroleptic malignant syndrome, and preventative strategies are emphasized.
- In "Practical Management of Alzheimer's Dementia," authors **JEFFREY BUROCK, MD**, and **LILLY NAQVI, BS**, review molecular mechanisms operative in Alzheimer's disease and newly developed anti-amyloid therapies, and focus on the treatment of cognitive dysfunction and neurobehavioral symptoms in dementia.

- **ELIE AOUN, MD**, **PAUL CHRISTOPHER, MD**, and **JAMES INGRAHAM, MD**, in "Emerging Drugs of Abuse: Clinical and Legal Considerations," focus on the clinical presentations, recognition, and management of novel toxidromes associated with newer illicit drugs. Neurotransmitter mechanisms operative in these intoxication states are reviewed. Emergency departments and psychiatric services in Rhode Island and nationally have seen a remarkable rise in these complicated, severe, and sometimes lethal syndromes.

Why are these subjects treated together in this issue of RIMJ? These illness and clinical problems are prevalent, tax our health care system, and cut across medical specialties. To effectively address and manage diagnoses like dementia, delirium, toxidromes, substance abuse, and health-rejecting patients, physicians must work collaboratively, bringing their various areas of expertise to bear on complex clinical presentations. Health care reform has only hastened the increasing interest in collaborative care, with an eye towards psychiatry's role in an integrated system to improve outcomes and reduce health care costs. The reader is encouraged to consider these diagnoses in the context of an integrated model of health care delivery.

Guest Editors

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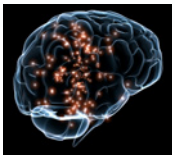
DARPA WORKS



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Delirium: Presentation, Epidemiology, and Diagnostic Evaluation (Part 1)

COLIN J. HARRINGTON, MD; KALYA VARDI, MD

ABSTRACT

Delirium is a highly prevalent and complex neuropsychiatric disorder marked by attentional dysfunction, disturbances in multiple cognitive domains, and changes in motor behavior, perception, sleep, and thought process. Delirium results from diverse toxic, metabolic, infectious, and structural etiologies and is associated with a number of adverse outcomes. Delirium pathophysiology involves perturbation of multiple neurotransmitter systems. Behavioral presentations of delirium are common and are often misattributed to primary psychiatric processes. Diagnostic assessment of delirium includes thorough physical examination, careful cognitive testing, appropriate metabolic and infectious studies, review of medications, and structural brain imaging and electroencephalography as indicated. Pharmacologic and non-pharmacologic interventions have been documented to reduce the incidence and severity of delirium. Antipsychotics are the treatment of choice for delirium-related agitation and psychosis.

KEYWORDS: Delirium, encephalopathy, cognitive disorder, agitation

INTRODUCTION

Delirium is a complex neuropsychiatric disorder marked by an alteration in level of consciousness, attentional dysfunction, disturbances in other cognitive domains including memory, orientation, and language, and associated changes in non-cognitive domains of motor behavior, perception, affect, sleep-wake cycle, and thought process.[1,2] Delirium results from diverse etiologies and is associated with a number of adverse clinical and systems outcomes including secondary infections, falls, violence, and increased hospital length-of-stay, healthcare costs, and mortality.[1-8] While the pathophysiology of delirium is poorly understood, the neurobehavioral syndrome likely represents a final common pathway of perturbation of multiple neurotransmitter systems operative across widely distributed neural networks.[1,9-11]

At its core delirium is a cognitive disorder and, as such, associated neurobehavioral changes and psychiatric signs and symptoms are considered *secondary*. Delirium has been described in the medical literature since antiquity and has acquired many diagnostic labels including acute confusional state, acute brain dysfunction, acute brain failure, acute organic brain syndrome, ICU psychosis, and metabolic encephalopathy, amongst others. The term *delirium* is derived from the Latin roots *de* (translated "away from") and *lira* (translated "furrow of a field") thus suggesting that one is derailed from the plowed or straight path.[11]

The term *encephalopathy* is often employed in place of or alongside delirium and allows for the proper grouping together of delirium and dementia as cognitive disorders – while also providing for the longitudinal course-based distinction between delirium and dementia, as acute and reversible, and chronic and progressive forms of encephalopathy, respectively. Use of this terminology also allows for description of the intermediate syndrome of sub-acute encephalopathy where cognitive dysfunction is often less obvious and neuropsychiatric symptoms predominate.

EPIDEMIOLOGY, RISK FACTORS, AND OUTCOMES

Delirium is a highly prevalent disorder estimated to occur in 10%-15% of general medical-surgical inpatients, in 25%-45% of hospitalized cancer patients, and in 80%-90% of terminally ill palliative care patients.[1,4,5,11,12] Rates of delirium are particularly high in the intensive care unit (ICU) where studies suggest that 30% of patients are delirious on admission and 60% develop delirium during the course of their critical illness.[1,3,5,13-15] Upwards of 80% of mechanically ventilated ICU patients are estimated to be delirious.[14-16]

Models of delirium etiology suggest predisposing, precipitating, and perpetuating factors.[1,2,4,11,17] Illness, pharmacologic, and environmental factors likely play roles in the development and persistence of delirium. Identification of modifiable factors is crucial to prevention and optimal management of delirium. Older age, premorbid cognitive dysfunction, medical illness burden, baseline poor functional status, and medication exposure are most highly predictive of delirium development.[1,2,4,5,11] Baseline cognitive dysfunction is the most robust predictor of incident delirium in the hospitalized patient with upwards of 60% of acute encephalopathy episodes thought to occur atop a baseline of cognitive impairment.[1,13,17,18] Delirium superimposed on dementia or other types of cognitive dysfunction appears more resistant to treatment.[1,19] Surgical patients, especially those undergoing total joint replacement and cardiac procedures requiring bypass, are at particularly high risk for the development of delirium.[4,20-22]

Delirium is associated with numerous adverse outcomes including prolonged hospital length of stay,[1] increased rates of discharge to institutional care settings,[3] increased health-care costs,[8] reduced quality of life,[1,11] increased short- and long-term mortality,[5-7] and long-term cognitive impairment.[9,13,14,18] Delirium in the ICU, after controlling for numerous confounders, is associated with an increase in ventilator dependent days and ICU length of stay, and is an independent predictor of increased mortality in mechanically ventilated patients.[16] Delays in diagnosis and treatment of delirium are associated with increased mortality in ICU patients.[23]

CLINICAL PRESENTATION, EXAMINATION, AND COURSE

There are many definitions of delirium in the literature. Factor analysis studies suggest that the broad and heterogeneous phenotype of delirium loads onto three core symptom domains including a "cognitive" domain (orientation, attention, short-term memory, long-term memory, and visuospatial ability), a "higher level thinking" domain (language and thought process), and a "circadian" domain (sleep-wake cycle and motor behavior).[24] Common to all definitions of delirium is a disruption in attention, often signaled by a frank alteration in level of consciousness or sensorium. On a spectrum between stupor and normal consciousness, delirium presentations can range from frank somnolence to more awake and alert states marked by subtle concentrational difficulty.[1] Intact attentional *function* includes the ability to focus, maintain, and shift attention according to environmental demands. Attentional *dysfunction* may manifest in clinical findings of obvious confusion with incongruent responses to the examiner's queries and in more subtle ways where patients can focus initially but are distractible, impersistent, or perseverative on bedside and formal neurocognitive testing. If basic attention and concentration are impaired, then more complex cognitive functions of language, orientation, memory, and thought process are secondarily disturbed. In cases of severe delirium, attentional impairment can frankly preclude adequate assessment of other higher order cognitive domains.

When attention and awareness are altered, the delirious patient's navigation of the environment is impaired. The surgical dictum to "look, listen, and feel" regarding the examination of the acute abdomen is applicable to the examination of the delirious patient as well. Observation of patients from a distance can provide clues about their cognitive function. Disheveled appearance, restless fidgeting, picking behavior, and talking out loud when alone in the room suggest inattention to self, disconnection from the environment, and response to internal stimuli. Just as palpation of the abdomen can alter the findings of auscultation, so too can more formal examination of delirious patients alter their cognitive performance. When engaged with a more structured cognitive assessment, the confused patient can sometimes "borrow the frontal lobe" of the organized examiner and respond more appropriately than expected – a particularly relevant issue in the assessment of the less obviously encephalopathic patient where proper diagnosis of abnormal behavior hinges on a comprehensive neuropsychiatric assessment. In this regard, the act of examining the patient may change the examined – and thus should come after a period of simple observation and casual engagement.

Delirium typically develops over hours to days. Subacute encephalopathies due to smoldering infection, slowly developing metabolic derangements, chronic lithium intoxication, and other drug toxicities can evolve over days to weeks. Cognitive and behavioral changes frequently fluctuate and follow a diurnal pattern. Assessment during periods of more lucid behavior can lead to the conclusion that patients are cognitively intact, making subsequent behavioral changes and agitation diagnostically difficult to understand.

Changes in motor behavior are common in delirium. Hypoactive and hyperactive subtypes of delirium have been identified. Different pathophysiologies have been proposed for the two motor subtypes but have not been supported to date. Patients often fluctuate between these two forms of delirium making single cross-sectional assessment diagnostically insufficient. Hyperactive delirium, often the result of drug intoxication and withdrawal states, can be associated with agitation and related patient and staff injury. Some studies suggest prognostic relevance to the motor subtypes, with hyperactive delirium more responsive to pharmacologic treatment and hypoactive delirium predictive of worse outcome.[1,2,11]

Psychiatric symptoms and neurobehavioral changes are common in delirium and range from frank agitation, to restlessness, anxiety, dysphoria, tearfulness, apathy, withdrawal, disinhibition, disordered thinking, and perceptual disturbances of hallucinations and delusions. In contrast to behavioral symptoms of *primary* psychiatric syndromes that occur in a clear sensorium, behavioral changes in delirium occur atop a substrate of clinically demonstrable abnormal brain function and are properly considered *secondary* phenomena. New onset psychiatric symptoms should trigger examination of cognitive *function* and evaluation for causes of cognitive *dysfunction* when it is demonstrated, especially in the elderly and medically ill.

Despite its high prevalence and associated morbidity and mortality, delirium often goes undetected. Behavioral changes of delirium are commonly attributed to primary psychiatric processes, leading to delays in diagnosis and treatment of its causes.[1,15,19,23] Hypoactive delirium is often mistaken for depression – where psychomotor slowing, poor oral intake, and limited engagement with family and staff are attributed to vegetative dysfunction and psychological withdrawal of a mood disorder. Restlessness and anxiety in the medically ill patient are often considered appropriate psychological responses to the illness experience (rather than symptoms

of delirium). Failure to cognitively probe these behavioral changes and to recognize them as manifestations of delirium often leads to delays in diagnosis of the causative medical-surgical illness, the introduction of unnecessary antidepressant medications, and the initiation of potentially deliriogenic benzodiazepines.

Hallucinations, illusions, and delusional ideation, typically paranoid, are particularly common in delirium and are highly distressing to patients, families, and staff.[12,25,26] These misperception symptoms result from cognitive misprocessing that leads to misinterpretation of sensory phenomena and misattribution of meaning to routine hospital events. Patients often report that they are being poisoned, experimented on, plotted against, or held captive (note, many *are* physically restrained and treated with injectable medications). Psychiatric consultation for a question of "psychosis" is often requested in these cases. Onset of primary psychosis in the elderly and medically ill is extremely unusual and new hallucinations or delusions in this population should be considered diagnostic of delirium or dementia until proven otherwise.

While considered a transient syndrome and indicative of typically reversible processes, recent data suggest that many delirium episodes last longer than initially presumed. As many as 30%-40% of patients discharged to nursing homes and skilled nursing facilities remain delirious at the time of transfer.[1] Delirium is a risk factor for long-term cognitive impairment, especially in survivors of critical illness and in cases of sepsis-related encephalopathy.[3,9,13,14,18,27]

RISK FACTORS AND CAUSES

Delirium is caused by a wide variety of etiologies including metabolic, toxic-pharmacologic, infectious, vascular, traumatic, and post-surgical conditions.[1,11,24] Though the vast majority of delirium episodes are not caused by structural disease, brain imaging is performed in most delirious patients as part of the initial evaluation. Structural causes of delirium are typically heralded by a history of trauma or a focal neurological exam. Delirium often evolves in hospitalized stroke patients and is typically the result of metabolic and infectious complications. Stroke as a direct cause of delirium is less common.

The pathophysiology of delirium is poorly understood. Inflammatory mechanisms are active in infectious, metabolic, traumatic, and other processes linked to delirium. Animal and human studies have documented numerous adverse mood, cognitive, and behavioral effects of various inflammatory mediators including interferon-alpha, interleukin-1, interleukin-6, and tumor necrosis factor-alpha. Illness-related *systemic* inflammation is thought to play a central role in delirium etiology of multiple causes.[28,29]

Dysfunction of various neurotransmitter systems has been implicated in the pathophysiology of delirium. Derangement of dopaminergic and serotonergic neurotransmitter function is likely causative in diagnoses of neuroleptic malignant

Table 1. Selected causes of delirium

Autoimmune	**Metabolic**
Acute graft versus host disease	Acidosis or alkalosis
Autoimmune encephalopathy (voltage-gated potassium channel, NMDA receptor)	Anemia
Central nervous system vasculitis	Hepatic failure
Hashimoto's encephalopathy	Hypercapnea
Systemic lupus erythematosus	Hypoalbuminemia
Cardiac	Hypo- or hypercalcemia
Acute myocardial infarction	Hypo- or hyperglycemia
Heart failure	Hypo- or hyperkalemia
Cerebrovascular	Hypo- or hypermagnesemia
Stroke (ischemic, hemorrhagic)	Hypo- or hypernatremia
Transient ischemic attack	Hypophosphatemia
Subarachnoid hemorrhage	Hypoxemia
Hypertensive encephalopathy	Uremia
Drug intoxication	Other (carcinoid, porphyria, etc)
Alcohol	**Neoplastic**
Bath salts	Carcinomatous meningitis
Cannabinoids (marijuana, synthetic)	Intraparenchymal brain tumor
Gamma-hydroxybutyrate	Lymphomatous meningitis
Hallucinogens	Parenchymal metastasis
Opiates	Paraneoplastic syndrome
Psychostimulants	**Systemic infection**
Sedative-hypnotics (benzodiazepines, barbiturates)	Bacteremia
Drug withdrawal	Cellulitis
Alcohol	Pneumonia
Sedative-hypnotics (benzodiazepines, barbiturates)	Sepsis
Endocrine	Urinary tract infection
Adrenal insufficiency or excess	**Traumatic brain injury**
Hypo- or hyperthyroidism	Diffuse axonal injury
Hypo- or hyperparathyroidism	Parenchymal contusion
Panhypopituitarism	Subdural hematoma
Intracranial infection	**Other**
Abscess	Central nervous system radiation
Encephalitis (HSV, arboviruses)	Disseminated intravascular coagulation, thrombotic thrombocytopenic purpura
Human immunodeficiency virus	Malignant hyperthermia, neuroleptic malignant syndrome, serotonin syndrome
Meningitis (bacterial, viral, fungal)	Postoperative state (cardiotomy, joint arthroplasty)
Neurosyphilis	Seizures

*See Table 2 for drugs causing delirium

Adapted from:Trzepacz PT, Meagher DJ, and Leonard M. (2011). Delirium. In Levenson JL (Ed), *Textbook of Psychosomatic Medicine*. Arlington, VA: American Psychiatric Publishing, Inc.

syndrome and serotonin syndrome, respectively. Deficient gamma-aminobutyric acid (GABA) function and glutamate hyperactivity have been implicated in the encephalopathy of sedative-hypnotic withdrawal. The anti-cholinergic properties of numerous medications (**Table 2**) play a role in the development of delirium. Opiate narcotics drive delirium via both their opioid and anti-cholinergic effects.

Causes of delirium cut across all organ systems. Derangements in sodium and calcium metabolism, hypoalbuminemia, hypoxemia, hypercapnea, hepatic and renal insufficiency, hyper and hypoglycemia, drug intoxication and withdrawal, infection, and primary central nervous system diseases including stroke, seizure, and traumatic brain injury have all been associated with delirium.[1,11] (**Table 1**).

Medications from multiple classes, via both well-understood and more idiosyncratic mechanisms, have been associated with delirium (**Table 2**). Antimicrobials (antiviral acyclovir, macrolide antibiotics including clarithromycin, fluoroquinolones such as ciprofloxacin, penicillins, cephalosporins, and metronidazole), anticonvulsants (phenytoin, phenobarbital, valproic acid), corticosteroids, antiparkinson agents (amantadine, levodopa), cardiac drugs (digitalis, lidocaine, quinidine, and beta-blockers), and various antineoplastic agents (5-fluoruracil, methotrexate, procarbazine, vincristine, interferon alpha, and ifosfamide) have all been implicated in the development of delirium. Opioid analgesics and benzodiazepines are especially common causes of delirium in hospitalized medical-surgical patients.

Acute *intoxication* with virtually any abuseable prescription or illicit drug can drive a delirium. Drug *withdrawal* delirium, however, is more specifically associated with use of sedative-hypnotic agents (i.e., alcohol, benzodiazepines, and barbiturates) that share a GABA-ergic mechanism of action and drive a delirium tremens-like encephalopathy syndrome. While there are case reports of delirium associated with abrupt discontinuation of opioid narcotics (methadone), these agents typically do not produce a withdrawal delirium. Presumption of opioid withdrawal as the cause of delirium in opioid abusers or medical-surgical patients exposed to prolonged courses of narcotic analgesics is ill advised as these patients are often affected by and at risk for multiple delirium-related conditions.

Emergency department presentations for acute mental status change are extremely common and have given rise to protocol driven empiric treatment of frequently occurring reversible causes of delirium. Emergency protocols, in parallel with appropriate diagnostic testing, include the administration of supplemental oxygen, intravenous dextrose, intravenous normal saline, naloxone, and thiamine targeting, respectively, hypoxemia, hypoglycemia, hypovolemia, opioid intoxication, and Wernicke's encephalopathy. Flumazenil, a benzodiazepine reverse agonist, is sometimes administered for suspected benzodiazepine intoxication, but reports of benzodiazepine withdrawal-induced seizures have led to more cautious use of this agent.

Table 2. Selected drugs causing delirium

Analgesics	**Antiparkinsonian drugs**
Opiates	Amantadine
Salicylates	Bromocriptine
Antimicrobials	Dopamine agonists
Acyclovir, gancyclovir	(ropinirole, pramipexole)
Aminoglycosides	Levodopa
Amphotericin B	**Cardiac drugs**
Antimalarials	Beta-blockers
Cephalosporins	Captopril
Ethambutol	Clonidine
Interferon	Digoxin
Isoniazid	Lidocaine
Macrolides (clarithromycin)	Methyldopa
Metronidazole	Procainamide
Quinolones (ciprofloxacin)	Quinidine
Rifampin	Tocainide
Sulfonamides	**Sedative-hypnotics**
Vancomycin	(intoxication or withdrawal)
Anticholinergic	Barbiturates
Antihistamines (H_1)	Benzodiazepines
Antispasmodics	**Stimulants**
Atropine and atropine-like drugs	Amphetamines
Benztropine	Epinephrine, phenylephrine
Phenothiazines	Pseudoephedrine
Tricyclics (amitriptyline, doxepin, imipramine)	Theophylline
Trihexiphenidyl	**Miscellaneous**
Anticonvulsants	Antihistamines (H_2)
Phenobarbital	Baclofen (intoxication or withdrawal)
Phenytoin	Bromides
Valproic Acid	Disulfiram
Anti-inflammatory drugs	Ergotamine
Corticosteroids	Lithium
Nonsteroidal anti-inflammatory drugs	Propylthiouracil
Antineoplastic drugs	Quinacrine
Asparaginase	Timolol (ophthalmic)
Dacarbazine	
Diphosphamide	
5-Fluorouracil	
Methotrexate	
Procarbazine	
Vinblastine	
Vincristine	

Adapted from: Trzepacz PT, Meagher DJ, and Leonard M. (2011). Delirium. In Levenson JL (Ed), *Textbook of Psychosomatic Medicine*. Arlington, VA: American Psychiatric Publishing, Inc.

EVALUATION

Delirium evaluation begins with a thorough physical examination with particular attention paid to findings suggestive of metabolic derangement, infection, and neurologic focality. Routine metabolic studies should be checked and urinalysis and chest X-ray obtained. Brain imaging is often performed in the assessment of delirium, but is typically unrevealing. Brain computed tomography (CT) scanning is indicated for evaluation of intraparenchymal or subdural hemorrhage in patients with a history of trauma or focal neurologic examination findings. Magnetic resonance imaging (MRI) is more sensitive in evaluating for space occupying lesions, white matter disease processes, and new ischemic stroke as causes of delirium.

Electroencephalography (EEG) in delirium typically reveals diffuse bilateral background slowing in the delta to theta range. These EEG changes are non-specific and common to encephalopathies of diverse etiologies. Certain causes of delirium are associated with specific EEG findings including triphasic waves in hepatic encephalopathy, excess beta-range activity in benzodiazepine intoxication, and periodic discharges and burst suppression in prion diseases.

EEG is not particularly helpful when neuropsychiatric assessment is consistent with a diagnosis of delirium and physical examination and laboratory investigation suggest its cause(s). In contrast, even non-specific background slowing on EEG can be very helpful in distinguishing between abnormal behavior of psychiatric disease and that of more subtle, subacute encephalopathy where cognitive dysfunction is *less obvious* – as the EEG in most psychiatric disorders is normal.

When patients are *obviously* encephalopathic but evaluation for toxic, metabolic, infectious, and structural causes is unrevealing, EEG is indicated to evaluate for non-convulsive status epilepticus (NCSE). Recent studies have documented unexpectedly high rates of NCSE in critically ill and ICU patients.[30] This is a notable finding that argues for more liberal use of EEGs in encephalopathic critically ill patients who typically have multiple non-epileptic processes driving their delirium and in whom EEG has previously been thought to be less indicated.

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Disclosures

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Delirium: Treatment and Prevention (Part 2)

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ABSTRACT

Delirium management begins with non-pharmacologic interventions and treatment of the underlying causes. There are no FDA-approved medications for delirium-related psychosis and agitation, although numerous agents have been studied. Small sample size, narrow inclusion criteria, lack of placebo controls and variable methodologies limit the generalizability of findings to date. Studies and expert guidelines support the use of antipsychotics for delirium-related psychosis and agitation, and demonstrate comparable efficacy and safety between first- and second-generation agents. Mounting evidence also suggests that antipsychotics and dexmedetomidine are effective in preventing delirium in surgical and mechanically-ventilated patients, respectively.

KEYWORDS: delirium, encephalopathy, cognitive disorder, agitation

INTRODUCTION

Delirium management begins with evaluation and treatment of its causes, discontinuation of potential offending agents, and institution of non-pharmacologic strategies to limit its incidence, course and complications. Pharmacologic treatment is typically reserved for neurobehavioral symptoms of agitation and psychosis that are unresponsive to these primary interventions. Despite its high prevalence and association with multiple adverse outcomes, there are no FDA-approved treatments for delirium.

Studies of delirium management have explored both treatment and prevention, have been conducted in general medical-surgical patients and in critically ill, intensive care unit (ICU) populations, and have included both pharmacologic and non-pharmacologic interventions. Unfortunately, small sample size, narrow inclusion criteria, lack of placebo controls, and variable methodologies limit the generalizability of findings to date.

Numerous agents have been studied for delirium management including antipsychotics, benzodiazepines, cholinesterase inhibitors and other pro-cholinergic drugs, ketamine, and, more recently, dexmedetomidine. Published guidelines from numerous subspecialty societies and recent meta-analyses recommend haloperidol and other antipsychotic agents for the treatment of delirium.[1,2] Based on these and other consensus statements, antipsychotic agents remain the treatment of choice for delirium and related agitation.

NON-PHARMACOLOGIC INTERVENTIONS

The landmark study by Inouye et al tested a multi-disciplinary protocol of non-pharmacologic interventions to reduce delirium incidence, duration and severity in 852 elderly patients admitted to the general medical service of an academic hospital.[3] The protocol consisted of both global interventions and targeted interventions for patients with specific risk factors. Interventions included early mobilization, noise reduction and scheduling adjustments to minimize sleep disruption, early recognition and treatment of dehydration, orientation boards and frequent verbal reorientation for patients with cognitive impairment, and communication aids for patients with visual and hearing impairment. The incidence of delirium was 40% lower in the intervention group compared with the control group. The total number of days spent in delirium was also significantly lower in the intervention group. Zaubler et al replicated these results and reported $841,000 in cost savings over 9 months in a community hospital setting.[4] These protocols are considered the standard of care and have been put in place at institutions across the country. Similar non-pharmacologic interventions have been designed and implemented by the Brown-based Geriatric Medicine Program, and form the basis of the Close Observation Medical Unit (COMU) and other elder-care protocols at Rhode Island Hospital and The Miriam Hospital, respectively (L. McNicoll, personal communication, July 2012).

PHARMACOLOGIC INTERVENTIONS – TREATMENT AND PREVENTION

Overview

First generation antipsychotics (FGA), such as haloperidol, are the mainstay for treating the neurobehavioral symptoms of delirium.[1,5,6] Their utility is thought to derive from dopaminergic blockade, based on the hypothesis that dopaminergic hyperactivity and cholinergic deficiency contribute to the onset and persistence of delirium. For this reason, cholinesterase inhibitors have also been tried with mixed results.[6] Haloperidol has minimal hemodynamic side effects and

remains the best studied and most recommended treatment for delirium-related agitation. Haloperidol can be administered orally, intramuscularly (IM) or intravenously (IV), has a wide therapeutic window, and can be titrated across a broad dose range, from 0.5 mg as needed to 10 mg hourly, with onset of action between 30-60 minutes for the IV and IM routes of administration. Peak serum concentrations occur 2-6 hours after oral administration. There are case reports of safe and effective haloperidol administration up to 500 mg per day.[5] Intravenous and IM forms of haloperidol are particularly helpful in uncooperative patients and in critically ill patients where gastrointestinal absorption is unreliable. Numerous reports suggest that IV administration is associated with less risk of extrapyramidal symptoms (EPS).[5] Emerging data suggests that, in addition to its anti-dopaminergic action, haloperidol may also counter delirium by decreasing oxidative stress and inflammation via σ-1 receptor blockade and interleukin-1 antagonism.[6]

There is a literature supporting the use of second-generation antipsychotics (SGAs) in the treatment of delirium-related agitation and psychosis.[2,5-9] SGAs studied to date include risperidone,[10,11] quetiapine,[12] olanzapine,[9,13] ziprasidone,[5] and aripiprazole.[5] The main advantage of the SGAs over haloperidol is their relatively reduced risk of EPS, which is particularly relevant in patients with parkinsonian syndromes such as dementia with Lewy bodies (DLB) and idiopathic Parkinson's disease (PD). Quetiapine is least likely to produce or exacerbate EPS and is the agent of choice in treating agitation and psychosis in parkinsonian patients. Unlike haloperidol, none of the SGAs are available IV. Olanzapine, ziprasidone, and aripiprazole can be administered in immediate-release intramuscular forms and are indicated when the oral route is unavailable and haloperidol is contraindicated. Risperidone and paliperidone are available in long-acting intramuscular depot formulations which are utilized in the treatment of patients with chronic psychotic illnesses, but are not indicated in delirium.

The FDA issued "black box" warnings in April 2005 and June 2008 regarding the use of antipsychotic agents in the elderly. These warning were based upon evidence of increased cerebrovascular events and all-cause mortality in studies of extended courses of antipsychotic treatment in elderly, demented nursing home patients.[14] The relevance of these findings and warnings to the short-term use of these agents in patients with delirium is unclear. Given the high prevalence of co-morbid dementia in delirium patients, these warnings should be taken into consideration when weighing the potential risks and benefits of brief antipsychotic treatment against those of untreated delirium.

Haloperidol and all SGAs carry a risk of QTc prolongation (QTP) and QTP is the best predictor of torsade de pointes (TdP), a malignant ventricular dysrhythmia. The QT prolonging effects of antipsychotic and other agents are catalogued at www.torsades.org. Low-dose oral haloperidol has minimal QT prolonging effects. Thioridazine, ziprasidone and high-dose IV haloperidol have the most significant QT prolonging effects of the antipsychotic agents. Although the degree of QTP and absolute risk of TdP associated with these agents is small, most guidelines advise caution when using IV haloperidol in patients with risk factors for QTP or TdP (**Table 1**). The absolute risk of TdP for IV haloperidol has been estimated at 0.27%.[5]

Table 1. Assessing and Monitoring Risk for Drug-Induced QTc Prolongation (QTP)

Risk Factors for QTP:
• Advanced cardiac disease
• Known history of long-QT syndrome
• Baseline QTc > 450 msec
• Hypokalemia
• Hypomagnesemia
• Concomitant use of other QTc prolonging agents
Prior to Initiating a QTc Prolonging Drug:
• Obtain electrocardiogram to measure baseline QTc interval
• Obtain serum potassium and magnesium levels
• Correct any electrolyte abnormalities
• Review medication list for QTc-related interactions
After Initiating a QTc Prolonging Drug:
• Repeat electrocardiogram at regular intervals (typically once daily)

Dexmedetomidine is a highly selective, centrally-acting alpha-2 agonist with sedative, analgesic and anxiolytic properties, and has been studied for both prevention of delirium and treatment of delirium-related agitation in ICU patients. Trials comparing dexmedetomidine to benzodiazepine and opioid ICU sedation protocols have demonstrated its efficacy, safety and favorable side effect profile.[15-19] Unlike most other sedatives employed in the ICU, dexmedetomidine is not associated with significant respiratory depression; however, hypotension and bradycardia can complicate its use, especially at high infusion rates.[6,15-19] Multiple studies have reported decreased opiate requirements in ICU and post-operative patients sedated with dexmedetomidine.[5] Reduced opioid use likely contributes to the lower incidence of delirium observed in dexmedetomidine-treated patients. Dexmedetomidine is also thought to have mild cholinergic activity which may favorably affect the sleep-wake cycle.[5]

Benzodiazepines are potentially deliriogenic. Except for cases of alcohol and sedative-hypnotic withdrawal where they are the treatment of choice, benzodiazepines are not considered first-line agents in the treatment of delirium-related agitation.[20] *Adjunctive* use of benzodiazepines is appropriate in cases of agitation related to certain toxidromes and neuroleptic-malignant syndrome, or when delirium is complicated by catatonia or severe EPS that limit the use of antipsychotic agents.

The existing literature is summarized below with special attention to differences between *general medical-surgical* patients versus *ICU* patients. Outcome measures vary across these studies and include delirium incidence, severity and duration, length of hospitalization, length of time in the ICU, number of ventilator dependent days, and disposition to home versus other medical facilities or institutional settings.

Typical teaching recommends the use of antipsychotic agents for the treatment of delirium-related psychosis and agitation but not for the delirium syndrome proper. Animal studies suggest that dopaminergic mechanisms play a role in the development of delirium irrespective of the presence or absence of agitated behavior. Additionally, recent studies and personal accounts suggest that a significant proportion of non-agitated, "hypoactive" delirium patients experience distressing psychotic symptoms and that these frightening symptoms may drive the development of a post-traumatic stress disorder (PTSD)-like syndrome.[21,22] Taken together, these observations may argue for more liberal use of dopamine-blocking agents in the treatment of delirium, even in the absence of problem behaviors.

TREATMENT STUDIES

General Medical and Surgical Patients

Multiple case reports and small, open-label trials suggest that SGAs (including risperidone, quetiapine, olanzapine, aripiprazole and ziprasidone) are effective and safe in the treatment of delirium.[5,9-13] Several single-blind, randomized trials comparing SGAs to haloperidol for the treatment of delirium found no significant differences between the two interventions in treatment outcomes or adverse effects.[5] One double-blind RCT of risperidone versus haloperidol in 28 delirious patients reported comparable improvement across groups.[10] A 2007 Cochrane review of antipsychotic use in delirium included a meta-analysis of haloperidol, olanzapine, risperidone and placebo treatment studies, and concluded that (1) haloperidol does not significantly reduce delirium *incidence* compared with placebo, (2) low-dose haloperidol reduces delirium severity and duration in post-operative patients, (3) low-dose haloperidol and the SGAs have similar efficacy and EPS incidence, and (4) higher dose haloperidol is associated with more severe EPS.[8]

ICU Patients

In the MIND study, which evaluated prevention and treatment, 101 mechanically-ventilated ICU patients were randomized to receive oral haloperidol, oral ziprasidone, or placebo for up to 14 days according to a protocol which allowed for dose adjustments based on delirium severity, level of sedation and side effects.[23] Neither agent significantly reduced the duration of delirium, although the study was most likely underpowered due to small sample size, inclusion of patients without delirium at baseline, and open-label IV haloperidol use across groups. There was no difference in duration of coma between groups, a measure included due to concern that the sedating effects of antipsychotics may prolong coma. Rates of EPS, including akathisia, were comparable across groups. Extrapyramidal signs and symptoms were assessed by physical exam. Akathisia in particular, could only be assessed when patients were neither comatose nor delirious, and could participate in the assessment. A 2013 international study used similar methods to compare IV haloperidol to placebo for prevention and treatment of delirium in mechanically-ventilated patients, and found no significant difference between groups in duration of delirium.[24]

Devlin et al randomized 36 delirious, ICU patients to receive oral quetiapine or placebo.[12] Treatment with quetiapine was associated with shorter total duration of delirium, shorter time to first resolution of delirium, and less hours of agitation compared with placebo. Significantly more adverse effects were reported in the quetiapine group, especially sedation; however, no EPS or QTP were observed.

In a small, open-label trial, mechanically-ventilated ICU patients with severe agitation secondary to delirium were randomized to receive a continuous infusion of either dexmedetomidine or haloperidol.[15] The dexmedetomidine group spent more time with minimal or no delirium symptoms, less time intubated, less time in the ICU and less time in mechanical restraints. Three patients receiving haloperidol could not be extubated and underwent tracheostomy, compared with none in the dexmedetomidine group. Haloperidol was discontinued early in one patient due to QTP.

A qualitative meta-analysis of antipsychotic use for delirium in ICU patients reviewed three studies including the MIND and Devlin trials and a study by Skrobik et al of 73 delirious ICU patients randomized to oral olanzapine or haloperidol.[9] Evidence was strongest for the beneficial effects of quetiapine in the treatment of delirium. Guidelines from the American College of Critical Care Medicine (ACCM) report similar evidence for quetiapine and other SGAs in comparison to haloperidol in reducing the duration of delirium in ICU patients.[2,9]

An RCT of rivastigmine versus placebo as adjunct to haloperidol for ICU delirium was stopped early due to increased mortality in the rivastigmine group.[25] The median duration of delirium, severity of delirium, length of ICU stay, and cumulative doses of *as needed* haloperidol, lorazepam and propofol were all higher in the rivastigmine group. The dosing schedule for rivastigmine was different from the regimen used in Alzheimer's disease, with increases allowed every 2-3 days based on the assumption that correction of the functional cholinergic deficit of delirium would be more rapid than that of chronic dementia.[25] The ACCM advises against using rivastigmine for delirium in adult ICU patients.[2]

PREVENTION STUDIES

General Medical and Surgical Patients

At least three studies have examined prophylactic anti-

psychotic use in patients undergoing orthopedic or gastrointestinal surgery. In a double-blind study, Kalisvaart et al randomized 430 hip surgery patients to receive oral haloperidol or placebo from admission until the third post-operative day.[26] The *incidence* of delirium was similar between groups; however, delirium episodes were shorter and less severe in the haloperidol group. Kaneko et al randomized 78 gastrointestinal surgery patients to receive haloperidol or normal saline IV on post-operative days one through five.[7] The incidence, severity and duration of delirium were significantly lower in the haloperidol group. In a double-blind study, Larsen et al randomized 400 patients undergoing hip or knee replacement surgery to receive one dose of olanzapine or placebo immediately pre- and post-operatively.[13] Delirium incidence was significantly lower in the olanzapine group (14.3% vs. 40.2%, $p < 0.0001$) and more patients in the olanzapine group were discharged to home. Notably, when delirium did occur in the olanzapine group, it lasted longer and was more severe. The latter findings were attributed to the unexpected development of alcohol withdrawal in five of the 28 patients in the treatment group versus none in the control group.

ICU Patients

Two studies have examined prophylactic antipsychotic use in postoperative ICU patients. Prakanrattana et al randomized 126 cardiac surgery patients to receive a single dose of risperidone or placebo postoperatively.[11] Delirium incidence was significantly lower in the risperidone group. Wang et al randomized 457 cardiac surgery patients to receive a continuous infusion of either haloperidol or normal saline postoperatively.[27] Haloperidol treatment was associated with a lower 7-day incidence of delirium, longer time to delirium onset, and a greater number of delirium free-days. A recent meta-analysis of studies examining delirium prevention in general and ICU surgical patients calculated a relative risk of 0.5 for developing delirium in patients receiving prophylactic antipsychotic medication compared with placebo.[7]

Three RCTs have examined the incidence of delirium among ICU patients sedated with dexmedetomidine versus benzodiazepines or opioids. The MENDS trial randomized 106 mechanically-ventilated ICU patients to sedation with dexmedetomidine or lorazepam.[16] The number of days alive without coma or delirium was significantly higher in the dexmedetomidine group. Maldonado et al randomized 118 mechanically-ventilated, cardiac surgery patients to dexmedetomidine, propofol or midazolam sedation protocols.[17] Delirium incidence was significantly lower in the dexmedetomidine group but there were no significant differences in length of ICU or hospital stay. In the DEXCOM study, 306 cardiac surgery patients were randomized to either dexmedetomidine or morphine for sedation and analgesia on admission to the ICU.[18] Delirium incidence was comparable, but dexmedetomidine-treated patients spent three fewer days in delirium, were extubated earlier, experienced less hypotension and required less norepinephrine. Dexmedetomidine use was associated with significantly higher incidence of bradycardia. Dexmedetomidine is an expensive drug, but a recent cost analysis comparing it to midalozam for sedation in mechanically-ventilated ICU patients reported a median savings of $9,679 per ICU stay in dexmedetomidine treated patients.[19]

Two placebo controlled studies reported no benefit of cholinesterase inhibitors for delirium prevention in surgical ICU patients.[6] In contrast, ketamine administered during anesthesia induction was associated with a lower incidence of postoperative delirium compared to placebo in cardiac surgery patients (3% versus 31%).[28]

CONCLUSION

Studies and expert guidelines support the use of antipsychotics for the *treatment* of delirium-related psychosis and agitation. First- and second-generation agents have demonstrated comparable efficacy and safety. Non-pharmacologic interventions significantly reduce delirium incidence, duration and severity. There is growing evidence that antipsychotics and dexmedetomidine are effective in *preventing* delirium in surgical and mechanically-ventilated patients, respectively.

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The 'Problem Patient': Modest Advice for Frustrated Clinicians

ROBERT BOLAND, MD

ABSTRACT

"Problem patients" are rare, but they take up a disproportionate amount of clinician time and energy. They often are defined in terms of the effect they have on clinicians rather than any specific behavior – such effects can include frustration, self-doubt and unprofessional behavior. The key to avoiding those pitfalls is to take a deeper look and understand what is behind patients' problematic behaviors. Given the vagueness of the term there are many potential etiologies, most of which are addressable, at least in part. This article presents a brief guide to identifying and managing the various conditions that can cause a disruption of the usually rewarding doctor-patient relationship, and also encourages us to consider the role we might play in this disruption.

KEYWORDS: Problem patient, difficult patient, hateful patient, physician-patient relations, professionalism, conflict (psychology)

INTRODUCTION

'A Typical Problem Patient (Part 1)'

As you pack your children into the car, the physician calls with the psychiatric consult. "The patient is refusing his medication," she says.

"What medication?" you ask.

"Acetaminophen."

"Really, you're calling me because he won't take 'Tylenol'? On a holiday, seriously?"

"Well, his fever is rising and I have to give him something; if I don't control his fever this could get dangerous."

"Well, why is he refusing?"

"I don't know – maybe he's suicidal. Maybe he's just being difficult."

"Well, which do you think it is?"

Irate, she says, "like you said, it's a holiday and I'm the only doctor for this whole service. It's really busy and I don't have time for this. I don't know why he's being so difficult – that's your job to figure out," and abruptly hangs up.

You prepare to tell your children that the parade is off.

THE PROBLEM PATIENT

A PubMed search of the term "problem patient" yields more than 100 articles. Although the term dates back to the 1950s, the definitive treatment of the subject was a now-classic 1978 article by James E. Groves,[1] in which he used a particularly dramatic synonym: the "hateful" patient.

What is a Problem Patient?

Finding a useful definition is elusive. Descriptions in the literature often say less about patients and more about how we react to them.[2] These patients leave us feeling frustrated, angry and helpless. We then feel ashamed at our unprofessional attitude. We may even worry about our ability to provide appropriate care in light of these feelings.

How Should we Approach Such Patients?

First, we must understand them. We need an algorithm, lest we use "problem patient" as if it were an explanation in itself. This article will attempt to organize the different possible etiologies that might account for a patient's seeming attempt to disrupt the normal treatment alliance.

We begin with the most basic of decision points:

Is the Patient's Behavior Deliberate?

Much of our frustration stems from our conviction that a patient's problematic behaviors are "on purpose." Often, this is not the case.* Many disorders can affect a patient's behavior and the ability to cooperate with care. How does one decide? A focused medical interview can inform our hypotheses regarding what might underlie a patient's problematic behavior. One must be careful – provocative metaquestions ("why are you being so difficult?") are rarely helpful, but an empathic inquiry into a patient's behavior can help one assess the level of awareness and control over this behavior.

NON-DELIBERATE BEHAVIORS

Delirium†

Delirious patients may actively resist treatment, sometimes

*It is understood that a discussion of "deliberate behavior" introduces dilemmas regarding concepts of consciousness and free will. These will be deferred to philosophers and this author will not attempt to rise above a lay understanding of these concepts.

† This and the next few diagnoses are discussed in more detail elsewhere in this issue; here the discussion is restricted to a consideration of their role in causing problematic behaviors.

violently; such "agitated patients" are relatively easy to identify. Less dramatic, but more common, are the hypoactive delirious patients who do not resist treatment but cannot consistently participate.[3] They may not take their medications or may not cooperate with physical rehabilitation. In such cases, the critical issue is to recognize the delirium and treat the underlying cause. When the cause is unknown or not easily treated, medications (usually antipsychotics) may help address problematic behaviors, but given their side effects and questionable efficacy, such medications are usually reserved for the most dangerous behaviors. Otherwise, the main treatments are behavioral, emphasizing frequent reassurance and reorientation. Questions of competency may arise, but given that delirium is usually a transient condition, decisions around treatments and disposition should be deferred if possible until the patient is more coherent.

Dementia

The uncooperative demented patient has a more permanent condition that is likely to deteriorate. In the unfamiliarity of the hospital setting, they may become more confused, if not frankly delirious, and the focus should be on returning the patient to their usual baseline. Family members may help determine what that baseline is. Once there, the "problem" in their problematic behavior usually lies in their inability to understand their situation. The priority should be to identify a substitute decision-maker, such as a guardian who can act on the patient's behalf.

Major psychiatric disorders

In addition to cognitive disorders, major psychiatric disorders can impair one's ability to cooperate with treatment. Psychotic patients may not trust their clinicians, depressed patients' negatively distorted world view may cloud their judgment and depressed or anxious patients may lack concentration or seek to avoid stressful decisions altogether. In each case, the focus of treatment should be the psychiatric disorder itself, with the problematic behaviors conceptualized as secondary to the psychiatric illness.

Somatic Symptom Disorders

Although DSM-5[4] has revised the classification of the "Somatoform Disorders,"[5] the central concepts remain the same: there are patients who appear to experience pathological symptoms for which there is no clear medication explanation. In addition, some patients are so worried about having an illness that they cannot function properly. Both types of patients can drain the medical system as well as the patience of their clinicians.

The classic approach to the somatizing patient is to schedule frequent and regular medical visits. This seems simple, but it is contrary to the "problem-driven" focus of modern medicine. To schedule visits regardless of the current status of the patient seems counterintuitive; however, this preventive approach is grounded in behavior theory with its attempt to decrease the association between symptoms and medical attention (for a fuller discussion of the approach to somatic symptom disorders, see Oyama et al[6]).

DELIBERATE BEHAVIORS

Factitious disorder and malingering

At times, we suspect patients are lying to us. Usually they are not, but rarely patients do deliberately fabricate their medical history or symptoms. Lying is not a medical or psychiatric disorder, it is a common human behavior – the issue here is the motivation for the behavior.

A patient with factitious (or Munchausen) disorder fabricates symptoms: the reasons for this are not clear but presumably derive from a desire to be treated as a patient. Most of us are familiar with the care and attention that come with being a patient; few of us, however, are willing to lie or fake symptoms to obtain this. Our understanding of those who do is poor; however, it is assumed that most have underlying severe psychiatric disorders.

Malingering is simpler, in that patients lie for some rational (that is, easily understandable and identifiable secondary) goal: money, relief from responsibility, shelter or protection for example. It is *not* a disorder, it *is* "bad" – but usually understandable – behavior. It need not occur as part of another psychiatric disorder, and although we associate malingering with sociopathy, this is not always the case: we can all empathize with a homeless patient who presents to an emergency department with vague symptoms in a desperate attempt to get out from the cold.

At times, the "practical" goals associated with malingering can overlap with a desire to assume the patient role, and differentiating malingering from factitious disorder can be challenging, particularly as it seems to require us to look into the hearts and minds of our patients to discern their motivations. It may be helpful to remember that patients with factitious disorder are often very psychologically ill people who may have a number of comorbid psychiatric disorders (particularly personality disorders) requiring careful assessment and an offer of treatment, whereas as noted above, malingering can be independent of any other psychiatric disorder.

Many clinicians find untruthful patients to be particularly trying; however there is no benefit from taking an unprofessional stance. It is usually best to avoid direct confrontation, which is likely to be met with anger, denial and an abrupt discharge against medical advice. Patients should be approached forthrightly and empathically in an attempt to clarify the diagnosis and engage the patient in a treatment that includes education about the disorder and its potential consequences (C Harrington, personal communication). It may be useful to consider what the patient seeks to gain from their behavior and it may be helpful to address this goal, particularly if the behavior is not part of a larger personality issue. A patient seeking shelter, for example, may

not be aware of the options available and providing practical assistance is not only kind, but likely to decrease their reliance on the medical system for survival. Most important, is to do no harm, by, for example, performing unnecessary diagnostic procedures or starting unnecessary medications.

Personality Disorders

Personality disorders include, by definition, difficulties with normal relationships. It should be no surprise, then, that these patients interact poorly with the medical system. Instead of DSM-5's rigid categories, it may be more helpful to use Grove's original approach[1] by recognizing certain broad personality types that have particular difficulties with the medical system:

The Dependent Clinger: These patients require an unreasonable degree of explanation and attention that challenges a clinician's professionalism, as well as one's time-management skills. The usual inclination to appease a patient fails in light of their bottomless pit of need, resulting in mutual frustration and anger.

The Entitled Demander: These patients seek attention through intimidation and devaluation. They may demand tests, refuse payment, or threaten legal proceedings. Clinician reactions can range from helplessness to defensiveness to outright malevolence.

The Manipulative Help-Rejecter: Although professing to want medical help, these patients are more interested in the relationship with their clinicians. Improvement risks losing that relationship, thus they remain ill. They may justify their noncompliance by devaluing their clinicians, leaving them to feel guilty or inadequate.

The Self-Destructive Denier: Unlike Help-Rejecters, who desire a clinical relationship, the self-destructive patient seems motivated only by a desire for self-harm. These patients can challenge the essence of our professional ethic – our desire to help the sick – and our resulting frustration can lead to anger and a wish to abandon these patients.

Such categories derive more from clinical wisdom than empirical investigations, and only roughly correlate with the (recently abandoned) DSM symptom clusters. For example, some Entitled Demanders might belong in the prior DSM's "dramatic cluster" whereas the more dependent ones would belong in the "anxious" cluster; however, obtaining an official diagnosis is probably less important than recognizing the patterns of behavior, in order to guide therapeutic responses to these patients.[7]

There is no simple method to successfully treat each of these patients, but the key is to first recognize and then understand them.[8] The unaware clinician risks either adopting the patient's point of view or feeling personally attacked. Once recognized, the clinician can step back and realize that the behaviors are part of a larger interpersonal problem affecting all areas of a patient's life.[9] It may also help to realize that some of the unpleasant feelings experienced by the clinician provide insights into the degree of inadequacy and self-hatred that the patient experiences every day. Understanding this can, hopefully, encourage empathy (or, at least, sympathy) and professional distance. Once achieved, the clinician can decide on an appropriate treatment plan, as well as appropriate boundaries and limits to the professional interaction.

CODA: WHEN THE PATIENT ISN'T THE PROBLEM

'A Typical Problem Patient (Part 2)'

Walking into the patient's room, you see him comfortably lying in his hospital bed, watching the very basketball game you were listening to as you drove to the hospital. A few questions about the game convince you that he is cognitively intact and his animated and intelligent discussion of the game start to make depression or some other psychiatric disorder seem unlikely. Getting down to business, you tell him, "the reason I'm here is that your doctors are concerned that you won't take your medications."

"That again?" he says with exasperation.

"Well," you explain, "apparently they think you really need the acetaminophen – why are you refusing it?"

"Because I have cirrhosis," he answers. "I've had it for years, and the doctor who diagnosed it told me I should never use Tylenol again."

You admit that the explanation makes perfect sense.

Later, you find the consultee, who admits that she forgot about the patient's liver disease, but is unapologetic, saying that she had a long night on call, and that the patient's inappropriate flirtatiousness combined with a questioning of her expertise during her initial evaluation caused her to cut the interview short.

Sometimes, the "problem" lies with us. One large general medical survey found that physicians who reported high frustration with patients were less experienced, worked longer hours and had more symptoms of depression, stress and anxiety than other doctors.[10] Fatigue, stress and burnout can affect our ability to maintain a professional demeanor.

Even at our best, there will always be patients who "push our buttons."

Before branding a patient as a problem, we should examine ourselves, our reaction to the patient and consider why we are having that reaction. It is helpful to avoid assigning fault, and instead seeing a problematic relationship as a mutual "failure to communicate." Reestablishing rapport should be the overriding issue. Then, the clinician must work to create a trusting, empathic and professional relationship. Even when a patient does fit into one of the categories of "problem patient" listed here, this approach will be more fruitful than explaining (or dismissing) a patient with a label.

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Serotonin Syndrome: A Concise Review of a Toxic State

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ABSTRACT

The serotonin syndrome is a toxic state caused by increased intrasynaptic serotonin and characterized by a triad of altered mental status, autonomic instability and neuromuscular abnormalities. It can result from exposure to a single serotonergic agent but is more likely to be due to polypharmacy, often with drugs from multiple classes. It develops over a short period of time and resolves just as quickly once identified and treated. Diagnostic criteria have been developed to assist in clinical practice. Treatment is largely supportive and prognosis is generally very favorable. Pharmacologic vigilance and prevention are key.

KEYWORDS: Serotonin syndrome, polypharmacy, myoclonus

INTRODUCTION

Frequently considered diagnostically but not always recognized or well understood, the serotonin syndrome (SS) is best conceptualized as a potentially life-threatening neurotoxic state rather than a distinct idiosyncratic reaction. It results from excess intrasynaptic serotonin, with symptoms developing over hours, and is characterized by the triad of mental status alteration, neuromuscular hyperactivity and autonomic instability.[1,2]

Initially described in 1960[3] and brought into mainstream awareness with the case of Libby Zion,[4] its true incidence is likely underestimated given the wide spread use of selective serotonin reuptake inhibitors (SSRIs) and other serotonergic drugs, and because mild cases often go undetected.[2,5] Serotonin syndrome occurs in approximately 14%-16% of patients who overdose with SSRIs.[6]

Serotonin syndrome has been reported to occur with numerous drugs and in various combinations, and is overwhelmingly the result of polypharmacy, including illicit and over-the- counter drugs (OTCs). Occurrence of SS with a single agent is unusual, though it does occur, sometimes after a single dose.[7] Case reports document numerous drugs from different classes as precipitants for this toxic state.[8-12]

In this article we review the pathophysiology, clinical presentation, differential diagnosis, precipitating drug classes, and general management of the SS. The aim of this paper is to provide a brief review of the SS in order to promote greater awareness, increased understanding, and more effective prevention of this toxidrome.

PATHOPHYSIOLOGY

Serotonin (5-hydroxytryptamine or 5-HT) is a product of hydroxylation and decarboxylation of L-tryptophan.[8] The majority of serotonin is found in the periphery where it is involved in regulation of GI motility and vasomotor function. Approximately 2% of serotonin is found in the CNS and synthesized primarily in the raphe nucleus of the brainstem.[13] Serotonin is involved in modulating multiple CNS functions including core body temperature, emesis, eating behavior, analgesia, wakefulness, sexual behavior, mood, affect, perception, and personality.[2,8,14,16]

The SS toxidrome is thought to result from hyperstimulation of postsynaptic serotonergic receptors. Clinical findings do not correlate with serum serotonin levels; it is the concentration at the nerve terminal that is most important. While 5-HT2A receptor agonism has been implicated,[2,8,15,16] activation of the 5-HT1A receptor is thought to be primarily responsible for the clinical syndrome.[2, 8, 13-14, 16-18] Increased serotonergic activity is driven by various mechanisms including increased serotonin synthesis and release, decreased catabolism and reuptake, and increased receptor agonism and sensitivity.[8,14,19]

Genetic variability in the activity of the monoamine oxidase (MAO) enzyme responsible for serotonin metabolism is a predisposing factor for the development of SS. Acquired defects in MAO activity and serotonin metabolism related to cardiovascular disease, liver disease, and pulmonary disease associated with chronic tobacco use are identified risk factors for SS development.[18]

Drugs and drug classes that can contribute to the development of this toxic state include, but are not limited to: opioids (and related agents including tramadol), antimicrobials (including antiretrovirals), SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), norepinephrine-dopamine reuptake inhibitors (NDRIs), monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), atypical antidepressants such as trazodone and mirtazapine, lithium, triptans, anxiolytics, antihistamines, antitussives, anti-emetics, antiepileptic drugs (AEDs), muscle relaxants, anti-obesity drugs, methylene blue, herbal preparations, OTCs, and drugs of abuse.[8,19]

CLINICAL PRESENTATION AND DIAGNOSIS

SS is a clinical syndrome that requires a careful history, complete medication reconciliation, and comprehensive physical and mental status examinations to diagnose. It presents with a triad of mental status changes (anxiety, agitation, confusion, restlessness, disorientation, coma), neuromuscular abnormalities (rigidity, tremor, nystagmus, myoclonus, hyper-reflexia, ataxia, increased tone, particularly in the lower extremities), and autonomic instability (hypertension, hypotension, tachycardia, tachypnea, mydriasis, diaphoresis, hyperthermia).[5, 14-15, 17, 20]

The majority of cases present within 24 hours, and most within six hours of starting, changing, adding, and even withdrawing a drug.[21] Clinical presentation varies across a spectrum of severity. Mild cases can present with only anxiety and tremor and often go undetected. When severe, SS can present with hyperthermia, rhabdomyolysis, acute renal failure, metabolic acidosis, disseminated intravascular coagulation, respiratory failure, seizure and coma. Fatalities associated with SS are often the result of poorly treated hyperthermia.[11,12,19] Associated laboratory findings are non-specific, and can include elevated aminotransferases, creatinine, serum potassium, and creatinine phosphokinase (CPK), as well as leukocytosis, and myoglobinuria.[12,19]

The differential diagnosis of SS is broad and includes malignant hyperthermia, anticholinergic toxicity, opioid withdrawal, CNS infection, delirium tremens, non-convulsive seizures, sympathomimetic toxicity, stiff man syndrome, and heat stroke, but diagnostic consideration of neuroleptic malignant syndrome (NMS) in patients treated simultaneously with dopamine blocking agents is most common and challenging.[8,14] A number of findings aid in the differentiation between SS and NMS including abrupt onset, rapid resolution, mydriasis, myoclonus, hyper-reflexia, and clonus (especially in the lower extremities) in SS[2,14] (**Table 1**).

Several diagnostic criteria have been developed for the accurate identification of SS.[17, 22] The Hunter criteria[20] provide decision rules that are simple to apply and have been shown to have good sensitivity (75%) and specificity (86%) (**Table 2**).

Table 1. Differentiating SS from NMS.

	SS	NMS
Onset	Abrupt > gradual	Gradual > abrupt
Course	Rapid resolution	Prolonged
Neuromuscular findings	Myoclonus + tremor	Diffuse rigidity
Reflexes	Increased	Decreased
Pupils	Mydriasis	Normal

Table 2. The Hunter criteria for serotonin syndrome.

Presence of a serotonergic agent *plus one* of the following:
Spontaneous clonus.
Inducible clonus + agitation or diaphoresis.
Ocular clonus + agitation or diaphoresis.
Tremor + hyperreflexia.
Hypertonia + temperature >38°C + ocular or inducible clonus.

TREATMENT

Successful treatment is based on prompt recognition, after which the offending drug(s) are removed and supportive treatment instituted. Serotonin syndrome has a generally favorable prognosis and often resolves without specific intervention, other than supportive measures, including intravenous hydration and provision of a safe environment for the management of delirium.[24, 25] Most cases resolve within 24 hours. In approximately 30%-40% of cases, however, symptoms persist beyond 24 hours and may require more intensive care.[16]

Beyond supportive measures in mild cases, level of intervention is based on severity of presentation. Agitation is treated with benzodiazepines and external cooling is used to prevent complications of hyperthermia.[14] Moderate symptoms may be treated pharmacologically with cyproheptadine, a 5-HT2A antagonist and nonselective H1 antagonist.[23,25] Chlorpromazine, a 5-HT2A antagonist and dopamine antagonist, is a second-line agent, but caution is advised due to the risk of hypotension and the drug's ability to decrease the seizure threshold. In cases where NMS is a diagnostic consideration, chlorpromazine and other dopamine blocking agents should be avoided so as to minimize diagnostic confounding.

Significant neuromuscular hyperactivity and autonomic instability suggest a severe course of illness and require aggressive treatment that may include sedation, intubation, and paralysis. Succinylcholine should not be used in cases of rhabdomyolysis to avoid exacerbation of hyperkalemia. Restraints should be avoided as they are associated with isometric muscle contraction that can drive lactic acidosis and worsen hyperthermia. Bromocriptine and dantrolene sodium, used in cases of severe NMS, have no proven role in the treatment of SS. Antipyretics are not indicated as hyperthermia in SS is thought to be due to excessive muscle contraction rather than to a change in hypothalamic set point.

Reinstitution of serotonergic drugs and other potentially offending agents needs to be carefully considered according to specific clinical indications and risk of recurrent toxicity. Serotonin syndrome is much easier to prevent than to treat.

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Practical Management of Alzheimer's Dementia

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ABSTRACT

Alzheimer's disease (AD) is the most common cause of dementia in the elderly. There currently is no effective treatment that delays the onset or slows the progression of AD. Significant advances in neuroscience, genetics and molecular biology over the past 25 years have changed the way we think about AD. This article reviews the literature on diagnosis and treatment of AD so that primary care physicians can manage this complex disease.

KEYWORDS: Alzheimer's disease, dementia, dementia medications

INTRODUCTION

Every 68 seconds, a person in the United States is diagnosed with Alzheimer's dementia (AD). By 2050, this rate is expected to double. An estimated 5.2 million Americans currently have Alzheimer's dementia, and it is predicted that by 2050 that number will approach 13.8 million.[1] AD has emerged as a serious public health concern, placing an immense burden on patients, families, the community, and health care resources. AD accounts for approximately 60% of all cases of dementia in the developed world. The focus of this review will be on practical management of primary care patients with probable AD.

A common misperception is that AD is a normal or expected occurrence of aging, and that it is part of the typical trajectory of age-related cognitive decline. Healthy aging has been found to be associated with generally stable performance on measures of cognitive functioning, such as the Mini-Mental Status Examination (MMSE). However, as individuals live to advanced ages (over the age of 80), it is more challenging to differentiate between the subtle changes of aging and those caused by early dementia. Unfortunately, family members and caregivers may fail to recognize or be in denial about the significance of their loved one's cognitive decline, leading to delayed diagnosis and late treatment of dementia when behavioral problems become problematic or unmanageable. Pathologic changes that underlie AD begin to accumulate decades before cognitive and behavioral changes emerge.[2] Markers of brain health versus cognitive decline may be identifiable earlier in life. In the seminal Nun Study published in JAMA,[3] approximately 80% of nuns whose early-life writing samples were measured as lacking in complexity went on to develop Alzheimer's disease in old age as opposed to 10% of those whose writing was rated as more complex.

Nearly a hundred years ago, post-mortem analysis of human AD brains provided the first clues to the pathophysiology of AD and potential interventions. Senile plaques composed of extracellular deposits of amyloid-β (Aβ) and neurofibrillary tangles formed by intracellular aggregation of phosphorylated tau protein were found in regions of cortex that serve memory and other cognition functions. Based upon demonstrated deficiencies in choline acetyltransferase, the enzyme responsible for the synthesis of acetylcholine, the "cholinergic hypothesis" of AD was proposed.[4] The more recent "amyloid cascade" hypothesis of AD proposes that Aβ, specifically the least soluble forms Aβ 40 and 42, have a central role in AD. Aβ 40 and Aβ 42 are cleaved from amyloid precursor protein (APP) by beta and gamma secretase enzymes known as presenilin 1 and 2. Innovative studies over the last decade have evaluated enzyme inhibitors and immunotherapies that interfere with Aβ production, inhibit Aβ aggregation, and enhance Aβ clearance. Evidence for the reduction of amyloid and related AD pathology by these agents in transgenic mouse models has been very encouraging. Unfortunately, phase III human trials have been disappointing, including a recent trial of bapineuzemab, a human anti-Aβ monoclonal antibody, that failed to show benefit.[5] These and other basic science mechanisms operative in AD and novel treatment approaches are reviewed elsewhere.[6] Therapies targeting amyloid-based pathology have dominated recent drug development. Trials of tau-based therapies are newly underway.

Mutations in three genes – APP, presenilin 1 and presenilin 2 – all predispose to early onset (autosomal dominant) AD. In Trisomy 21, where there is duplication of the APP gene on chromosome 21, symptoms of AD may begin in the third or fourth decade of life. The E4 allele of the apolipoprotein E (APOE) gene has been identified as a major risk factor for late-onset AD.[7] No specific environmental toxin has been consistently associated with AD.

DIAGNOSIS

AD typically progresses along a continuum from normal aging to amnestic, mild cognitive impairment (a-MCI) and

finally frank AD. Patients with a-MCI present with memory deficits that are greater than would be expected based on age and education; however, functional abilities remain intact and behavioral problems are rare. Amnestic-MCI progresses to AD at a rate of 5-15% per year. There are no FDA-approved treatments for a-MCI. In a 3-year placebo controlled trial, Peterson et al evaluated vitamin E 2000IU and donepezil 10mg for the treatment of MCI. Donepezil reduced the rate of conversion to AD at 12 months, but neither agent separated from placebo at three years.[8] Nonetheless, this stage presents an opportunity for closer follow-up, modification of pre-morbid risk factors such as smoking, diabetes, and depression, and education and empowerment of the patient and family. Early diagnosis provides the patient and family an opportunity to anticipate problems and plan for the future (e.g., advanced health care wishes, wills) while the patient is still capable of making medical decisions.

A thorough history should be taken, preferably with a knowledgeable spouse or other family member present, in order to determine the time of onset and the course of cognitive decline. Recommended diagnostic tools include the Mini-Mental Status Examination (MMSE), the Clinical Dementia Rating Scale (CDR), and formal neuropsychological testing. Although neuropsychological testing remains the gold-standard for diagnosis, it is expensive and not available to all patients. No laboratory or imaging tests are sufficient to diagnose AD, although they may rule out reversible causes of dementia such as Vitamin B-12 deficiency, thyroid disease, electrolyte abnormalities, and certain structural lesions.

CT and MR imaging of AD typically demonstrate cerebral volume loss, especially in the temporal lobe structures such as the hippocampus. Brain single-photon emission computed tomography (SPECT) and fluorodeoxyglucose positron emission tomography (FDG-PET) studies in AD typically demonstrate, respectively, reduced cerebral blood flow and hypometabolism in posterior temporo-parietal regions. New biomarkers, such as cerebrospinal fluid measures of amyloid-β42 and phosphorylated tau have demonstrated impressive sensitivity and specificity in diagnosis of AD, but neither is utilized in routine practice or universally supported by published guidelines. In 2012, a PET scan that selectively binds amyloid-β plaques was approved by the FDA for AD testing. Unfortunately, this test is still not covered by the Centers for Medicare or Medicaid Services or any private insurers.[9] This test should be reserved for patients with early-onset cognitive dysfunction (usually defined as 65 years or less in age), atypical clinical presentations or course of illness, or other unexplained cognitive decline.[10]

PHARMACOLOGIC TREATMENT OF COGNITIVE SYMPTOMS

There are no available therapies that can stop or reverse the course of AD. The pharmacologic agents approved for the treatment of AD remain limited and include the three cholinesterase inhibitors (ChEI) donepezil (Aricept™), rivastigmine (Exelon™), and galantamine (Razadyne™) and a single N-methyl-d-aspartate receptor antagonist, memantine (Namenda™). The ChEI are approved for all three stages of AD, from mild to severe, and serve primarily to reduce the rate of cognitive decline. Memantine is approved for moderate to severe AD. Studies suggest no benefit from memantine in early disease. The American Psychiatric Association (APA) recommends that all patients with mild to moderate AD be offered treatment with a ChEI. Consistent with recent FDA approval of ChEIs for severe AD, the APA suggests

Summary of all the available FDA-approved medications for Alzheimer's dementia

Generic Name	Trade Name	Indication	Available Formulations	Start dose	Target dose	Renal dosing	Hepatic dosing
Donepezil	*Aricept™*	Mild-mod AD: 5,10mg Mod-severe AD: 10mg, 23mg	5, 10mg tabs 5, 10mg ODT 23mg tabs	5mg QD	10mg QD	No change	No change
Galantamine	*Razadyne™*	Mild to moderate AD	4,8, 12mg tabs 4mg/ml sol'n	4mg BID	12mg BID	16mg max	16mg max
	Razadyne ER™	Mild to moderate AD	8,16,24 mg caps	8mg QD	24mg QD		
Rivastigmine	*Exelon™*	Mild to moderate AD	1.5,3,4.5, 6mg caps 2mg/ml sol'n	1.5mg BID	6mg BID	No change	No change
	Exelon Patch™	Mild to severe AD	4.6,9.5,13.3mg patch				
Memantine	*Namenda™*	Moderate to severe AD	5, 10mg tabs	5mg QD	10mgBID	5mg BID max	No change
	Namenda XR™	Moderate to severe AD	7,14,21,28mg tabs	7mg QD	28mg QD		

Summary of SGAs used in dementia-related psychosis and agitation

Generic Name	Trade Name	Available Formulations	Start dose	Typical dose	Common side effects
Aripiprazole	Abilify™	2,5,10,15,20,30mg tablets 10,15mg ODT 1mg/ml oral sol'n 9.75mg single dose injection	2mg	5-10mg	Somnolence, EPS, fatigue, nausea, akathisia Least likely to cause QT prolongation
Olanzepine	Zyprexa™	2.5,5,10,15,20,30mg tabs 10mg,15mg ODT 10mg single dose injection	2.5mg	5-10mg	Postural hypotension, constipation, weight gain, dizziness Doses >10mg/day may cause anticholinergic side effects
Quetiapine	Seroquel™	25,50,100,200,300,400mg tabs	12.5mg	25-50mg	Somnolence, dizziness, nausea, fatigue Least likely to cause parkinsonism
Risperidone	Risperdal™	0.25,0.5,1,2,3,4mg tabs 0.5,1,2,3,4mg ODT 1mgl/ml oral sol'n	0.5mg	1-2mg	Parkinsonism, akathisia, dystonia, tremor, sedation
Ziprasidone	Geodon™	20,40,60,80mg tabs 20mg/ml single dose injection	20mg	40-60mg	Somnolence, EPS, dizziness May cause significant QT prolongation

consideration of cholinergic therapies in late disease as well.[11] Evidence suggests that ChEI treatment for at least six months delays the need for nursing home admission.[12] There are reports of marked improvement in cognitive and neuropsychiatric status with initiation of cholinesterase inhibitors in cases of dementia with Lewy bodies (DLB), perhaps consistent with pathologic observations of more significant loss of cholinergic neurons in DLB. Rivastigmine is FDA-approved for PD dementia, though its clinical benefits are modest.

There are no specific recommendations regarding the discontinuation of ChEIs or memantine. Some reports suggest subacute cognitive deterioration when these agents are abruptly stopped. Typical practice in the US includes early treatment with a ChEI and addition of memantine when disease progresses to the moderate-to-severe stage. Howard et al compared continued treatment with donepezil alone to addition of memantine to donepezil and memantine alone (after donepezil discontinuation) in moderate-to-severe AD. Continued treatment with donepezil alone and memantine alone were associated with similar cognitive benefit compared to placebo. In contrast to earlier studies, the combination of donepezil and memantine provided no additional benefit compared to continued donepezil alone.[13]

The most common adverse effects of ChEIs include nausea, vomiting, diarrhea, anorexia, insomnia, muscle cramps, and fatigue. Less common, but notable side effects of ChEIs include nightmares, weight loss, gastrointestinal bleeding, symptomatic bradycardia, and syncope. Rivastigmine is available as a once-daily transdermal formulation, *Exelon patch*™, that may improve gastrointestinal tolerability. Memantine is typically dosed at 10 mg twice daily. Namenda™ is now available in a 20 mg XR formulation that is intended for once daily dosing. Adverse effects of memantine include fatigue, dizziness, constipation, headache and occasionally worsening of AD-related behavioral problems.

NEUROPSYCHIATRIC-BEHAVIORAL SYMPTOMS AND THEIR PHARMACOLOGIC TREATMENT

Behavioral symptoms in dementia are common and include anxiety, apathy, depression, irritability, agitation, aggression, delusions, and hallucinations. The occurrence of these symptoms varies depending on the cause and stage of dementia. Apathy, irritability, and depression are common in early dementia while agitation, delusions, and hallucinations tend to occur in the later stages of the disease.[14] Aggressive behaviors can be verbal and physical. It is often difficult to distinguish between psychotic and non-psychotic forms of aggression.

Depression is often a harbinger of dementia in patients with no prior psychiatric history of a mood disorder. Indeed, late-onset depression may represent a presenting behavioral syndrome of an overarching neurodegenerative disorder

such as AD or vascular dementia. The evidence base for pharmacologic treatment of depression in dementia patients is limited. SSRIs are considered first line agents for treating depression in dementia patients.[15] Sertraline and citalopram have minimal pharmacokinetic interactions and are particularly indicated in elderly patients who are often on multiple medications. SSRIs have a broad range of additional effects including attenuation of anxiety, irritability, hostility, and obsessions and compulsions. Compared to placebo, citalopram (Celexa™) at 30mg daily significantly reduced agitation and caregiver distress in patients with probable AD.[16] Mild decline in cognitive performance and mild prolongation of the QTc interval (mean 18 msec) were noted in the citalopram-treated group.

Tricyclic antidepressants (TCAs) are associated with numerous adverse effects including cardiac arrhythmias, urinary retention, constipation, delirium, and overdose risk and should be used with caution in dementia patients. The anti-cholinergic effects of TCAs may be additive to the cholinergic loss of AD and exacerbate cognitive dysfunction. Mirtazapine (Remeron™) may be particularly effective in addressing complaints of poor appetite and insomnia that are common in depressed AD patients. There is some evidence that ChEIs can improve mood and other non-cognitive behavioral symptoms in AD. For this reason, a trial of a ChEI targeting both cognitive and neuropsychiatric symptoms in behaviorally dysregulated AD patients makes sense before the addition of a primary psychotropic agent. A trial of stimulants, such as methylphenidate, may be warranted in those patients with prominent apathy or those who partially respond to SSRIs.

Neuropsychiatric symptoms of agitation, aggression, and psychosis are associated with global decline in patient function and have a very negative effect upon caregiver and family quality of life.[17] These symptoms typically evolve over months; but when they emerge abruptly, it is important to evaluate for a diagnosis of delirium. Delirium is particularly common in demented patients. Medications with anticholinergic properties, benzodiazepines, and narcotics are often implicated as causes of delirium atop a baseline dementia. Uncontrolled pain, constipation, malnutrition, dehydration, and infection, particularly urinary tract infections, may also precipitate delirium. It is imperative that these conditions are addressed before assuming that agitation is due primarily to underlying AD or disease progression.

Although there are currently no FDA-approved agents for the treatment of dementia-related agitation and psychosis, second-generation antipsychotics (SGA) have been utilized to treat these symptoms. A recent study of Medicare beneficiaries in nursing homes found that 27% were prescribed antipsychotics.[18] The use of these medications in dementia management remains controversial, especially in light of the 2005 "black box" warning. Schneider et al found a significant increase in cerebrovascular events, especially with risperidone, when using SGAs for the treatment of agitation and psychosis in demented nursing home patients.[19] Additional analysis of the data documented an increase in all-cause mortality in dementia patients treated with SGAs compared to placebo. Antipsychotic use in dementia has declined since the issuance of this warning, particularly in nursing homes.

There is a limited evidence base regarding the effectiveness of SGAs for the treatment of dementia-related agitation and psychosis. The CATIE-AD trial examined the effectiveness of the three most commonly used SGAs – quetiapine, risperidone, and olanzapine. All of these agents, but particularly olanzapine, were associated with significant weight gain. Sedation and confusion were common side effects of all three medications. Olanzapine and risperidone were associated with Parkinsonism and other extra-pyramidal symptoms (EPS). Quetiapine was relatively free of EPS side effects. The CATIE-AD trial concluded that the adverse effects of these medications may outweigh any benefit they provide for the treatment of behavioral symptoms in dementia patients. Given their "black box" warning, SGAs are likely best reserved for patients with prominent psychosis and/or agitation who have not improved with non-pharmacologic treatments, cholinesterase inhibitors, or SSRIs. If ineffective, these agents should be discontinued rather than adding a second drug. Even when clinically beneficial, noting the evolving course of the underlying dementia, SGAs should be periodically tapered or discontinued to reassess their indication. Typical suggested starting doses of these drugs include risperidone 0.5mg, quetiapine 25mg, or olanzapine 2.5mg, all dosed once daily at bedtime. Given the limited evidence base and the warning regarding the use of these agents in dementia, careful informed consent discussion with patient and family about the risks and benefits of treatment versus the risks of untreated agitation should precede the initiation of any antipsychotic medication.

Behaviors such as wandering, yelling, and stubbornness can be particularly difficult to manage, often precipitate nursing home placement, and frequently persist in the institutional care setting. It is important that medication not be used as a "chemical restraint" to control these relatively benign behaviors. A multidisciplinary approach with input from properly trained nursing staff, social workers, and family can be helpful in designing a non-pharmacologic plan to help manage these behaviors. Novel approaches such as aromatherapy are being increasingly utilized in long-term care with success.[20]

Psychosocial interventions include cognitive and social stimulation such as adult day care participation, behavioral-oriented therapies, and caregiver support. Since activities of daily living (ADLs) such as self-care, personal hygiene, and dressing tend to worsen with progression of AD, patients with advanced AD require a greater level of caretaker commitment. Management of medical decisions and financial affairs, and cessation of driving often emerge as problems for caregivers. It is important to provide adequate caregiver

support, as "caregiver burden" is associated with high rates of AD patient nursing home placement.[21] Caregivers often benefit from referral to Alzheimer's Association support groups. When at-home care is no longer viable, families face the difficult decision of placing their loved one in an assisted-living facility or nursing home. The onset of behavioral problems such as aggression and delusions, rather than frank cognitive decline proper, often hastens this transition to long-term care.

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Emerging Drugs of Abuse: Clinical and Legal Considerations

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ABSTRACT

Over the past several decades, nontraditional drugs of abuse, including bath salts, synthetic cannabinoids, and salvia, have increased in popularity and use. Despite this fact, they remain unfamiliar to many healthcare providers. Commonly marketed as "legal highs," these substances are being used for their desired neuropsychiatric effects, taking advantage of their accessibility, low cost, variable legality, and limited detection on traditional urine drug screens. Similar to traditional drugs of abuse, these substances have varying degrees of toxicity and may lead to potentially adverse effects, ranging from benign to life threatening. This paper offers a review of three of the more widely-used emerging drugs (or classes of drugs): bath salts, synthetic cannabinoids, and salvia. For each we review its history and development, the neurochemical basis for its clinical effects, the nature and route of ingestion, the range of desired effects, potential toxicities, diagnostic and therapeutic approaches, as well as social and legal considerations.

KEYWORDS: Emerging drugs, drug abuse, bath salts, salvia, synthetic cannabinoids

INTRODUCTION

The past decade has been witness to a growing number of drugs of abuse. These include designer drugs, which are synthesized to mimic the structure and/or psychoactive properties of existing substances, and herbal substances, which contain one or more molecules that elicit a range of psychoactive effects. The prevalence of the use of these drugs and a growing understanding of their toxicity has sparked concern among medical and public health professionals alike. Of additional concern is the manner in which many of these drugs are advertised and sold. They are commonly marketed as "legal highs" with packaging that appeals to youth and young adults, and are relatively inexpensive, readily available online, in "head shops," at gas stations and convenience stores, and are not detected by standard drug screens. Keeping legal regulations at pace with the development of these drugs has proved challenging. Although the Synthetic Drug Abuse Prevention Act of 2012 added 15 synthetic cannabinoid receptor agonists and 11 synthetic cathinones to Schedule I of the Controlled Substances Act,[1] new analogues continue to be developed to evade this and other state-specific bans.

This paper offers a review of three of the more widely-used emerging drugs (or classes of drugs): bath salts, synthetic cannabinoids, and salvia. For each substance, we will outline its history and development, the neurochemical basis for its clinical effects, the nature and route of ingestion, the range of desired effects, potential toxicities, diagnostic and therapeutic approaches, as well as social and legal considerations (**See Table 1**).

Bath salts

Background

'Bath salts' is a general term referring to more than 30 available synthetic derivatives of cathinone[2] which was identified in 1975 as the principal psychoactive component of Khat.[3]

Table 1. Summary of desired effects, toxicities and management

	Desired effects	Toxicities	Management
Bath salts	○ Stimulation ○ Elation ○ Friendliness ○ Fluency ○ Sexual arousal ○ Perceptual disturbances	○ Sympathetic overstimulation ○ Aggression ○ Agitation ○ Memory deficits ○ Hallucinations ○ Paranoia	○ Supportive measures ○ Low-stimulation environment ○ Benzodiazepines, ○ IV fluids ○ Brief low-dose antipsychotics for psychosis only
Synthetic cannabinoids	○ Euphoria ○ Relaxation ○ Disinhibition ○ Altered perception ○ Altered consciousness	○ Anxiety ○ Mood dysregulation ○ Memory deficits ○ Hallucinations ○ Paranoia ○ Seizures ○ Nausea/vomiting ○ Diaphoresis ○ Hot flushes ○ Mydriasis ○ Tremor ○ Tachycardia ○ Hypertension	○ Supportive measures ○ Low-stimulation environment ○ Benzodiazepines
Salvia	○ Trance-like state ○ Hallucinations ○ Sensory disturbances ○ Synesthesia ○ Extra-bodily experiences ○ Elevated mood	○ Depersonalization ○ Anxiety ○ Dysphoria ○ Confusion ○ Fear ○ Headaches ○ Drowsiness ○ Tachycardia ○ Hypertension	○ Supportive measures ○ Low-stimulation environments ○ Benzodiazepines

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Bath salts

Cathinones have been investigated for their stimulant, antidepressant and appetite suppressant properties, but such studies have been halted because of concerns for abuse and dependence.[2,3] Mephedrone, MDPV (3,4-methylenedioxypyrovalerone) and methylone are the most common recreationally-used cathinones because of their structural, and clinical, similarities with amphetamine.[4] They are most widely produced in China, Pakistan and India and are typically sold as powder or pellets. Bath salt can be administered by oral, intranasal, inhaled (smoked), intravenous, or rectal routes.[3]

Mechanism of action and neurochemical considerations

Bath salts exert their effects by inhibiting vesicular monoamine transporters for serotonin, dopamine and norepinephrine, thereby increasing presynaptic neurotransmitter levels.[5] They also act as potent monoamine oxidase (MAO) inhibitors, with increased selectivity for MAO-B.[6] When compared to amphetamine and MDMA, bath salts were found to produce a greater increase in serotonin and dopamine levels in the nucleus accumbens.[2]

Desired effects, toxicities and long term effects

Although the pharmacokinetic properties of bath salts vary with the specific analogue used, the average onset of subjective effects occurs within 30 minutes. Effects peak at 45 to 90 minutes after administration and last up to 3 hours. The subjective effects include stimulation, elation, friendliness, talkativeness, sexual arousal and perceptual disturbances.[7]

Adverse neurobehavioral reactions include anxiety, hallucinations, delusions (paranoid and other), agitation, aggression, impaired working memory, and bruxism.[4] Bath salts have also been associated with metabolic derangements including hyponatremia, rhabdomyolysis, disseminated intravascular coagulation, acute kidney injury, and hepatic failure.[4] Additional toxicities range from sympathetic overstimulation (including hypertension, tachycardia, and hyperthermia) to seizures and death.[4,8] Cases of excited delirium, known as "bath salts psychosis," have been reported and are associated with significant mortality.[8,9] Bath salts withdrawal symptoms include depression, impulsivity, anhedonia with cognitive complaints of poor concentration and attention.[15] Long-term bath salt use is complicated by tolerance and a marked tendency to re-dose, thereby increasing the risk for accidental overdose.[2]

Diagnostic and therapeutic considerations

Bath salts are not detected by standard urine toxicology tests. Mass spectroscopy and gas chromatography can be used to detect specific cathinones but these tests are expensive.[7] Result reporting from these methods is often delayed, making them less helpful in guiding differential diagnosis and treatment during the acute phase of illness.[7] At present, there are no validated guidelines for the management of acute bath salts intoxication but current recommendations include supportive measures, low stimulation environments, benzodiazepines for sedation and seizure prevention, and intravenous fluids for prevention of rhabdomyolysis.[10] More serious metabolic and hemodynamic adverse effects may require admission to a medical or intensive care unit. Brief courses of low-dose antipsychotics can be helpful in managing the psychotic symptoms of an excited delirium but prolonged use is discouraged.[11]

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K2/Spice

Synthetic cannabinoids (Spice)

Background

Synthetic cannabinoids, commonly referred to as "Spice" and "K2," act as agonists at the cannabinoid (CB) receptor.[7] These agents are synthesized and then sprayed on dried herbs that may possess their own implicit psychotropic properties. They are often marketed as "incense" and are typically labeled "not for human consumption" in order to circumvent the Controlled Substances Analogues Enforcement Act of the United States.[7] Synthetic cannabinoids were developed by independent laboratories following research

on the development of CB1/CB2 receptor agonists for the treatment of pain and nausea.[7] Similar to marijuana, they are ingested orally or smoked.

Mechanism of action and neurochemical considerations

Cannabinoid agonists vary in conformation and belong to specific structural groups. The most commonly identified analogues belong to the JWH (John W. Huffman), CP (Cyclohexyl Phenol) or HU (Hebrew University) structural groups.[7,12] Whereas THC is only a partial agonist at the CB1 and CB2 receptors, synthetic cannabinoids act as full agonists at these receptors with an affinity up to 800 times that of THC.[12] Cannabinoid receptors play a role in sensory perception and emotional processing of stimuli in the hippocampus, amygdala, and prefrontal cortex via reduction in GABA release and increase in dopamine and glutamate release.[13] In addition to CB receptor agonism, Spice products are often contaminated with Clenbuterol, which drives sympathetic nervous system activation via agonism at β2 adrenergic receptors.[7,13]

COURTESY OF DRUG ENFORCEMENT ADMINISTRATION (DEA)

K2/Spice

Desired effects, toxicities and long-term effects

The desired effects of synthetic cannabinoids closely resemble those of smoked and orally ingested marijuana, including euphoria, relaxation, disinhibition, and altered perception and consciousness.[7,13] Adverse reactions and toxic effects of synthetic cannabinoids result predominantly from activation of central CB receptors and β2 adrenergic receptors. Somatic and autonomic effects related to the cannabinoid toxidrome include nausea, vomiting, diaphoresis, hot flushes, xerostomia, mydriasis, tachycardia, hypertension, and tremors. Neuropsychiatric toxicities include anxiety, mood dysregulation, perceptual disturbances (hallucinations and delusions), memory impairment, sedation or psychomotor agitation, depersonalization, increased sensitivity to sensory stimuli, suicidal ideation, and seizures. Vascular reactivity and dysfunction have been reported in association with synthetic cannabinoid intoxication and is especially concerning in patients with a history of ischemic heart disease.[13] Tachyphylaxis has been described and is thought to be due to the long half-life of many of the synthetic cannabinoids and their active metabolites.[14] Clinical reports of deaths related to Spice intoxication and its complications are on the rise.[13,14]

Long-term Spice users may develop tolerance. Spice related withdrawal effects include sleep disturbances, seizures and cardiac conduction abnormalities with associated palpitations.[15] As with marijuana, there are several reports of new-onset psychosis following synthetic cannabinoid use that persists beyond the initial intoxication phase. Associated symptoms include paranoid and other delusions, disorganized speech and behavior, affective blunting, and waxing and waning psychomotor slowing. These symptoms may require inpatient management and treatment with antipsychotic medication. Thirty percent of these patients remained psychotic after eight months.[13-15] Other neuropsychiatric sequelae include depressed mood, neurovegetative dysfunction, and suicidal ideation.

Available evidence suggests that prolonged use of synthetic cannabinoids is more strongly associated with persistent psychosis than marijuana. This may be due to the higher affinity of these agents at CB1 and CB2 receptors, dose and potency variation of the active compounds found in synthetic cannabinoids, and the fact that natural cannabis contains cannabidiol, a compound with antipsychotic properties.[16,17]

Diagnostic and therapeutic considerations

Liquid gas chromatography tandem mass spectrometry (LC-MS/MS) and matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDY-TOF) are able to detect synthetic cannabinoids and their metabolites in urine.[13] Like bath salts, testing for synthetic cannabinoids requires use of specialty reference labs with related high costs and delays in reporting of results. There are no published guidelines for the management of the synthetic cannabinoid toxidrome but current recommendations include supportive care, provision of a low-stimulation environments, and use of benzodiazepines for anxiety and sedation.[7,13]

Salvia

Background

Unlike bath salts and synthetic cannabinoids, salvia (*salvia divinorum*) is a naturally occurring herb from the mint family that has been used in Mexico for centuries for its psychogenic effects.[18] Recreational use of salvia has surged over the last decade in the United States and Europe owing to its low cost, ease of purchase online, and a lack of legislation controlling its access and use. Salvia is most commonly smoked but can also be chewed with resulting mucosal absorption.[18]

Mechanism of action and neurochemical considerations

Salvinorin A has been identified as the active chemical responsible for salvia's clinical effects.[18] Salvinorin A is a diterpene compound with highly selective kappa opioid receptor agonist properties resulting in hallucinations, diuresis,

mood improvement and spinal analgesia. In contrast to μ opioid receptor agonists, diterpenes are not associated with respiratory depression. The kappa receptor has been extensively researched for its antidepressant and anxiolytic properties, making it unclear why salvia can produce a paradoxical increase in anxiety.[19,20] The onset and duration of salvia's effects depend upon the route of administration and range from minutes to up to an hour.[20] Salvia is hepatically metabolized by the cytochrome oxidase isoenzyme system and undergoes first pass metabolism, explaining why oral ingestion does not produce neuropsychiatric effects.[20]

Desired effects, toxicities and long-term effects

The desired effects of salvia include a state of "trance" or "reminiscent meditation" that is similar to that produced by lysergic acid diethylamide (LSD), ketamine, and cannabis.[21] The intoxication state is marked by hallucinations, other sensory-perceptual distortions, increased sensitivity to sensory stimuli, synesthesia, out-of-body experiences, and mood elevation.[18,21] Unwanted effects of salvia intoxication include anxiety, dysphoria, confusion, language impairments and fear associated with "bad trips." Symptoms of headaches and drowsiness have been reported to last for several hours after the most recent use.[18] Withdrawal episodes marked by tachycardia and hypertension have been described but these are uncommon.[19] Cases of persistent psychosis in the setting of chronic use have been described and it has been suggested that salvia can unmask or exacerbate preexisting mental illness.[19,21] Cases of salvia addiction have been reported but its prevalence has not been studied.[21]

Diagnostic and therapeutic considerations

Similar to synthetic cannabinoids and bath salts, salvia testing is not part of routine urine drug screens. It, too, can be detected by the use of high-performance liquid chromatography (HPLC) LC–MS/MS or gas chromatography–mass spectrometry (GC–MS) – but with related high cost and delayed result reporting. It remains uncommon for a patient to seek medical care solely for salvia intoxication, but current management recommendations include supportive care treatment with benzodiazepines as indicated for agitation or severe anxiety.[19]

CONCLUSION

Bath salts, synthetic cannabinoids, and salvia are three novel agents in a constantly evolving list of drugs of abuse. Abuse of these substances is particularly worrisome because they are readily available, inexpensive, perceived as harmless by the general public, result in severe somatic and neuropsychiatric toxidromes, and because they are not readily detected by routine drug screening methods. Despite the protean and severe effects of the toxidromes associated with these drugs, medical professionals may be unfamiliar with their presentation and management. The adverse effects of these

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Salvia

and other novel drugs of abuse have been made clear on a local level with a recent report from the Rhode Island Department of Health of 10 deaths from Acetyl-Fentanyl overdose, a fentanyl analogue that is up to five times more potent than heroin. These drugs pose unique challenges to the medical community and regulatory bodies, as advancements in molecular chemistry have paved the way for the continuous development of newer and more potent substances of abuse.

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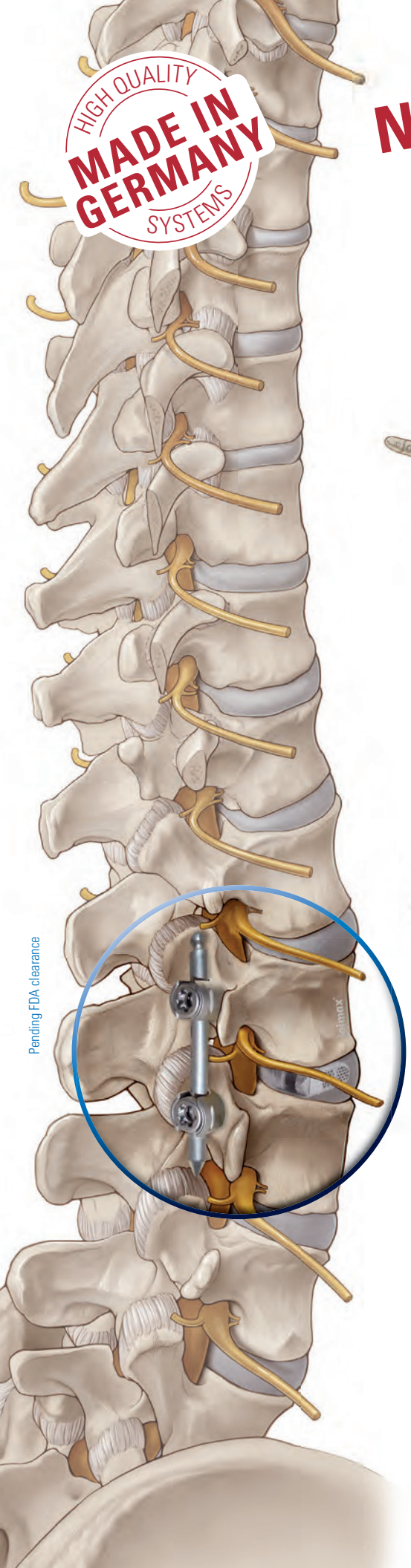

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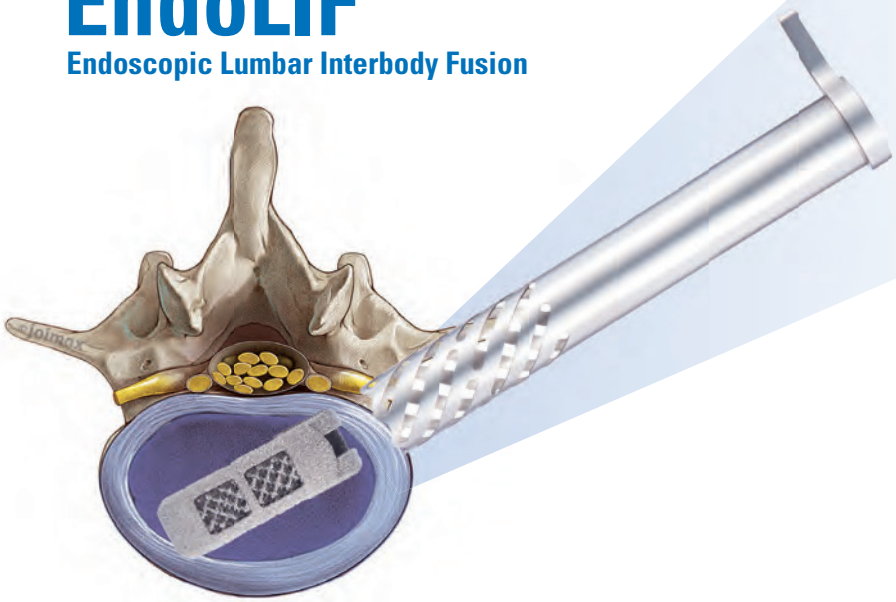

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Outpatient, Awake, Ultra-Minimally Invasive Endoscopic Treatment of Lumbar Disc Herniations

GABRIELE P. JASPER, MD; GINA M. FRANCISCO, BSC; ALBERT E. TELFEIAN, MD, PhD

ABSTRACT

BACKGROUND: Endoscopic discectomy is an ultra-minimally invasive outpatient surgical option for the treatment of lumbar herniated discs. The purpose of this study was to assess the benefit of tranforaminal versus interlaminar endoscopic discectomy in patients with single level Lumbar 5-Sacral 1(L5-S1) disc herniations and lumbar radiculopathy.

METHODS: After Institutional Review Board Approval, charts from 41 consecutive patients with complaints of lower back and radicular pain and an L5-S1 herniated disc who underwent an endoscopic procedure between 2007 and 2012 were reviewed. The transforaminal approach was used for patients with far lateral, foraminal, and paracentral disc herniations and the intralaminar approach was used for herniations that were more central.

RESULTS: The average pain relief 1-year postoperatively was 75.9% for the transforaminal group and 75.3% for the interlaminar group, both excellent results as defined by MacNab. The average preoperative visual analogue scale (VAS) scores were 8.2 and 8.4 for the transforaminal and interlaminar groups respectively, indicated in our questionnaire as severe and constant pain. The average 1-year postoperative VAS scores were 1.7 and 2.1, indicated in our questionnaire as mild and intermittent pain. There were no complications in the series of patients treated.

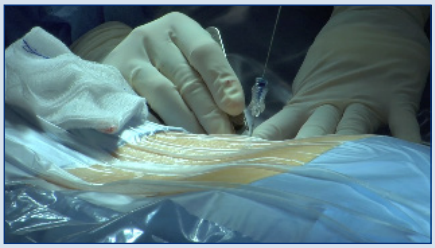
CONCLUSIONS: The 1-year follow-up data presented here for transforaminal and intralaminar approaches to L5-S1 disc herniations appears to indicate that either approach can be used as determined to best suit the pathology without sacrificing the probability of postoperative pain improvement.

KEYWORDS: Endoscopic discectomy, minimally-invasive, transforaminal, interlaminar

IRB approval: Meridian Health: IRB Study # 201206071J

BACKGROUND

Minimally invasive spine surgery is a broad term covering several different surgical approaches, but all are designed to access spine pathology while minimizing damage to the surrounding tissue. Transforaminal endoscopic lumbar discectomy represents the current pinnacle in minimally invasive spine surgery because the surgery is performed through a pea-sized incision (5-6 mm) in awake patients. This means faster recovery of the patient. Studies have shown shorter hospital stays and quicker return to work after endoscopic disc surgery.[1,2]



VIDEO: Endoscopic Lumbar Discectomy Surgical Procedure

Advances in endoscopic visualization and instrumentation, as well as increased patient demand for more minimally invasive procedures, have led to an increased popularity of the technique, particularly outside of the United States. Other studies have shown that endoscopic discectomy is a safe and effective alternative to conventional procedures, and has the advantages of being a truly minimally invasive procedure.[3-5] Rhode Island Hospital will be the first academic center in New England to offer this awake, ultra-minimally invasive endoscopic treatment for lumbar disc herniations this spring.

The authors describe here their experience with treating patients, who present with L5-S1 disc herniations and persistent lumbar radiculopathy despite conservative non-operative treatment, with endoscopic discectomy. Surgical approaches presented were chosen based on the location and morphology of the disc herniation, the height of the iliac crest and the need for foraminotomy. A retrospective study on average patient pain relief 1- year post-L5-S1 endoscopic discectomy is presented.

METHODS

Participants

After Institutional Review Board Approval, charts from 41 consecutive patients aged 25-87 (mean age of 46, 15 women (37%) and 26 men (63%)) with complaints of lower back and radicular pain who received endoscopic discectomy procedures for L5-S1 disc herniations between 2007 and 2012 were reviewed.

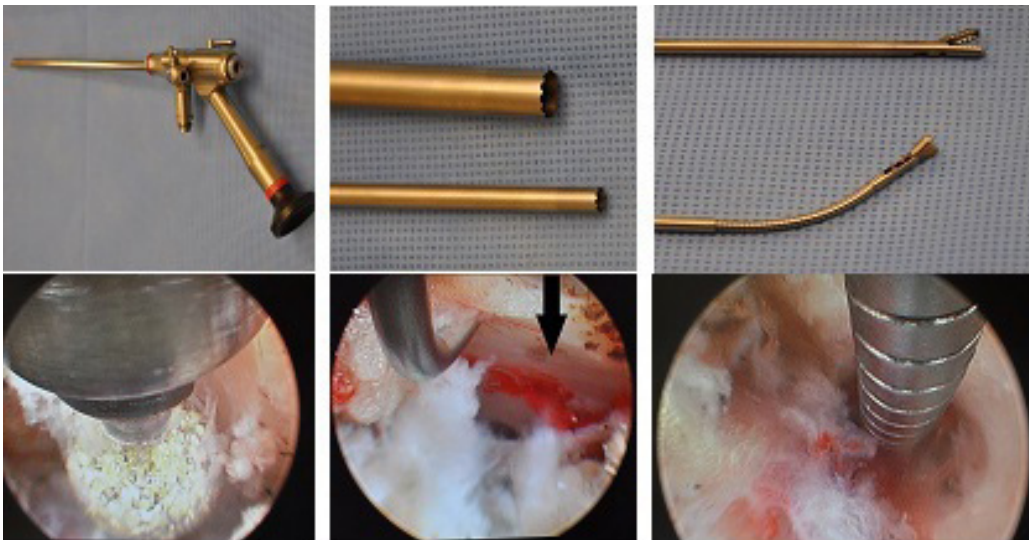


Figure 1. Instruments used in the TESSYS™ procedure are shown. Endoscope with working channel **(top left)**, large and small reamers for enlarging the neural foramen by removing the ventral portion of the superior articulating process **(top middle)**, straight and bendable graspers **(top right)**, diamond drill for enlarging the foramen **(bottom left)**, nerve hook for retracting the nerve root (*arrow*) **(bottom middle)**, and bendable grasping forceps reaching through the expanded foramen behind the pedicle for an extruded disc fragment **(bottom right)**.

Surgical Technique

Patients were selected for treatment based on the results of their MRI, physical exam, dermatomal pain pattern, and favorable response to transforaminal steroid injection. Patients were positioned on their sides (lateral decubitus) or lying face down (prone on a Wilson frame). Versed and fentanyl were given for conscious intravenous sedation and the rest of the procedure was performed with just local anesthetic. The surgeon began by inserting a set of guide rods and then a 6 mm working cannula under fluoroscopic guidance. Any bony removal necessary was performed with small bone reamers or an endoscopic drill (**Fig.1**). Rotating the cannula and endoscope allowed for 360-degree visualization of the annulus and exiting and traversing nerve roots (**Fig. 2**). The technical success of the foraminotomy procedure was determined by the visualization of the traversing nerve root (**Fig. 1**). Discectomy was performed with straight, upgoing, and bendable graspers (**Fig. 1**). At this point, whether using a transforaminal approach or interlaminar approach, the herniated disc and any bony overgrowth causing nerve root compression could be resected endsocopically under magnification.

The difference between the transforaminal approach and the interlaminar approach is the location of the operative "window." The entry point for the transforaminal approach is 8-18 cm off the midline with the target area being the neural foramen. This works well for lateral, foraminal and paracentral disc herniations. The interlaminar approach uses an entry point that is near midline and targets central disc herniations that are either above or below the exiting nerve root, which in the case of L5-S1 is the S1 nerve.

Measures

Follow-up questionnaires were filled out by the patient with each visit indicating the location, severity, and duration of pain. Patients were asked to rate their pain using a 0 – 10 scale, a modified form of the Visual Analog Scale (VAS). Each patient had MRI confirmation of disc herniation or protrusion prior to the procedure. Comparison was made between the two groups of patients: receiving endoscopic discectomies by transforaminal and interlaminar approaches. The overall pain relief in patients was calculated as a percentage of improvement between the preoperative and the 1-year postoperative VAS score. Overall success rate was then calculated on each patient. MacNab criteria

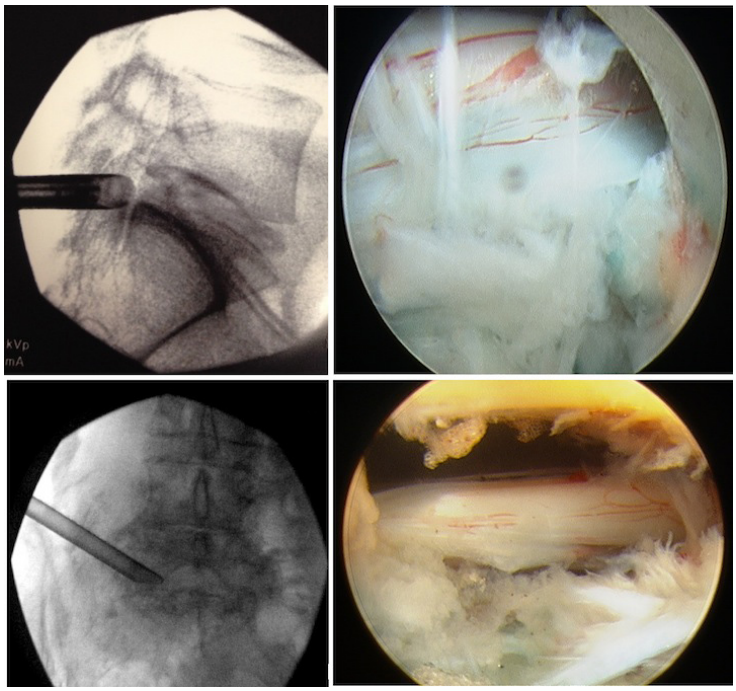


Figure 2. Fluoroscopic and endoscopic views from interlaminar and transforminal L5-S1 discectomies. Working channel seen in the L5-S1 interlaminar space **(top left)** and endoscopic view of the S1 nerve root (**above**) and herniated disc (below) **(top right).** Working channel seen in the L5-S1 transforaminal approach **(bottom left)** and endoscopic view of the ligamentum flavum (top and yellow) S1 nerve root (middle) and herniated disc (below) **(bottom right).**

was applied to each patient by characterizing pain relief of 75%-100% as excellent, 50%-74% as good, 25%-49% as fair, and 0%-24% as poor.[6] Success is based on an excellent, good, or fair outcome.

RESULTS

Of the 41 patients undergoing awake endoscopic surgical treatment for an L5-S1 disc herniation, 24 underwent a transforaminal approach and 17 an interlaminar approach. The average pain relief 1-year postoperatively was 75.9% for the transforaminal group and 75.3% for the interlaminar group, both excellent results as defined by MacNab.[6] The average preoperative VAS scores were 8.2 and 8.4 for the transforaminal and interlaminar groups respectively, indicated in our questionnaire as severe and constant pain. The average 1-year postoperative VAS scores were 1.7 and 2.1, indicated in our questionnaire as mild and intermittent pain. Only 1 patient in the transforaminal surgery group and 2 patients in the interlaminar group had results that were not at least excellent, good, or fair.

During the 1-year follow-up there were no cases of disc reherniations in either group. There were no complications of cerebrospinal fluid leak, nerve injury, or hemorrhage requiring return to the operating room. Previously reported complications can include infection, dysesthesia, thrombophlebitis, dural tear, vascular injury, and death.[4]

DISCUSSION

Other studies have shown that endoscopic spine surgery is an effective procedure for treating multiple pathologies in the lumbar spine including lateral, paracentral, central, extruded and even contralateral herniated discs as well as lateral recess stenosis.[2,7-10] The 41 patients treated here included cases in which sequestered herniated discs seen cephalad or caudal to the disc space were removed using specialized flexible instruments. The instruments enabled the surgeon to circumnavigate and reach into the epidural space and as far as the mid-vertebral body (**Fig. 1**). The unique surgical method and instrument design allowed for high success even in the more challenging area of L5-S1 presented here. The patients were sedated intraoperatively but conscious so nerve damage could be avoided. Each patient was asked throughout the procedure if he or she was experiencing leg pain, characteristic of manipulation of the nerve root. This nerve could be viewed and identified endoscopically allowing for further caution when working in the epidural space, adding to the safety of the procedure.

Changes in health care in the United States present challenges, among them how to deliver the highest-quality, most-effective care in the most cost-efficient way. In the United States, from 2002-2007, a study of Medicare patients showed a 15-fold increase in the frequency of complex spinal fusions performed in this older population – these included 360-degree and multilevel lumbar spinal fusions.[11] Multilevel complex spinal fusions represent a complex solution to the problem of degenerative spine disease. Most practitioners and patients in Rhode Island would likely agree that the availability of more "non-instrumented" minimally-invasive surgical options to spine care would be a welcome addition to our treatment armamentarium.

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Promoting Medical Student Research Productivity: The Student Perspective

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ABSTRACT

One-third of medical students complete medical school without significant exposure to research. This gap in their medical education is significant: research not only exposes medical students to scientific methodology and academic writing, but also encourages them to multitask, communicate, and critically analyze the scientific literature – valuable skills that will serve them well in their future medical careers. We report herein the proceedings from a student-led symposium that aimed to promote student involvement in research at the Alpert Medical School of Brown University by providing practical information on how to successfully complete a research project.

KEYWORDS: medical student, research, publication

INTRODUCTION

Due to the declining numbers of physician scientists, there is a recent push to expose medical students to research.[1] Medical students who acquire research experience are more likely to choose academic careers[2-4] and are better prepared for residency training.[5] Moreover, research teaches students how to ask scientific questions and critically review literature – valuable skills for future physicians irrespective of their career choices.[6]

The primary barriers to student involvement in research include time constraints, difficulty finding mentors, and absence of training in research methodology.[7] To begin addressing these barriers, we presented a symposium titled, "Publications and Pitfalls: Our Tips as Medical Students," at the Alpert Medical School (AMS) in January 2014. Supported by two faculty members and led by a panel of five AMS students with experience in scientific research, the symposium sought to share the successes and failures of the student panelists and encourage first- and second-year medical students to become involved in research. This paper synthesizes the proceedings of the symposium.

Picking a Faculty Mentor

Identifying a committed mentor is vital to a successful research experience. Students should begin by determining if they wish to do basic science or clinical research. Compared to laboratory-based projects, clinical science often lends itself to smaller projects, which are more amenable to beginning researcher and student schedules. Students should then find an area of interest and arrange to meet with faculty members who have experience in that subject. If a student cannot decide on a specific field, it is helpful to speak to peers about possible interests and good mentor experiences.

The initial face-to-face meeting with the faculty member will allow students to assess the potential mentor's interest in working with them. Good mentors will be enthusiastic, have multiple publications with students as co-authors, work with the student directly instead of through research assistants, and understand the constraints (e.g., time) and expectations (e.g., desire to explore the field and publish findings) of medical students. Students should shy away from mentors who are unresponsive to emails, lack recent publications, and have had poor reviews from former students.

Beginning and Managing a Project

For students who have a research topic in mind, it is essential they begin with forming a research question and then conducting a literature review to ensure that they are not reinventing the wheel. This exercise will also teach students how to read academic papers and determine what makes a good research project and publication. For students unsure of a project, they can begin the literature review after they meet with their mentor.

Other important considerations when deciding upon a project are group versus individual work, funding, and establishing a timeline. Students should determine if they want to work with a group or by themselves. A team can take on a larger project, especially when time is limited. However, group projects can be weighed down by the complexity of large-team dynamics; there may be more opportunities for any one person to delay the project, which can be difficult for students with significant time constraints. Inexperienced students should consider taking on small individual projects where they can benefit from a close working relationship with a primary faculty mentor and increase their chances of obtaining a publication. Regardless of the size of the research team, students should have a discussion with their research mentor to establish authorship requirements, especially for students aiming to be a first author on an abstract or manuscript.

Funding for a project may not always be available, though

Table 1. Sample Timeline for a Summer Research Project

DATES	Planned Work	Objectives for Mentor Interactions*
October	Search for topic and meet with prospective mentor(s)	Finalize topic
November	Conduct background research and literature review	Plan project, timeline and mentor meeting schedule
December	Write project's introduction, purpose, methods and limitations and incorporate into funding proposal (e.g., SA); provide updated CV to mentor for letter of support	Revise funding proposal
January	Submit funding proposal	Finalize funding proposal
February–April	If applicable, meet with IRB coordinator and prepare and submit IRB proposal	Revise and finalize IRB proposal
June	Collect data	Organize results
July	Analyze data	Review primary findings
Late July to Early August	Prepare abstract and manuscript	Revise abstract and manuscript
September	Submit abstract to target conference and manuscript to target peer-reviewed journal	Project summary and future plans

*Email, telephone calls and face-to-face meetings as needed.

Abbreviations: SA, Summer Assistantship; IRB, Institutional Review Board.

students should thoroughly investigate research-funding opportunities at their institutions. At the AMS, there are numerous funding opportunities for student research and research-related travel.[8] Beginning students should consider choosing projects such as chart reviews, which are less likely to require financial support.

Developing a detailed timeline will significantly increase the chance of completing a project. Medical students often have only a few months to dedicate to research due to the demands of their academic schedules. Students should ensure their mentor understands these limitations. Ideally, students and mentors should set target dates for each of the important components of the project, including Institutional Review Board (IRB) proposal submission, data collection, data analysis, and abstract and manuscript preparation. While targets may change as the project continues, good mentors will advise students on their timelines. Students should also be frank about their commitment to making these deadlines achievable. A sample timeline for a summer project is listed in **Table 1**. Notably, we recommend aiming to complete the project, including manuscript writing, by the end of the summer (or the allotted research time): the remaining project tasks – such as revising a manuscript in response journal reviewers' comments – are less likely to interfere with the demands of students' academic schedules in the fall.

Establishing rules of communication with faculty mentors can help avoid significant delays. Students and mentors should agree on rules of communication: for example, an accepted time frame to respond to emails and when to send follow-up emails. It is important to set dates for regular meetings in advance, come prepared to each meeting with a written agenda, and leave with clear action items for both parties to keep the project on track.

Writing: Institutional Review Boards, Abstracts, and Manuscripts

Beginning student researchers often believe that abstract and manuscript writing occur after data analysis. However, introductory elements can be written even before any data is collected. By writing the introduction, purpose, and methods in abstracts and manuscripts, students can better understand their research question and methodology. This process also clarifies the goals of data collection and analysis.

Writing these portions of the manuscript can also help students with their IRB proposals, if their projects require it. Learning how to prepare and submit an IRB proposal is an excellent experience, but also time consuming. Additionally, a project can be derailed by a delay in the IRB-approval process. If students need to complete IRBs for a project, it is essential they start working early with experienced mentors and staff (e.g., institutional IRB coordinator) who can help guide them through the IRB process. Students should plan to have IRB approval obtained *before* the summer (or allotted research time). Students without adequate experience and time to navigate the IRB process should consider, if possible, starting with projects (e.g., a systematic literature review) that will not need IRB approval or projects that are already IRB approved.

When data collection and analysis is completed, students should establish a target conference and journal with their mentor and understand all conference abstract and journal

Table 2. Five Tips for Success as a Medical Student Researcher

1. Find a good mentor: look for those who are interested in medical students, understand the constraints of medical school, have a track record of recent student-authored publications, and communicate promptly and directly.
2. Start projects with a literature review to establish a knowledge base on the topic of interest and find new ideas.
3. Set realistic deadlines for all stages of the project, including preparing the institutional review board application (if required), collecting the data, analyzing the data, and writing the abstract and manuscript.
4. Prepare the preliminary sections of the abstract and manuscript in advance and read major journals for models.
5. Begin with a small, more manageable project to increase its likelihood of being completed.

requirements before writing the results and discussion portions of the abstract and manuscript. Students should expect and allot time for multiple revisions, especially if they lack experience in writing scientific papers. Reviewing articles from major journals can help students understand the anatomy of a clear abstract and concise paper.

CONCLUSION

In summary, we hope that this symposium will assist AMS students in bringing their research projects to fruition. A list of key take-home messages is provided in **Table 2**. We plan to continue this symposium annually, incorporating new information to meet the changing needs of student researchers. Future topics include research software, poster design, and conference presentation style.

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Disclosures

The authors report no conflict of interest.

Disclaimer

The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government.

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Gastrointestinal CMV in an Elderly, Immunocompetent Patient

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ABSTRACT

An 83-year-old male with a history of diabetes but with an otherwise intact immune system presented with melena. Upper endoscopy showed gastric and duodenal ulcers. Colonoscopy showed colonic ulcers. Biopsies revealed cytomegalovirus (CMV). Therapy with an antiviral such as ganciclovir should be considered even in an immunocompetent patient if male and over the age of 55, or if they have chronic diseases such as diabetes or chronic kidney disease.

KEYWORDS: CMV, Colitis, Immunocompetent, Ganciclovir

INTRODUCTION

Gastrointestinal Cytomegalovirus (CMV) infection is well-described in patients immunocompromised by HIV and low CD4 counts, chemotherapy, chronic steroids, or immunosuppressive therapy after organ transplantation. However, GI CMV can also represent a very rare yet significant problem in immunocompetent patients. We report an elderly immunocompetent patient with GI CMV disease, and we provide a management algorithm (Table 1) to determine whether or not to treat such a patient with antivirals.

CASE REPORT

An 83-year-old male with a past history of diabetes mellitus presented with melena. EGD showed multiple small antral ulcers, gastritis, and a 1-cm, non-bleeding, duodenal ulcer. One month later a repeat EGD showed persistence of the gastric and duodenal ulcers despite a trial of PPI therapy. Biopsies for H pylori was positive, yet for some reason the patient was not treated.

Over the next four months he had no further bleeding or symptoms. A repeat EGD and colonoscopy demonstrated two 3-cm antral ulcers, a duodenal ulcer, and colitis. Biopsies revealed gastric, duodenal, and colonic CMV. Serum CMV antibody level was elevated, and HIV test was negative. Since he was asymptomatic at this time, CMV therapy was not initiated. The patient was referred to us to evaluate for underlying inflammatory bowel disease and to confirm that the CMV had resolved.

Table 1. Treatment algorithm for Gastrointestinal CMV

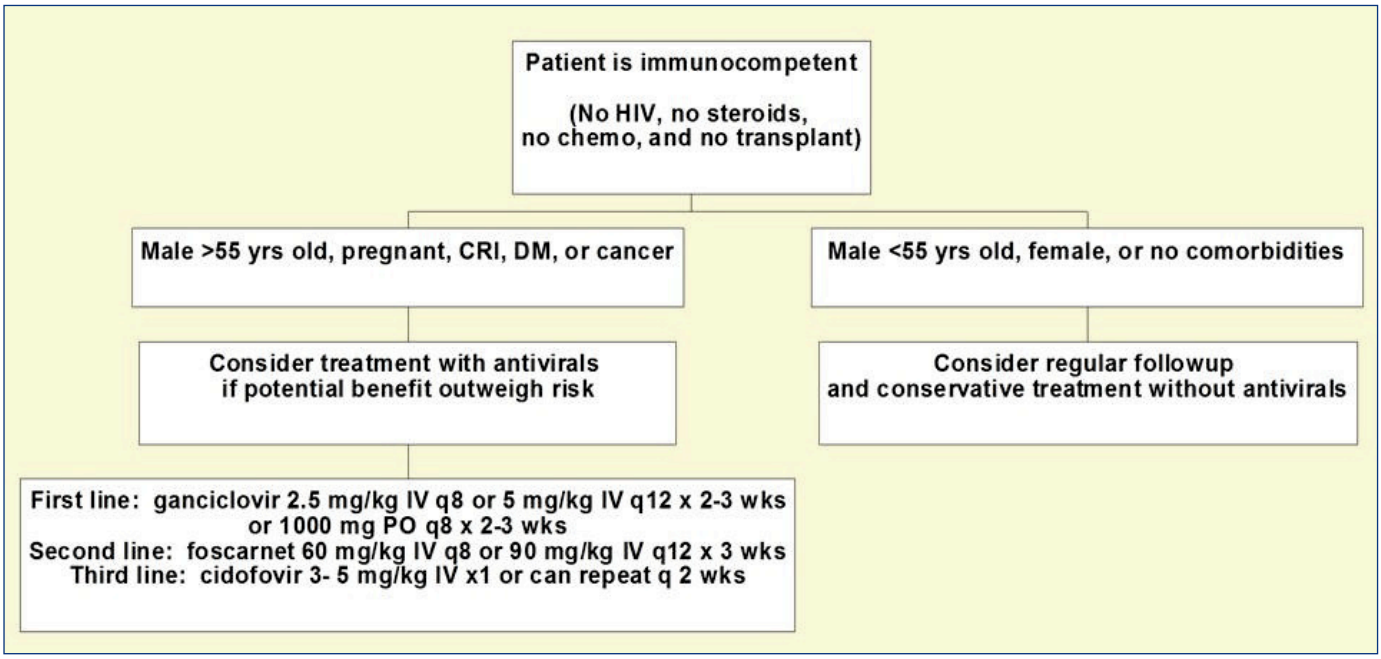


Image 1. Duodenal ulcer

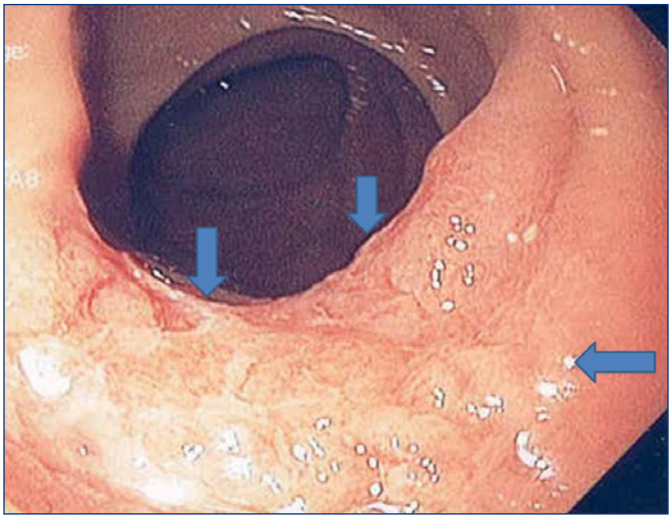


Image 2. Colonic ulcer

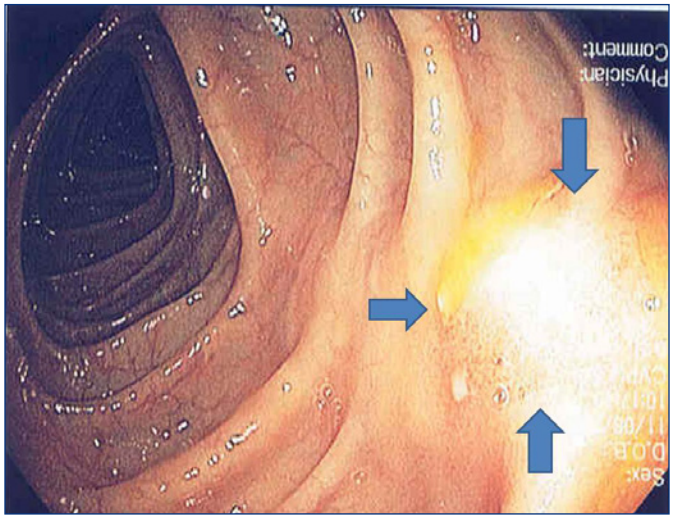


Image 3. Duodenal CMV on histology

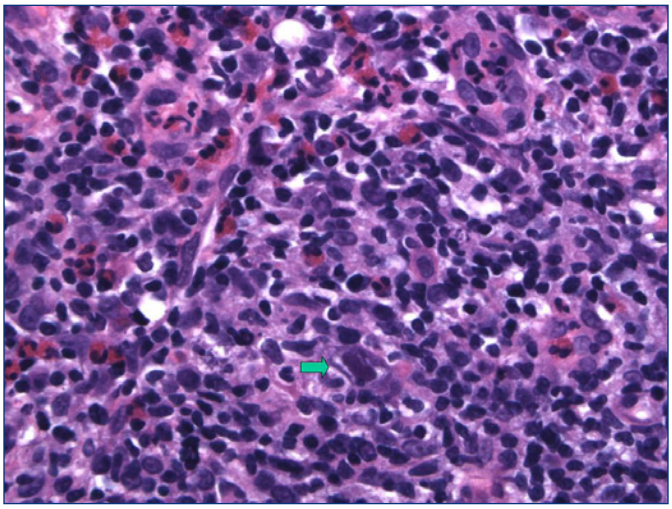


Image 4. Colonic CMV on histology

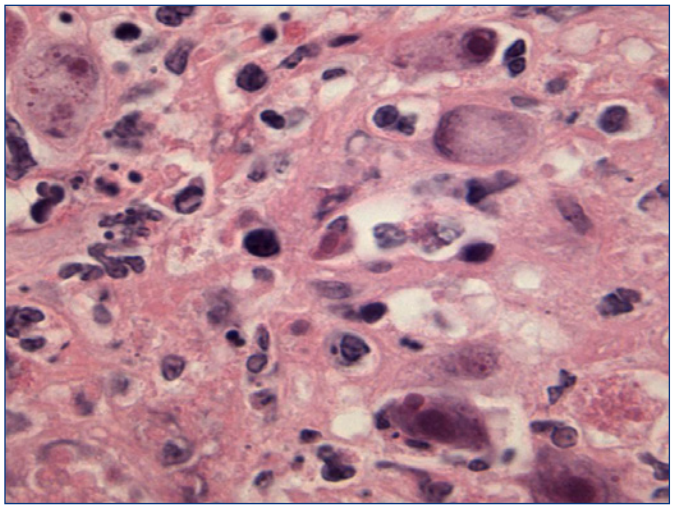
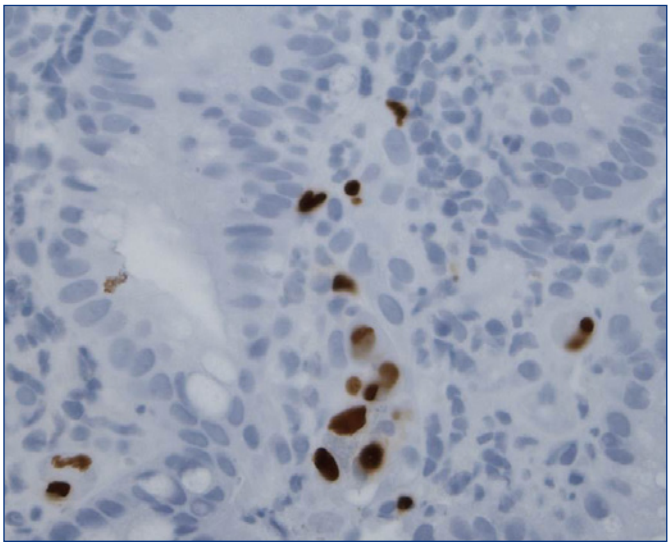


Image 5. CMV on Immunohistochemistry



Another EGD showed antral and duodenal ulcers (Image 1). Colonoscopy revealed scattered colonic ulcers (Image 2). Antral, duodenal, and colonic biopsies were positive for CMV (Images 3 and 4). Immunohistochemistry was positive for CMV (Image 5). Because Helicobacter pylori was positive in the past, he was treated with 2 weeks of triple therapy. One year later, the patient expressed concern about the ulcers, so endoscopies were repeated. Biopsies this time continued to show persistence of the antral, duodenal, and colonic CMV. CMV viral culture was positive, and CMV DNA was positive as well.

Because the patient had been asymptomatic for quite some time, whether or not to treat him was controversial, and a literature review was performed. One large case series suggested treatment for older male patients or patients with any chronic systemic disorder in contrast with observation for younger and healthier patients. Because of the possibility of increased mortality from the patient's male sex, age, and

diabetes, we decided to treat him with a 21-day course of oral ganciclovir. Post-treatment colonoscopy showed resolution, but EGD showed persistence of the duodenal ulcer and biopsies showed CMV. A second round of treatment was started with intravenous ganciclovir. The EGD after this round of treatment showed a partially healed duodenal ulcer and less CMV on biopsy, but not full resolution. Because the elderly patient had received two attempts at antiviral treatment and was asymptomatic, we decided not to pursue anything further except clinical follow-up. Four years later he remained asymptomatic, and EGD showed no ulcer but continued persistence of the CMV.

DISCUSSION

CMV is a double-stranded DNA virus in the Herpes virus family. It is often acquired in infancy or through sexual contacts, and most adults in the United States are colonized with CMV. Initial infection usually causes flu-like symptoms, and most CMV disease is due to reactivation of latent virus. CMV can affect any organ in the body, but it most often causes retinitis, gastrointestinal disease, or encephalitis.[1] Most CMV disease occurs in patients immunocompromised by HIV,[2,3] organ transplantation,[4] chronic steroids, or chemotherapy. One third of AIDS patients have CMV disease, and the greatest risk occurs to HIV patients when the CD4 count falls below 50. Clinical manifestations of GI CMV disease are very rare in immunocompetent people being the subject of only a few case reports.[5] The elderly are at particular risk of CMV disease and related mortality because T cell function declines with normal aging.[6,7]

CMV gastrointestinal disease can affect the gastrointestinal tract from the mouth to the anus,[8] and it can also affect the pancreas, liver[9] and bile duct. Colitis is the most frequent gastrointestinal manifestation, but often multiple discrete areas of the GI tract can be involved. Gastrointestinal CMV can present in many ways, but most often it presents as diarrhea, abdominal pain, and bleeding. On a cellular level, vascular endothelial cells are damaged leading to erosion and ulceration. Because symptoms of GI CMV are diverse and nonspecific, CMV can often be mistaken for other GI disorders like inflammatory bowel disease (IBD) or ischemic colitis.[10] CMV can also be a potential causative factor in exacerbations of IBD (particularly in severe UC not responding to treatment).[11]

The gold standard for diagnosis is visualization of large cells containing intra-nuclear and intracytoplasmic inclusions surrounded by a clear halo ("Cowdry owl eye") in tissues samples. Immunohistochemical studies like monoclonal antibodies and in-situ DNA hybridization can be confirmatory tests. Serum antibodies, viral cultures, and stool cultures are generally not useful.

Treatment is usually with either oral or intravenous ganciclovir12 (5 mg/kg twice daily) or foscarnet (90 mg/kg two twice daily), both of which are viral DNA polymerase inhibitors. Cidofovir is used less commonly. Immunocompetent patients often do not need treatment with antivirals.

A meta-analysis of cases with CMV colitis in immunocompetent hosts was published in Digestive Diseases and Sciences in 2005.[13] Galiatsatos and colleagues found that there was higher mortality rate in patients who were males over the age of 55 and in patients with chronic diseases such as diabetes or chronic kidney disease. Young patients with no co-morbidities had an excellent prognosis without any intervention. Among patients younger than 55 years, 50% of those older than 55 years, only 32% had spontaneous resolution, and survival for their group as only 45%. Eleven of the 14 deaths in their study were directly caused by CMV colitis. Therefore it was suggested that antiviral therapy be used in patients who are males older than 55 years or in patients with chronic diseases that may affect the immune system. A summary of the proposed treatment algorithm is presented in Table 1.

CONCLUSION

Our case was a male older than 55 years with diabetes. Since he was at risk for significant mortality based on this meta-analysis, we decided to treat him with antiviral therapy. As of the current time, our patient remains asymptomatic.

There are only a few published case reports of CMV gastrointestinal disease in immunocompetent hosts. Here we presented a case of CMV in an elderly patient with a normal immune system, and we discuss our management based on the literature reviewing when to treat CMV in an immunocompetent host. The decision to use antivirals can be a complex and challenging one, but one with likely benefit when a patient has certain risk factors.

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An Unusual Case of Pulmonary Embolism in a Young Healthy Female Competitive Rower

KATHERINE M. RAND, CHARLES B. SHERMAN, MD

ABSTRACT

Young healthy women without a genetic predisposition are considered to be at low risk for deep vein thrombosis and pulmonary emboli. We present an unusual case of pulmonary embolism in a 21-year-old female competitive rower likely caused by oral contraception and trauma of the axillary-subclavian vein by extrinsic compression due to repetitive arm movements.

KEYWORDS: Pulmonary Embolism, Effort Thrombosis, Oral Contraception, Elite Athletes, Crew

INTRODUCTION

Pulmonary embolism (PE) affects over 1 in 1,000 Americans each year and has a mortality rate greater than 15% in the first 3 months after diagnosis.[1] The most common risk factors for pulmonary emboli and deep vein thrombosis (DVT) include prolonged immobility, older age, history of smoking, inherited clotting factors, and post-operative states.[2-5] Additionally, the use of oral contraceptives (OCP) is understood to introduce an increased risk,[6-10] often in conjunction with genetic predisposition such as factor V Leiden mutation.[11-13] Young women without genetic predisposition who are healthy and active are considered to be a low risk population for DVT and PE. We present the unique case of a young woman, a competitive collegiate crew athlete, who developed multiple PE's likely the result of OCP use and repetitive arm movement with effort thrombosis.

CASE REPORT

CR was a 21-year-old female athlete who presented to the emergency department of a local hospital with a 6-week history of increasing muscle fatigue, dizziness and exhaustion. As a competitive National Collegiate Athletic Association Division I crew athlete, she routinely trained over 22 hours per week, with most workouts involving intense repetitive arm and leg movement. During this 6-week period she continued to train at the same high intensity levels, but her performance decreased dramatically. Within six minutes into any workout her legs felt heavy and her breathing became significantly more difficult. With the development of sharp chest pain and more exertional dypsnea, she presented to the emergency department for further evaluation. She denied cough, hemoptysis, wheeze, palpitations, or upper arm or lower leg pain or swelling. Just prior to the development of her initial symptoms she had taken a 3-hour flight home after an intensive training program. In addition, the patient

Figure 1. Bilateral segmental pulmonary emboli

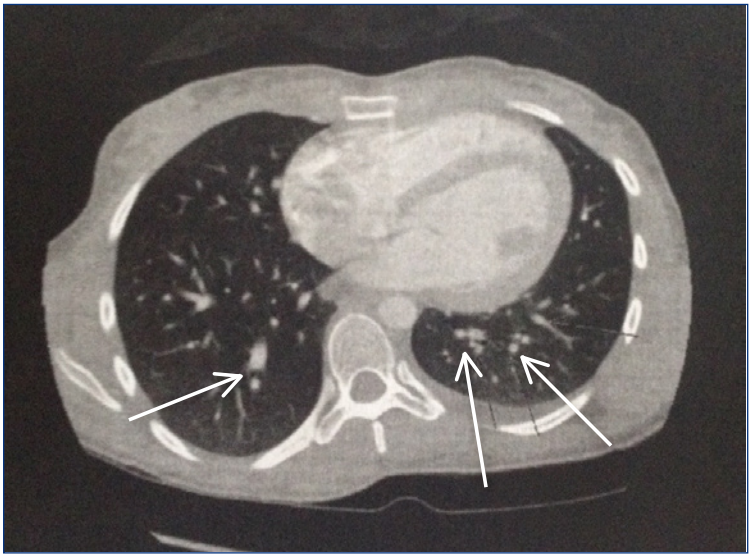

Figure 2. Left lower lobe pulmonary infarction

had a 16-month history of using the NuvaRing (etonogestrel 0.120 milligram (mg) and ethinyl estradiol 0.015 mg per day) and Loestrin 24 LE (norethindrone acetate 1 mg and ethinyl estradiol 20 mcg tablets) for contraception. She was a never smoker without a personal or family history of any clotting disorder.

Her physical exam was remarkable for: BP: 134/60; pulse: 80; respirations: 14; and oxygen saturation on room air: 98%. Her heart and lung exam were normal. She had no swelling or tenderness in upper or lower extremities.

Her laboratories revealed: normal electrolytes and a normal complete blood count; normal non-invasive lower extremity Doppler studies, no evidence of thrombophilia on a comprehensive screen, and a CT angiogram showing extensive pulmonary emboli, left greater than right, (**Figure 1**) a small, left pleural effusion and left lower lobe airspace disease likely representing a pulmonary infarction (**Figure 2**).

Her hospital course was remarkable for clinical improvement with the use of fluids and anticoagulation, first with IV heparin and then oral warfarin. She completed 6 months of anticoagulation and remains healthy. She has resumed exercise but has not returned to crew activities. She is currently using the Mirena intrauterine device (IUD) (52 mg levonorgestrel with an initial release rate of 20 microgram (ug) per 24 hours) for contraception.

DISCUSSION

Our female athlete developed multiple PE's over a 6-week period likely as the result of both OCP use and crew induced repetitive arm movement. Oral contraception is a recognized risk for thromboembolic disease in young women. Estrogen is known to be involved in multiple prothrombotic alterations in proteins associated with coagulation, and OCP therapy has been shown to increase levels of factors II, VII, VIII, X and fibrinogen and decrease levels of antithrombin and protein S.[14] Varying doses of estrogen are known to correlate with different levels of risk.[15,16] In comparison to the most commonly used estrogen dose (30 µg), oral contraceptives containing 20 µg estradiol were found to be associated with a decreased risk of thrombosis, whereas those containing 50 µg estradiol were found to be associated with an increased risk of thrombosis.[16] Given the reduced risk of venous thromboembolic disease with low-dose estrogen, it is likely that additional factors contributed to the development of PE in this patient.

Pulmonary embolism has been reported in other young female athletes using OCP. There have been case reports of PE and OCP in a competitive collegiate gymnast[17] and a competitive collegiate cross-country runner.[18]

Effort thrombosis or Paget-Schroetter syndrome is a condition seen in young athletes due to trauma of the axillary-subclavian vein by extrinsic compression due to sports such as crew that involve repetitive arm movements. External compression of the axillary and subclavian veins by the musculoskeletal components of the thoracic outlet can create pooling of blood in these veins. This may then lead to venous hypertension and chronic stasis, contributing to acute thrombosis.[19] Presenting symptoms may include pain or swelling in the upper extremity; however, some patients have no localizing symptoms. A 25-year-old major league professional baseball pitcher presented with only complaints of dizziness and shortness of breath. An angiogram showed segmental PE's in both the upper and lower lobes and a small infiltrate in the left lower lobe. A lower extremity ultrasound showed no evidence of deep venous thrombosis, yet an ultrasound of upper extremities revealed acute DVT involving the right subclavian and axillary veins.[20]

It is not possible to absolutely confirm that effort thrombosis contributed to our patient's PE's as no upper extremity imaging was performed. However, her lower extremity, non-invasive studies were negative, making leg DVT less likely as a cause for her PE's. Further, other risk factors such as high dose estrogen OCP, cigarette smoking, and thrombophilia were not present. Finally, effort thrombosis has been detected in patients without complaints or physical findings involving the upper extremity.

It is important for clinicians to recognize repetitive motion as a risk factor for thromboembolic disease in young athletes involved in appropriate sports even without complaints of upper extremity symptoms. Only then can rapid and potentially life-saving interventions be instituted.

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Disclosures

None of the authors has potential conflict of interest with any companies/organizations/ whose products or services may be discussed in this article.

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Rhode Island *Clostridium difficile* Infection Trends and Laboratory ID Events Ranking

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In January 2013, the Centers for Medicare & Medicaid Services (CMS) began requiring acute-care hospitals to submit any laboratory-identified ("LabID") *Clostridium difficile* cases to the Centers for Disease Control and Prevention's surveillance system, the National Healthcare Safety Network (NHSN).[1] By collecting data from acute-care hospitals across the nation, Medicare was able, for the first time, to systematically assess the burden of *C. difficile* nationwide and to publicly report LabID incidence on Hospital Compare.[2]

CMS's requirement to collect *C. difficile* surveillance data reflects the fact that *C. difficile* infection (CDI) is a high public health priority—both because of the impact on patients, who suffer diarrhea due to mucosal inflammation and damage[3] and because it is the most common healthcare-associated infection (HAI).[1,4,5] In 2011, there were 383,498 cases of CDI at hospital discharge in just 36 states with available data.[6] The cost of an inpatient CDI is more than $35,000 and estimates of annual medical costs exceed $3 billion nationally.[1]

The recent inclusion of CDI LabID data in Hospital Compare provides an opportunity to assess Rhode Island's performance. The objectives of this analysis were to: (1) describe RI's longitudinal trends in CDI using available historical data, and (2) compare RI's performance to neighboring states and the nation, using the newly-available LabID events data.

METHODS

Data sources

We used two data sources: (1) Healthcare Cost and Utilization Project (HCUP) data from 2002 to 2012, which includes CDI, and (2) Hospital Compare data for the first quarter of 2013, which includes LabID events. Of note, these two data sources use different measures of *C. difficile:* CDI is based on clinical diagnosis, whereas LabID events do not distinguish between *C. difficile* colonization and infection. As a result, LabID events overestimate the true CDI infection rate.[7]

HCUP databases are sponsored by the Agency for Healthcare Research and Quality and include longitudinal administrative data (inpatient, ambulatory surgery, and emergency department) for all patients, regardless of payer.[8]

Hospital Compare includes data on care processes and outcomes for selected conditions, and patient experience with care.[2] CMS requires the acute-care hospitals that participate in the Inpatient Prospective Payment System (IPPS) to submit select data, including *C. difficile* LabID event, and penalizes facilities that fail to comply. We downloaded the most recently available data (Q1 2013), which includes standardized infection ratios (SIRs)[2] comparing each hospital's and state's observed number of infections to the predicted number of infections, estimated using regression models based on data from 2010-2011.[9] SIRs are summary measures used to track and compare HAIs at the facility, state and national levels. If the upper limit of the SIR 95% confidence interval (CI) is less than 1.0, the infection rate is better than predicted; if the 95% CI includes 1.0, it is the same as predicted; if the lower limit of the 95% CI is greater than 1.0, it is worse than predicted.

Statistical Analyses

We used HCUP to query the number of CDIs by primary or secondary *C. difficile* diagnosis (ICD-9-CM code 008.45) and the number of hospital discharges. We calculated CDI rates (the number of infections per 1,000 hospital discharges) from 2002-2012 for Rhode Island, the two neighboring states with available data (Massachusetts and Vermont) and the U.S. as a whole, and then graphed these results. We also downloaded *C. difficile* LabID event SIRs from Hospital Compare and used Geographic Information System 10.2 (Environmental Systems Research Institute, Inc., Redlands, CA) software both to rank the 50 states and D.C. and to map the rankings.

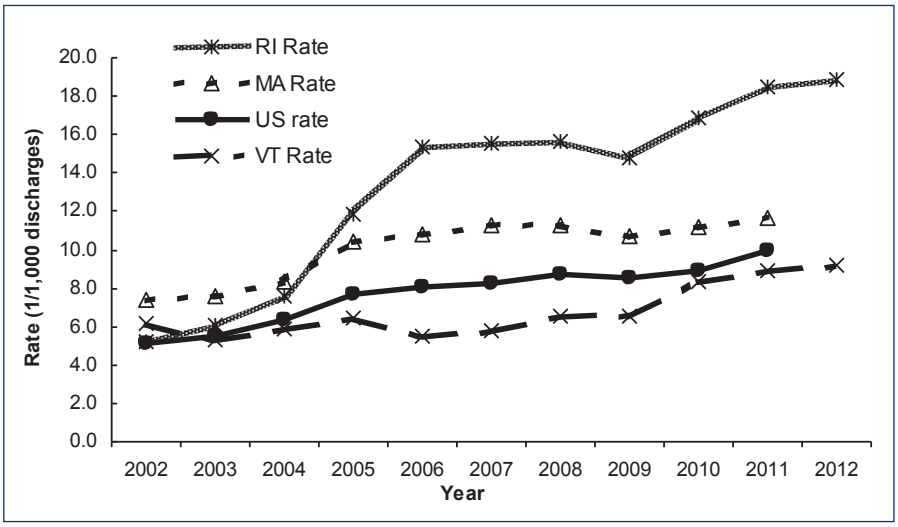
RESULTS

HCUP data reveal that the rate of CDI (listed as any diagnosis in administrative data) in Rhode Island increased more than three-fold over the past decade (5.21 per 1,000 discharges in 2002 vs. 18.87 per 1,000 in 2012), outpacing national trends and neighboring states (**Figure 1**). In comparison, CDI slightly increased in Massachusetts, Vermont, and U.S. between 2002 and 2011.

In the first quarter of 2013, RI ranked 51st among the 50 States and Washington, D.C., for *C. difficile* LabID SIRs (Figure 2). There were 19 states with upper limits of 95% CI of the SIR below 1.0 (i.e., better than the U.S. average); 22 states with 95% CI of the SIR crossing 1.0 (i.e., same as U.S. average); and 10 states, RI, AZ, NM, MD, NV, NJ, VA, NY, CA, and MA with lower limits of 95% CI of the SIR above 1.0 (i.e., worse than U.S. average).

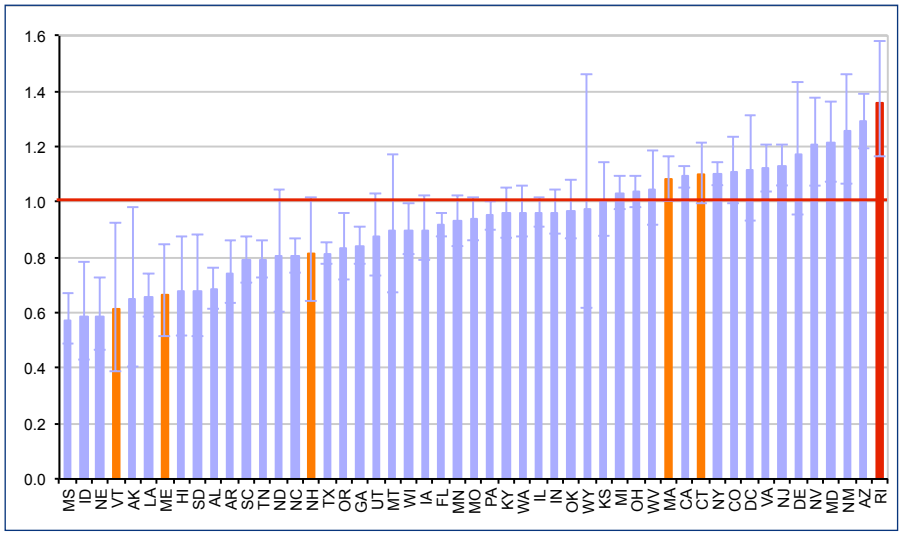
The SIRs display some region clustering, with the highest (worst) SIRs in the Northeast (VA, MD, D.C., DE, NJ, NY, RI) and West (NV, AZ, NM, CO) (Figure 3). The states with the 10 lowest (best) rankings were more widespread and included states in the Midwest (ID, SD, NE), South (LA, MS, AL) and elsewhere (VT, ME, AK, HI). In New England, VT and ME were better than the U.S. as a whole; NH and CT were same as U.S.; and MA and RI were worse than U.S. (**Table 1**), first quarter of 2013.

Figure 1. *Clostridium difficle* Infection Rate, New England Area and U.S. 2002–2012



Note: Data from Healthcare Cost and Utilization Project (HCUP) (http://www.hcup-us.ahrq.gov/)

Figure 2. States Ranked by Standardized Incidence Ratio (SIR) of *Clostridium difficile* LabID Events, First Quarter of 2013



Note: Data from Hospital Compare Website (https://data.medicare.gov/)

DISCUSSION

Between 2002 and 2012, CDI increased throughout the U.S., but the increase was greater in RI compared to other New England states (MA and VT) and the U.S. as a whole. In the first quarter of 2013, RI ranked 51st among the 50 States and D.C. for *C. difficile* LabID SIRs. The highest (worst) *C. difficile* LabID SIRs are in the Northeast and West.

CDI is spread by the fecal-oral route[3] and is strongly associated with antibiotic overuse; widespread use of broad-spectrum antibiotics is a likely contributor.[1,3] A resistant strain of *C. difficile* (BI/NAP1/027) appeared in 2004. This strain is associated with more severe clinical outcomes and may be contributing to the rapid global spread of CDI[1,3,4,8,10] and the increasing trends we noted between 2002 and 2012. Robust antibiotic stewardship programs can reduce CDI risk.[3] Although all RI hospitals have antibiotic stewardship programs in an effort to reduce targeted antibiotic use, none have a full-time physician or infectious diseases-trained pharmacist whose sole responsibility is to manage an antibiotic stewardship program, as is done in some hospitals around the country.[11] It may be that the thin profit margin of hospitals in RI compared to other states has limited the resources needed to further control CDI.

Elderly patients and those with comorbidities are the most affected by CDI.[10] Over two-thirds of patients with CDI are 65 years of age or older[1,8] and nearly 90% of CDI deaths are in elderly persons.[4] This may partially explain the regional trends we noted because the Northeast has the highest proportion of the population at least 65 years of age (14.1%) and at least 85 years of age (2.2%) in the U.S. based on 2010 census data.[12] More specifically, RI has a higher proportion of the population 65 years of age and older (14.4% in RI vs. 13.0% on average in the U.S.); and a higher proportion of those 85 years of age and older (2.5% in RI vs. 1.8% on average in the U.S.).[12]

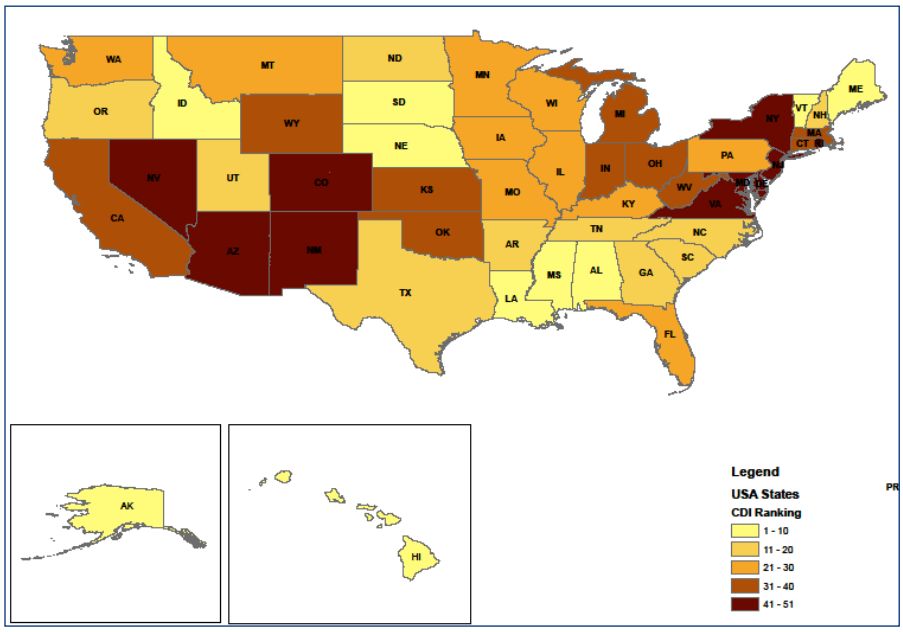
Although the CDC uses a regression model to risk-adjust the Hospital Compare data based on numerous factors, including hospital bed size, medical school affiliation, admission prevalence rate of community-onset *C. difficile* LabID events, and the test type used to detect *C. difficile* in stool,[9] HCUP does not adjust for the diagnostic test type and it is important to note that the various tests have differing sensitivities. Possibly unlike any other states, 100%

of RI hospitals currently use the most sensitive CDI diagnostic testing method, nucleic acid amplification test (NAAT) testing.[13] Ten of 11 hospitals in RI switched to NAAT from other test types over the past few years and, if these changes occurred more rapidly and uniformly than in other states, this may partially account for some of the difference in rates of CDI or *C. difficile* LabID events in RI compared to other states or national benchmark data. Although the CDC risk adjusts for diagnostic test method used, it is unclear if this is robust enough to address what is likely a statewide difference from other states or to account for facilities' changes in tests over time.

We note several additional limitations. First, HCUP uses administrative data that is collected for billing purposes and may not accurately measure HAIs.[14] Second, HCUP data cannot distinguish community-onset CDI from hospital-onset CDI, so we are unable to attribute infections to hospital care. Third, HCUP data for CDI are limited to 37 states and some states are missing data for one or more years. There is no CDI data for CT, precluding us from comparing RI against both adjacent states (MA and CT); ME does not have data for 2004 and 2005; and NH does not have data for 2002 and 2010-2012. Finally, we have only a single quarter of Hospital Compare data (Q1 2013) and are therefore unable to assess longitudinal trends or to compare CDI and *C. difficile* LabID estimates for the same time period.

These findings highlight the need to focus additional financial and human resources on reducing CDI. Although wearing gowns and gloves when entering the room of a patient with CDI and rigorous environmental cleaning of their room can decrease *C. difficile* transmission by 20%,[4] such interventions require sufficient staffing (e.g., to perform rigorous daily and discharging cleaning) and, in some cases, costly adjunctive measures (e.g., the use of portable robotic ultraviolet lights and hydrogen peroxide vapor to disinfect rooms when terminally cleaned). In RI hospitals, infection preventionists are now responsible not only for providing education and leading multi-disciplinary interventions across the hospital, but also for conducting surveillance and reporting results to the CDC and elsewhere. Additional resources may help to improve our state's *C. difficile* performance relative to past trends and our peers.

Figure 3. States Ranked by Standardized Incidence Ratio (SIR) of *Clostridium difficile* LabID Events, First Quarter of 2013.



Note: Data from Hospital Compare Website (https://data.medicare.gov/)

Table 1. Hospital *Clostridium difficile* LabID Events in New England States, First Quarter of 2013

State	Observed Cases	Predicted Cases	SIR	95% CI	Rank
Vermont	23	37.4	0.614	0.389-0.922	4
Maine	65	97.8	0.665	0.513-0.847	7
New Hampshire	77	94.6	0.814	0.642-1.017	16
Massachusetts	693	640.0	1.083	1.004-1.167	38
Connecticut	397	356.9	1.100	0.994-1.213	40
Rhode Island	170	125.2	1.358	1.162-1.578	51

SIR, standardized incidence ratio; CI, confidence interval.
Note: Data from Hospital Compare Website (https://data.medicare.gov/)

Acknowledgements

We would like to express our particular thanks to Steve Sawyer, Rhode Island Department of Health, for his GIS technical assistance.

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Disclosure

The authors have no financial interests to disclose.

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Using the Rhode Island Prescription Drug Monitoring Program (PMP)

JAMES V. MCDONALD, MD, MPH

Prescription drug abuse is an epidemic that will not be controlled without a well-coordinated effort. Prescribers in Rhode Island can contribute substantively to this effort by using the Rhode Island Prescription Drug Monitoring Program ("PMP") consistently. The PMP is a simple on-line tool that helps prescribers monitor patient-prescription histories. Every prescription filled in the state is input to the PMP system within seven days of filling (and the average lag is less).

Why use the PMP? In the words of an old axiom from medical school, "It's what you don't know you don't know that will hurt you" – and your patients. I work with physicians every day who are genuinely surprised by the patient-prescription histories they review in the PMP. Consider. In the year 2013, 1,394 Rhode Island residents used five or more pharmacies to fill prescriptions from five or more prescribers. Are at least *some* of these people diverting prescription drugs from their intended purposes? Yes, of course. Did *you* unknowingly write prescriptions for any of these people? Possibly. Using the PMP helps you avoid this problem. Less ominously, but also of potentially great concern, are those patients who do not inform you of prescriptions written for reasons unconnected with the care *you* provide. For example, a patient taking a benzodiazepine for anxiety may forget to mention this fact when being seen for severe pain following a serious injury – pain for which you would normally (and appropriately) prescribe an opioid. Does the benzodiazepine prescription matter? Of course. Using the PMP helps you avoid potentially dangerous prescribing conflicts such as this.

REGISTERING

Registering to use the PMP is simple. Go to RIPMP.com, where you will be directed to a log-in screen to register. You will need your DEA number. You will be asked why you wish to register. You do not need a detailed reason. A phrase such as "direct patient care" will suffice.

GENERATING A PATIENT REPORT

Once you have a user name and password, you are ready to log into the system. To see a patient report, generate a "New Request." (This is something you will do often, ideally before you write any and every prescription for a controlled substance.) Enter the patient's last name, first name, and date of birth. (It is important to enter the last name completely and to spell it correctly. It is also important to enter the correct date of birth.) After you have entered this information, click "Create," and when the report is generated, verify that it is the report of your patient, and not the report of a patient of the same name, recalling how easy it is to mis-enter a date of birth.

I work with physicians every day who are genuinely surprised by the patient-prescription histories they review in the PMP.

REVIEWING A PATIENT REPORT

In the vast majority of cases, when you review a patient's report, you will find few surprises. Prescription records will match your prescribing, with an occasional prescription the patient has neglected (or thoroughly forgotten) to report.

Yet, prescribers who use the PMP do find surprises! People who divert prescription drugs may be quite devious, using several addresses and several pharmacies. Other than these signs, look for prescriptions that have been filled early.

The PMP is also useful for conducting simple reviews of the safety of a drug regimen. For example, a patient may be taking several medications containing acetaminophen. The PMP may be used as a handy summary to compute the usual daily dose of acetaminophen, looking for potentially toxic levels.

ADDRESSING PROBLEM BEHAVIOR

Once you begin using the PMP, you will eventually see patients whose PMP reports raise substantial questions, leading to potentially awkward moments in the exam room. Difficult questions will need to be asked, but of course, the sooner the correct diagnosis is made, the better. You may uncover addiction, pseudo-addiction, under-treated pain, tolerance, opioid-induced hyperalgesia, and many other treatable problems.

You may also suspect prescription diversion. In this case, you must avoid jumping to conclusions, on the one hand, and gullibility, on the other, but you *must* talk about it with the patient. The issue at stake is whether or not to dismiss the patient without tapering the medication(s) in question. *Proceed as you would with any other medical problem*. Take a good history. Create a differential diagnosis. Work it through. Sometimes, the correct course of action is to

summarily dismiss a patient without any taper of medications, keeping in mind that patients who divert prescription medications may also be seriously addicted to a variety of substances, some prescribed, some not. Nonetheless, if you conclude that a patient is diverting medications, dismissal *is* justified, *especially* because *knowingly giving medication to someone who is diverting prescription medications is unprofessional conduct*.

TAPERING A PRESCRIPTION

In any case, if you decide to taper a prescription medication, do so over two to four weeks to avoid withdrawal. Decrease the dose by one-third every three days. In the case of long-acting medications, decrease the dose by one-third every five to seven days.

Then refer the patient to addiction treatment.

ADDRESSING PRESSURE FROM THE PATIENT TO PRESCRIBE

There is no place for bullying or violence in a therapeutic relationship. Address this forthrightly with a patient if you feel pressured to prescribe. Advise the patient that you cannot be pressured. If the patient persists, talk to your employer and colleagues about the situation. It should never be kept a secret. If law enforcement is needed, call them. Protect yourself, while remaining professional.

IDENTITY THEFT

As you make use of the PMP, you may see prescriptions in your name that you did not write. *Contact law enforcement immediately*. The State Police and the Drug Enforcement Agency (DEA) conduct this type of investigation; local enforcement can coordinate.

It is not uncommon for office staff to call in prescriptions without the prescribers' knowledge. Controlled substances have a high street value and are subject to diversion. *Do not let staff call in controlled substances.*

YOUR PRESCRIBING PRACTICES

You may wish to brush up on your prescribing practices. Many resources are currently available online. Consider, for example, http://www.scopeofpain.com.

PMP USER'S GUIDE

A user's guide to the Rhode Island PMP, covering all of the above in greater detail and including detailed examples of patient histories, is available online:
http://www.health.ri.gov/publications/guides/HowToUseThePMP.pdf

LIMITATIONS

Ideally, the PMP would contain information on *all* prescriptions dispensed for every patient, but currently, its scope is limited to prescriptions dispensed by pharmacies located in Rhode Island and by mail-order pharmacies licensed to do business in the state. Information on prescriptions dispensed by other out-of-state pharmacies and from Veterans Administration (V.A.) or military pharmacies is not available at this time. Being cognizant of these limitations, it is prudent to ask patients about the use of pharmacies not covered by the PMP, especially in the case of patients who have moved into the state recently or who have been recently deployed out of state by the military (or another employer).

Author

James V. McDonald, MD, MPH, is Chief Administrative Officer of the Board of Medical Licensure & Discipline of the State of Rhode Island.

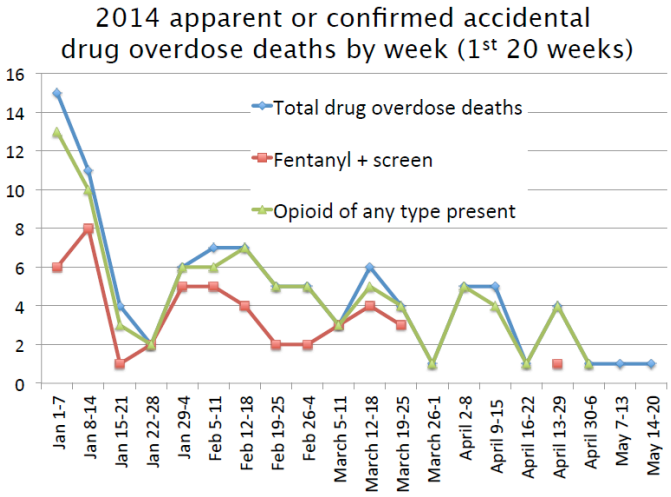
Enhanced Surveillance for Opioid Overdose in Rhode Island

[REPORTED BY STAFF OF THE RHODE ISLAND DEPARTMENT OF HEALTH]

Currently, Rhode Island is experiencing an epidemic of opioid overdosing. As with any complex social phenomenon, the epidemic has multiple causes, some known and some unknown. Clearly, opioids from multiple sources are plentiful. Clearly, recreational opioid use has become popular across social strata. And clearly, today's common street mixes, such as heroin and fentanyl, are very powerful and have contributed to overdose deaths. Far less clear is what drives these trends. Nonetheless, Public Health must respond, and response begins with comprehensive assessment of the problem. Therefore, the Rhode Island Department of Health (HEALTH) has enhanced its real-time surveillance of opioid overdosing in three ways.

DEATH INVESTIGATIONS

The Rhode Island Office of the State Medical Examiners is paying particularly close attention to all deaths caused by apparent overdoses, focusing on *motive* (intentional or unintentional), *type and combination of drugs* (prescription drugs vs. street drugs), *source of manufacture* (licit vs. illicit, as in the case of fentanyl), *social characteristics of the victim* (gender, age, race, ethnicity, etc.), and *comorbidities* (pain, mental problems, health problems). After careful evaluation, data thus developed are plotted to monitor trends in overdose deaths by type, as illustrated by the following example.



Since January 1, 2014 the Rhode Island Office of the State Medical Examiners has investigated 94 apparent accidental drug overdose deaths (74 confirmed, 20 under investigation). Most of the deceased were men (68/94 or 72%) and most were white (85/94 or 90%). Of the 74 *confirmed* accidental overdose deaths, the following drug involvement has been established:

- 13/74 (18%) only pharmaceutical drugs
- 43/74 (58%) only illicit drugs
- 18/74 (24%) both pharmaceutical and illicit drugs
- 68/74 (92%) some opiate or opioid
- 41/74 (55%) fentanyl

EMERGENCY DEPARTMENT VISITS

Second, HEALTH has asked hospital-based emergency departments in the state to report all overdose events (daily), using a newly developed "Opioid Overdose Case Report Form for Poisoning or Suspected Poisoning by Opioids" which collects information on the *patient* (gender, age, ethnicity, race, municipality of residence), the *event* (location, single or multiple overdose incidents at the scene of the poisoning), the *response* (Naxolone (opioid antagonist) given? where? by whom?), the *principal diagnosis*, and the *outcome* (recovery or death). In the first month of reporting (April 2014), about 50 episodes of opioid poisoning or suspected poisoning were reported. The ages of victims ranged from 19 to 72 years with a mean of 37 years. Most of the victims (69%) were men. Naxolone was administered in 85% of the episodes.

AMBULANCE RUNS

Third, HEALTH has added four questions about Naxolone use to its "Emergency Medical Service Ambulance Run Report," as follows:

- Was Naxolone (Narcan) administered *prior to the arrival* of EMS?
- If yes, who administered Naxolone (Narcan)?
- How was it administered?
- What was the dosage administered?

These questions have been incorporated in the Run Report form for about one month at the time of this writing. Thus far, no reports of Naxolone administration *prior to the arrival* of EMS have been received.

These three enhancements in public health surveillance will increase our understanding of the deadly opioid abuse problem in Rhode Island. Based on coordinated, comprehensive, and carefully monitored data from autopsies, emergency department visits, and ambulance runs – in addition to data extracted from an array of standard surveillance systems – HEALTH is well-equipped to formulate public health policies for the prevention and control of opioid abuse and its sequelae.

VITAL STATISTICS
MICHAEL FINE, MD
DIRECTOR, RHODE ISLAND DEPARTMENT OF HEALTH
COMPILED BY COLLEEN A. FONTANA, STATE REGISTRAR

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

	REPORTING PERIOD		
VITAL EVENTS	DECEMBER 2013	12 MONTHS ENDING WITH DECEMBER 2013	
	Number	Number	Rates
Live Births	871	11,505	10.9*
Deaths	875	9,973	9.5*
Infant Deaths	9	83	7.2#
Neonatal Deaths	6	58	5.0#
Marriages	382	6,521	6.2*
Divorces	303	3,308	3.1*
Induced Terminations	No data available		
Spontaneous Fetal Deaths	No data available		
Under 20 weeks gestation	No data available		
20+ weeks gestation	No data available		

* Rates per 1,000 estimated poulation
# Rates per 1,000 live births

	REPORTING PERIOD			
Underlying Cause of Death Category	JUNE 2013	12 MONTHS ENDING WITH JUNE 2013		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	172	2,431	230.8	3,354.5
Malignant Neoplasms	179	2,235	212.2	5,945.0
Cerebrovascular Disease	32	429	40.7	627.0
Injuries (Accident/Suicide/Homicide)	32	632	60.0	9,236.5
COPD	28	508	48.2	512.5

(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 1,052,567 (www.census.gov)
(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.

Jaime Rampone from the Lincoln Central Elementary School is the 2014 winner of annual Tar Wars Poster Contest. She received an all-expenses paid trip to the national competition in Washington, DC. Held annually since 1993, the Rhode Island Academy of Family Physicians, the Rhode Island Chapter of the American Academy of Pediatrics and the Rhode Island Medical Society have cooperated to bring the national Tar Wars® anti-smoking educational program to fifth-graders in Rhode Island.

Volunteers and participants at the 2014 bike helmet distribution at the Mary Fogarty School in Providence. Vouchers for the helmets are distributed to RIteCare families in the state, along with bike safety material and other items donated by the RIMS Foundation.

At the Rhode Island Medical Society's Eleventh Hour Education Event held on May 17, participants included, from left, **Steve DeToy**, RIMS Director of Government Affairs; **Russell Settipane, MD**, program chair; **Kelly I. McGee, Esq.**, who participated in the panel discussion on medical marijuana; **Megan Turcotte**, RIMS Director of Member Services; and **Todd Handel, MD**, a panelist who specializes in interventional pain management and sports medicine.

Attendees listened to panelists discuss issues related to pain management, medical marijuana, and also heard updates from the leadership of RIMS.

Robin Webster, MHA, BSN, RN, a clinical risk management consultant at Coverys, spoke on her areas of expertise.

Afreen Siddiqui, MD, pain management speaker, answering questions from the audience. She is president of the RI Society of Anesthesiologists and Director of Interventional Pain Management at the Providence VA Medical Center.

Working for You: RIMS advocacy activities

May 1, Thursday

Legislative hearings, State House

Dr. Migliori and Mr. DeToy meet with the Speaker of the House regarding economic impact study.

Retirement party for HARI President

Chairman Keable fundraiser

Reach Out and Read RI Annual Gala

May 2, Friday

Tobacco Free Rhode Island conference call

NE Delegation to the AMA meeting, Meredith, NH; Drs. Hollmann, Adrain, and RIMS staff attending

May 3, Saturday

NE Delegation to the AMA meeting, Meredith, NH; Drs. Hollmann, Adrain, and RIMS staff attending

May 5, Monday

Meeting with Chairman Miller regarding RIMS legislation

Executive Committee Meeting

May 6, Tuesday

RIMS Physician Health Committee (Herbert Rakatansky, MD, Chair)

Meeting of interested parties regarding DOH proposed pain regulations

Meeting with Chairman Miller regarding general health care legislation

Legislative hearings, State House

Health care professionals fundraiser, co-host Peter Karczmar, MD, on behalf of Providence mayoral candidate Brett Smiley

May 7, Wednesday

Legislative hearings, State House

RI State Nurses Association awards dinner honoring RIMS members Sen. Christopher Ottiano, MD, and James Carney, PA-C.

May 8, Thursday

US Attorney's office planning committee June 7 CME Event

New England MGMA annual conference, Newport; RIMS-IBC staff attending

RI Chapter American College of Physicians annual conference; RIMS staff attending and staffing exhibit table

Legislative hearings, State House

Rep. Frank Ferri fundraiser

May 9, Friday

Tobacco Free RI conference call

May 10, Saturday

RIMS annual bike helmet giveaway; Jim Carney, PA-C, Kristin Carney, PA-C, WAMS member students, and RIMS staff attending

Annual Tar Wars poster contest - Art Frazzano, MD, Chair; RIMS President Elaine Jones, MD, celebrity judge; and RIMS staff attending

May 12, Monday

Rep. Malik fundraiser

May 13, Tuesday

Health Services Council

AMA State Litigation conference call; Newell Warde, Chairman

Legislative hearings, State House

Brown University Health Council

May 14, Wednesday

Board of Medical Licensure and Discipline Meeting

Legislative hearings, State House

Chairman Gallison fundraiser

Rep. Cimini fundraiser

Rep. Tanzi fundraiser

Rep. Ajello fundraiser

May 15, Thursday

Legislative hearings, State House

Felice Freyer farewell event

Sen. Lombardi fundraiser

Speaker Mattiello fundraiser

May 16, Friday

Meeting with Neighborhood Health Plan

May 17, Saturday

Eleventh Hour CME event; RIMS Vice President Russ Settipane, MD, Moderator, RIMS and RIMS-IBC staff attending

May 19, Monday

Lobbyists meeting

RIQI monthly update, RIMS staff

AMA Advocacy Resource Center conference call

Chairman Shekarchi fundraiser

Sen. Ottiano fundraiser

May 20, Tuesday

Chronic Care Sustainability Initiative (CSI) Annual Meeting

Meeting with Health Care Lobbyists to discuss proposed DOH opioid prescribing regulations

Tobacco Free RI Coalition meeting with Speaker

Legislative hearings, State House

May 21, Wednesday

DOH Primary Care Physicians Advisory Committee meeting

Meeting with Lt. Governor's staff regarding AHSRI

Worker's Comp Advisory Committee meeting

Legislative hearings, State House

May 22, Thursday

Lt. Governor's LGBT Listening Session

Tobacco Free RI advocacy day

Legislative hearings, State House

Rep. Guthrie fundraiser

Rep. Amore fundraiser

May 23, Friday

WAMS Awards Day, RIMS staff attending

DOH Health Professional Student Loan Program executive committee meeting

May 24, Saturday

Stanley Aronson Event at WAMS, RIMS staff attending

May 27, Tuesday

DOH public hearing regarding proposed controlled substances prescribing regulations

Meeting with Dr. Fine, Dr. Jones, Dr. Karczmar, and RIMS staff

Legislative hearings, State House

Rep. Bennett fundraiser

May 28, Wednesday

RIMS Membership Committee meeting

Legislative hearings, State House

Rep. Abney fundraiser

May 29, Thursday

Johnson & Wales University Physician Assistant program building dedication, RIMS staff attending

RI Prescription Drug Abuse Collaborative, RIMS staff attending

Legislative hearings, State House

May 30, Friday

TFRI conference call

Why You Should Join the Rhode Island Medical Society

The Rhode Island Medical Society delivers valuable member benefits that help physicians, residents, medical students, physican-assistants, and retired practitioners every single day. As a member, you can take an active role in shaping a better health care future.

RIMS offers discounts for group membership, spouses, military, and those beginning their practices. Medical students can join for free.

Above: State House press conference on health care, Brown MSS at the AMA, CPT update seminar, bike helmet distribution, medical student volunteers; Upper right: Meeting of RIMS membership committee

APPLY FOR MEMBERSHIP ONLINE

RIMS MEMBERSHIP BENEFITS INCLUDE:

Career management resources

Insurance, medical banking, document shredding, and independent practice association

Powerful advocacy at every level

Advantages include representation, advocacy, leadership opportunities, and referrals

Complimentary subscriptions

Publications include *Rhode Island Medical Journal*, *Rhode Island Medical News*, annual *Directory of Members;* RIMS members have library privileges at Brown University

Member Portal on www.rimed.org

Password access to pay dues, access contact information for colleagues and RIMS leadership, RSVP to RIMS events, and share your thoughts with colleagues and RIMS

SPECIAL NOTICE: 2014 AMA DUES PAYMENTS

The American Medical Association (AMA) will direct bill its Rhode Island members for their 2014 dues. Beginning August 2013, AMA members will receive a separate dues statement from the AMA instead of paying AMA membership dues through the Rhode Island Medical Society (RIMS) membership invoice. This is simply an operational change so that both RIMS and AMA can concentrate on their respective member satisfaction. There remains no requirement for RIMS members to join the AMA.

Please let us know if you have questions concerning this change by emailing Megan Turcotte or phoning 401-331-3207.

JWU Opens State's First Physician Assistant Program

BY MARY KORR
RIMJ MANAGING EDITOR

PROVIDENCE – Johnson & Wales University has added another 'White Coat' to its experiential programs with the grand opening of the first Center for Physician Assistant Studies Program in Rhode Island on May 29.

The 24 inaugural students, selected from an applicant pool of nearly 1,000, took visitors on a tour of the former jewelry facility at 35 Claverick Street, several blocks from one of the program's partners, the Alpert Medical School. Their future is as bright as the white coats they donned for the first time last week.

During his welcoming remarks, **GEORGE BOTTOMLEY, DVM, PA-C**, program director, said the university's preliminary study into launching the program predicted a robust 10-year job growth rate in the PA field, with a median starting salary of $93,000.

The 24-month program, with a year of classroom/laboratory studies followed by a clinical year, culminates in a master of science degree in physician assistant studies. The Accreditation Review Commission on Education for the Physician Assistant, Inc. (ARC-PA) has granted Accreditation-Provisional status.

Dr. Bottomley, who returned to his native Rhode Island to found the program, noted having a relationship with a medical school is an essential partnership to the program. "All of our students will benefit from the interdisciplinary opportunities," he said.

He and the PA program faculty and staff have been working closely with Alpert's Dean Jack Elias, Associate Dean Allan Tunkel and Associate Dean for Academic Affairs, Dr. Michele G. Cyr. At the inaugural ceremony she quoted an African proverb which, she said, "aptly captures the spirit of the partnership that our schools have forged. 'If you want to go fast, go alone. If you want to go far, go together.'

"All of the opportunities we create for our students to work side by side will lay the groundwork for them to work together as a team in their careers. Together they will provide the best care for patients and populations. Alone, they might go faster but together they will go farther," she said.

JWU's Providence Campus President Mim L. Runey, LP.D, said the mission of the Center is to educate students

PHOTOS BY MARY KORR

Center Director George Bottomley, DVM, PA-C, cuts the blue ribbon on the first Center for Physician Assistant Studies in Rhode Island on May 29. The former jewelry manufacturing plant comprises 18,000 square feet and cost a total of $13.3 million for building, land, design and construction.

Gov. Lincoln Chafee spoke at the opening ceremony and noted Johnson & Wales University's Centennial this year. The Center expands his concept of a "meds and eds" revitalization occurring in the former Jewelry District, now the Knowledge District, of downtown Providence.

Administration/Faculty

George Bottomley, DVM, PA-C
program director

Anthony Mega, MD
medical director

Rebecca Scott, PA-C, PhD
assoc. professor, senior academic coordinator

Andrew Mackie, PA-C, MPAS
assist. professor, academic coordinator

Allison Jackson, PA-C
asst. professor, clinical coordinator

Thomas P. Meehan, PA-C
assist. professor

Katie Spoidoro
admissions coordinator

Speakers at the opening ceremony listen to Center Director George Bottomley's welcoming remarks. From left are Chancellor John J. Bowen, Gov. Lincoln Chafee, Campus President Mim L. Runey, Dr. Michele G. Cyr, Associate Dean for Academic Affairs at the Alpert Medical School, and Marie Ghazal, Chief Executive Officer of the Rhode Island Free Clinic.

Krista Murphy, in front, spoke at the welcoming ceremony on behalf of her fellow PA students. She said the inaugural class would build the cornerstone of the Center's mission to educate collaborative practitioners embodying humanistic medicine.

to become "collaborative practitioners with the respect, empathy and trust inherent to patient-centered, humanistic health care."

It was an emotional day for JWU Chancellor John J. Bowen '77, who described himself as the son of a factory worker, and then recalled the jewelry workers who worked here when the building opened in 1948. "Their lives never got any better. It is very symbolic to take this old dilapidated building and bring new life into it and transform it. What will really make the reputation of this program are the students we educate here to help others."

Maria Ghazal, RN, chief executive officer of the Rhode Island Free Clinic, spoke at the welcoming ceremony and described the clinic as a place which "provides a medical home for those who don't have any other options in the state."

She put faces on the populations the clinic serves: "Adults who now have insurance but can't get an appointment for 6 months. Our diverse populations have difficulties understanding the present health care system and how to access it. This program will help our state in so many meaningful ways. We cannot do this work alone; it takes partnerships with academia, business, and other healthcare organizations."

The free clinic will be a placement site for students where clinic physicians have readily volunteered to serve as preceptors.

Inside the temperature-cooled anatomy lab, half a dozen students showed visitors the state-of-the-art equipment at each station. They pondered their first lab experience in the room a few days hence with excitement and a bit of trepidation, and then moved on to show visitors the brightly-colored student lounge and locker rooms.

And for the university it is a beginning as well; JWU plans a further expansion into the health sciences as part of its five-year strategic plan. ❖

Former hospital lab technician and new PA student Andrew Rowles explains the technology in the Clinical Skills Lab, which replicates a hospital ED room or physician's exam room.

Students in the Gross Anatomy Lab which feature e-study guides at each station and screens which can project close-ups during instruction.

PHOTOS BY MARY KORR

Robert Petrie checks assays being analyzed on the state-of-the-art High Speed Connected Automation (HSCA) system in Miriam's core biochemistry lab.

New System Vaults Lifespan's Core Laboratory into Future

Only second in nation, fourth in world, installed at Miriam Hospital

MARY KORR
RIMJ MANAGING EDITOR

PROVIDENCE – One physician viewing the High Speed Connected Automation (HSCA) system for the first time in The Miriam Hospital's core biochemistry laboratory likened it to a million-dollar Lionel train set. Hundreds of test tubes travel the four-lane track, which stretches 70 feet into the lab, in all directions. "This is futuristic and will take the lab through another decade," said **DAVID MORRIS, PhD**, Director of Clinical Biochemistry for Lifespan's Pathology Laboratories.

The approximately $3.8 million Beckman Coulter system went live in February – after ramping up for months not only at Miriam, but also at Rhode Island Hospital and Newport Hospital. Those systems had to be retrofitted and required the technologists to do yeoman's work – manually centrifuging, for example, for several months. One Miriam technologist said it was like going back to the Dark Ages of testing.

So far the transition has been seamless, with only a few minor glitches. Since it is only the second HSCA system in the nation, and the fourth in the world, the lab is expected be a showplace for those interested in viewing the cutting-edge system in operation. Laboratorium experts from across the country are expected to visit Providence and see the Lifespan HSCA line.

DOUGLAS ANTHONY, MD, PhD, Lifespan's Chief of Pathology and Laboratory Medicine, compared the system's capabilities to a superhighway. "There's even a passing lane," he noted. "Think of 1-95 North to Boston at 5 p.m. We used to have to handle samples from the emergency rooms or the ICUs manually. Now, we have the HOV (high-occupancy vehicle or carpool) lanes to bypass routine testing samples."

In addition to a dedicated STAT input area, there is a centrifuge bypass lane for tubes which have been pre-spun.

Dr. Anthony said because of the volume of testing the laboratory performs – perhaps as much as half of the tests done in the state – there were 'traffic' jams on the previous two-track system, which reached the end of its life after more than a dozen years of service.

The lab begins to hum with activity in the afternoon, as couriers arrive from 50 service centers, hospital laboratories and physicians' offices throughout the state and southeastern Massachusetts with specimens for testing. A pneumatic tube deposits the in-hospital samples. The average is 2,000-2500 samples tested daily.

Each sample has been barcoded when the sample was obtained. The sample vacutainer tubes have specific cap colors to validate required sample type against test ordered, are automatically loaded into instrument-specific racks, prioritized and queued for testing. Barcode readers double-check the sample identity and analysis requested multiple times, minimizing any chance for error.

The HSCA tube holders are equipped with radio frequency identification technology (RFID) chips to track the location of each sample in real time, verifying the sample's location with the patient's computerized record, and directing them along the tracks to one or more of the four analyzers and two

Robotic arms and pipette fingers inside the system.

centrifuges that are connected to the Automation Line. The read-through labels (RTLs) allow volume detection through three layers of labels.

The whole line is powered by compressed air; tiny air valves produce bursts of pneumatic air to propel the tubes north, east, south and west and into inlets for analysis. The unit features a consolidation of testing disciplines – chemistry, immunochemistry and immunology.

The new system has expanded capacity; for example, a chemistry analyzer can handle 1,200 tubes per hour. Dr. Morris estimates a 25 percent quicker turnaround time; all assays requested are usually completed within 30 minutes. Normal tests are reported instantly to the physician's office via direct computer interfaces.

He stops at the aliquotter unit to illustrate the preciseness and intelligence of the robotic components. Robotic "fingers" pick up the primary tube sample; the computer calculates how much serum or plasma is available to make "daughter" tubes, and once that is determined, it moves it on to an adjacent unit.

Here, pipette tips on the two robotic arms transfer serum from the primary to the secondary tubes, printers label the daughter aliquots with identification and barcodes, and then robotic arms direct them to an outlet and towards analyzers or for storage. "This is 100 percent accurate. There is no contamination. No hands touch it," Dr. Morris said.

The "command center" operator monitors the entire process on three computer screens. All testing is auto-verified, Dr. Morris said. For example, "If there's a potassium below 3 or critical values, the analysis is repeated instantly," he said.

At the end of the line is a pair of computer-controlled car parks or stockyards, which are refrigerated units that hold 5,400 tubes each on four levels for automated storage, instant retrieval if additional or repeat tests are required, and subsequent disposal.

The HSCA offers "standardization across the systems," said Dr. Anthony. "So it doesn't matter if your patient is seen in Newport, Rhode Island Hospital or here at The Miriam. All of the information is available in one format and is consistent."

In addition to streamlining workflow, increasing capacity while decreasing turnaround time, Dr. Anthony sees another advantage to the system. "It reduces the incremental costs to add on a research study since it doesn't take a lot of extra time to set it up." It has allowed the Laboratory to insource millions of tests per year creating job opportunities for Rhode Islanders.

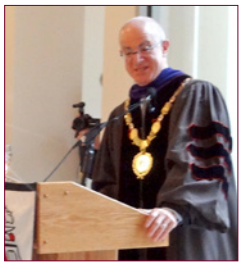
"It's a brilliant system," reflected Dr. Morris. "If you can't make it work, it's you and not the system." ❖

The so-called refrigerated and automated stockyard stores 5,400 samples. There are two in operation at Miriam's lab.

Brown Honors Dr. Aronson, Founding Medical School Dean, with $3M Endowed Fund

MARY KORR
RIMJ MANAGING EDITOR

Alpert Medical School Dean Jack A. Elias, MD, greets those attending the ceremony to announce the formation of an endowed fund to honor Stanley M. Aronson, MD, the school's founding dean.



Brown Chancellor Thomas J. Tisch formally announced the Dean Stanley M. Aronson Fund for Research and Innovation during commencement weekend.

PHOTOS BY MARY KORR

PROVIDENCE – In formal regalia, Brown Chancellor Thomas J. Tisch formally announced the Dean Stanley M. Aronson Fund for Research and Innovation on Saturday, May 24, during a reception and ceremony at the Warren Alpert Medical School to honor the school's founding dean.

"Dr. Aronson is an adored giant in the worlds of medicine and medical education – and also in the life of Brown and Rhode Island," Tisch, a Brown alumnus, said. "To have this important fund named in his honor is a wonderful and fitting tribute."

The fund is endowed with $3 million. Proceeds will allow the medical dean to make strategic investments in faculty, educational programs, and research facilities that would not otherwise be possible.

"Every dean builds on the work of previous deans," said Dr. Jack A. Elias, dean of medicine and biological sciences at Brown, "but Stanley Aronson was asked to build a medical school from the ground up. Nothing compares to that."

The event was attended by Dr. Aronson's family, friends, supporters, colleagues and former students during his tenure; many of whom reminisced about visiting Dr. Aronson's farm in Rehoboth where he nurtured a seedling from the Tree of Hippocrates in Greece, and which now stands tall in front of the Arnold Laboratory. They recalled the gift of his mentorship, his boundless love of learning, and his work ethic which inspired them. Others recalled the resonance of his deep, eloquent voice and his tall presence, matched with great warmth, empathy, and admonishment to call him anytime if they were struggling or had a particular problem. To many, he was a father-figure.

Dean Emeritus Stanley M. Aronson, MD, celebrates with Jack A. Elias, MD, dean of medicine and biological sciences at Brown, and Allan Tunkel, MD, associate dean.

Dr. Aronson beamed as he greeted guests, among whom were several of his successors to the deanship. During his brief remarks, he paid homage to them and noted that there were several deans in medical schools nationwide who graduated from Brown's medical school.

He said he was pleased that Dr. Elias and future deans will have a significant additional resource to meet the needs of students and those who will benefit from their training. "This is a wonderful thing that will give him a wider range of creativity in research, teaching, and certainly in the care of the sick in Rhode Island," Dr. Aronson said.

The endowed fund certainly was a timely gift. The event was capped with a chorus of Happy Birthday, as the ever-humble nonagenarian prepared to reach another milestone several days after the ceremony. ❖

Brown University Oncology Research Group Celebrates 20th Anniversary

DAVID ORENSTEIN
BROWN UNIVERSITY SCIENCE NEWS OFFICER

PROVIDENCE – For 20 years, The Brown University Oncology Research Group (BrUOG) has provided the administrative and financial infrastructure for Rhode Island cancer specialists to develop and test their best ideas for fighting the disease in its many forms.

In 1994, none of Rhode Island's hospitals was big enough to sustain even small cancer trials, said **DR. HOWARD SAFRAN**, BrUOG's medical director, a Brown professor of medicine, and a Lifespan physician.

"To be successful, you have to have enough patients to complete your study," Dr. Safran said. "So we thought that if all the hospitals got together – this was before Lifespan or any mergers – we thought collectively we could compete [with other cancer centers]. We looked at Brown as a neutral ground and so we put our central office at Brown and all the hospitals decided they would be part of it."

COURTESY OF BROWN UNIVERSITY/KAYLA ROSATI

Dr. Howard Safran is the medical director of BrUOG.

The first trial that put BrUOG on the map was a study led by BrUOG founder **DR. HAK CHOY**, a former Brown professor, who showed that the ovarian and breast cancer drug paclitaxel also made radiation more effective in treating lung cancer.

"That work has really been enduring," Dr. Safran said. "That work has become the standard of care that is still used around the world."

Further BrUOG studies, led by Dr. Safran, extended it to esophageal and stomach cancer. He and his colleagues have also made other advances against esophageal cancer by trying out a drug called trastuzumab, which had shown some efficacy in breast cancers associated with a genetic mutation called HER2.

When BrUOG researchers discovered that HER2 was also found in esophageal cancer, they designed a trial combining trastuzumab with taxol and radiation.

"We treated 19 Rhode Islanders and we thought it worked terrifically," Dr. Safran said. Seven years later the idea gained further support in a much larger study in Asia and Europe. And now there's a major national study in the United States.

"That work is based on a Brown study," Dr. Safran said.

Dozens of doctors, thousands patients

Over the years BrUOG has involved dozens of local doctors, working with a wide range of experimental treatments for cancers all over the body. Twenty years into the effort, they have treated roughly 3,000 Rhode Island patients in scores of small "phase I" or "phase II" trials. They collaborate with similar groups around the country as well.

Rhode Island Hospital radiation oncologist **DR. JAROSLAW HEPEL**, assistant professor of radiation oncology in the Alpert Medical School, said BrUOG provides many "indispensible" advantages, starting with the statewide community of colleagues it brings together. At regular meetings, surgeons, clinical oncologists, and medical oncologists all discuss current trials and new ideas and protocols.

Meanwhile, with a staff of two, BrUOG not only helps finance trials but also supports them logistically with the needed regulatory filings, data

Farrah Fawcett Foundation Awards BrUOG $50,000 Grant

In April, The Farrah Fawcett Foundation (FFF) presented a $50,000 grant to the Brown University Oncology Research Group (BrUOG) for "BrUOG 276: A Phase II Evaluation of ADXS11-001, Mitomycin, 5-fluorouracil (5-FU) and IMRT for Anal Cancer."

The study is investigating whether the addition of the immunotherapy drug, ADXS11-001 can be tolerated and if it will increase response rates when added to the standard care treatment of chemotherapy and radiation. While almost all anal cancers are HPV positive, Advaxis's immunotherapy drug "stimulates a person's immune system to assist in the attack of cells made cancerous by HPV," stated Howard Safran, MD, medical director of BrUOG.

After Advaxis showed promise in a Phase II cervical cancer trial, BrUOG is optimistic about the applicability of this treatment regimen in anal cancer.

collection and management, safety monitoring, and other essential functions that safeguard patient care and trial integrity throughout the process.

Dr. Hepel is now leading his second BrUOG-supported trial in which he's studying a noninvasive but precise means of delivering radiation to the site of breast lumpectomies. Rather than delivering radioactive material via catheters or other implants, the technology he's studying, called AccuBoost, essentially zaps the tumors. It's precise because it targets imaging markers left in the surgical area and because the breast is held firmly in place during radiation (but with much less pressure than in a mammogram).

The current trial "BrUOG 291," is meant to assess how patients tolerate a five-session course of treatment that conveniently can be performed in less than a week. Dr. Hepel expects the dose to be as effective as standard care, but he is checking for cosmetic outcomes, skin irritation or other possible side effects.

Meanwhile, **DR. KIMBERLY PEREZ**, assistant professor of medicine and a physician at Rhode Island Hospital and The Miriam Hospital, has been working through BrUOG to understand the underlying genetics of rectal cancer and to develop better treatments. She said the group's support is part of what convinced her to practice in Rhode Island.

"The Brown University Oncology Research Group was a significant factor in my decision to take the job at RIH/TMH Cancer Center," she said. "It has provided me with opportunities to ask critical questions in GI oncology clinical care and develop protocols in which to answer them. As a result it has provided me with the opportunities for growth as a clinical scientist locally and on the national stage in cancer clinical research."

She means that literally. Later this spring she'll speak about some of her BrUOG-supported results at the American Society of Clinical Oncology Conference in Chicago. ❖

Board of Ed OKs RIC/URI Shared Nursing Education Center at South Street Landing

Would become co-tenant with Brown University

PROVIDENCE – At the May 12, 2014 board meeting, the Rhode Island Board of Education unanimously endorsed draft legislation that would enable the University of Rhode Island (URI) and Rhode Island College (RIC) to locate a shared nursing education facility in the former South Street Power Station. The draft legislation will be delivered to the Rhode Island General Assembly for consideration.

As proposed, URI and RIC would occupy approximately 50 percent of the abandoned power station and would be a co-tenant with Brown University, which would occupy the remaining half of the facility for administrative offices. The proposed legislation for the state's investment entails the construction, outfitting and occupancy of approximately 130,000 SF to be shared by the state's two public nursing education programs.

All other components of the $206M development project, including construction of a residential and retail building and construction of a new garage, will be developed and financed privately.

Shared sim centers, labs

The design of the shared nursing education center respects the uniqueness of both programs, which will remain separate, while allowing each program to expand and share state-of-the-art simulation laboratories and equipment, enhancing educational opportunities for students and faculty. The Shared Nursing Education Center will also serve as a focal point for inter-professional education and collaborative research in the area, particularly with its proximity to the Brown University Warren Alpert Medical School and the state's major hospitals.

The legislation mirrors the lease that is currently in final negotiations between the State and Commonwealth Venture Properties (CV), a private developer. A team comprised of members of the Department of Administration, led by Director Richard Licht; the URI and RIC administrations representing each institution's academic, finance and facilities interests; the deans and faculty of the two nursing programs; and the Board of Education have been working on the development of this project over the past ten months.

The submittal of draft legislation is one step in the approval process. The General Assembly must pass legislation enabling the state to enter into the lease.

The final lease must be approved by the Board of Education and the State Properties Committee.

"Simulation laboratories are a critical component of our education strategy, and this project greatly expands the opportunities for integrating technology into the curriculum," said **DEAN JANE WILLIAMS**, Rhode Island College School of Nursing.

"The shared center is an opportunity to enhance the classroom and laboratory teaching for our students at all levels of nursing preparation in a facility with advanced learning environments that will be unique in our region. We are excited about the proximity to the hospitals and peoples with health inequities in the urban core, the Alpert Medical School, and the health and life science research initiatives that hold the potential for fruitful collaborations aimed at tackling some of our state's most pressing health care challenges," said Interim Dean Mary Sullivan, College of Nursing at the University of Rhode Island. ❖

CVS

The proposed MinuteClinics are located in Woonsocket, Cranston, North Smithfield, East Greenwich, Westerly, Providence and Wakefield. They will be staffed by nurse practitioners or physician assistants, who will be under the supervision of a Rhode Island physician.

Health Dept. Issues Conditional CVS Application to Operate MinuteClinics

PROVIDENCE – **MICHAEL D. FINE, MD**, Director of Health, has approved the application of CVS MinuteClinics Diagnostics of Rhode Island, LLC to license seven healthcare facilities in Rhode Island, but with a number of significant conditions attached.

In deciding to approve the license application, and in determining the conditions upon which that approval depends, the Department investigated and considered the effect these services will have on Rhode Islanders' access to primary care, and on the quality of patients' relationships with primary care providers within both the MinuteClinics and primary care practice settings.

In assessing the expediency of conditions of licensure, the state agency addressed concerns regarding (1) potential conflicts and the appearance of conflicts of interest incident to the corporate structure and relationships between pharmacy and prescribers; (2) the potential fragmentation of primary care delivery and effect on the primary care business model; (3) the appropriateness of pediatric care in the MinuteClinic setting, and; (4) patient access for underserved communities.

"Primary care based delivery systems around the nation and around the world create the best population health outcomes at the lowest cost," Dr. Fine said. "Primary care practices have been significantly challenged by the necessity of functioning as businesses in a world in which they have no effective market power, while obligated to meet regulated standards of professional practice, and by their own ethical commitments."

Conditions

The following are among the conditions stipulated by the Health Department which may be subject to revision after review by all pertinent parties:

- Each clinic must maintain a roster of primary care practitioners or community health centers who are currently accepting new patients.
- Only provide care to children 18 months and older; each clinic must be enrolled in Kidsnet to provide vaccination information for minors under the age of 19.
- Treatment limited to three repeat visits for an individual for the same condition or illness.
- Clinic must provide a copy of the visit's medical record to the patient and, with the patient's consent, provide an electronic copy to the patient's primary care provider.
- All prescribers must be enrolled in Currentcare and the Prescription Monitoring Program before prescribing any medications.
- Each clinic must have an Electronic Medical Record that is fully integrated with various EPIC systems utilized by Rhode Island hospitals within 6 months of each of the hospitals going live with EPIC.
- CVS (the applicant) shall freely provide uncompensated care to patients who have been determined eligible for charity care.

Approval of MinuteClinics' request for licensure is contingent upon MinuteClinics' acceptance of the Health Department conditions or a mutually agreeable revised set of conditions.

Full report: http://www.health.ri.gov/news/temp/201405MinuteClinic.pdf

New Law Expands Access to Prescription Monitoring Program

PROVIDENCE – Last week, Gov. Lincoln Chafee signed into law legislation to expand the categories of individuals authorized to access and use the Prescription Monitoring Program database and requiring all practitioners to register with the Department of Health monitoring database as a condition of the initial approval of or renewal of the practitioner's authority to prescribe controlled substances.

The new law takes immediate effect. It will allow other authorized designees of a practitioner or pharmacist to access the database on the practitioner's or pharmacist's behalf, provided the designee is employed by the same professional practice or pharmacy, that that practitioner or pharmacist takes reasonable steps to ensure that such a designee is sufficiently competent to use the database and that the ultimate decision as to whether or not to prescribe or dispense a controlled substance remains with the practitioner or pharmacist.

Under the ongoing DoH monitoring program, prescribers and pharmacies must use the program each time a controlled substance is prescribed and review the database to see if other prescribers have already given a patient a similar medicine or medication that might cause a serious drug reaction.

If a pattern of overuse or over-prescribing is detected, prescribers and pharmacists are encouraged to help stop it; pharmacists, for instance, may refuse to fill a prescription based on a concern of addiction. ❖

State Troopers now Equipped with Narcan

PROVIDENCE – Colonel Steven G. O'Donnell, Superintendent, of the Rhode Island State Police and Commissioner of Public Safety, announced the full deployment of Narcan to members of the Rhode Island State Police. This is in response to the epidemic of drug overdose deaths in Rhode Island this year. Narcan counteracts the effects of opioid overdoses.

The Rhode Island Disaster Medical Assistance Team (DMAT) conducted a training for all sworn members of the Rhode Island State Police on the administration of Narcan, which is delivered by nasal spray. Concurrent with the training, the State Police Planning, Research, and Accreditation Unit, in consultation with other law enforcement agencies, developed a policy for Narcan use and administration. This policy is now serving as a model policy for other state and municipal police departments.

DMAT ordered 300 doses of Narcan for the State Police that they made up into a kit including a tamper evident, sealable carrying case, a single dose of Narcan, a laminated instruction card, gloves, and atomizer to deliver the Narcan nasal spray. The total cost to the State Police for the 300 complete kits is $35.50 per kit. DMAT also assembled the kits at no cost to the State Police. The kits were paid for with federal drug forfeiture funds.

The kits will be distributed as follows: 158 kits to uniformed patrol troopers and 23 kits to detectives. Training will then be held for the Rhode Island Division of Sheriffs, who will receive 55 kits, and the Rhode Island Capitol Police, who will receive 15 kits. At the request of Richmond, Burrillville, and Hopkinton Police, they will receive 15 kits each. The remaining 4 kits will be kept for surplus. ❖

Health Department Reports Number of Babies Born Dependent on Drugs Doubles

Neonatal Abstinence Syndrome rates rising in tandem with drug overdose rates

PROVIDENCE – Rates of Neonatal Abstinence Syndrome have continued to rise in Rhode Island after nearly doubling from 4.4 per 1,000 live births in 2005 to 8.3 per 1,000 live births (90 cases) in 2012. Already in the first quarter of 2014, 26 newborns (11.0 per 1,000* live births) have received the Neonatal Abstinence Syndrome diagnosis. The rising rates are significant in that they parallel the rising rates of unintentional drug overdose deaths in recent years.

Neonatal Abstinence Syndrome refers to the withdrawal and series of ill effects often experienced by a child born to a mother dependent on illicit drugs or pharmaceutical drugs (most commonly opioids like prescription pain medications or heroin).

"This is an example of the intergenerational tragedy in our state caused by the disease of addiction," said Director of Health Michael Fine, MD. "Every baby deserves a healthy start in life. We can—and must—minimize the devastating impact of Neonatal Abstinence Syndrome by supporting women and families at risk for addiction before, during, and after pregnancy through evidence-based services like our Nurse-Family Partnership, Healthy Families America, and Parents as Teachers home visiting programs."

Mothers giving birth to babies with Neonatal Abstinence Syndrome are on average about 30 years old, and many have completed some post-secondary education. The majority holds at least a high school diploma or GED and is single, on public health insurance, white, and non-Hispanic.

HEALTH analyzed newborn screening and hospital discharge data for babies born to Rhode Islanders in the state's birthing hospitals to calculate rates of Neonatal Abstinence Syndrome and associated maternal demographics.

Rhode Island already screens all newborns for a variety of health conditions and risk factors, including Neonatal Abstinence Syndrome. I

* Data are provisional

Kent and Memorial Hospitals Using Germ-Zapping Robots to Fight Infection

PROVIDENCE – As hospitals across the nation look for new and innovative ways to battle deadly pathogens and kill multi-drug resistant organisms that put patients at risk, Care New England has begun using germ-zapping robots that eliminate hard-to-kill microorganisms in hard-to-clean places. Two robots are in place at Kent Hospital in Warwick, and one is in place at Memorial Hospital in Pawtucket.

Xenex Disinfection Services' UV disinfection system is the fastest, safest and most effective method for the advanced cleaning of hospital rooms, and is scientifically proven to destroy all major classes of microorganisms that can cause hospital-acquired infections (HAI).

Hospital-acquired infections, which are caused by such deadly pathogens as methicillin-resistant staphylococcus aureus (MRSA), *Clostridium difficile* (C. diff), pneumonia and Acinetobacter, are the fourth-leading cause of death in the United States, according to the Centers for Disease Control and Prevention.

The Xenex disinfection device uses pulsed xenon ultraviolet (UV-C) light that is 25,000 times more powerful than sunlight to destroy harmful bacteria, viruses, fungi and even bacterial spores. The system is effective against even the most dangerous pathogens, including C. diff, norovirus, and influenza and staph bacteria like MRSA. In minutes the device can disinfect a patient room, patient bathroom or operating room with a pulsing light that washes over the surfaces where germs reside.

The Xenex system has been credited for helping other health care facilities in the U.S. decrease their MRSA and C. diff infection rates. The Xenex UV disinfection system can disinfect a room in minutes and is easily portable, allowing it to be used in virtually any location within the hospital. Because the light is extremely intense, the machine operates on its own once it's set up in a room. For enhanced safety, a sign placed outside the door warns people not to enter, and a motion sensor automatically shuts the machine off if someone should enter.

CNE

Paul Petit and Lewis Rodrigues, Environmental Services with Memorial Hospital's robot germ-slayer.

CNE

David Raymond, Patty Cameron, Clyde Vittum, and Maria Furtado, Environmental Services, Kent Hospital, are shown with new robotic disinfection system.

Staff at Kent and Memorial Hospitals helped to name their Xenex robots in a contest sponsored by the Environmental Services Departments at both operating units. Kent's robots are now referred to as, "Adam and Eve," and Memorial's robot is named "Violet."

"One hospital-acquired infection is one too many, so we are excited to be using the Xenex system to help us achieve our goals of infection prevention, while improving quality and patient outcomes," said Edward Schottland, acting president, Memorial Hospital. "Our environmental services team is very enthusiastic to be using this kind of advanced technology in their daily work." ❖

Bradley/Hasbro Center Launches Asthma Study for Latino Students

PROVIDENCE – **DAPHNE KOINIS-MITCHELL, PhD**, a researcher and staff psychologist at the Bradley Hasbro Children's Research Center, and director of the Community Asthma Program at Hasbro Children's Hospital, has launched a new asthma intervention program for Latino middle school students in urban public schools to study how best to help them manage their asthma. The Rhode Island Puerto Rico ASMAS Program (Asthma Management in Schools) team will develop and test a peer-facilitated asthma self-management intervention for Latino children in the 7th and 8th grades.

"Asthma health disparities continue to exist in children, with Latino children of Puerto Rican and Dominican descent having the highest rate of complications from asthma," said Koinis-Mitchell. "Middle school children suffer from asthma more than children from any other age group. This same group spends a majority of their day in school, and when faced with symptoms, must manage their illness in school. So, it is vitally important to reach these children where their health and academic success are affected on a daily basis and teach them to self-manage their asthma."

The ASMAS program will create and evaluate a culturally tailored asthma self-management program for Latino middle school students through a partnership with high schools in the Central Falls and Pawtucket school districts. Latino high school students (juniors and seniors) who have asthma will be selected to administer the intervention to their younger middle school peers from the same school districts. The high school students, who are nominated by school personnel, will use their participation in this program as an independent study and as a community service requirement fulfillment.

Although guidelines for managing asthma in the school setting currently exist, translating these guidelines into the context of urban schools raises many challenges.

"During the middle school years, older peers have a major influence on children's health behaviors. However, traditional formats of health education delivery don't capitalize on this influence," said Koinis-Mitchell. "We hope this new peer-based intervention can help us overcome the traditional challenges for health education in this group, such as language barriers and limited school supports for children who have asthma."

Koinis-Mitchell hopes the study will result in improved asthma self-management among study participants, such as managing symptoms better, as well as keeping a rescue inhaler on hand and having an action plan with a school nurse.

This study is funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) under grant number 1R21HD074855. ❖

MEMORIAL HOSPITAL OF RI

Sara Watson, MD, a second-year Family Medicine resident at Memorial Hospital, co-led an effort to teach students about healthy eating with the construction of a community garden at the Baldwin Elementary School in Pawtucket.

Memorial Family Medicine Staff Plant Seeds of Healthy Eating

PAWTUCKET – Staff from the Department of Family Medicine at Memorial Hospital of Rhode Island recently rolled up their sleeves and broke out the shovels to help build a community garden at the Elizabeth Baldwin Elementary School located in Pawtucket. The school, which has over 750 students in grades K-5, has had a long history of finding innovative ways to fight childhood obesity.

Lead by **FADYA EL RAYESS, MD**, a family medicine physician at Memorial and **SARA WATSON, MD**, a second-year Family Medicine resident at Memorial, the garden is designed to help students and their families learn about healthy eating. Made possible by $7,000 in grant funding from Lowes Home Improvement and the Whole Kids Foundation, the project is part of an on-going partnership between Memorial staff and the school in which health care providers teach students about the importance of regular exercise and healthy eating habits.

"This is just one of many innovative projects Baldwin has implemented to address childhood obesity, and a natural extension of the weekly teaching from Family Medicine residents on nutrition and physical activity," said Dr. El Rayess.

As part of The Warren Alpert Medical School of Brown University's Family Medicine Residency Program, residents do a nutrition rotation at the school. Dr. El Rayess says this garden project will become an important part of that education. ❖

Bradley/Hasbro Study: CBT Benefit Youngsters with OCD

PROVIDENCE – A new study from the Bradley Hasbro Children's Research Center has found that family-based cognitive behavioral therapy (CBT) is beneficial to young children between the ages of five and eight with Obsessive-Compulsive Disorder (OCD). The study, published online in *JAMA Psychiatry*, found developmentally sensitive family-based CBT that included exposure/response prevention (EX/RP) was more effective in reducing OCD symptoms and functional impairment in this age group than a similarly structured relaxation program.

BRADLEY HOSPITAL

Jennifer Freeman, PhD

JENNIFER FREEMAN, PhD, a staff psychologist at the Bradley Hasbro Children's Research Center and clinical co-director of the Intensive Program for OCD at Bradley Hospital, led the study. "CBT has been established as an effective form of OCD treatment in older children and adolescents, but its effect on young children has not been thoroughly examined," said Freeman. "These findings have significant public health implications, as they support the idea that very young children with emerging OCD can benefit from behavioral treatment."

During the 14-week randomized, controlled trial, which was conducted at three academic medical centers over a five-year period, the team studied 127 children between the ages of five and eight with a primary diagnosis of OCD. Each child received either family-based CBT with EX/RP or family-based relaxation therapy.

The family-based CBT focused on providing the child and parent "tools" to understand, manage and reduce OCD symptoms. This includes psychoeducation, parenting strategies, and family-based exposure treatment, so children can gradually practice facing feared situations while learning to tolerate anxious feelings. The family-based relaxation therapy focused on learning about feelings and implementing muscle relaxation strategies aimed at lowering the child's anxiety. At the end of the trial period, 72 percent of children receiving CBT with EX/RP were rated as "much improved" or "very much improved" on the Clinical Global Impression-Improvement scale, versus 41 percent of children receiving the family-based relaxation therapy.

According to Freeman, the traditional approach for children this young presenting with OCD symptoms has been to watch and wait. "This study has shown that children with early onset OCD are very much able to benefit from a treatment approach that is uniquely tailored to their developmental needs and family context," said Freeman. "Family-based EX/RP treatment is effective, tolerable and acceptable to young children and their families."

"The findings from this study support extending downward the age range that can benefit from CBT with EX/RP for pediatric OCD treatment," said Freeman. "With appropriate parental support, young children with OCD can make significant gains beyond what can be expected from having parents attempt to teach relaxation strategies to their children with OCD."

This study was funded by the National Institute of Mental Health (NIMH) under grant number 1R01MH079217.

Freeman's principal affiliation is the Bradley Hasbro Children's Research Center, a division of the Lifespan health system in Rhode Island. She is also co-director of the Pediatric Anxiety Research Clinic at the Bradley Hasbro Children's Research Center and clinical co-director of the Intensive Program for OCD at Bradley Hospital. She is an associate professor (research) at The Warren Alpert Medical School of Brown University, Department of Psychiatry and Human Behavior. ❖

RIH Study: Medicare Patients with Dementia have Increased Readmission Rates

PROVIDENCE – A review of more than 25,000 admissions of Medicare beneficiaries to Rhode Island hospitals has found that patients with a documented diagnosis of dementia are nearly 20 percent more likely to be readmitted within 30 days than those without dementia. The study by Rhode Island researchers is published online in advance of print in the journal *Archives of Gerontology and Geriatrics.*

"Persons with dementia may have difficulties comprehending and following important discharge instructions, (e.g. medication changes, decision making, self care)," said principal investigator **LORI DAIELLO, PharmD**, of the Alzheimer's Disease and Memory Disorders Center at Rhode Island Hospital. "In addition, many patients with dementia have multiple medical conditions, so it's not surprising that this group of vulnerable older adults might be at a higher risk of being readmitted to the hospital shortly after discharge."

Daillo added, "Because dementia often goes undiagnosed, or is not documented in a patient's medical record, we believe that the current findings may underestimate readmission rates and risks in this population. " Our results suggest that a better understanding of the peridischarge period for patients with dementia may inform initiatives aimed at decreasing readmissions for hospitalized elderly patients." ❖

CharterCARE and Prospect joint venture receives state approval

PROVIDENCE – The Rhode Island Department of Health has approved the hospital conversion and change in effective control applications of Prospect Medical Holdings and CharterCARE to establish a joint venture to be called Prospect CharterCARE, LLC that will own Roger Williams Medical Center, St. Joseph Health Services of Rhode Island d/b/a Our Lady of Fatima Hospital and related healthcare facilities. Each of these facilities will be converted from not-for-profit to for-profit statuses.

"I am pleased to approve the applications, as conditioned in the Decisions," said HEALTH Director, **MICHAEL D. FINE, MD**. "I hope the implementation of these approvals, as conditioned, will strengthen the fiscal condition of these valued hospitals. I also hope the implementation of these approvals, as conditioned, will improve the overall healthcare provided by our Rhode Island hospitals as we work together to make healthcare affordable and work together to improve the health of all Rhode Islanders."

Approval and implementation of these applications will result in (1) the issuance of new hospital licenses to Prospect CharterCARE RWMC, LLC and Prospect CharterCARE SJHSRI, LLC; (2) issuance of a new nursing home license to Prospect CharterCARE Elmhurst, LLC; (3) the issuance of a new organized ambulatory care facility license to CharterCARE RWMC, LLC d/b/a Roger Williams Sleep Disorders Center; and (4) the issuance of a new home nursing care provider license to Prospect CharterCARE RWMC, LLC d/b/a CharterCARE Home Health Services.

To view the Decisions, visit: http://www.health.ri.gov/programs/hospitalconversionsmerger/ ❖

Joint Statement from Chartercare and Prospect

We are gratified by the decisions of Attorney General Peter F. Kilmartin and Department of Health Director Michael Fine, MD, to grant final approval to our joint venture. We also express our thanks to the members of the Health Services Council, which voted unanimously to recommend approval of our joint venture on May 13, and to the Department of Health staff and counsel and assistant Attorney Generals who conducted a thorough and fair review.

Through our unique and innovative partnership, we look forward to building on the tradition of high-quality, compassionate care at Roger Williams Medical Center and Our Lady of Fatima Hospital and preserving both institutions, as well as Elmhurst Extended Care and the St. Joseph Health Center clinics, as vital components of the Rhode Island health care network.

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Women & Infants Opens Expanded Infusion Center, Integrative Care Suite

PROVIDENCE – Women & Infants Hospital has opened the Murray Family Infusion Center and the Carter Family Integrative Care Suite within its Program in Women's Oncology facility in the Bernard and Ina Wasserman Family Building.

The Murray Family Infusion Center is more than twice the size of the Program's former facility, offering private and semi-private treatment spaces, and a lounge and nourishment center for patients and their families and caregivers. In addition, the Carter Family Integrative Care Suite was created as a dedicated space for wellness programs and complementary therapies for patients undergoing cancer treatment and their caregivers.

"The Program in Women's Oncology has been providing superior care to women with cancer and their families for 25 years, drawing hundreds of women from as far away as Cape Cod and Connecticut for its clinical excellence and skilled, compassionate staff," says Mark Marcantano, president and chief operating officer of Women & Infants. "This Program is a regional and national leader in the field and the new facilities now better reflect that excellence."

The former Infusion Center, located in one part of the building's third floor became too small to comfortably accommodate the more than 6,000 chemotherapy and other infusion treatments being given there each year.

The Murray Family Infusion Center now occupies a portion of the first floor of the building and was designed with the latest in ergonomics in mind, as a mix of private infusion areas and double infusion rooms was created for patients who prefer company during treatments, which can last up to six hours. Each infusion station has enough room for a caregiver to accompany the patient for treatment. The Center also includes expanded consultation space.

The Murray Family Charitable Foundation stepped forward early with a leadership grant giving tremendous momentum to the campaign. The hospital later received an inspiring challenge grant from the Carter Family Charitable Trust which was instrumental in completing the effort. In recognition of their generosity, the new Integrative Care Suite honors the Carters.

In addition, the Champlin Foundations also played a significant role with very generous funding. In all, more than 1,300 individuals, corporations and foundations contributed $3.4 million.

"The outpouring of gifts for this project in particular has been exceptional. We are grateful to all of our donors. Every oncology patient and her family will benefit from the community's support," Marcantano says.

"This new space is absolutely beautiful and helps us fulfill our mission of providing safe, quality care for women with cancer," says Cornelius "Skip" Granai III, MD, director of the Program in Women's Oncology. "The increased capacity afforded by this larger space will not only help us care for more women, but will allow us to continue to attract top residents, fellows and other providers to train here at Women & Infants." ❖

Rhode Island Hospital Acquires New Gamma Knife

PROVIDENCE – Rhode Island Hospital has acquired the Leksell Gamma Knife® Perfexion™ for the treatment of intracranial tumors, vascular malformations and other neurological disorders. It provides patients with a safer, less-invasive option to neurosurgery for complicated diagnoses, and can be used for the treatment of brain tumors, obsessive-compulsive disorder (OCD), trigeminal neuralgia, essential tremor and more. It also can be used in place of whole-brain radiation, in essence, targeting multiple brain tumors without radiating the entire brain.

"For some patients, neurosurgery simply isn't an option due to the location of the tumor, or the severity of the diagnosis," said **WAEL ASAAD, MD**, of the Department of Neurosurgery. "For these patients, targeted radiation is often the best course of treatment."

Perfexion allows noninvasive cerebral surgery to be performed with extreme precision, without opening the skull. It also minimizes the amount of radiation delivered to surrounding tissue. As with the previous gamma knife, patients are fitted with a stereotactic frame to prevent movement of the head during treatment. Perfexion then delivers a single dose of ionizing radiation from multiple sources simultaneously. Procedures generally take 15 to 40 minutes, and are typically performed with local anesthesia as an outpatient procedure.

"Patients have had a few options over the last few years, but Perfexion will provide patients with the most targeted, and fastest, treatment possible, allowing them to have fewer side effects, and the ability to go home the same day, in most cases returning to normal activities the next day," Assad said. ❖

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Pitch Perfect: Piyush Gupta, MD, Wins at Google Glass Challenge

MARY KORR
RIMJ MANAGING EDITOR

Bye, bye beepers? Probably, according to innovators in mobile health technology who presented their concepts of clinical wearable intelligence at a recent Google competition sponsored by the Presidential Innovation Fellows program, the Massachusetts Institute of Technology, and the website MedTech Boston.

"It's inevitable," said **PIYUSH GUPTA, MD**, who won the "Best Pitch" award at the Google Glass Challenge held at Google Boston headquarters on April 23rd for his entry: Glass on Call.

Dr. Gupta is a PGY3 medical resident at Rhode Island Hospital. He earned his bachelor's degree in biological sciences at Carnegie Mellon University and his MD at the University of Vermont College of Medicine.

RIMJ asked Dr. Gupta to elaborate on his award-winning idea and the event for our readers.

Q. The Google event must have been exciting. What were your thoughts as you delivered your pitch to the experts such as keynote speaker Rafael Grossmann, MD, the first surgeon to use Google Glass in the OR, and Google's healthcare industry execs?

A. I was really excited to be able to present at Google in Boston. It was a wonderful experience meeting the other contestants and judges. Also, it was incredible that most of the audience was not directly in healthcare! This goes to show how diverse and popular healthcare innovation is becoming.

I see this as a huge opportunity for providers to shape healthcare. If engineers and clinicians are able to work together, we can create new technologies which prioritize safer, more efficient patient care rather than creating sexy looking devices that don't truly impact medical practice.

Q. Glass on Call: Can you explain to RIMJ readers how this might, in the future, replace their current beeper system and how it exactly works?

A. Glass on Call is essentially augmented paging. First off, it allows caregivers to focus on their task at hand while responding to messages and alerts. Second, it allows for automatic alerts to be sent from an EMR. Third, it allows for group messages, picture messages, video messages, etc., expanding on the basic text message that we get now.

Q. Is it difficult to get used to reading data on a pair of glasses or on a face screen?

A. Not at all! You need to play around with the Glass initially, yes, but soon enough it becomes second nature to you.

Q. How are the Google Glass prototypes used in Boston ERs and at RIH?

COURTESY PIYUSH GUPTA, MD

Dr. Piyush Gupta, a resident at Rhode Island Hospital, pitched a homerun in Cambridge, Mass., recently at the Google Glass competition to create clinical uses for Glass.

A. Glass at RIH is being used for telemedicine consults, allowing access to a specialist quicker for more efficient care. [At RIH, emergency room doctors are using the device to stream video of patients who arrive with burns or rashes to dermatologists who can help direct the course of treatment.]

Boston is using glass as an extension of its EMR: Accessing data on the go while delivering care.

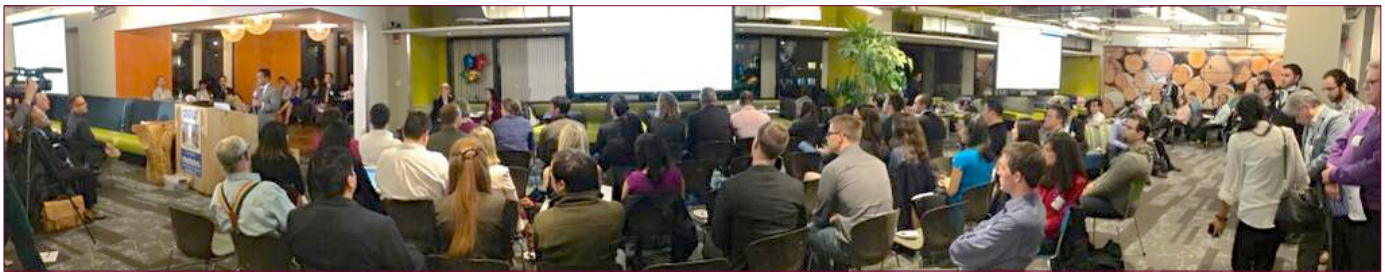
Q. What about intellectual property rights for Glass on Call?

A. My presentation was only an idea. I would love if someone developed it, and if I could be a part of that.

Q. Will you buy a pair of Google Glass when it becomes available?

A. Yes! ❖

View Dr. Gupts's presentation here: http://prezi.com/zjgily7otg_d/glass-on-call/



MEDTECH BOSTON

Over 200 people turned out to see the MedTech Boston Google Glass Challenge "Final Smackdown" Pitch Competition held at Google Cambridge Center in April.

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Recognition

Women & Infants Earns National Achievement Award

From American College of Surgeons' Commission on Cancer

PROVIDENCE – The Commission on Cancer (CoC) of the American College of Surgeons announced recently that Women & Infants Hospital of Rhode Island is one of 74 accredited cancer programs nationwide – and one of just two in Rhode Island – to earn its 2013 Outstanding Achievement Award.

"The Commission on Cancer is a respected national organization that will only send a team to evaluate a cancer program if it meets certain criteria. To earn one of its Outstanding Achievement Awards is a distinct honor and tribute to the tireless, compassionate and innovative ways the leadership and staff in our Program in Women's Oncology help women with cancer every day," says **MARK R. MARCANTANO**, president and chief operating officer of Women & Infants.

The Program in Women's Oncology earned a three-year accreditation with commendation from the CoC in late 2013 after a successful site visit in September.

"Everything we do in the Program in Women's Oncology – every doctor we hire, every service we offer, every decision we make – is based on our desire to help women with cancer. Our entire purpose is to diagnose as early as possible, treat them as effectively and compassionately as possible, and support them as they face the world as survivors," says **CORNELIUS "SKIP" GRANAI III, MD**, director of the Program in Women's Oncology. "We have access to the full scope of services, research and leading technology and science, but it is our humane approach and the way we are always looking to answer the question 'What more can we do?' that continues to set us apart."

The purpose of the award is to raise the bar on quality cancer care, with the ultimate goal of increasing awareness about quality care choices among cancer patients and their loved ones. In addition, the award is intended to:

- Recognize those cancer programs that achieve excellence in providing quality care to cancer patients.
- Motivate other cancer programs to work toward improving their level of care.
- Facilitate dialogue between award recipients and health care professionals at other cancer facilities for the purpose of sharing best practices.
- Encourage honorees to serve as quality-care resources to other cancer programs.

"More and more, we're finding that patients and their families want to know how the health care institutions in their communities compare with one another," said **DANIEL P. MCKELLAR, MD, FACS**, chair of the CoC. "They want access to information in terms of who's providing the best quality of care, and they want to know about overall patient outcomes. Through this recognition program, I'd like to think we're playing a small, but vital, role in helping them make informed decisions on their cancer care.

"These 74 cancer programs represent the best of the best when it comes to cancer care," he added. "Each of these facilities is not just meeting nationally recognized standards for the delivery of quality cancer care, they are exceeding them." ❖

Dr. James Padbury Honored by Pediatric Society

WOMEN & INFANTS HOSPITAL

James F. Padbury, MD

PROVIDENCE – **JAMES F. PADBURY, MD**, was recently presented with the Mentor of the Year Award at the 26th annual meeting of the Eastern Society for Pediatric Research, part of the Society for Pediatric Research of the American Pediatric Society.

Each year the award is presented to an outstanding teacher who has had a major impact on developing research skills in trainees and launching productive research careers.

Dr. Padbury is pediatrician-in-chief and chief of Neonatal/Perinatal Medicine at Women & Infants Hospital and the William and Mary Oh-William and Elsa Zopfi Professor of Pediatrics for Perinatal Research at The Warren Alpert Medical School. ❖

RIH

Esther Choo, MD

Esther Choo, MD, Receives Young Investigator Award

PROVIDENCE – Rhode Island Hospital emergency medicine physician and researcher **ESTHER CHOO, MD**, is a recipient of the 2014 Young Investigator Award from the Society of Academic Emergency Medicine (SAEM) for her research addressing the high occurrence of substance use and intimate partner violence in women. Her research is supported with funding from the National Institutes of Health.

The award recognizes researchers who have a clear commitment to research during the early stage of their academic career. Dr. Choo, a national advocate for innovation in nurturing and training young researchers, has consistently presented and published in her research field, including 27 original manuscripts published in peer-reviewed journals, and 22 scientific presentations at national meetings. She also co-created the Women's Health in Emergency Care division in the Rhode Island Hospital department of emergency medicine, the first of its kind in the country, which provides care that is specific to women and offers an academic rotation to focus on gender-specific research.

She also created and co-directs a SAEM-approved research fellowship program, and serves on the Executive Committee of the 2014 Academic Emergency Medicine Gender-Specific Research in Emergency Care Consensus Conference. ❖

Recognition

Miriam Hospital Receives 8th Consecutive Award for Quality Care

PROVIDENCE – The Miriam Hospital has received the Get With The Guidelines-Stroke Gold-Plus Quality Achievement Award for using American Heart Association/American Stroke Association quality improvement measures when treating stroke patients. The distinction, which recognizes evidence-based clinical guidelines, acknowledges The Miriam's commitment to quality, excellent care. The hospital treats more than 600 stroke patients each year and has received the Gold or Gold Plus designation for stroke care every year since 2008.

"Receiving this acknowledgment from the Heart Association/American Stroke Association over the last eight years validates the proven, comprehensive model of care we use when treating our stroke patients," said **THOMAS F. TRACY, JR., MD**, chief medical officer and senior vice president of medical affairs at The Miriam Hospital. "Our exemplary team of physicians, nurses, and staff in The Miriam Stroke Center and emergency department work together as one to consistently administer the highest level of quality care."

"We are pleased to recognize The Miriam for their commitment and dedication to stroke care," said **DEEPAK L. BHATT, MD, MPH**, national chairman of the Get With The Guidelines steering committee and executive director of Interventional Cardiovascular Programs at Brigham and Women's Hospital and professor of medicine at Harvard Medical School. "Studies have shown that hospitals that consistently follow Get With The Guidelines quality improvement measures can reduce patients' length of stays and 30-day readmission rates and reduce disparity gaps in care."

The Get With The Guidelines-Stroke quality program embodies adoption of the latest, research-based treatment guidelines intended to speed recovery and reduce death and disability among stroke patients. ❖

LIFESPAN

Dr. Joseph Sweeney

Joseph Sweeney, MD, Receives Milton Hamolsky Lifetime Achievement Award

PROVIDENCE – The Rhode Island Chapter of the American College of Physicians has awarded the 2014 Milton Hamolsky Lifetime Achievement Award to **JOSEPH SWEENEY, MD**.

The award, recognition for distinguished service, was given to Dr. Sweeney for his outstanding contributions in both the field of internal medicine and to the Rhode Island Chapter. As medical director of the blood banks at The Miriam and Rhode Island hospitals, Dr. Sweeney oversees the transfusion of about two-thirds of all the blood transfused in the state of Rhode Island. And, as Lifespan's director of coagulation and transfusion medicine, he is responsible for ensuring safe and appropriate transfusion and managing blood coagulation problems.

"Since coming to Rhode Island 20 years ago from Virginia, where he was chief medical officer and head of research at the Norfolk American Red Cross, Dr. Sweeney has pioneered the use of new technologies," said Thomas F. Tracy, Jr., MD, chief medical officer and senior vice president of medical affairs at The Miriam. "As a result, he has been a recognized leader in safe transfusion practices, while eliminating waste and inefficiencies."

A resident of Barrington, R.I., Dr. Sweeney is medical director of the School of Technology at Rhode Island Hospital, where he oversees curriculum and teaching of technologists in training. He is also medical director of the blood bank at Roger Williams Hospital and is a professor of pathology and laboratory medicine at the Warren Alpert Medical School. He has extensive experience and expertise in coagulation and transfusion medicine, writing more than 230 scientific papers and abstracts.

"Dr. Sweeney provides that critical knowledge for many of the patients who come into our Level 1 Trauma Center at Rhode Island Hospital in the middle of the night in need of immediate, quality care," Dr. Tracy added. "He is the one fielding those time-sensitive, critical questions and advising on the best care."

He is a fellow of the American College of Physicians; the Royal College of Pathologists in the United Kingdom; and the Royal College of Physicians in Ireland in the faculty of pathology. He has served as a member of the Technical Committee of the American Association of Blood Banks; currently serves on the board of directors of the Rhode Island Blood Center and the editorial board of *Transfusion*; and is an honorary scientific member of the Biomedical Excellence for Safer Transfusion Collaborative.

In addition to teaching residents and fellows, Dr. Sweeney also engages in blood transfusion research. His recent publications on blood management have received special recognition by The Joint Commission, and he was recently accepted as a member of the Brown University Alpha-Omega-Alpha, a U.S. medical school honor society.

Dr. Sweeney received his medical degree from the National University of Ireland at Galway. He trained in internal medicine and hematology in Dublin, Ireland, becoming a member of the Royal College of Physicians of Ireland. He subsequently trained in clinical hematology and blood banking at Montefiore and the Bronx Municipal Hospitals in New York City, and in medical oncology at the Roswell Park Cancer Institute in Buffalo, New York. ❖

Recognition

Lynn E. Taylor, MD, Honored as Woman Physician of the Year

PROVIDENCE – **LYNN E. TAYLOR, MD, FACP**, was honored as the 2014 Woman Physician of the Year by the Rhode Island Medical Women's Association (RIMWA) at the organization's annual meeting held May 13th at the Providence Marriott.

Dr. Taylor, an assistant professor of medicine at the Alpert Medical School, is an HIV specialist focusing on HIV and viral hepatitis coinfection. She developed and directs The Miriam Hospital's HIV/Viral Hepatitis Coinfection Program, providing multidisciplinary care to HIV/hepatitis C virus (HCV) and HIV/hepatitis B coinfected persons.

Established in 2001, the HIV/Viral Hepatitis Coinfection Program, part of The Miriam Hospital's Immunology Center, serves patients living with HIV infection. The goals of the clinic include preventing new viral hepatitis infections; educating patients about viral hepatitis; promptly diagnosing viral hepatitis; evaluating liver disease; treating viral hepatitis with medications; providing hepatitis A virus (HAV) and hepatitis B virus (HBV) vaccinations; screening for other forms of liver disease, as well as for liver cancer; and serving as a springboard for viral hepatitis-related research.

She was also one of two recipients of the 2013 Rhode Island Innovation Fellowship, an annual program designed to stimulate solutions by Rhode Islanders to Rhode Island challenges. She is the first physician to be selected. Her project, Rhode Island Defeats Hep C, aims to make Rhode Island the first state to eradicate the Hepatitis C virus infection. ❖

Lynn E. Taylor, MD

Whah Wonder
an interpretive portrait in wool of Jimi Hendrix

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Recognition

Podiatrists Celebrate Centennial Year in Newport

NEWPORT – The Rhode Island Podiatric Medical Association (RIPMA) kicked-off their Centennial celebration with an awards luncheon recently held at the Newport Marriott. The luncheon highlighted 100 years of community service with a Centennial Year Journal.

At the event, **ROBERT S. CRAUSMAN, MD**, of Rehoboth, MA, received the Myron Keller Award for his outstanding service to podiatry and for the development of a curriculum for podiatric residents at Memorial Hospital of Rhode Island. Dr. Crausman holds an MD and MMS from Brown University. He specializes in internal medicine, pulmonary disease, and geriatric medicine in Massachusetts and Rhode Island. He currently serves as Clinical Professor of Medicine at The Alpert Medical School of Brown University and is President of Trumed, Inc., in Fall River, Mass.

Dr. Clyde S. Fish was awarded the Centennial Year Merit Award.

CLYDE S. FISH, DPM, of West Greenwich, RI, was awarded the Centennial Year Merit Award for his outstanding service to podiatry and the RIPMA. He has served as RIPMA board treasurer since 1997, has been on the board since 1990 and first joined the Association in 1983.

In presenting the award, Dr. Peter Lewis said, "Dr. Fish has served on numerous committees including the health insurance advisory committee and took a leadership role on the highly successful Shoes for the Homeless campaign conducted by the Association."

Robert S. Crausman, MD, received the Myron Keller Award.

Dr. Fish is a Fellow of the American College of Foot Surgeons. He was former Chief of Podiatry at Kent County Hospital and serves at Roger Williams Medical Center, wherehe is director of the Podiatric Resident Clinic and a member of the Residency Training Committee. He is a graduate of Temple University School of Podiatric Medicine and the University of Rhode Island.

DR. DAVID RUGGIERO, president of the RIPMA, **DR. KRYSIA LEPOER**, president-elect, and 13 past presidents attended the Centennial Luncheon; a total of about 60 podiatrists attended the event. ❖

RIPMA

Past, present and future presidents of the Rhode Island Podiatric Medical Association celebrated the Association's 100th year at a luncheon recently held at the Newport Marriott.

Recognition

Memorial Hospital Recognizes Emergency Medical Workers

PAWTUCKET – Memorial Hospital and The Blackstone Valley Regional Emergency Medical Services (EMS) Council honored EMS workers in the Pawtucket area with an appreciation breakfast at the hospital on May 20th.

The Administration and staff at Memorial Hospital recognizes the value of EMS providers as a vital public service for the local community. EMS workers provide immediate lifesaving care and transportation to those in need 24 hours a day, seven days a week. ❖

Pictured left to right, front row kneeling, John Potvin, director of Emergency Medical Services, East Providence Fire Department; Tim Pacheco and Paul Richard, both Pawtucket fire fighters; and Brendan Johnson and Jake Morgan, both Pawtucket lieutenants. Left to right, back row, Thomas Gough, senior vice president, site operations; Sherri Sprague, RN, nurse manager, Emergency Department; Robert Howe, regional sales manager, Rosenbauer of New England, LLC; Laura Forman, MD, physician-in-chief, Emergency Department; Steven Guadalupe, director of Marketing, Med Tech Ambulance Service; Lynne Rivard, RN, Emergency Department director; Captain Raymond Medeiros, director of Emergency Medical Services, North Providence Fire Department; Dr. Karl Machata, Emergency Department staff physician, BVEMS director; Shelley MacDonald, MS, RN, senior vice president, Patient Care Services, chief nursing officer; John Vernancio, director, New England Ambulance; Wes Meyer, Pawtucket lieutenant; Gregg Noury, Business Development, New England Ambulance Service; Joe DeAngelis, Cumberland Fire Department; and Lori-ann Gagne, secretary to the Emergency Department's physician-in-chief.

Appointments

Joseph A. Diaz, MD, named Physician-In-Chief of Medicine at Memorial Hospital

MEMORIAL HOSPITAL

Joseph A. Diaz, MD, MPH

PAWTUCKET – Memorial Hospital of Rhode Island recently appointed **JOSEPH A. DIAZ, MD, MPH, FACP**, as physician-in-chief of medicine. He had served in the role of interim physician-in-chief of medicine at Memorial since September of 2012, and continues to serve as the chief of the Division of General Internal Medicine.

As Physician-in-Chief, Dr. Diaz oversees the Department of Medicine including the medical sub-specialty divisions as well as the Department's educational programs. "During this time of transition, there is no better person to lead the Department of Medicine than Dr. Diaz," said Edward Schottland, acting president. "An accomplished educator and leader in the fields of general internal medicine and primary care, Joe is exactly what the hospital needs as it continues its transformation."

Dr. Diaz earned his B.A. at Boston College, and both his medical degree and master of public health at Brown University. He completed his residency and fellowship in general internal medicine at Rhode Island Hospital prior to joining the faculty at Memorial Hospital of Rhode Island and The Warren Alpert Medical School of Brown University.

At the Alpert Medical School, Dr. Diaz is an associate professor of medicine in the Division of General Internal Medicine, co-director of the Department of Medicine Dominican Republic Exchange Program, and a lead faculty member in the medical school's academy system for student advising.

Dr. Diaz is a member of the American College of Physicians, Society of General Internal Medicine, and American Society of Preventive Oncology. He has published peer-reviewed articles and book chapters that pertain to his research interests which center on cancer prevention and control, disparities in healthcare, and medical education. ❖

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Appointments

Kent's Lisa J. Gould, MD, named President of Wound Healing Society

KENT HOSPITAL

Lisa J. Gould, MD

WARWICK – **LISA J. GOULD, MD, PHD, FACS**, associate medical director of the Wound Recovery and Hyperbaric Medicine Center at Kent, has been named president of the Wound Healing Society, a national scientific organization focused on wound healing. The announcement was made at their annual meeting in Orlando, FL, in May.

Dr. Gould is a board-certified plastic surgeon, a nationally recognized researcher and educator, and a wound-care clinician. She served on the executive board of the Wound Healing Society for more than 10 years and chaired its Education Committee for six years. She has authored numerous publications and was instrumental in creating the Basics of Wound Care Course, a regular feature at the Symposium on Advanced Wound Care, the nation's largest wound-care conference.

"This is a great accomplishment for Dr. Gould and The Wound Recovery and Hyperbaric Medicine Center at Kent, as she will be representing such a large, respected, national organization focused on wound healing," said **GEORGE PERDRIZET, MD**, medical director of the Wound Recovery and Hyperbaric Medicine Center at Kent. "Dr. Gould's expertise in wound care, in addition to her strong clinical background makes her a leader in this field of medicine and I am confident she will excel as president of WHS."

In her tenure, Dr. Gould plans to launch a wound education web-portal, develop standardized clinical trial protocols for wound care, and promote an advocacy campaign for patient-centered wound care.

The Wound Recovery and Hyperbaric Medicine Center at Kent is a unique regional referral center, offering advanced wound care, treatment for diabetic ulcers, surgical wounds, ostomy problems and other chronic concerns. The center cares for patients throughout New England and is housed on the Kent Hospital grounds. Its advanced hyperbaric oxygen chambers are available 24-hours a day for emergency referrals needing immediate intervention. It is the only 24-7 hyperbaric medicine facility outside of Boston. ❖

Position Available — Live on Block Island!

Block Island Health Services seeks a board certified family practice physician to provide primary and urgent care at the only medical facility in an Island community. Share practice with a certified family nurse practitioner. Generous benefits including housing. The Center serves approximately 2,200 unduplicated patients per year. In the winter there are about 1,000 residents, but in the summer the population swells to 13,000 or more. October through early June is a slower pace, but there is a busy pace mid June through Labor Day.
Block Island Health Services is affiliated with Warren Alpert Medical School of Brown University and University of New England College of Osteopathic Medicine.

Block Island was designated by the Nature Conservancy as one of twelve "last great places" due to its commitment to sustain natural habitat in balance with human recreation. This position is ideal for someone who appreciates a small town, the natural environment, ocean-based recreation, and is comfortable with both primary and emergency care.

Contact Barbara Baldwin, Executive Director
Block Island Medical Center, PO Box 919, Block Island, RI 02807
or e-mail bbaldwin@bihealthservices.com
Please indicate your salary requirements.

Photo courtesy of Kari Curtis/Block Island Times

Appointments

WOMEN & INFANTS HOSPITAL

Jennifer Gass, MD

Jennifer Gass, MD, elected President of RI ACS

PROVIDENCE – **JENNIFER GASS, MD, FACS**, co-director of the Breast Health Center, part of the Program in Women's Oncology, and chief surgeon at Women & Infants Hospital, was elected president of the Rhode Island chapter of the American College of Surgeons (ACS).

Dr. Gass, a breast surgeon also affiliated with the Breast Health Center at Kent Hospital, is also entering her second year as president-elect of the National Consortium of Breast Centers (NCBC).

"Dr. Gass is at the forefront of our understanding and treatment of breast cancer. Recognized as a consummate leader in breast disease regionally and nationally, I am not surprised she has been asked to lead these two prominent organizations," says **ROBERT D. LEGARE, MD**, co-director of the Breast Health Center. "This is also a tribute to her great skills as a surgeon and clinician."

The ACS is a scientific and educational association of surgeons founded 100 years ago to improve the quality of care for patients by setting high standards for surgical education and practice. The RI chapter has representation from each hospital in the state.

Board certified in both general surgery and critical care, Dr. Gass is director of the breast fellowship at Women & Infants and is an associate professor at The Warren Alpert Medical School of Brown University. She is a member of the American Society of Breast Surgeons, Rhode Island Medical Women's Association, the Rhode Island Medical Society, and the American Medical Association. ❖

CARE NEW ENGLAND

Margaret Howard, PhD

Margaret Howard, PhD, named Director of Women's Behavioral Health at W&I

PROVIDENCE – **MARGARET HOWARD, PHD**, has been named director of the Division of Women's Behavioral Health at Women & Infants Hospital. Dr. Howard, who is also director of the Day Hospital there and a clinical professor in the Departments of Psychiatry and Human Behavior and Medicine at the Alpert Medical School, has served as interim director since 2011.

"Dr. Howard has long been an invaluable member of our clinical and administrative team," said **RAYMOND O. POWRIE, MD**, interim chief of the Department of Medicine and senior vice president for quality and clinical effectiveness at Women & Infants Hospital, chief medical quality officer at Care New England, and professor of obstetrics, gynecology and medicine at the Alpert Medical School. "We are delighted to have her expertise and leadership as we enhance our women's behavioral health services, working in collaboration with our other Care New England hospitals."

Dr. Howard received her PhD in clinical psychology from Southern Illinois University. She completed her internship and postdoctoral fellowship at the Alpert Medical School of Brown University's Department of Psychiatry and Human Behavior. She has served as the director of the Mother Baby Perinatal Psychiatric Partial Hospital (Day Hospital) at Women & Infants Hospital since 2000.

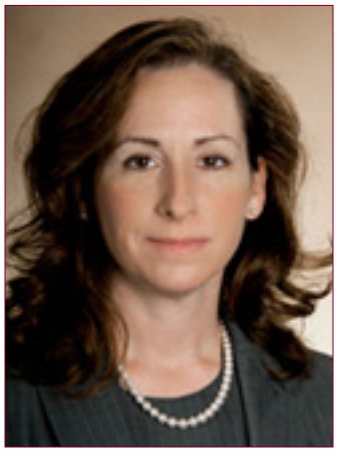
Dr. Howard is also the associate director of the Women & Infants/Brown University Women's Mental Health Fellowship and serves as the vice chair of the Care New England Brain and Behavioral Health Council. She is the primary Women & Infants Day Hospital rotation supervisor for clinical psychology residents and also supervises psychiatry residents, primary care residents and Brown medical students.

Her clinical and research interests center on postpartum mood disorders, mother-infant attachment, perinatal anxiety disorders, and novel and integrated treatment approaches for perinatal women. ❖

Karen L. Furie, MD, installed as Inaugural Kennison Professor

PROVIDENCE – **KAREN L. FURIE, MD**, was installed as the inaugural Samuel I. Kennison, MD, and Bertha S. Kennison Professor in Clinical Neuroscience on April 29. Dr. Furie is chair of the Department of Neurology at the Alpert Medical School.

The professorship was established with gifts from the estate of the late Grace Kennison Alpert, Brown University class of 1951.



BROWN

Karen L. Furie, MD

The Esoteric Prefixes of Medicine (Part II)

STANLEY M. ARONSON, MD

A PREFIX CONSISTS OF ONE OR MORE SYLLABLES PLACED BEFORE A root thus providing the root with direction, quantitation, color, severity, nuance or any of a vast number of qualifying syntactical adjuncts. The liberal use of prefixes adds greater meaning and substance to the roots to which they are affixed.

Medical vocabulary, leaning heavily on Greek, is thus blessed with prefixes that more narrowly define the word, particularly prefixes that give proportion, direction or dimension. There are prefixes such as *platy-*, meaning flat as in platyhelminths or platypus; *mio-*, meaning less/lesser as in miosis or Myocene; *cata-*, meaning down, as in cataplasm or catastrophe; *dolicho-*, meaning lengthy, as in dolichocephaly or indulge; *ortho-*, meaning straight or correct, as in orthopedics or orthodox; *oligo-*, meaning few, as in oligodendroglia or oligarchy; *syn-*, *sym-*, meaning joined or together, as in syndrome or syntax; *leio-*, meaning smooth, as in leiomyoma or leisure; *proximo-*, meaning nearest, as in proximal or approximate; *pachy-*, meaning thick, as in pachymeningitis or pachyderm; *meta-*, meaning between, over or after, as in metabolite, metastasis or metamorphosis; and *ceno-*, meaning common or newly arrived as in cenocyte or cineole.

The ancient Greek language has provided most of the standard prefixes in medical terminology. These include prefixes such as *iso-*, meaning equal or similar to, as in isogenesis, isolate or isomer; *pleo-*, *plio-*, meaning more than as in pleocytosis, pleomorphic or Pliocene; *plesio-*, meaning near or close to as in plesiomorphic or plesiosaur.

And then there are the many prefixes beginning with the Greek letter *xi*, the fourteenth letter of the Greek alphabet. For example, xeno-, variously meaning stranger, alien and sometimes guest as in xenophobia, xenograft or xenolith; *xero-*, meaning dry as in xeroderma, xerophthalmia or xerography; *xylo-*, meaning a relationship to wood as in xylenol or xylospasm; *xipho-*, meaning sword-shaped as in xiphoidalgia or xiphoid; and *xantho-*, meaning yellow in color as in xanthochromia or xanthodermia.

PAGE FROM *CATOPTRUM MICROSCOPICUM*, JOHANN REMMELIN, 1619 FROM THE RIMS COLLECTION AT THE HAY LIBRARY

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100 Years Ago: Dr. Blumer Calls for Experts to Assess Mental Health of 'Insane Aliens'

MARY KORR
RIMJ MANAGING EDITOR

PROVIDENCE – At the annual meeting of the Rhode Island Medical Society on June 4, 1914, **DR. G. ALDER BLUMER**, superintendent at Butler Hospital from 1899-1921, offered several resolutions on the topic of the mental health of immigrants and the need for trained professionals to evaluate psychiatric disorders and for the federal government to assume the costs for the care of those already admitted.

Among the resolutions Dr. Blumer proposed to send to President Woodrow Wilson, immigration authorities and the state Congressional delegation, were the following:

WHEREAS, The entry of insane and mentally defective immigrants to this country is a menace to the mental health of the nation, not only in the present, but in succeeding generations, and

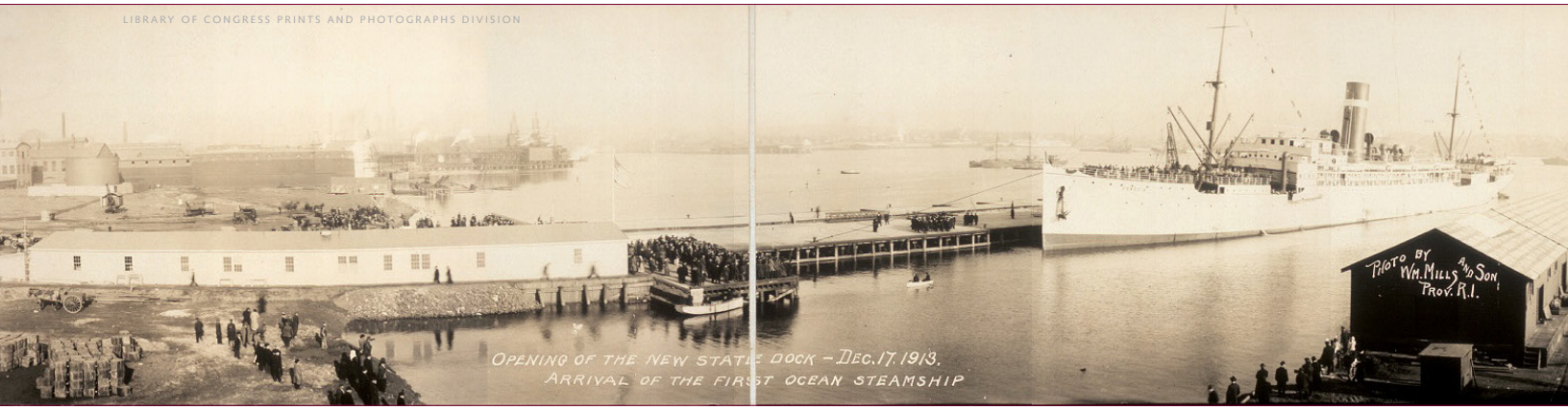
WHEREAS, This State bears a large part of the burden of caring for the insane and mentally defective aliens; and

WHEREAS, The present immigration laws, although providing for the exclusion of such immigrants, do not provide means for their examination by trained experts, nor for effective measures for the return home of insane aliens who become inmates of our institutions; and

WHEREAS, These are primarily matters of public health; therefore be it

Resolved by the Rhode Island Medical Society, That Congress be urged to provide for the mental examination of arriving immigrants by physicians in the United States Public Health Service especially trained in the diagnosis of insanity and mental defects; to provide adequate facilities for the detention and careful examination of all immigrants at large ports of entry; to provide for the detail of American medical officers on vessels bringing immigrants to this country in order that their welfare may be safeguarded and those with mental diseases or defects discovered; to provide for the assumption by the Federal Government of an equitable share of the burden of caring for dependent aliens, which is now borne entirely by the States; and to provide for the safe and humane return to their own home of those immigrants whom it is necessary to exclude and of those aliens in our public institutions who desire to return.

The matter was referred to the medical society's House of Delegates. ❖



Because of overcrowding at Ellis Island, ships bringing immigrants during the heyday of immigration to this country began arriving in Providence and New Bedford. Shown here is the first steamship to arrive in the new Port of Providence in December 1913. The French Fabre Line vessels, which left from Marseilles, France, stopping en route at Mediterranean ports in Portugal and Italy, were the main carriers to New England.

Hats Off to The Way We Were

VINTAGE PHOTO BY J. HERZOG, PASCOAG, RI

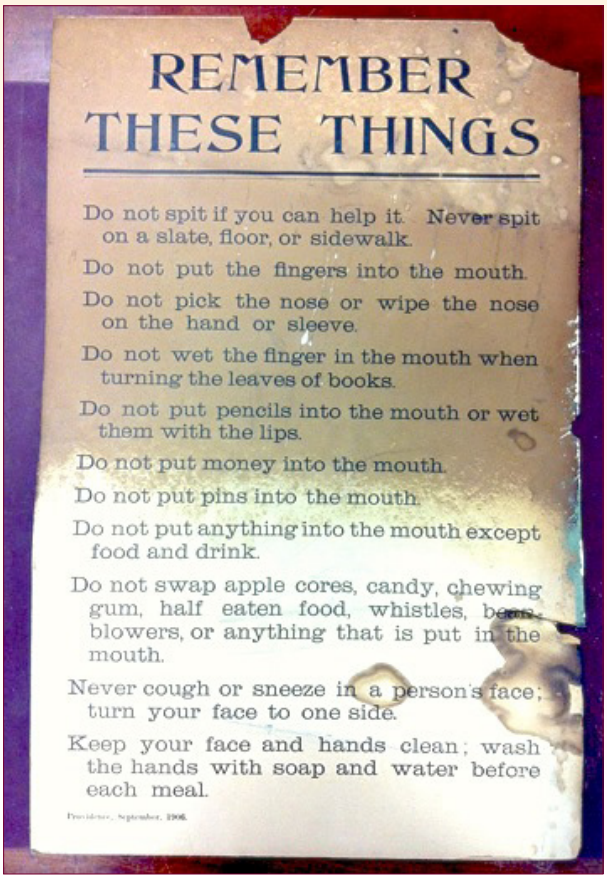
This photograph shows the quarterly meeting of members of the Rhode Island Medical Society held on Sept. 3, 1914 at the State Sanatorium at Wallum Pond in Burrillville, R.I. It was published in the November 1914 issue of the *Providence Medical Journal.*

Providence City Hall Workers Find Century-Old Poster

PROVIDENCE – According to the Providence City Hall website, maintenance workers made a surprising discovery recently while carrying out renovation work in the Recorder of Deeds Office.

The website states: "Tucked behind a cabinet was a large poster printed in 1906 with the headline, "Remember These Things."…This public announcement is undoubtedly the work of **DR. CHARLES V. CHAPIN**, who at this time was serving as the Superintendant of Health for Providence…Four years after this poster was issued, Dr. Chapin published his classic study, *The Sources and Modes of Infection*, and in 1911 another book, *Contact Infection at the Providence City Hospital*, further advanced his thesis regarding the spread of disease."

Charles V. Chapin, MD



REMEMBER THESE THINGS

Do not spit if you can help it. Never spit on a slate, floor, or sidewalk.

Do not put the fingers into the mouth.

Do not pick the nose or wipe the nose on the hand or sleeve.

Do not wet the finger in the mouth when turning the leaves of books.

Do not put pencils into the mouth or wet them with the lips.

Do not put money into the mouth.

Do not put pins into the mouth.

Do not put anything into the mouth except food and drink.

Do not swap apple cores, candy, chewing gum, half eaten food, whistles, bean blowers, or anything that is put in the mouth.

Never cough or sneeze in a person's face; turn your face to one side.

Keep your face and hands clean; wash the hands with soap and water before each meal.

Providence, September, 1906.