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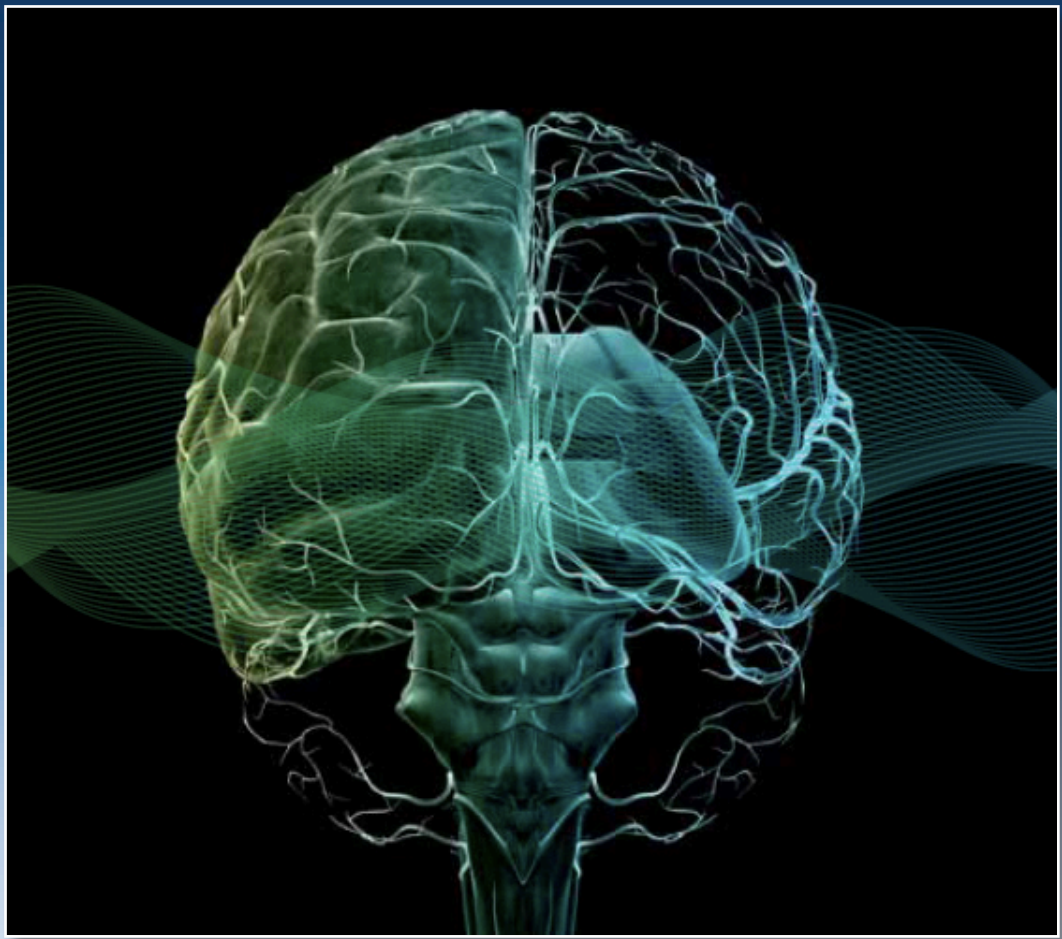

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NORMAN PRINCE NEUROSCIENCES INSTITUTE

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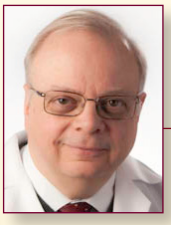

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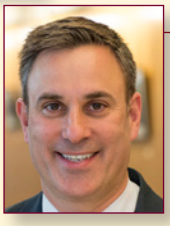

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RIMJ Mission Statement

The Rhode Island Medical Journal (RIMJ), published by the Rhode Island Medical Society, is an independent, monthly, electronic publication which aims to reflect the views and purposes of the entire medical community of Rhode Island.

We see the Journal as a vehicle aimed at the practicing physicians of Rhode Island – whether they are in private practice, on the staff of the state's hospitals or as part of the many colleges and universities of the state. It offers a venue for them to express their clinical or investigative findings, and for the academic faculty to publish their clinical or research results. It also serves as a platform for local medical students, resident physicians and fellows to contribute to the medical literature while honing the rudiments of medical writing.

In addition, it offers the opportunity for medical professionals to make the community aware of testing or clinical expertise that may not be widely known, even within our small state. And finally, RIMJ is a forum where allied health professions such as local schools of public health, pharmacy and nursing may share their concerns and aspirations as the business of health care takes on new and unanticipated challenges.

Joseph H. Friedman, MD
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Stanley M. Aronson, MD
Editor Emeritus

Small Research

JOSEPH H. FRIEDMAN, MD
joseph_friedman@brown.edu

There are many studies that need to be done to improve medical treatment. We worship the cult of evidenced-based medicine, ignoring the fact that the evidence often doesn't reflect the patients we're applying it to because they would have been excluded from study participation. We use drugs for off- label indications because no one will pay for a study that proves a treatment might work on-label.

I don't think I'm a troglodyte in these matters. But I'm increasingly annoyed by the daily clinical questions we face that are relatively easy to solve, but cannot be because they are unfundable. I've planned four studies that will answer potentially important clinical questions, at least in the world of Parkinson's disease, that simply require the administration of questionnaires to consecutive subjects, who are simply consecutive patients who agree to participate. None of these studies are of earth- shattering importance, but are sufficiently relevant to justify publication in a major neurological journal if the studies are done correctly and have interesting results. And, more importantly, might improve care. However, there is no possibility that any of these studies could possibly be funded. I can do these only because a student asked to do a research study. I don't think this scenario is much different than it has been over the past several decades.

There are few funding mechanisms. The NIH funds major studies, requiring hundreds of thousands of dollars, most of which are big-ticket items costing millions, to answer very important questions involving thousands of patients. These are crucial studies and the results do, in fact, alter our treatments, and, even if the benefits are meager, they apply to tens of thousands of people. On the other hand, studies of symptoms like fatigue, apathy, feelings of tremor internally may cost more to design for an NIH grant submission than to carry out. A study that might require $20,000 of a study coordinator's time would probably require significantly more than that to simply put together a submission to the NIH, and stands less than a 15% chance of ever being funded and, even if funded, usually requires at least two submissions and a year's worth of effort.

I spent a decade trying to prove that clozapine was the treatment of choice for psychosis in Parkinson's disease. I was assured by many senior colleagues that a grant submission to the NIH would be a waste of time since that wasn't the sort of study they liked to fund at the time. The neurological institute wasn't interested in psychiatric problems, and the psychiatric institute wasn't then interested in problems from neurology. The drug company that had the drug under patent wasn't interested in funding the study because of fear that the frail population was at too high a risk for side effects (read law suits) and the market was too small to justify it. So it was only after a colleague suggested applying for an FDA orphan drug grant that the study was funded. The maximum grant allowed still underfunded the study, but was sufficient for it to be done, with a lot of unpaid participation by my highly motivated colleagues. Not only was the drug company not interested in funding the study, they actually tried to renege on supplying free drugs, which it had promised.

Small research, in my view, is like "small ball" in baseball. It involves chipping away at the edges – bunts, stolen bases, hit and run, rather than home runs. To do small studies requires volunteerism. The patient advocacy organizations are primarily interested in cures. The NIH is interested in "big picture" projects which must be performed with incredible amounts of detail and statistical analysis. They also require pilot information, for which mechanisms for federal funding via competitive grants were recently developed. Drug companies are interested primarily in studies that can be used for marketing. Even getting IRB approval for studies where a few questions are asked requires an investment of several

hours. So, for example, if I want to find out how many of my PD patients suffer from anxiety, and how severe it is, I will need IRB approval, and then written informed consent to have patients rate their anxiety on a scale of 0–10. If I ask the question as part of a routine office visit, and record the answer, I can then obtain IRB approval for a chart review, thus obviating the need for informed consent, speeding up the process.

I am frustrated, and I'm unsure if I really should be. There is a limited amount of money available and endless numbers of important research questions. Our colleagues' abuse of patients, from the syphilis projects at Tuskegee, to the U.S. military's use of unknowing soldiers for experiments involving radiation or mind-altering drugs, to Willowbrook, led to our use of IRBs to protect patients from abuse, and now to our increasing use of them to protect the institution from law suits.

I think I'm grumpy because I have less time to do the studies I used to do on my own time. The press of the financial vise in medicine has made "small research" increasingly difficult. Even involving residents in collaborative research projects is challenging since they have too little time to do their clinical work due to time restrictions without concomitantly reduced workloads. Luckily there are students who can afford to offer unpaid summer time either out of interest or to buff their resumes before applying to medical school. ❖

Author

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

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The Origins of the Sneeze: Divine Gift or Mere Goldenrod Pollen?

STANLEY M. ARONSON, MD
smamd@cox.net

There are some who become so dismayed by monosyllabic words of robust Germanic origin that they compulsively seek out polysyllabic terms inherited from the two ancient Mediterranean cultures. And so, when they are obliged to acknowledge a sneeze, they will pause, seek through their thesauruses and then brightly declare: " 'Tis not a sneeze, it's a *snatiation*.' "

Snatiation, with its four syllables, sounds more cultured and eminently more authoritative. (Truly, a word not to be sneezed at.) Sadly, though, it is neither Greek nor Latin in origin. Instead, it is an acronym for **S**neezing **N**on-controllably **A**t a **T**ime of **I**ndulgence of the **A**ppetite – a **T**rait **I**nherited and **O**rdained to be **N**amed, and was specifically contrived in 1990 by the geneticist, J.G.Hall, to bring comfort to those feeling diminished by the use of monosyllabic words.

Sneezing has not gone unnoticed in the ancient texts. Xenophon the historian relates that sneezes were regarded by the armies of Athens as good omens. And Greek mythology is awash with sneezes and their consequences.

Yet other humans are burdened by paroxysms of sneezing after an unduly heavy meal (for want of a better name, this is called The Achoo Syndrome).

Odysseus, after years of indolent island-hopping, and now disguised as a beggar, ventures home to his wife, Penelope. Her son, Telemachus, then sneezes, bringing her much joy since it is a divine sign that Odysseus has returned.

The Romans, however, had a more conventional word for sneezing, the English spelling of which is sternutation. Sneezing in the Roman Empire, and its formulaic responses, had become so common that Pliny (23–79 CE) had idly wondered, "*Cur sternutamentis salutamus?*" (Why greet sneezings?)

Indeed, why greet sneezes? And why not sniffles, snorts, sneers or even coughs? Yet every known culture has determined that sneezing is an involuntary act and clearly a divine omen. Some cultures have then decided that sneezes are felicitous events; and thus, when hearing a sneeze, will declare such responses as *Sante* or *gesundheit*, *Reichtum*, *ola*, *Dieu te*, *dominus tecum*; and for the pragmatic Dutch, *morgen mooi weer* (nice weather tomorrow).

CDC/JAMES GATHANY

This photograph captured a sneeze in progress, revealing the plume of salivary droplets as they are expelled in a large cone-shaped array from this man's open mouth, thereby, dramatically illustrating the reason one needs to cover his/her mouth when coughing, or sneezing, in order to protect others from germ exposure.

Other cultures, more cautious about their futures, may utter: May God forgive you (Amharic), All Praise for Allah (Arabic), May good happenings arise (Assamese), May Jupiter preserve you (Latin), A fortunate occurrence (Cantonese), May you live long (Nepali), May you recover (Lugandese), and May it go right (Irish.)

Since a sneeze renders the soul of the sneezer to be transiently vulnerable, some responses are designed to create a temporary shield against impending evil. In some parts of Europe there is the further belief that one's heart stops momentarily during the sneeze; and this belief reinforces yet further the compulsion to bless the sneezer. Accordingly, no culture is without its rituals of sneeze-response. And with the possible exception of a rare anchorite meditating in some remote cave, a sneeze anywhere in the world will elicit an immediate response even from neighboring strangers. (The sneezes associated with seasonal release of goldenrod pollen have not yet infiltrated the texts of mythology.)

Modern physicians, too busy to study the mythic roots of sneezing, have determined that a proneness to sneezing might be an inheritable trait, particularly so when people with this genetic variant are suddenly exposed to bright sunlight (helio-ophthalmic outburst syndrome). Yet other humans are burdened by paroxysms of sneezing after an unduly heavy meal (for want of a better name, this is called The Achoo Syndrome). And finally there are the sneezing-prone neuroses, amongst adolescents, that respond favorably to psychotherapy.

The secular advances of modern medicine have diminished the value of sneeze-generated responses. And so, when a person now sneezes in public, two societal responses become apparent: People will studiously ignore the event; or alternatively, someone will chastise the sneezer, accusing him of willfully contaminating the atmosphere with exotic viruses.

With all the perils assigned to sneezes – including cardiac arrest and the loss of one's soul – some sneezes persist in their innocence. There is, for example, A.A.Milne (1882–1956) and his clinical observations on the upper respiratory activities of Christopher Robin:

Christopher Robin
Had wheezles
And sneezles…

And then there is the earnest advice given by The Duchess in *Alice's Adventures in Wonderland* by Lewis Carroll (1832–1898):

Speak roughly to your little boy,
And beat him when he sneezes;
He only does it to annoy,
Because he knows it teases. ❖

Original illustration by John Tenniel (1914) in *Alice's Adventures in Wonderland.*

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.

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{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, atop the Harbor Bridge Pylon in Sydney, Australia

RIMS' Steve DeToy in Union Square, New York City

Michael Migliori, MD, at the World Ophthalmology Conference, Tokyo

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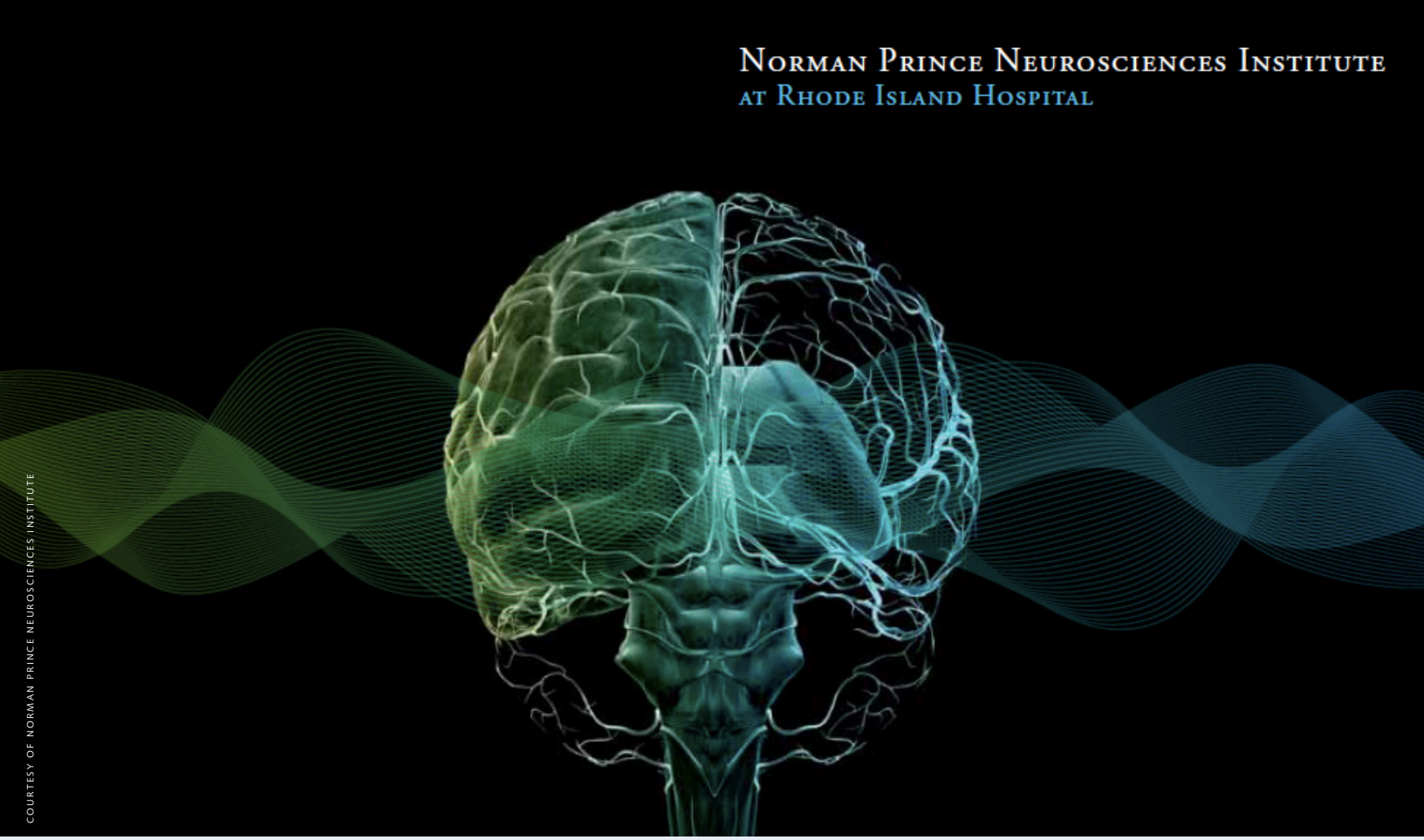

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The cover image is an artist's semitransparent rendering of the brain looking from the back. It shows features of the vascular system on the surface, the cerebral cortex on the left, deep structures of the cerebral hemisphere on the right, and brain stem in the lower center.

The Norman Prince Neurosciences Institute: Linking Research to Clinical Care

JOHN A. ROBSON, PhD; KAREN FURIE, MD; STEVEN RASMUSSEN, MD

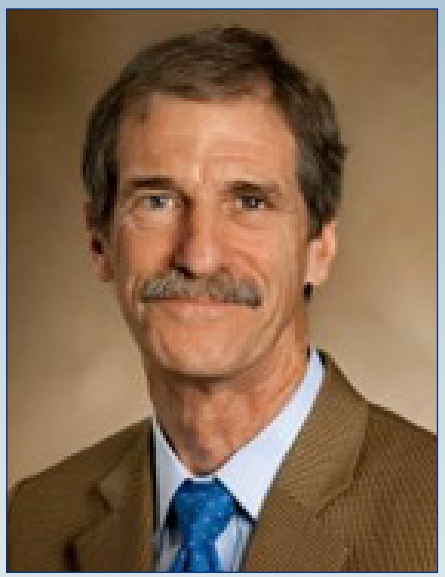
Over the past 50 years the expansion and advances in neuroscience have been astonishing. The Society for Neuroscience illustrates this growth. It is the world's largest organization of scientists and physicians devoted to understanding the brain and nervous system. In 1969 it had 500 members. Today it has almost 42,000 and its annual meeting attracts over 30,000 researchers. This tremendous growth in research has led to discoveries that have fundamentally changed our understanding of the nervous system.

We are gaining an ever-more sophisticated understanding of the functioning of neurons through the development of advanced imaging technologies in combination with genetic manipulations, and the human genome project is providing new insights about diseases and disorders of the nervous system. Advances in brain imaging technologies, such as Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI), have revolutionized the ways that we diagnose disorders of the nervous system and they are showing, on a global scale, how information is processed in the brain. At the same time researchers are developing devices, like electrodes for deep brain stimulation and implantable multi-electrode arrays that take advantage of progress in computational neuroscience and computer science to better diagnose and treat a variety of neurological disorders, ranging from depression to epilepsy to Parkinson's disease and paralysis.

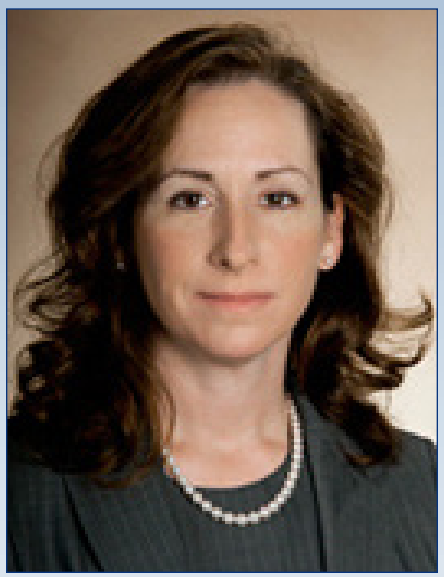
In 2013 the White House announced a new national initiative in neuroscience – BRAIN (Brain Research through Advancing Innovative Neurotechnologies). It is targeted at one of the great mysteries of the brain – how networks of neurons interact to create sensations, movements and thoughts. It will lead to even more breakthroughs in our understanding of how populations of neurons work together normally and how changes in network interplay lead to symptoms associated with neurological and psychiatric disease. These recent and anticipated future advances are creating opportunities for devising new treatments for diseases of the brain and nervous system that are greater than at any time in history.

In Rhode Island

This excitement about brain science is having a profound impact in Rhode Island. In the past few years the Alpert



John A. Robson, PhD



Karen Furie, MD

Steven Rasmussen, MD

PHOTOS: BROWN UNIVERSITY

Medical School at Brown University, in partnership with its affiliated hospitals, has been moving toward the creation of a coordinated academic medical center in Providence. One goal of such a center is to create links between research scientists and clinicians to encourage disease-targeted research and to create a pipeline that will facilitate the conversion of research findings into benefits for patients. In this area neuroscience is leading the way.

In December 2009 descendants of Frederick Henry Prince, a New England entrepreneur who made his fortune during the Gilded Age, around the turn of the 20th century, approached Dr. Timothy Babineau, President of Rhode Island Hospital, about making a gift from the Frederick Henry Prince 1932 Trust. Over the next several months that idea crystallized into a $15-million donation, the largest in the history of Rhode Island Hospital, from Elizabeth J.M. Prince and her children, Diana Oehrli, Guillaume de Ramel and Regis de Ramel, to endow the Norman Prince Neurosciences Institute (NPNI), named after the son of Henry Frederick Prince, who died from a head injury suffered in a plane crash during World War 1.

Although the gift was made to Rhode Island Hospital, the Institute was expected to develop as a collaborative venture with Brown University and other hospitals affiliated with the Alpert Medical School, including Bradley Hospital, Butler Hospital, Women and Infants Hospital, The Miriam Hospital and the Providence VA Medical Center. In that respect, the timing could not have been better. The chairs of the clinical neuroscience departments of neurology, neurosurgery and psychiatry were vacant, creating an opportunity to recruit new leadership with a shared vision for building interdisciplinary programs. In addition, Brown University was planning a major expansion of brain science on its campus through its own neuroscience institute, the Brown Institute for Brain Science (BIBS). The fit was obvious and these initiatives have coalesced into a broad-based, interdisciplinary and inter-institutional effort.

Launching the Norman Prince Neurosciences Institute

In 2011 NPNI began to develop a vision for growth. A steering committee was created that included the leaders in neurology, neurosurgery, psychiatry and basic neuroscience at Rhode Island Hospital, Brown and its other affiliated hospitals. Dr. G. Rees Cosgrove was recruited from Boston in 2010 to serve as chair of neurosurgery and take a major leadership role in the NPNI, which he did until resigning in 2014. Dr. Cosgrove did his neurosurgical training at the Montreal Neurological Institute, a self-contained, highly integrated clinical and research institute at McGill University that, in several respects, serves as a model for NPNI. In 2011 he was joined by Dr. John Robson as executive director. He is a neuroscientist who also worked at the Montreal Neurological Institute as associate director from 1997–2007. In 2012 Dr. Karen Furie, a Brown graduate and stroke specialist at Harvard University and the Massachusetts General Hospital, was recruited to be the chair of neurology and Dr. Steven Rasmussen accepted the chair of psychiatry and human behavior. Dr. Rasmussen has been on the Brown faculty for almost 30 years and is a leading expert on the treatment of obsessive-compulsive disorder. Both Drs. Furie and Rasmussen also serve as co-clinical directors of NPNI.

Building on Excellence: Brown Institute for Brain Science

Brown University is well known for its strengths in neuroscience research. It was one of the first universities in the United States to establish a Department of Neuroscience and, as a group, its neuroscientists have been very successful building excellence and attracting research funds.

However, Brown's neuroscientists are not confined to one department; they are found across the campus. Consequently the Brown Institute for Brain Science (BIBS) was established as an umbrella organization to advocate for all "brain scientists" and to facilitate interdisciplinary research. This institute now lists more than 100 faculty members from 15 different departments. Represented disciplines range from applied math, engineering and computer science, to cell and molecular biology and physiology, to cognitive neuroscience and brain imaging. Similarly, the clinical neurosciences are distributed across several departments, including neurology, neurosurgery, pathology, psychiatry and radiology, and they are found in many different hospitals affiliated with the Alpert Medical School. Like BIBS, NPNI strives to unite their efforts and create new opportunities for growth and collaboration.

From the onset there has been a major emphasis on collaboration between NPNI and BIBS. The two organizations have worked closely together to create joint programs intended to benefit all of brain science across the campuses of Brown and its affiliated hospitals. These efforts have included funding for collaborative research projects, a symposium, workshops and seminar speakers. BIBS and NPNI also partnered with the Rhode Island Medical Society for its highly successful "200th Anniversary Lecture Series."

Efforts are also underway to find ways to collaborate with scientists at the University of Rhode Island, which started an interdisciplinary neuroscience graduate program in 2012. That program and others related to neuroscience at URI are sure to grow in size and prominence in the coming years due to the recent creation of the Ryan Institute for Neuroscience.

These are exciting times for neuroscience in Rhode Island. There is a real opportunity to make Providence a nationally recognized center of excellence in this area. In some areas we are already there but further investment will be needed. The clinicians and scientists are eager and many of the parts are in place.

This issue of the *Rhode Island Medical Journal* contains articles by members of NPNI. They provide examples of programs being developed that focus on important clinical issues. It is not a comprehensive review of all programs that fall under the NPNI umbrella. However, these articles describe programs that illustrate the approach that we are developing. They focus on autism, stroke, traumatic brain injury and emerging uses of technology to treat a variety of neurological and psychiatric disorders. Each of these efforts involves teams that are collaborative, interdisciplinary and inter-institutional.

Authors

John A. Robson, PhD, is Administrative Director of the Norman Prince Neurosciences Institute, Rhode Island Hospital and Associate Director, Brown Institute for Brain Science, Brown University.

Karen Furie, MD, is Co-Clinical Director of the Norman Prince Neurosciences Institute, Rhode Island Hospital, and Professor and Chair, Department of Neurology, The Alpert Medical School of Brown University.

Steven Rasmussen, MD, is Co-Clinical Director of the Norman Prince Neurosciences Institute, Rhode Island Hospital and the Mary E. Zucker Professor and Chair of the Department of Psychiatry and Human Behavior, The Alpert Medical School of Brown University.

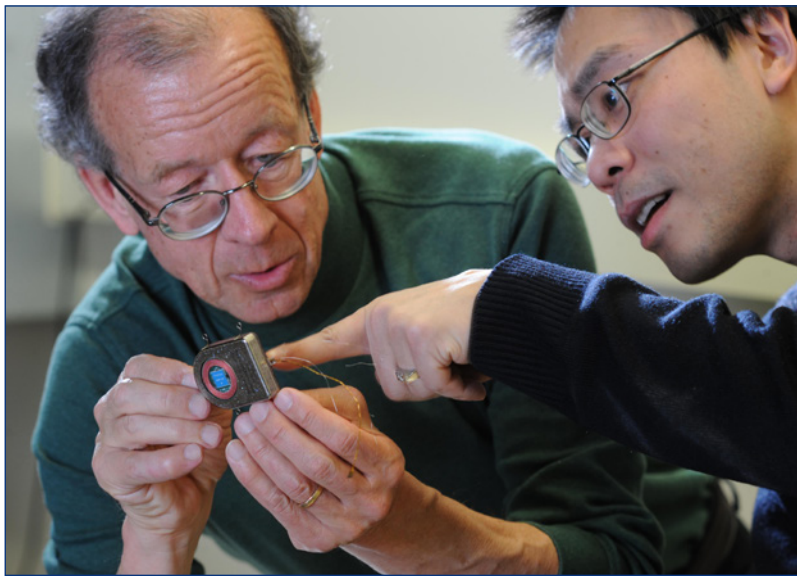
Neurotechnology: A New Approach for Treating Brain Disorders

JOHN A. ROBSON, PhD; R. JOHN DAVENPORT, PhD

ABSTRACT

Advances in neuroscience, engineering and computer technologies are creating opportunities to connect the brain directly to devices to treat a variety of disorders, both neurological and psychiatric. They are opening a new field of neuroscience called "neurotechnology." This article reviews efforts in this area that are ongoing at Brown University and the hospitals affiliated with Brown's Alpert Medical School. Two general approaches are being used. One uses advanced electrodes to "sense" the activity of many individual neurons in the cerebral cortex and then use that activity for therapeutic purposes. The other uses various types of devices to stimulate specific networks in the brain in order to restore normal function and alleviate symptoms.

KEYWORDS: Neurotechnology, neuroscience advances, BrainGate



FRED FIELD FOR BROWN UNIVERSITY

In a significant advance for brain-machine interfaces, engineers in the Brown Institute for Brain Science have developed a novel wireless, broadband, rechargeable, fully implantable brain sensor that has performed well in animal models. Here engineers Arto Nurmikko and Ming Yin examine their prototype device.

INTRODUCTION

Diseases and disorders of the nervous system have proven to be especially difficult to treat in part because of the complexity of the brain. Most efforts have focused on the development of behavioral or pharmacological therapies. However, with advances in engineering and computer technologies, alternative "device-based" approaches are being explored as potential tools for treating a number of conditions ranging from paralysis to movement disorders to mental illness.

Researchers at Brown University and its affiliated hospitals are international leaders in this approach, known as "neurotechnology." This collaborative, interdisciplinary effort has followed two approaches. One takes advantage of devices to detect brain activity and then uses that information for therapeutic purposes. The second uses devices to change brain activity in ways that can restore normal function. The work has benefited from the collaboration between the Norman Prince Neurosciences Institute (NPNI) and the Brown Institute for Brain Science (BIBS).

SENSING THE BRAIN

BrainGate research

The BrainGate research project is a multi-institutional effort based at Brown that is focused on improving the ability of paralyzed people to interact with the world. It uses a technologically advanced array of 96 electrodes implanted in the motor cortex of patients paralyzed as the result of stroke, injury or disease. These electrodes are able to measure the activity of individual neurons while people imagine moving their own arm. Computer algorithms translate that input to output that can be used to move a cursor on a computer screen[1] or, more recently, to move a robotic arm in a coordinated and purposeful manner.[2] In a dramatic demonstration in 2012, a paralyzed woman used BrainGate to control a robotic arm to give herself a drink of coffee[2] – the first time she has been able to do that in 15 years! In 2013, the BrainGate team received the inaugural Israel Brain Prize for this advance.

A remarkable finding of this project is that a very small number of neurons – fewer than 100 – can provide sufficient information to encode such complex movements. The current system does not replicate the speed and dexterity of natural arm and hand movements. However, innovations in signal decoding are improving control and "sensing" technology is making it possible to incorporate the activity of

more neurons into the system. As this trend progresses, the ability of paralyzed patients to control robotic devices should improve dramatically.

Engineers at Brown are also making rapid progress in developing a next-generation BrainGate device that transmits neural signals wirelessly.[3] That technology will enable patients to use the BrainGate approach in more ambulatory, real-life situations, untethered from a computer. It will also advance the possibility of amputees using this approach to better control prosthetic limbs. Other studies, using non-human primates, suggest that it will eventually be possible to use this approach to control movements of a patient's paralyzed limb by stimulating muscles directly.[4]

VIDEO: Paralyzed woman uses thoughts to sip coffee

Multi-electrode arrays

Multi-electrode arrays are also providing new insights into brain activity during epileptic seizures. To plan for epilepsy surgery, doctors often record activity from the brains of patients using electrocorticography (ECoG). In this procedure a large array of 50 or more electrodes is placed directly on the surface of the cortex in the region suspected to be the source of the seizures. Recordings can be made over a week or more while the patients are alert and off anti-seizure medications in an effort to record seizure activity and localize its source. These standard ECoG arrays do not, however, reveal the activity of single neurons.

As part of this procedure it is now possible to insert the same 96-electrode array used in the BrainGate system into the region suspected to be the source of seizure activity. This is being done by a team of clinicians, scientists and engineers at Brown and Rhode Island Hospital, in collaboration with colleagues at Massachusetts General Hospital. Thus, for the first time, the activity of individual neurons is being recorded and analyzed before, during, and after seizures. An initial report of the results from four research participants illustrates the potential power of this approach.[5] This study showed that seizures are not comprised of hyper-synchronized neuronal firing as previously suspected. Instead the patterns of activity are quite heterogeneous during the seizure. In comparison, at the end of the seizure almost all neural activity is suppressed for several seconds.

Perhaps the most surprising and significant finding in this study was the discovery that many neurons, even ones well outside the area of seizure origin, showed significant changes in activity minutes prior to the onset of the seizure. Thus, chronically implanted electrodes that record individual neurons could become reliable tools for identifying seizures prior to their onset. If this proves to be the case, it could lead to closed-loop devices able to treat epilepsy by stopping seizures before they start, by injecting a drug or an electrical current into the region of the seizure's onset. The FDA recently approved such a device based on ECoG recording technology and implanted stimulating electrodes (NeuroPace RNS System®).

ALTERING ACTIVITY

Deep brain stimulation (DBS) use in various disorders

Physicians have been altering brain activity to treat psychiatric disorders since the 1930s in those patients with the most severe and intractable symptoms.[6] However, in recent years, these techniques have become progressively more refined.

In the 1980s a new form of stimulation was developed primarily to treat tremors and other abnormal movements in patients with Parkinson's disease[7,8] who had severe medication-related problems. Neurosurgeons had discovered that small lesions deep in the brain, in the sub-thalamus and the globus pallidus, could greatly reduce certain symptoms in patients whose responses to drug therapy were problematic. Subsequently, they discovered that high-frequency stimulation in these same areas had similar effects. Since lesions are not reversible and can cause complications, if not properly placed, deep brain stimulation (DBS) has become increasingly common as it causes minimal brain damage, can be adjusted with changes in stimulation and the electrodes can be removed. Today there are close to 100,000 people worldwide with DBS electrodes. The vast majority has been implanted for the treatment of Parkinson's disease and other movement disorders, including essential tremor and dystonia.

DBS is also being tested as a potential treatment for a number of other conditions. These include epilepsy,[9] Tourette's syndrome,[10] motor problems of multiple sclerosis[11] and several others. Within NPNI and BIBS, most research using DBS has focused on mood disorders – depression[12] and obsessive-compulsive disorder (OCD).[13] The rationale behind this is a growing body of evidence that these disorders are related to dysfunctions of networks of neurons involving the prefrontal cortex,[14-16] much like the symptoms of Parkinson's disease are related to networks involving the motor cortex.

Researchers do not yet agree on the best target for treating depression with DBS. A group from Butler Hospital and the Providence Veterans Affairs Medical Center has focused on an area deep in the forebrain that includes the ventral portion of the anterior limb of the internal capsule and the adjacent striatum (VC/VS). In 2009 they reported that about half of a group of 15 patients with refractive major depression benefitted from DBS in this region with no adverse effects.[12]

Of those who responded, all showed significant improvement in standard mood-rating scales and about 40% were in remission when last examined (up to 4 years postoperatively). In comparison, others have stimulated the medial

surface of the cortex in an area known as the sub-callosal cingulate gyrus (area 25) – also part of the mood disorder circuitry – and they report similar benefits.[17]

Efforts are also underway to evaluate the effectiveness of DBS in the VC/VS for treating severe, unresponsive OCD. In a recent multi-center study, about two-thirds of patients responded positively to treatment for 12 months.[13] When the stimulation was interrupted, the responders quickly fell into a severely depressive state, which was reversed when the stimulation resumed.

The reason that some patients do not respond to stimulation is not understood, although it is presumed to be related to the placement of the stimulating electrode. This is currently being addressed by a large multi-institutional team, including researchers from Brown, Harvard, the University of Rochester, the University of Pittsburgh and the University of Puerto Rico, that is supported by a grant from the National Institute of Mental Health. They are studying the neural mechanisms that underlie DBS stimulation and the cortical networks that are associated with OCD with the expectation that the results will reveal more effective targets and stimulus parameters.

The use of DBS to treat Alzheimer's disease has also received attention recently. Lozano and colleagues[18] stimulated the fornix and hypothalamus in a patient who was part of a study using DBS to treat obesity and observed that stimulation invoked memories. This led to a preliminary study of six patients with early-stage symptoms of Alzheimer's disease. Of the six, two showed improved function on standard memory tests for a year. The performance of a third patient was unchanged although it would normally be expected to get worse during this period. The other three patients continued to worsen as typical Alzheimer's patients do. This study lacked controls but was suggestive of positive cognitive benefits from DBS.

Based on these preliminary results, a phase 1–2 clinical trial is now underway to test safety and efficacy in 20–30 patients. Rhode Island and Butler Hospitals are collaborating as one of the sites. Surgery is being done at Rhode Island Hospital and testing is being conducted at Butler. In this one-year trial, only half of the patients will be stimulated and neither the patients nor the testers will know who was stimulated until the end of the trial. After the results are known, all patients will have the option of turning on their stimulators if they want. This study design will greatly mitigate placebo effects and investigator bias.

DBS shows great promise for a number of conditions. However, DBS is an invasive surgical technique that comes with small risks for bleeding and infection. It is also expensive. NPNI and BIBS researchers are exploring other techniques to stimulate the brain non-invasively and inexpensively. These techniques include transcranial magnetic stimulation (TMS) and transcranial direct or alternating current stimulation (tDCS or tACS). All involve the excitation or inhibition of brain activity by passing a current outside the head. TMS uses a strong magnetic pulse, placed next to the skull, to induce an electric current in the adjacent cortical surface. TDCS and tACS apply a direct (tDCS) or alternating (tACS) current to the scalp, which causes subtle changes in the activity of the underlying region of the cerebral cortex. The equipment required for all three is relatively inexpensive and can be used on patients by trained technicians. All of these techniques have been shown capable of affecting mood[19] and compulsions.[20]

In 2008 the FDA approved TMS as a treatment for severe, intractable depression and all three stimulation techniques are being actively explored for a variety of other applications by research teams at the Center for Neurorestoration and Neurotechnology at the Providence VA Medical Center. Disorders being studied include OCD, Post Traumatic Stress Disorder and chronic pain. In addition, evidence suggests that TMS and tDCS may enhance plasticity in the cortex. Thus, this research team is also investigating the possibility that stimulation could be used to enhance the benefits of rehabilitation therapy following stroke or other forms of brain injury.

SUMMARY

Researchers in NPNI and BIBS are collaborating on all of the efforts described above. They are located at different institutions in Providence, including Brown University and hospitals affiliated with Brown's Alpert Medical School. They are members of teams that are using neurotechnology to develop novel treatments for patients suffering with a wide variety of neurological and psychiatric disorders. This area of research demands coordination and collaboration between clinicians, neuroscientists, engineers, mathematicians and computer scientists. It is also an area where Providence already stands out on the world stage and is poised to expand its prominence.

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Authors

John A. Robson, PhD, is Administrative Director, Norman Prince Neurosciences Institute, Rhode Island Hospital, and Associate Director, Brown Institute for Brain Science, Brown University.

R. John Davenport, PhD, is Associate Director, Brown Institute for Brain Science, and Adjunct Assistant Professor of Neuroscience, Brown University.

Disclosures

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Correspondence

John A. Robson, PhD
Administrative Director
Norman Prince Neurosciences Institute
Rhode Island Hospital
593 Eddy Street
Providence, RI 02903
401-793-9132
john_robson@brown.edu

The Brown University Traumatic Brain Injury Research Consortium and the Norman Prince Neurosciences Institute

JEFFREY ROGG, MD; HEATHER SPADER, MD; BETHANY J. WILCOX, BS; ANNA ELLERMEIER, MD; STEVE CORREIA, PhD; ADAM CHODOBSKI, PhD; JOANNA SZMYDYNGER-CHODOBSKA, PhD; NEHA RAUKAR, MD; JASON T. MACHAN, PhD; JOSEPH J. CRISCO, PhD; W. CURT LAFRANCE, JR, MD, MPH, FOR THE BROWN UNIVERSITY TRAUMATIC BRAIN INJURY RESEARCH CONSORTIUM*

ABSTRACT

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).

KEYWORDS: Traumatic brain injury (TBI), concussion, biomechanics of head impact

INTRODUCTION

Traumatic brain injury (TBI) has become a health issue of major concern in recent years due to increasing numbers and evidence of long-lasting effects. Between 2000 and 2012 the US military reported more than 250,000 cases of TBI[1] whereas, in the civilian population, there are an estimated 1.7 million cases per year, most of which are classified as mild TBI (mTBI) or concussion.[2]

The Brown TBIRC was established in 2012 at Rhode Island Hospital (RIH) under the NPNI umbrella, uniting basic and clinical neuroscience researchers at RIH, Providence Veterans Affairs Medical Center, Butler Hospital, the Brown Institute for Brain Sciences and Alpert Medical School of Brown University. Members of the consortium consist of a diverse group of clinician scientists (including the Departments of Neurosurgery, Neurology, Psychiatry, Neuroradiology, Emergency Medicine, Orthopedics and Neuropsychology), biomechanical engineers, biostatisticians and basic neuroscientists. TBIRC members are conducting studies to better understand the mechanisms of brain injury, to find methods to identify features that affect prognosis, and to develop treatments for patients with TBI. Linking clinical neuroscience and public health, members of the TBIRC also serve on the State of Rhode Island Governor's Permanent Advisory Commission on TBI, the Sports Medicine Advisory Committee of the Rhode Island Interscholastic League and have served on the Institute of Medicine's Committee on Sports Related Concussion in Youth. The following describes several of the research projects currently underway.

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Contact sports: Helmets with special sensors allowed researchers to gather data on the strength, number, and direction of blows to the head in contact sports like football. Data from the sensors shows that running backs and quarterbacks suffer the hardest hits to the head, while linemen and linebackers are hit on the head most often.

MECHANISM OF INJURY

Biomechanics of Head Impact

While concussions are a growing health care concern, the mechanism and the basis for prevention and treatment remain poorly understood. Head acceleration after impact is the primary mechanical factor in concussion injury. However, the relationship between the biomechanics of impact and its clinical effect is unknown. The Head Impact Telemetry (HIT) System is an accelerometer-based head impact monitoring device (Simbex, Lebanon, NH) that

allows researchers to record the frequency and severity of head impact sustained by helmeted athletes during play. This provides information toward understanding the biomechanical basis of concussion and repeated subconcussive impacts.

In our approach to understanding the biomechanics of concussions, we have used data collected by the HIT System to quantify *head impact exposure*, a multifactorial term that includes the frequency, magnitude, and location of head impacts. Our objective is to quantitatively measure head impact exposure in contact-sport athletes, in relation to their head impact mechanism. These data are then correlated with clinical outcome.

Previously, we have quantified and reported *head impact exposure* based on player position in collegiate football players.[3] In a subsequent study that evaluated impact associated with clinical concussion, we identified a relationship between type of *head impact exposure* and incidence of concussion.[4] We are now applying this analysis to men's and women's collegiate ice hockey to determine the additional role that gender may play in the athlete's biomechanical tolerance to concussion.

We propose that reducing an athlete's *head impact exposure* is a practical approach for reducing their risk for brain injury.[5] In order to investigate strategies for reducing *head impact exposure*, we developed a tool that synchronized HIT data with game video footage to associate the biomechanics of head impact with specific impact mechanisms (e.g., head contact with the ice in hockey). Using this technique, we have identified the circumstances of play that result in the most frequent or high-magnitude head impact.[6] By quantifying the biomechanics of concussion we have accomplished the first step in understanding concussion injury with practical application to furthering our exploration of early detection and prevention.

CLINICAL SEVERITY ASSESSMENT

Attention Network Task for Acute Concussion Modified

The development of an easily administered, reliable, and valid measure of mTBI-related attention dysfunction was motivated by a need to understand when U.S. military veterans of Iraq and Afghanistan could be safely redeployed to combat after having sustained mild traumatic brain injury (mTBI). One such test would also have clear utility and application to the sports arena where augmentation of current return-to-play guidelines would have expected benefit for preventing severe or chronic brain injury.

In order to achieve this goal, investigators at Brown and the Providence VA Medical Center have modified the computer-administered Attention Network Task (ANT),[7] a well-established visual flanker task, to serve as a screening measure for changes in attention during the acute and near-term post-acute period following mTBI. The modified ANT (mANT) includes distracting sounds (e.g., beeps, buzzes) paired with visual stimuli. The sounds are intended to magnify mTBI-mediated attention dysfunction in military, sports, or other highly stimulating situations.

The ANT is a computer task designed to evaluate alerting, orienting, and executive aspects of attention. It requires the participant to rapidly determine the left-right direction of a central arrow surrounded by congruent or incongruent flankers (e.g., ← ← ← ← ← or ← ← → ← ←).The arrows are preceded either by no cue, an alerting cue or an orienting cue (indicating where the arrows will appear). Prior studies show reduced reaction times (RT) for congruent compared to incongruent arrows, alerting cue compared to no cue, and orienting cue compared to alerting cue.[5]

Using mANT, an initial validation study in 20 healthy young adults tested the hypothesis that RT would be longer and accuracy poorer for sound vs. no sound conditions.[8] However, results showed faster RT for sound compared to no-sound conditions with no differences in accuracy. This unexpected result could be due to additional alerting from the second sensory channel (auditory) since the sounds were designed to occur slightly (400 ms) before the visual presentation of the arrows.

This result raised the question of whether the RT enhancement effect of positive sound conditions would be attenuated following mTBI, and thereby serve as a potentially rapid, easily applied measure of post-concussion disability. Early application of this technique to Brown football players diagnosed with sports-related mTBI where mANT was performed within 72 hours of injury showed that the RT advantage for sound compared to no-sound conditions was significantly smaller for the mTBI group compared to the control group. There were no significant group differences in accuracy. These results provide limited initial support for the mANT as a sensitive measure of acute mTBI.

EFFECT OF CONCUSSION ON THE YOUNG DRIVER

Participation in high school and collegiate sports is on the rise, with more than 7 million high school students participating in 2005–2006 and almost 385,000 collegiate students participating in 2004–2005.[9] Concussions represented 11.6% of all high school athletic injuries and 5.8% of all collegiate athletic injuries.[10] Concurrently, novice drivers have the highest crash rate per miles driven of any age group, and it is not until age 25 that the rate starts to approach the rate seen throughout most of adulthood.[11]

The combination of inexperience and developmental and structural risk factors contribute to the statistic that motor vehicle collisions are a leading cause of death in this age group in both boys and girls.[11] Young drivers exhibit diminished ability to judge risk and inhibit impulses, have increased distractibility, and an increased propensity towards risky behavior.[11] During the post-concussive phase, there is evidence of a reduction in visual memory, reaction time, impulse control composite score and processing speed.[12] All of these brain functions are used during the act of driving.[13]

It was purported that during the acute post-concussive period, these alterations will translate to deficits in driving ability. In an Australian study, concussed adult drivers demonstrated impaired hazard perception when compared to non-concussed aged matched controls.[14,15]

We conducted a pilot research study that enrolled male and female collegiate hockey players from Brown University. The athletes underwent pre-season ImPACT testing, Trail-Maker B (TM-B) and Driving Simulator testing. TM-B is an assessment tool that provides information about visual search speed, scanning, speed of processing, mental flexibility, as well as executive functioning. It is also sensitive to detecting several cognitive impairments. Following concussion, the athletes repeated both the Driving Simulator and TM-B within 48 hours and then serially until their symptom score and ImPACT tests normalized. Early results of comparison of preseason testing with concussed testing identified deficits in both the Trail-Maker B and the Driving Simulator sections.

Our intention is to expand our study population to include both high school and additional college athletes in order to better inform driving recommendations for our young drivers who have sustained mild traumatic brain injury.

ASSESSMENT OF MORBIDITY AND PROGNOSIS

Inflammatory Biomarkers for Mild Traumatic Brain Injury

Mild TBI or concussion, which represents the majority of TBI cases, is increasingly being recognized in adolescents,[16] and the associated morbidity can be significant in this age group. A substantial subset of these children has delayed recovery, resulting in the loss of productivity and psychosocial distress.[17] Compared to adults, adolescents are more susceptible to repetitive injuries and post-concussion syndrome (PCS). Currently, there is no established method for predicting the recovery period and determining the optimal treatment for individual mTBI patients. Certain patient characteristics or symptoms observed at admission appear to be predictive of PCS.[18] However, more objective measures would improve clinicians' ability to provide prognostic information and potentially guide therapy.

There has been a considerable interest in identifying serum biomarkers that would allow for diagnosis and prognosis in neurotrauma. However, defining such biomarkers for mTBI has been particularly challenging.[19] Among the potential biomarkers S100B, a predominantly astrocyte-derived protein, has been extensively studied but demonstrates low sensitivity and specificity as a biomarker for mTBI. Neuronal proteins, such as neuron-specific enolase, ubiquitin C-terminal hydrolase-L1, cleaved tau protein, and αII-spectrin breakdown product of 145 kDa, were also found to have significant limitations as serum biomarkers in mTBI. It has been generally assumed that the levels of serum biomarkers should reflect the magnitude of damage of neural tissue caused by injury. However, the extent of damage of neural tissue in mTBI is likely to be quite limited, which may explain the low sensitivity of serum biomarkers that have been studied. We are pursuing an alternative approach to identify proteins that are produced in the brain but whose serum levels would reflect functional changes in brain parenchymal cells rather than the cellular damage resulting from injury.

Our studies involve both pediatric (adolescent) and adult populations of mTBI patients, and include control groups of patients with long-bone fractures and healthy volunteers. These investigations focus on inflammatory biomarkers. Although the pathophysiological processes accompanying mTBI/concussion are not fully understood, studies in animal models of mTBI suggest that neuroinflammation plays a significant pathophysiological role in mTBI.[20] In this context, it is also important to note that the immature brain likely exhibits a much stronger inflammatory response to injury than the adult central nervous system.[21] There is ample evidence of adverse effects of neuroinflammation on various aspects of brain function, which are highly relevant to mTBI and PCS. Neuroinflammation has a detrimental effect on neurogenesis, learning and memory, and appears to play a part in the pathophysiology of depressive disorders. Our preliminary observations stress the importance of how the collected blood samples are processed. While the serum levels of circulating proteins are commonly assessed, the coagulation process involved in harvesting serum may liberate some proinflammatory mediators that are carried by circulating leukocytes or bound to Duffy antigen receptors expressed on erythrocytes.[22,23] For example, we have found that the serum levels of CXCL1, a neutrophil chemoattractant, are considerably higher than those measured in plasma. This indicates that some published data should be evaluated with caution. Our studies have nearly completed enrollment. If our hypothesis is correct, the results may have prognostic potential for mTBI, may assist clinicians in tailoring recommendations to patients, and may provide the mechanistic basis for new therapeutic approaches in mTBI patients.

NOVEL MRI FINDINGS IN COLLEGIATE ATHLETES WITH MILD TRAUMATIC BRAIN INJURY

A team of clinical neuroscientists, radiologists, statisticians and brain imagers at RIH and Brown University is investigating the utility of routine, advanced and novel MR imaging sequences in collegiate athletes for identifying early features that define subjects at risk for long-term sequelae of mTBI. In addition, we are studying subacute functional and microstructural brain MR changes that may correlate with the quality and severity of long-term post-mTBI disability.

To investigate this question we have designed a research trial that enrolls scholastic athletes with sports-related concussion (Glasgow Coma Scale[24] of 13-15). 3T-MR imaging is performed at Brown University or RIH within 72 hours of concussion and then repeated three months later. The MR imaging protocol includes standard clinical sequences that

measure brain anatomy and edema, (T1 (MPRAGE), FLAIR), as well as newer imaging techniques with improved sensitivity to very small quantities of brain hemorrhage (SWI), white matter tract integrity (DTI) and cerebral blood flow (ASL). A novel imaging sequence, developed by researchers at Brown, for quantification and localization of brain myelin (mcDESPOT[25]) is also included in the research trial. Athletes enrolled in the study also complete post-concussive symptom surveys at each imaging time point, and at one month following concussion.

The preliminary findings of routine MR imaging have paralleled existing concussion literature. Standard T1 and FLAIR routine imaging sequences, even at 3T appear insensitive to the effects of mild traumatic injury and appear to be of little diagnostic value.[26] The high sensitivity heme sequence (SWI) identified punctate deep white matter hemorrhage in a small group of subjects. Although present in subjects with severe acute subjective symptoms, this finding did not affect treatment decision-making or affect long-term outcome.

The early data supports a potential role for cerebral blood flow (CBF) analysis imaging, suggesting regionally altered CBF in the acute post-injury state. Of note, limited recent literature has also identified early-altered CBF in deep grey matter structures following mTBI.[27] We plan to assess the utility of this finding for predicting long-term clinical and structural sequelae.

DTI findings have thus far been consistent with existing literature that demonstrates decreased white matter tract integrity (FA values) in frontal and mesial temporal lobe structures susceptible to head injury, such as the uncinate fasciculus and genu of the corpus callosum.[28] The relevance of these microstructural changes to long-term clinical sequelae is currently being explored.

The preliminary findings of disordered myelin content revealed by mcDESPOT in the chronic post-injury phase have been significant and unexpected. With further exploration using this technique in a larger study population, we hope that it will demonstrate utility for identifying sites of microstructural brain injury, and for furthering our understanding of myelin repair and its potential impact on long-term disability.

INFLUENCE OF COMORBID DISORDERS AND POSSIBLE TREATMENTS FOR PATIENTS WITH MTBI

A focus of study in the RIH division of neuropsychiatry and behavioral neurology is the relationship between mTBI seizures, and psychiatric comorbidity. Patients with mTBI have seizures that are not always epileptic. In fact, mTBI appears to be a significant risk factor in patients with psychogenic nonepileptic seizures (PNES), and is associated with increased psychiatric co-morbidity, symptom severity, poor functioning and increased disability.

In a study that compared patients with PNES and TBI to those without TBI, we found that 45% of patients with PNES also had TBI, and 73% of those TBIs were mild TBI.[29] The study revealed that if a patient had both PNES and TBI, the combination resulted in 2.75 odds increase of having posttraumatic stress disorder (PTSD) and triple the odds increase of having a history of trauma abuse. This finding illustrates the importance of the 'double hit' of emotional and physical traumatic experiences that may occur with abuse or a head injury, commonly found in the PNES population.

This study shows that TBI and PNES are significantly associated with a cluster of diagnoses including depression and PTSD, personality, or trauma and abuse history, all of which may affect functioning. Developing appropriate protocols to more accurately diagnose these patients is the first step to ensure proper care.

The neuropsychiatric approach to brain-behavior disorders research is being applied to other studies discussed in this article, including a pilot study of neuroimaging, cognitive measures and psychiatric symptoms in college athletes who sustained concussion. Given the significant numbers of veterans with TBI,[30] a study proposal of mTBI diagnosis and treatment in veterans at the Providence VA Medical Center has been recently submitted. Ultimately, the goal of the division of neuropsychiatry is to develop prevention strategies and clinical treatments for patients with mTBI.

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Authors

Jeffrey Rogg, MD, is Associate Professor, Department of Diagnostic Imaging at the Warrren Alpert Medical School of Brown University where he is the Director of Neuroradiology.

Heather Spader, MD, is Chief Resident in the Department of Neurosurgery at the Warren Alpert Medical School of Brown University.

Bethany J. Wilcox, BS, is a PhD candidate working in the Bioengineering Lab directed by Joseph J. Crisco, PhD, Professor, Department of Orthopaedics at The Warren Alpert Medical of Brown University.

Anna Ellermeier, MD, is a Third-year Resident in the Department of Diagnostic Imaging at the Warren Alpert Medical School of Brown University.

Steven Correira, PhD, is Assistant Professor, Department of Psychiatry and Human Behavior, based at the Providence VA Medical Center.

Adam Chodobski, PhD, is Associate Professor, Department of Emergency Medicine, Warren Alpert Medical School of Brown University, where he is Director of Neurotrauma and Brain Barriers Research.

Joanna Szmydynger-Chodobska, PhD, is Assistant Professor of Emergency Medicine (Research), Emergency Medicine.

Neha Raukar, MD, is Assistant Professor, Department of Emergency Medicine, Warren Alpert Medical School of Brown University, where she is Director of the Division of Sports Medicine.

Jason T. Machan, PhD, is Assistant Professor in the Department of Orthopaedics (Research) at the Warren Alpert Medical School of Brown University, where he is in charge of the Rhode Island Hospital Biostatistics Core.

Joseph J. Crisco, PhD, is the Henry F. Lippitt Professor of Orthopedics in the Department of Orthopaedics at The Alpert Medical School of Brown University.

W. Curt LaFrance, Jr., MD, MPH, is Assistant Professor, Departments of Psychiatry and Neurology (Research) at the Warren Alpert Medical School of Brown University, Director of the Rhode Island Hospital Division of Neuropsychiatry and Behavioral Neurology and Staff Physician at the Providence VA Medical Center

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Correspondence

Jeffrey Rogg, MD

Department of Diagnostic Imaging, Rhode Island Hospital

593 Eddy Street, Providence, RI 02903

401-444-5184

jrogg@lifespan.org

Advances in Stroke Over the Past Decade

BRIAN SILVER, MD

ABSTRACT

Over the last decade, a number of advances in the care of stroke and TIA patients have been made. These advances include prevention, acute management, and recovery. Some of this work has occurred in Rhode Island. This review will focus on the revised definition of stroke and TIA; short-term risk of TIA; rapid management of TIA; targeted use of medication and lifestyle changes; monitoring for atrial fibrillation; novel anticoagulants for atrial fibrillation; a better understanding of the limitations of intra-arterial therapy for acute ischemic stroke; clinical treatment trials for intracerebral hemorrhage; and the use of robotic, magnetic, and chemical interventions to improve function after stroke.

KEYWORDS: Stroke, TIA, risk factors, acute intervention, recovery

INTRODUCTION

In this brief review, some of the advances in stroke over the past decade will be reviewed. Of note, many of these advances occurred as a result of work done here in Rhode Island.

DEFINITION OF STROKE AND TIA

The definitions of stroke and transient ischemic attack (TIA) have evolved over the last decade. The term TIA was first used in the 1960s to designate a presumed ischemic neurologic event from which a complete recovery occurred in under 24 hours. In 2002, a panel of experts proposed a new, tissue-based, definition of TIA: "a brief episode of neurological dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction." In 2009, the American Stroke Association proposed a modification of that definition which eliminated time altogether and also included spinal cord ischemia as follows: "a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction (on neuroimaging)."[1]

The basis for the change in these definitions comes from research over the last decade. Among 19 studies of 1,117 patients with the time-based definition of TIA, the rate of positive findings on diffusion-weighted imaging (DWI) was 39%.[1] DWI is an MRI sequence sensitive to the diffusion of water molecules. During acute ischemic stroke, there is a restriction of the normal Brownian movement of water which manifests as brightness on DWI. The longer the event, the more likely DWI will be positive. Nevertheless, short-lasting events can also result in a positive DWI. As imaging technology evolves, smaller areas of suspected tissue damage will also become apparent, further increasing the percentage of patients who are reclassified as having had a stroke. Indeed, it is possible that all such events cause some tissue damage and would be obvious if we had the capability of performing non-invasive microscopic imaging.

Brian Silver, MD

SHORT-TERM RISK AFTER TIA AND ITS MODIFICATION

Though it was well known that stroke carried a substantial risk of recurrence, it was not until a study in 2000 that the high short-term risk of TIA became apparent.[2] In that study, which used the 24-hour definition of TIA, approximately 10% of patients returned with stroke within 90 days, half within the first 48 hours. Patients in that study did not have

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Robotic training enhances arm motor recovery after stroke.

urgent evaluation or treatment. A risk-stratification model called ABCD2 was then developed which allocated points for presenting variables (age, blood pressure at presentation, clinical symptoms, duration, diabetes).[3] The range of scores is 0-7 with higher scores being associated with greater risk.

The finding of high risk of stroke following TIA led to clinical studies evaluating urgent intervention. The first study, called SOS-TIA, and conducted in France, evaluated an urgent management program including rapid carotid imaging, rhythm monitoring, carotid revascularization when appropriate, anticoagulation when appropriate, and lipid management.[4] Compared with the expected rate of stroke (based on ABCD2 risk stratification), the authors found an approximate 80% reduction in risk. Simultaneously, the EXPRESS study, conducted in England, using a before-and-after design, found a similar 80% reduction in stroke recurrence using a rapid evaluation and treatment program.[5] A 2012 study from Australia demonstrated a 1.5% risk of stroke at 90 days in patients with TIA who had all investigations and management conducted in the emergency department.[6] The expected rate, based on the ABCD2 scheme, was 10%.

On the basis of these findings, Rhode Island Hospital developed a TIA unit in the emergency department in March 2013. The rate of stroke at 7 days, based on telephone contact, has been less than 1% to date.

LONG-TERM RISK MODIFICATION

INTERSTROKE was a landmark case-control study which matched 3,000 stroke patients with 3,000 controls in 22 countries.[7] The authors found that 10 risk factors were associated with 90% of all stroke [hypertension, current smoking, increased waist-to-hip ratio, poor diet, physical inactivity, diabetes mellitus, excessive alcohol intake, psychosocial stress and depression, cardiac causes and abnormal ratio of apolipoproteins B to A1. The authors concluded that interventions that targeted these factors could substantially reduce the burden of stroke. The newly formed School of Public Health at Brown University will focus on initiatives at improving risk factors that lead to cardiovascular disease. A recent study by Wing and colleagues at Brown University found that the addition of intensive lifestyle changes (diet and exercise) did not reduce the rates of death, stroke, or myocardial infarction compared with medication use alone.[8] However, those assigned to intensive lifestyle changes used less medication.

Additional advances in the last decade include the observation that longer heart rhythm monitoring leads to an increased detection of atrial fibrillation. In a Canadian study which randomly assigned patients to Holter monitoring versus 30 day monitoring in patients with cryptogenic stroke, detection rates of atrial fibrillation were 3% and 16%, respectively.[9] What is unclear is what duration of atrial fibrillation on these monitors confers increased risk. For example, does a 20-second episode of atrial fibrillation during 30 days of monitoring suggest increased risk requiring anticoagulation? The standard definition of paroxysmal atrial fibrillation is at least 30 continuous seconds of the abnormal rhythm. Further study will be required to determine prognosis and optimal medical treatment. There are now many options for anticoagulation for patients with atrial fibrillation including vitamin K antagonists (warfarin), direct thrombin inhibitors (dabigatran), and factor Xa inhibitors (apixaban, rivaroxaban).[10] These agents can be expected to reduce the risk of embolism by approximately 60%-70% relative to no treatment and approximately 40%-50% relative to aspirin. Individualized determination of risk can be accomplished with the CHADS2 and CHA2DS2Vasc scoring systems.[11] Specific risk assessment for neurovascular processes may be helpful in shared decision-making processes, with careful attention to presentation format.

At this time, there does not appear to be a role for anticoagulation in intracranial atherosclerosis, cervical arterial dissection, or patent foramen ovale (PFO)-related stroke. Recurrence risk of stroke is highest with intracranial atherosclerosis (approximately 12% per year) and much lower with PFO-related stroke (approximately 1%–2% per year), and cervical arterial dissection (3% in the 12 months after ictus). In addition, interventional approaches do not appear to mitigate risk in these conditions, and even if subgroup analyses suggest benefit, the absolute reduction is very small (less than 1%) with an increased risk of procedure-related complications.

ACUTE INTERVENTIONS

Despite the wide use of intra-arterial procedures for the treatment of acute stroke, definitive evidence of overall benefit is lacking at this time. Three trials failed to show net benefit for intra-arterial therapy added to intravenous thrombolytic therapy within 3 hours (IMS III), intra-arterial compared to intravenous therapy within 4.5 hours (SYNTHESIS), and imaging-guided intra-arterial therapy compared to placebo within 8 hours (MR RESCUE).[12] Post-hoc analyses suggest that there are subgroups which may benefit. The most important variable is time to treatment. There is a strong correlation between time to intra-arterial recanalization and outcome.[13] Further, the completeness of recanalization at earlier time points is also important.[14] Because approximately 2 million neurons, 14 billion synapses, and 7.5 miles of myelinated fibers are lost every second during a large vessel ischemic stroke,[15] recanalization at late time points may only serve to perfuse already destroyed tissue, analogous to putting out a fire after a house has already burned down.

Intracerebral hemorrhage carries a worse prognosis than ischemic stroke yet an acute treatment which improves outcome remains elusive. Potential promising interventions include rapid control of blood pressure and targeted removal of clot. The INTERACT2 study failed to show a statistically significant benefit in favor of rapid blood pressure reduction

below a target of 140 mmHg systolic within the first 6 hours of bleeding but sample size may have precluded detection of benefit.[16] The ongoing ATACH-II study,[17] which is also evaluating rapid reduction in blood pressure to less than 140 mmHg systolic should yield a definitive answer on the question of blood-pressure reduction, particularly when data are pooled with INTERACT2.

Another intriguing option for the treatment of intracerebral hemorrhage is thrombolysis-assisted clot evacuation. The procedure consists of creation of a burr hole ipsilateral to the bleeding, insertion of a catheter into the center of the clot, injection of tPA into the center of the clot, and then evacuation of the dissolved material. Moreover, the procedure can be performed as late as 24 hours. MISTIE II was a small study which suggested benefit of this procedure with good recovery at one year, reduced length-of-stay in the hospital, and total cost of care.[18] Mortality, however, was not decreased. MISTIE III,[19] the phase III version of the study, will provide a definitive answer on whether this procedure is truly of value in the case of patients with intracerebral hemorrhage.

RECOVERY OPTIONS

Recovery after stroke is an exciting area of research opportunity. The notion that the nervous system was incapable of regeneration was dispelled in the 1990s. Since that time, a number of potential interventions to augment recovery after stroke have been posited. These include robotic, electromagnetic, and pharmacological therapies. Cellular therapy remains an active area of interest but logistical and regulatory issues in the United States have not led to a trial in stroke at this time. In addition, the concept that electrical energy from the brain can be converted to kinetic action through an external device has now become a reality.

Lo and colleagues, from the Providence VA, published a randomized trial of robot-assisted therapy for upper-limb impairment in stroke in 2010.[20] It was the first such study ever published in the *New England Journal of Medicine*. Though the study did not find that robot-assisted therapy was superior to intensive or usual care at 12 weeks, there was a suggestion of benefit over usual care at 36 weeks. Since then, the research group at the VA has continued to explore different robot options for the purpose of augmenting limb recovery.

Hochberg, Donoghue and colleagues from the Brown Institute of Brain Sciences made headlines worldwide with the publication of an article in *Nature* regarding the implantation of a 96-channel microelectrode array that allowed two patients with long-standing tetraplegia to control an external robot arm.[21] In one patient, the arm was used to lift a bottle of coffee to her mouth. Remarkably, the complex robotic arm movements could be controlled by a very small pool of neurons. This groundbreaking research paves the way for next-generation devices that can be controlled through implanted chips.

Multiple studies now suggest that transcranial magnetic stimulation (TMS) may be used to augment both motoric and linguistic recovery after stroke. Of note, excitatory stimulation of the affected hemisphere appears to produce benefit while inhibitory stimulation of the unaffected hemisphere may produce benefit.[22] A transcranial magnetic stimulation device now exists at Butler Hospital and will allow additional study in this area.

Pharmacological therapy, such as fluoxetine and PDE5 inhibitors, are also of potential benefit. The FLAME study suggested that fluoxetine not only improved depression but also improved motor function after stroke.[23] Sildenafil has been shown in young and aged animals to improve neurological outcome though neurogenesis, angiogenesis, and synaptogenesis.[24,25] Preliminary human studies[26] have served as the basis for larger pilot randomized trials.

SUMMARY

Evolving understanding of the concept of cerebral ischemia and recurrent risk has led to improved treatments and short-term outcomes for patients. Large international studies of recurrent stroke have now helped focus the agenda for what needs to be done to lower long-term risk. Beneficial acute treatments of both ischemic and hemorrhagic stroke continue to be defined and many exciting options are now available. Strategies for improving recovery after disabling stroke are now entering an active phase of development. Rhode Island, the Brown Institute for Brain Sciences, and the Norman Prince Neurosciences Institute have the tools and expertise to be leaders in these areas.

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Author

Brian Silver, MD, is Director, Stroke Center, Rhode Island Hospital; Associate Professor of Neurology, The Warren Alpert Medical School of Brown University.

Disclosures

The author reports no conflicts of interest.

Correspondence

Brian Silver, MD
Department of Neurology
110 Lockwood Street, Suite #324
Providence, RI 02903
401-444-8806
Fax 401-444-8781
Brian_Silver@brown.edu

The Rhode Island Consortium for Autism Research and Treatment (RI-CART): A New Statewide Autism Collaborative

ALAN GERBER, MA; ERIC M. MORROW, MD, PhD; STEPHEN J. SHEINKOPF, PhD; THOMAS ANDERS, MD

ABSTRACT

Autism is a neurodevelopmental disorder characterized by core deficits in social interaction, language and repetitive behaviors. The need for services is rising sharply as the number of children identified with autism increases. The Rhode Island Consortium for Autism Research and Treatment (RI-CART) was founded in 2009 with the goal of increasing communication among autism researchers throughout the state and improving treatment for children with autism. RI-CART members have several exciting projects in progress, with its larger aim being the creation of a statewide research registry. A statewide registry would benefit research in Rhode Island and allow for larger collaborations nationally.

KEYWORDS: RI-CART, autism, autism spectrum disorder, registry, Rhode Island

WHAT IS AUTISM?

Autism, usually referred to as an autism spectrum disorder (ASD), is a highly heterogeneous, neurodevelopmental disorder with symptoms that typically appear by the second year of life.[1] The main symptoms include core deficits in social interaction, communication and repetitive and inflexible behaviors.[2] In order to receive a diagnosis of autism, the symptoms must be present by age three, and not be better explained through another developmental disorder. While the genetic underpinnings of autism are not completely understood, it is clear from twin studies that autism is a highly heritable disorder.[3] Recent advances in genetic research have been able to account for between 10%-20% of autism spectrum diagnoses.[4]

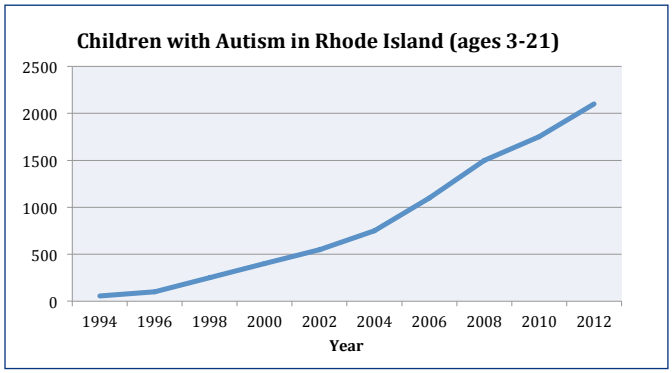
Current estimates indicate that 1 in 88 children have been diagnosed with an autism spectrum disorder, a sharp rise from the prior estimate of 1 in 110.[5,6] Boys receive a diagnosis of autism spectrum disorder at almost five times the rate of girls.[6] Unfortunately, epidemiological work beyond the school years is almost nonexistent. In addition to the difficulties of raising a child with autism, the lifetime costs can be substantial for both families and communities as a whole.[7,8] In order to meet these rising needs, the National Institutes of Health (NIH) has increased federal funding for autism research from $132 million in 2009 to $192 million in 2012 and funding is projected to stay at that level for the next two years.[9]

RI·CART
RHODE ISLAND CONSORTIUM FOR AUTISM RESEARCH & TREATMENT

AUTISM IN RHODE ISLAND

Similar to the national numbers, according to the Rhode Island Department of Elementary and Secondary Education there has been a constant rise in the number of school-age children receiving services for an autism spectrum disorder. (**See Figure 1**.) In the 2011–2012 school year, there were approximately 140,143 children in all Rhode Island schools between preschool and 12th grade. Of those children, approximately 2,099 were receiving support for an autism spectrum disorder, which totaled about 8% of the 24,836 children receiving special education services.[10] If national prevalence estimates can be applied throughout the lifespan, we estimate that there are about 10,000 individuals living with an autism spectrum disorder across the state.[6]

Figure 1. Children with Autism in Rhode Island 1994-2012



WHY RI-CART?

Rhode Island has a proud and impressive history of supporting children and families with special needs. It was the first state to offer a public special education class and among the first to adopt regulations requiring special education in public schools. Additionally, Rhode Island is the nation's leader in identifying special learning needs among its students.[11] Rhode Island is also among the nation's leaders in caring for its children. According to the

U.S. Census, 94% of its children are covered by insurance, which is the 7th best in the nation.[12] Despite increasing uncertainty over health care reform, in 2011 Rhode Island became one of 31 states to mandate that insurance covers autism. Benefits to families include coverage for identification, assessment and treatment of autism spectrum disorders.

VIDEO: Eric M. Morrow, MD, PhD, discusses his genetics and autism research

Rhode Island also has an excellent mixture of demographic factors and a unique population density that make it appealing to researchers. In addition to having a small population of a little over 1 million people, the state is the smallest in the United States by a significant margin, making it conceivable to reach a large percentage of its residents. These qualities reduce the burden for participants, as well as researchers, and reduce a bias to collect data from families who are capable of traveling the farthest for a study. Additionally, Rhode Island's population is remarkably stable and diverse. Its population reflects the racial and ethnic diversity found in the United States. Moreover, according to the U.S. Census, about 56% of its residents were born in Rhode Island, with 97% remaining in the state from year to year.[13]

This combination of demographic factors and progressive thinking has led to a rich history of successful longitudinal studies in Rhode Island such as the New England Family Study,[14] the Neonatal Follow-Up Program,[15] and several long-standing, longitudinal studies in psychiatry, including anxiety, depression, OCD and children born after specific neonatal exposures such as amphetamine. What makes Rhode Island unique is that its numerous hospitals are united by one medical school. Despite its size, Rhode Island contains several well-known research institutions and is a national leader in medical research. Furthermore, its academic, research, and clinical programs have strong relationships with governmental representatives and state agencies such as the Department of Health and the Department of Education. This makes Rhode Island strongly positioned to lead innovative research in autism assessment and treatment.

WHAT IS RI-CART?

In 2009, a small group of interested parties began to meet at Bradley Hospital to discuss autism research and treatment in Rhode Island. As this group of collaborators grew, it became known as the Rhode Island Consortium for Autism Research and Treatment (RI-CART). From the beginning, RI-CART researchers broke barriers by including treatment providers, community agencies, and parent advocacy groups in the discussion. RI-CART has since expanded to include a diverse array of disciplines such as psychologists, psychiatrists, pediatricians, neurologists, geneticists, neuroscientists, epidemiologists, and educators. Members represent many of the institutions throughout the state, including Brown University and its affiliated hospitals, Rhode Island College, the University of Rhode Island, parent advocacy groups (The Autism Project), community programs (The Groden Center, The Neurodevelopment Center, Gateway Healthcare), and the RI Departments of Education and Health. A list of our members can be found on our website.[16] The group continues to search for further collaborators throughout the state.

This issue of the *Rhode Island Medical Journal* discusses the exciting contributions of the Norman Prince Neurosciences Institute to neuroscience and brain research. This model of cooperation across disciplines for a common goal directly mirrors the aims of RI-CART members. The Norman Prince Neurosciences Institute (NPNI) at Rhode Island Hospital and the Brown University Institute for Brain Science (BIBS) are spearheading an effort to bridge basic and clinical neuroscience research and bring laboratory discoveries to the bedside. RI-CART is thrilled to be a partner in their focus on neurodevelopmental disorders and brain development.

What are RI-CART's Goals?

RI-CART members believe that the best way to improve the lives of children with autism spectrum disorder and their families is to improve and expand knowledge of these disorders. We believe that this needs to be accomplished through collaboration between all invested parties. Thus, RI-CART members are united by three overarching goals:

1. To foster research directed at improving treatments and a better understanding of the basic mechanisms of autism spectrum disorders.
2. To enhance communication among parents, educators, and researchers throughout Rhode Island.
3. To use data-driven advocacy and education to inform state health and education programs about the special needs of this population.

RI-CART Research Projects

RI-CART members have several noteworthy projects underway that will help to shed light on the complexities of autism. One of the first funded RI-CART research projects is a study of barriers to health care and potential improvements to care in an adult population with autism. This project is directed by Dr. Henry Sachs of Bradley Hospital and currently funded by the Rhode Island Foundation. Typically, when a person with an intellectual or developmental disability turns 21, their access to state and federal benefits becomes highly restricted, making this a transition marked

by difficulty. Research has demonstrated that adults with intellectual and developmental disabilities have greater medical needs and decreased access to health care than the general population.[17,18] The autism literature has generally focused on school-age children, ignoring the large number of adults, making this a vital project. One previous study that focused on the experiences of adults with autism in accessing health care reported that adults with autism experienced significantly less satisfaction with patient-provider communication, as well as significantly higher odds of unmet physical and mental health care needs. This study utilized online survey methods adapted to facilitate the inclusion of adults with autism; however, researchers were unable to reach populations that were not able to use a computer.[19] In the current study, researchers are working together with community institutions and families to conduct interviews and examine medical records of adults with autism to further investigate barriers to health care and possible solutions for this population.

Another currently funded project is the Rhode Island Multi-site Genetic Study of Autism and Intellectual Disabilities. This project is directed by Dr. Eric Morrow and currently funded by the Simons Foundation for Autism Research Initiative (SFARI), representing a collaboration with the third largest national funding agency for autism research.[20] While research has clearly demonstrated that autism spectrum disorders have a strong genetic component,[4] the utility of clinical testing requires a great deal more research.[21] Dr. Morrow's laboratory uses genome-wide strategies to identify genes involved in autism spectrum disorders. This research will contribute to the advancing understanding of the complex genetic underpinnings of autism spectrum disorders with the long term goal of improving diagnosis and treatments. Other complementary projects to examine the role of gene-environment interactions are also planned and follow-up projects that build on this initial SFARI-funded project are likely.

Future projects will be enabled through the creation of a statewide research registry. This model is drawn from other pediatric illness, such as pediatric cancers, where all patients in major centers were enrolled in clinical treatment trials. This approach has subsequently led to a number of curative treatments for cancers that previously carried a very high mortality rate. RI-CART's aim is to enroll all individuals in Rhode Island with an autism spectrum disorder diagnosis into this registry. Participants will be evaluated using the Autism Diagnostic Observation Schedule (ADOS), a clinical interview considered the gold standard of autism assessment. Registrants and their immediate family members will also be invited to provide biological samples for genetic, stem cell, and environmental exposure studies. The registry data will be stored on a secure web-based platform where de-identified data may be shared with qualified investigators in the future. The implementation of further research will be augmented by the existing ADOS assessments and genetic data already collected.

In the near future, RI-CART plans to welcome an education specialist and a parent liaison to its staff and increase the number of clinicians conducting the ADOS assessment. Families will benefit from participation in RI-CART by virtue of receiving state-of-the-art autism assessments as well as long-term access to RI-CART staff and expertise. These efforts will allow us to provide an infrastructure of support for families in a range of domains, working collaboratively with community service providers and educators. Ultimately, RI-CART members have several larger goals as part of our long-term aims. These include the first complete statewide study of autism, large scale genetic and epidemiological studies, the ability to provide high-quality targeted treatments to people with autism spectrum disorders and their families as well as potential collaborations with the National Database for Autism Research (NDAR) and Interactive Autism Network (IAN).

SUMMARY

Despite the rising rates of autism in Rhode Island and across the United States, there is reason for optimism. Through its unique multi-disciplinary approach that allows for wide collaborations among all interested parties in the state, RI-CART will serve as a national model for biomedical and treatment research. RI-CART members are already making strong progress towards our goal of improved communication throughout the state and are working hard towards improving the lives of children with autism as well as their families.

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Authors

Alan Gerber, MA, is a Clinical Research Assistant at Bradley Hospital.

Eric M. Morrow, MD, PhD, is an Assistant Professor in Brown University's Departments of Biology, and Psychiatry & Human Behavior. He is also the director of the Developmental Disorders Genetics Research Program at Bradley Hospital.

Stephen Sheinkopf, PhD, is an Assistant Professor in Brown University's Department of Psychiatry & Human Behavior.

Thomas Anders, MD, is an Adjunct Professor in Brown University's Department of Psychiatry & Human Behavior. He is also a Senior Research Scientist at Bradley Hospital.

Disclosures

The authors report no conflict of interests.

Correspondence

Alan Gerber, MA
Bradley Hospital
1011 Veterans Memorial Parkway
East Providence, RI 02915
401-432-1624
Fax 401-432-1607
Agerber@Lifespan.org

HPV Knowledge and Vaccine Acceptance in an Uninsured Hispanic Population in Providence, RI

JEFF CHAU, FARZANA KIBRIA, MACAYLA LANDI, MELISSA REILLY, TANIA MEDEIROS, MPH; HEATHER JOHNSON, MLIS; SHAHLA YEKTA, PhD, MPH; ANNE S. DE GROOT, MD

ABSTRACT

The Food and Drug Administration has approved two human papillomavirus (HPV) vaccines for use by men and women in the United States. The vaccines not only protect against HPV infection, but also reduce the risk of cervical cancer in women. Despite the widespread availability of these vaccines, vulnerable populations such as those with low incomes have been reported to have limited access to and knowlege about HPV vaccines. In order to evaluate and improve HPV vaccination uptake in a population of uninsured, low-income Spanish-speaking individuals attending a free clinic in Rhode Island, we administered a questionnaire regarding knowledge, attitudes, and practices (KAP) and performed an education intervention. We found that knowledge of HPV infection and cervical cancer among the patients sampled was low when comparing Hispanics to non-Hispanics (47.2%, 85.7%, respectively) but willingness to vaccinate oneself or one's child was very high after a brief video-based intervention.

KEYWORDS: HPV, HPV vaccine, Hispanic, Uninsured, Free Clinic

INTRODUCTION

HPV is the most common sexually transmitted infection (STI) in the United States (US).[1] Lifetime risk of acquiring at least one HPV strain is above 50% in sexually active individuals. More than 100 strains of HPV have been identified, 40 of which can infect the genital region, thereby causing genital warts and malignancies such as cervical cancer. In the US, an estimated 26,000 cancers are attributed to HPV, and of these, 18,000 occur in women, most commonly as cervical cancers, but also as cancer of the anus, vulva, oropharynx, and vagina; the remaining 8,000 cases occur in men as oropharyngeal, anal, and penile cancers.[2] Often, HPV-infected cells are shed within one to two years of onset of infection, thus minimizing the rate of cancer conversion. In 10% of cases, however, the infection can reach the basal layer of cervical tissue and become precancerous or malignant.[3]

Seventy percent of cervical cancer cases are caused by two strains of HPV: Types 16 and 18.[1] In 2006 and 2009, the Food and Drug Administration approved two highly-effective prophylactic vaccines for females aged nine to twenty-six or nine to twenty-five: Gardasil (Merck) and Cervarix (GlaxoSmithKline), respectively. Both vaccines protect against types 16 and 18, but Gardasil, which also received FDA approval for use in males ages nine to twenty-six, also protects against HPV types 6 and 11, the cause of over 90% of genital warts.

The practice of HPV vaccination has significantly reduced the prevalence of HPV infection in the United States. In a study taking place between 2003 and 2010, the incidence of infection among young women, aged 14-19 years old, decreased by 56% from 477 infections in 2003-2006 to 217 infections in 2007-2010.[4] While vaccination is critical in preventing the spread of disease, vaccines can only be effective if accepted and easily available to the population at risk of acquiring disease. One impediment to vaccine uptake is lack of knowledge. Currently, members of at-risk populations (individuals from impoverished and underserved communities) often report low awareness regarding the widespread availability of the HPV vaccine.[5]

In this study, we evaluated the gaps in knowledge of HPV vaccination among low-income, uninsured, and a predominantly Hispanic patient population at a free clinic in Rhode Island through a questionnaire and administered a brief video intervention. The purpose of the questionnaire was to evaluate their knowledge of HPV, HPV vaccination, and cervical cancer and their related attitudes and practices, while the intervention was designed to improve patient health literacy on HPV and inform them of vaccine availability. We found that self-identified Hispanics in our study reported lower rates of STIs, less knowledge of HPV and its link to cervical cancer, and equal willingness to be vaccinated or to vaccinate their children, as compared to non-Hispanic individuals who participated in this study. In addition, we identified a high rate of autonomy with regard to vaccination among all participants who were eligible for vaccination.

METHODS

Study Population

One hundred participants over the age of 17 were recruited between May 2012 and June 2013 from Clinica Esperanza/Hope Clinic (CEHC), a free, urban primary care clinic in Providence, RI. In addition to the primary care clinic, CEHC operates a free walk-in clinic to unaffiliated patients from the surrounding community. CEHC serves a predominantly Hispanic cohort of 2,000 low-income patients, all of whom

are uninsured and most of whom do not speak English as their first language. Seventy-nine percent of CEHC patients are Central and South American immigrants, and 80% of patients at CEHC report having an annual household income of less than $25,000. During the study period, the CEHC population was 67% Hispanic, slightly less than 10% Non-Hispanic White, 8% African American and 67% female.

Study Design

This study protocol was approved by the University of Rhode Island Institutional Review Board. Over a 13-month period, survey administrators (JC, FK, ML, and MR) approached CEHC patients in the clinic's waiting room. These patients were either continuing-care patients or walk-in clients. Patients were recruited at random, and provided either written or verbal informed consent in their preferred language (Spanish or English). Participants anonymously completed an online (computer-based) or paper-based version of the survey in their preferred language in one of the clinic's private rooms. Participants watched a video about HPV and HPV vaccines in English or Spanish midway through the interview. The two-part survey included pre- and post-intervention sections separated by an educational video.

The pre-intervention survey ascertained information regarding participant demographics, sexual history, gynecological history, and incidence and knowledge of STIs, including HPV. Immediately following their completion of the pre-intervention section of the survey, participants viewed a video about HPV and cervical cancer. After watching the brief video ("Cervical Cancer: What is Human Papilloma Virus? (HPV)" by HealthiNation [English] or "Vacuna contra el VPH" by Leopoldo Vaszquez Matute [Spanish]), regarding HPV and cervical cancer, study participants completed the post-intervention section of the survey, which addressed the study participants' knowledge of the HPV virus and of cervical cancer. Study participants were also asked if they had previously been vaccinated against any diseases, including HPV, and their attitude and willingness to vaccinate against HPV. After completing the survey, study participants were given a $10 grocery gift card and (for those participants who were eligible for vaccination), the option to file an application for a free Gardasil vaccine.

Statistical Methods

Descriptive statistics were calculated for all relevant variables. Differences in means between groups were tested using two-tailed t-tests assuming equal variance between two independent samples (significant values are indicated in the data tables with bold font and underline). Study coordinators also used chi square and Fisher's exact test to test for differences in proportions when applicable. The data were analyzed with IBM SPSS Statistics v22.

RESULTS

Demographic Characteristics of the Participants

As shown in Table 1, a greater number of women than men participated in this research study (66% female, 34% male). Thirty-one percent of participants reported their race to be White, 7% Black/African American, 3% Asian, 2% Native Hawaiian/other Pacific Islander, and 57% Other; 73% reported their ethnicity (separate from race) as being Hispanic. The mean age of participants was 39.6 years (SD = 13.4). Of the 90% of individuals who reported information regarding their level of education, 73% of participants reported having completed at least high school. This population did not differ significantly from the overall clinic population.

Gynecological Health Information, Knowledge, and Practices

The survey also contained information regarding age of first

Table 1. Demographic and sexual history characteristics

	Total (N = 100)	Female (N = 66)	Male (N = 34)	Hispanic (N = 72)	Non-Hispanic (N = 28)
Age (Mean Years ± SD)	39.6 ± 13.4	39.2 ± 13.5	40.4 ± 13.3	40.2 ± 12.9	38.0 ± 14.8
Marital Status (% Married)	27.0%	24.0%	32.4%	27.8%	25.0%
Highest Education					
Any Education	90.0%	93.9%	82.4%	88.9%	92.9%
Completed High School	56.2%	51.6%	64.3%	60.3%	46.2%
Some College	10.1%	11.3%	7.1%	9.5%	11.5%
Completed College	31.5%	33.9%	25.0%	28.6%	38.5%
Completed Graduate School	2.2%	1.6%	3.6%	1.6%	3.9%
Sexual Debut					
No Sexual Relations	8.0%	9.2%	6.1%	5.7%	14.3%
Age of Sexual Debut (Mean Years ± SD)*	18.6 ± 3.9	19.1 ± 4.0 (59)	17.7 ± 3.2	18.7 ± 3.9	18.9 ± 3.6 (24)
< 15 Years*	5.6%	3.4%	9.7%	7.6%	0.0%
Between 15 and 18 Years*	55.5%	54.2%	58.1%	53.0%	62.5%
> 18 Years*	38.9%	42.4%	32.4%	39.4%	37.5%
(Lifetime) Sexual Partners (Number ± SD)*	4.2 ± 3.7	3.3 ± 2.7	6.1 ± 4.4	3.6 ± 2.8	5.5 ± 4.8
Ever Experienced Forced Sexual Relations*	9.0%	13.6%	0.0%	5.6%	17.9%
Ever Exchanged Sex for Something	4.0%	6.1%	0.0%	5.6%	0.0%
Money**	50.0%	50.0%	0.0%	50.0%	0.0%
Food**	25.0%	25.0%	0.0%	25.0%	0.0%
Other**	25.0%	25.0%	0.0%	25.0%	0.0%

*Note: Number of respondents for questions with response rates below 90% is reported in parentheses next to the corresponding value. *Of those who reported any sexual relations. **Of those who reported ever exchanging sex for something.*

menstruation, first gynecological examination, and general knowledge of Pap smears (Pap tests). The average age of first menstruation was reported as 12.9 years (SD = 1.7). Of the 51 women who reported having had a gynecological exam, the average age for their first Pap smear was 24.9 years (SD = 8.4). Twelve of the female participants (19.1%) of those who answered this question reported never having been to or having seen a gynecologist, their ages ranging from 20 to 51 years. Nearly 10% of female survey respondents reported that they did not know what a Pap test was. There were no differences between Hispanic and non-Hispanic participants for any of these topics.

Table 2. Knowledge regarding STIs, safe sex practices, HPV, and cervical cancer

	Total (N = 100)	Female (N = 66)	Male (N = 34)	Hispanic (N = 72)	Non-Hispanic (N = 28)
Sexually Transmitted Infections (STI)					
Knows what an STI is	87.0%	89.4%	82.4%	87.5%	85.7%
Knows how to protect against an STI	77.0%	78.8%	73.5%	**70.8%**	**92.9%**
Knows where to get an STI exam	64.0%	75.4%	44.1%	**54.9%**	**89.3%**
Has had an STI	8.0%	7.8%	9.1%	4.4%	17.9%
Don't know	12.0%	10.9%	15.2%	17.4%	0.0%
Safe Sex Practices					
Uses protection during sex	51.0%	50.0%	65.6%	56.7%	52.0% (25)
Knows what "contraception" means	85.0%	93.6%	79.4%	84.5%	92.6%
Have spoken to, or plans to speak to children about safe sex (N = answered)	49.0%	84.6% (39)	72.7% (22)	**76.6%** (47)	**92.9%** (14)
Human Papillomavirus (HPV)					
Knows HPV is an STI	58.0%	62.1%	50.0%	**47.2%**	**85.7%**
Knows that HPV can affect					
Women	86.0%	95.1%	84.9%	91.0%	92.6%
Men	74.0%	82.3% (55)	83.9%	83.6% (61)	92.0% (25)
Adolescent girls	73.0%	90.9% (55)	79.3% (29)	88.7% (62)	81.8% (22)
Adolescent boys	63.0%	80.4% (51)	78.6% (28)	81.0% (58)	76.2% (21)
Cervical Cancer					
Knows HPV can cause cervical cancer	81.0%	81.8%	79.4%	83.3%	75.0%
Don't know	16.0%	13.6%	20.6%	16.7%	14.3%
Knows cervical cancer can cause death in women	78.0%	78.5%	79.4%	80.3%	75.0%
Don't know	20.0%	12.3%	17.7%	15.5%	10.7%
Knows where to get tested for cervical cancer	62.0%	74.2%	38.3%	56.9%	75.0%
Has been tested for cervical cancer*	--	68.2%	--	68.8% (48)	66.7% (18)

*Note: Number of respondents for questions with response rates below 90% is reported in parentheses next to the corresponding value. *Among female participants.*

Knowledge of Sexually Transmitted Infections, HPV, and Cervical Cancer

As shown in Table 2, 87% of participants reported knowledge of sexually transmitted infections (STIs), while 77% reported an understanding of how to protect against such infections. A greater percentage (29.2%) of Hispanics was not aware of measures that could be taken to protect against STIs as compared to non-Hispanics (7.2%). With respect to their knowledge of where to test for STIs, 64% of participants knew where to get an STI exam. Among the 64%, a greater number of females and a greater number of non-Hispanics compared to Hispanics knew where to receive testing (75.4% females, 44.1% males; and 54.9% Hispanics, 89.3% non-Hispanics). When female participants were asked if they knew where to receive cervical cancer screening, 25.8% responded that they did not know where to receive this test. In addition, 31.8% of respondents indicated never having been screened for the disease.

Table 3. Attitudes toward and decision-making regarding the HPV vaccine

	Total (N = 100)	Female (N = 66)	Male (N = 34)	Hispanic (N = 72)	Non-Hispanic (N = 28)
Ever received a vaccination	48.0%	50.8%	44.1%	49.3%	46.4%
Willing to receive HPV vaccine	93.2% (73)	89.8% (49)	91.7% (24)	90.4% (52)	90.5% (21)
Willing to vaccinate child(ren) against HPV	97.3% (75)	96.1% (51)	100% (24)	96.4% (55)	100% (20)
Preferred contact method to receive information about vaccination appointments					
Phone Call	69.0%	69.7%	67.7%	76.3%	50.0%
Email	17.0%	12.1%	26.5%	15.3%	21.4%
Text Message	9.0%	7.6%	11.8%	9.7%	7.1%
Letter	13.0%	12.1%	14.7%	9.7%	21.4%
Other	9.0%	13.6%	0.0%	6.9%	14.3%
HPV Vaccination Decision-Making					
Would decide autonomously to receive vaccine	96.0%	97.0%	94.1%	97.2%	96.4%
Would decide autonomously to vaccinate child(ren)	78.0%	78.8%	76.5%	76.4%	82.1%

Note: Number of respondents for questions with response rates below 90% is reported in parentheses next to the corresponding value.

When participants were asked to describe their knowledge of HPV, a greater proportion of Hispanics than non-Hispanics were unaware of HPV (62.8% vs. 14.3%, respectively). While 24.3% of Hispanics reported knowing one or more causes of cervical cancer, 53.6% of non-Hispanics specified knowing one or more causes of cervical cancer.

Risk Factors for Sexually Transmitted Infections

Ninety percent of study participants reported being sexually active, with about 20% of participants having six or more sexual partners since their first sexual encounter. Of these 90 sexually active participants, 51% reported using a method of contraception during sexual activity (50% females, 65.6% males). Only eight individuals reported having been infected with an STI and 12 participants were not aware of whether or not they have ever been infected with an STI. There were no statistical differences between men, women, Hispanic, and non-Hispanic participants for any of these topics.

This study also sought to evaluate participants' attitudes toward discussing safe sexual practices with their children. Forty-nine percent of participants indicated they have previously spoken with their children, or are planning to do so. Fewer Hispanics (76.6%) than non-Hispanics (92.3%) reported having plans to speak with their children about STIs.

Willingness and Autonomy Associated with Vaccination against HPV

As seen in Table 3, 48% of study participants reported having been previously vaccinated against a variety of diseases such as hepatitis, flu, tetanus, and varicella. Of the 73 individuals who responded during the post-intervention portion of the survey concerning HPV vaccination, 68 (93%) expressed a willingness to receive the HPV vaccine. Hispanic and Non-Hispanic participants were equally willing to be vaccinated (>90%, both groups).

Since many of the study participants were older than the appropriate age for HPV vaccination, study participants were also asked if they would be willing to vaccinate their children against HPV; 97.3% (100% male, 96.1% female) indicated they would be agreeable to vaccinating their children against the disease. Nearly all study participants (96%) indicated they would autonomously decide whether to receive the HPV vaccine. The same study participants noted that, with respect to their children, 22% would allow their children to make the decision autonomously.

DISCUSSION

When compared to the non-Hispanic study participants in this survey and intervention, Hispanics reported a lower incidence of knowledge of HPV, causes of cervical cancer, locations for STI testing, and methods for protection against these infections. This is consistent with published studies and reflects a need for increased education of low-income Hispanics, particularly since they are at increased risk for cervical cancer.[2,5] Also consistent with the published literature regarding cervical cancer, Pap testing, HPV, and the association between HPV and cervical cancer among patients of Hispanic origin, we confirmed that Hispanic study participants had more limited knowledge of HPV and cervical cancer than non-Hispanics.[6] Hispanic survey participants were also less likely to know where to get tested for cervical cancer.

Possible explanations for this lack of awareness and for lack of Pap screening for some members of our population include limited access to healthcare, due to lack of insurance and under-utilization of preventative care services.[7] In addition, lack of HPV and cervical cancer awareness may be attributed to cultural norms that have been reported to limit the exchange of information about sexual health topics between Hispanic individuals, their families, their peers, and their healthcare providers.[8] In our study, Hispanics reported they were less likely than non-Hispanics to discuss STIs with their children. Research suggests Hispanics are more likely to experience fear, anxiety, and stigma when discussing sexual health topics.[6-9] These fears, in addition to other more commonly reported factors such as access to health care, may contribute to the increased incidence of later-stage diagnosis of cervical cancer, and therefore, higher mortality rates in Hispanic women.[2]

FUTURE DIRECTIONS

We found important deficiencies in knowledge of HPV and its link to cervical cancer among Hispanic patients attending our free clinic for uninsured patients, and limited knowledge about sites where STI and pap testing could be performed. In order to address this disparity, we believe that it will be important to encourage healthcare providers, locally and nationally, to encourage providers serving predominantly Hispanic populations to discuss HPV and cancer risk, reinforce the need for Pap tests, and recommend HPV vaccination for eligible patients. It is notable that fully 14.2% of adolescent health providers fail to recommend the HPV vaccine to adolescent girls despite administering other vaccinations.[10] Studies have also shown a positive correlation between provider encouragement and vaccine acceptance in Hispanics and other ethnic minorities.[11,12,13]

Thus, in addition to determining whether populations of patients are aware of and interested in receiving the HPV vaccine, in future studies, we will examine whether healthcare providers for low-income, uninsured populations require additional education pertaining to HPV and its linkage to cervical cancer. Since we already provide access to gynecological exams and Pap and HPV screening at our clinic, recommending the vaccine to members of the Hispanic community who qualify for vaccination is an important intervention that is likely to have a significant impact on cervical cancer outcomes in this at-risk population.

In order to improve HPV vaccination uptake, we plan to implement two means of improving access: patient education and provider reinforcement (a "push-pull" intervention). In addition, CEHC will continue to provide free access to Pap smears and free vaccinations to eligible patients who are interested in the HPV vaccine. These methods are consistent with our overall approach to improving health care outcomes in the uninsured, predominantly Spanish-speaking populations that we serve.[14,15,16] We look forward to

redressing the knowledge, attitudes, and practices problems related to HPV vaccination and sexual health that were identified in the course of this survey.

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Authors

Jeff Chau, College of Pharmacy, University of Rhode Island, Kingston, Rhode Island

Farzana Kibria, Clínica Esperanza/Hope Clinic, Providence, Rhode Island, Smith College, Northampton, Massachusetts

Macayla Landi, Clínica Esperanza/ Hope Clinic, Providence, Rhode Island, College of Pharmacy, University of Rhode Island, Kingston, Rhode Island

Melissa Reilly, Clínica Esperanza/Hope Clinic, Providence, Rhode Island; Institute for Immunology and Informatics, University of Rhode Island, Kingston, Rhode Island

Tania Medeiros, MPH, Clínica Esperanza/Hope Clinic, Providence, Rhode Island

Heather Johnson, MLIS, Institute for Immunology and Informatics, University of Rhode Island, Providence, Rhode Island

Shahla Yekta, PhD, MPH, Clínica Esperanza/Hope Clinic, Providence, Rhode Island; Institute for Immunology and Informatics, University of Rhode Island, Kingston, Rhode Island

Anne S. De Groot, MD, Clínica Esperanza/Hope Clinic, Providence, Rhode Island; Institute for Immunology and Informatics, University of Rhode Island, Providence, Rhode Island; EpiVax, Providence, Rhode Island

Disclosures

The authors have no disclosures to report.

Correspondence

Anne S. De Groot, M.D
Volunteer Medical Director
Clinica Esperanza/ Hope Clinic
CEO, CSO, EpiVax, Inc.
146 Clifford Street
Providence RI 02903
401-272-2123
dr.annie.degroot@gmail.com

Solitary Pulmonary Nodule: Pleuropulmonary Synovial Sarcoma

ROBERT C. WARD, MD; ARIEL E. BIRNBAUM, MD; BASSAM I. ASWAD, MD; TERRANCE T. HEALEY, MD

ABSTRACT

Pleuropulmonary synovial sarcoma (PPSS) is an extremely rare primary malignancy of the lung. We present a case of a middle-aged female with PPSS that was initially discovered as an incidental indeterminate nodule on chest radiograph. Following evaluation with computed tomography (CT), the patient went on to positron-emission tomography (PET)/CT for work-up of the solitary pulmonary nodule, which demonstrated mild FDG-avidity and no other evidence of FDG-avid disease. The patient then underwent thoracotomy and right upper lobectomy for definitive treatment. Only after evaluation of the gross pathology, histology, immunohistochemistry and cytogenetics was the diagnosis of synovial sarcoma made. Importantly, the preceding PET/CT, in addition to physical exam of the upper and lower extremities, helped exclude the more common extra-thoracic soft-tissue variety of synovial sarcoma, which frequently metastasizes to lung, carrying a worse prognosis. Discussion of synovial sarcoma and PPSS follows.

KEYWORDS: Solitary pulmonary nodule, Lung cancer, Synovial sarcoma, Sarcoma

CASE PRESENTATION

A 44-year-old female with a past medical history of hypertension and hyperlipidemia presented with an incidental, right, upper lobe, solitary pulmonary nodule identified on a chest radiograph performed for evaluation of chest pain (**Figure 1**). Given the small size and location of the lesion, the symptom of chest pain was considered unrelated. A chest radiograph performed eight months earlier for chest pain showed no evidence of the pulmonary nodule (**Figure 2).**

The recommended chest CT demonstrated a circumscribed 1.7 cm right, upper lobe, solitary pulmonary nodule containing a small peripheral focus of calcification (**Figure 3**). There was no evidence of emphysema (**Figure 4**), and there was no suspicious hilar or mediastinal lymphadenopathy. The subsequent PET/CT demonstrated mild FDG-avidity (maximum SUV of 2.3) associated with the nodule (**Figures 5 and 6**). Histologic correlation and surgical consultation was recommended for suspicion of malignancy.

The patient underwent right thoracotomy with right upper lobectomy and mediastinal lymph node dissection. The nodule was well-circumscribed and unencapsulated with areas of internal necrosis and foci of calcification. Gross pathology (**Figure 7**), histology (**Figure 8**), immunohistochemistry (**Figure 9**) and fluorescence in situ hybridization

Figure 1. PA chest radiograph demonstrates a solitary pulmonary nodule within the right upper lung (red arrows).

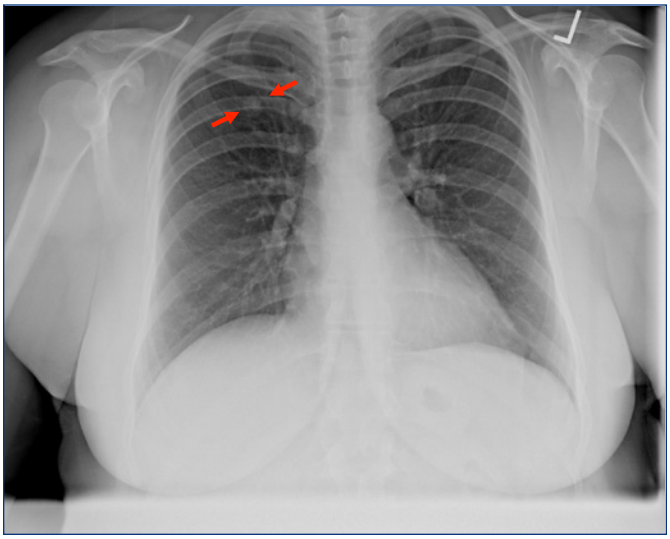


Figure 2. PA chest radiograph eight months earlier shows no evidence of the solitary pulmonary nodule seen in Figure 1.

Figure 3. Axial non-contrast CT of the chest in soft tissue windows demonstrates a 1.7 cm right upper lobe pulmonary nodule with a focus of peripheral calcification (red arrow). There was no evidence of hilar or mediastinal lymphadenopathy.

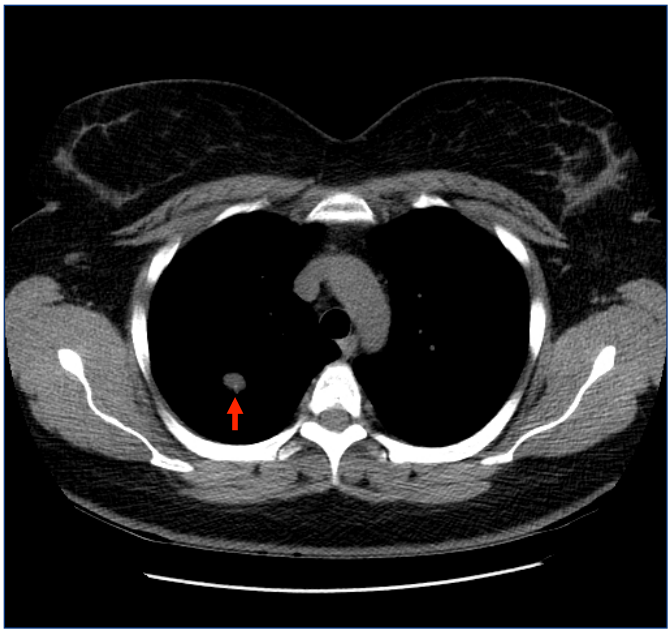


Figure 4. Axial non-contrast CT of the chest in lung windows re-demonstrates the 1.7 cm right upper lobe pulmonary nodule with circumscribed margins (red arrow). No evidence of emphysema.

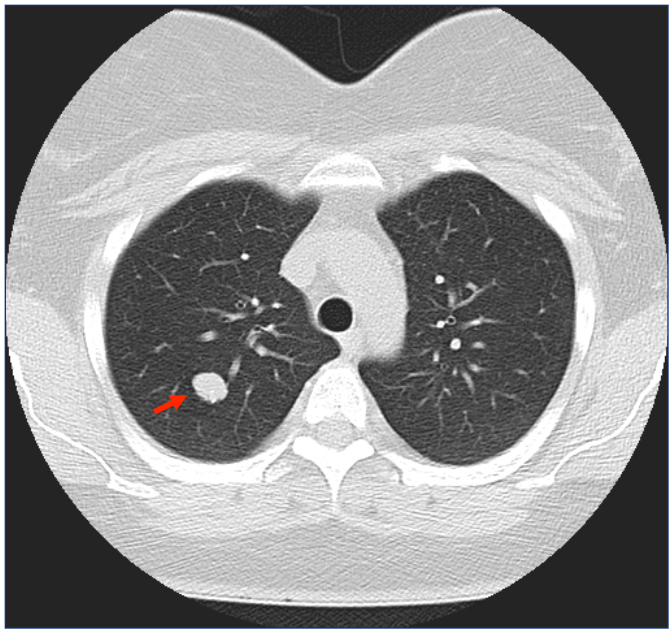


Figure 5. Fused axial PET/CT at the level of the great vessels demonstrates mild FDG-avidity (maximum SUV of 2.3) associated with the right upper lobe solitary pulmonary nodule (red arrow). There was no evidence of FDG-avid nodal or distant metastatic disease.

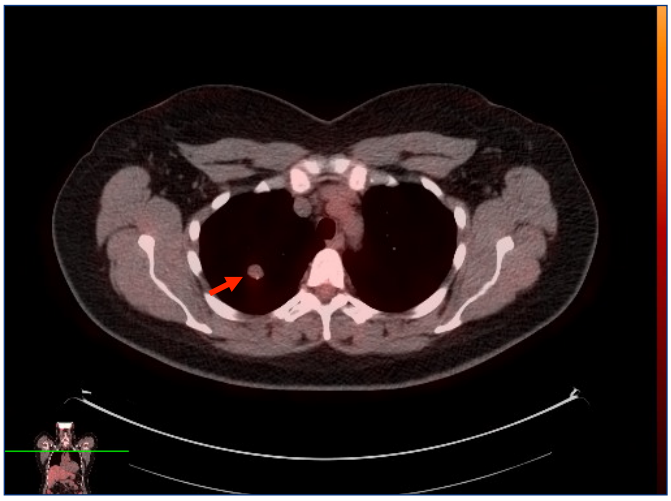
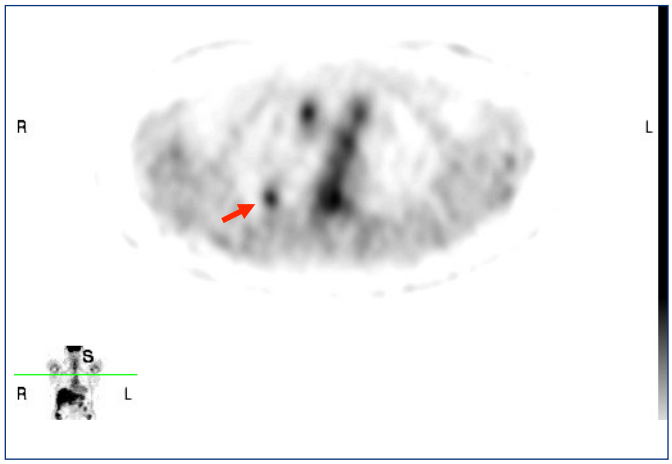


Figure 6. PET scan at the same location as Figure 5 demonstrates the FDG-avidity associated with the right upper lobe solitary pulmonary nodule to better advantage (red arrow). Also note physiologic FDG activity within the great vessels, esophagus and degenerative endplate change of the thoracic spine.



(FISH) results were consistent with synovial sarcoma of the monophasic spindle cell type. All sampled lymph nodes were negative for malignancy.

Although synovial sarcomas have been reported to occur as a primary malignancy in the pleuropulmonary region, soft tissue sarcomas are far more common. Because the patient had undergone a pre-operative PET/CT, which revealed no additional sites of FDG-avid disease, it was concluded the patient had the rare primary pleuropulmonary variety of synovial sarcoma.

Because this patient's tumor was identified early as an incidental finding, surgical resection was considered definitive therapy, and therefore, chemotherapy and radiation therapy were not pursued.

PLEUROPULMONARY SYNOVIAL SARCOMA

Historically, synovial sarcomas were thought to be associated with the synovium. The term synovial sarcoma first appeared in the German surgical literature in the 1865, where it was used to describe a complex multinodular lesion apparently arising from synovial tissue in the knee of an adult patient.[1] Nearly 120 years later, in 1984, pathologists definitively demonstrated that these neoplasms actually have no demonstrable relationship to synovial tissue.[2] Instead, they represent mesenchymal spindle cell tumors characterized by variable epithelial differentiation.[3] Thus, the term *synovial* sarcoma is a misnomer. Nonetheless, the name lives on.

Soft-tissue synovial sarcoma is far more common than pleuropulmonary synovial sarcoma (PPSS). Soft-tissue synovial sarcomas typically occur in juxta-articular locations of the extremities in young and middle-aged adults.[3] Synovial sarcomas account for 7%-10% of all soft-tissue sarcomas.[3] Pulmonary sarcomas, in general, constitute only 0.1%-0.5% of all primary lung malignancies.[3] The most frequently reported subtypes of sarcomas in the lung are leiomyosarcomas, malignant fibrous histiocytoma, fibrosarcoma, and PPSS, which is increasingly recognized as a subtype of sarcoma because of the relatively recent identification of a distinctive chromosomal translocation specific to synovial sarcoma.[4,5]

Relatively speaking, the occurrence of synovial sarcoma as an extra-thoracic soft-tissue primary tumor is relatively common compared to PPSS. Furthermore, distant metastases develop in 40%-50% of patients with extra-thoracic soft tissue synovial sarcoma; the lung is the most common site of metastatic disease, and massive pleuropulmonary metastases are the leading cause of death.[6] Because the morphologic features of primary and metastatic synovial sarcomas are similar, clinical and radiologic evaluation is essential to exclude the presence of tumor outside the thorax.

Patients with PPSS typically present with a cough, chest pain, or dyspnea.[3] Alternatively, PPSS may be found incidentally, as in the index case. PPSS typically appears as a sharply marginated mass with uniform opacity of chest radiographs.[7] CT images show a well-circumscribed heterogeneously enhancing lesion, and have been reported as lacking calcification,[7] in contradistinction to the index case. MRI provides superior demonstration of nodular soft tissue and multilocular fluid internal components, in addition

Figure 7. Gross pathology demonstrates a 1.4 cm tan to white, unencapsulated, homogeneous, well-circumscribed lesion. The pleural surface overlying the lesion is inked blue, and the staple line is inked orange. The surrounding lung tissue is unremarkable.

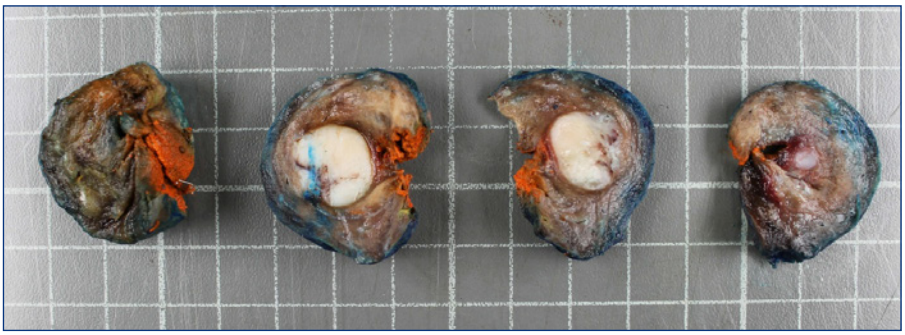


Figure 8 a/b. Hematoxylin and Eosin stain at 200x and 400x, respectively, demonstrate mitotic count of 10 mitoses/10 high-powered fields, approximately 20% necrosis, and foci of calcification.

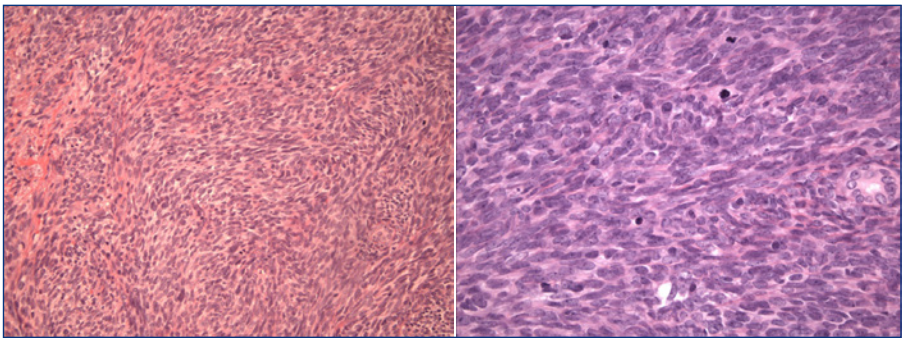
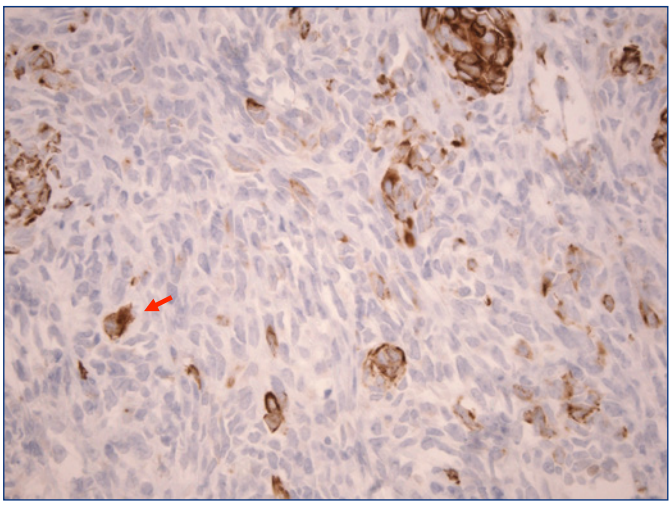


Figure 9. Immunohistochemistry cytokeratin cocktail at 400x demonstrates focal areas of positivity (e.g. red arrow). This finding along with diffuse strong BCL-2 positivity, and synaptophysin, EMA, Ewing's sarcoma, and Ki-67 positivity support the diagnosis of synovial sarcoma. FISH (not shown), demonstrated the SYT (18q11.21) rearrangement specific to synovial sarcoma.



to peripheral rim enhancement after administration of a gadolinium-based contrast material.[7]

Unfortunately, the radiographic manifestations of PPSS overlap significantly with those of many other lesions of the lung and pleura, including primary and metastatic lung neoplasms, localized fibrous tumor of the pleura, malignant mesothelioma, and other rare, primary, parenchymal sarcomas. The presence of significant adenopathy, however, argues against PPSS.[3]

Treatment typically consists of multimodality therapy for synovial sarcomas, including surgical resection, chemotherapy and radiation therapy.[8,9] However, no randomized studies in any age group have been reported to assess therapeutic approaches in patients with synovial sarcoma. There is no prognostic data for PPSS, but the broader and more long-term clinical experience of soft-tissue sarcomas has shown an overall 5-year survival rate of 50%-80%.[10] Poor prognostic factors include tumors greater than 5 cm, greater than 50% necrosis, the presence of hemorrhage, poorly differentiated subtypes, location other than extremities, and patients older than 40 years of age.[10,11]

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Authors

Robert C. Ward, MD, is a Resident in the Department of Diagnostic Imaging, Warren Alpert Medical School of Brown University, and Rhode Island Hospital, Providence, RI.

Ariel E. Birnbaum, MD, is an Assistant Professor of Medicine, Warren Alpert Medical School of Brown University, and Rhode Island Hospital, Providence, RI.

Bassam I. Aswad, MD, is an Associate Professor of Pathology, Warren Alpert Medical School of Brown University, and Rhode Island Hospital, Providence, RI.

Terrance T. Healey, MD, is an Assistant Professor of Diagnostic Imaging, Warren Alpert Medical School of Brown University, and Rhode Island Hospital, Providence, RI.

Disclosures

The authors have no financial relationships to disclose.

Correspondence

Terrance T. Healey, MD
Rhode Island Hospital
593 Eddy Street, Providence, RI 02903
401-444-5184.
thealey@lifespan.org

What is MOLST?

EDWARD MARTIN, MD, MPH; JAMES V. MCDONALD, MD, MPH

A Medical Order for Life Sustaining Treatment (MOLST) is used by terminally patients and clinicians to document end-of-life wishes, regardless of who provides the patient's medical care or where the patient's medical care is given. MOLST became a reality in Rhode Island in 2013.[1] MOLST, POLST (Physician Order for Life Sustaining Treatment) or COLST (Clinician Order for Life Sustaining Treatment) is currently used in 42 states in the U.S.

MOLST is a medical order, similar to a prescription, and as such, is transportable and enduring, regardless of clinical setting. It is appropriate only for a patient with a terminal condition, defined in Rhode Island as "an incurable or irreversible condition that, without the administration of life sustaining procedures, will, in the opinion of the attending physician, result in death."[2] MOLST is strictly voluntary. Decisions are made by the patient and a MOLST-qualified health care provider – physician, physician's assistant, or advanced practice registered nurse. When a patient is not competent, a health care decision maker may make MOLST decisions.

Rhode Island's MOLST form[3] may be found at the Rhode Island Department of Health website,[4] and is easily downloadable. The form should be printed on cardstock and completed with the patient. It is signed by the patient (or the patient's health care decision maker) and a MOLST-qualified health care provider. It has five discrete sections, A through F.

- **Section A** addresses the issue of cardio-pulmonary resuscitation.
- **Section B** delineates allowable medical interventions, from comfort measures to full medical treatment.
- **Section C** controls transfer to a hospital setting and requires a "Yes" or "No."
- **Section D** contains four nutrition choices, from no artificial nutrition to long-term artificial nutrition.
- **Section E** contains four hydration choices, from no artificial hydration to long-term artificial hydration.
- **Section F** indicates if one of several advanced care directives – e.g., durable power of health care; health care proxy; living will, etc. – exists.

See sample MOLST form on the following pages.
Download MOLST form.

The form also contains spaces for signatures.

On January 1, 2014, it became mandatory[5] for several types of health care facilities to offer MOLST to terminally ill patients: nursing facilities, assisted living residences, hospices, kidney dialysis centers, home health agencies, and hospitals (in the case of hospitals, only if a patient is to be discharged or transferred to another health care facility).

The MOLST form is of no value if it is not discussed. Even though a patient does not bring up the topic does not mean that he or she does not wish to discuss the matter. Introducing a patient to the concept of MOLST is one way to begin a dialogue about end-of-life issues.

References

1. Medical Orders for Life-Sustaining Treatment: Rhode Island Department of Health
2. Medical Orders for Life-Sustaining Treatment: Rhode Island Department of Health (Page 2, Section 1.25)
3. http://www.health.ri.gov/forms/medical/OrdersForLifeSustainingTreatment.pdf
4. http://www.health.ri.gov
5. http://sos.ri.gov/documents/archives/regdocs/released/pdf/DOH/7387.pdf (Page 3)

Authors

Dr. Edward Martin is Chief Medical Officer of Home & Hospice Care of Rhode Island.

Dr. James McDonald is Chief Administrative Officer of the Board of Medical Licensure and Discipline for the State of Rhode Island.

HIPAA PERMITS DISCLOSURE OF MOLST TO OTHER HEALTH CARE PROFESSIONALS AS NECESSARY.
MOLST IS VOLUNTARY. NO PATIENT IS REQUIRED TO COMPLETE A MOLST FORM.

Medical Orders for Life Sustaining Treatment (MOLST)

Follow these orders, then contact a MOLST-Qualified Health Care Provider. This is a **Medical Order Sheet** based upon the person's wishes in his/her current medical condition. Any section not completed implies full treatment. **This MOLST remains in effect unless revised.**

Patient's Last Name _____ Patient's First Name _____

Gender: ☐ M ☐ F Patient's Date of Birth / / Date/Time Form Prepared _____

A CHECK ONE

CARDIOPULMONARY RESUSCITATION (CPR): *Person has no pulse and is not breathing.*

☐ **Attempt Resuscitation/CPR** ☐ **Do Not Attempt Resuscitation/DNR** (Allow Natural Death)

- No defibrillator (including automated external defibrillators) should be used on a person who has chosen "Do Not Attempt Resuscitation."
- When not in cardiopulmonary arrest, follow orders in sections B and C.

B* CHECK ONE

MEDICAL INTERVENTION: *Patient has a pulse and/or is breathing.*

☐ **Comfort Measures Only:** Use medication by any route, positioning, wound care and other measures to relieve pain and suffering. Use oxygen, suction and manual treatment of airway obstruction as needed for comfort. Use antibiotics only to promote comfort.

☐ **Limited Additional Interventions:** Includes care described above. Use medical treatment, antibiotics, and IV fluids as indicated. Do not intubate. May use non-invasive positive airway pressure. Generally avoid intensive care.

☐ **Full Treatment:** Includes care described above in Comfort Measures Only and Limited Additional Interventions, as well as additional treatment, such as intubation, advanced airway interventions, mechanical ventilation, and defibrillation/cardioversion as indicated.

C CHECK ONE

TRANSFER TO HOSPITAL

☐ Do not transfer to hospital for medical interventions. ☐ Transfer to hospital if comfort measures cannot be met in current location.

D CHECK ONE

ARTIFICIAL NUTRITION (For example a feeding tube): *Offer food by mouth if feasible and desired.*

☐ No artificial nutrition ☐ Defined trial period of artificial nutrition
☐ Long-term artificial nutrition, if needed ☐ Artificial nutrition until not beneficial or burden to patient

E CHECK ONE

ARTIFICIAL HYDRATION: *Offer fluid/nutrients by mouth if feasible and desired.*

☐ No artificial hydration ☐ Defined trial period of artificial hydration
☐ Long-term artificial hydration, if needed ☐ Artificial hydration until not beneficial or burden to patient

F

ADVANCE DIRECTIVE (if any): *Check all advance directives known to be completed.*

☐ Durable Power of Health Care ☐ Health Care Proxy ☐ Living Will ☐ Documentation of Oral Advance Directive

Discussed with:

☐ Patient ☐ Health Care Decision Maker ☐ Parent/Guardian of Minor ☐ Court-Appointed Guardian ☐ Other: _____

G

SIGNATURE OF MOLST-QUALIFIED HEALTHCARE PROVIDER (Physician, RNP, APRN, or PA)

My signature below indicates to the best of my knowledge that these orders are consistent with the person's medical condition and preferences.

Signature (required) _____ Phone Number _____ Date/Time / /

Print Name _____ Rhode Island License # _____

SIGNATURE OF PATIENT, DECISION MAKER, PARENT/GUARDIAN OF MINOR, OR GUARDIAN

By signing this form, the patient or legally-recognized decision maker acknowledges that this request regarding resuscitative measures is consistent with the known desires of, and with the best interest of, the individual who is the subject of the form.

Signature (Required) _____ Phone Number _____ Relationship (if patient, write self) _____

Print Name and Address _____

SEND MOLST FORM WITH PERSON WHENEVER TRANSFERRED OR DISCHARGED.

HIPAA PERMITS DISCLOSURE OF MOLST TO OTHER HEALTH CARE PROFESSIONALS AS NECESSARY.
MOLST IS VOLUNTARY. NO PATIENT IS REQUIRED TO COMPLETE A MOLST FORM.

Review and Renewal of MOLST Orders on This MOLST Form (this MOLST form remains in effect unless another MOLST form is executed.)

The MOLST-Qualified Health Care Provider may review the form from time to time as the law requires, and also:

- If the patient moves from one location to another to receive care; or
- If the patient has a major change in health status (positive or negative); or
- If the patient or other decision-maker changes his/her mind about treatment.

Date/Time	Reviewer's Name and Signature	Location of Review (e.g., Hospital, Nursing Home, Provider's Office, Patient's Residence)	Outcome of Review
			☐ No change ☐ Form voided, new form completed ☐ Form voided, ***no*** new form
			☐ No change ☐ Form voided, new form completed ☐ Form voided, ***no*** new form
			☐ No change ☐ Form voided, new form completed ☐ Form voided, ***no*** new form

Directions for MOLST-Qualified Health Care Providers Completing MOLST

- Must be completed by a MOLST-Qualified Health Care Provider based on patient preferences and medical indications. A MOLST-Qualified Health Care Provider is defined as a physician, nurse practitioner, advanced practice registered nurse, or a physician assistant.
- MOLST must be signed by a MOLST-Qualified Healthcare Provider (physician, nurse practitioner, advanced practice registered nurse, or physician assistant) and the patient/decision maker to be valid. Verbal orders are acceptable with follow-up signature by provider in accordance with facility/community policy and documentation that there was discussion with the patient or the patient's advocate about discontinuing the MOLST order.)
- This is the ONLY MOLST FORM that is acceptable for completion in Rhode Island. Do not make your own MOLST form. Photocopies and faxes of signed MOLST forms are legal and valid.
- Any incomplete section of the MOLST form implies full treatment for that section.

***Section B:**

- When comfort cannot be achieved in the current setting, the person, including someone with "Comfort Measures Only," should be transferred to a setting able to provide comfort (e.g., treatment of a hip fracture)
- IV medication to enhance comfort may be appropriate for a person who has chosen "Comfort Measures Only".
- Non-invasive positive airway pressure includes continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP), and bag valve mask (BVM) assisted respirations.
- Treatment of dehydration prolongs life. A person who desires IV fluids should indicate "Limited Interventions" or "Full Treatment."

Modifying and Voiding MOLST

- A patient with capacity can, at any time, void the MOLST form or change his/her mind about his/her treatment preferences by executing a verbal or written advance directive or a new MOLST form.
- To void MOLST draw a line through Sections A through E and write "VOID" in large letters. Sign and date the line.
- A health care decision maker may request to modify the orders based on the known desires of the individual or, if unknown, the individual's best interests.

DEFINITIONS

"Medical orders for life sustaining treatment" or "MOLST" means a voluntary request that directs a health care provider regarding resuscitative and life-sustaining measures. Rhode Island General Laws §23-4.11-2 (10).

"Qualified patient" means a patient who has executed a declaration in accordance with this chapter and who has been determined by the attending physician to be in a terminal condition. Rhode Island General Laws §23-4.11-2 (16).

"Terminal condition" means an incurable or irreversible condition that, without the administration of life sustaining procedures, will, in the opinion of the attending physician, result in death." Rhode Island General Laws §23-4.11-3.1 (20).

This form is approved by the Rhode Island Department of Health. For more information or a copy of the form, visit **www.health.gov**

SEND MOLST FORM WITH PERSON WHENEVER TRANSFERRED OR DISCHARGED.
Rhode Island General Laws §23-4.11-3.1 authorizes this MOLST form. **(Rev. 9-2013)**

Increasing Trend of HPV-Associated Oropharyngeal Cancers among Males in Rhode Island, 1987–2011

JUNHIE OH, BDS, MPH; JOHN FULTON, PhD; TRICIA WASHBURN, BS

Evidence linking human papillomavirus (HPV) with the development of oropharyngeal cancers has accumulated since the 1980s, culminating in the conclusion that HPV plays a *causal* role in the development of some oropharyngeal neoplasms.[1] These particular cancer types are on the rise in the United States,[2-4] and as this report will show, in Rhode Island as well. Authors will discuss strategies for prevention and control efforts, based on Rhode Island-specific epidemiology and growing body of research of HPV-associated oropharyngeal cancers.

METHODS

The Rhode Island Cancer Registry (RICR) has collected cancer case reports since October 1986. Since 1995, this effort has been supported in part by the National Program of Cancer Registries of the Centers for Disease Control and Prevention (CDC). Using RICR data for the period 1987–2011, newly diagnosed malignant squamous cell carcinomas of the head and neck were identified. In parallel with a previous analysis of similar data,[5] these cancers were categorized either as "HPV-associated oropharyngeal cancers" or as "comparison cancers."

HPV-associated malignancies include those of the tonsil (including the pharyngeal lymphoid ring), posterior one third (base) of the tongue and lingual tonsil, and certain oropharyngeal sites (including overlapping lesions of the tongue, the lateral wall of the oropharynx, overlapping lesions of the oropharynx, non-specified oropharynx and pharynx, and overlapping lesions of the lip, the oral cavity, and the pharynx). Comparison cancers were those diagnosed in selected sites in the head and neck that are anatomically near the oropharyngeal cancer sites but are sites not associated with HPV infection based on epidemiologic and pathologic studies.[5] **Table 1** contains a complete description of HPV-associated oropharyngeal cancers and comparison cancers with specific cancer classification codes.

Please note that tumors categorized as "HPV-associated" were *not verified* as testing positive for HPV DNA. The RICR does not routinely collect this information. Nonetheless, recent studies reveal HPV positivity as high as 70% in "HPV-associated oropharyngeal cancers." [4,6]

Incidence rates for HPV-associated oropharyngeal cancers and comparison cancers in a subset of head and neck cancers were examined by sex and year of diagnosis. SEER*Stat software was used to calculate the number of cancers and age-adjusted rates per 100,000 population, standardized to the U.S. 2000 standard population (see http://www.seer.cancer.gov/seerstat/index.html). Annual percentage change (APC) was computed for cancer trends, using the CDC's JoinPoint regression software (see http://surveillance.cancer.gov/joinpoint/), evaluating statistical significance of at the $p \leq 0.05$ significance level.

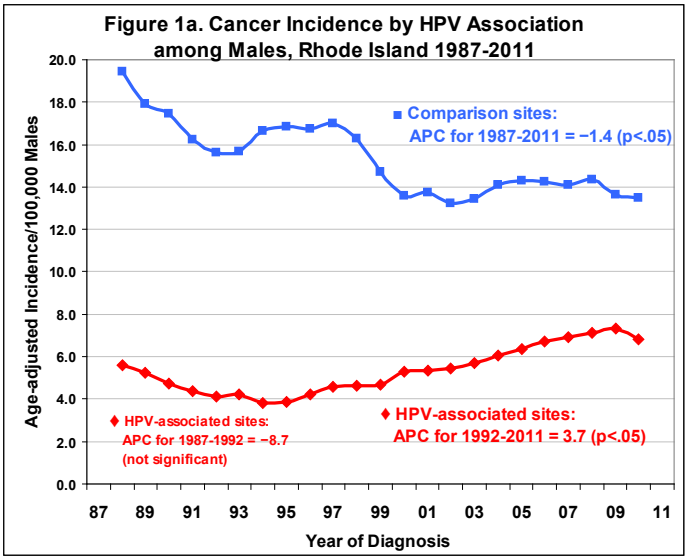
RESULTS

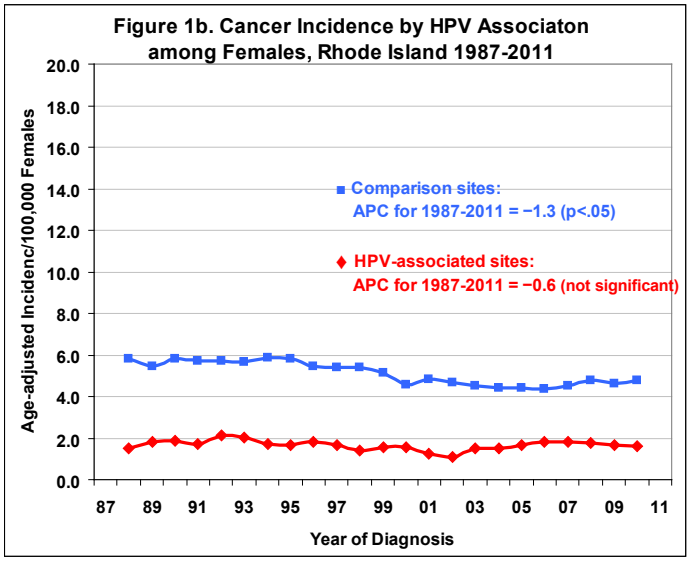
A total of 940 HPV-associated oropharyngeal cancers were reported to RICR during 1987–2011, as compared with a

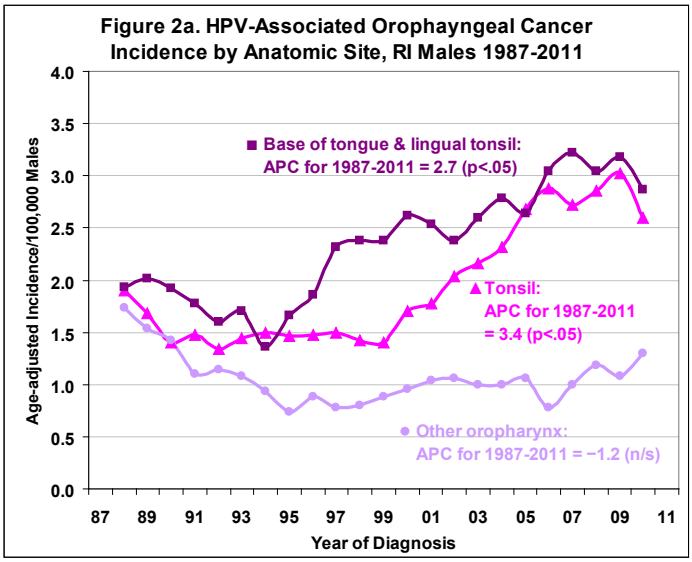
Table 1. ICD-O-3 topography code* and anatomic site description used to define HPV-associated and comparison cancers in selected sites in the head and neck.

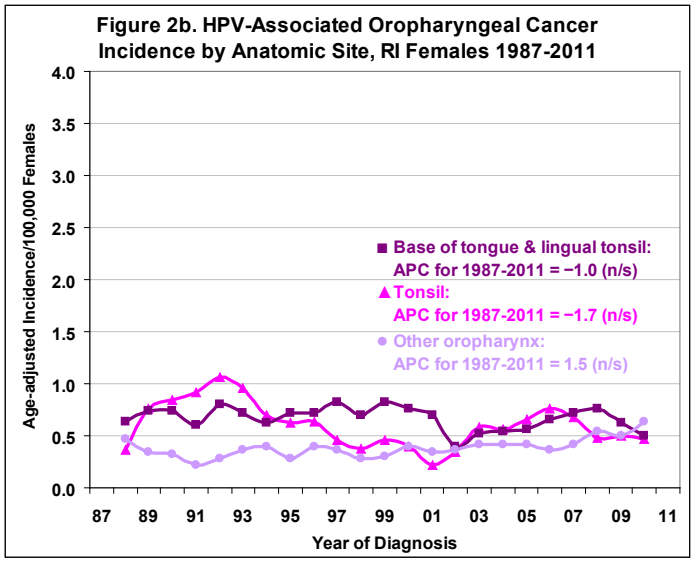
HPV-associated sites	
Tonsil, including pharyngeal lymphoid ring	C090, C091, C098, C099 (Tonsil) C142 (Pharyngeal lymphoid ring or Waldeyer's ring)
Base of tongue and lingual tonsil	C019 (Base of tongue) C024 (Lingual tonsil)
Other oropharynx	C028 (Overlapping lesion of tongue) C102, C108, C109 (Oropharynx) C140 (Pharynx) C148 (Overlapping lesion of lip, oral cavity and pharynx)
Comparison sites	
Tongue	C020, C021, C022, C023, C029 (Tongue)
Other oral cavity	C030, C031, 039 (Gum) C040, C041, C048, C049 (Floor of mouth) C050 (Hard palate) C060, C061, C062, C068, C069 (Other/unspecified parts of mouth)
Larynx	C320, C321, C322, C323, C328, C329 (Larynx)
Other oropharynx	C051, C052, C058, C059 (Palate) C100, C101, C103 (Other Oropharynx)

** International Classification of Disease for Oncology, 3rd edition, [ICD-O-3].*









total of 2,675 comparison cancers in a subset of head and neck cancers.

Among Rhode Island males, the annual age-adjusted incidence rate of HPV-associated cases increased between 1992 and 2011 (APC = 3.7, p<0.05), whereas the incidence of comparison cases steadily decreased between 1987 and 2011 (APC= −1.4, p<0.05) (**Figure 1a**). Among women, the annual percent change in age-adjusted incidence of HPV-associated cases was not statistically significant over the period of observation, whereas the incidence of comparison cases steadily decreased between 1987 and 2011 (APC = −1.3, p<0.05) (**Figure 1b**).

Assessment of HPV-associated oropharyngeal cancers by anatomic site revealed that tumors of the tonsil and base of the tongue (including the lingual tonsil) increased between 1987 and 2011, particularly among males (APC=3.4 and 2.7, respectively, **Figure 2a**). A similar trend was not observed among women (**Figure 2b**).

DISCUSSION

The findings in this report are subject to at least two limitations. First, the potential exists for misattribution of oral and pharyngeal cancers to HPV infection. HPV association is based solely on anatomic site, not on case-specific HPV data. Second, only incomplete information on comorbidities, smoking history, and alcohol use history is available in cancer case reports made to the RICR, that prevents use of such variables for further assessment. In the future, focused surveillance of oropharyngeal cancers, including the careful collection of information on HPV positivity and other risk factors, will assist in unraveling the importance of HPV as an emerging risk factor in the development of tumors at specific anatomic sites, and also in establishing the effectiveness of HPV vaccination in preventing those tumors.

Meanwhile, using the information available to us for the past two-and-a-half decades, RICR data reveal a *robust* increase in HPV-associated oropharyngeal cancer incidence

among men, in contrast to a steady decrease in the incidence of non-HPV-associated head and neck cancers among men *and* women.

Historically, tobacco use and heavy alcohol consumption were considered the major risk factors for head and neck cancers.[7] Recent research, however, reveals an increasing occurrence of oropharyngeal cancers in young(er) men who have never smoked, but whose sexual behaviors are consistent with increased risk of HPV infection, e.g., reporting numerous sexual partners or an early sexual debut.[6,8]

As in the case of other HPV-associated cancers, HPV infection in the mouth and throat, typically HPV-16 infection, is a precursor of oropharyngeal cancer development.[9] Recent analysis of data from the 2009-2010 National Health and Nutrition Examination Survey (NHANES) estimated an overall prevalence of oral HPV infection among United States residents aged 14–69 years of 10.1% among males and 3.6% among females.[10]

Recognizing the significant contribution of HPV infection to recent oropharyngeal cancer trends – especially among men – suggests important implications for oropharyngeal cancer prevention and control. Available HPV vaccines *may* be effective in reducing the burden of HPV-associated oropharyngeal cancers, either *directly*, by preventing HPV infection of the mouth and throat, or *indirectly*, by preventing HPV infection of the genitals or anus, potential sources of oral HPV infection.

CDC's Advisory Committee on Immunization Practices (ACIP) has recommended routine vaccination against HPV for young females since 2007 and young males since 2011.[11,12] As recommended, Rhode Island includes HPV vaccine as part of the universal state supplied vaccine program, for all adolescents regardless of insurance status, through primary care providers and school- and community-based vaccination clinics. Although clinical trials have as yet to determine the efficacy of HPV vaccines for the prevention of oropharyngeal cancers, currently available HPV vaccines offer good protection against HPV-16, the dominant strain associated with oropharyngeal cancers.[11,13]

On the basis of current, state-specific epidemiologic trends of HPV-associated cancer rates, healthcare professionals are encouraged to promote vaccines and other preventive measures in their practices. However, many healthcare professionals may be reticent to discuss sexual behavior with their patients, and, understandably, may be undecided about the role of HPV vaccines in the prevention of oropharyngeal cancers. The Rhode Island Department of Health, partnering with a statewide cancer coalition, and immunization and oral health advocates, conducts educational sessions on this subject for licensed medical and dental care professionals and also develops educational modules to be used in the curricula of health professionals-in-training.

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2. Jemal A, Simard EP, Dorell C, *et al.* Annual report to the nation on the status of cancer, 1975–2009, Featuring the burden and trends in human papillomavirus (HPV)–associated cancers and HPV vaccination coverage levels. *J Natl Cancer Inst.* 2013;105(3):175-201.
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4. Chaturvedi AK, Engels EA, Pfeiffer RM, *et al.* Human papillomavirus and rising oropharyngeal cancer incidence in the United States. *J Clin Oncol.* 2011;29(32):4294-4301.
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Authors

Junhie Oh, BDS, MPH, is the Senior Public Health Epidemiologist in the Oral Health Program and the Office of Immunization, Rhode Island Department of Health.

John Fulton, PhD, is the Administrator in the Rhode Island Cancer Registry.

Tricia Washburn, BS, is the Chief in the Office of Immunization, Rhode Island Department of Health.

Disclosures

The authors and/or spouses/significant others have no financial interests to disclose.

Correspondence

Junhie Oh, BDS, MPH
Rhode Island Department of Health
3 Capitol Hill
Providence, RI 02908-5097
Junhie.Oh@health.ri.gov

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	OCTOBER 2013	12 MONTHS ENDING WITH OCTOBER 2013	
	Number	Number	Rates
Live Births	1,008	11,561	11.0*
Deaths	821	9,943	9.4*
Infant Deaths	6	81	7.0#
Neonatal Deaths	4	56	4.8#
Marriages	777	6,394	6.1*
Divorces	253	3,360	3.2*
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	APRIL 2013	12 MONTHS ENDING WITH APRIL 2013		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	209	2,444	232.1	3,387.0
Malignant Neoplasms	200	2,225	211.3	5,787.5
Cerebrovascular Disease	34	443	42.1	667.0
Injuries (Accident/Suicide/Homicide)	43	624	59.2	8,896.5
COPD	47	520	49.4	535.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 estimated population of 1,052,567 (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.

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	NOVEMBER 2013	12 MONTHS ENDING WITH NOVEMBER 2013	
	Number	Number	Rates
Live Births	942	11,535	11.0*
Deaths	833	9,961	9.5*
Infant Deaths	7	82	7.1#
Neonatal Deaths	6	58	5.0#
Marriages	419	6,495	6.2*
Divorces	227	3,307	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	MAY 2013	12 MONTHS ENDING WITH MAY 2013		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	163	2,417	229.5	3,234.5
Malignant Neoplasms	175	2,232	211.9	5,732.5
Cerebrovascular Disease	31	432	41.0	649.5
Injuries (Accident/Suicide/Homicide)	46	612	58.1	8,724.5
COPD	43	514	48.8	522.5

(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.

There's a...

.002% chance you'll ever need a neuro-oncologist.

.001% chance you'll ever need a surgical epileptologist.

.00135% chance you'll ever need a certified Burn Center.

There's a 100% chance we'll have them.

You didn't plan on being here, but we did.

Many hospitals can give you the care you need. World class hospitals are prepared to give you *all* the care you *may ever* need. With the area's only Level I trauma center, some of the most advanced equipment on earth and literally hundreds of specialists, Rhode Island Hospital is truly a world class hospital, ready to meet the needs you expect— as well as those you don't.

Rhode Island Hospital

A Lifespan Partner

Rhode Island Hospital is the principal teaching hospital of The Warren Alpert Medical School of Brown University.

CME EVENT

Eleventh Hour Education Event

May 17, 2014, 7:00 am
Crowne Plaza Hotel
801 Greenwich Avenue, Warwick RI 02886

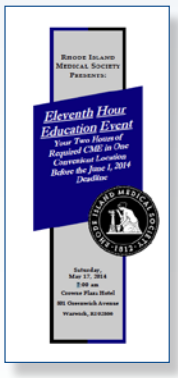
The RI Medical Society has organized your opportunity to obtain required Continuing Medical Education (CME) on Saturday, May 17, 2014.

The required topics to be covered are **Pain Management** and **Risk Management**, while we will also cover important education on a non-required topic.

The Rhode Island Department of Health states that "unless you were in training or became Board Certified or Re-Certified within the past two years, (physicians) need to complete 40 hours of Continuing Medical Education (CME) during each two-year license cycle. The current license renewal cycle requires that you obtain and submit your credits no later than **June 1, 2014**. At least two hours of this education must be related to one of the following topics:

- Risk management
- Opioid pain management/chronic pain management
- End of life/palliative care
- Ethics"

Registration



Program and Registration form

The program agenda and registration details for this event can also be found at www.rimed.org. RIMS members may log onto the Member Portal to register or complete the form and return as noted.

If you are not a RIMS member but would like to join, please complete the online membership application. The member rate will be offered to applicants upon receipt of your membership application.

Please email Megan E. Turcotte with questions, or call 401-331-3207.

NOTICE

The Rhode Island Medical Society no longer endorses the collection agency **IC System** and is currently seeking a high-quality, professional collection agency that will provide superior service to RIMS members at favorable rates.

RIMS Director of Govt. and Public Affairs, Steve DeToy recently spoke to more than 30 medical students on the R.I. General Assembly. His message was: Democracy is not a spectator sport. Pictured, from left, are Dan Ebner, MD'17, chair of WAMS AMA; Steve DeToy, Allison Chen, MD'17, vice chair; and Jason Bowman MD'16, outgoing chair.

RIMWA ANNUAL MEETING
and Woman Physician of the Year Celebration

Lynn E. Taylor, MD, FACP
Assistant Professor of Medicine
The Warren Alpert Medical School of Brown University

Tuesday, May 13, 2014
6:00 pm Reception
7:00 pm Dinner and Program

Providence Marriott Hotel
One Orms Street
Providence, RI

Open to medical and non-medical communities.
Please RSVP by May 9.

Invitation/Reservation Form

Working for You: RIMS advocacy activities

April 1

Physician Health Committee, Herbert Rakatansky, MD, Chair

Meeting with chain drug stores regarding pharmacists performing limited CLIA test

Meeting with other lobbyists on political matters

Legislative hearings, State House

Representative Kazarian and Senator Crowley Fundraisers

April 2

DOH hearing, medical records regulations; Peter Evangelista, MD, attending,

Legislative hearings, State House

Senator Pichardo fundraiser

April 3

Attended meeting, University of RI; US Attorney, DEA, Brown, URI Planning Committee for June 7 CME event

RI Public Health Association Gun Violence Day, State House

Legislative hearings, State House; Drs. Alyn Adrain, Richard Terek, and Phillip Lucas testifying

Senator Nesselbush Fundraiser, Dr. Adrain attending

April 4

HealthRIght meeting regarding health care cost-containment legislation

April 7

Senator Whitehouse meeting with coalition to transform advanced care, at BCBSRI

Meeting with Drs. Rakatansky, Hollmann, Adrain; Mssrs. Warde and DeToy to discuss draft changes to the Code of Medical Ethics proposed by AMA's Council on Ethical and Judicial Affairs

RIMS Council Meeting

April 8

Health Source RI's Expert Advisory Committee

Legislative hearings, State House

Senator Goldin Fundraiser

April 9

BMLD

Workers Comp Advisory Council

YMCA Day at General Assembly (AMA and YUSA have formed a strategic partnership)

Litigation Center Executive Committee conference call, Newell Warde chairing

Legislative hearings, State House; Drs. Siddiqui, Arron, and Griffin testifying

April 10

Mental Health and Addiction Services Coalition Meeting at the Drug and Alcohol Treatment Association of RI offices

Meeting with Governor's Policy Staff regarding health care legislation

Health Services Council

Meeting with new House Finance chair, Radiology and Orthopedic Societies, to discuss provider tax repeal legislation,

Legislative hearings, State House; Peter Evangelista, MD, testifying

Senate HHS Chair Josh Miller Fundraiser, Dr. Migliori and RIMS staff attending

April 11

Meeting on *RI Medical Journal,* RIMS Staff and Journal Staff

April 12

Celebration of the new Stanley M. Aronson Chair at Butler Hospital, installation of its first occupant, *RI Medical Journal* Editor-in-Chief, Joseph H. Friedman, MD

April 14

Meeting with BCBSRI staff to discuss support for RIMS Physician Health Program

Meeting with RI Quality Institute, update on CurrentCare status

Conference call with AMA Advocacy Resource Center to discuss release and rollout of 2014 Economic Impact Study,

April 15

Meeting with Sen. Miller, Rep. Bennett, Pat Recupero, MD, and others to discuss mental health legislation

Legislative hearings, State House

April 16

Sen. Whitehouse meeting regarding RI health care system, Department of Health; attending were: Lt. Gov. Roberts, BCBSRI, UHC, Lifespan, Care NE, Director of the Dept. of Health, Health Insurance Commissioner; Coastal Medical, RI Primary Care, Brown University, Alpert Medical School, RI Quality Institute, and South County Hospital

Legislative hearings, State House; Drs. Terek, Blazar, Paletta, Banki, Brousseau, and Sweeney testifying

New House Majority Leader DeSimone fundraiser, Dr. Migliori and RIMS staff attending

Gubernatorial candidate Gina Raimondo fundraiser, sponsored by multiple physicians and other providers; Drs. Migliori and Karczmar, RIMS staff attending

Board of Directors Meeting, RIMS Insurance Brokerage Corporation, Peter A. Hollmann, MD, President

April 17

Meeting with Lt. Governor to discuss Sen. Whitehouse meeting and other topics

Health Care Reform Executive Committee

Health Services Council, Drs. Lange, Solomon, and Hollinshead attending

Legislative hearings, State House

Meet with RI Society of Anesthesiologists and CRNAs to discuss legislation

April 23

Reach Out and Read RI/Providence Community Health Centers event for RI's First Lady, Stephanie Chafee

April 24

Interview with reporter for national trade magazine regarding UnitedHealthcare

Drs. Jones, Karczmar and RIMS staff meet with representatives of Primum Healthcare, LLC, regarding virtual ACO,

RIMS Nominating Committee meeting, Drs. Jones, Karczmar, Adrain, Bubly, Siedlecki, Settipane and staff

April 25

Meet with Lt. Governor's staff regarding health care legislation

April 28

Tobacco-Free RI Coalition conference call

April 29

Legislative hearings, State House

April 30

Senator Ottiano and RIMS staff hosting medical students at the State House,

Legislative hearings, State House

Rep. Corvese fundraiser, Dr. Migliori and Mr. DeToy attending

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.

Cardiovascular Institute Researcher Develops First Blood Test to Predict Risk of Sudden Cardiac Death

Pilot trial shows blood test much more effective than current risk stratifications

PROVIDENCE – A researcher at the Cardiovascular Institute (CVI) at Rhode Island, The Miriam and Newport hospitals has found that a simple blood test can predict a person's risk for sudden cardiac death, enabling physicians to more quickly and accurately assess a patient's need for an implantable cardiac defibrillator (ICD).

That paper by **SAMUEL C. DUDLEY, MD, PhD**, chief of cardiology at the CVI, is published online in advance of print in the *Journal of the American College of Cardiology*.

"This is the first test of its kind; never before have clinicians been able to accurately assess a patient's risk of sudden cardiac death by performing a blood test," Dr. Dudley said. "The primary prevention model for at-risk patients in the U.S. is to implant an ICD before a cardiac event happens. While it's better to be safe, this has led to widespread overuse of ICDs throughout the U.S. and abroad."

Dr. Dudley continued, "With this blood test, we can refine the need for such a device, and instead implant the cardiac defibrillators only in the most severe cases of sudden cardiac death risk."

LIFESPAN

Samuel C. Dudley, MD

The new blood test is in a pilot phase in a large, multisite trial led by Dr. Dudley and other researchers at Lifespan's CVI anticipated to start this fall. ❖

RIH Researchers Find Increase in Patients Admitted with Infections Resistant to Common Antibiotics

Study reviewed patients with community-acquired, healthcare-associated and hospital-acquired infections

PROVIDENCE – The emergence of community-acquired infections, such as urinary tract infections (UTI), due to strains resistant to common antibiotics are on the rise, according to Rhode Island Hospital researchers. The study is published online in the journal *Antimicrobial Resistance and Infection Control*.

"Over the last several years, we've seen an increase in the number of bacteria – many of which are forms of E. coli – that are resistant to commonly administered antibiotics," said **LEONARD MERMEL, DO**, medical director of the department of epidemiology and infection control at Rhode Island Hospital. "However, we also found that many of these bacteria causing urinary tract infections were susceptible to an older, inexpensive antibiotic, nitrofurantoin."

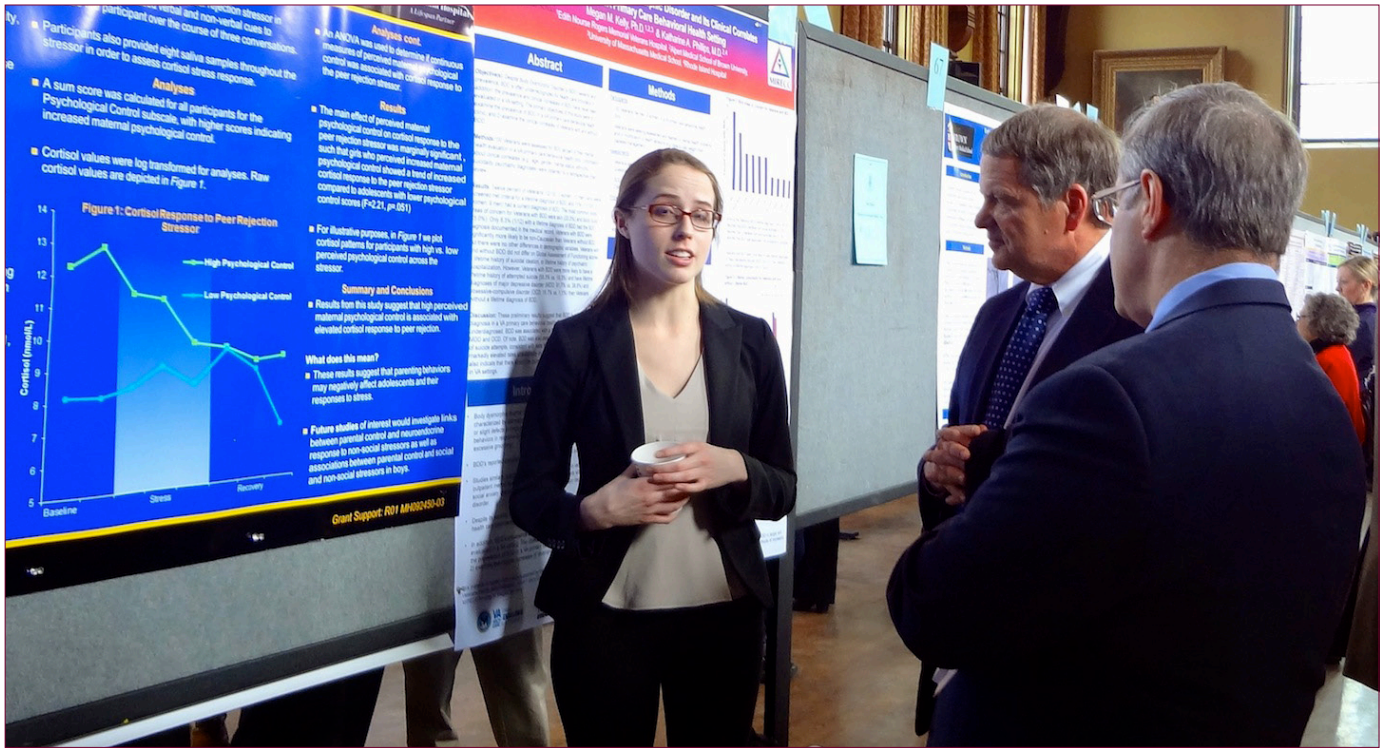
The study involved patients with infections documented from 2006 to 2011 that were due to extended-spectrum beta-lactamase (ESBL)-producing bacteria. These bacteria are resistant to most antibiotics in the penicillin and cephalosporin families of antibiotics. The incidence of infections due to these microorganisms is increasing, which creates a challenge regarding appropriate antimicrobial therapy, especially in a community or outpatient setting where oral antibiotics are used.

The study noted the emergence of community-acquired infections due to ESBL-producing bacteria, a significant increase in healthcare-associated infections, as well as E. coli becoming the predominant pathogen in all three acquisition groups (community-acquired, healthcare-associated, and hospital-acquired). The researchers found high levels of resistance to the antibiotics Ciprofloxacin and Trimethoprim-Sulfamethoxazole (TMP-SMZ), which could lead to poor outcomes in the community as these are the commonly used antibiotics in outpatient settings for urinary tract infections.

"Recognizing the strains that are resistant to common antibiotics is critical to providing proper treatment and better outcomes," Dr. Mermel said. "The incidence of overall antibiotic resistance is also on the rise, likely due to overuse in both humans and farm animals, so what may have been effective in the past, may no longer work to fight infection today. Therefore, greater efforts in controlling unnecessary antibiotic use in the community, healthcare settings, and in agriculture are critical."

"The overuse of antibiotics is a big concern, with real implications for patients," said co-author **STEVE KASSAKIAN, MD**. "It's imperative that we determine why these bacteria are resistant to some antibiotics so that we can develop new ones to combat dangerous, and possibly fatal infections." ❖

MindBrain Research Day



PHOTOS BY MARY KORR

Dr. Steven Rasmussen and Alpert Medical School Dean Jack Elias speak to one of the presenters at the inaugural MindBrain Research Day held March 25th at Brown University. The poster display was followed by a keynote lecture, given by Emory University Professor Helen Mayburg, MD, a psychiatrist and an expert on deep brain stimulation (DBS) and the neurocircuitry of depression

Students, physicians and researchers affiliated with the Brown Institute for Brain Science and the Norman Prince Neurosciences Institute and the Alpert Medical School and its affiliated hospitals presented 157 research projects in a poster display in a packed Sayles Hall. The day builds upon an 18-year tradition begun by the Department of Psychiatry and Human Behavior in the Alpert Medical School, and was also sponsored by the Departments of Neurology and Neurosurgery.

WOMEN & INFANTS

Pictured at the ribbon cutting for Women & Infants' new Obstetric Evaluation Unit are, left to right: Angelleen Peters-Lewis, RN, PhD, senior vice president of patient care services and chief nursing officer; Dr. Roxanne Vrees, medical director of emergency obstetrics & gynecology; Dr. Maureen Phipps, chief of obstetrics & gynecology; Mark Marcantano, president; Dr. Ray Powrie, Care New England chief medical quality officer and senior vice president for quality and clinical effectiveness; and Tracey Casala, nurse manager, emergency obstetrics and gynecology.

Women & Infants Unveils Obstetric Evaluation Unit

PROVIDENCE – Women & Infants Hospital held a ribbon-cutting ceremony on April 3 for its new Obstetric Evaluation Unit in the Division of Emergency Obstetrics and Gynecology. This new, state-of-the-art, seven-bed unit, an expansion to the hospital's current Emergency Department, will serve as a dedicated space to provide high quality, efficient care to obstetric patients. In addition, the Obstetric Evaluation Unit will foster a more integrated model of care between the Emergency Department and the hospital's Labor, Delivery and Recovery Unit.

The expansion increases the Emergency Department's bed capacity by 60% to 19 total beds, and also provides two dedicated ultrasound rooms, a three-bed triage bay, and a dedicated infant resuscitation area for Women & Infants' neonatal intensive care unit team to safely and effectively evaluate infants following an imminent delivery.

"This new unit provides a beautiful, state-of-the-art space for pregnant women. Our new space will improve a patient's experience by reducing emergency department wait times, enabling health care providers to see patients sooner and streamlining care," said **MAUREEN G. PHIPPS, MD, MPH**, chief of obstetrics and gynecology at Women & Infants Hospital, executive chief of obstetrics and gynecology at Care New England Health System, Chair and Chace-Joukowsky Professor in the Department of Obstetrics & Gynecology and assistant dean for teaching and research in women's health at The Warren Alpert Medical School of Brown University.

ROXANNE VREES, MD, medical director of emergency obstetrics and gynecology at Women & Infants, said, "Our new Obstetric Evaluation Unit allows our highly skilled team to continue to provide efficient, high quality care while emphasizing our dedication to a family-centered model." ❖

Women & Infants Researchers Present Study at National Conference

Work uses technology to isolate cancer in the sentinel lymph node

PROVIDENCE – A team of researchers from Women & Infants Hospital of Rhode Island's Program in Women's Oncology and Division of Pathology and Laboratory Medicine presented the results of a study evaluating the use of sentinel lymph node dissection in women with vulvar malignancies, and then follow the patients for complications and recurrence.

The team – **DRS. RICHARD G. MOORE, DARIO ROQUE, CAROLYN MCCOURT, ASHLEY STUCKEY, PAUL A. DISILVESTRO, JAMES SUNG, MARGARET STEINHOFF, CORNELIUS GRANAI III, AND KATINA ROBISON** – presented their work at the annual meeting of the Society of Gynecologic Oncologists (SGO) in Tampa. The oral presentation was part of the main plenary session at the meeting.

The study is entitled "Isolated sentinel lymph node biopsy with conservative management in women diagnosed with vulvar cancer." Using radioactive dye and blue dye, gynecologic oncology surgeons are able to identify and remove just the sentinel node.

"The object of this study was to examine the sentinel lymph node alone in women with squamous cell carcinoma of the vulva and evaluate their recurrence in the groin and any complication rates," Dr. Moore explains. "We discovered that removing just the sentinel node had decreased complication while maintaining a low rate of further occurrence of malignancy.

"This should be considered an option for women with squamous cell carcinoma of the vulva."

The study, the largest prospective trial on sentinel lymph node dissection among women with vulvar cancer in the United States, included 73 women with 69 undergoing sentinel node dissection. Fifty-seven of those women were managed conservatively. Three experienced groin recurrences, for a recurrence rate of 5.2 percent.

Women whose sentinel node tested negative for metastasis were followed clinically without further treatment. Women with metastasis to the sentinel lymph node underwent full groin node dissection and were then followed by standard treatment protocols. ❖

Researchers Identify Similarities Between HIV-AIDS and Opioid Addiction Epidemics

PROVIDENCE – There are important parallels between the early years of the HIV/AIDS epidemic and the current epidemic of opioid addiction – ones that could trigger a significant shift in opioid addiction prevention, diagnosis and treatment.

Josiah D. Rich, MD, MPH

These are the findings of a comparative review of HIV/AIDS and addiction by researchers **JOSIAH D. RICH, MD, MPH**, director of the Center for Prisoner Health and Human Rights, based at The Miriam Hospital; **TRACI C. GREEN, PHD, MSC**, Department of Emergency Medicine at Rhode Island Hospital and assistant professor of Emergency Medicine and Epidemiology at the Warren Alpert Medical School of Brown University; and lead author **SARAH E. WAKEMAN, MD**, Department of Medicine and Center for Community Health Improvement, Massachusetts General Hospital. The paper is published online in advance of print in the *American Journal of Medicine*.

"Deaths documented by the Centers for Disease Control and Prevention have been on the rise, and that profile bears a striking resemblance to the beginning stages of the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) epidemic," said Dr. Rich. "There are lessons learned from the HIV/AIDS epidemic that should be heeded and should drive a parallel response to today's crisis: addiction."

In the paper, "From Documenting Death to Comprehensive Care: Applying Lessons from the HIV/AIDS Epidemic to Addiction," researchers detail how the HIV/AIDS epidemic spurred a novel public health approach centered on human rights. That included biomedical breakthroughs and life-saving treatment, and community advocacy and activism played key roles. Fast forward 30 years and the global response to HIV/AIDS has attracted an unprecedented commitment of resources and international aid, and there are predictions for its end. Researchers assert that a parallel response is needed in response to the epidemic of addiction.

Similar to HIV/AIDS, many addiction victims are young, previously healthy and already stigmatized. Effective care is compromised by a public perception that only certain groups become addicts. The death toll of the two epidemics is comparable, but the response to opioid addiction is not yet as effective: every 19 minutes another American dies from an unintentional overdose.

Affecting 40 million Americans, or 15.9 percent of the population, addiction to drugs, alcohol and tobacco has a greater public impact than heart conditions, diabetes or cancer. Opioid-use disorders are the fastest-growing type of drug problem. According to researchers, much of the current exposure to opioids is linked to the explosion of widely available, potent prescription painkillers that have an identical effect in the brain as heroin. Although many benefit from substantial pain relief and improved quality of life, prescription opioids now kill more people than heroin and cocaine combined. Researchers note that while prevalent, addiction has been marginalized as a social problem setting it apart from other diseases, with barriers to treatment ranging from stringent criteria for entry to limited availability of treatment.

Dr. Rich and others are spearheading a RI "collaborative practice agreement" that allows anyone to walk into a Walgreens in RI and obtain naloxone (or Narcan) – a drug that quickly reverses an opioid overdose, along with training on how to use it.

Researchers described the need for a comprehensive prevention, diagnosis and treatment campaign to fight overdose, along with standard-of-care treatment models based on existing evidence. They propose more education for the medical community and that educational resources for addiction in medical training be on par with that of other chronic diseases. Also, as with HIV/AIDS, patients suffering from addiction should be involved in the design and implementation of programs and products designed to serve them.

Immediate steps that can address the catastrophic death toll from unintentional overdose include a balance of harm reduction and supply-side and demand-oriented interventions, such as:

Regularly prescribe, train in use of, and distribute naloxone.

Reformulate pain medications and decrease availability of painkillers through physical education, prescription drug-monitoring programs, and crackdowns on "pill mills."

Increase access to evidence-based treatment, including medications like buprenorphine and methadone.

Funding to support the investigators, all of whom are affiliated with The Center for Prisoner Health and Human Rights, has been received from The National Institute on Drug Abuse (NIDA), The National Institute on Allergy and Infectious Diseases (NIAID), and the Centers for Disease Control and Prevention (CDC). ❖

Sen. Sheldon Whitehouse gave the keynote lecture on health and climate change at Brown's annual Dr. and Mrs. Frederick W. Barnes Jr. Lecture.

Sen. Whitehouse Sounds Alarm on Climate Change, Health

MARY KORR
RIMJ MANAGING EDITOR

PROVIDENCE – Brown's Public Health Research Day in April took on a sense of urgency as Sen. Sheldon Whitehouse delivered a sobering lecture on climate change and its effects on public health "in a time of unprecedented carbon release in the air and oceans."

Introduced by Brown President Christina Paxson, Senator Whitehouse delivered the annual Dr. and Mrs. Frederick W. Barnes Jr. Lecture on the interface of medicine, society and public health. He targeted climate-change deniers "who ignore all the scientific evidence," including colleagues in Congress.

He also stated his opposition to the Keystone XL Pipeline. "Keystone would pump tar sands oil – one of the filthiest fuels on earth – a carbon impact equivalent of adding 5.7 million cars to our roads," he said.

Recently he met with doctors, researchers and people who live near tar sands mining operations, refineries and dumps to discuss the specific health problems they see there: asthma, lung disease, cancer, heart disease. "With the support of the American Public Health Association and the National Association of County and City Health Officials, Sen. Barbara Boxer (CA) and I have asked the State Department to conduct an independent study of the human health effects of tar sands oil and the Keystone pipeline before making a decision on whether it should proceed."

Sen. Sheldon Whitehouse considers a question from Brown School of Public Health Dean Terrie Fox Wetle during his Public Health Research Day keynote lecture.

Carbon pollution

In the lecture, Senator Whitehouse also noted the improvements in air quality and health savings ($30 saved in health costs for every $1 spent) achieved through the Clean Air Act are being eroded as ground-level ozone (smog), a major pollutant on 'bad air' days, increases.

In Rhode Island, he said, about 12% of children and 9% of adults suffer from asthma, higher than the national average, so these bad air days hit home. There are days in summer when "even healthy people are urged to limit their activities."

> **'In Rhode Island, about 12% of children and 9% of adults suffer from asthma, higher than the national average, so these bad air days hit home.' —Sen. Whitehouse**

He also noted:

- Climate change prolongs the allergy season; since 1995, ragweed season has increased across the country anywhere from 13-25 days.
- Warming oceans and lakes cause rising algae bloom levels, 'red tides', which can lead to neurotoxic shellfish poisoning.
- Longer summers and shorter winters are predicted to increase exposure to ticks, mosquitoes and the diseases they carry.
- Increased risk of floods, sewage overflow and potential contamination to the water supply, as happened in Warwick several years ago, resulting in the city shutting down the sewage treatment plant.
- Increases the risk for more severe weather, heat waves and droughts.

What RI is doing

Sen. Whitehouse said the R.I. Climate Change and Health Project, part of a national effort supported by a CDC initiative, is helping the state and public prepare for the health effects related to climate change with an emphasis on identifying vulnerable populations. For example, the Rhode Island Dept. of Health is working with the Dept. of Elderly Affairs in this effort.

He also said the Dept. of Health is working with the Dept. of Environmental Management (DEM) and the Dept. of Transportation (DOT) to pilot a Lyme disease prevention program for outdoor workers.

In 2010, he added, Rhode Island created a Climate Change Commission, which has identified climate risk to key infrastructures. He also noted that for the past four years, the state has been a part of the Regional Greenhouse Gas Initiative (RGGI). "Our region caps carbon emissions and sells emission allowances through auctions, which has created economic incentives for utilities to invest in renewable energy development," he said. "This spurs innovations and creates green jobs."

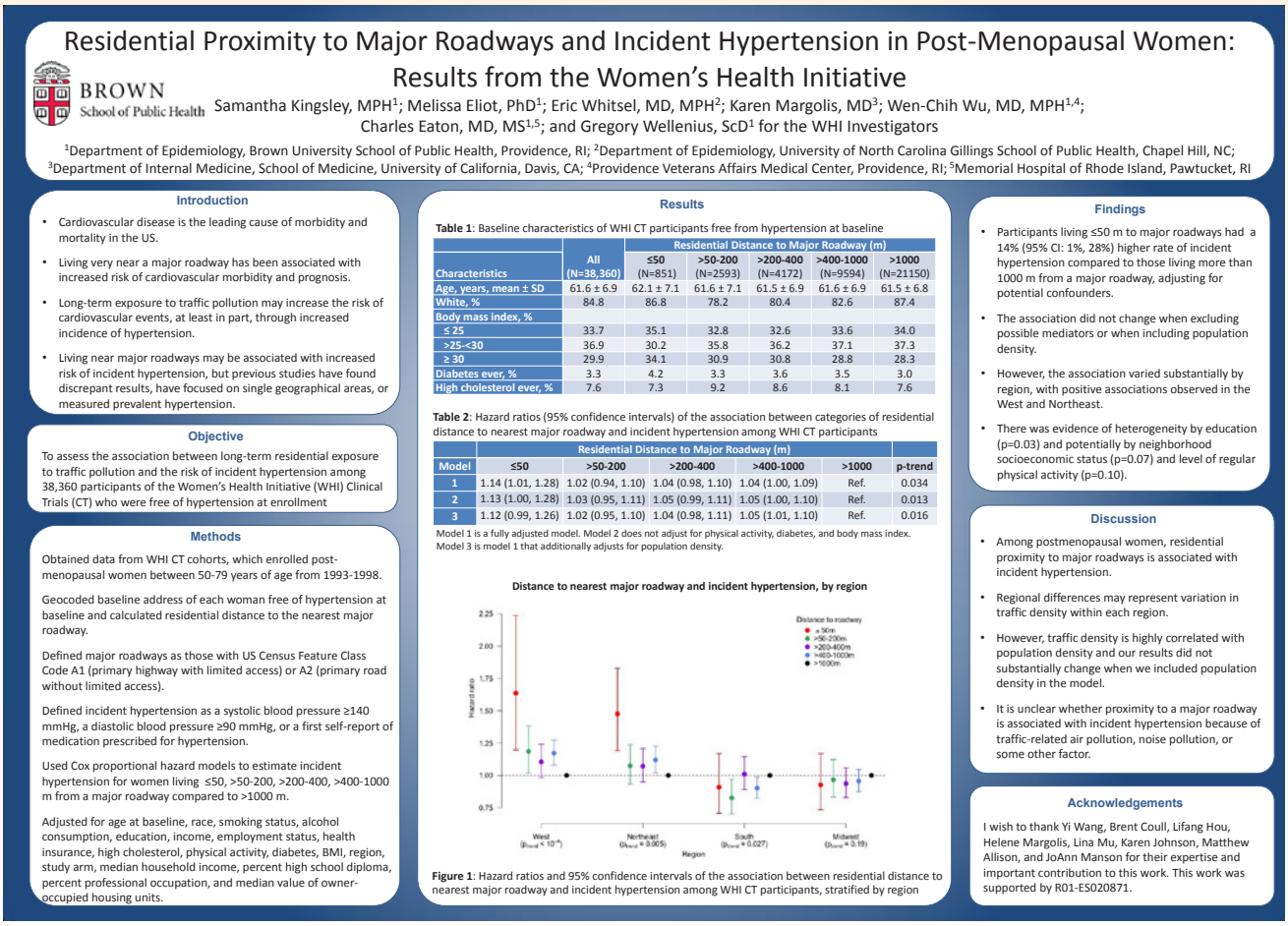
He ended his talk by stating that "Congress is asleep and Congress needs to wake up."

In the Q&A following the talk, Dr. Richard Besdine, professor of medicine and professor of health services policy & practice, said: "The health consequences of what we've done to the planet are so striking…Public health is out in front of this, but in organized medicine there might be some allies to bring to the battle who can be more effective in the health argument."

Data-driven evidence is key, Sen. Whitehouse responded, and noted the partnership of Brown's School of Public Health and the Dept. of Health to examine correlations between rising temperatures and hospital admissions.

Another member of the audience expressed concern about possible toxins in the plastic baby bottles she uses. Sen. Whitehouse admitted the road ahead to fight carbon and other pollutants is a tough one, exacerbated by industry lobbyists, but the duty of this generation.

The research day was sponsored by the Brown School of Public Health, the Environmental Change Initiative, the Rhode Island Department of Health, and the Rhode Island Public Health Association.



Residential Proximity to Major Roadways and Incident Hypertension in Post-Menopausal Women: Results from the Women's Health Initiative

BROWN School of Public Health

Samantha Kingsley, MPH[1]; Melissa Eliot, PhD[1]; Eric Whitsel, MD, MPH[2]; Karen Margolis, MD[3]; Wen-Chih Wu, MD, MPH[1,4]; Charles Eaton, MD, MS[1,5]; and Gregory Wellenius, ScD[1] for the WHI Investigators

[1]Department of Epidemiology, Brown University School of Public Health, Providence, RI; [2]Department of Epidemiology, University of North Carolina Gillings School of Public Health, Chapel Hill, NC; [3]Department of Internal Medicine, School of Medicine, University of California, Davis, CA; [4]Providence Veterans Affairs Medical Center, Providence, RI; [5]Memorial Hospital of Rhode Island, Pawtucket, RI

Introduction

- Cardiovascular disease is the leading cause of morbidity and mortality in the US.
- Living very near a major roadway has been associated with increased risk of cardiovascular morbidity and prognosis.
- Long-term exposure to traffic pollution may increase the risk of cardiovascular events, at least in part, through increased incidence of hypertension.
- Living near major roadways may be associated with increased risk of incident hypertension, but previous studies have found discrepant results, have focused on single geographical areas, or measured prevalent hypertension.

Objective

To assess the association between long-term residential exposure to traffic pollution and the risk of incident hypertension among 38,360 participants of the Women's Health Initiative (WHI) Clinical Trials (CT) who were free of hypertension at enrollment

Methods

Obtained data from WHI CT cohorts, which enrolled post-menopausal women between 50-79 years of age from 1993-1998.

Geocoded baseline address of each woman free of hypertension at baseline and calculated residential distance to the nearest major roadway.

Defined major roadways as those with US Census Feature Class Code A1 (primary highway with limited access) or A2 (primary road without limited access).

Defined incident hypertension as a systolic blood pressure ≥140 mmHg, a diastolic blood pressure ≥90 mmHg, or a first self-report of medication prescribed for hypertension.

Used Cox proportional hazard models to estimate incident hypertension for women living ≤50, >50-200, >200-400, >400-1000 m from a major roadway compared to >1000 m.

Adjusted for age at baseline, race, smoking status, alcohol consumption, education, income, employment status, health insurance, high cholesterol, physical activity, diabetes, BMI, region, study arm, median household income, percent high school diploma, percent professional occupation, and median value of owner-occupied housing units.

Results

Table 1: Baseline characteristics of WHI CT participants free from hypertension at baseline

		Residential Distance to Major Roadway (m)				
Characteristics	All (N=38,360)	≤50 (N=851)	>50-200 (N=2593)	>200-400 (N=4172)	>400-1000 (N=9594)	>1000 (N=21150)
Age, years, mean ± SD	61.6 ± 6.9	62.1 ± 7.1	61.6 ± 7.1	61.5 ± 6.9	61.6 ± 6.9	61.5 ± 6.8
White, %	84.8	86.8	78.2	80.4	82.6	87.4
Body mass index, %						
≤ 25	33.7	35.1	32.8	32.6	33.6	34.0
>25-<30	36.9	30.2	35.8	36.2	37.1	37.3
≥ 30	29.9	34.1	30.9	30.8	28.8	28.3
Diabetes ever, %	3.3	4.2	3.3	3.6	3.5	3.0
High cholesterol ever, %	7.6	7.3	9.2	8.6	8.1	7.6

Table 2: Hazard ratios (95% confidence intervals) of the association between categories of residential distance to nearest major roadway and incident hypertension among WHI CT participants

	Residential Distance to Major Roadway (m)					
Model	≤50	>50-200	>200-400	>400-1000	>1000	p-trend
1	1.14 (1.01, 1.28)	1.02 (0.94, 1.10)	1.04 (0.98, 1.10)	1.04 (1.00, 1.09)	Ref.	0.034
2	1.13 (1.00, 1.28)	1.03 (0.95, 1.11)	1.05 (0.99, 1.11)	1.05 (1.00, 1.10)	Ref.	0.013
3	1.12 (0.99, 1.26)	1.02 (0.95, 1.10)	1.04 (0.98, 1.11)	1.05 (1.01, 1.10)	Ref.	0.016

Model 1 is a fully adjusted model. Model 2 does not adjust for physical activity, diabetes, and body mass index. Model 3 is model 1 that additionally adjusts for population density.

Distance to nearest major roadway and incident hypertension, by region

Figure 1: Hazard ratios and 95% confidence intervals of the association between residential distance to nearest major roadway and incident hypertension among WHI CT participants, stratified by region

Findings

- Participants living ≤50 m to major roadways had a 14% (95% CI: 1%, 28%) higher rate of incident hypertension compared to those living more than 1000 m from a major roadway, adjusting for potential confounders.
- The association did not change when excluding possible mediators or when including population density.
- However, the association varied substantially by region, with positive associations observed in the West and Northeast.
- There was evidence of heterogeneity by education (p=0.03) and potentially by neighborhood socioeconomic status (p=0.07) and level of regular physical activity (p=0.10).

Discussion

- Among postmenopausal women, residential proximity to major roadways is associated with incident hypertension.
- Regional differences may represent variation in traffic density within each region.
- However, traffic density is highly correlated with population density and our results did not substantially change when we included population density in the model.
- It is unclear whether proximity to a major roadway is associated with incident hypertension because of traffic-related air pollution, noise pollution, or some other factor.

Acknowledgements

I wish to thank Yi Wang, Brent Coull, Lifang Hou, Helene Margolis, Lina Mu, Karen Johnson, Matthew Allison, and JoAnn Manson for their expertise and important contribution to this work. This work was supported by R01-ES020871.

At the poster session, researchers in the Brown University School of Public Health, the Environmental Health Initiative, the Rhode Island Department of Health, and others displayed and discussed posters describing their research in Rhode Island and around the world. The environmental theme winner was Samantha Kingsley for the poster entitled "Residential Proximity to Major Roadways and Incident Hypertension in Post-Menopausal Women: Results from the Women's Health Initiative."

MEMORIAL HOSPITAL

From left, Memorial Hospital of Rhode Island's, Michael Pepi, MD, obstetrician/ gynecologist-in-chief; Shirley Picard, RN, nurse manager of The Birthing Center; Susanna Magee, MD, MPH, director of the Maternal Child Health Program; and Edward Schottland, acting president, at the ceremonial opening of the renovated Birthing Center.

Memorial Cuts Ribbon on Updated Labor-Delivery-Recovery Rooms

PAWTUCKET – Clinical staff and leadership at Memorial Hospital of Rhode Island recently cut the ribbon on newly refreshed labor-delivery-recovery (LDR) rooms in the hospital's Birthing Center.

Each of the four LDRs and the adjacent hallway and nurse's station were repainted, flooring was repaired and a new counter was installed at the nurse's station, configured for improved staff workflow. The result is a larger, more inviting and more patient- and family-centered environment.

The work was made possible through a fundraiser "Labor of Love," coordinated by staff in The Birthing Center, which raised more than $20,000.

"Memorial Hospital has distinguished itself as the place for a personalized birthing experience," says **MICHAEL PEPI, MD**, obstetrician- and gynecologist-in-chief at Memorial, noting that The Birthing Center is recognized by the Childbirth and Postpartum Professional Association for providing excellence in mother-friendly maternity care.

"Our laboring mothers deserve a serene place in which to give birth and these updated LDRs reflect the commitment we have to providing a homey, comfortable environment for them," adds **SUSANNA MAGEE, MD, MPH**, who helped coordinate the fundraising efforts for the work.

The Birthing Center offers showers and a spacious labor tub for hydrotherapy during labor. There are also birth balls, music therapy, aromatherapy and a labor support box for each LDR so partners, nurses and doulas have supplies on hand to provide for individualized birth experiences. ❖

Memorial Dedicates Room to Honor Blood Donors

PAWTUCKET – Memorial Hospital of Rhode Island recently dedicated the main lobby waiting room in honor of its own and its employees' commitment to blood donation.

It was dedicated as a Seasons' Pass room. The Rhode Island Blood Center's Seasons' Pass program was initiated 12 years ago, to recognize and thank four-time-a-year blood donors and four-time-a-year blood drive sponsors.

Since the program began, the number of four time a year donors has more than doubled to over 10,000. Conservatively in its first 11 years more than 55,000 additional pints of blood have been collected because of the program, meaning that more than 165,000 individuals and families have been given hope and life – virtually the population of Providence.

MEMORIAL HOSPITAL

Pictured left to right, Christine Hannon, artist; Edward Schottland, acting president, Memorial Hospital of Rhode Island; Scott Asadorian, chief operating officer, Rhode Island Blood Center; Frank Prosnitz, communications manager, Rhode Island Blood Center; and Michael Gama, a former Narragansett police officer who received a marrow transplant and several blood transfusions while battling leukemia a few years ago.

Memorial Hospital, which has been running four or more blood drives a year, held its first blood drive in November 1980. Since then, hospital blood drives have collected nearly 6,200 pints of blood. Each pint of blood that is collected is separated into three components, distributed to three different recipients, resulting in the Memorial blood drive program potentially helping well over 18,000 individuals.

At the press conference, Michael Gama, a former Narragansett police officer, shared his story of survival. Michael, who was suffering from leukemia, received a marrow transplant and several blood transfusions on his road to recovery. Recently, he met his marrow donor, Catherine Prince of North Carolina at an event sponsored by the Rhode Island Blood Center.

Edward Schottland, acting president, Memorial Hospital, praised the dedication of blood donors and the hospital's commitment to blood donation. Scott Asadorian, the Rhode Island Blood Center's chief operating officer, recognized that it is organizations like Memorial Hospital that help assure a regular and consistent blood supply for patients that need it. Christine McIntyre-Hannon, this year's Seasons' Pass artist, signed prints of her painting for four-time-a-year donors. ❖

2014
Heart Ball
SATURDAY
June 14th
Marble House Mansion
Newport, Rhode Island
Join us for an elegant evening of dinner and dancing at one of Newport's architectural gems, as we highlight research and education, focused on children with congenital heart defects.
David Rozen, Chair
CFO, Alex and Ani
Reserve your seat at
SNEHeartBall.heart.org
or call 401-330-1706
American Heart Association®
heart ball

Memorial Opens Comprehensive Hernia Center

PAWTUCKET – Memorial Hospital of Rhode Island has opened The Comprehensive Hernia Center, led by surgeons **PETER S. GILL, MD, FACS**, surgeon-in-chief at Memorial, and **ALFREDO C. CORDOVA, MD**, both members of Affinity Physicians, an affiliate of Care New England Health System. The center offers highly specialized care for people with all types of hernias, including all the latest treatments in hernia surgery, to ensure the best possible outcomes.

"This is the only place where a patient with a hernia can find expert surgical care as well as access to a comprehensive group of medical professionals, including wound care specialists, nutritionists, physical therapists, pain service specialists, gastroenterologists and diagnostic imaging specialists," Dr. Gill explains.

"Surgery isn't always the answer. Some patients may feel relief from dietary changes or other lifestyle modifications," adds Dr. Cordova, who is Spanish speaking. "We provide both medical and surgical approaches to caring for all types of abdominal cavity hernias and carefully tailor the approach to each patient's needs."

Both doctors are part of the American Hernia Society Quality Collaborative and specialize in the most advanced minimally invasive techniques. ❖

Total Joint Center at Miriam Awarded Joint Commission Gold Seal of Approval

PROVIDENCE – The Total Joint Center at The Miriam Hospital has earned The Joint Commission's Gold Seal of Approval for its total knee and total hip replacement programs. The certification recognizes the Total Joint Center's compliance with national standards for health care quality and safety in a disease-specific care set by The Joint Commission. It also acknowledges the center's dedication to continuous compliance with The Joint Commission's state-of-the-art standards.

"Achieving The Joint Commission's Gold Seal of Approval is a terrific show of support for the unprecedented integrated way we deliver total joint replacement surgery at The Miriam Hospital," said **JOHN A. FROEHLICH, MD**, program director. "In using the most advanced technologies and with our ongoing commitment to meeting high standards, the Total Joint Center reflects our dedication to providing exceptional multi-faceted medical and surgical services, and personalized, patient-centered care."

To receive this designation, The Miriam Hospital's Total Joint Center recently underwent a rigorous on-site review that evaluated its compliance with standards of care specific to the needs of patients and families, including infection prevention and control, leadership and medication management. Certification requirements address three core areas: compliance with consensus-based national standards; effective use of evidence-based clinical practice guidelines to manage and optimize care; and an organized approach to performance measurement and improvement activities.

Now in its third year, the Total Joint Center at The Miriam Hospital is a program of the Orthopedic Institute at Rhode Island and The Miriam hospitals that focuses on patient education, patient satisfaction, exceptional surgical technique and nursing care, and consistent post-operative therapy in a welcoming, comforting setting. The center invests in the most advanced and current technologies and equipment to meet high targets on quality measures. More than 1,300 joint procedures were performed in 2013. ❖

Samuels Sinclair Dental Center at RIH helps to 'Give Kids a Smile'

PROVIDENCE – On April 4th the Samuels Sinclair Dental Center celebrated the 12th annual "Give Kids a Smile Day" (GKAS) with underserved, uninsured and underinsured children throughout Rhode Island receiving dental care in clinics and private dental offices statewide. Eighty-seven children received dental care at Rhode Island Hospital's event.

"Dentists, hygienists and dental assistants from private practices, and other volunteers donated their time and talents along with the staff at the Samuels Sinclair Dental Center to make this event happen for the 12th year now," said **SHIRLEY SPATER FREEDMAN, DMD**, center director. "We were able to provide chair-side education, preventive and restorative care to dozens of low-income children who don't have access to dental care, ultimately providing them with a dental home, and a much needed level of primary care."

As the centerpiece to National Children's Dental Health Month, and sponsored by the Rhode Island Dental Association and the American Dental Association, GKAS was designed to provide dental care to low-income children who would not otherwise have access to care, while also raising awareness of the importance of dental coverage for children's health.

The event included visits from Paws, the PawSox mascot, a group of superheroes, pet therapy dogs and the Tooth Fairy. Members of Team Hasbro, Hasbro, Inc's employee volunteer program, brought toys and games to entertain the children while they waited to see their dentist and dental hygienist, many for the very first time. Dental supplies for the day were donated by national sponsor Henry Schein and Patterson Dental. ❖

RHODE ISLAND HOSPITAL

Children received dental screenings, oral examinations, radiographs, cleanings, fillings and educational materials at Rhode Island Hospital's Samuels Sinclair Dental Center.

Hasbro Designated Level 1 Pediatric Trauma Center by ACS

PROVIDENCE – Hasbro Children's Hospital, the pediatric division of Rhode Island Hospital, has been designated a Level 1 Pediatric Trauma Center by the American College of Surgeons (ACS). This is the first time the hospital has been verified specifically for the care of injured children. Rhode Island Hospital has been a Level 1 Adult Trauma Center for more than 20 years, and has been reverified.

Hasbro Children's Hospital had previously been included as a "pediatric commitment" in the Rhode Island Hospital Level 1 Trauma Center certification, but is now eligible to apply for standalone Level 1 status under the new ACS guidelines. The two hospitals are the only Level 1 Trauma Centers in Rhode Island.

This three-year certification is the highest designation a trauma center can receive, and recognizes the hospital's dedication to providing optimal care for injured patients. Level 1 trauma centers provide a full range of services, including designation as an academic medical center, conducting research and providing medical education.

"This certification is a validation of the fully coordinated, multidisciplinary care we have been providing to injured children since Hasbro Children's Hospital opened its doors 20 years ago," said **FRANCOIS LUKS, MD**, director of pediatric trauma. "It is the first time that we have sought – and obtained – independent verification for the care we provide to injured children, and that is a recognition of how comprehensive our pediatric trauma care has become."

To qualify as a Level I trauma center, a hospital must be fully prepared to treat victims of traumatic injuries – from falls, car crashes, gunshots, assaults, etc. – and offer the highest level of medical and surgical care, with surgeons and anesthesiologists on duty 24 hours a day. Level 1 trauma centers must have a wide range of specialists, such as orthopedic surgeons and neurosurgeons, promptly available if needed, and be involved in education and efforts to prevent traumatic injuries in the community.

Dr. Luks added that the designation means the hospital has to be ready for anything. "Being a Level 1 Trauma Center means that whoever comes through our doors, regardless of the type of injury, we are prepared to offer the entire spectrum of care," he said. "This means more than just initial life-saving efforts, ready and available at a moment's notice, but also everything a patient needs throughout the entirety of his or her healing process."

To be verified as a trauma center, Hasbro Children's Hospital underwent an on-site review earlier this year under the guidelines established by the ACS. The criteria the hospital must meet and maintain include:

- An ongoing quality assurance program.
- Standard response for treatment of major trauma.
- Nurses trained and experienced in delivering acute care.
- Operating rooms open and staffed around the clock.
- State-of-the-art imaging and monitoring equipment to provide quick evaluation and diagnosis.
- Rescue squads and response teams that are prepared to maximize pre-hospital care and fast transport. ❖

$1 Million Gift Funds New Nursing Graduate Program at Salve Regina

NEWPORT – At a ceremony April 23rd, Salve Regina officials were joined by Sen. Jack Reed (D-RI) in announcing the establishment of the University's new graduate program in nursing, as well as a $1 million gift from the Rodgers Family Foundation to help launch it.

Enrollment for the 78-credit, practice-based program resulting in the terminal degree in the field, the Doctor of Nursing Practice (DNP), is underway for classes beginning in fall 2014.

"We are proud to continue our longstanding tradition of educating nursing professionals to be exceptional caregivers and leaders in their field – hallmarks of the Salve Regina nursing graduate," said President Jane Gerety, RSM.

Established in 1948, Salve Regina's baccalaureate degree nursing program is the oldest in Rhode Island. The new DNP curriculum builds on the baccalaureate program by providing clinical preparation as an advance practice nurse, education in evidence-based practice, quality improvement, and systems thinking among other key areas.

DNP graduates will likely seek practice leadership roles such as advanced practice nurses, managers of quality initiatives, executives in health care organizations, directors of clinical programs, and faculty responsible for clinical program delivery and clinical teaching.

The program will admit nurses prepared with Bachelor of Science degrees in nursing. The first 48 credits of the program will allow students to earn a Master of Science degree in nursing and prepare them to sit for the family nurse practitioner certification examination. The second 30 credits of the program will allow students to proceed to the terminal DNP degree.

Offered at the Center for Adult Education in Warwick, hybrid courses are specifically designed for nurses seeking to balance their professional careers and academic pursuits. Part-time students can complete the DNP program in five years, including summer instruction.

Salve Regina's baccalaureate program is accredited by the Commission on Collegiate Nursing Education (CCNE), which represents the highest level of nursing accreditation possible for baccalaureate nursing programs. ❖

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

Brown School of Public Health to Launch Center for Long-Term Care

PROVIDENCE – The American Health Care Association and the National Center for Assisted Living have awarded the Brown University School of Public Health $1 million to launch the Long Term Care Quality and Innovation Center.

The center will work to improve the quality of long-term and post-acute care by studying best practices, conducting other research, and developing training and leadership programs in the field.

"A major goal of our research and teaching is to improve the quality of care, and therefore the quality of life, for our nation's elderly and post-acute populations," said **VINCENT MOR, PhD**, the Florence Pirce Grant Professor of Health Services, Policy, and Practice, who will direct the center. "We look forward to working with AHCA and NCAL's support to discover, evaluate, advance, and apply practices that could benefit millions of people and their loved ones."

The center is designed to become self-sustaining after three to five years. ❖

Flu Declared Widespread

Masking Rule in Effect

PROVIDENCE – Director of Health **MICHAEL FINE, MD**, recently declared the flu to be widespread again in Rhode Island. This declaration triggers the requirement that healthcare workers who have not been vaccinated against the flu wear surgical masks during direct patient contact.

Rhode Island is seeing a second wave of flu that is even more intense than the first. The dominant strains in this late-season wave have been H3N2 – which has a great impact on the elderly – and influenza B.

The majority of the 13 flu-related deaths this season have been people in their 80s and 90s. There have been 464 flu-related hospitalizations this season. Seventy of these hospitalizations occurred between April 6 and April 12.

The masking requirement for healthcare workers will remain in effect until the widespread declaration is lifted. The flu was also widespread this year from January 8 until February 27. ❖

Kent Hospital to Seek Regulatory Approval to Develop Angioplasty Program

WARWICK – Kent Hospital is seeking approval to perform both emergency and elective coronary angioplasty procedures. The hospital submitted a letter of intent (LOI) to the Rhode Island Department of Health recently stating "intent to develop a coronary angioplasty program within one year" and within the next eight weeks Kent will submit a full application for a certificate of need.

Currently, there are three hospitals in the state (The Rhode Island and Miriam Hospitals and Landmark in Woonsocket) that offer the procedure.

"Kent Hospital is an extremely busy and important community hospital that is vital to its large catchment area in the southern half of Rhode Island. Community hospitals, like Kent, need to be able to provide emergency cardiac services for its patients," said **CHESTER HEDGEPETH, III, MD, PhD**, executive chief of cardiology for Care New England Cardiovascular Care and the Brigham and Women's Cardiovascular Associates at Care New England. "Kent Hospital has made major investments in building its cardiology program in the last four years and is well-positioned to provide this lifesaving program to the community."

Kent Hospital and Care New England have entered into a clinical affiliation with Brigham and Women's Hospital of Boston (BWH), whose cardiovascular specialists serve on staff at Kent and Memorial hospitals. The design of the proposed angioplasty program is happening under the supervision of BWH.

"Ample data now convincingly demonstrate the value of acute angioplasty for patients with heart attacks. With proper supervision, equipment and training of physicians and staff, PCI can be provided in the community setting with excellent results. By making PCI more accessible, patients with heart attacks can have treatment earlier and expect to experience less heart damage," said **DAVID O. WILLIAMS MD**, senior physician at Brigham and Women's Hospital and Care New England director of invasive cardiac services.

In 2008, Kent was granted a certificate of need to pursue angioplasty, but the program was not launched because of difficulty in securing on-call coverage, a program requirement. During that implementation process, Kent worked with its staff and rescue personnel around its service area to provide advanced training while equipping ambulances with the latest monitoring equipment to assess patients for the possible need for angioplasty.

When the decision was made in 2010 to suspend the pursuit of angioplasty, it was noted that Kent would conduct a thorough review of its cardiology services to determine the future of the program.

The creation of the Brigham and Women's Cardiovascular Associates at Kent Hospital and more recently the expansion of this service across the Care New England Health System, including the integration of existing BWH cardiology services at Memorial Hospital, means patients have improved local accessibility to advanced cardiac care.

Cardiovascular services available now include advanced imaging such as cardiac CT, valvular heart disease service, heart failure and transplant consultation. Cardiovascular clinical trials, telemedicine, congestive heart failure management and a full range of cardiac arrhythmia diagnostic and therapeutic procedures are also available. When appropriate, patients can receive seamless coordination of care at BWH and then quickly return home for follow up care. ❖

Whah Wonder

an interpretive portrait in wool of Jimi Hendrix

In the words of the designer Ned Baker:

I am a lifelong student and admirer of 60's-70's music - particularly the explosive evolution of the electric guitar and the iconic imagery of the albums and posters from that era.

This rug is a tribute to this period of social unrest and the breaking of barriers AND new ground. The contrast of bold design against a plainer, more organic background shows how the music and sentiments of the time contrasted with what was heretofore considered "normal."

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Phase I Cancer e Trial at Roger Williams Shows Promising Results

PROVIDENCE – Researchers at the Roger Williams Cancer Center have shown encouraging results from a recently completed trial involving immunotherapy for cancer patients. Final results from the "Hepatic Immunotherapy for Metastases (HITM) Phase 1 trial (NCT01373047)" for patients with stage IV colon cancer and liver metastases were recently presented at the 2014 Society of Surgical Oncology (SSO) meeting. The SSO funded the study. In six patients whose disease had been progressing on standard therapy, genetically-modified T cells were delivered directly into the liver's arterial circulation. The treatment was shown to be well tolerated.

In several patients, the team – which included **DR. STEVEN KATZ**, **DR. RICHARD JUNGHANS**, and **DR. N. JOSEPH ESPAT** – reported encouraging evidence of clinical activity. Tumor markers decreased and biopsies of liver tumors demonstrated evidence of tumor cell killing in patients who had been treated with multiple lines of conventional chemotherapy. One patient has survived more than 12 months following treatment.

"This is an important advance for the treatment of liver metastases," said Dr. Katz, the principal investigator for the HITM trial. "We are combining a potent immunotherapeutic tool with a powerful and rational delivery strategy to minimize side effects and optimize clinical effect. Our platform is still at an early stage and we look forward to future clinical trials to define the best immunotherapy strategy for liver metastases."

Ongoing work in the Roger Williams Immunotherapy Laboratory, funded by the NIH, will guide the design of future trials. ❖

RIH physician finds legalizing medical marijuana does not increase use among adolescents

Study reviewed data of self-reported marijuana use in high school students

PROVIDENCE – According to a new study at Rhode Island Hospital which compared 20 years worth of data from states with and without medical marijuana laws, legalizing the drug did not lead to increased use among adolescents. The study is published online in advance of print in the *Journal of Adolescent Health*.

"Any time a state considers legalizing medical marijuana, there are concerns from the public about an increase in drug use among teens," said principal investigator **ESTHER CHOO, MD**, an attending physician in the department of emergency medicine at Rhode Island Hospital. "In this study, we examined 20 years worth of data, comparing trends in self-reported adolescent marijuana use between states with medical marijuana laws and neighboring states without the laws, and found no increase in marijuana use that could be attributed to the law."

Dr. Choo continued, "This adds to a growing body of literature published over the past three years that is remarkably consistent in demonstrating that state medical marijuana policies do not have a downstream effect on adolescent drug use, as we feared they might."

Currently, medical marijuana is legal in 21 states and the District of Columbia.

The study examined a nationally representative sample of high school students. The data showed that past-month marijuana use was common, at nearly 21 percent of the study population. However, there were no statistically significant differences in marijuana use before and after policy changes in any state pairing.

"Researchers should continue to monitor and measure marijuana use," Dr. Choo said. "But we hope that this information will provide some level of reassurance to policymakers, physicians, and parents about medical marijuana laws." ❖

RI scientists, collaborators closer to designing vaccine for H. pylori pathogen

PROVIDENCE – Researchers from the University of Rhode Island are championing a recent breakthrough in the laboratory with hopes it could lead to a vaccine against the pathogen responsible for stomach cancer and to therapeutics for inflammatory diseases.

The results were published in April in the journal PLOS ONE in an article titled, "Human Immune Response to H. pylori HLA Class II Epitopes Identified by Immunoinformatic Methods." This is the first time that human immune responses to the H. pylori pathogen have been described in such detail, and the researchers believe that a vaccine against the pathogen is within reach.

Helicobacter pylori, or H. pylori, is a bacterium that infects the stomach of half of the human population, leading to chronic gastric inflammation in all of those infected while also causing other adverse health effects. It is the most common cause of peptic ulcers, and its persistence in the stomach also gradually promotes gastric cancer development.

Recently, H. pylori infection has also been found to have some beneficial effects. It has been linked to protection against unrestrained inflammation in conditions such as asthma, inflammatory bowel disease, esophageal reflux and esophageal adenocarcinoma.

"The dual personality of H. pylori is a novel, unexpected finding," said URI Assistant Research Professor **LENNY MOISE, PhD**. Dr. Moise is one of the leaders on the project, working alongside URI Research Professor **ANNIE DE GROOT, MD**, and Brown Alpert Medical School Professor **STEVEN MOSS, MD**.

To investigate how H. pylori stimulates both harmful and beneficial human immune responses, the research team used the recent availability of multiple H. pylori genome sequences coupled with advances in computerized algorithms (provided to the researchers by local biotech company EpiVax, Inc.) to identify 90 H. pylori-derived peptide sequences considered as potential immune epitopes. Testing them against human immune cells, the researchers found that these sequences elicited significantly higher inflammatory and immunosuppressive responses in those patients already infected by H. pylori.

"These experiments demonstrate the utility of immunoinformatics to identify vaccine and immunotherapeutic candidates," said Dr. De Groot, director of the Institute for Immunology and Informatics located on the URI Providence campus.

The research program is funded by a $13 million National Institutes of Health award entitled "Translational Immunology Research and Accelerated [Vaccine] Development," also known as the TRIAD program headed by Dr. De Groot. ❖

Q & A with Dr. Stanley Aronson on Butler Hospital's First Endowed Chair

MARY KORR
RIMJ MANAGING EDITOR

PROVIDENCE – Following the recent celebration of The Aronson Chair for Neurodegenerative Disorders on April 12th, Butler Hospital's first endowed Chair, Dr. Stanley Aronson shared his vision for the initiative.

Q. What were your thoughts at the Chair inaugural event, surrounded by friends, family, physicians, philanthropists and former students?

A. The metaphor that I used was this: Let's not celebrate the bottle of champagne that we used to launch the ship. It is the ship, not the champagne, that is our future and is the only purpose of the establishment of this Chair. My name on it is an irrelevance. There is a desperate need for the care and better understanding of these neurodegenerative diseases: Alzheimer's, Parkinson's, multiple sclerosis, Huntington's, etc. A lot has been known and offered to palliate the progress of these diseases but patients still need years and years of competent care. None of these disorders have been conquered in terms of a cure.

PHOTOS BY AL WEEMS/COURTESY OF BUTLER HOSPITAL

Butler Hospital inaugurated its first endowed chair, The Aronson Chair for Neurodegenerative Disorders on April 12 at a celebration held at the Providence Marriott. Pictured from left, Gale Aronson, Dr. Stanley M. Aronson, Butler's President Patricia Recupero, MD, JD; and the inaugural Chair, Joseph H. Friedman, MD.

Brown medical school graduate Dr. Sarah Aronson spoke at the celebration honoring her father.

Q. How do you envision the journey of this 'ship' as you metaphorically described it?

A. The ship is just venturing into the waters. It will first assemble, by its very nature, people from different disciplines who might be interested in aspects of the same disease. You form a kind of nucleus and pretty soon you have a weekly research discussion group. This happens so often. By talking to each other, sharing ideas, that's what I'm hoping the neurodegenerative unit will be. There's always a first – as a medical school we began with a very limited faculty. Under Joe Freidman and others, the degenerative unit will continue and advance the care of people with incurable diseases of the brain. Secondly, it will educate medical students in the nature, complexity and dimension of these diseases. And the third arm of this ship is research and to gather in funds for it.

Q. Dr. Friedman, the inaugural Chair, has described you as a polymath. How would you describe Dr. Friedman?

A. First and foremost Joe is a superb neurologist, superbly trained. People come from all over to receive care at his Movement Disorders Clinic. And, I think he's unique and let me tell you why. Before going to medical school, he spent two years in Africa in the Peace Corps, working in various areas of West Africa. Since he has come here, he has used his vacations to go back to Africa to train individuals; this past autumn he was in Kigali, Rwanda, a place of immense sorrow and people trying to rebuild after the genocide. So to me his humanity is a gift and an example.

Q. Final thoughts on the Chair?

A. There are very few centers in the U.S. devoted directly to these diseases. We need to get the brightest and the youngest and the most dedicated individuals to work here and in the process perhaps come up with ideas, get research money, and build labs step-by-step; it is a long process. It does not come about by miracles; it comes about by hard work, continuous work, and for every success there will be three or four failures, but you keep working on it.

If, by having a Chair or a nucleus, you can bring people together harmoniously to do something on behalf of people with these diseases, and gather in funds for research, from Bethesda and from the generosity of Rhode Island families, then we've accomplished our purpose. ❖

Dr. Aronson is given a round of applause by celebrants. In front row, from left, are Campaign Chair Arthur Robbins, Judy Robbins, Dr. Sarah Aronson, Dr. Susan Mates, Dr. Joseph H. Friedman, and Butler President Dr. Patricia Recupero.

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Recognition

Dr. Robert Carnevale to Accept the Irving Addison Beck Laureate Award

PROVIDENCE – On May 8, Dr. Robert Carnevale, an internist and cardiologist at Coastal Medical, and an associate professor of medicine (clinical) at the Alpert Medical School, will be awarded the Irving Addison Beck Laureate Award. This American College of Physicians recognized award is presented annually to a physician in practice who is a senior College member, usually at the Fellow or Master level.

COASTAL MEDICAL

Robert Carnevale, MD

The award is given in recognition of peer approval, excellence in the specialty of internal medicine, and for distinguished service to the Chapter and to the Rhode Island community.

Dr. Carnevale will be presented with his award at the RI ACP Annual Scientific Meeting on May 8, Rhodes on the Pawtuxet, Cranston. Dr. Yul Ejnes will be introducing the award and Dr. Carnevale will be present to accept the award in the presence of his peers.

Dr. Carnevale was born in Providence and educated at Classical High and Providence College, graduating with honors in 1972. He went on to study medicine at the New York Medical College in Manhattan and Valhalla and came back to Rhode Island for internal medicine residency and cardiology fellowship at the Rhode Island Hospital in 1975.

In 1995, together with friends and colleagues who had also started neighborhood practices in internal medicine and its subspecialties, he was involved with the creation of a new concept in care that was considered a group practice but without walls. The medical practice was called Coastal Medical Inc. which soon also led to the formation of a sister, more business oriented, Coastal Care Medical Management LLC where Dr. Carnevale served for many years as a founder, treasurer, chairman of finance committee and later medical director.

The recipient of this award epitomizes the attributes Dr. Irving Beck. Dr. Beck was born and raised in Rhode Island and was a dedicated, compassionate internal medicine doctor who served as chief of medical service at the former Providence Lying-In Hospital (now Women & Infants' Hospital), Miriam Hospital and Rhode Island Hospital. He authored many papers and lectured frequently at Brown University. He also was a fellow of both the Royal Society of Medicine and the American College of Physicians, and served as chapter governor from 1962 to 1968. ❖

Constance A. Howes, executive vice president of women's health at Care New England and former president and CEO of Women & Infants Hospital, and Dennis Keefe, president and CEO of Care New England, hold up a check for $200,000 marking the launch of the Constance A. Howes Women's Health Innovation Research Fund.

Women & Infants Honors Howes for Leadership Roles

Establishes Women's Health Innovation Research Fund

PROVIDENCE – After more than 30 years of leadership at Women & Infants Hospital, Constance (Connie) A. Howes, now executive vice president of women's health at Care New England, recently stepped down from her position as president and CEO of the hospital. Women & Infants hosted a recent event to commemorate her three decades of leadership on behalf of the women, newborns and families in our state, our region and the nation.

At the event, Dennis Keefe, president and chief executive officer of Care New England, announced the launch of the Constance A. Howes Women's Health Innovation Research Fund. The fund has already received donations totaling $200,000 from more than 140 donors.

Mr. Keefe said, "This fund honors Connie's legacy by providing seed funding to our rising stars in the area of women's health research, and, we believe it will help to attract residents and fellows to Women & Infants to continue the tradition of research that has thrived under Connie's leadership."

In addition to the establishment of the fund, Ms. Howes' name has been engraved on the cornerstone of Women & Infants Hospital's South Pavilion.

"This cornerstone is a fitting tribute to Women & Infants' former president and CEO whose visionary leadership, along with Board Chair Anne Szostak and the entire Women & Infants Board, resulted in the opening of the nationally and internationally recognized Carter Family Neonatal Intensive Care Unit, located in the hospital's South Pavilion," said Mr. Keefe. "On behalf of the CNE Board and its Governance and Nominating Committee, I want you to know how very much we appreciate all that you have already accomplished in your career on behalf of our patients and their families, the faculty, caregivers and employees."

Jack A. Elias, MD, dean of medicine and biological sciences at The Warren Alpert Medical School of Brown University and Frank L. Day Professor of Biology at Brown University, presented Connie with an official Brown University chair in "gratitude and admiration for our long and valued partnership."

She was also presented with a Certificate of Appreciation from Women & Infants Hospital and a citation from Mayor Angel Taveras on behalf of the City of Providence. ❖

The Rhode Island Podiatric Medical Association is pleased to congratulate the recipient of the Centennial Year Myron Keller Memorial Award

ROBERT S. CRAUSMAN, MD, MMS, FACP, FCCP

Dr. Crausman was selected for his outstanding service to podiatry in Rhode Island. He developed a curriculum for podiatric residents at Memorial Hospital of Rhode Island. He has written several articles and peer reviewed publications about the program and podiatric medicine for geriatrics in such publications as the Journal of the American Podiatric Medical Association.

The Myron Keller Memorial Award is given to Dr. Crausman because he exemplifies the high ideals and dedicated spirit so nobly portrayed in the life of RIPMA's past Treasurer and editor, Dr. Myron Keller.

Dr. Crausman is a board-certified Internal Medicine Physician with a distinguished career in clinical healthcare and public health. He holds a MD and MMS from the Brown University School of Medicine. He specializes in internal medicine, pulmonary disease, and geriatric medicine in Massachusetts and Rhode Island. He currently serves as Clinical Professor of Medicine at Brown University School of Medicine and is President of Trumed, Inc in Fall River, Massachusetts.

RHODE ISLAND PODIATRIC MEDICAL ASSOCIATION

Appointments

Dr. Vincent MacAndrew, Jr., Orthopedic Surgeon, Joins Westerly

WESTERLY – L+M Medical Group welcomes Dr. Vincent MacAndrew, Jr. to the Westerly Hospital Department of Orthopaedic Surgery. Dr. MacAndrew will provide patient care alongside Westerly Hospital's board-certified orthopaedic surgeons Dr. Paul Benoit and Dr. Stephen Gross at the L+M Medical Group.

Dr. MacAndrew earned his medical degree from Jefferson Medical College in Philadelphia, Pennsylvania and completed his residency at Thomas Jefferson University Hospital in Philadelphia. His areas of specialty include total joint replacement surgery, arthroscopic surgery, hand surgery, and sports medicine. ❖

Marcantano Named President and Chief Operating Officer of Women & Infants

WOMEN & INFANTS

Mark R. Marcantano

PROVIDENCE – Dennis D. Keefe, president and chief executive officer of Care New England, announced that Mark R. Marcantano has been named president and chief operating officer of Women & Infants Hospital of Rhode Island. Marcantano has been serving as acting president since October 1, 2013.

"I am so pleased to officially welcome Mark Marcantano to the helm at Women & Infants. I am confident he will carry on the proud traditions and take Women & Infants to its next level of excellence," said Keefe.

"I am overjoyed," Marcantano said. "It is very exciting to have the opportunity to lead Women & Infants Hospital forward in this era of health care reform and to be a part of Dennis Keefe's vision to build the integrated delivery system for Care New England."

He continued, "To guide us this year, I have four priorities for Women & Infants: to provide the highest quality care and best experience to our patients and families; to reduce cost and become more efficient; to recruit and retain the best and the brightest talent; and to continue to advance research and innovation."

Prior to being named acting president, Marcantano served as executive vice president and chief operating officer of Women & Infants since January 2010. He came to Women & Infants from Boston Children's Hospital where he served as vice president of ambulatory and network services.

Prior to his position at Boston Children's Hospital, Marcantano was executive dean, senior vice president and chief operating officer of Albany Medical College, affiliated with Albany Medical Center, in New York.

Marcantano earned a bachelor of science degree in finance from New York University and went on to earn his juris doctor from Albany Law School of Union University. He currently serves as a member of the boards of Meeting Street and the Women & Infants Health Care Alliance. ❖

Souza Appointed Acting President of HARI

CRANSTON – Michael R. Souza has been appointed acting president of the Hospital Association of Rhode Island (HARI), where he will oversee day-to-day operations of the association and direct member services. Souza previously served as senior vice president.

Current president Edward J. Quinlan has announced his retirement, effective May 1.

"Ed Quinlan has served our association with distinction for nearly two decades," said Dennis D. Keefe, chair of the HARI Board of Trustees and president and CEO of the Care New England Health System. "Mike's background and skills in hospital finance and reimbursement have strengthened the association and will assist him in leading HARI during this tumultuous time of change."

Quinlan's diverse career has spanned the fields of health care, business and government. He served as vice president of the Washington Capitals of the National Hockey League. Prior to that, he was press secretary for U.S. Senator John Chafee. He also served as director of public relations for Gilbane Building Company.

He started his career working as Director of Public Relations/Development at two medical facilities – North Miami General Hospital (North Miami, FL) and Kent County Hospital.

His professional and community commitments have included service to: the American Hospital Association Regional Policy Board, Innovation Providence, Greater Providence Chamber of Commerce Board of Trustees, RI Health Insurance Advisory Council, RI Health Planning Advisory Council, RI Health Reform Council, University of Rhode Island (URI) Health Studies Council, URI College of Pharmacy Advisory Board, Opportunities Industrialization Center Board of Directors, Rhode Island Commodores.

Souza joined HARI in 2009 from Signature Healthcare in Brockton, MA, where he served as corporate controller and was responsible for the accounting, reporting and control functions of the corporation's various entities. He also served as director of financial planning at Landmark Medical Center.

Souza was awarded a Master of Science management degree by Bridgewater State College. He received a Bachelor of Arts degree in humanities and social sciences from the University of Massachusetts at Dartmouth. The Healthcare Financial Management Association (HFMA) has awarded him the certification of fellow. ❖

Appointments

Brown names Abrar Qureshi, MD, Chair of Dermatology

Will also serve as chief of dermatology at RIH

PROVIDENCE – Rhode Island Hospital has appointed Abrar Qureshi, MD, MPH, as chief of the department of dermatology, effective March 3, 2014. Dr. Qureshi comes to Rhode Island Hospital from Brigham & Women's Hospital and the Dana-Farber Cancer Institute. In this role, Dr. Qureshi will be responsible for managing clinical services, educational and research activities, and administration of the department of dermatology. He also will be the chair of dermatology at The Warren Alpert Medical School of Brown University.

Abrar Qureshi, MD, MPH

Dr. Qureshi succeeds Charles McDonald, MD, who retired from the position after 44 years of service, 15 of which he served as chief of the department.

At Brigham & Women's Hospital and the Dana-Farber Cancer Institute, Dr. Qureshi served as associate physician in the department of dermatology. He also has held academic appointments at Brigham & Women's Hospital, Massachusetts General Hospital and the Boston Veterans Administration Hospital.

He received his medical degree from Aga Khan University in Karachi, Pakistan, and his master of public health degree in clinical effectiveness from the Harvard School of Public Health. He completed his internship in internal medicine at Beth Israel Deaconess Medical Center, his residency in dermatology in the Combined Harvard Residency Training Program and a research fellowship at Massachusetts General Hospital.

He has received numerous awards, among them: several mentorship awards from the Medical Dermatology Society, and the Outstanding Service Award and Diversity Mentorship Award from the American Academy of Dermatology.

He is a member of numerous professional organizations, including the Society for Investigative Dermatology, the Society for Epidemiology Research, the American Dermato-Epidemiology Network, the American Association for Cancer Research and the North American Rheumatic Dermatologists.

His research interests include teledermatology, skin cancer, vector-borne illnesses and psoriasis. ❖

RWMC Names Dr. Joseph C. Cambio Director of Urology

PROVIDENCE – Joseph C. Cambio, MD, has been named Director of the Division of Urology at Roger Williams Medical Center. Dr. Cambio has been a leader in advancing urological practice in Rhode Island, taking major roles in the introduction of prostate ultrasonography and laser lithotripsy to the state.

RWMC

Joseph C. Cambio, MD

Dr. Cambio attended St. Louis University in Missouri and the University of Bologna in Italy. He received his medical degree from the Universidad Autonoma de Guadalajara with additional training at St. Louis University School of Medicine, and completed surgical training and a residency in urology at Rhode Island Hospital/Brown University School of Medicine.

Dr. Cambio is a founding member of Urologic Specialists of New England, which has seven offices throughout Rhode Island. In addition to general urology, his practice interests include prostate disease, vasectomy and vasectomy reversal.

He is certified by the American Board of Urology. Dr. Cambio is fluent in Spanish, Italian and English. ❖

Constance A. Howes Joins Women's Choice Award Healthcare Advisory Board

PROVIDENCE – Constance A. Howes, FACHE, Esq., executive vice president of women's health at Care New England, has joined the Women's Choice Award Healthcare Advisory Board. The board is comprised of executive level health care professionals who have a deep expertise in health care issues and patient experience.

WomenCertified Inc., home to the Women's Choice Award, announced the formation of the Advisory Board which will help fuel and advance its mission to elevate standards of patient care for women and their families by empowering them to make smart health care choices. Board members will provide insight, findings, expertise and thought leadership on the trends and challenges facing today's consumers when choosing hospitals and health care providers, and provide solutions aimed at helping women who are responsible for 90% of health care decisions.

Howes presides over the multidisciplinary Women's Health Council which guides program development in women's health for Care New England. She was recently elected to the Board of Trustees of the American Hospital Association (AHA) and also serves in a number of industry and civic leadership posts, including chairing the Governor's Workforce Board and chairing Innovation Providence which is working to advance the state's knowledge economy and economic development.

Howes, of Providence, was president and chief executive officer of Women & Infants Hospital from 2002 to 2013, formerly serving as executive vice president and chief operating officer. ❖

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Obituaries

MICHAEL J. BACCARI, MD, of Warwick, passed away peacefully after a short illness at Massachusetts General Hospital in Boston on April 17. He was a well-respected physician with a medical career that spanned over 45 years.

Dr. Baccari was born on September 29, 1933 in Providence. He is survived by his loving spouse of 32 years, Alberta Baccari and his five children: Catherine Mulcahy and her husband Stephen, Michael Baccari and his wife Lily, Daniel Baccari, Esq., Robert Baccari and his wife Jenny, and Brian Baccari and his wife Kate. He was an adored "Poppy" to his 10 grandchildren. He also leaves his former spouse, Irene Tanner and her husband Frank.

He was a graduate of Providence College and graduated cum laude from Georgetown University School of Medicine. He served in the United States Navy as a medical officer. Following his honorable discharge, he returned to Rhode Island where he practiced internal medicine until his retirement in 2011.

Dr. Baccari served as the first medical director of Cherry Hill Manor and remained active there for 36 years. He was a member of the National Medical Honor Society, the Rhode Island Medical Society and the American Medical Association.

Dr. Baccari found great joy in his family and friends. He enjoyed spending time with his children and grandchildren, especially when he could share his favorite hobbies, fishing, gardening and golfing. He loved afternoons relaxing in his yard, reading a book, and watching his fig tree grow in the company of his two dogs.

Next to his family, Dr. Baccari's greatest love was for his patients, many of whom became his lifelong friends. His dedication and compassion were admired by all. In his own words, "Medicine was my life."

In lieu of flowers, donations in his memory may be made to the Massachusetts General Hospital Cancer Center, Boston, Massachusetts 02114.

LEON D. PUPPI, MD, a pulmonary and critical care specialist, died March 15, 2014. He was the beloved husband of Angela S. (Wallwork) Puppi and the devoted father of Thomas C. Puppi, Michael V. Puppi, Christina V. Puppi and James S. Puppi and was the brother of Ileana V. Ward.

Dr. Puppi was a graduate of LaSalle Academy, class of 1971. He received his bachelor of arts in mathematics at Clark University in 1975 and his medical degree from the Institute of Medicine and Pharmacy in Bucharest, Romania.

Upon graduation, he served his residency in internal medicine and pulmonary fellowship at the Brooklyn Hospital Center and a critical care fellowship at The Miriam Hospital. He was most recently practicing at South County Pulmonary Inc. and at South County Hospital, where he also had headed the critical care unit and took an active role in its development. He also served on its ethics, critical care and bylaw committees as well as serving as past president of the medical staff.

He also had a love for music and enjoyed playing the guitar, cycling and skiing.

RICHARD SHULMAN, MD, 71, of Harpswell, Maine, succumbed to cancer at his home surrounded by his family on March 21, 2014. He is survived by his wife Kristin, son Scott Shulman and wife Ilsa, daughters Wendy Donner and husband Andy, and Deborah Shulman Dutra and husband Steven; grandchildren Jasper, Anya, Dylan, Aiden; two loving nephews, former wife Judith Shulman, and a large community of extended family, friends and colleagues. He was preceded in death by his sister, Ann Rozen.

Dr. Shulman was born in Boston to Frances and Charles Shulman and was raised in Swampscott, MA. He earned his bachelor's and MD degrees from Harvard University magna cum laude. He started his career as a researcher at the National Institutes of Health and then moved to Barrington, RI.

Dr. Shulman spent the first decade of his career as chief of cardiology at Brown University and The Miriam Hospital and the next two decades in the private practice of cardiology as managing partner of Cardiovascular Associates of RI. He also served as director of the Southcoast Hospital Systems cardiac catheterization laboratory. He completed fellowships in Cardiac MRI at Washington University in St. Louis and cardiac CT in New York.

In 2011, he moved to Harpswell, Maine, and began a chapter of semi-retirement. He spent his winters skiing at Sunday River in Bethel and worked part time in Lewiston, ME. Throughout his life, he was an avid skier, runner, sailor, and cyclist. One of his proudest accomplishments was winning the Lighthouse Trophy in the Newport Bermuda Race. He lived life to the fullest and was full of life. In lieu of flowers, donations can be made to US Sailing, a program that supports youth sailing education.

The Esoteric Prefixes of Medicine (Part I)

STANLEY M. ARONSON, MD

Beyond the commonly used and generally understood binary prefixes of the basic medical vocabulary (eg, *infra-/supra-*, *macro-/micro-*, *hypo/-hyper-*, etc.) are a gathering of less commonly employed prefixes which promote a more accurately defining of technical words – but simultaneously serve to make the language of medicine more arcane and therefore more dependent on a smattering of Greek (G) and Latin (L).

Some of these less commonly employed Greek/Latin prefixes serve to define, metaphorically at times, an animal such as *draco-*, (G) meaning dragonlike as in draconculiasis or draconic; *cyno-*, (G) meaning dog as in cynophobia or cynic; *hippo-*, (G) meaning horse as in hippocampus or hippopotamus; *ichthyo-*, (G) meaning fishlike, as in ichthyosis or ichyophobia; *echino-*, (G) meaning hedgehog or sea urchin as in echinococcosus or echinosis; and *bufo-*, (G) meaning toad-like as in bufogenin or bufotoxin.

Other prefixes refer to body parts such as *rostro-*, (L) meaning toward the beak or nose, as in rostriform; *rumen-*, (L) meaning gullet or throat as in rumenotomy or rumination; *rhino-*, (G) meaning nose as in rhinitis or rhinocerus; *labio-*, (L) meaning rim or lip as in labiogingival or labioplasty; *ischia-*, (G) meaning hip as in ischiodynia or ischium (but not ischo-, (G) meaning to hold back as in ischemia ischuria); *gnatho-*, (G) meaning jaw, as in gnathology and gnathocephalus; *tricho-*, (G) meaning hair as in trichinosis or oligotrichia; *ptero-*, (G) meaning wing as in pterygium or helicopter; *carpo-*, (G) meaning wrist or sometimes to seize as in carpal bone or carpe diem (L, seize the day); *metro-*, (G) meaning uterus or mother as in metrorrhea or metropolis; *chiro-*, (L) meaning hand as in chiropractic or chirurgical; *cheilo-*, (G) meaning lips as in cheilitis or cheilophagia; *cervico-*, meaning neck as in cervix or cervical; *prosopo-*, (G) meaning face or countenance, prosopospasm or prosopalgic.

Still other prefixes denote specific clinical features such as *sudor*, (L) meaning sweat as in sudorosis or sudatorium; *psora-*, (G) meaning itching as in psoriasis or psoralea; *causticus-*, (G,L) meaning burning as in cautery or holocaust.

And, of course, *irido-*, (G) meaning rainbow as in iridoplegia or iridescent.

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1913: Dr. Friedmann's 'Turtle Cure' for Tuberculosis Comes to RI

MARY KORR
RIMJ MANAGING EDITOR

On April 8, 1913, Dr. Franz Friedrich Friedmann of Berlin arrived in Rhode Island with his 'turtle cure' for tuberculosis. Dr. Friedmann described the vaccine as a strain of living tubercle bacilli extracted from the lungs of turtles and avirulent to human beings. He claimed to have cured over a thousand patients.

R.I. Gov. Aram J. Pothier, who caught wind of the turtle treatment from newspapers of the day, invited Dr. Friedmann to the Ocean State. Dr. Friedmann had arrived in New York City two months prior and began treating patients with his reptilian remedy in his Waldorf-Astoria hotel room. However, the desperate mobs of consumptives impelled the hotel manager to evict the 'miracle' worker, who was also an entrepreneur. While in New York, Dr. Friedmann formed a partnership with businessman Morris Eisner, and they began to plan a network of Friedmann Institutes.

Upon his arrival in Rhody, Dr. William L. Harris of the R.I. State Board of Health and Dr. W.G. Dwinell welcomed the 'turtle man,' as newspapers had dubbed Dr. Friedmann, at the Narragansett Hotel. He opined: "While here I shall instruct a certain number of physicians in the use of my vaccine. They will be permitted to observe me, and I shall explain from time to time the method of treatment. The Providence doctors will be the first to benefit by my discovery, as I have decided to give the secrets to them owing to the great courtesy they have shown to me and the cordial welcome I have received from your Governor," reported the *New York Times* of April 9, 1913.

In short order, Dr. Friedmann visited the State Sanatorium at Wallum Lake, where 200 TB patients resided. Dr. Harry Lee Barnes, superintendent of the sanatorium, wrote about the doctor's 'turtle cure' in the November 1913 issue of the *Providence Medical Journal.* "It was obvious that the reports of animal experiments with this vaccine were too meager and inconclusive, the case reports of human beings injected too scanty, and the time elapsed after such injections too short to be sure either of its safety or its value…I accordingly replied to Dr. Harris that the patients would be notified, after which they would be allowed to take it on their own responsibility."

LIBRARY OF CONGRESS

Dr. Franz Friedmann leaves a hospital in New York City in 1913 after discussing his 'turtle cure' with physicians.

The patients harbored no such reservations and Dr. Friedmann injected 69 patients on the first day of his visit. On May 28, Dr. Friedmann administered a second injection to 43, and on June 8, Dr. Dwinell, who was in charge of the nascent Friedmann Institute in Providence, injected 40 additional patients.

In the *Providence Medical Journal* article several months later, Dr. Barnes reported his conclusions regarding the 'turtle cure': "The 120 patients having pulmonary tuberculosis have shown none of the immediate and wonderful results reported by Friedmann…On the contrary, about 17 percent have shown an increased activity of the disease…"

That spring, the New York Board of Health called a halt to the 'turtle cure' and outlawed "the use of living bacterial organisms in the inoculation of human beings for the prevention of treatment and disease."

Dr. Friedmann dispatched forthwith to Germany, but not before selling the vaccine's rights for $125,000, and $1.8 million in stock of the 36 Friedmann Institutes, which did not materialize, rendering the stock worthless. No doubt the turtles in the Berlin Zoo, the original source of the bacilli, breathed a sigh of relief. ❖

RHODE ISLAND HISTORICAL SOCIETY COLLECTION

Wallum Lake Sanatorium and Hospital from *The Wallum Pond Estates* by Dr. Harry Lee Barnes, a booklet published in 1922.